# The Use of Machine Learning in the Evaluation of VA and Anti-VEGF Efficacy During the First Year of Treatment in nAMD

Mandeep Kumar Gupta

Doctor of Optometry

Aston University

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## Thesis abstract

Introduction: Neovascular age related macular degeneration (nAMD) is a sight threatening, ocular condition that can be managed with varying doses of anti-vascular endothelial growth factor (anti-VEGF) drugs and is routinely monitored with optical coherence tomography (OCT) retinal scans. Artificial intelligence (AI) based technologies also now offer automated analysis of such scans making available additional information on features within the scanned area.

Purpose: This study aims to use OCT determined information to predict anti-VEGF treatment frequency and visual prognosis in nAMD, potential influence on treatment regimen and the role AI might play in managing nAMD in the future.

Methods: This was a retrospective, non-interventional, observational study of patients aged 50 and over diagnosed with nAMD between May 2016 and March 2020. From electronic medical records, measures of visual acuity (VA), demographic information and anti-VEGF dosing for the duration of the management were included. OCT characteristics from the baseline visit and the post loading visits were extracted by automated segmentation and AI-enabled retinal segmentation. These were analysed using AI driven technology to predict outcomes.

Results: 327 eyes of 308 individuals were enrolled within the study. It was found that classification modelling differentiating between eyes that required 3 or >3 injections could predict between the classes to an area under the receiver operating characteristic curve (AUC) of 0.63 with ganglion cell layer and drusenoid PED found to be the most informative features. In attempting to sort between eyes that lost or gained VA over 12 months, classification accuracy of AUC 0.88 was achieved with baseline VA deemed the most informative feature.

Conclusion: This study evaluated the application of AI based technologies in investigating anti-VEGF dosing and visual outcomes. The results determined the presence of relationships in predicting injection numbers and VA and perhaps gave some further insights into the role AI may play in the future nAMD management.

Keywords: neovascular age related macular degeneration, optical coherence tomography, anti-vascular endothelial growth factor, artificial intelligence, model

For my parents who set a foundation to allow me attempt such an undertaking.

To my wife Leah and daughter Lowri for their support, encouragement to chase my dreams and especially those grounding moments of warmth, fun and laughter.

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Finally, I remain grateful to Kesh Aggarwal for sharing your expertise in Microsoft Excel and all the times you guided me on how to merge and curate the various datasets created during the study.

# Contents

## List of abbreviations

| Abbreviation | Definition |
|---|---|
| AI | artificial intelligence |
| AMD | age related macular degeneration |
| anti-VEFG | anti-vascular endothelial growth factor |
| AUC | area under the ROC curve |
| AUC | area under the receiver operating characteristic curve |
| BM | Bruch's membrane |
| CA | classification accuracy |
| CA | classification accuracy |
| CC | choriocapillaris |
| CI | chief investigator |
| CM | central macular |
| CMT | central macular thickness |
| CNN | convolutional neural network |
| CNVM | choroidal neovascular membrane |
| CV | curriculum vitae |
| CVRMSE | coefficient of variation root mean squared error |
| DL | deep learning |
| DR | diabetic retinopathy |
| ELM | external limiting membrane |
| EMR | electronic medical records |
| ETDRS | Early Treatment Diabetic Retinopathy Study |
| Excel | Microsoft Excel |
| EZ | ellipsoid zone |
| FP | false positives |
| GA | geographic atrophy |
| GCL | ganglion cell layer |
| GCL-IPL | ganglion cell layer-inner plexiform layer |
| GCP | good clinical practice |
| GDPR | General Data Protection Regulation |

| | |
|---|---|
| HCRW | Health and Care Research Wales |
| HEYEX | Heidelberg Eye Explorer |
| HRA | Health Research Authority |
| HRF | hyperreflective foci |
| ICO | Information Commissioner's Office |
| ILM | inner limiting membrane |
| INL | inner nuclear layer |
| IOPRSI | interface of the inner and outer segments of the photoreceptor layer |
| IPL | inner plexiform layer |
| IRAS | Integrated Research Application System |
| IRC | intraretinal cysts |
| IRF | intraretinal fluid |
| IRL | inner retinal layers |
| kNN | k-Nearest Neighbours |
| LOF | local Outlier Factor |
| logMAR | logarithm of the minimum angle of resolution |
| M | mean |
| MAE | mean absolute error |
| MCC | Matthews correlation coefficient |
| MEH | Moorfields Eye Hospital NHS Foundation Trust |
| min CMT | minimum layer thickness values |
| ML | machine learning |
| MSE | mean squared error |
| n | number of instances |
| N1 | no evidence of nAMD in the fellow eye either prior to or during the initial 12 months of study |
| N1FA | no prior evidence of nAMD in the fellow eye but where the condition did subsequently develop and was treated with anti-VEGF in the fellow eye during the initial 12 months of study |
| N2FA | prior evidence of nAMD in the fellow eye and where anti-VEGF treatment was administered to the fellow eye during the initial 12 months of study |

| | |
|---|---|
| N2FI | prior evidence of nAMD in the fellow eye and where treatment was not administered to the fellow eye during the initial 12 months of study |
| nAMD | neovascular age related macular degeneration |
| NB | nAMD was diagnosed in both eyes at the same visit and anti-VEGF treatment loaded bilaterally, although subsequent treatment patterns may have varied in both study eyes |
| NFL | nerve fibre layer |
| NHS | National Health Service |
| NICE | National Institute for Health and Care Excellence |
| OCT | optical coherence tomography |
| ODM | Orange data mining |
| OLM | outer limiting membrane |
| ONL | outer nuclear layer |
| OPL | outer plexiform layer |
| OPRT | photoreceptor outer segment-RPE interdigitation |
| ORL | outer retinal layers |
| PED | pigment epithelial detachment |
| PR | photoreceptor |
| PR1 | myoid zone of the photoreceptor layer |
| PR2 | ellipsoid component of the photoreceptor layer |
| PRL | photoreceptor layer |
| PRN | pro re nata |
| $R^2$ | coefficient of determination |
| RCT | random control trial |
| RMSE | Route mean squared error |
| RNFL | retinal nerve fibre layer |
| ROC | receiver operating characteristic |
| RPE | retinal pigment epithelium |
| SD | standard deviation |
| SD-OCT | spectral domain optical coherence tomography |
| SHRM | subretinal hyper reflective material |
| SRF | subretinal fluid |

| | |
|---|---|
| st dev | standard deviation |
| SVM | support vector machine |
| TN | true negatives |
| TNR | true negative rate |
| TP | true positives |
| TPR | true positive rate |
| um | microns |
| V0 | baseline visit |
| V12 | visit at 12 months from initiation of treatment |
| VA | visual acuity |
| VP | post loading dose visit |
| WUTH | Wirral University Hospital Trust |

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## Preface

Neovascular age related macular degeneration (nAMD) is a sight threatening, ocular condition that can be managed with anti-vascular endothelial growth factor (anti-VEGF) drugs; a vast amount of research has been already undertaken and remains ongoing studying the management and outcomes of this condition.

One method of evaluating nAMD treatment is through the analysis of retinal scans which are undertaken on a regular basis on those receiving treatment. Such scans can provide global values of retinal changes or be subdivided to consider specific regions within the retina. Artificial intelligence based technologies also now offer automated analysis of such scans making available additional information on features within the scanned area.

Studies evaluating nAMD have previously researched and published findings of the prognostic value of changes within individual retinal layers, groups of layers and features derived from retinal scanning.

This study aims to develop this previous work by investigating retinal scan determined information that might: predict anti-VEGF treatment frequency, have a significant bearing on visual prognosis and might influence decisions on treatment regimens. Additionally, the role advanced algorithms and machine learning might play in managing nAMD will be considered.

A novel approach within the project will be to investigate a larger number of variables, derived from retinal scans, than have previously been collectively considered. Potential benefits of this method include a more detailed analysis of effects of changes within specific retinal regions and the relative influence of such changes compared to each other.

# 1 Introduction

## 1.1 Neovascular age related macular degeneration

A highly regarded Cochrane review of anti-VEGF use for nAMD by Solomon et al. (2019) states that age related macular degeneration (AMD) is the most common cause of uncorrectable severe vision loss in people aged 55 years and older in the developed world with incidence increasing with age.

nAMD usually occurs when abnormal, new blood vessels, often originating from the choroid, breach the outer layers around the retina causing pathological changes which eventually result in loss of visual function (Grossniklaus and Green, 2004). The condition accounts for about 10% of all cases of AMD and approximately 80% of those with severe visual loss caused by AMD.

## 1.2 Anti-VEGF

The anti-VEGF agents have been shown in studies to block the growth of abnormal vessels helping to reduce vision loss and, in some cases, improve vision (Solomon et al., 2019). This therapy has been credited in playing a significant role in halving the incidence of legal blindness attributed to AMD in Denmark from 2000 to 2010 (RCOPHTH, 2013).

A review of random control trials (RCTs) has also deemed anti-VEGF agents were associated with significantly better visual acuity outcomes, reporting fewer patients reaching visual acuity equivalent to legal blindness (Colquitt, 2008).

Both the National Institute for Health and Care Excellence (NICE) and the Royal College of Ophthalmologists issued guidance recommending ranibizumab as an option for the treatment of nAMD in 2008 (NICE, 2008, Amoaku et al., 2009), followed by aflibercept in 2013 (NICE, 2013), brolucizumab in 2021 (NICE, 2021) and faricimab in 2022 (NICE, 2022). Since 2022 ranibizumab biosimilar drugs have also become available and recommended for the treatment of nAMD by National Health Service (NHS) England (2023).

Treatment of nAMD itself however has economic implications with the cost of ranibizumab required for one year of treatment of monthly injections estimated at £9134 with additional costs of £3120 for service provision (Colquitt, 2008) and costs projected as £8498 over two years if following a model where treatment was stopped and recommenced (Dakin et al., 2014).

Optometrists have been involved in various aspects of service delivery for nAMD from detection and referral, to assessments in secondary care and delivery of anti-VEGF agents (Harper et al., 2016). As the

burden of treatment nAMD is expected to continue to grow both financially and in terms of service provision, options of trying to manage the condition have been discussed including shared cared schemes involving community based optometrists (Townsend et al., 2015).

### 1.3 nAMD dosing

Diagnosis of nAMD and decisions on commencement of anti-VEGF therapy, where appropriate treatment criteria are fulfilled, are undertaken in medical retina consultant led services. If suitable, therapy is recommended to be initiated within two weeks of referral with a mandated, initial loading dose of anti-VEGF intravitreal injections; the previously accepted loading phase of monthly injections for three months (Chandra et al., 2022) having been superseded by advice to follow drug summary of product characteristics (RCOPHTH, 2024) to reflect developments within the field.

Dosing of patients with anti-VEGF agents can then occur at regular monthly, two monthly or three monthly intervals, can be based solely on clinical and OCT findings on a pro re nata (PRN) schedule or be administered at set intervals determined by disease activity, with progressive attempts at lengthening periods between treatments in a method named 'treat and extend'. The merits of treatment modalities have been investigated with guidance issued by the Royal College of Ophthalmologists taking a neutral stance, when issued in 2013, recommending the regimen most appropriate for the patient be adopted by the clinician (RCOPHTH, 2013) but revised in 2022 to since support a treat and extend regimen (Chandra et al., 2022).

Several systematic reviews have considered the effect of treatment regimen on structural and functional outcomes. Li et al. (2020) found dosing at monthly intervals to yield a statistically better level of vision at one year when compared against PRN treatment, but that the difference was not clinically relevant. There appeared to be no statistically significant inferiority when monthly dosing was compared against a treat and extend regimen. There was also a greater mean decrease in retinal thickness found in those treated monthly compared to the alternative treatment modalities. Rosenberg et al. (2023) compared results of a treat and extend regimen against PRN and monthly dosing to find similar visual and retinal thickness outcomes in treat and extend and monthly dosing. A small statistically and clinically significant benefit to vision was found in the treat and extend regimen over PRN dosing in most of the studies they considered, where as only one RCT found retinal thickness to be less well maintained in PRN compared to treat and extend dosing. No significant difference in vision or macular thickness was however found in the review by Nichani et al. (2023).

No difference in quality of life indicators was reported between the treatment regimens but few studies were found to report on such measures (Li et al., 2020).

All reviews reported those treated monthly received the greatest number of injections over a period of one year, followed by the treat and extend regimen with PRN dosing requiring the fewest treatments to be administered. Cost implications were logically linked to injection numbers and thus, where reported, highest in the group medicated monthly, followed by the treat and extend course of therapy. Service provision however includes drug administration and patient monitoring. Frequent observation is thus an aspect which impacts PRN models less favourably financially and is a significant, additional budgetary factor which was estimated at 15% of the total costs in one RCT studying ranibizumab. Despite requiring the most review visits, PRN treatment was reported by Li et al. (2020) as the most cost effective modality with a reduced risk of endophthalmitis believed to be proportionally linked to the reduced number of interventions. In keeping with developing consensus however, the latterly authored review articles favoured the balance of lower treatment burden and favourable or non-inferior visual outcomes of a treat and extend regimen.

### 1.4 Optical coherence tomography

Optical coherence tomography (OCT) is an imaging technology that uses infrared light sources and detectors to create a two dimensional map of reflection sites within a three dimensional body and can thus reproduce a representative slice image through an object such as an eye (Fercher et al., 2003). The human eye lends itself to examination using such technology due to its optical qualities, high transmittance and the non-invasive, in vivo, high resolution imaging possible of the layer structure of the retina (Figure 1.1) (Puliafito, 1996).

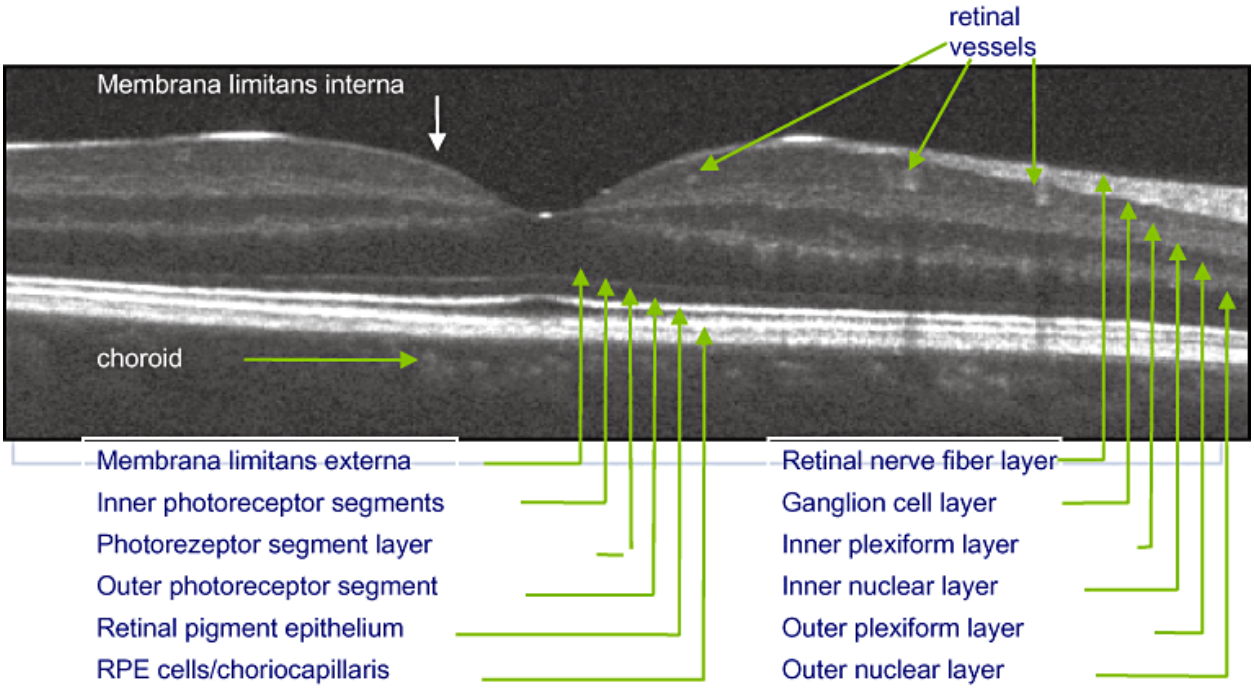


*Figure 1.1: OCT defined high resolution view of the layered architecture of the retina (Hassenstein and Meyer, 2009). Reproduced with permission.*

Component retinal layers can be differentiated by their varying reflectivity patterns and have shown a high level of agreement with the histological structure of the retina (Figure 1.2) which allows the visualisation of pathogenic and morphological changes in retinal disease (Hassenstein and Meyer, 2009).

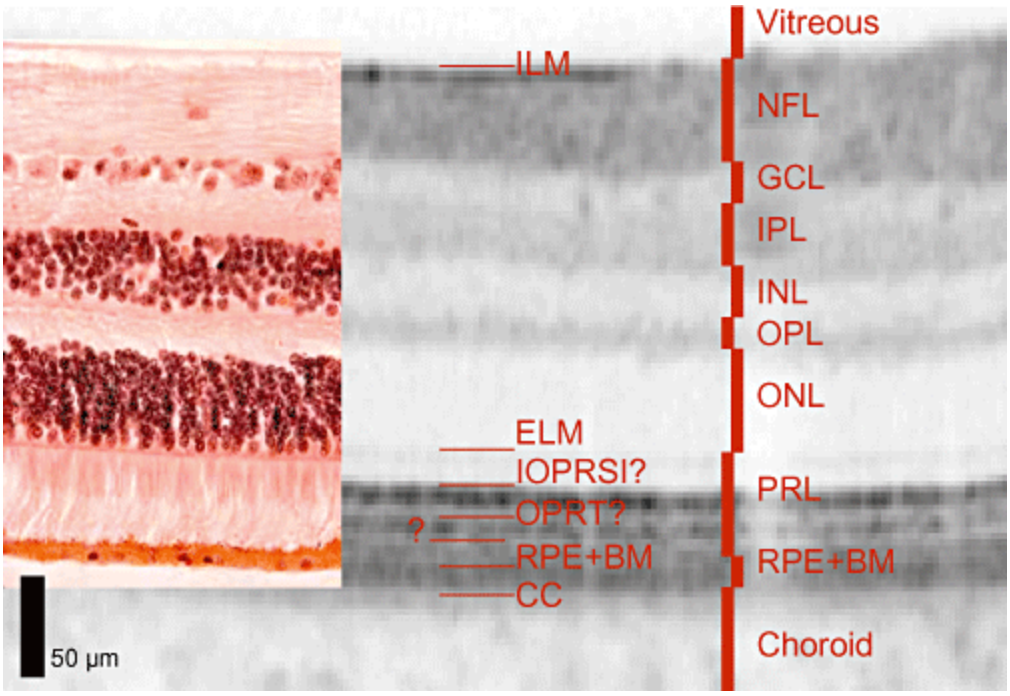


*Figure 1.2: Relationship between retinal structure and reflectivity pattern on OCT with bands representing interfaces between the vitreous, inner limiting membrane (ILM), nerve fibre layer (NFL), ganglion cell layer (GCL), inner plexiform layer (IPL), inner nuclear layer (INL), outer plexiform layer (OPL), outer nuclear layer (ONL), external limiting membrane (ELM), interface of the inner and outer segments of the photoreceptor layer (IOPRSI), photoreceptor layer (PRL), photoreceptor outer segment-RPE interdigitation (OPRT), retinal pigment epithelium (RPE), and Bruch's membrane (BM), choriocapillaris (CC) and choroid. Adapted from Hassenstein and Meyer (2009). Reproduced with permission.*

This availability of such cross-sectional and volumetric information of retinal architecture has led to OCT being widely adopted in the management of retinal disease (Lim et al., 2012) with OCT also now recommended on initial assessment of those with suspected nAMD and as the primary method for ongoing monitoring of those with the disease (NICE, 2018).

## 1.5 Segmentation

The ability of OCT technology to automatically detect retinal layer boundaries, in a process termed segmentation, enables the measurement of component retinal thicknesses at various locations within the scanned region (Keane et al., 2012).

The Spectralis SD-OCT (spectral domain optical coherence tomography) device, produced by Heidelberg Engineering, Germany, utilises mapping patterns to acquire multiple scans of the central macula. From the scans, the proprietary image analysis software Heidelberg Eye Explorer (HEYEX) produces measures of average central foveal thickness, macular volume as well as segmentation of eight distinct retinal layers to allow interpretation of the thickness of individual, component retinal layers with a high level of

repeatability and reproducibility of measurements demonstrated in young, healthy individuals (Ctori and Huntjens, 2015).

Oberwahrenbrock et al. (2015) undertook a literature review and patient study of automated OCT segmentation data produced by several device manufacturers to find that when averaged over a larger region rather than single locations, a high level of repeatability was found in the measures for all layers except the outer plexiform layer using the Heidelberg Spectralis.

## 1.6 Retinal subfields

A pattern commonly used to grade central retinal thicknesses uses three concentric circles overlaying the central macula with diameters of 1mm, 3mm and 6mm (Figure 1.3) derived from ratios relating to a third, one and two disc diameters was first described in the landmark Early Treatment Diabetic Retinopathy Study (ETDRS) (1991b). This ETDRS grid pattern was further subdivided to form nine standardised sections within which observations could be made. This model has more recently been described as comprising a central foveal ring, an inner macular (perifoveal) ring and an outer macular ring (Röhlig et al., 2019).

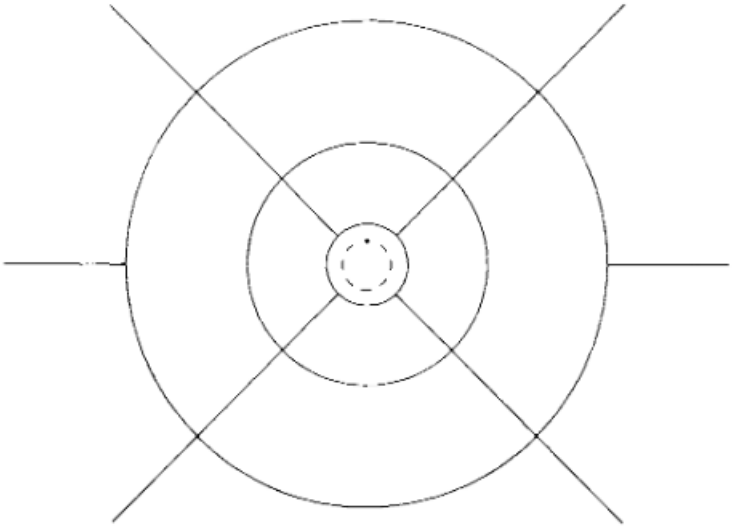

*Figure 1.3: Standard ETDRS grid subfields (1991b). Reproduced with permission.*

Alternative square grid patterns have been studied (Röhlig et al., 2019) and maps using concentric circular patterns considering only the central 3.45mm diameter region of the macula have been used in studies (Khanifar et al., 2010, Panozzo et al., 2019) and are available as OCT overlays within HEYEX alongside the

standard ETDRS grid. A literature search however failed to find any obvious evidence that might confer superiority of a particular mapping strategy but did find the standard 1mm, 3mm and 6mm zones most commonly described as those considered in research. Perhaps more relevantly however, it is changes within the central 1mm subfield have conventionally been studied in large scale RCTs investigating the effect of anti-VEGF in nAMD (Pawloff et al., 2022).

### 1.7 Biomarkers

Structural changes, seen on OCT, predictive of disease progression have been studied in nAMD with retinal morphology shown to relate strongly to visual function and efficacy of anti-VEGF therapy (Schmidt-Erfurth et al., 2015).

Subretinal fluid (SRF), intraretinal fluid (IRF), pigment epithelial detachment (PED) and subretinal hyper reflective material (SRHM) are changes visible within retinal layers on OCT, commonly cited as being indicative of nAMD (Jaffe et al., 2013, Schmidt-Erfurth et al., 2015, Phadikar et al., 2017, Borrelli et al., 2024, Gale et al., 2024).

Refractory cystoid IRF is believed to be a relevant finding on OCT with intraretinal cysts (IRCs) associated with a higher risk for visual loss (Gianniou et al., 2015, Schmidt-Erfurth et al., 2015) than subretinal fluid or fluid beneath the retinal pigment epithelium (RPE) (Jaffe et al., 2013). IRCs have also been associated with poorer levels of improvement in vision and citied as the most relevant imaging marker for visual function (Schmidt-Erfurth et al., 2015).

PED, when present as an initial indicator of neovascular activity, has been associated with poorer visual outcomes in PRN dosing regimens, particularly in the presence of secondary IRC formation. Presence of PED was also found to be the strongest indicator for progressive disease activity and consecutive vision loss in PRN treatment by Schmidt-Erfurth et al. (2015). SHRM is believed to be constitute various exudative substances but is generally regarded as negative prognostic indicator (Borrelli et al., 2024) and is associated with the development of macular scarring and atrophy (Casalino et al., 2018).

A comprehensive literature review of imaging biomarkers in nAMD undertaken by Schmidt-Erfurth and Waldstein (2016) again associated persistent IRCs, SRHM and PED with poorer visual outcomes, but conversely found subretinal fluid to have a less detrimental effect on vision and disease progression.

Abnormal levels of retinal thinning or thickening, increasing choroidal neovascular membrane (CNVM) area and foveal scarring have also been associated with the larger decreases in visual acuity (Jaffe et al., 2013).

## 1.8 Significance of retinal layer thickness and volumes in nAMD

The relevance of retinal thickness in nAMD has been considered in various aspects including the significance to disease activity, visual outcomes and in a novel attempt at predicting treatment frequency.

An increase in sub-retinal drusen volume and increased RPE thickening where shown as features more prevalent in those that developed nAMD by Roberts et al. (2017) while nerve fibre layer (NFL), ganglion cell layer (GCL), inner plexiform layer (IPL) thickness was found to be greater in treatment naïve patients with nAMD, than in control subjects in a separate study by Muftuoglu et al. (2018).

A reduction in thickening of the NFL and ganglion cell layer-inner plexiform layer (GCL-IPL) was found in a study of those with nAMD treated with anti-VEGF over a period of 12 months by Lee et al. (2020), whereas over the review period of 6 months when assessing the effect of anti-VEGF, Kim et al. (2019) found a significant reduction in GCL-IPL thickness but no significant change in NFL thickness.

Research comparing baseline results to those after 12 months of therapy with aflibercept included work by Aşikgarip et al. (2021), which reported statistically significant thickening of the GCL, NFL and IPL at baseline in their retrospective control study. Significant central macular GCL thickening at baseline was also reported by Gunay and Esenulku (2022) in their study, but no significant change in the NFL thickness was found. The group also reported mean central macular thickness (CMT) and sub foveal choroidal thickness were significantly increased prior to treatment (Gunay and Esenulku, 2022).

The outcomes of a group considering treatment using ranibizumab however found NFL and GCL thicknesses did not alter significantly over the period of the first year (Zucchiatti et al., 2017).

A study by Shin et al. (2011) assessing prognostic factors relating to visual acuity, in those with nAMD, determined that preservation of the inner segment/outer segment layer and external limiting membrane, thinner CMT, and lesser CNVM lesion height before treatment were associated with better final visual acuity. The study did not however find that CMT, outer nuclear layer thickness or RPE regularity were significant prognostic factors.

Separately sub RPE volume, sub RPE drusenoid complex thickness and inner segment layer thickness have been reported as the most statistically significant features in predicting anti-VEFG treatment frequency over the first 12 months by Pfau et al. (2021).

## 1.9 Limitations of OCT in nAMD

It has been shown that measurements of macular thickness and segmentation vary dependant on OCT manufacturer (Mylonas et al., 2009) and that structures arranged obliquely in the retina are often poorly visualised in OCT images as detection of features by OCT is related to the angle light reflected from the area of study (Keane et al., 2012).

Errors in automated measurements are further compounded by nAMD presenting in multiple forms, where complex alterations in morphology diminish the ability of segmentation algorithms to detect normal boundaries (Sadda et al., 2006, Keane et al., 2012, Song et al., 2012) with OCT enabling determination of a cross-sectional outline of a neovascular complex, but being limited in definitively allowing internal neovascular components to be distinguished from features such as fibrosis, haemorrhage or dense exudate (Lim et al., 2012).

It has previously been recommended that manual measurement of central macular thickness is undertaken when two or more line scans are affected by segmentation errors in the central 1mm region (Patel et al., 2009) but newer algorithms and more modern SD-OCT have been associated with improved levels of accuracy (Krebs et al., 2009).

Studies assessing relationships between retinal thickness or volumes and changes found in nAMD have also more often tended to consider the sum of the component retinal layers, thus failing to account for subtle pathological changes within individual layers and the potential prognostic impact of such alterations (Schmidt-Erfurth and Waldstein, 2016) with a similar recommendations made by Keane et al. (2008) that more detailed OCT evaluation may lead to refining the relationship between anatomical change and visual acuity.

## 1.10 Artificial intelligence in retinal conditions

Methods based on machine learning (ML) and supervised, deep learning (DL) have been shown to accurately identify pathological features in retinal disease by recreating the multi-layered neural structure seen in the visual cortex, in an artificial, convolutional neural network (CNN). When trained using existing large scale data sets, such as databases of images, CNNs have shown, in task specific recognition, a level of performance equivalent to ophthalmologists in evaluating retinal images and OCT scans. In other specific examples, including mapping electrocardiograms to detect arrhythmias and evaluating complete patient medical records to predict hospital admission, CNN deployment has been shown to exceed human performance (Schmidt-Erfurth et al., 2018b).

Management of retinal conditions may draw benefits from such artificial intelligence (AI) based systems with applications in fields including disease classification and predictive analyses extending beyond solely image identification (Figure 1.4).

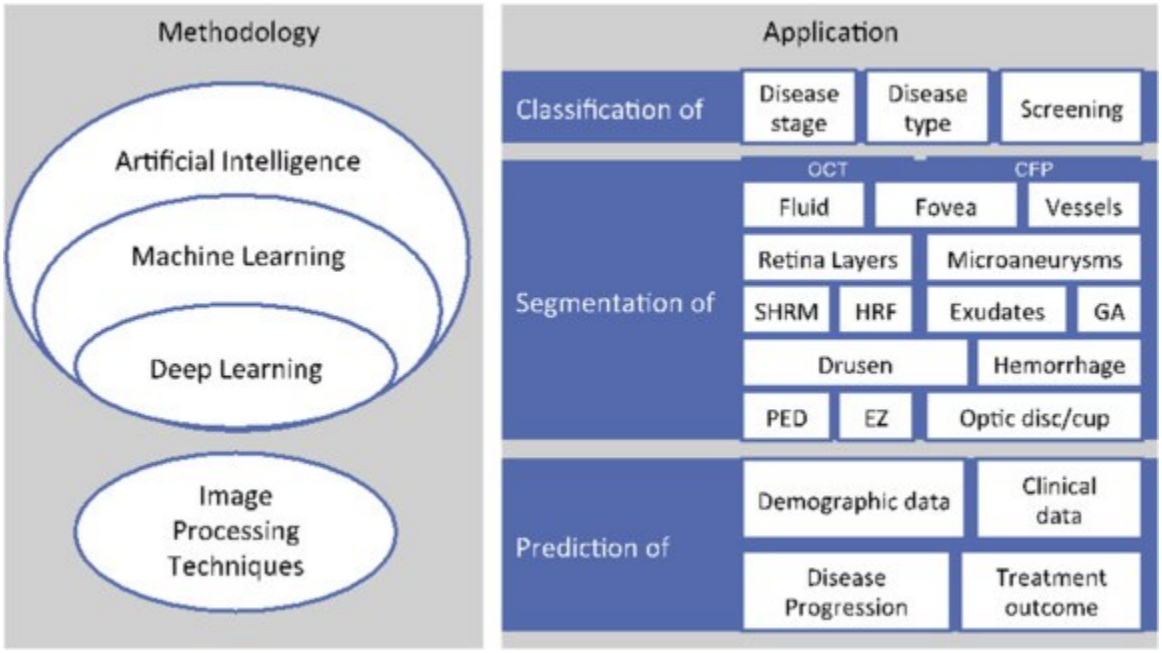


*Figure 1.4: Applications of AI within management of retinal conditions including detection of retinal properties such as subretinal hyper reflective material (SHRM), hyperreflective foci (HRF), geographic atrophy (GA), pigment epithelial detachment (PED) and the ellipsoid zone (EZ) (Schmidt-Erfurth et al., 2018b). Reproduced with permission.*

The CNN U-Net has been utilised in a collaboration between Google DeepMind Health and Moorfields Eye Hospital to develop a validated, device independent, segmentation network that interprets raw OCT scan data to extract 15 attributes (Table 1.1) including information on anatomical structures, pathological features and image artefacts (De Fauw et al., 2018).

| |
|---|
| Vitreous and subhyaloid |
| Posterior hyaloid |
| Epiretinal membrane |
| Neurosensory retina |
| Intraretinal fluid |
| Subretinal fluid |
| Subretinal hyper reflective material |

| |
|---|
| Retinal pigment epithelium (RPE) |
| Drusenoid pigment epithelium detachment (PED) |
| Serous PED |
| Fibrovascular PED |
| Choroid and outer layers |
| Mirror artefact |
| Clipping artefact |
| Blink artefact |

*Table 1.1: Classifications of features extracted from OCT scans (De Fauw et al., 2018)*

AI based attempts, using retrospective data, have also been made at predicting anti-VEGF dosing over a period of one year by using CNN adapted OCT segmentation and feature extraction followed by ML based probabilistic forecasting, Lasso regression and random forest regression, with the model employing random forest regression found to yield the most accurate prediction (Pfau et al., 2021).

Most recently in 2024, promising results have been reported from a study using CNN derived automated quantification of retinal fluid to distinguish between those that required more and less frequent dosing with anti-VEGF in patients actively undergoing management of nAMD (Mares et al., 2024).

## 1.11 AI in data analysis

To statistically evaluate data to investigate relationships between multiple variables, a multivariate analysis may establish the probability of potential correlations while simultaneously taking into account a number of characteristics. Multivariate analyses of data are assisted by powerful, modern computers which allow the simultaneous application of multiple, statistical processes and can facilitate computationally demanding methods (Press, 2005).

Developments in ML are predicted to have a further transformative effect on such analyses through an augmented ability to yield traditional binary outputs from pre-defined algorithms and additionally learn rules from data by sifting through vast numbers of variables (Yoo et al., 2012). Such data mining methods, have in broad terms been described as the analysis of large quantities of data to either find unsuspected relationships that may be relevant to an effect being studied or that may be predictive of a response being investigated (Bellazzi and Zupan, 2008).

Modern data analysis tools, including the open source software Orange, developed at the University of Ljubljanacan, can perform such functions (Demšar et al., 2013) with notably greater options for data modelling when considered alongside similar software (Zupan and Demsar, 2008).

Such programmes also enable data visualisation described as 'the use of computer-supported, interactive, visual representations of data to amplify cognition'. This approach helps present information in an accessible and concise format by employing processes like mapping, selection, and interactivity, allowing the information to be tailored to various relevant aspects of the material or data being studied (Khan and Khan, 2011).

Benefits to healthcare, from such AI based data analysis systems, are predicted to include improved diagnostic and prognostic accuracy and a reduction in work load through savings in repetitive, interpretive activities (Obermeyer and Emanuel, 2016) with a review by Ting et al. (2019) reporting on the notable performance of DL technologies in detecting diabetic retinopathy (DR) in digital imaging based DR screening programmes, the clinically acceptable performance of a DL diagnostic system in detecting referable AMD on digital images and the use of computer programmes in analysing visual field plots in earlier detection of field loss and progression of loss in glaucoma.

### 1.12 Topol review and the significance of AI in the education of healthcare professionals and patients

The Topol review published in 2019 set out recommendations on incorporation of digital technologies within the NHS. The review stated 'advances in mathematics, computing power, cloud computing and algorithm design have accelerated our ability to analyse, interpret and make decisions using artificial intelligence'.

The review considered technological advances in digital medicine including telemedicine, remote triage and remote monitoring, as well as the widespread adoption of smart phone apps, which were recognised as the future of healthcare in both managing and empowering patients to be able to access services and to understand and participate in the management of their conditions. Focus, it was anticipated, would shift to prevention and earlier, more accurate recognition of diseases through processes including genomics, where the likelihood of an individual developing a given condition is mapped. The use of AI based technologies, including automated image analysis, the gathering of patient-generating data and its interpretation to clinically useful information has also been highlighted as key areas where significant benefits were envisaged and rapid development was encouraged.

It was also recommended that patients should be included as partners in the process of digital transformation, collaborating with healthcare facilities and their workforces which, through a process of education, it was deemed, would encourage adoption and development of the relevant systems and skills to be able to take advantage of the benefits these technologies will bring.

A core recommendation in the report was thus provision of continuous professional development within the emerging fields, including development positions in academia and industry, with additional recommendations that future undergraduate education for healthcare professionals incorporate topics including genomics, data analytics and AI, reinforcing the inherent value and changing landscape that this digital future represents (Topol, 2019).

### 1.13 Challenges and limitations to AI application in healthcare

The predictive power of machine algorithms have been found to be dependent on the size and quality of the datasets (Silver et al., 2016) and AI based systems have also shown susceptibility to error by finding overly favourable correlations; predictors and results are therefore recommended to be carefully validated. Additionally, while algorithms have shown an advanced ability to predict outcomes, determinants of causes from data analysis can be more elusive and ML has been shown to remain confronted with fundamental problems in statistical analyses including the detection of causal inference in observational data sets (Obermeyer and Emanuel, 2016).

Data quality can also be detrimentally affected by certain groups being overrepresented within datasets owing to inequalities in access to healthcare and capturing of results (Miotto et al., 2017) and information can also exist in a vast manner of forms, sometimes termed heterogeneity, with Cios and Moore (2002) reporting variants existing in the following:

- acquisition methods (images/scans/interviews/measurements)
- recording of data
- reporting of subjective results
- clinician interpretation
- conditions, such as inflammation, that are typically not mathematically described
- variation and non-standardisation in nomenclature defining conditions

Data complexity is further amplified in healthcare by disease heterogeneity with conditions existing in various subsets and disease processes evolving and advancing over time which models may not take account of, instead preferring static conditions. A limitation in the volume of data available on a specific

characteristic or phase of a condition can thus be a constraint of studies within such fields (Miotto et al., 2017).

The ease with which the language or form in which results generated by AI may be interpreted by the intended user may also influence the assimilation of the technology (Ting et al., 2019). Visualisation of data sets with larger volumes and multiple variables is limited by the number of visual dimensions or vectors available to effectively display such information thus often requiring multiple charts and maps to display material derived through processes such as self-organising maps (Vesanto, 1999). Improved interpretability of results from an AI model, to readily enable the end user understand how a prediction has been derived, has been thought, may facilitate acceptance of findings from such systems and subsequent implementation into healthcare practice (Miotto et al., 2017).

The deployment of AI in healthcare presents particular challenges, including ethical and legal implications around data ownership and privacy (Cios and Moore, 2002). There are also potential vulnerabilities to data breach and cyberattack, concerns over accountability and legal liability of decisions made by AI systems, the governance responsibility of such devices both in the UK and internationally, and financial and environmental implications associated with the increasing computation demands (Gajjar, 2023). Additionally, inherent scepticism and education may pose further challenges in the adoption of AI technology in healthcare (Ting et al., 2019).

## 1.14 Conclusion

Thus, while studies have previously reported on, OCT determined, retinal layer changes typically seen in nAMD treated with anti-VEGF, their evaluation as predictors, particularly using ML driven tools, appears limited.

The use of ML technology to extrapolate biomarkers in OCT scans, considered relevant in nAMD, and their use in modelling disease activity has however received a greater level of attention. Biomarkers do not however appear to have been frequently considered alongside retinal layer segmentation in predicting nAMD outcomes.

Of the various typically described anti-VEGF dosing regimens in nAMD, given that a PRN schedule is administered solely based on disease reactivation, this treatment modality perhaps offers the greatest insights into the activity of various nAMD phenotypes however does not appear to have been frequently modelled.

## 1.15 Rationale

This body of work therefore aims to consider relationships between a greater number of variables predictive of disease activity, disease progression and markers associated with declining visual acuity than previously collectively considered. In particular thicknesses of individual retinal layers and disease biomarkers derived by ML driven technology will be evaluated, with statistical analysis also facilitated by the use of AI based platforms which seems to be a novel approach in this project.

The study will also attempt to identify relevant OCT determined features that may predict how often nAMD requires treatment, with a focus on data from treatment naïve patients with a view this may positively impact the future management of nAMD in differentiating cases which are likely to require more frequent therapy from those in which the condition is inactivated more readily.

### 1.15.1 Primary outcome measures for the study

To investigate which OCT determined features influence treatment frequency.

To consider which OCT determined changes have the greatest bearing on visual prognosis.

### 1.15.2 Secondary outcome measures for the study

To establish whether OCT determined features can help differentiate patients that may benefit from a PRN based treatment regimen versus a pre-determined number of treatments in the management of nAMD.

To determine the impact advanced algorithms and ML might have in managing nAMD.

# 2 Methodology

## 2.1 Introduction

This chapter aims to present the method used to devise the study, obtain results and perform the statistical analysis of the investigation undertaken.

## 2.2 Literature review

A comprehensive literature review was conducted to evaluate the existing knowledge relevant to the field of study. Strategies were employed to ensure only relevant material was reviewed focusing on studies regarded as having produced the highest level of evidence.

Appropriate literary articles were identified on databases including the Cochrane Library, Medline, Web of Science, Scopus and Google Scholar.

Where available, standardised search terms were used and acronyms avoided or considered carefully before used as search terms. Boolean operators were employed to narrow the searches, with greater emphasis placed on search terms appearing in titles or abstracts. Relevant date ranges were applied if pertinent to the topic being explored.

Search terms and key words included:

- Anti-VEGF
- Neovascular AMD OR neovascular age related macular degeneration
- Epidemiology OR incidence OR prevalence
- Pathophysiology
- Service delivery
- Regimen
- Optical coherence tomography OR OCT
- Retinal layers
- Segmentation
- Retinal thickness
- Spectralis SD-OCT
- Heidelberg Eye Explorer OR HEYEX
- ETDRS
- Mapping patterns

- Biomarkers
- Subretinal fluid
- Intraretinal fluid
- Pigment epithelial detachment
- Machine learning
- Deep learning
- Artificial intelligence
- Data analysis
- Healthcare
- Data mining
- Prediction
- Model
- Visual acuity
- Outlier
- Ophthalmic
- Imaging
- NOT diabetic retinopathy
- NOT angiography
- NOT glaucoma

Limits Applied to Search Results:

- Peer-reviewed material only
- Availability in English
- Preference for articles published in journals with higher scientific rankings

Types of Studies Included:

- Randomised controlled trials
- Observational studies
- Case controlled studies
- Cohort studies
- Meta-analyses
- Systematic reviews

Citation searching within relevant articles, in particular systematic reviews and meta-analyses, was further used to source appropriate literature.

Furthermore, nationally issued guidance from regulatory bodies including the National Institute for Health and Care Excellence (NICE) and Royal College of Ophthalmologists and the material considered by such bodies in developing relevant guidelines was considered in this review along with publications used by the National Health Service (NHS) in developing national recognised healthcare strategies and legislation.

### 2.3 Study design

This was a retrospective, non-interventional, observational study using fully anonymised data. Analyses performed in the study were on data from electronic medical records (EMR) systems and human eye scans using OCT. No patient identifiable information was transferred to the research team at Aston University.

### 2.4 Ethical and legal approval

The study conformed to ethical principles underlying the Declaration of Helsinki and good practice guidelines on the proper conduct of research. Approval for the project was gained from the Health Research Authority (HRA) and Health and Care Research Wales (HCRW) (Appendix 1). A data sharing agreement between the study centre, Aston University, and principal research site, Wirral University Hospital Trust (WUTH), was contained within the HRA research application.

An additional data sharing agreement between the primary research site and secondary research site, Moorfields Eye Hospital NHS Foundation Trust (MEH), was established separately (Appendix 2) before proceeding with the study.

### 2.5 Study risk assessment

The study only considered fully anonymised data for analysis where personal identifiers, both direct and indirect, that could lead to an individual being identified, had been removed.

Any patients preferring not to have their information shared or used for research were invited to advise WUTH of their wishes and such cases were highlighted within the Trust EMR. It was accepted that data from patients who had previously requested that their information not be shared, even for research purposes in anonymised form, would not be included in the study. The project was deemed to present no obvious risk to patients as all would had previously received a diagnosis and clinical management plan from a consultant ophthalmologist responsible for their care and furthermore the study only involved the retrospective analysis of anonymised data and of known features, seen on OCT scans, that have formerly been reported in literature. It was however planned that should the study find any previously unknown

relationships relevant to the management of patients from this dataset, or in the unlikely event the study uncovered any anomalies in the re-analysis of the data, such outcomes would be reported back to the participating NHS organisation supplying the data. Such information could perhaps help to guide the future management of individuals but it was deemed, would not impact on those who have already been diagnosed and received treatment, being considered by the project.

In considering consent and disclosure of data, in retrospective studies using non-identifiable, anonymised data of patients who have previously undergone investigations and treatment, the Information Commissioner's Office (ICO) code of practice was consulted and found to state that consent was generally not necessary in such cases (ICO, 2021).

Study data was additionally processed using an algorithm developed by MEH and Google DeepMind Health. The data however was not at any time be accessed by Google or DeepMind Technologies eliminating the risk it could have been retained by such organisations. The study was thus considered to present a very low risk for disclosing identifiable data but regardless strict adherence to ICO advice on managing data protection risk (ICO, 2019) and ICO guidance on anonymisation (ICO, 2012) was followed.

Where pseudonymised data was to be shared between WUTH and Moorfields Eye Hospital NHS Trust, this was on the basis of the completed data sharing agreement where both parties followed appropriate technical and organisational measures to comply with the obligations under Article 32 of the General Data Protection Regulation (GDPR).

### 2.6 Study population and date range

While ranibizumab had been recommended for the treatment of nAMD in 2008 (NICE, 2008), aflibercept was developed subsequently and did not become available until July 2013 (NICE, 2013). Furthermore, the adoption and integration into clinical use of a novel pharmaceutical agent would likely not have been instant, thus January 2014 was chosen as the start date of the study, a period from which both drugs recommended to treat the condition were first available for the full calendar year.

On 16th March 2020 an official lockdown was announced in response to the COVID-19 pandemic. Data published on NHS outpatient activity reported over a 50% decrease in attendances by April 2020 but as shown in charts plotting outpatient appointments and attendances by week (Figure 2.1) , appointment activity started to show a decline by the start of March 2020 (Secondary Care Analytical Team, 2021). February 2020 was thus taken as an endpoint for the study to thus allow for the accumulation of results

from a minimum period of 12 months of patient attendances unaffected by the response to the COVID-19 pandemic.

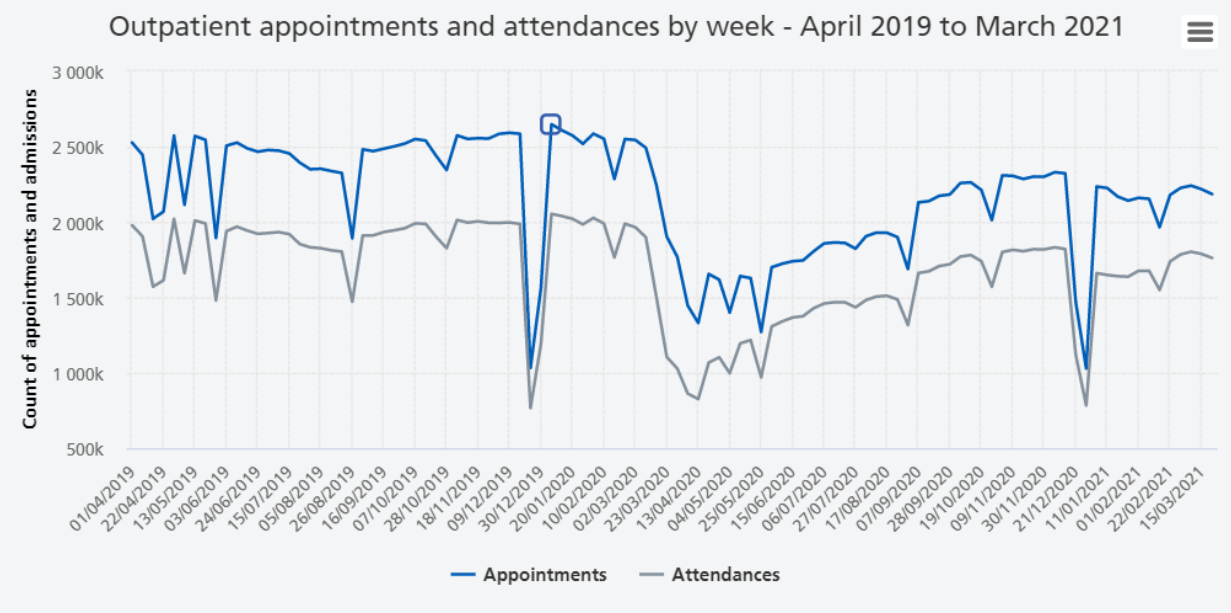


*Figure 2.1: Outpatient appointments and attendances by week - April 2019 to March 2021 (Secondary Care Analytical Team, 2021). Reproduced with permission.*

Prior to collecting data, a study population estimate was also made based on statistics from the Wirral Intelligence Service (2019), which reported population data up to 2018, and UK prevalence data from a meta-analysis referenced by NICE (NICE, 2018), which estimated 1.2% of those aged over 50 as having nAMD (Owen et al., 2012). Using these figures, it could be estimated that 1646 individuals had the condition in 2018 on the Wirral. A literature search for UK incidence data found a number of estimates but using the most conservative of these figures from the same group that supplied the prevalence data, 0.14% of those aged over 50 developed the condition annually and again using Wirral population statistics between 2014 and 2018, this extrapolated a figure of 756 individuals hypothetically having developed the condition during this period.

As it was deemed unlikely that all patients with the condition at any one time would be under the care of a Trust, the estimate derived using prevalence data was likely overestimated. Similarly, the incidence of the disease was likely underestimated as it used most conservative incidence estimate and did not take

account of 2019 population figures thus it was expected that the potential number of cases available for investigation would lie somewhere between 756 and 1646.

As the prognostic abilities of AI based analytical systems are linked to the size of the dataset inputted (Silver et al., 2016), it was decided for the purposes of this study that all eligible cases would be included for evaluation. Furthermore on reviewing studies, already consulted in this report, that have previously described retinal layer changes in nAMD, they were found to have considered population sizes of between 24 and 99 eyes (M = 54.00, SD = 29.41, N = 9) or if taking into account retrospective studies only, the cohort size was between 52 and 99 eyes (M = 78.25 eyes, SD = 20.79, N = 4) (Shin et al., 2011, Roberts et al., 2017, Zucchiatti et al., 2017, Muftuoglu et al., 2018, Kim et al., 2019, Lee et al., 2020, Aşikgarip et al., 2021, Pfau et al., 2021, Gunay and Esenulku, 2022). It was thus felt that the approach of using the maximum available population size would both optimise the development of AI driven learning models while minimising the risk that any statistical inferences drawn by the study would be negatively affected by inadequate sample sizes.

### 2.7 Data collection

The ophthalmology EMR database, Medisoft, at WUTH was electronically searched by Trust staff to acquire the relevant datasets for adult patients that had attended WUTH for the treatment of any form of nAMD that met the inclusion and exclusion criteria.

Using the OCT image analysis software, HEYEX, scans acquired using Heidelberg Spectralis SD-OCT of those identified from the EMR as eligible to be included in the study were reviewed by Trust staff in line with the exclusion criteria to extract numerical values of component retinal thicknesses.

These data were anonymised, uploaded to a spreadsheet and forwarded to the research student undertaking the project for further evaluation.

Additionally, Trust staff at WUTH securely transferred exported anonymised copies of the OCT scans to MEH, in line with an established data sharing agreement, where additional processing by OCTANE API, an automated machine learning algorithm, generated further quantitative outputs of retinal features. These data were returned to WUTH and in turn forwarded to the research student for analysis.

### 2.8 Study analysis

To statistically evaluate the data collected and investigate relationships between the variables being considered, analyses were conducted using the AI driven platform Orange Data Mining, developed by the University of Ljubljana and Microsoft Excel (Excel).

Analyses were carried out by the research student undertaking the project and assisted by the project supervisor, associate supervisor and colleagues from Aston University.

### 2.9 Project timetable

The project began in April 2022 once approvals had been granted. With the agreement to an extension of the project completion, data collection was concluded by August 2023. The data analysis and reporting then commenced inline with a completion deadline for the project of January 2024.

### 2.10 Inclusion criteria

The primary inclusion criterion was an adult patient aged 18 years and over that attended WUTH for the diagnosis and subsequent treatment of any form of nAMD from January 2014 to February 2019.

For the dataset, the inclusion criteria were set as digital OCT images acquired using Heidelberg Spectralis OCT and demographic and treatment information recorded on the EMR.

### 2.11 Exclusion criteria

The principal exclusion criteria initially set were:

- Data of patients who had requested that their records should not be shared and had informed WUTH of this decision
- Datasets from individuals in whom OCT scanning could not be performed
- Datasets from individuals with incomplete records
- Images that did not permit analysis of the required features
- Datasets from cases where treatment was withdrawn within the first 12 months due to safety concerns, vision falling below eligibility criteria and patients declining treatment

### 2.12 Additional exclusion criteria

A criterion of age 50 and over was additionally used to exclude cases within the project as a systematic review of anti-VEGF use in nAMD (Solomon et al., 2019) reported the condition to be associated with those aged 55 years and older and UK AMD related services commissioning guidance stating the condition to typically affect those over the age of 50 years (Chandra et al., 2022). Additionally the pivotal ANCHOR, MARINA and VIEW trials (Brown et al., 2006, Rosenfeld et al., 2006, Heier et al., 2012), which helped to establish guidelines for the use of ranibizumab and aflibercept in nAMD, only included patients aged 50 and over within their cohorts with future studies seeming to adopt similar thresholds, thus if attempting

to draw conclusions between this study and prior work, to ensure that cohorts considered were from similar age groups, this approach seemed consistent.

A further exclusion criterion of the availability of a minimum of six instances of follow up episode information within the first year of management was also set to ensure an appropriate number of integers existed with which to carry out data interpolation or form any statistical inference as detailed in chapter 4.

Instances where additional therapies related to nAMD management, including surgical vitrectomy, intravitreal tissue plasminogen activator and photodynamic therapy, were employed during the study period also resulted in exclusion of the given record.

### 2.13 Security arrangements

A copy of the research data will be securely held at Aston for 6 years from date of study closure in accordance with Aston University Record Management Policies and Procedures and any staff members accessing the data will have been appropriately trained to handle and process data in accordance with Aston University Data Protection Policies and Procedures.

# 3 Data collection and rationale

## 3.1 Introduction

This chapter provides a detailed account of how data was collected and the rationale behind how variables were to be considered by the study.

## 3.2 EMR database search and data extraction

An initial EMR database search found that 1322 eyes of 1123 adult patients aged 18 years and over had been diagnosed and subsequently treated for nAMD from January 2014 to February 2019. During this period all patients received a loading dose of 3 anti-VEGF injections at 4-week intervals with further treatment determined on a PRN basis.

On applying inclusion criteria to these cases, as it was discovered that results of VA were not kept electronically at WUTH until May 2016, this reduced the potential pool of 724 eyes of 638 individuals that met the inclusion criteria.

Data was thus extracted from the EMR for the period between May 2016 and March 2020 for naïve eyes receiving anti-VEGF for nAMD using auditing tools contained within the software and case review. From the initial, baseline visit onwards, information on following characteristics were considered for extraction for each clinic visit:

- Ethnicity
- Laterality of studied eye
- Age at given visit
- Sex
- Anti-VEGF drug type administered to studied eye
- Adjunctive interventions to the studied eye
- VA studied eye
- VA fellow eye
- Number of injections administered at visit to studied eye
- Number of injections administered at visit to fellow eye

## 3.3 OCT

### 3.3.1 OCT capture method

All OCT images were acquired by either qualified ophthalmic photographers or ophthalmic technicians trained in the use of the Heidelberg Spectralis in capturing scans.

The device had preset scanning patterns for use in capturing images, centred on the fovea, in macular diseases such as nAMD, with the two scanning patterns employed at WUTH within the AMD service comprising 19 or 25 B-scan sections (also termed slices or frames) of the central macula. The variation in scanning patterns resulted from the device defaulting to 19 frames for macular imaging, thus 25 slice scans were performed either at clinician request or due to this becoming the preferred option over time due to manufacturer advice on this extended pattern being more conducive to nAMD management.

An automatic retinal tracking (ART) mode, available within Heidelberg Spectralis, was engaged in macular tomography to ensure that all B-scans, required to image the area of interest, were acquired consistently despite any eye movements. In ART mode, the device additionally acquires a specified number of B-scans per retinal location allowing averaging of the multiple sections, enhancing image quality further by boosting the signal-to-noise ratio and reducing motion artifacts.

Details of the two scan patterns are catalogued in Table 3.1.

| Number of B scans | 19 | 25 |
|---|---|---|
| Pattern size | 20x15 (5.9x4.5mm) | 20x20 (5.9x5.9mm) |
| Distance between B-scans | 247um | 247um |
| Scan angle | 20˚ | 20 ˚ |
| ART mode | 9 images averaged | 9 images averaged |

*Table 3.1: OCT scan pattern parameters*

The ‘Auto Rescan’ function within Heidelberg Spectralis used active eye tracking to automatically acquire OCT scans at the same location of the retina as during the previous exam thus allowing high reproducibility of thickness measurements and allowing specific retinal loci to be more readily compared in images over varying timeframes.

The accepted practice at WUTH was to use Auto Rescan at all follow up visits to reacquire macular scans based on the template of the prior examination unless a specific scan was requested by the examining

clinician or the ophthalmic imager felt the scanning pattern required to be altered to better capture the area of interest.

### 3.3.2 OCT analysis and review

OCT image analysis software, HEYEX, allowed review of captured scans.

Automated segmentation of acquired scans by HEYEX detected 11 retinal boundaries (Figure 3.1) from which the programme extrapolated thickness and volumetric information for component retinal layers and layer groups (Table 3.2).

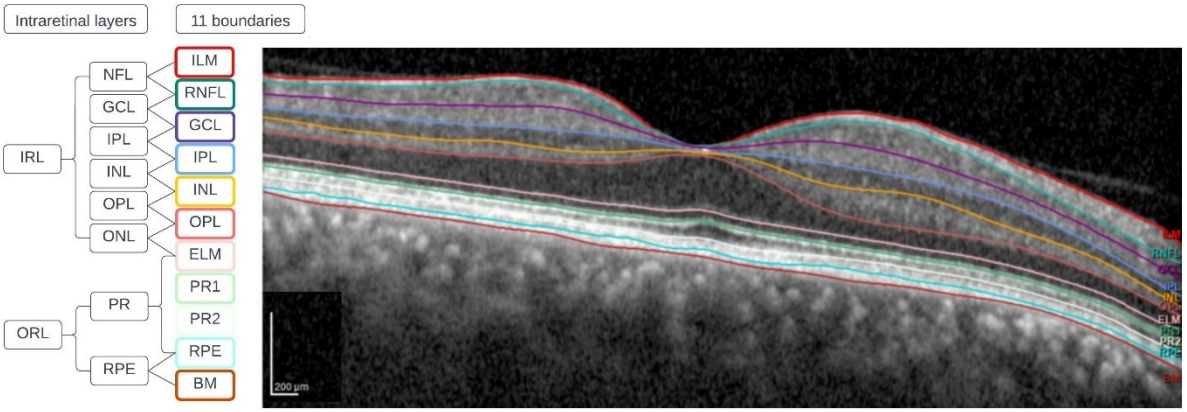


*Figure 3.1: Representation of retinal boundary detection and intra-retinal layer segmentation a normal eye by Spectralis SD-OCT: inner limiting membrane (ILM), retinal nerve fibre layer (RNFL), ganglion cell layer (GCL), inner plexiform layer (IPL), inner nuclear layer (INL), outer plexiform layer (OPL), outer limiting membrane (OLM), myoid zone of the photoreceptor layer (PR1), ellipsoid component of the photoreceptor layer (PR2), retinal pigment epithelium (RPE), and Bruch's membrane (BM), and secondary derivation of intraretinal layers and layer groups (Table 3.2)*

| Intraretinal layer or layer group | Segmentation boundaries |
|---|---|
| $Retina_t$ | ILM-BM (Sum of all retinal layers) |
| NFL (nerve fibre layer) | ILM-RNFL |
| GCL | RNFL-GCL |
| IPL | GCL-IPL |
| INL | IPL-INL |
| OPL | INL-OPL |
| ONL | OPL-ELM |
| RPE | RPE-BM |
| IRL (inner retinal layers) | ILM-ELM |
| ORL (outer retinal layers comprising photoreceptor [PR] layer) | ELM-BM |

*Table 3.2: Intraretinal layers as defined by composite boundaries in HEYEX*

Using a modified ETDRS grid overlaying the central 3mm of the macula (Figure 3.2), the software determined tissue volumes for the central 3mm and 1mm zones centred over the fovea as well as average thickness data in the central 1mm zone and the minimum thickness measure from the analysed region.

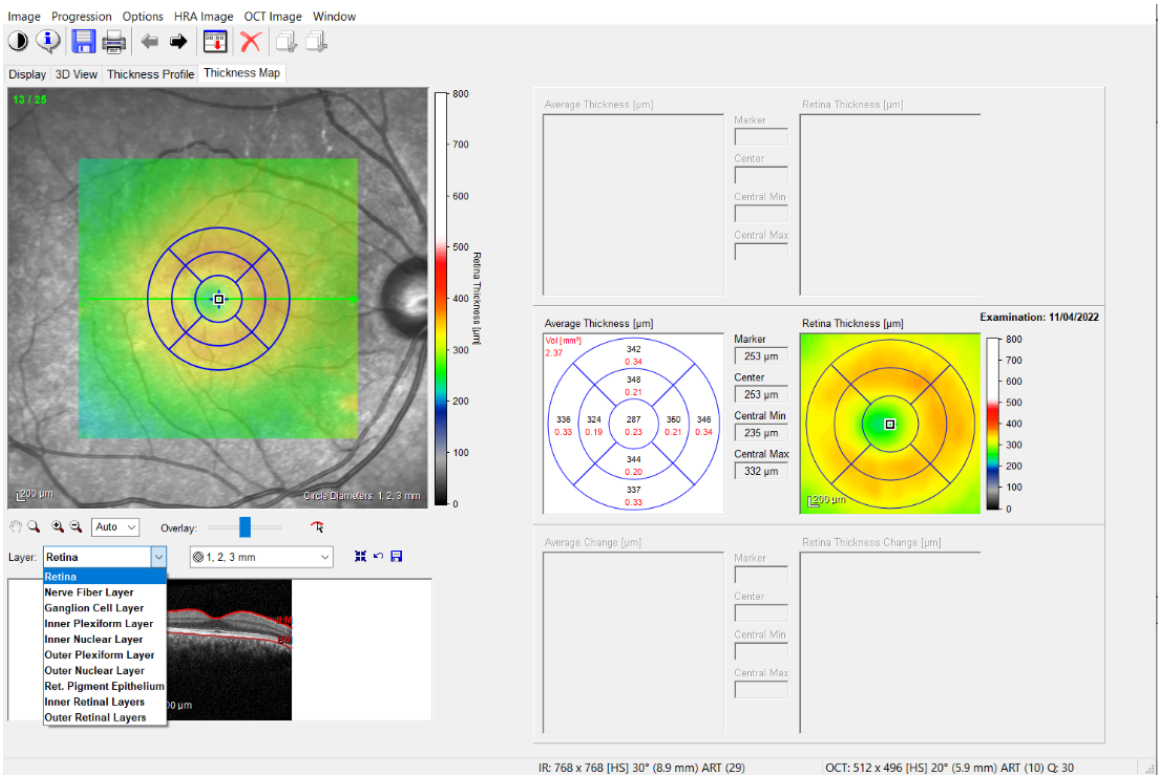


*Figure 3.2: Representation of OCT interpretation within HEYEX*

### 3.3.3 OCT database search and data extraction

OCT scans from the baseline visit (V0), the post loading dose visit (VP) and at 12 months from initiation of treatment (V12) were initially considered most pertinent to the investigation and chosen as the episodes from which OCT data would be extracted. It became apparent, during the extraction process, that the V12 data could not however be used as a predictor for changes observed in treatment patterns or VA at 12 months as V12 was in effect the primary endpoint considered in the project. These V12 data were thus superfluous and omitted from further extraction within the study.

As the 19 and 25 slice scan patterns, used to acquire OCTs of the central macula in nAMD at WUTH, covered either a region comprising the central 5.9 x 4.5mm or 5.9 x 5.9mm zone, it was decided to consider the retinal data from within only the 1mm and 3 mm central ETDRS rings as a modified 3mm overlay would overfit all image frames independent of the scan pattern and thus study would avoid being affected by incomplete capture affecting the 6mm zone from the standard ETDRS subfield map. Thickness data from individual superior, nasal, inferior and temporal subfields offered by the ETDRS grid analysis were not however considered within this project.

From the HEYEX derived 10 retinal layers and layer groups in which thickness and volumetric data were available, the following measures were extracted to a datasheet:

- volume ($mm^3$) within the 3mm subfield (3mm vol)
- volume ($mm^3$) within the 1mm central subfield (1mm CM vol)
- mean layer thickness ($mm^2$) within the 1mm central subfield (1mm CMT)
- minimum layer thickness ($mm^2$) within the 1mm central subfield (min CMT)

Extraction of OCT data from HEYEX involved the inspection of each file to ensure layers were correctly segmented and that the region of interest had been correctly scanned. Once the exclusion criteria had been appropriately applied, the extracted OCT values were collated with the EMR workbook, anonymised and transferred to Aston for analysis.

In applying the exclusion criterion of images that did not permit analysis of the required features, it was decided to omit scans where two or more line scans are affected by segmentation errors in the central 1mm region as suggested as a limit in prior research (Patel et al., 2009).

OCT scans of datasets meeting all study criteria were additionally compiled on a secure server for additional processing at MEH once the extraction process at WUTH was completed.

### 3.3.4 MEH OCTANE dataset

Extracted OCT files were electronically transferred to MEH by WUTH for analysis by for AI-enabled retinal segmentation.

This retrospective OCT processor, OCTANE API (OCTANE), employed a deep learning tool with a U-Net based architecture with previously published validation (De Fauw et al., 2018) to produce quantitative tissues volumes by evaluation of component retinal features within each scan slice (Figure 3.3, Figure 3.4 and Figure 3.5).

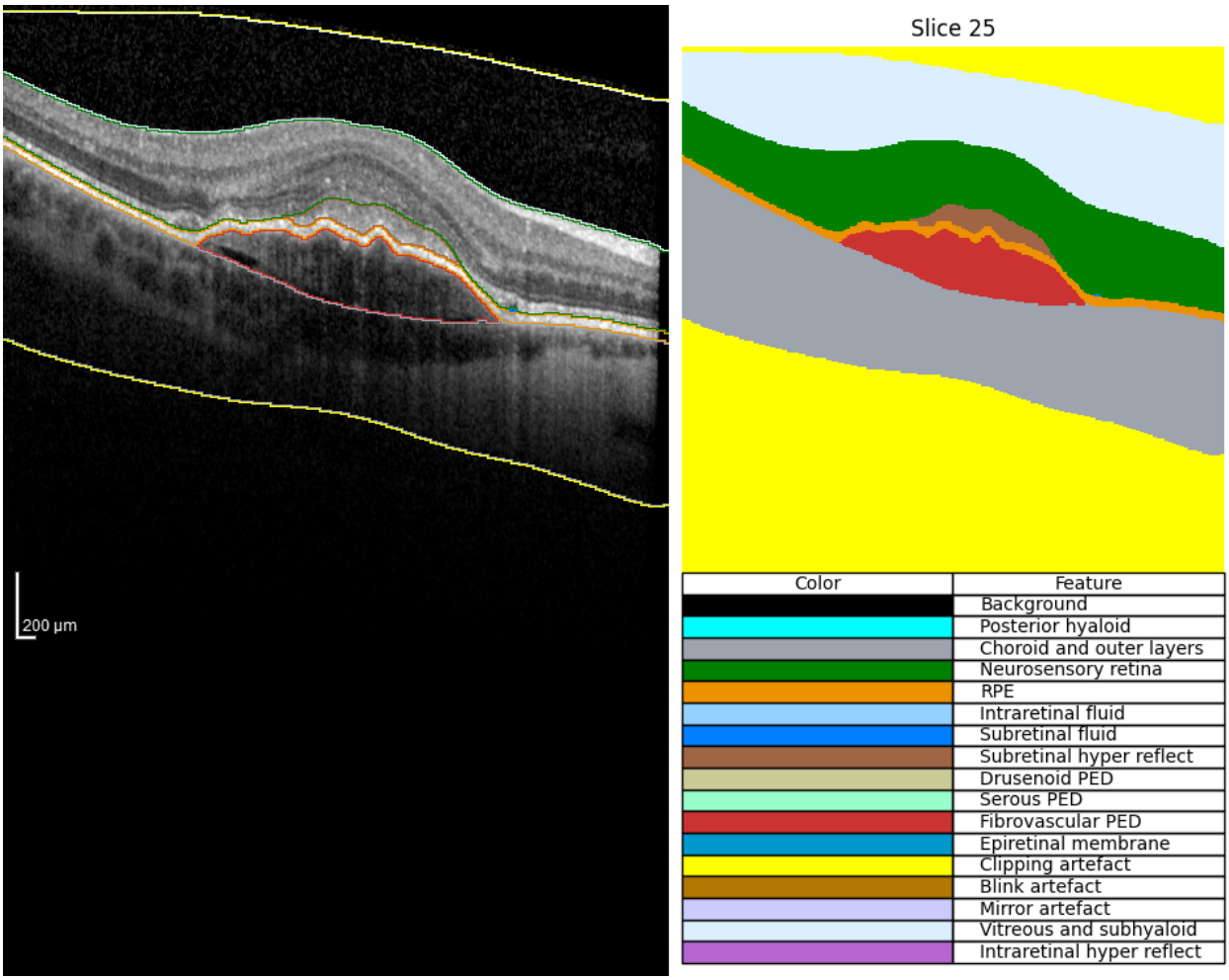


*Figure 3.3: OCTANE output showing tissue segmentation and determination of features including subretinal hyper reflective material, subretinal fluid and fibrovascular PED*

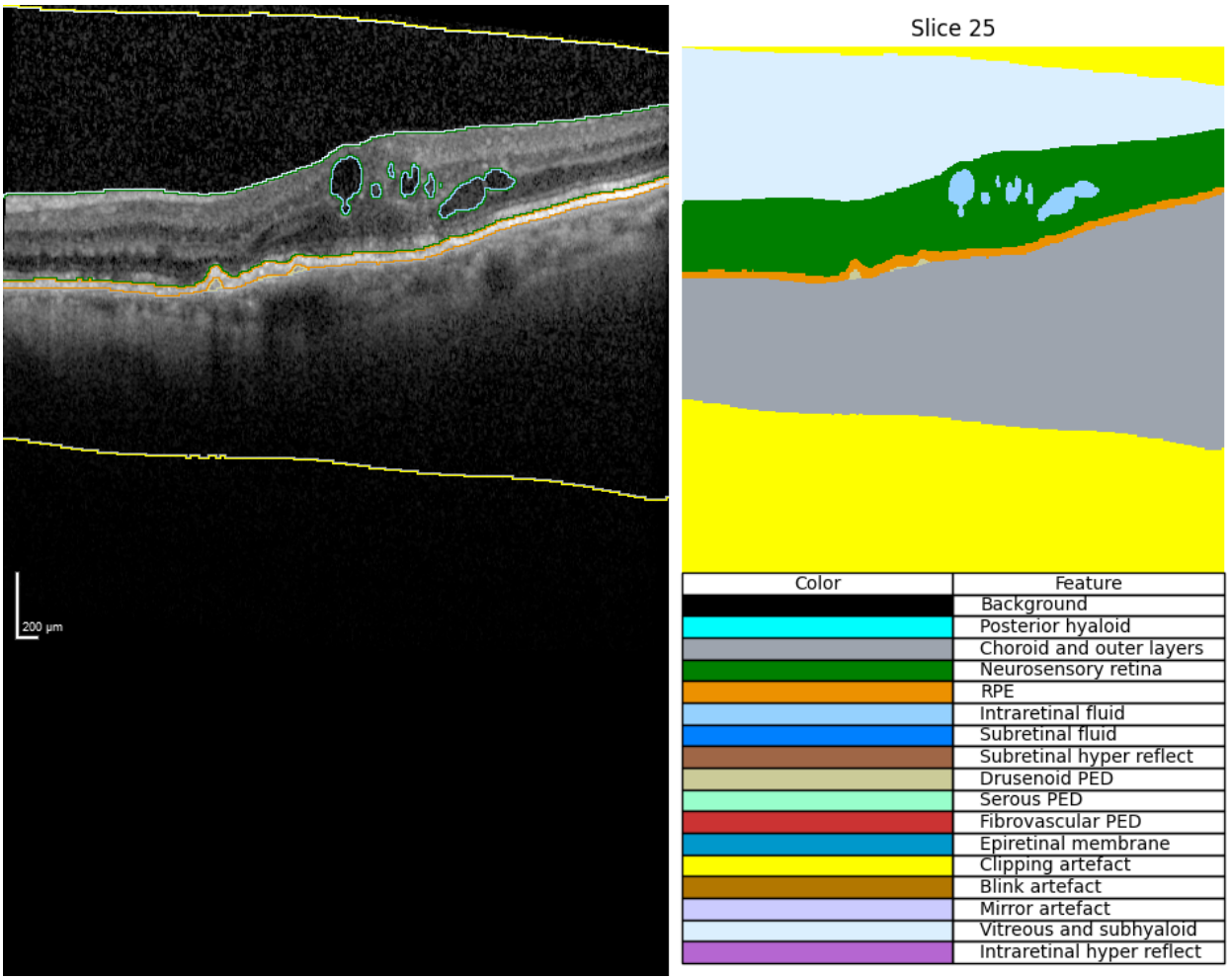


*Figure 3.4: OCTANE output showing tissue segmentation and determination of features including intraretinal fluid and drusenoid PED*

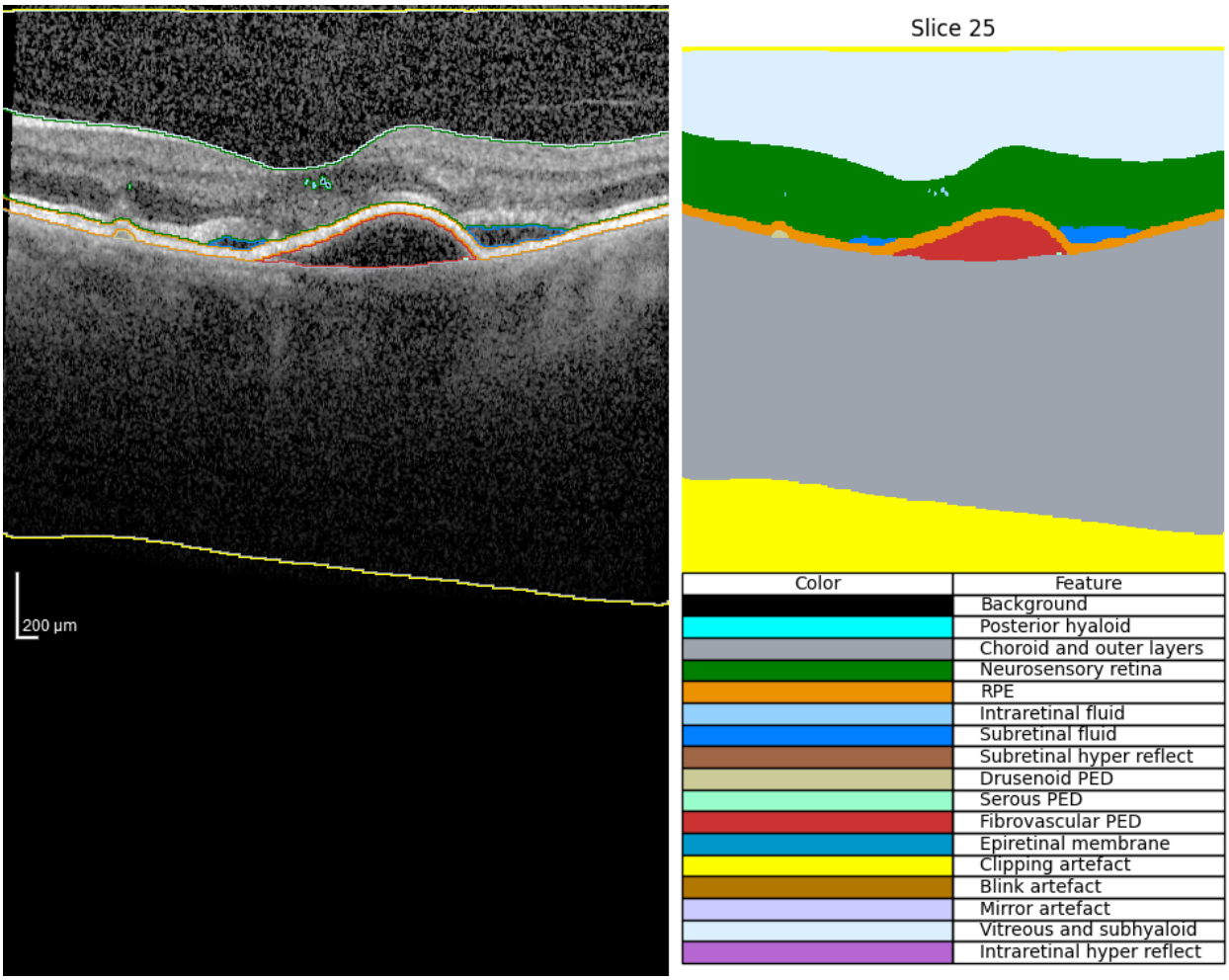


*Figure 3.5: OCTANE output showing tissue segmentation and determination of features including intraretinal fluid, subretinal fluid, drusenoid PED, fibrovascular PED and serous PED*

It was discovered however that the algorithm could only consider data from 25 slice OCT scans where the data captured at WUTH comprised a combination of 19 and 25 section scans.

The outputted tissue data (Table 3.3) from the scans which could be interpreted was returned within an Excel file with volumes displayed in the units $um^3$.

| |
|---|
| Background |
| Vitreous and subhyaloid |
| Posterior hyaloid |
| Epiretinal membrane |
| Neurosensory retina |
| Intraretinal fluid |

| |
|---|
| Intraretinal hyper reflective material |
| Subretinal fluid |
| Subretinal hyper reflective material |
| RPE |
| Drusenoid PED |
| Serous PED |
| Fibrovascular PED |
| Choroid and outer layers |
| Mirror artefact |
| Clipping artefact |
| Blink artefact |

*Table 3.3: Scan features reported on within OCTANE output Excel file*

This data was carefully merged to the existing, complied study data using the supplied and returned anonyms and the VLOOKUP function within Excel to ensure that files were correctly matched. Tissue volumes were converted to $mm^3$ to match the existing units in which volumetric OCT was extracted from HEYEX.

## 3.4 Visual acuity

### 3.4.1 Measurement and documentation

VA of patients attending WUTH in relation to nAMD management was assessed using logarithm of the minimum angle of resolution (logMAR) ETDRS charts scored by counting individual letters correctly identified (Ferris et al., 1982). The use of this letter score method adheres to the gold standards recommended in clinical trials (Ferris and Bailey, 1996) and is widespread within the assessment of those with nAMD. A change of five letters within this score relates to one line of logMAR VA and measures can be related to approximate Snellen VA equivalent (Table 3.4).

| ETDRS Letter score | LogMAR | Snellen equivalent (m) |
|---|---|---|
| 0 | 1.7 | |
| 5 | 1.6 | |
| 10 | 1.5 | 6/192 |
| 15 | 1.4 | 6/152 |
| 20 | 1.3 | 6/120 |
| 25 | 1.2 | 6/96 |

| | | |
|---|---|---|
| 30 | 1.1 | 6/76 |
| 35 | 1.0 | 6/60 |
| 40 | 0.9 | 6/48 |
| 45 | 0.8 | 6/38 |
| 50 | 0.7 | 6/30 |
| 55 | 0.6 | 6/24 |
| 60 | 0.5 | 6/19 |
| 65 | 0.4 | 6/15 |
| 70 | 0.3 | 6/12 |
| 75 | 0.2 | 6/9.5 |
| 80 | 0.1 | 6/7.5 |
| 85 | 0 | 6/6 |
| 90 | -0.1 | 6/4.8 |
| 95 | -0.2 | 6/3.8 |
| 100 | -0.3 | 6/3 |

*Table 3.4: The relationship between the ETDRS letter score, LogMAR and the approximate Snellen visual acuity*

All staff engaged in the process of measuring visual acuity were trained on the use of ETDRS charts and the letter scoring method and undertook the activity giving consistent instructions to patients, in standardised testing conditions including the use pre-determined testing distances, employing an appropriate visual correction, with charts presented in ETDRS illuminator cabinets in accordance with the protocols derived at WUTH based on established standardised methods in measuring visual acuity (Ferris and Bailey, 1996) and those reported in the benchmark ETDRS (1991a) and AREDS (2000) studies.

Since May 2016 VA results for patients undergoing treatment for nAMD at WUTH were recorded on Medisoft. The programme allowed the selection of the ETRDS chart version used for the assessment, with different charts using varied letter selections but employing a homogenised level of difficulty (Ferris et al., 1982) utilised in testing either eye. The selected chart version was replicated by the EMR as an electronic grid on screen with the assessor able to indicate the letters correctly identified and the software in turn tabulating the letter score VA.

### 3.4.2 Evaluation of change in VA and managing fluctuation

The method of evaluating the change in visual acuity was considered carefully. A literature review of work investigating the repeatability of VA found reports of significant variability within measures. Siderov and Tiu (1999) found a change of 8 logMAR letters was required to be secure in the decision that a genuine change in VA had occurred. When considering VA in those with AMD, patient related factors, change in refraction and variation in disease state have been reported to play an additional role, thus the coefficient

of repeatability has been found to increase in such cohorts with studies reporting intersessional VA measures of 12 and 14.9 letters respectively (Patel et al., 2008, Aslam et al., 2014).

Prior work researching nAMD and using VA as an outcome measure has tended to either consider VA at the end of the period of interest or where examining change in VA, have utilised a measure of the difference between baseline VA and at the end of the studied timeframe. These approaches have been repeated within this body of work but it was also thought worthwhile to apply an alternative method to studying VA whereby some degree of the variation in repeatability of measures could be addressed and indeed to consider whether the degree of variance was of significance.

It was thus thought the slope of the linear regression line of the VA values for each individual (Figure 3.6) might better describe the trend in VA change over 12 months using the available data points and perhaps be less affected by variability of any individual VA datapoint. In addition to the fluctuation in measurements of VA between visits, some rationalisation could also be administered to account for the inconsistency in the number of follow up visits, ranging from between six and 13 (as discussed in section 4.5).

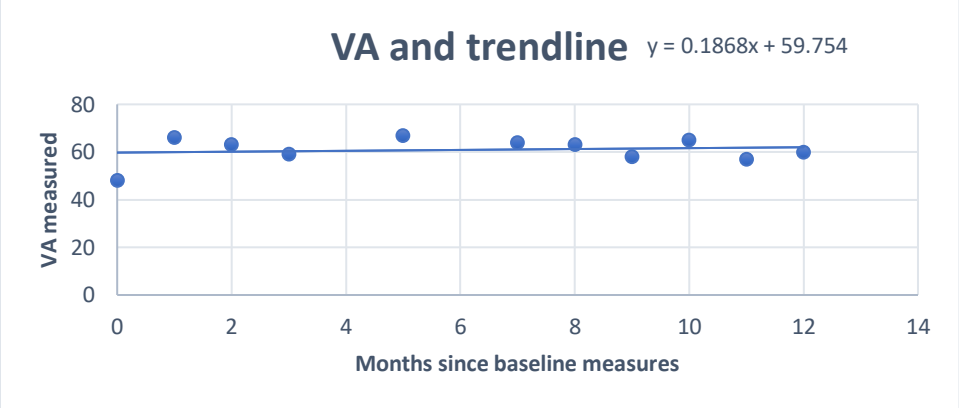


*Figure 3.6: Linear regression of sample data from Microsoft Excel plotting VA against time*

While the value of the slope of the regression line was displayed within scatterplot charts overfitted with trendlines, within Excel, this was more readily obtained by applying the command:

=SLOPE(known_ys, known_xs)

to VA data within workbooks which returned either a positive or negative value indicating whether visual acuity had improved or declined. These slope values were thus used to extract classifications of whether

vision was lost or gained during the study period and this data added to that already extracted for further evaluation.

As treatment with anti-VEGF has been shown to improve VA in those with nAMD and maintenance after two years has largely been considered against baseline measures of VA (Colquitt, 2008) it was felt that a further worthwhile aspect of investigation might be to assess whether the improved level of VA, found after anti-VEGF therapy was initiated, could be maintained and whether predictive factors of any such maintenance or decline could be determined. To thus account for the initial recovery in VA, change in VA over time was established against both baseline untreated levels of VA, when there was a likelihood of some immediate recovery, and VA results immediately post loading with anti-VEGF when it could be better interpreted whether this recovery was maintained over time.

Only a solitary measure of VA prior to treatment with anti-VEGF was available within the extracted data, rendering the ability to consider a mean of this result unachievable. The mean of the VA recorded at the two visits immediately post loading was however determined as well as the mean of the VA measure at 12 months, found by averaging the measure of VA at 12 months and the reading from the immediately preceding visit.

To consider the variability of VA and whether this could be predicted or indeed whether this measure had any predictive influence, the standard deviation of the mean of the VA measures immediately post loading until 12 months from initiation for therapy was considered. The baseline VA was not included as there would be an expected increase in VA after initial receipt of anti-VEFG therapy, as noted by Colquitt (2008), which could skew results.

### 3.5 Loading dose timeframe

Guidelines from the Royal College of Ophthalmologists at the time required that a loading dose of anti-VEGF was administered monthly for three months (RCOPHTH, 2013). The importance that intervals between these treatments were not delayed was supported by findings from a study by Relton et al. (2022) where those receiving the initial course of three treatments promptly within less than or equal to eight weeks were found to have a small but statistically significant improvement on visual outcomes compared to where this timeframe was greater than 10 weeks.

Through a combination of database search and case review, the timeframe over which loading with three doses of anti-VEGF took place was determined, and allowed the effective classification of

treatment delays and analysis to be carried out on whether this was a factor in treatment and visual outcomes.

### 3.6 Adjunctive interventions

The additional review of records to determine injectional intervals allowed the discovery and exclusion of cases where additional therapies related to nAMD management, including surgical vitrectomy, intravitreal tissue plasminogen activator and photodynamic therapy, were employed that might adversely affect the studied outcomes similar to an approach taken by the VIEW study (Heier et al., 2012).

### 3.7 Visits

Baseline VA and OCT measures were taken at the visit when diagnosis was made, prior to anti-VEGF therapy being initiated. Patients at WUTH were subsequently invited to attended monthly monitoring visits, starting one month after the third loading dose was administered, where OCT scans were taken and VA measured with further therapy initiated based on clinical findings in line with the PRN regimen. It would thus be expected that 9 episodes of such records would exist if considering a period of 12 months from when treatment was commenced. The number of such attendances over the first 12 months however varied from three to 13 visits with factors causing a reduction in visits including appointment delays due to circumstances arising at WUTH, delays arising from patient illness and non-attendance. Above expected numbers of episodes arose in cases where individuals were receiving bilateral treatment, hence requiring monthly review for the fellow eye and inevitably having additional measurements taken of the eye considered within the study, or where patients had been followed up at intervals shorter than one month for a period during the first year.

A minimum number of six follow up episodes was thus set as a further exclusion criterion to ensure that an appropriate number of data points existed such that change in visual acuity could be appropriately assessed over an adequate timeframe.

### 3.8 Fellow eye involvement

Both eyes being affected by nAMD is a commonplace finding with a largescale retrospective cohort study, evaluating 22,553 patients with unilateral nAMD, reporting development of the condition in the fellow eye in 38% of patients within 3 years of the primary eye being commenced on treatment (Starr et al., 2021). Chopra et al. (2018) also undertook a comprehensive study of those developing nAMD in fellow eyes at MEH reporting bilateral involvement in 22% of the patients. Their analysis additionally

found an improved level of baseline acuity in the second eye developing nAMD with closer observation, more frequent OCT imaging and those affected being more alert to sudden visual alteration cited as potential factors leading to earlier diagnosis.

Beneficial therapeutic effects of anti-VEGF agents in untreated fellow eyes have also been described in case reports (Wu and Sadda, 2008, Isildak et al., 2018), in statistically significant numbers of cases in a prospective study by Michalska-Małecka et al. (2016) and a retrospective study of patients enrolled in landmark MARINA and ANCHOR studies (Rouvas et al., 2009). The reports did not identify the exact mechanism of this response but unanimously suggested a likely systemic effect via entry of anti-VEGF into the blood stream with the prospective trial group also postulating a change in gene expression found in those having received ranibizumab as a potential mediator (Michalska-Małecka et al., 2016).

Although all eyes entered into this study at Aston University were treatment naïve, it did however seem sensible to consider subsets of the complete cohort to eliminate factors arising from therapy given to a fellow eye. During data extraction it was therefore determined:

- patients in whom there was no evidence of nAMD in the fellow eye either prior to or during the initial 12 months of study (N1)
- patients in whom there was no prior evidence of nAMD in the fellow eye but where the condition did subsequently develop and was treated with anti-VEGF in the fellow eye during the initial 12 months of study (N1FA)
- patients in whom there was prior evidence of nAMD in the fellow eye and where treatment was not administered to the fellow eye during the initial 12 months of study (N2FI)
- patients in whom there was prior evidence of nAMD in the fellow eye and where anti-VEGF treatment was administered to the fellow eye during the initial 12 months of study (N2FA)
- patients in whom nAMD was diagnosed in both eyes at the same visit and anti-VEGF treatment was loaded bilaterally over the same interval, although subsequent treatment patterns may have varied in both study eyes (NB)

## 3.9 Discussion

This chapter thus provided a detailed description of the data collection process from the electronic medical records and the subsequent analysis of visual acuity and OCT data.

Key aspects of the methodology included:

Patient selection: A rigorous selection process was employed to identify eligible patients with nAMD who received anti-VEGF therapy during the specified study period.

Data extraction: Relevant clinical data, including demographic information, treatment regimen, visual acuity measurements, and OCT scans, were extracted from the EMR.

OCT analysis: OCT scans were analysed using both automated segmentation software and AI enabled retinal segmentation to quantify various retinal layer thicknesses and volumes.

Visual acuity assessment: VA was measured using standardised ETDRS charts, and changes in visual acuity over time were evaluated using methods including linear regression analysis.

Adjunctive interventions and fellow eye involvement: The impact of adjunctive interventions, such as surgical procedures, and categorisation based on fellow eye involvement was accounted for in the analysis.

By systematically collecting and analysing these data, this study aimed to provide valuable insights into the efficacy and outcomes of anti-VEGF therapy in managing nAMD.

# 4 Data disposition, collation and processing

## 4.1 Introduction

This chapter aims to present the methods by which data was processed for further analysis during the study.

## 4.2 Data disposition

Once the extracted EMR results and Heidelberg HEYEX OCT outputs were complied, the project exclusion criteria could be applied yielding a total of 327 eyes of 308 patients for enrolment in the study (Figure 4.1). As explained in section 2.7, all 327 eligible cases were evaluated to optimise the predictive capabilities of the ML based systems used for analysis within the study.

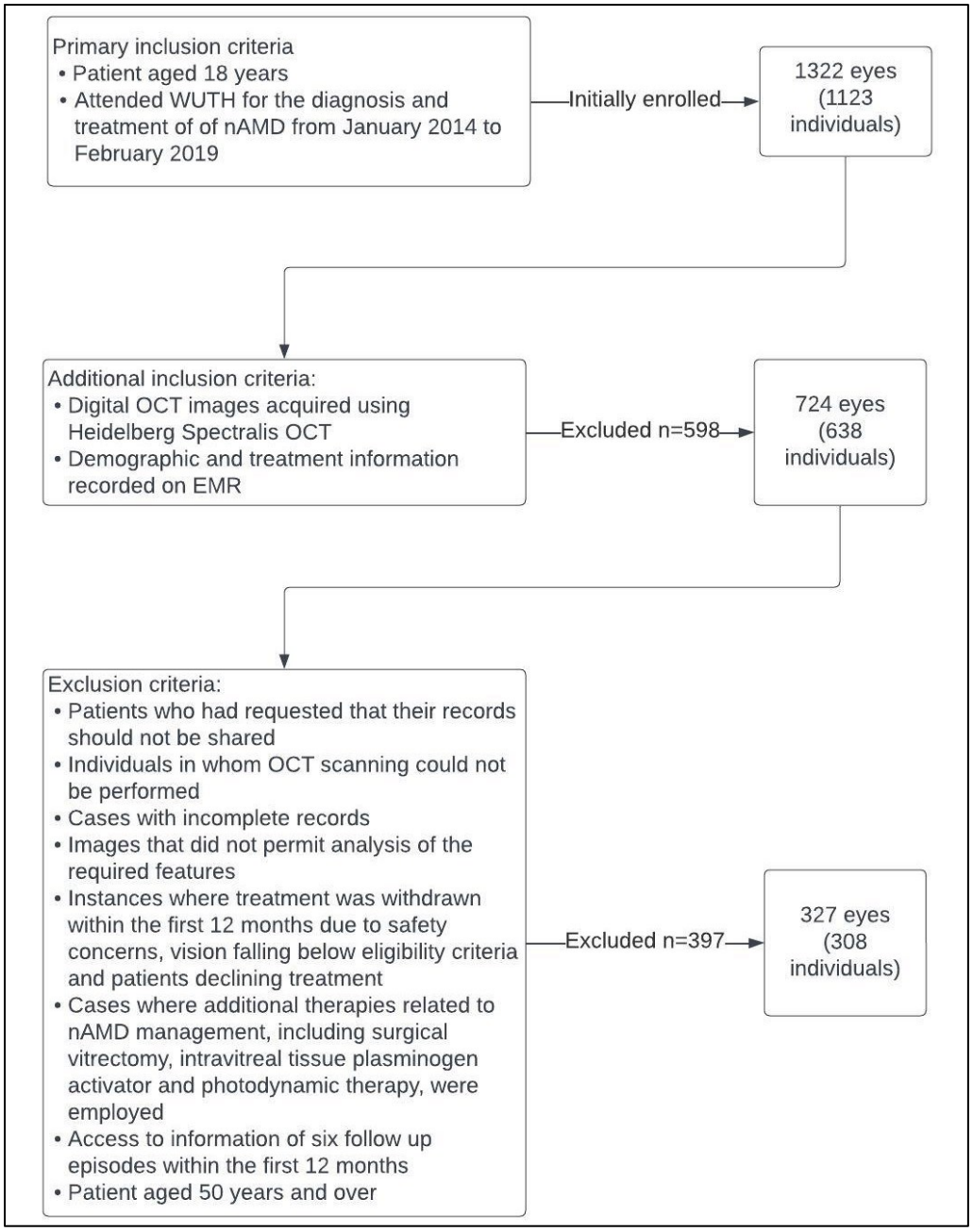


*Figure 4.1: Application of inclusion and exclusion criteria in disposition of cases*

## 4.3 EMR data extrapolation

On reviewing data extracted from within the EMR, the parameters displayed in Table 4.1, could either immediately be defined or the relevant details were readily extrapolated using tools available in Excel, with results added to the study datafile.

| |
|---|
| Ethnicity |
| Laterality |
| Age At First Injection |
| Sex |
| Anti-VEGF drug type over the course of treatment |
| Initial visit (baseline) VA studied eye |
| Initial visit (baseline) VA fellow eye |
| Time interval for loading dose, studied eye |
| Fellow eye nAMD activity |
| Month 12 VA studied eye |
| VA mean, month 11-12, studied eye |
| Slope of best fit line, VA post loading (post loading - month 12), studied eye |
| Slope of best fit line, VA 1st year (baseline - month 12), studied eye |
| St deviation of mean VA post loading (post loading - month 12), studied eye |
| St deviation of mean VA first year (baseline - month 12), studied eye |
| Total Injections First Year |
| Clange in VA, baseline – month 12, studied eye |
| Injections first year, studied eye |

*Table 4.1: EMR defined study variables*

### 4.3.1 Additional EMR data processing

The patterns in which injections were administered to the studied eye over the first year were additionally considered using hierarchical modelling of the administration records at each visit. The

model outputs were again added to the study data file and the method will be described in greater detail in chapter 6.

## 4.4 HEYEX OCT outputs

Extracted Heidelberg HEYEX OCT data (Table 4.2) for the 3mm subfield volume, 1mm subfield volume, the central 1mm average CMT and minimum CMT over the 10 retinal layers and layer groups, on which the programme reported measurements, yielded 40 quantitative instances for both baseline visits (V0) and post loading visits (VP) which were compiled with the extracted EMR results in the study workbook.

| OCT data<br>• 3mm vol<br>• 1mm CM vol<br>• 1mm CMT<br>• min CMT<br>for the following 10 layers at V0 and VP |
|---|
| Retina |
| NFL |
| GCL |
| IPL |
| INL |
| OPL |
| ONL |
| RPE |
| IRL |
| ORL |

*Table 4.2: Extracted HEYEX OCT data*

## 4.5 Datasets

The enrolled study dataset of 327 eyes of 308 patients thus featured a complete set EMR and HEYEX OCT records available for investigation with no missing instances of data. Additional subsets of data were however available for supplementary analyses and sub-cohorts were created to consider effects within particular groups during the project.

### 4.5.1 MEH OCTANE dataset

As scans were captured variably in both 19 and 25 slice patterns at WUTH, this produced some limitations to the data available for processing at MEH. The information returned by OCTANE therefore allowed the further analysis of:

- 232 eyes of 214 patients at baseline (V0)
- 230 eyes of 212 patients post loading (VP)

The study omitted the OCTANE determined features; background and intraretinal hyper reflective material, due to a complete absence of any returned integers and the features; mirror artefact, clipping artefact and blink artefact, as not being deemed to have a potential significance to the studied outcomes, while investigating the remaining 12 features (Table 4.3) which were added to the study datafile.

| |
|---|
| Vitreous and subhyaloid |
| Posterior hyaloid |
| Epiretinal membrane |
| Neurosensory retina |
| Intraretinal fluid |
| Subretinal fluid |
| Subretinal hyper reflective material |
| RPE |
| Drusenoid PED |
| Serous PED |
| Fibrovascular PED |
| Choroid and outer layers |

*Table 4.3: Studied OCTANE outputs*

### 4.5.2 Treatment naïve eyes with no fellow eye involvement

Although all eyes entered into this study at Aston University were treatment naïve, many fellow eyes had disease activity in varying states (Figure 4.2).

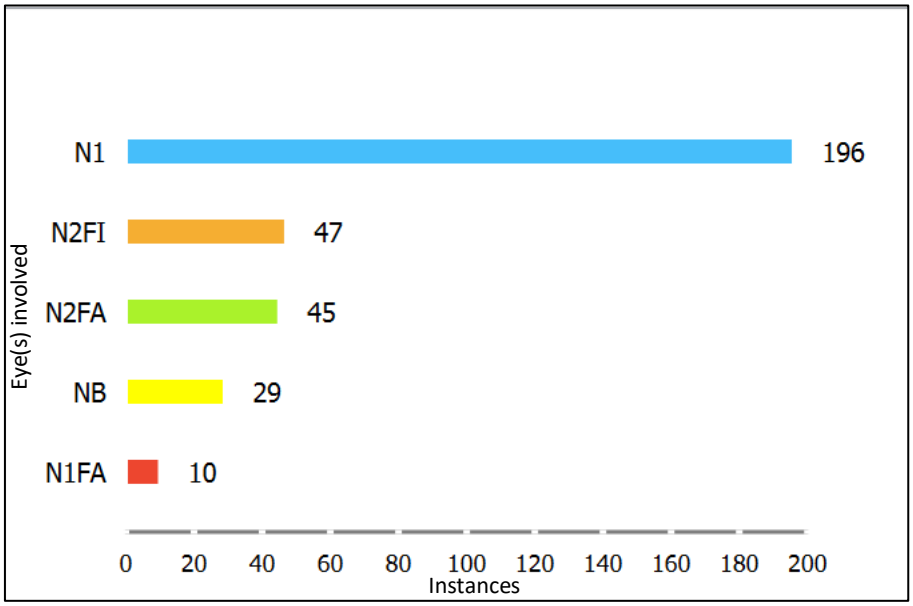


*Figure 4.2: Histogram of fellow eye involvement (N1: fellow eye - no evidence of nAMD in either prior to or during study period , N2FI: fellow eye - prior evidence of nAMD but disease state was inactive during study period, N2FA: fellow eye - prior evidence of*

*nAMD and was actively treated with anti-VEGF in during study period, NB: nAMD diagnosed in both eyes at the same visit and anti-VEGF treatment was loaded bilaterally over the same interval, with subsequent variation in treatment patterns, N1FA: fellow eye - no prior evidence of disease but nAMD did develop and was actively treated with anti-VEGF during study period)*

It thus seemed sensible, where appropriate, to consider a subset of the complete cohort to eliminate factors arising from therapy given to a fellow eye. The 196 patients in whom there was no evidence of nAMD in the fellow eye either prior to or during the 12 months of the study period would therefore be considered as a separate subgroup in addition to analyses performed on the whole cohort.

### 4.5.3 No further therapy past loading dose

As anti-VEGF therapy was administered using a PRN regimen at WUTH, this produced a variation in the number of doses individual eyes would receive over a defined period of time. It was thus found that a significant proportion of cases only required three loading doses of a given drug during the initial 12months of management and were as such evaluated in an additional analysis. This approach eliminated the compounding effect on variation of VA mediated by treatable disease activity.

## 4.6 Discussion

This chapter thus offered a detailed description of the data extraction, cleaning, and preparation processes.

Key aspects of the data processing included:

Case selection: Patients with nAMD who received anti-VEGF therapy were subjected to inclusion and exclusion criteria.

Data cleaning and preparation: Relevant clinical data and OCT measurements were extracted from EMR, HEYEX and OCTANE datasets and the extracted data was processed to remove inconsistencies and errors, and missing values were handled appropriately.

Data categorisation: The dataset was divided into various subsets based on factors such as fellow eye involvement and treatment regimen to enable more targeted analysis.

By effectively processing and preparing the data, this study aimed to provide a solid foundation for subsequent statistical analysis and machine learning modelling.

# 5 Orange data mining and data analysis

## 5.1 Introduction

The chapter aims to explain the AI based data analysis methods used in the study

## 5.2 Orange data analysis

Data analysis was carried out with Orange data mining and machine learning software (ODM), allowing access to a vast array of advanced analytical tools useful in healthcare research. The platform was accessed through a computer programme available to download through the company website and was operated by uploading a CSV data file containing potential determinants or features of interest and the studied outcomes or targets to an interface where various instructions and operations, termed widgets, could be combined to pre-process, evaluate and visualise data forming a 'workflow'. Data modelling tools or learners were additionally available allowing the development of predictive models of a particular outcome. To determine modelling accuracy and the informativity of features for a given, investigated effect, further widgets and statistical outputs were available to consider such potential relationships.

## 5.3 Features

From the collected study data, the parameters available as potential predictors in searching for relationships in evaluating the study outcomes were collated to the following seven groups (Table 5.1) and used in each analysis. VA, as a feature group, was however considered with and without including the standard deviation of mean VA, post loading until 12 months. This approach was taken as some of the measures considering VA at 12 months were also used in determining the mean VA over this period. As the standard deviation in the mean was also thus derived from these results in part, an overlap of the data within both groups potentially may have created an artefactual relationship which it was felt should be taken into account.

| Feature group | Description | No. features |
|---|---|---|
| Demographic & qualitative | Ethnicity<br>Laterality<br>Age At First Injection<br>Sex<br>Anti-VEGF drug type<br>Time interval 1st to 3rd injection<br>Fellow eye activity | 7 |
| VA | VA baseline visit (V0)<br>VA fellow eye (V0)<br>VA post loading (VP)<br>VA mean of 2 visits immediately post loading | 4 |
| VA_st dev | VA baseline visit (V0)<br>VA fellow eye (V0)<br>VA post loading (VP)<br>VA mean of 2 visits immediately post loading<br>Standard deviation of VA mean, post loading -12 months (VP-V12) | 5 |
| V0_OCT | HEYEX OCT results from baseline visit (V0) | 40 |
| VP_OCT | HEYEX OCT results from post loading visit (VP) | 40 |
| V0_OCTANE | OCTANE results from baseline visit (V0) | 12 |
| VP_OCTANE | OCTANE results from post loading visit (VP) | 12 |

*Table 5.1: Feature groups for analysis in ODM*

Groupings were created to allow systematic yet efficient evaluation of the features relevant to the study. These sets were based on feature type, the algorithmic method in which OCT data was collected and

treatment stage at which the feature data was acquired. In the case of the standard deviation of the VA mean from post loading to 12 months, as this metric contained data from all VA points from the first year, additional regard was considered appropriate in developing models with this attribute in the event that determined relationships were biased by the manner in which it was construed.

## 5.4 Targets

Some outcome variables were immediately available from the spreadsheets returned by WUTH the remainder; VA means, standard deviation of means, slope of best fit line through VA points and change in VA, were extrapolated from the results using various functions available in Excel.

Hierarchical clustering methods, available in ODM, were additionally employed to separate injection patterns, based on treatment frequency and intervals between injections, for investigation as a target characteristic.

Study targets were thus considered as those investigating injection associated treatment outcomes and those exploring visual outcomes.

Further rationalisation took place to identify discrete outputs and categorisation of continuous data to allow classification modelling. Regression analyses conversely, where continuous target ranges were more appropriate but where discrete variables could be considered with care, had appropriate variables grouped for evaluation separately.

Many of the target classifications were immediately apparent in cases of discrete data, principally where considering injections data. However, where determining target classes for continuous data, divisions used in prior work were considered and where such classification did not exist, a sensible approach was applied to section data and rationale explained within this document.

### 5.4.1 Anti-VEGF treatment models

Injection administration data existed in a discrete form and was thus used in both classification models and regression analyses considered in following groups (Table 5.2).

| Data type | Target variable | Range/classification |
|---|---|---|
| Numeric discrete: | Injections First Year | no. of injections 3-10 |
| Categorical: binary | Injections First Year | categories 3, >3 |
| Categorical: ordinal | Injections First Year | categories 3, 4, 5, 6, 7, 8, 9, 10 |
| Categorical: nominal | Injection pattern first year | Hierarchical model defined clusters 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 |

*Table 5.2: Anti-VEGF target variables*

### 5.4.2 VA models

VA data when initially extracted was present in a continuous range but was manipulated to develop the following outputs (Table 5.3), with standard deviation of VA also considered as a feature variable.

| Data type | Target variable | Classification |
|---|---|---|
| Numeric continuous | VA at 12 months, letter score | |
| | VA at 12 months, months 11-12 mean, letter score | |
| | VA post loading (post loading - month 12) slope of best fit line | |
| | VA baseline - 12 months, slope of best fit line | |
| | St deviation of mean VA, post loading (post loading - month 12) | |
| | St deviation of mean VA, baseline - 12 months | |
| | Change in VA, baseline – month 12, letter score | |
| Categorical: binary | Change in VA post loading (month 4 - month 12), slope of best fit line | 2 categories (lost/gained) |
| | Change in VA (baseline – 12months), slope of best fit line | 2 categories (lost/gained) |
| | Change in VA (baseline – 12months), letter score | 2 categories (lost/gained) |
| Categorical: ordinal | Change in VA post loading (month 4 - month 12), letter score | 3 categories (5 letter loss/gain/maintained) |
| | Change in VA (baseline – 12months), letter score | 3 categories (5 letter loss/gain/maintained) |
| | Change in VA (baseline – 12months), letter score | 3 categories (5 letter loss/gain/maintained) |
| | VA month 12, letter score | Categories <30, 31-40, 41-50, 51-60, 61-70, 71-80 |

*Table 5.3: VA target variables*

## 5.5 Modelling with learners

Machine learning algorithms were trained in ODM. These supervised learners, which utilised labelled datasets, attempted to sort test data to relevant, predefined categories or to predict a relationship between input features and output targets in classification and regression models (Alloghani et al., 2020).

## 5.6 Classification and regression analyses

Models were developed to utilise the following learners which ODM could apply to classification and regression analyses:

<u>kNN</u>

The k-Nearest Neighbours (kNN) algorithm works by finding the k closest training examples in the dataset and using them to make a prediction (Demšar et al., 2013). This clustering learner, capable of interpreting both categorical and numerical data, is considered to handle noisy data and outliers well and to develop outputs which are simple to understand. The model can however be sensitive to irrelevant features hence performance can deteriorate as the number of features increases (Cunningham and Delany, 2021)

Tree

The decision tree model works by repeatedly splitting the data into subsets based on the values of the input features until a prediction can be made about the target variable (Demšar et al., 2013). Easy to understand and interpret, the learner can handle both categorical and numerical data and manage non-linear relationships. Trees can however easily overfit the training data if not properly pruned and may not perform well on datasets with larger numbers of features (Breiman et al., 1984).

Random forest

Random forest models use bootstrap ensemble learning where multiple decision trees are created on different, arbitrary subsets of the data and then combined to form a prediction (Demšar et al., 2013). Highly accurate and able to manage both categorical and numerical data, the learner is less prone to overfitting than decision tree. The structure of individual trees in the forest can provide a degree of interpretability into significance of different attributes but overall feature importance can be difficult to interpret (Breiman, 2001).

Gradient boost

Gradient boosting models are an ensemble learning method that is used for classification and regression. They work by creating multiple decision trees on different subsets of the data and then combining the results to make a prediction (Demšar et al., 2013). With a high degree of accuracy and being less prone to overfitting than decision tree models the algorithm can also handle non-linear relationships but can be difficult to interpret and shows sensitivity to outliers (Hastie et al., 2009).

SVM

Support vector machine (SVM) models are a type of supervised learning algorithm that work by finding the hyperplane that best separates the data into different classes. The algorithm repeatedly optimises the process by selecting a small subsets of data points to update the model and using a separate subset

to test model performance and accuracy. While more often used for classification problems, in regression tasks, SVM performs linear regression in a high dimension feature space with the widget classing predictions based on a SVM Regression (Demšar et al., 2013).

SVM models are deemed very accurate and can handle linear, nonlinear and high dimensional data. They are also less prone to overfitting than other algorithms but outputs can be difficult to interpret, as they do not provide a direct explanation of how the model makes its predictions. The learner can however be sensitive to outliers in the data, as they can influence the placement of hyperplanes and affect the model's decision boundaries (Hastie et al., 2009).

Logistic regression

Logistic regression is used for classification analyses by finding the line that best separates the data into different classes. In ODM the model offers L1 (LASSO) and L2 (Ridge) regularisation, with L1 considered to offer superior ability in feature selection (Demšar et al., 2013) and hence preferred in this project.

Model outputs tend to be readily interpretable with coefficients communicable as odds ratios. Results tend to be less prone to overfitting than more complex models however assume linearity between target and input characteristics, can only manage discrete variables and may not perform well on datasets with large numbers of features (Nick and Campbell, 2007).

Naïve Bayes

Naïve Bayes models manage classification problems by applying Bayes' theorem to calculate the probability of each class given the input features with the assumption of feature independence (Demšar et al., 2013). Outputs are readily explainable with feature relevance interoperability through classification and ranking of odds ratios, however the algorithm assumes that the input features are independent of each other and struggles with complex non-linear relationships and shows sensitivity to outliers and irrelevant features (Zhang and Su, 2004).

Adaboost

The adaptive boosting (AdaBoost) ensemble learning method suitable for both classification and regression analyses. The learner operates by combining the results of weaker learners and adapts to the difficulty of each training sample to make a prediction (Demšar et al., 2013). In considering more carefully the training instances that the predecessor underfitted the algorithm can thus improve the accuracy of other models but in turn is hampered by datasets with noisy data (Géron, 2022).

Neural network

Neural networks simulate the structure of the human brain to find patterns in the data that can fit complex data patterns (Demšar et al., 2013). In ODM the Neural Network widget uses a Multi-layer Perceptron algorithm and backpropogation that can train on a dataset for either classification or regression. It differs from logistic regression, in that between the input and the output layer, there can be several non-linear layers with the learner fine tuning the error rate from forward propagation and propagating this loss backward through the neural network layers to adjust the weights during the previous iterations of the layers. The resultant model yields a high level of accuracy and can handle both linear and nonlinear data but may overfit the data if the network is too complex (Fabian, 2011)

Linear regression

The Linear Regression widget, used for regression analysis only, constructs a model that can identify a line that best fits the data from a predictor and the response variable (Demšar et al., 2013). Linear Regression output can be straightforward to interpret but may not perform well on datasets with non linear relationships or large numbers of features and can be sensitive to outlying datapoints (James et al., 2013).

To balance overfitting against the ability of a model to make accurate predictions, regularisation in the form of LASSO and Ridge parameters modify the reliance of the learner on specific information obtained from the training samples (Fabian, 2011). LASSO regularisation was employed in this body of work due to the superior performance in feature selection.

## 5.7 Outliers

All models were trained on both complete datasets of the given attribute being studied and a reduced set where outliers had been removed.

### 5.7.1 Noise vs outlying data

These attributes may initially seem alike but noise relates to causes including data type errors, incorrectly captured data values and missing data resulting in worthless information (Smiti, 2020).

Landmark definitions of outliers include, an observation which deviates so much from other observations as to arouse suspicions that it was generated by a different mechanism (Hawkins, 1980), an observation (or subset of observations) which appears to be inconsistent with the remainder of that set

of data. Authors considering outliers (or spurious values of any sort) however can be citied as far back as the 18th century (Barnett and Lewis, 1994).

Outliers may result from measurement or recording errors, exceptional but true values, misreporting or sampling errors. In some cases outlier removal avoids an analysis from being misled where as in other instances their incorporation can prove insightful (Smiti, 2020).

Finding outlying data instances that do not fit well to the general data distribution is very important in many practical applications and deciding on how to identify and manage these inconsistent data points has in itself generated a field of study (Zimek and Filzmoser, 2018).

### 5.7.2 Pros and cons of removing outliers

The merits of considering and removing outliers and the methods in which this can be done have been considered at length. Type 1 and 2 errors within classic parametric hypothesis based statistical methods can be inflated where outliers are not adequately accounted or overly, readily removed. Modern statistical methods including bootstrapping have been suggested to improve the robustness of data to outliers (Erceg-Hurn and Mirosevich, 2008).

Identification of outliers and their removal should thus be considered as separate and by a method which is blind to the hypothesis of interest (i.e., across all the data, or based on the residuals of a model that omits all hypothesis-relevant predictors) has been suggested (André, 2022) with the alternative approach involving hypothesis-aware outlier removal offering a greater consideration of the naturally occurring differences in variance in different studied parameters in multivariate analysis (Karch, 2023).

Outlier removal has however been shown to improve model performance in machine learning based imaging based studies with Li et al. (2015) reporting an improvement from 63% to 76% in test accuracy with the improvement in results in turn yielding levels equivalent to gold standard clinician assessments of a burn injury classification. Outlier classification and removal has also been shown to have benefits in reducing variance of the structural analysis in automated RNFL measurement from OCT (Bergamin et al., 2004).

### 5.7.3 Statistical approaches to managing outliers

ODM provides a range of statistical methods to aid in the identification and removal outliers with Local Outlier Factor (LOF) and Isolation Forest methods more suited to moderately to highly dimensional datasets. For both methods, their effectiveness depends on the specific dataset and problem at hand

with LOF deemed to be better suited for datasets with moderate dimensionality, while Isolation Forest is more effective for high dimensional datasets (Demšar et al., 2013).

Data dimensionality is determined by considering the number of independent observations 'n' against 'p' the number of variables associated with each instance. This dimensional property increases as p increases and begins to exceed n, with genomic studies and imaging studies, considering signal values of pixels, frequently cited as high dimensional in nature (Rahnenführer et al., 2023).

### 5.7.4 Outlier detection with LOF

In this study LOF was applied to manage outlying data.

LOF is an unsupervised anomaly detection algorithm which computed the local density deviation of a given data point with respect to its neighbours. It considered as outliers, the samples that had a substantially lower density than their neighbours (Fabian, 2011) with this score reflecting the degree of abnormality of the observations, presenting an efficient manner to perform outlier detection on moderately high dimensional datasets. (Demšar et al., 2013).

Hyperparameter tuning was considered, but for the purposes of the study, the default values for contamination, neighbours, and metric used by ODM were applied as it was deemed unlikely that significant additional performance of LOF would be aggregated through any adjustments.

Contamination determined the proportion of the most isolated points to be deemed anomalous and was determined automatically in ODM as a percentage of the samples presumed to be normal.

In considering the number of neighbours, Fabian (2011) recommended adopting a value of 20 which appeared to work well in practice as determining this figure otherwise, as a quantity set between the minimum number of samples a cluster had to contain and the maximum number of close by samples that could potentially be local outliers, was generally not feasible.

The metric parameter, defining the system of measurement to use for distance computation within LOC, was also kept as the standard Euclidean setting where the straight-line distance between two datapoints in a Euclidean space was considered (Fabian, 2011).

## 5.8 Preprocessing

A preprocess widget was added to identify and remove instances with missing data and to randomise the order of the observations, a practice which has been recommended as beneficial in removing potential trends associated with the sequence in which data were collected (Chicco, 2017). This also

overrode any default preprocessing within the models applying only the custom preprocessing pipeline devised in the study.

## 5.9 Test and score

A test and score widget provided various sampling schemes and statistical results of how well the models formed predictions.

### 5.9.1 Sampling

Stratified k-fold cross validation was implemented where data was split into 10 sample groups representative of the original dataset. The algorithm was then trained on k – 1 folds and evaluated on the remaining subset. This process is repeated, so that each fold was used for testing just once with information then produced on the average accuracy of the model (Demšar et al., 2013).

This process improved model performance and managed overfitting, a phenomenon to which machine learning is prone where the algorithm excessively adapts to training data and predictions in turn relate poorly when applied to test sets (Chicco, 2017, Demšar and Zupan, 2021).

### 5.9.2 Determinants of model accuracy in classification models

Demšar et al. (2013) described the range of statistics returned by the programme and used in the project to help assess the performance of each model.

Precision is a measure of the accuracy of positive predictions made by a model and is expressed as the proportion of true positives (TP) among the total positive predictions, TP and false positives (FP), made by the model (Géron, 2022).

$$\text{precision} = TP/(TP+FP)$$

Recall, also referred to as sensitivity or true positive rate (TPR), is the ratio of true positives among all positive instances in the data, TP and false negatives (FN) (Géron, 2022).

$$\text{Recall} = TP/(TP+FN)$$

Specificity, or true negative rate (TNR) is the proportion of true negatives (TN) among all negative instances in the dataset are correctly identified by the model (Géron, 2022).

$$\text{Specificity} = TN / (TN + FP)$$

Classification accuracy (CA) measures the proportion of correctly identified examples from the total number of predictions by a model. Although straightforward to interpret, reliability of the metric declined in the presence of skewed distributions in classification analyses (GoogleDevelopers, 2023).

$$CA = (TP + TN) / (TP + TN + FP + FN)$$

Area under the receiver operating characteristic curve (AUC) is a metric used to evaluate model performance utilising the TPR and false positive rate (FPR), the ratio of negative instances that are incorrectly classified as positive found by subtracting the TNR from one. The receiver operating characteristic (ROC) curve is generated by plotting the TPR against the FPR, and AUC considered for different decision thresholds (Géron, 2022, IBMCorp., 2022).

F1: The F1 score combines precision and recall to a single metric allowing an efficient mechanism to assess the accuracy of a classifier. F1 forms the harmonic mean of precision and recall giving more weight to low values thus a classifier receives a high score if both recall and precision are high (Géron, 2022).

Matthews correlation coefficient (MCC) is a statistical metric taking into account sensitivity, specificity, precision, and negative predictive value, a of measure of the proportion of negative predictions that are actually correct calculated from the total number of true predictions.

$$\text{Negative predictive value} = TN / (TN + FN)$$

Instances where MCC indicates a significant level of accuracy thus signifies the constituent metrics have also all generated high scores (Chicco and Jurman, 2023) offering a balanced measure that can be used even where classes are different sizes. (IBMCorp., 2022).

### 5.9.3 Determinants of model accuracy in regression models

Mean squared error (MSE) is a common metric used to evaluate the performance of a regression model. It measures the average squared difference between the predicted and actual values of the target variable. As an error metric, MSE can be interpreted as showing greater model accuracy as the value approaches zero. (Demšar et al., 2013).

Route mean squared error (RMSE) like MSE is a measure of the imperfection of the fit of the estimator to the data (Demšar et al., 2013). RMSE generates smaller values which are typically considered more interpretable however is also more sensitive to outliers and perhaps therefore more appropriate when datasets contain outliers that need to be penalised more heavily (Steurer et al., 2021).

Mean absolute error (MAE), a measure of average absolute differences, is used to assess how close forecasts or predictions are to eventual outcomes. MAE has reduced sensitivity to outliers but may also mask outlier impact on model performance (Demšar et al., 2013).

The coefficient of determination ($R^2$) is used to evaluate the performance of a regression model by providing a measure of the proportion of the variance in the dependent variable that can be explained by the independent variable. In the case of ODM, the best possible score was 1.0 but $R^2$ could be negative as the model could be arbitrarily worse (Demšar et al., 2013).

Coefficient of variation root mean squared error (CVRMSE) is a unitless statistical metric used to evaluate the performance of a regression model. CVRMSE is a normalized measure of RMSE that takes into account the variability of the input data . CVRMSE is expressed as a percentage, where lower values indicate better model performance, can be used to calibrate model performance and compare accuracy between models (Demšar et al., 2013).

## 5.10 Determinants of modelling performance

### 5.10.1 ROC analysis

ROC curves for a derived model could be plotted showing the true positive rate against a false positive rate (Demšar et al., 2013).

### 5.10.2 Confusion matrix

Confusion matrices showed the proportions of correct and incorrect predictions made by the model (Demšar et al., 2013).

### 5.10.3 Correlations

This ODM widget computed Pearson or Spearman correlation scores for all pairs of features in the dataset being analysed (Demšar et al., 2013). The analysis was applied to models derived within dataset.

### 5.10.4 Scatter plot

Scatter plots allowed visualisation of the relationship between target and feature variables (Demšar et al., 2013).

## 5.11 Determinants of feature relevance

### 5.11.1 Distributions

Distribution curves and histograms showed how many times an attribute value appeared in a dataset and in the case of categorical analyses, class distributions for each of the features was displayed using the distribution widget (Demšar et al., 2013).

### 5.11.2 Rank

The Rank widget scored feature variables according to their correlation with targets. The widget automatically selected the most informative metrics and outputted a list ordered according to the best scoring attributes (Demšar et al., 2013). In the case of this study, where available, only the results of the best five scoring features were considered.

#### 5.11.2.1 Ranking indicators

Demšar et al. (2013) described the ranking indicators in ODM highlighting several key methods for feature scoring and ranking, which were used to evaluate the relevance of features in relation to the target variable.

- Information Gain was the expected amount of information or reduction of uncertainty that could be garnered from a feature in respect to a target
- Gain Ratio was a ratio of the information gain and the intrinsic information of the attribute. This normalisation acted to reduce the bias towards multivalued features that occurred in information gain.
- Gini measured the reduction in impurity achieved by splitting the data based on a specific feature, features that created the most homogenous subsets for each class, were ranked higher.
- Analysis of Variance (ANOVA): the difference between the means of the features in different classes
- Chi-square provided a measure of the dependence between the feature and the category
- ReliefF measured ability of an attribute to distinguish between classes on similar data instances
- Fast correlation based filter (FCBF) assessed the relevance of each feature by combining the strengths of information gain and feature redundancy analysis to identify informative features while reducing redundancy
- Univariate Regression provided linear regression for a single variable

### 5.11.3 Nomographic representation of feature importance

The nomogram widget could be applied to the Naïve Bayes classifier and Logistic Regression classifier allowing variable features to be ranked by relative importance. In Naïve Bayes, odds ratios or percentage points scale of a positive or negative influence of features in inducing a change in the target variable could be viewed and manipulated. In the case of Logistic Regression, these odds or percentage points were only available as positive integers but linear graphical representations were available for continuous attributes to help visually understand their relationships with classifiers and relative degree of influence in altering an outcome (Demšar et al., 2013).

### 5.11.4 Feature importance

This ODM widget used the Permutation Feature Importance technique to calculate the contribution of each feature towards the prediction by measuring the increase in the prediction error of the model after the relationship with each independent variable was disrupted (Demšar et al., 2013).

## 5.12 Workflow

Typical ODM workflows for classification analyses and regression analyses are shown in Figure 5.1 and Figure 5.2 respectively.

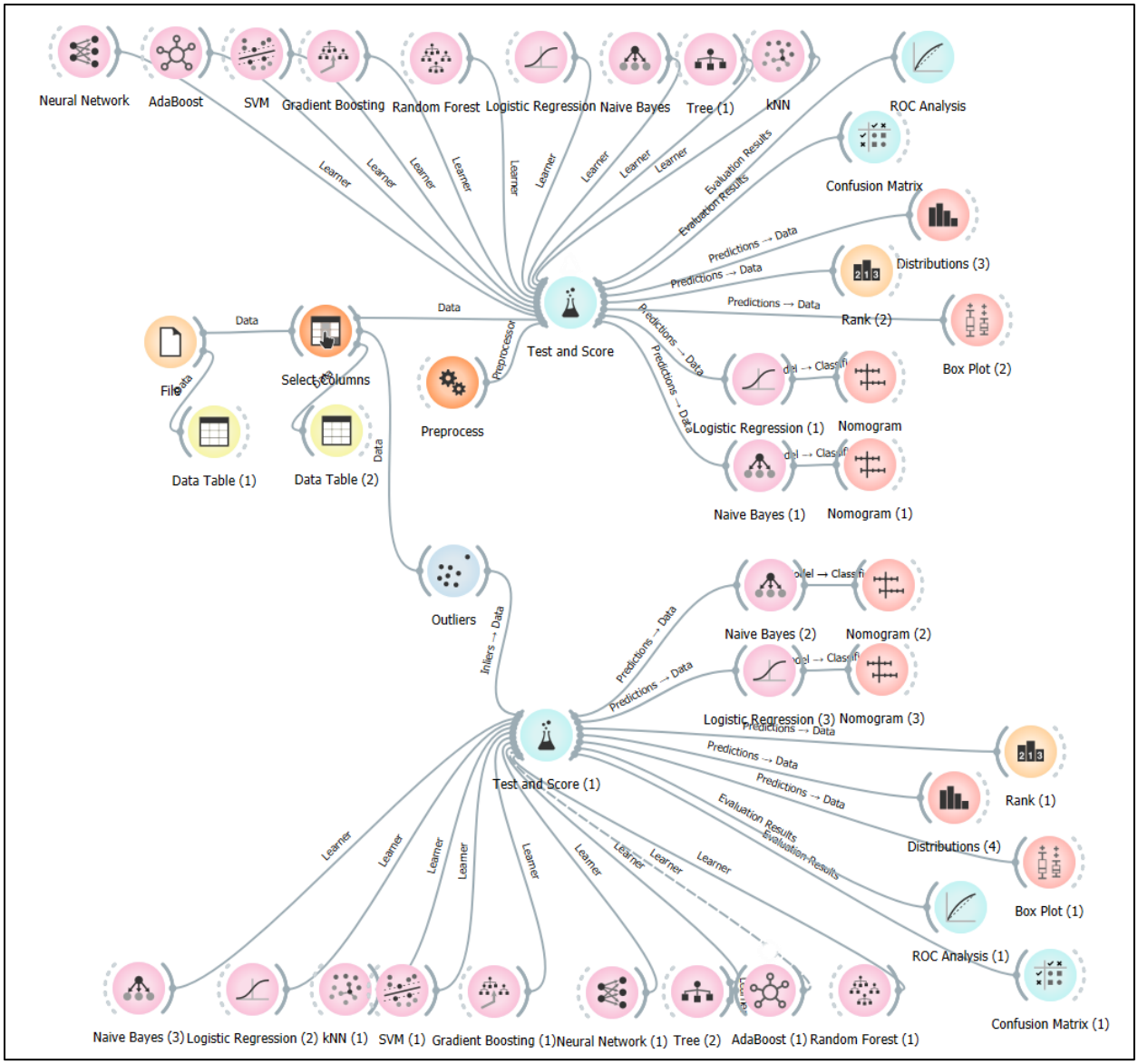


*Figure 5.1: ODM workflow of classification analysis*

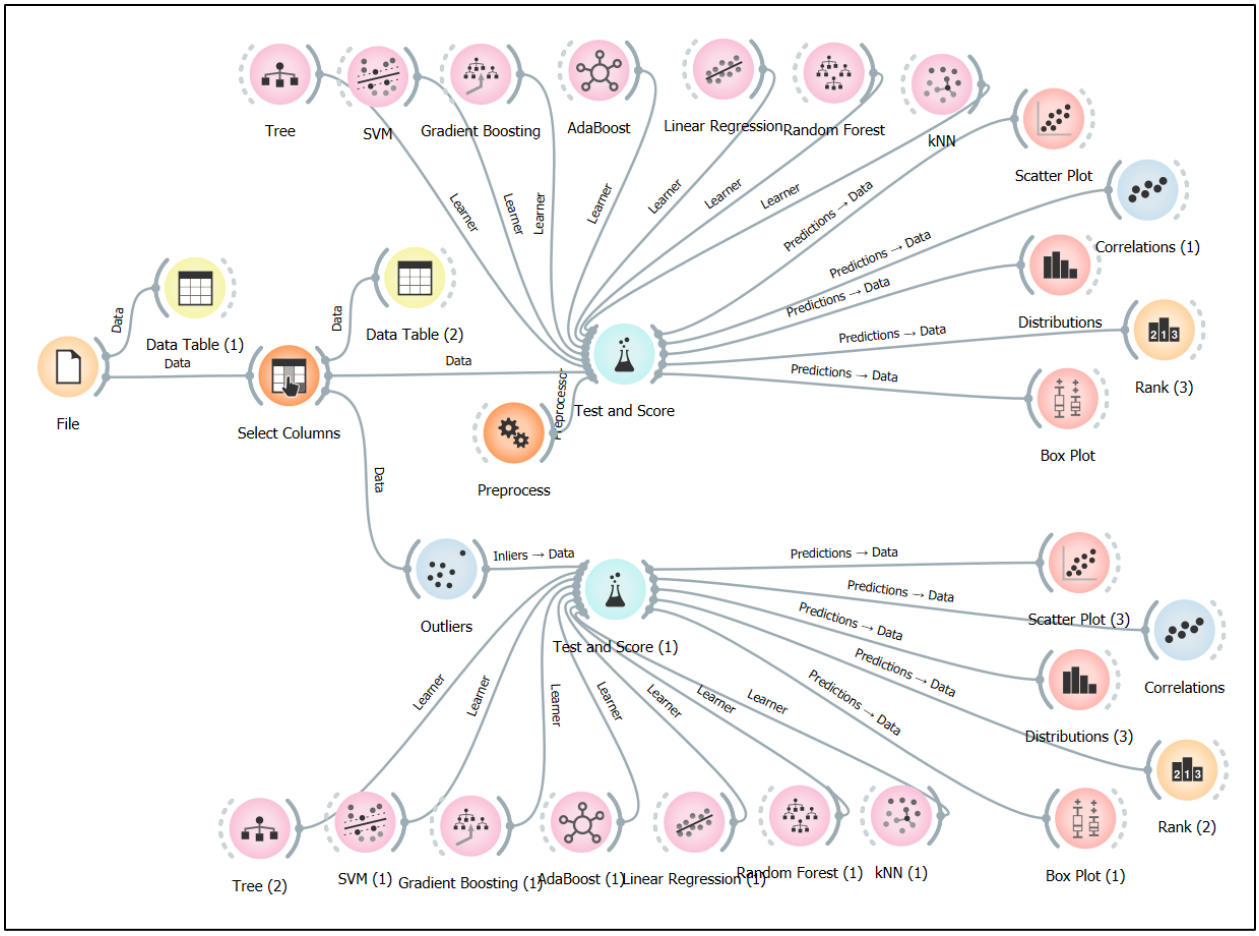


*Figure 5.2: ODM workflow of regression analysis*

## 5.13 Hierarchical clustering

Hierarchical clustering is an unsupervised learning technique that involves grouping unlabelled data instances into clusters based on patterns recognised within the information. The groups, or labels, devised by the algorithm can in turn be used for supervised learning tasks (Alloghani et al., 2020).

In ODM, widgets available within the hierarchical clustering pipeline allowed selection of Manhattan and Euclidean distance prediction, the number of nodes used to form clusters and pruning of clusters (Figure 5.3). Silhouette plots, which provide a graphical representation of consistency of data instances within clusters and scoring of the quality of clustering (Fabian, 2011), were used to optimise the number of clusters formed. Examination of means within the devised groups and plotting data in box and whisker charts within Excel allowed visualisation of the patterns within the clusters.

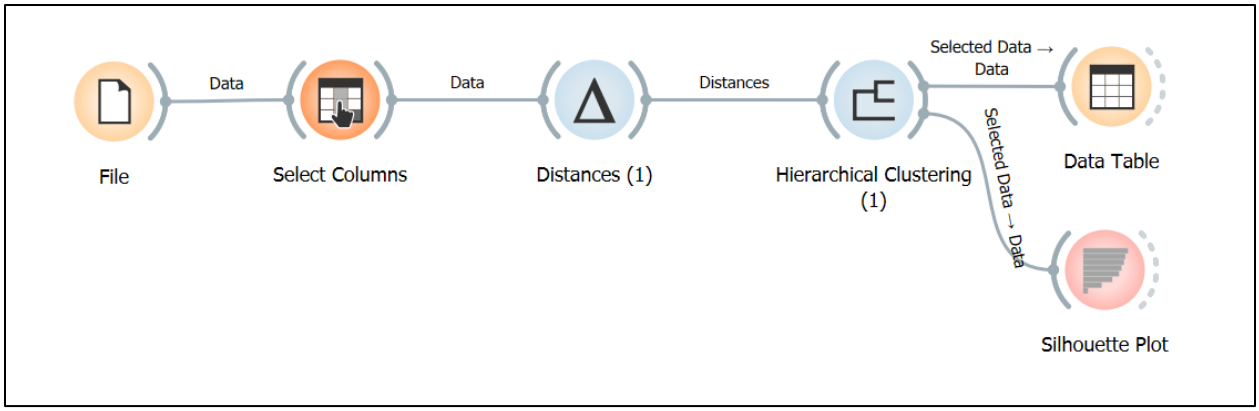


*Figure 5.3: ODM workflow of Hierarchical clustering*

## 5.14 Discussion

This chapter outlined ODM and the data analysis methods employed to analyse the extracted data.

Key aspects of the data analysis methodology included:

Feature engineering: Relevant features, including demographic, clinical, and OCT derived parameters, were identified and prepared for analysis.

Target variable definition: Target variables were defined, including both continuous and categorical outcomes.

Machine learning algorithms: The range of machine learning algorithms employed to build predictive models were defined.

Model and feature evaluation: Methods to evaluate modelling performance and feature importance were considered alongside techniques used to identify and manage outlying data.

By leveraging the capabilities of ODM and employing a variety of machine learning techniques, this study aimed to appropriately investigate the project outcomes measures.

# 6 Features influential in determining treatment doses and treatment frequency

## 6.1 Introduction

This chapter aims to present the analyses and results related to anti-VEGF injections administered over one year in the management of nAMD.

Anti-VEGF treatment was considered in terms of:

- The total number of injections administered during the first year
- The pattern of the injection administration over the first year

Analyses were undertaken by classification and regression modelling. These used the variables on which information was gathered during the study, including OCT based characteristics, visual acuity measures and demographic information, all of which were listed in chapter 5 within defined feature groups. These predictors were inputted to ODM based pipelines in an attempt to forecast anti-VEGF dosing over the first year treatment and the features relevant in forming such predictions.

The modelling accuracy and predictive strength of feature attributes from each ODM learner were considered and are reported in their entirety in appendices 3 and 4. The models which reached a significant level of performance and deemed further discussion have been reported within this chapter.

In order to more readily visualise classification model accuracy, models were initially ordered based on the AUC scores. A colour coding system was applied where model performance was described between a scale of 0 and 1 (Table 6.1). In the case of regression model interpretation, $R^2$ values were used to initially arrange learner outcomes prior to further investigation.

| Model performance range | Colour |
|---|---|
| 0 – 0.49 | No colour |
| 0.50 - 0.59 | Yellow |
| 0.60 - 0.69 | Orange |
| ≥ 0.70 | Green |

*Table 6.1: Key describing colours used to indicate model performance*

### 6.1.1 Sub-analyses : Injection doses within N1 cohort

In addition to assessment using the feature groups in section 6.3, some analyses were repeated. Where models were deemed to have attained a significant level of performance, these were re-evaluated considering the N1 group of 196 patients in whom there was no evidence of nAMD in the fellow eye, either prior to or during the 12 months of the study period. Where there was a significant improvement

in modelling outcomes, compared to the unfiltered study cohort, these results were reported within the thesis.

## 6.2 Predicting injection doses in year one

Considering the total study population of 327 treatment naïve eyes of 308 patients, all cases within this group completed the first year of treatment and monitoring. The minimum number of injections administered to any given eye within this group was three doses, effectively the loading phase only, and the maximum was 10 doses (Table 6.2). It can be seen that the distribution was right-skewed based on the higher instances of eyes injected with lower numbers of anti-VEGF doses (Table 6.3 and Figure 6.2) and a dispersion of 0.33 and a standard deviation of 1.5 around the mean of 4.56 (Figure 6.1).

| Distribution | Mean | Mode | Median | Dispersion | Standard deviation | Minimum | Maximum |
|---|---|---|---|---|---|---|---|
| Injections First Year | 4.56 | 3 | 4 | 0.33 | 1.50 | 3 | 10 |

*Table 6.2: Injections in first year summary statistics*

| Injections First Year | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|
| n | 106 | 77 | 55 | 48 | 30 | 7 | 3 | 1 |

*Table 6.3: Injections in first year instances*

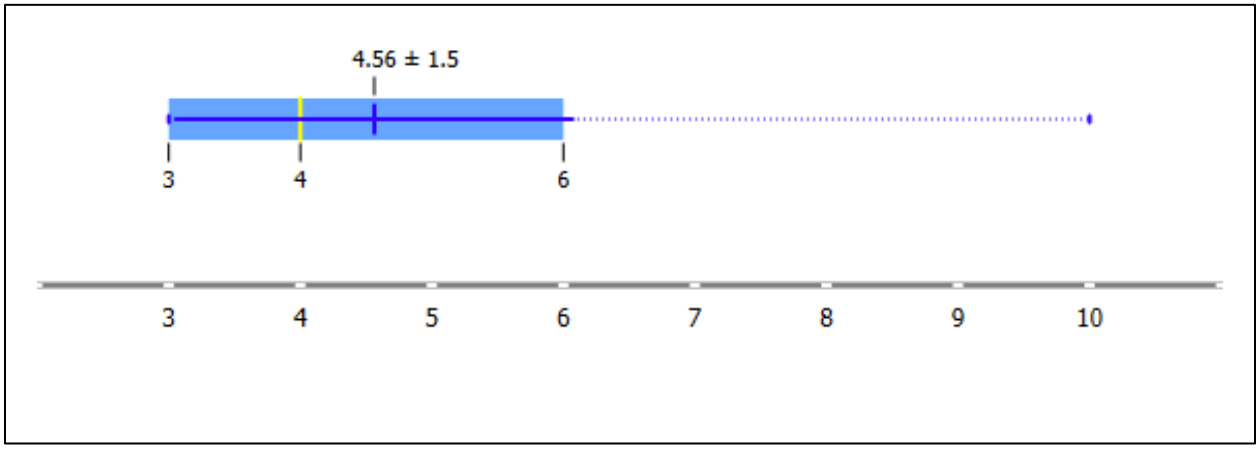


*Figure 6.1: Boxplot of Injections in first year*

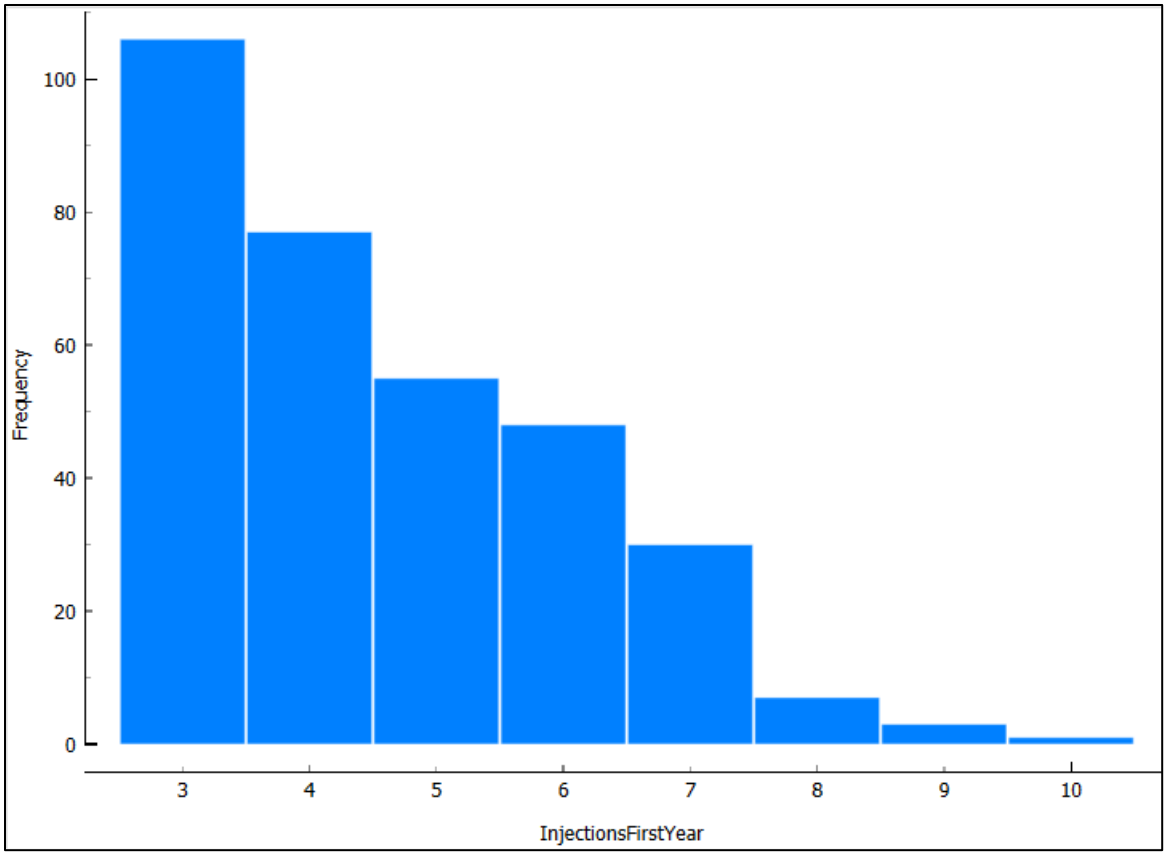


*Figure 6.2: Histogram of Injections in first year*

### 6.2.1 Classification analyses: Injections first year n=3, >3

The following classification analyses investigated the ability of different feature groups to differentiate between eyes that received only the loading dose of treatment (n=3) and those that required more than three injections (>3). The displayed results were averaged by ODM over both classes. The results for each class (injections n=3, injections n>3) were viewed individually and if a significant correlation was identified or if the model behaviour was notably improved compared to the averaged results, such findings were reported.

#### 6.2.1.1 Feature group 'VA'

The feature group 'VA' was considered in relation to eyes that received only the loading dose of treatment and those that required more than three injections.

Target: Injections first year (categories: 3, >3)

Feature group: VA

- VA baseline visit (V0)
- VA fellow eye (V0)
- VA post loading (VP)
- VA mean of 2 visits immediately post loading

6.2.1.1.1 ODM modelling

- AdaBoost was the only algorithm to yield results across all the performance metrics; AUC, CA, F1, precision, recall, MCC and specificity, at a level suggesting a relationship existed but with limited predictive power given the relatively low scores of just ≥ 0.50 (Table 6.4).
- Removing outliers in this series of models did not yield a significant improvement in performance.
- Feature prediction was not deemed accurate in this analysis and the removal of outliers, did not have a meaningful impact on performance.
- Sub-analysis of the N1 group (no nAMD in the fellow eye) shows similar results, with slightly reduced scores compared to the whole cohort.

| Model | AUC | | CA | F1 | Precision | Recall | MCC | Specificity |
|---|---|---|---|---|---|---|---|---|
| AdaBoost | 0.55 | | 0.60 | 0.60 | 0.60 | 0.60 | 0.10 | 0.50 |

*Table 6.4: AdaBoost classification model performance for total dataset of 'VA' group features for target 'Injections First Year categories 3,>3'*

6.2.1.2 Feature group 'VA_st dev'

The feature group 'VA_st dev' was considered in relation to eyes that received only the loading dose of treatment and those that required more than three injections.

Target: Injections first year (categories: 3, >3)

Feature group: VA_st dev

- VA baseline visit (V0)
- VA fellow eye (V0)
- VA post loading (VP)
- VA mean of 2 visits immediately post loading
- Standard deviation of VA mean, post loading -12 months (VP-V12)

#### 6.2.1.2.1 ODM modelling

- After removing outliers, the decision tree algorithm demonstrated statistically significant predictive ability but at a limited level given the low scores, particularly of AUC, MCC and specificity (Table 6.5).
- Post loading standard deviation of the VA mean (VP-V12) was the most informative feature in differentiating between the injection classes.

| Model | AUC | CA | F1 | Precision | Recall | MCC | Specificity |
|---|---|---|---|---|---|---|---|
| Tree | 0.57 | 0.61 | 0.62 | 0.62 | 0.61 | 0.13 | 0.52 |

*Table 6.5: Decision tree classification model performance with outliers removed of 'VA_st dev' group features for target 'Injections First Year categories 3,>3'*

### 6.2.1.3 Feature group 'V0_OCT'

The feature group 'V0_OCT' was considered in relation to eyes that received only the loading dose of treatment and those that required more than three injections.

Target: Injections first year (categories: 3, >3)

Feature group: V0_OCT

- 40 HEYEX OCT inputs from baseline visit (V0)

#### 6.2.1.3.1 ODM modelling

- After removing outlying data, Naïve Bayes, kNN, AdaBoost, and Decision Tree algorithms formed predictions at a statistically significant level across all metrics (Table 6.6) but with limited prognostic power owing to model proximity to the no-discrimination line in ROC curves (Figure 6.3 and Figure 6.4).

| Model | AUC | CA | F1 | Precision | Recall | MCC | Specificity |
|---|---|---|---|---|---|---|---|
| Naïve Bayes | 0.63 | 0.58 | 0.59 | 0.65 | 0.58 | 0.17 | 0.61 |
| kNN | 0.59 | 0.67 | 0.66 | 0.65 | 0.67 | 0.19 | 0.50 |
| AdaBoost | 0.55 | 0.60 | 0.60 | 0.61 | 0.60 | 0.09 | 0.50 |
| Tree | 0.54 | 0.60 | 0.61 | 0.61 | 0.60 | 0.11 | 0.51 |

*Table 6.6: Naïve Bayes, kNN, AdaBoost, and Decision Tree classification model performance with outliers removed of 'V0_OCT' group features for target 'Injections First Year categories 3,>3'*

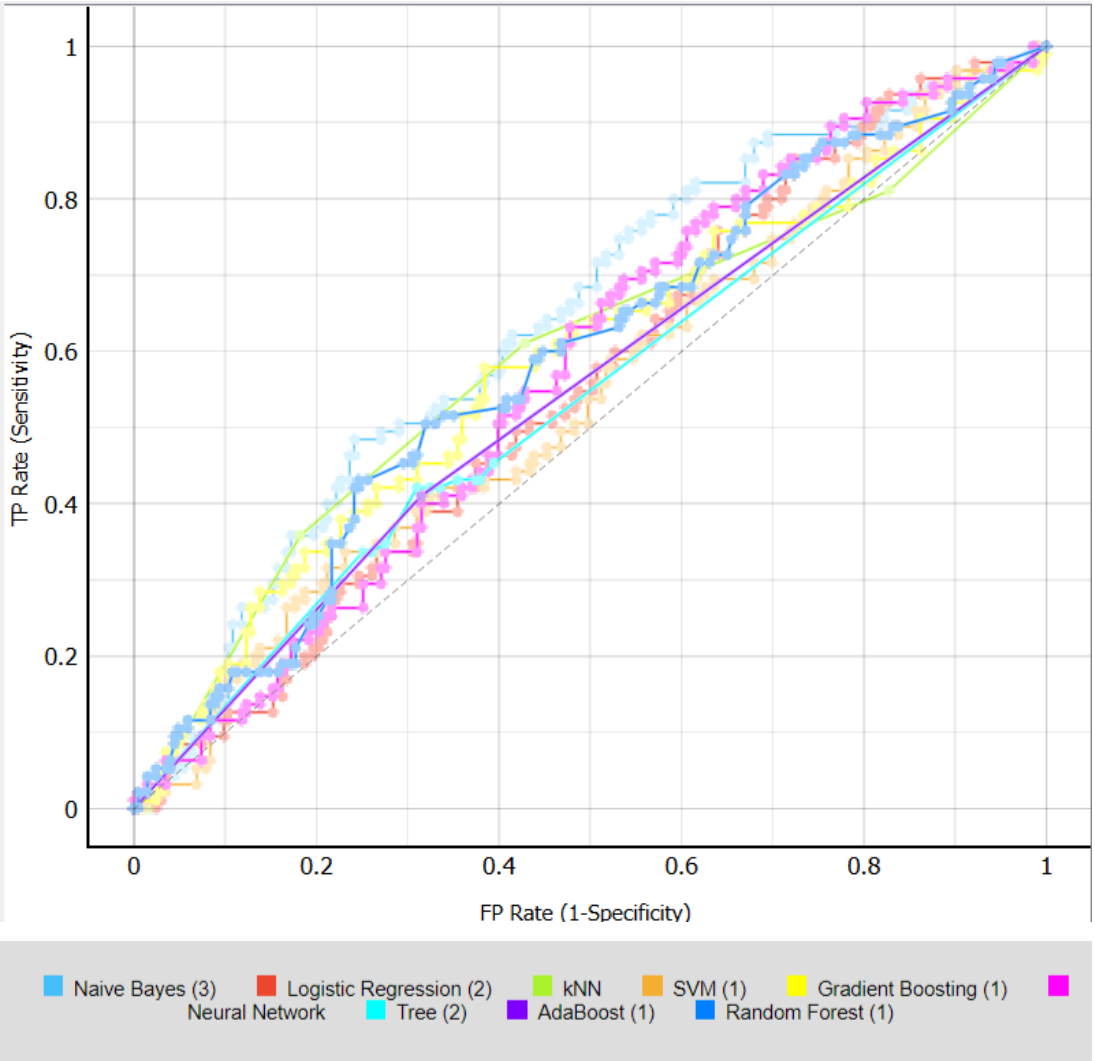


*Figure 6.3: ROC analysis of model performance with outliers removed of 'V0_OCT' group features for target Injections First Year n=3*

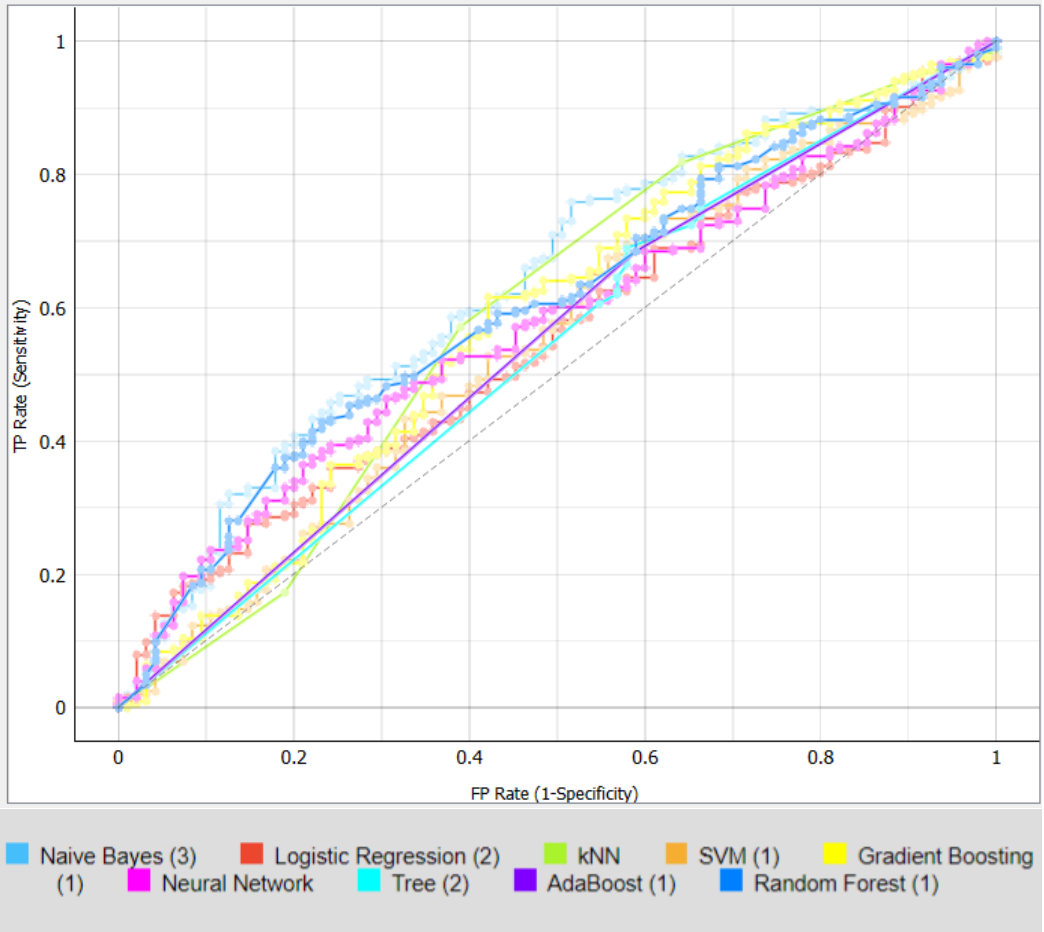


*Figure 6.4: ROC analysis of model performance with outliers removed of 'V0_OCT' group features for target Injections First Year categories n>3*

#### 6.2.1.4 Feature group 'VP_OCT'

The feature group 'VP_OCT' was considered in relation to eyes that received only the loading dose of treatment and those that required more than three injections.

Target: Injections first year (categories: 3, >3)

Feature group: VP_OCT

- 40 HEYEX OCT inputs from post loading (VP)

##### 6.2.1.4.1 ODM modelling

- After removing outliers, the Naïve Bayes model showed statistically significant predictive ability, but with limited accuracy (Table 6.7).

- Sub-analysis of the N1 group showed a significant improvement in accuracy after removing outliers, particularly for the Naïve Bayes model (Table 6.8), however considering the confusion matrix, a significant proportion of misclassifications persisted (Figure 6.5).

| Model | AUC | CA | F1 | Precision | Recall | MCC | Specificity |
|---|---|---|---|---|---|---|---|
| Naïve Bayes | 0.57 | 0.54 | 0.55 | 0.60 | 0.54 | 0.08 | 0.54 |

*Table 6.7: Naïve Bayes classification model performance with outliers removed of 'VP_OCT' group features for target 'Injections First Year categories 3,>3'*

| Model | AUC | CA | F1 | Precision | Recall | MCC | Specificity |
|---|---|---|---|---|---|---|---|
| Naïve Bayes | 0.61 | 0.60 | 0.61 | 0.64 | 0.60 | 0.21 | 0.62 |

*Table 6.8: Naïve Bayes classification model performance for N1 filtered dataset with outliers removed of 'VP_OCT' group features for target 'Injections First Year categories 3,>3'*

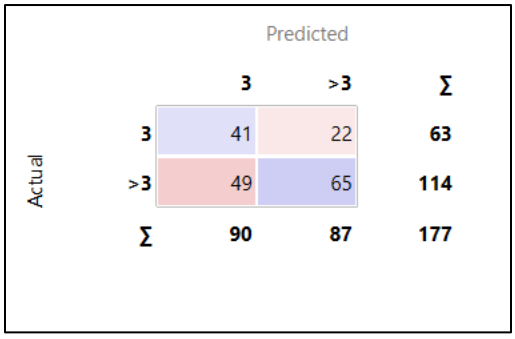


*Figure 6.5: Confusion matrix for Naïve Bayes model data instances for N1 filtered dataset of 'VP_OCT' group features for target 'Injections First Year categories 3,>3'*

### 6.2.1.5 Feature group 'VP_OCTANE' predictions of Injections first year (n=3, >3)

The feature group 'VP_OCTANE' was considered in relation to eyes that received only the loading dose of treatment and those that required more than three injections.

Target: Injections first year (categories: 3, >3)

Feature group: VP_OCTANE

- 12 OCTANE OCT inputs from baseline visit (VP)

#### 6.2.1.5.1 ODM modelling

- The Neural Network algorithm yielded the highest accuracy scores, attaining a statistically satisfactory level across all metrics but with overall predictive power remaining low (Table 6.9).

- Sub-analysis of the N1 group showed that kNN and AdaBoost models reach a statistically significant level of accuracy after removing outliers (Table 6.10). However considering predictions of the better performing kNN algorithm, a significant proportion of misclassifications persisted (Figure 6.6).

| Model | AUC | CA | F1 | Precision | Recall | MCC | Specificity |
|---|---|---|---|---|---|---|---|
| Neural Network | 0.56 | 0.55 | 0.56 | 0.60 | 0.55 | 0.09 | 0.55 |

*Table 6.9: Neural network classification model performance for total dataset of 'VP_OCTANE' group features for target 'Injections First Year categories 3,>3'*

| Model | AUC | CA | F1 | Precision | Recall | MCC | Specificity |
|---|---|---|---|---|---|---|---|
| kNN | 0.59 | 0.66 | 0.64 | 0.65 | 0.66 | 0.23 | 0.54 |
| AdaBoost | 0.56 | 0.58 | 0.58 | 0.59 | 0.58 | 0.12 | 0.54 |

*Table 6.10: kNN and AdaBoost classification model performance for N1 filtered dataset with outliers removed of 'VP_OCTANE' group features for target 'Injections First Year categories 3,>3'*

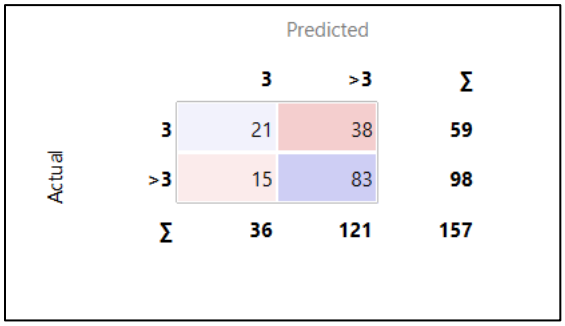


*Figure 6.6: Confusion matrix for kNN model data instances for N1 filtered dataset of 'VP_OCT' group features for target 'Injections First Year categories 3,>3'*

### 6.2.2 Classification analyses: Injections first year n=3, 4, 5, 6, 7, 8, 9, 10

Classification analyses were undertaken with the number of injections received over the first year of treatment considered in the categories n=3, 4, 5, 6, 7, 8, 9, 10. It was found that no learners in this series produced models with an adequate level of predictive accuracy. While many models reached AUC scores of 0.50 and specificity was generally high in the order of greater than or equal to 0.70, the sensitivity and precision of the models was however relatively low, in most cases less than or equal to 0.30. This was also the case in considering modelling indictor scores averaged over the classes and when evaluating performance in individual categories.

Feature determination was also relatively poor across all models as no HEYEX OCT or OCTANE features reached a significant level of prediction. Based on chi-squared values at the 0.05 significance level, the following features were suggestive of some degree of correlation but when considered alongside the level of modelling accuracy, any inference drawn would be disputable.

- Fellow eye activity (outliers removed)
- VA post loading (VP) (outliers removed)
- VA baseline visit (V0) (outliers removed)
- Standard deviation of VA mean, post loading -12 months (VP-V12) (outliers removed)

### 6.2.3 Regression analyses: Injections First Year

The following regression analyses investigated the devised feature groups abilities to predict the number of injections received over the first year of treatment.

#### 6.2.3.1 Feature group 'Demographic & qualitative'

The feature group 'Demographic & qualitative' was considered in relation to the number of injections received over the first year of treatment.

Target: Injections first year

Feature group: Demographic & qualitative

- Ethnicity
- Laterality
- Age At First Injection
- Sex
- Anti-VEGF drug type
- Interval 1st to 3rd injection
- Fellow eye activity

##### 6.2.3.1.1 ODM modelling

- After removal of outliers the linear regression model shows improved performance (Table 6.11) and Pearson correlation improved to 0.376 suggesting the presence of a relationship but at a weak level as suggested by scatterplot of the model (Figure 6.7).
- Sub-analysis of the N1 group showed further improvement in the performance of Linear Regression and SVM models after removing outliers (Table 6.12), with the resultant models also

yielding the highest levels of correlation; 0.441 Pearson correlation in the case of the linear regression model and 0.410 Pearson correlation in the case of the SVM algorithm. However, a high level of misclassified results persisted (Figure 6.8).

| Models | MSE | RMSE | MAE | $R^2$ | CVRMSE |
|---|---|---|---|---|---|
| Linear Regression | 2.00 | 1.42 | 1.19 | 0.13 | 30.94 |

*Table 6.11: Linear regression model performance with outliers removed of 'Demographic & qualitative' group features for target 'Injections First Year'*

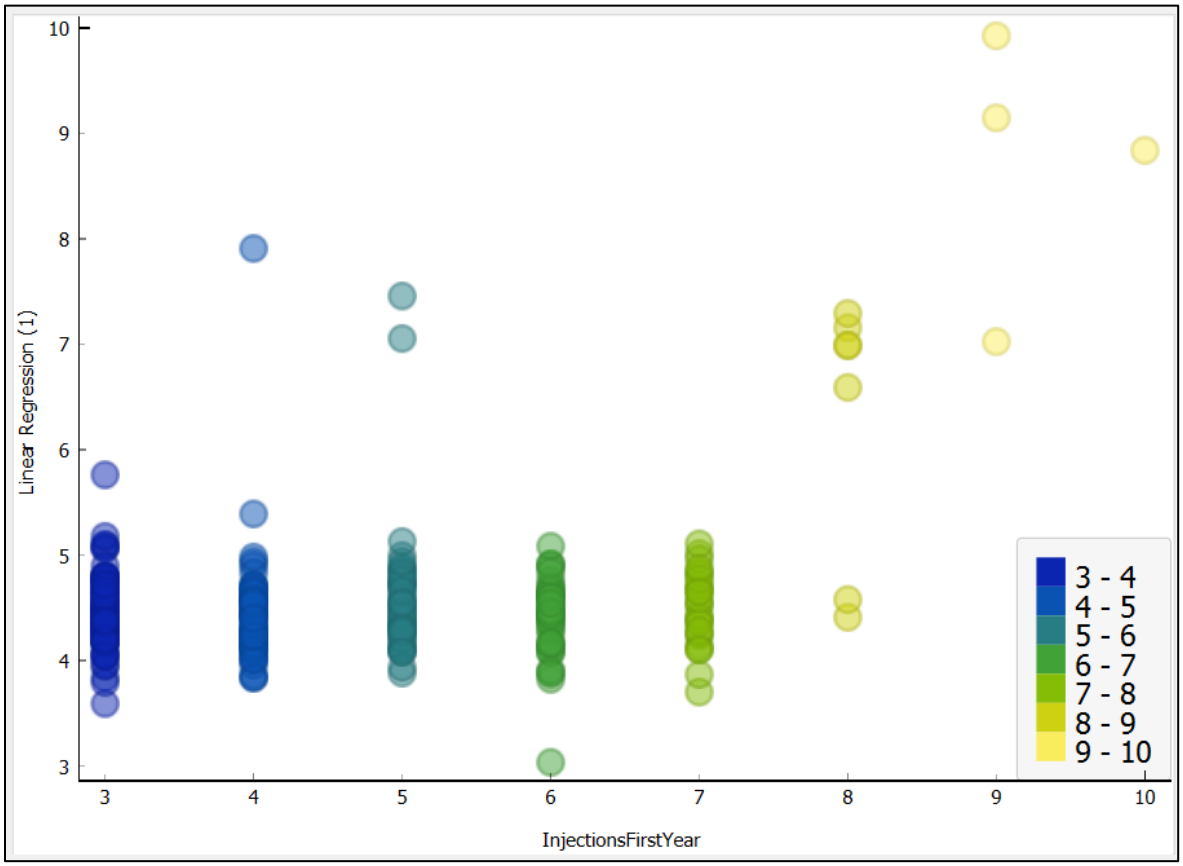


*Figure 6.7: Scatterplot of linear regression model predictions, with outlying data removed, of target 'Injections First Year'*

| Models | MSE | RMSE | MAE | $R^2$ | CVRMSE |
|---|---|---|---|---|---|
| Linear Regression | 2.14 | 1.46 | 1.23 | 0.18 | 31.62 |
| SVM | 2.28 | 1.51 | 1.25 | 0.13 | 32.66 |

*Table 6.12: Linear regression and SVM regression model performance with outliers removed for N1 filtered dataset of 'Demographic & qualitative' group features for target 'Injections First Year'*

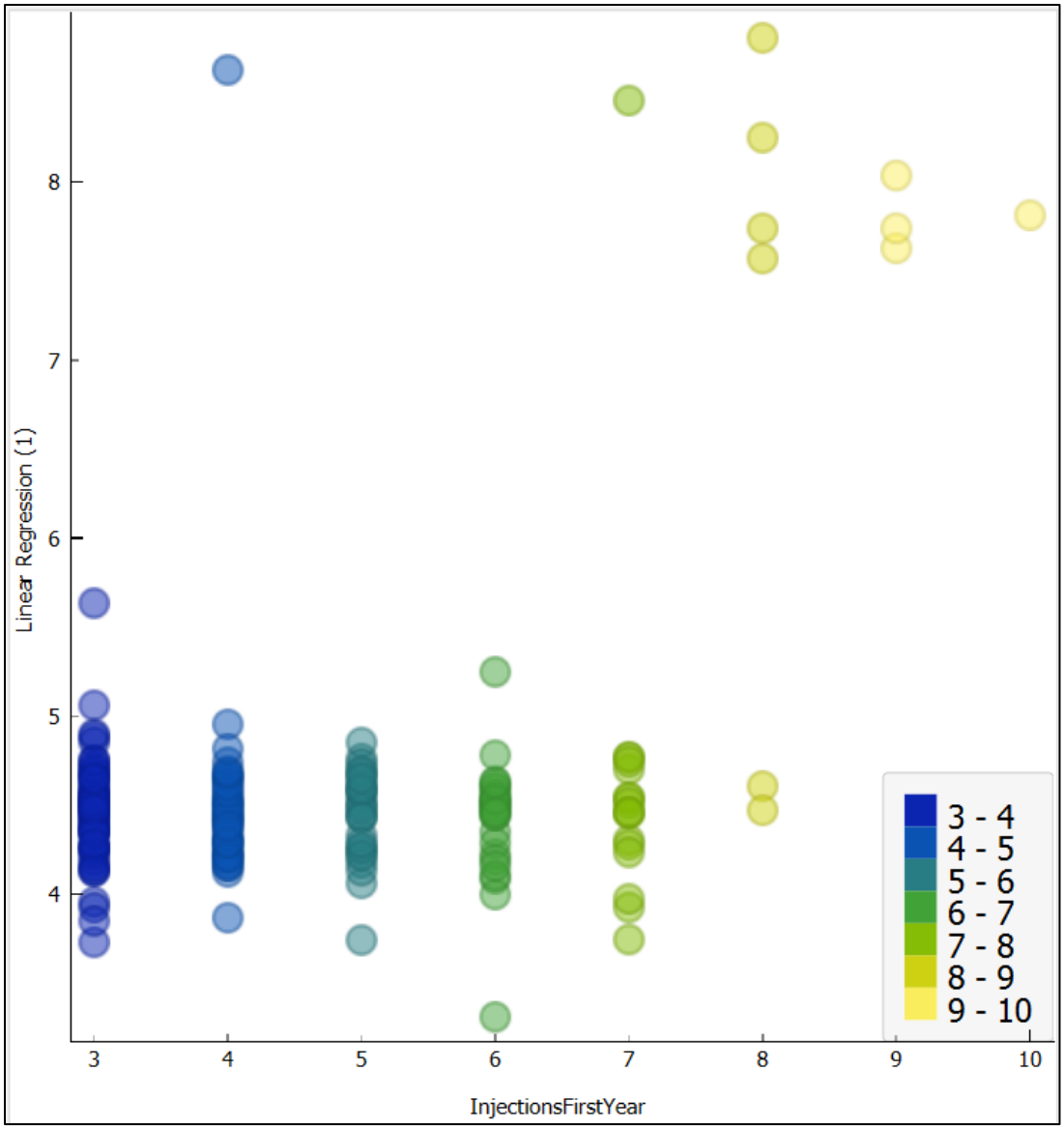


*Figure 6.8: Scatterplot of linear regression model predictions, of N1 filtered group with outlying data removed, of target 'Injections First Year'*

#### 6.2.3.2 Feature group 'VA_st dev'

The feature group 'VA_st dev' was considered in relation to the number of injections received over the first year of treatment.

Target: Injections first year

Feature group: VA_st dev

- VA baseline visit (V0)

- VA fellow eye (V0)
- VA post loading (VP)
- VA mean of 2 visits immediately post loading
- Standard deviation of VA mean, post loading -12 months (VP-V12)

6.2.3.2.1 ODM modelling

- Modelling performance was considered poor across all algorithms with minimal improvement on removing outliers.
- Standard deviation of the post loading VA mean was ranked as most important attribute (Table 6.13) in predicting anti-VEGF doses but the relatively low RReliefF score and Pearson correlation of 0.206 suggested that any inferences drawn would have to be treated carefully.

| Feature | Univariate Regression | RReliefF | Pearson correlation |
|---|---|---|---|
| Standard deviation of VA mean, post loading -12 months (VP-V12) | 14.454 | 0.083 | 0.206 |

*Table 6.13: Feature ranking in regression analyses of total dataset of 'VA_st dev' group features for target 'Injections First Year'*

6.2.3.3 Feature group 'V0_OCT'

The feature group 'V0_OCT' was considered in relation to the number of injections received over the first year of treatment.

Target: Injections first year

Feature group: V0_OCT

- 40 HEYEX OCT inputs from baseline visit (V0)

6.2.3.3.1 ODM modelling

- Modelling performance was poor across all algorithms, with minimal improvement after removing outliers.
- Central 3mm retina$_t$ volume was ranked as the most influential feature with univariate regression, RReliefF and Spearman correlation optimised on removing outliers (Table 6.14), however in view of the poor model performance scores, relatively weak correlation and comparatively low RReliefF values, any conclusions drawn from these ranking results would be guarded.

| Feature | Univariate Regression | RReliefF | Spearman correlation |
|---|---|---|---|
| V0_retina 3mm vol | 24.072 | 0.086 | 0.285 |

*Table 6.14: Feature ranking in regression analyses of dataset with outliers removed of 'V0_OCT' group features for target 'Injections First Year'*

#### 6.2.3.4 Feature group 'VP_OCT'

The feature group 'VP_OCT' was considered in relation to the number of injections received over the first year of treatment.

Target: Injections first year

Feature group: VP_OCT

- 40 HEYEX OCT inputs from baseline visit (VP)

##### 6.2.3.4.1 ODM modelling

- Modelling performance was considered poor across all algorithms in this dataset with minimal improvement in performance metrics on removing outliers.
- 3mm and 1mm $retina_t$ volumes and $retina_t$ 1mm CMT were ranked as the most influential features (Table 6.15). Removal of outliers from the data pool did not improve the ranking scores in this instance. In view of the poor model performance scores, relatively weak correlations and low RReliefF values, any conclusions drawn from these ranking results would also have to be considered carefully.

| Feature | Univariate Regression | RReliefF | Pearson correlation |
|---|---|---|---|
| VP_retina 3mm vol | 39.657 | 0.058 | 0.330 |
| VP_retina 1mm CMT | 34.611 | 0.061 | 0.310 |
| VP_retina 1mm CM vol | 33.624 | 0.060 | 0.306 |

*Table 6.15: Feature ranking in regression analyses of total dataset of 'VP_OCT' group features for target 'Injections First Year'*

### 6.3 Predicting injection patterns in year one

Beyond forming categories of anti-VEGF doses based on the number of injections received or those that received a loading phase of treatment only over three months, it proved difficult to readily extract frequency patterns from the dataset by conventional means, particularly where the time interval

between injections would be taken into account. It was thus decided to attempt to evaluate first year injection instances using ODM hierarchical clustering.

### 6.3.1 Injection frequency modelling using hierarchical clustering

Application of hierarchical clustering involved utilising unsupervised machine learning to separate eyes into clusters based on recognisable patterns of dosage intervals over the first year of treatment.

Within the ODM hierarchical clustering pipeline, the Euclidean distance metric was preferred to Manhattan distances due to improved cluster formation. The number of nodes used to form clusters was also tuned to optimise homogeneity within clusters and differentiation between clusters. Pruning did not appear to significantly impact on clustering results in this analysis.

Silhouette plots ( Figure 6.9) were used to visualise the number of nodes that yielded the best performance scores of clustering quality, optimising the consistency of data instances within clusters and ensuring adequate sample sizes within clusters. After evaluation, 10 clusters produced the best available results.

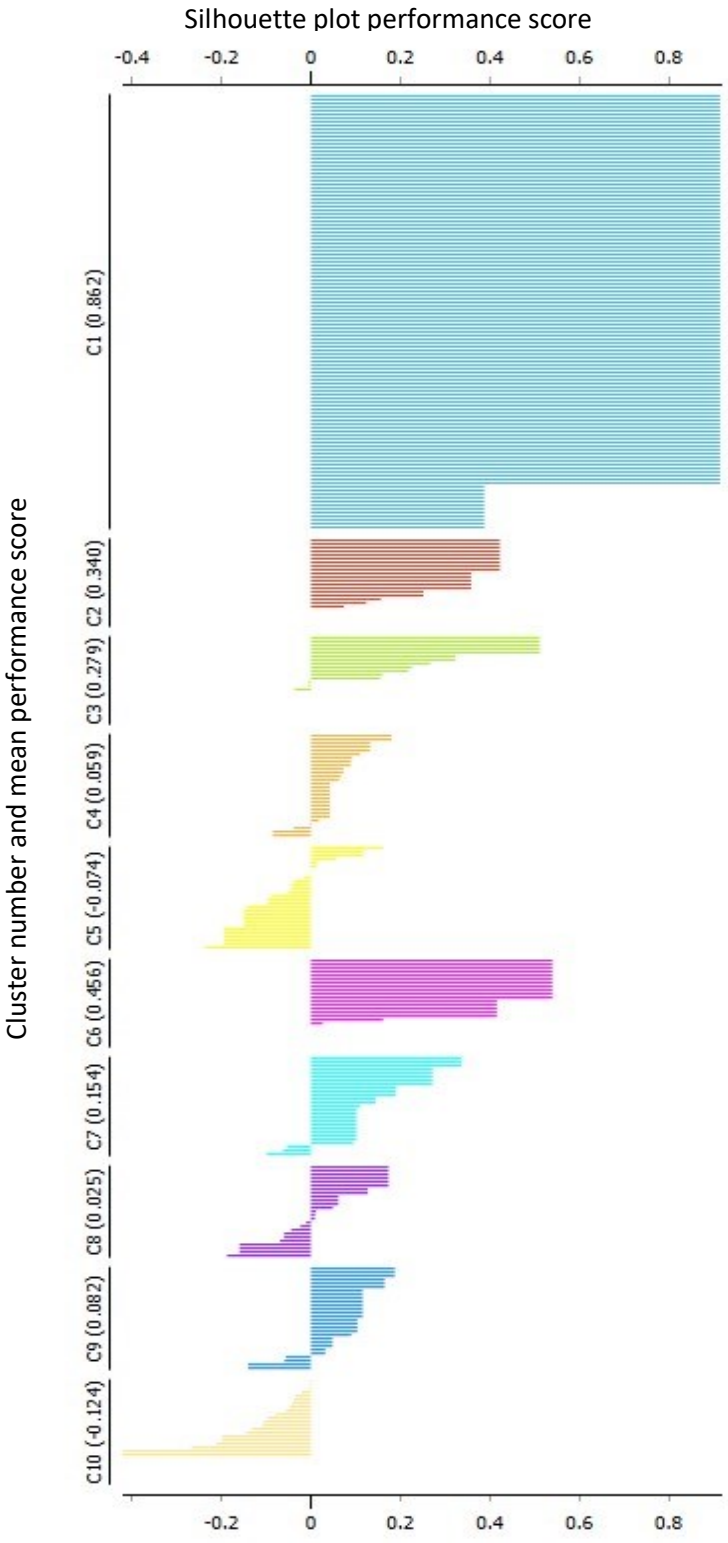


*Figure 6.9: Silhouette plot showing clustering to 10 groups by first year injection pattern with illustration of mean performance score, instance per cluster and homogeneity to determined pattern within clusters*

To understand the clustering patterns, results from each group were analysed in Excel. Averages were taken of the injections administered each month across each cluster, calculating the mean to a whole number to more easily visualise whether typically an anti-VEFG dose was received in any given month (Table 6.16). The standard deviation of the means of each month in turn indicated the confidence in each value and effectively how homogenous the treatment pattern was within cases assigned to a cluster. Combination scatter and column charts (Appendix 9) where additionally complied to help visualise the injection patterns and the spread in the results for each month.

| | Month | 0 | 1 | 2 | 3 | 4 | V5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Cluster 1 | **Mean of injections received** | **1** | **1** | **1** | **0** | **0** | **0** | **0** | **0** | **0** | **0** | **0** | **0** | **0** |
| | *Standard deviation* | *0.00* | *0.00* | *0.00* | *0.00* | *0.00* | *0.00* | *0.00* | *0.00* | *0.30* | *0.00* | *0.00* | *0.00* | *0.00* |
| Cluster 2 | **Mean of injections received** | **1** | **1** | **1** | **0** | **0** | **0** | **1** | **0** | **0** | **0** | **0** | **0** | **0** |
| | *Standard deviation* | *0.00* | *0.00* | *0.00* | *0.00* | *0.00* | *0.22* | *0.00* | *0.41* | *0.31* | *0.00* | *0.44* | *0.00* | *0.00* |
| Cluster 3 | **Mean of injections received** | **1** | **1** | **1** | **0** | **1** | **0** | **1** | **0** | **0** | **1** | **0** | **1** | **0** |
| | *Standard deviation* | *0.00* | *0.00* | *0.00* | *0.25* | *0.50* | *0.25* | *0.00* | *0.34* | *0.00* | *0.00* | *0.25* | *0.47* | *0.00* |
| Cluster 4 | **Mean of injections received** | **1** | **1** | **1** | **0** | **0** | **0** | **0** | **1** | **0** | **0** | **0** | **0** | **0** |
| | *Standard deviation* | *0.00* | *0.00* | *0.00* | *0.26* | *0.26* | *0.49* | *0.19* | *0.00* | *0.19* | *0.45* | *0.35* | *0.00* | *0.50* |
| Cluster 5 | **Mean of injections received** | **1** | **1** | **1** | **0** | **1** | **0** | **0** | **0** | **0** | **0** | **1** | **0** | **0** |
| | *Standard deviation* | *0.00* | *0.00* | *0.00* | *0.00* | *0.48* | *0.00* | *0.00* | *0.45* | *0.26* | *0.31* | *0.50* | *0.41* | *0.41* |
| Cluster 6 | **Mean of injections received** | **1** | **1** | **1** | **0** | **0** | **0** | **0** | **0** | **0** | **1** | **0** | **0** | **0** |
| | *Standard deviation* | *0.00* | *0.00* | *0.00* | *0.00* | *0.00* | *0.49* | *0.00* | *0.00* | *0.00* | *0.00* | *0.23* | *0.00* | *0.31* |
| Cluster 7 | **Mean of injections received** | **1** | **1** | **1** | **0** | **0** | **1** | **0** | **0** | **0** | **0** | **0** | **0** | **0** |
| | *Standard deviation* | *0.00* | *0.00* | *0.00* | *0.00* | *0.00* | *0.19* | *0.00* | *0.00* | *0.50* | *0.39* | *0.50* | *0.00* | *0.31* |
| Cluster 8 | **Mean of injections received** | **1** | **1** | **1** | **0** | **0** | **0** | **0** | **0** | **0** | **0** | **0** | **1** | **0** |
| | *Standard deviation* | *0.00* | *0.00* | *0.00* | *0.20* | *0.20* | *0.50* | *0.37* | *0.47* | *0.49* | *0.20* | *0.00* | *0.00* | *0.40* |
| Cluster 9 | **Mean of injections received** | **1** | **1** | **1** | **0** | **0** | **0** | **0** | **0** | **0** | **0** | **0** | **0** | **1** |
| | *Standard deviation* | *0.00* | *0.00* | *0.00* | *0.00* | *0.00* | *0.43* | *0.45* | *0.00* | *0.49* | *0.35* | *0.00* | *0.26* | *0.00* |
| Cluster 10 | **Mean of injections received** | **1** | **1** | **1** | **1** | **0** | **1** | **0** | **0** | **0** | **0** | **0** | **0** | **0** |
| | *Standard deviation* | *0.00* | *0.21* | *0.49* | *0.00* | *0.43* | *0.50* | *0.47* | *0.47* | *0.50* | *0.43* | *0.39* | *0.35* | *0.49* |

*Table 6.16: Injections patterns within clusters determined from mean of injections received at each visit and standard deviation in the mean*

Cluster one could be considered as having most readily interpretable pattern with injections received monthly for only the first three months of the entire year. Only the standard deviation in month eight was raised showing increased variability in the cluster pattern at this single interval. This analysis corresponded with results shown in the silhouette plot where a large proportion of the group could be seen as having a high and similar level of clustering scores. This homogeneity of treatment patterns could also be seen in the box and whisker chart for cluster one (Figure 6.10).

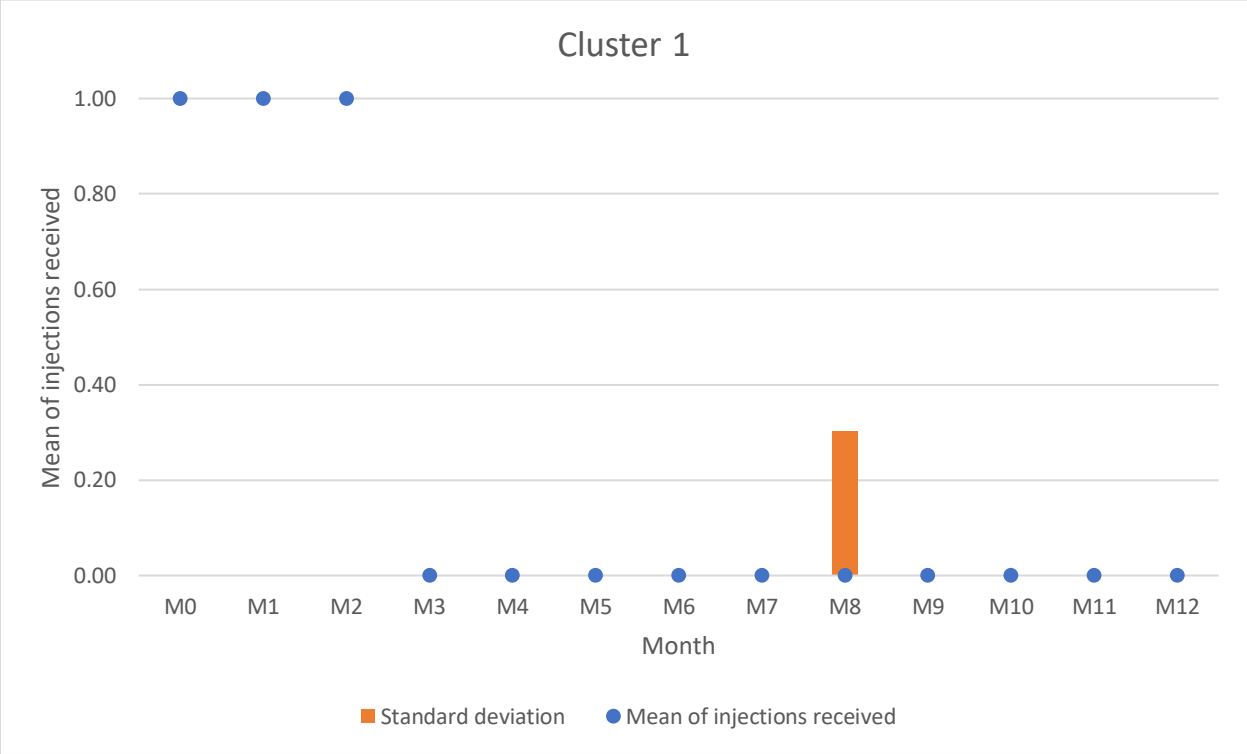


*Figure 6.10: Combination scatter and column chart of Cluster 1 showing distribution of injections received per month*

Cluster 10, in contrast to cluster one, had a treatment pattern where the results from the majority of months (barring months one and four) showed an elevated standard deviation in the mean injections received in each interval. The scatter and column chart (Figure 6.11) also showed greater dispersion of means and greater variability within the averaged results, particularly in months 2, 5, 6, 7, 8 and 12. The silhouette plot, which showed low clustering scores and a high degree of variability in the scores for cluster 10, was therefore in agreement with these findings.

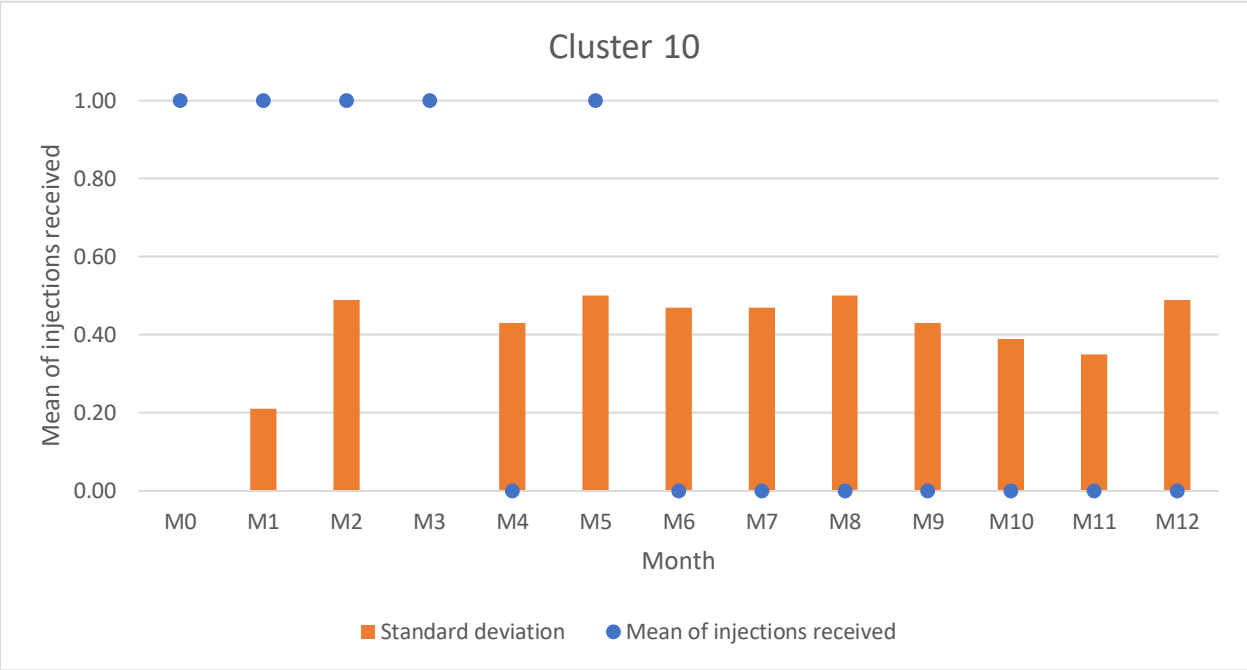


*Figure 6.11: Combination scatter and column chart of Cluster 10 showing distribution of injections received per month*

The remaining injections patterns and the standard deviation in the mean values, determined from table 6.16, and the box and whisker plots, from Appendix 3, were also evaluated in relation to the results form the silhouette plot. In general, there appeared to be a high level of concurrence where clusters with tighter distributions in the means corresponded to higher clustering scores and showed greater homogeneity within the plots with the reverse true of clusters with greater dispersion of dosing means.

In addition to evaluating the monthly pattern of injections, the mean of the total injections received by each eye over 12 months within each cluster and size of each cluster were also considered (Table 6.17). An immediate relationship was not however apparent which would relate these data to the silhouette plot clustering scores.

| | Mean of total injections in 12 months | Standard deviation of mean | Instances within cluster |
|---|---|---|---|
| Cluster 1 | 3.1 | *0.30* | 118 |
| Cluster 2 | 4.6 | *0.67* | 19 |
| Cluster 3 | 6.5 | *0.81* | 15 |
| Cluster 4 | 5.5 | *1.35* | 28 |
| Cluster 5 | 5.1 | *1.00* | 28 |
| Cluster 6 | 4.6 | *0.83* | 18 |
| Cluster 7 | 5.2 | *1.17* | 27 |
| Cluster 8 | 5.7 | *0.97* | 25 |
| Cluster 9 | 5.1 | *0.87* | 28 |
| Cluster 10 | 6.4 | *1.87* | 21 |

*Table 6.17: Cluster data of the mean of the total injections received by each eye over 12 months in each group, standard deviation of the mean and cluster size.*

The findings thus strongly suggested that the hierarchical clustering algorithm based the groupings on the monthly treatment pattern.

### 6.3.2 Classification analyses: Injection pattern first year (categories: clusters 1, 2, 3, 4, 5, 6, 7, 8, 9, 10)

Classification analyses were performed to in an attempt to predict treatment patterns determined by ODM hierarchical clustering. It was found however that no learners produced models with an adequate level of performance.

The following characteristics did reach a meaningful level of prediction in differentiating between the classes based on chi-squared values at the 0.05 significance level, however when considered alongside the level of modelling accuracy, any inferences drawn would be disputable.

- Time interval 1st to 3rd injection (full dataset)
- Fellow eye activity (full dataset)
- Age At First Injection (full dataset)
- VA fellow eye (V0) (full dataset)
- Standard deviation of VA mean, post loading -12 months (VP-V12) (full dataset)

## 6.4 Discussion

This section aims to summarise previous studies which have attempted similar investigations, discuss the results from this body of work in predicting anti-VEGF dosing and, in the cases of stronger relationships, to assess in more detail how individual features influence injection outcomes.

Prior work by Bogunović et al. (2017) to predict treatment frequency has included a reanalysis of the PRN arm of the landmark HARBOUR study which in 2013 published results on ranibizumab dosing (Busbee et al., 2013). The post-hoc study divided the cohort into low and high retreatment subgroups finding that random forest based models achieved AUC scores of 0.7 and 0.77, respectively, in differentiating between the classes. Feature analysis within their study determined SRF volume within the central 3mm subfield at month 2 to have the highest predictive value with 1mm total retinal thickness and IRF within the 3mm central macular zone to also deemed to be discriminative.

A study carried out by Pfau et al. (2021) has already been considered within chapter 1. Regression analyses from their work, attempting to predict anti-VEGF PRN treatment frequency over 12 months from OCT biomarkers, devised a random forest based model ($R^2$ = 0.39) and a natural gradient boosting model ($R^2$ = 0.094) which demonstrated significant relationships. Based on their retinal apportionment, sub RPE volume, sub RPE drusenoid complex thickness and inner segment layer thickness were found be the most statistically significant features in predicting anti-VEFG treatment frequency .

TREND was another pivotal study which helped to evaluate the safety and efficacy of delivering ranibizumab in a treat and extend regimen in nAMD (Silva et al., 2018). Bogunović et al. (2022) again performed a retrospective analysis of patients from this study to create models that would differentiate between those with high disease activity and requiring more frequent retreatment at shorter intervals against those in whom treatment intervals could be extended. Their random forest model predicted the extendable treatment interval group with an averaged AUC of 0.71. VA change from baseline to the first follow up, at one month, and volume of SRF remaining at the first follow up were found to be the most important predictive markers in predicting treatment intervals.

In this study, where anti-VEGF dosing modelling was attempted to categorise eyes by the actual number of injections received or the temporal pattern in which injections were administered, modelling accuracy failed to reach an acceptable level. This was based on AUC, CA, precision, recall and specificity collectively all failing to reach a level above 50%. This in turn rendered the clinical application of results from the models inappropriate. Fellow eye disease activity, baseline VA and the standard deviation of the VA mean, post loading until month 12, were only features within both series of analyses to yield chi-squared values, at an $\alpha$ level of 0.05, suggesting they had some bearing in predicting injection dosing.

In trying to differentiate between eyes that required three or more than three injections, modelling performance improved significantly. Of the feature groups where modelling accuracy was above 50%

collectively across AUC, CA, precision, recall and specificity, the most accurate model from each group is considered below (Table 6.18). It was found that the Naïve Bayes learner produced the highest degree accuracy, AUC of 0.63, in considering baseline HEYEX OCT (V0_OCT) variables. Considering however the confusion matrix for Naïve Bayes performance, there were still a significant proportion of misclassifications (Figure 6.12) thus results remained at a level where predictions would have to treated carefully in clinical applications.

| Feature group | Model | AUC | Dataset | Most informative feature |
|---|---|---|---|---|
| VA | AdaBoost | 0.55 | Full | VA fellow eye (V0) |
| VA_st dev | Tree | 0.57 | Outliers removed | VA fellow eye (V0) |
| V0_OCT | Naïve Bayes | 0.63 | Outliers removed | V0_GCL 1mm CM vol |
| VP_OCT | Naïve Bayes | 0.57 | Outliers removed | VP_GCL 1mm CM vol |
| VP_OCTANE | Neural Network | 0.56 | Full | VP_vol_drusenoid_ped |

*Table 6.18: Models predicting Injections first year (n=3, >3) with highest levels of accuracy from each feature group (where adequate level of performance was found), model AUC, dataset sample considered and most informative feature within model*

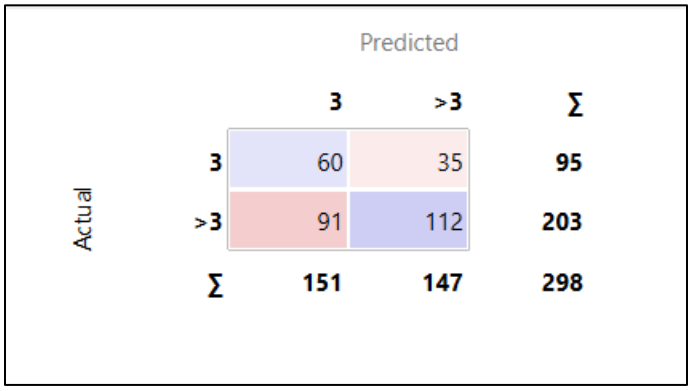


*Figure 6.12: Confusion matrix for Naïve Bayes model predictions of 'V0_OCT' group features with outliers removed for target 'Injections First Year categories 3,>3'*

Features predictive of differentiating between eyes that required three or more than three injections were more difficult to determine. While the most informative feature within each best performing model was extracted (Table 6.18), the indictors determining the prognostic ability of these variables suggested relatively poor performance. Standard deviation of the post loading VA mean showed the best level of predictive performance of any individual variable scoring relatively highly across all feature prediction indictors and reaching a chi-squared score which demonstrated significance but at an α level of 0.1. In considering the influence of the post loading VA standard deviation on dosing, it was easier to consider a logistic regression nomogram (Figure 6.13). The diagram effectively showed that as standard deviation decreased to a minimum of 0.4, probability increased to maximum of 50% of only requiring

three injections. The reverse was the case when considering those that required more than 3 injection where a standard deviation of 0.4 again implied a 50% probability of requiring more then 3 injections but this probability rapidly increased as the standard deviation rose.

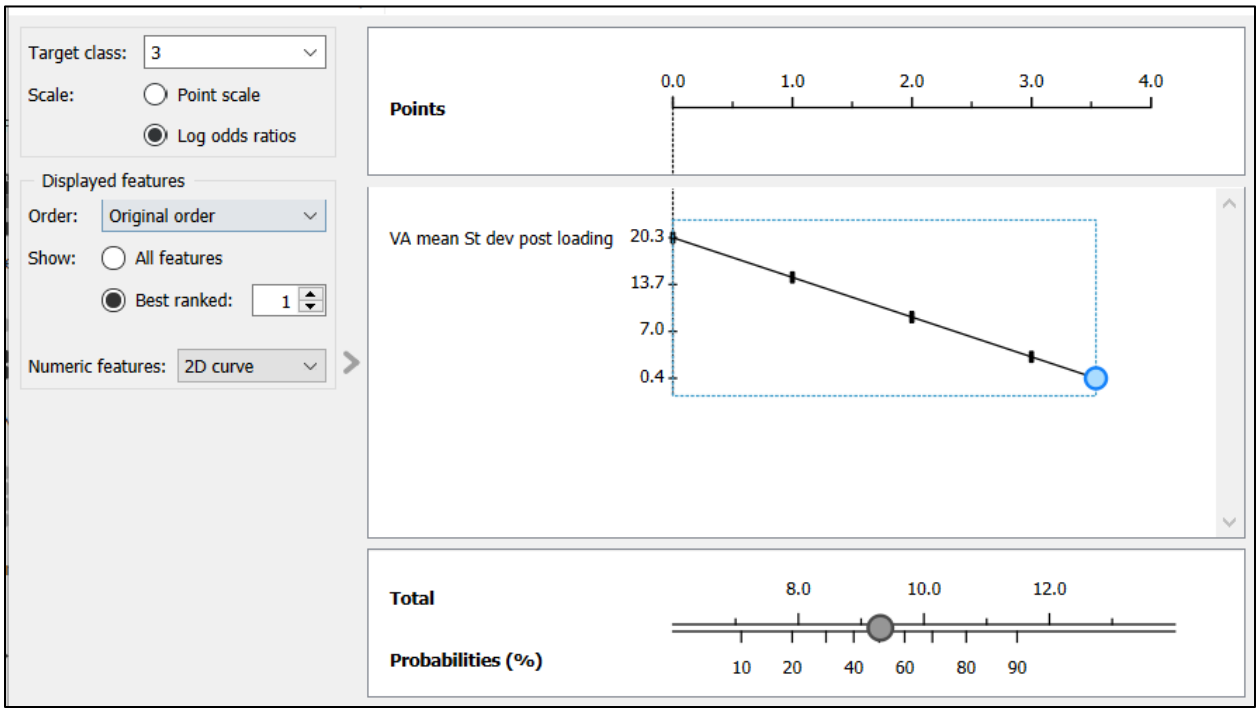


*Figure 6.13: Logistic regression nomogram demonstrating effect of the standard deviation of VA mean, post loading -12 months (VP-V12) on differentiating between the classes, Injections first year (n=3, >3)*

In evaluating eyes that required three or more than three injections, the only analyses where N1 filtering produced a significant improvement in performance was in the feature group 'VP OCT' (post loading HEYEX OCT variables). The Naïve Bayes model AUC improved to 0.61 in this case but as previously shown in the confusion matrix (Figure 6.5), a significant proportion of misclassifications persisted. Ranking performance also remained at a level where statistical significance was not demonstrated.

Regression models were also produced to investigate relationships between the features and doses of anti-VEGF administered. In this series of analyses, only the group comprising demographic & qualitative features were found to demonstrate a significant relationship with injection administered in year one. The best performing linear regression model coefficient of determination of 0.13 and 0.376 Pearson correlation however suggested a rather weak relationship which could be visualised within the model scatterplot (Figure 6.7). $R^2$ (0.18) and Pearson correlation (0.441) improved marginally when considering

the N1 sub-cohort of 196 patients in whom there was no evidence of nAMD in the fellow eye, but not to a level where there was an obviously increase in modelling performance.

Within regression analyses predicting anti-VEGF treatment doses, feature ranking failed to determine any characteristics which consistently scored at levels across univariate regression, RReliefF and correlation what would suggest appropriate predictive ability.

## 6.5 Key Findings

- Predicting the exact number of injections or the specific pattern of injections over one year proved challenging.
- Models differentiating between eyes that require only the loading dose (3 injections) and those that need more showed improved accuracy.
- The Naïve Bayes classifier, using baseline HEYEX OCT measures, predicted the need for more than 3 injections with an AUC of 0.63.
- Fellow eye visual acuity, baseline GCL volume, post loading GCL volume, and post loading drusenoid PED volume were the most informative features in predicting the need for more than 3 injections.
- The standard deviation of the VA mean post loading demonstrated a weak but statistically significant influence on predicting the number of injections.
- $Retina_t$ thicknesses and volumes measured at baseline and post loading showed weak positive relationships with the number of injections administered.

# 7 Features relevant in predicting visual acuity and visual prognosis

## 7.1 Introduction

This chapter aims to present the analyses and results related to visual acuity and visual prognosis over one year of those undergoing management of nAMD with anti-VEGF.

Visual acuity outcomes were considered in terms of:

- final visual acuity after 12 months of treatment
- change in visual acuity at 12 months from baseline
- change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints
- standard deviation of VA mean over 12 months

Analyses were undertaken by classification and regression modelling. These used the variables on which information was gathered during the study, including OCT based characteristics, visual acuity measures and demographic information, all of which were listed in chapter 5 within defined feature groups. These predictors were inputted to ODM based pipelines in an attempt to forecast VA over the first year of treatment and the features relevant in forming such predictions.

The modelling accuracy and predictive strength of feature attributes from each ODM learner were considered and are reported in their entirety in appendices 3 and 4. The models which reached a significant level of performance and deemed further discussion have been reported within this chapter.

In order to more readily visualise classification model accuracy, models were initially ordered based on the AUC scores. A colour coding system was applied where model performance was described between a scale of 0 and 1 (Table 7.1). In the case of regression model interpretation, $R^2$ values were used to initially arrange leaner outcomes prior to further investigation.

| Model performance range | Colour |
|---|---|
| 0 – 0.49 | No colour |
| 0.50 - 0.59 | Yellow |
| 0.60 - 0.69 | Orange |
| ≥ 0.70 | Green |

*Table 7.1: Key describing colours used to indicate model performance*

### 7.1.1 Sub-analyses : VA outcomes within N1 cohort

In addition to assessment using the feature groups in section 6.3, some analyses were repeated. Where models were deemed to have attained a significant level of performance, these were re-evaluated considering the N1 group of 196 patients in whom there was no evidence of nAMD in the fellow eye, either prior to or during the 12 months of the study period. Where there was a significant improvement in modelling outcomes, compared to the unfiltered study cohort, these results were reported within the thesis.

### 7.1.2 Follow up attendances first year

After the baseline measures and three loading doses of anti-VEGF were administered, the 308 patients within the study population attended between six and 11 follow up visits within the first year at which visual acuity was reassessed (Table 7.2 and Figure 7.1). The majority of the group attended for eight or nine visits with the mean number of visits found to be 8.28 with a standard deviation of 1.3.

| Distribution | Mean | Mode | Median | Dispersion | Standard deviation | Minimum | Maximum |
|---|---|---|---|---|---|---|---|
| Follow up attendances first year | 8.28 | 9 | 8 | 0.15 | 1.3 | 6 | 11 |

*Table 7.2: Follow up visits in first year summary statistics*

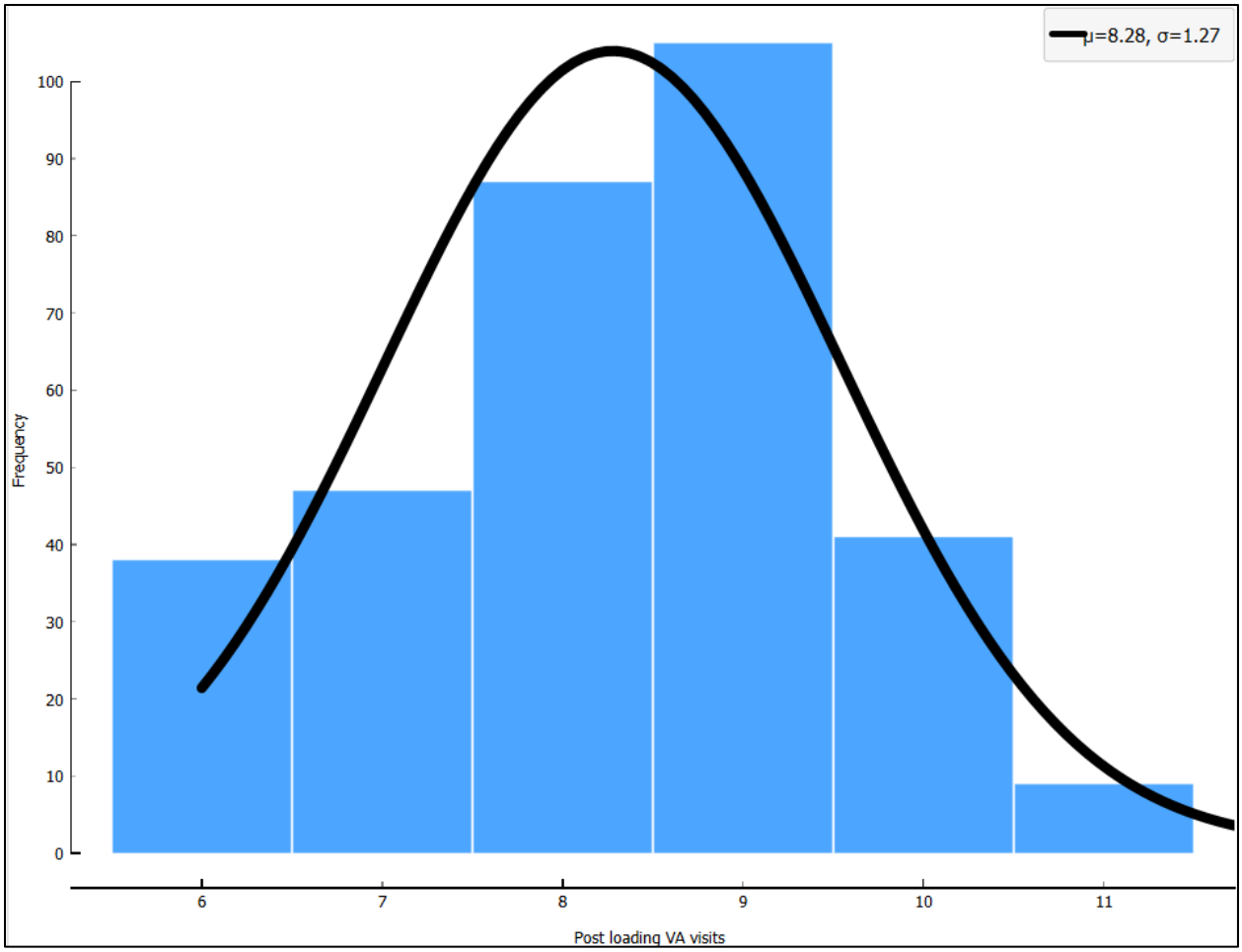


*Figure 7.1: Histogram of follow up visits in first year*

## 7.2 Visual acuity at 12 months

Visual acuity was recorded in letter score format and at 12 months varied between a maximum of 94 letters and a minimum of 18 letters (Table 7.3). It can be seen from the distribution plot (Figure 7.2) that VA had a left skewed distribution around a mean of 60.99 letters.

| Distribution | Mean | Mode | Median | Dispersion | Standard deviation | Minimum | Maximum |
|---|---|---|---|---|---|---|---|
| Visual acuity at 12 months | 60.99 | 73 | 64 | 0.25 | 15.44 | 18 | 94 |

*Table 7.3: VA at 12 months summary statistics*

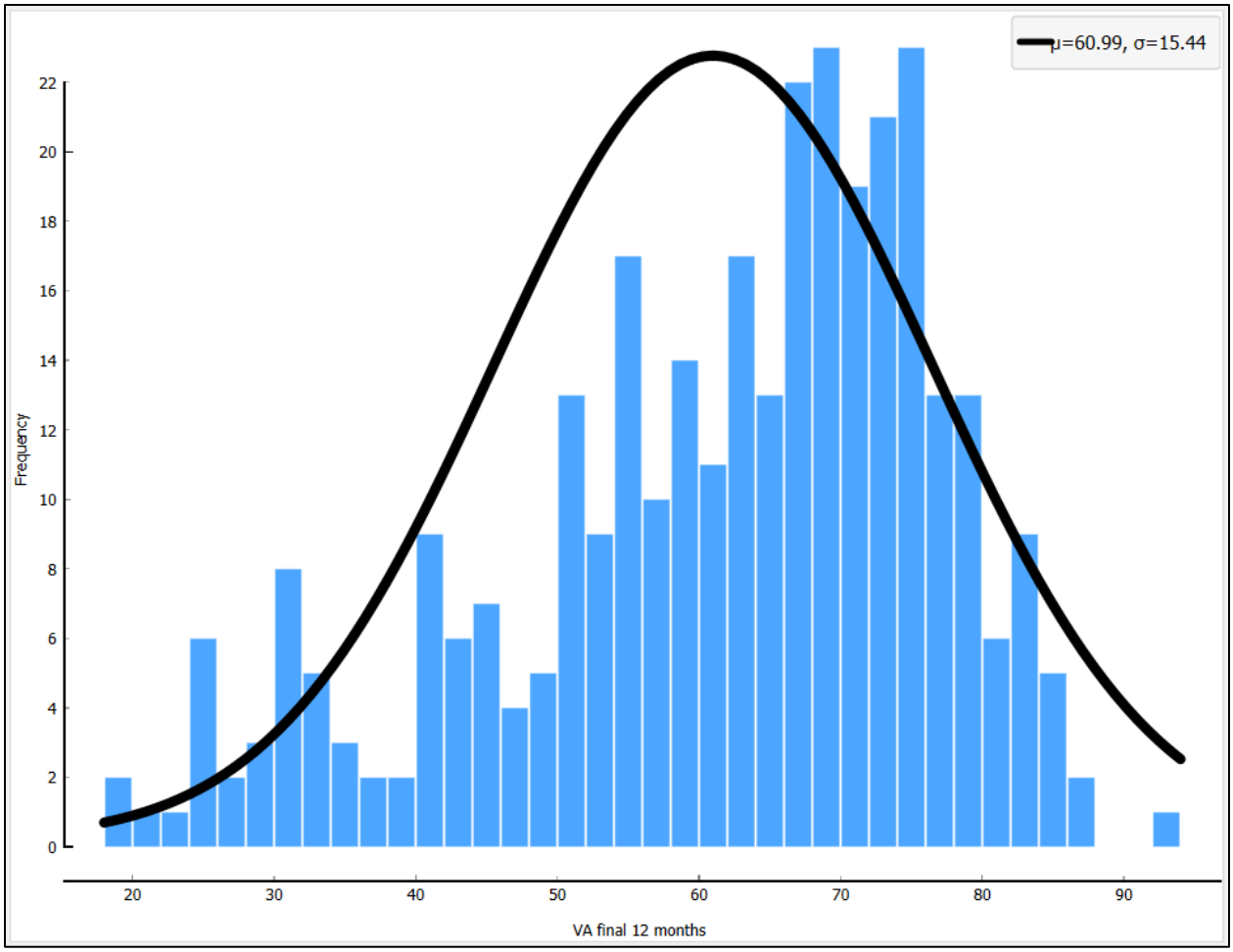


*Figure 7.2: Distribution of VA at 12 months*

VA was also sorted into categories based on the acuity measure gained at 12 months (Table 7.4 and Figure 7.3).

| Categories (letter) | <30 | 31-40 | 41-50 | 51-60 | 61-70 | 71-80 | >80 |
|---|---|---|---|---|---|---|---|
| Instances | 17 | 23 | 31 | 66 | 89 | 83 | 18 |

*Table 7.4: Categories of VA at 12 months and instances per group*

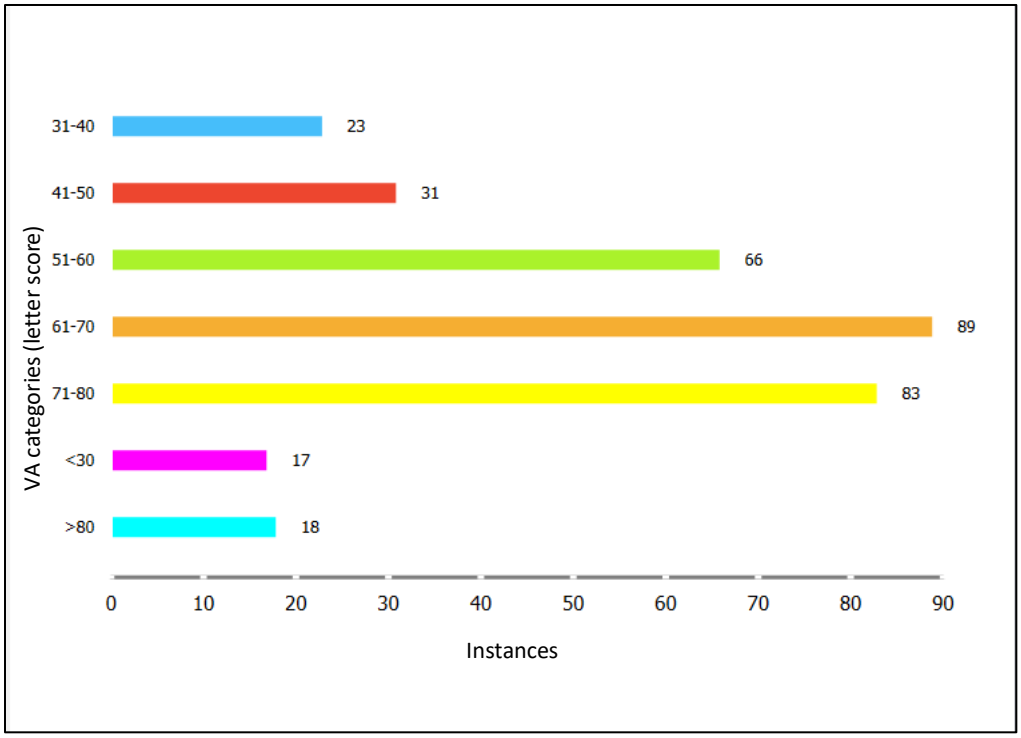


*Figure 7.3: Histogram of instances within categories of VA at 12 months*

### 7.2.1 Classification analyses: VA at 12 months (categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80)

The following classification analyses investigated the devised feature groups in relation to the visual acuity within the classes; letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80. The displayed results were averaged by ODM over the seven groups. The results for each category were however viewed individually and if a significant correlation was identified or if the model behaviour was notably improved compared to the averaged results, such findings were reported.

#### 7.2.1.1 Feature group 'VA'

The feature group 'feature group 'VA' was considered in relation to VA at 12 months.

Target: VA at 12 months (categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80)

Feature group: VA

- VA baseline visit (V0)
- VA fellow eye (V0)
- VA post loading (VP)
- VA mean of 2 visits immediately post loading

7.2.1.1.1 ODM modelling

- On considering the class VA 71-80 letters individually, with outliers removed, the models based on SVM, logistic regression and a neural network did reach an appropriate level of accuracy across all indictors (Table 7.5). The confusion matrix for SVM model (Figure *7.4*) did however continue to show a significant number of misclassifications, even within the VA 71-80 letters grouping, thus results remained at a level where prediction may be deemed unreliable.
- All attributes in this case demonstrated a significant relationship, at the 0.05 α level based on chi-squared scores, in predicting between the VA classes (Table 7.6). VA mean of the 2 visits post loading, in particular, performed satisfactorily across all indictors however given that the modelling accuracy was questionable, reported feature ranking results would have to be interpreted with care.

| Model | AUC | CA | F1 | Precision | Recall | MCC | Specificity |
|---|---|---|---|---|---|---|---|
| SVM | 0.81 | 0.75 | 0.60 | 0.52 | 0.70 | 0.43 | 0.77 |
| Logistic Regression | 0.80 | 0.74 | 0.59 | 0.51 | 0.69 | 0.42 | 0.76 |
| Neural Network | 0.79 | 0.74 | 0.57 | 0.51 | 0.64 | 0.39 | 0.78 |

*Table 7.5: Classification model performance with outliers removed for dataset of 'VA' group features for target 'VA at 12 months (categories: letter score VA 71-80)'*

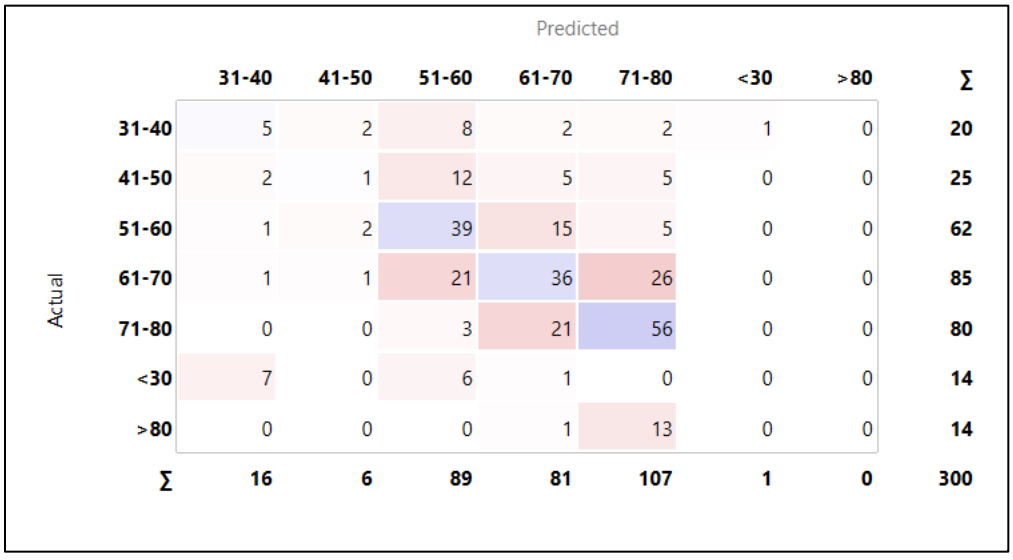


*Figure 7.4: Confusion matrix for SVM classification model predictions for dataset with outliers removed of 'VA' group features for target 'VA at 12 months (categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80)'*

| Feature | Info. gain | Gain ratio | Gini | ANOVA | $\chi^2$ | ReliefF | FCBF |
|---|---|---|---|---|---|---|---|
| VA mean initial 2 visits post loading | 0.528 | 0.264 | 0.107 | 58.458 | 129.364 | 0.037 | 0.305 |
| VA post loading (VP) | 0.480 | 0.240 | 0.095 | 48.903 | 120.513 | 0.030 | 0.000 |
| VA baseline visit (V0) | 0.201 | 0.101 | 0.037 | 19.715 | 63.427 | 0.015 | 0.000 |
| VA fellow eye (V0) | 0.073 | 0.037 | 0.017 | 3.059 | 17.115 | 0.010 | 0.033 |

*Table 7.6: Feature ranking in classification analyses of total dataset of 'VA' group features for target 'VA at 12 months (categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80)'*

#### 7.2.1.2 Feature group 'VA_st dev'

The feature group ''VA_st dev' was considered in relation to VA at 12 months.

Target: VA at 12 months (categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80)

Feature group: VA_st dev

- VA baseline visit (V0)
- VA fellow eye (V0)
- VA post loading (VP)
- VA mean of 2 visits immediately post loading
- Standard deviation of VA mean, post loading -12 months (VP-V12)

##### 7.2.1.2.1 ODM modelling

- After removing outliers, the model based on gradient boosting, reached an appropriate level of accuracy in predicting those within the 51-60 and 71-80 letter classes (Table 7.7 and Table 7.8). The confusion matrix for the gradient boosted model (Figure 7.5) did however continue to show a significant number of misclassifications, even within the 51-60 and 71-80 letters groupings, thus results remained at a level where prediction may not be of practical use.
- All attributes in this case demonstrated a significant relationship, at the 0.05 α level based on chi-squared scores, in predicting between the classes with the VA mean of the 2 visits post loading, being the most informative feature, performing well across all indictors (Table 7.9).

| Model | AUC | CA | F1 | Precision | Recall | MCC | Specificity |
|---|---|---|---|---|---|---|---|
| Gradient Boosting | 0.82 | 0.79 | 0.51 | 0.50 | 0.52 | 0.38 | 0.86 |

*Table 7.7: Classification models with adequate performance with outliers removed for dataset of 'VA_st dev' group features for target 'VA at 12 months (categories: letter score VA 51-60)'*

| Model | AUC | CA | F1 | Precision | Recall | MCC | Specificity |
|---|---|---|---|---|---|---|---|
| Gradient Boosting | 0.82 | 0.77 | 0.56 | 0.56 | 0.55 | 0.40 | 0.85 |

*Table 7.8: Classification models with adequate performance with outliers removed for dataset of 'VA_st dev' group features for target 'VA at 12 months (categories: letter score VA 71-80)'*

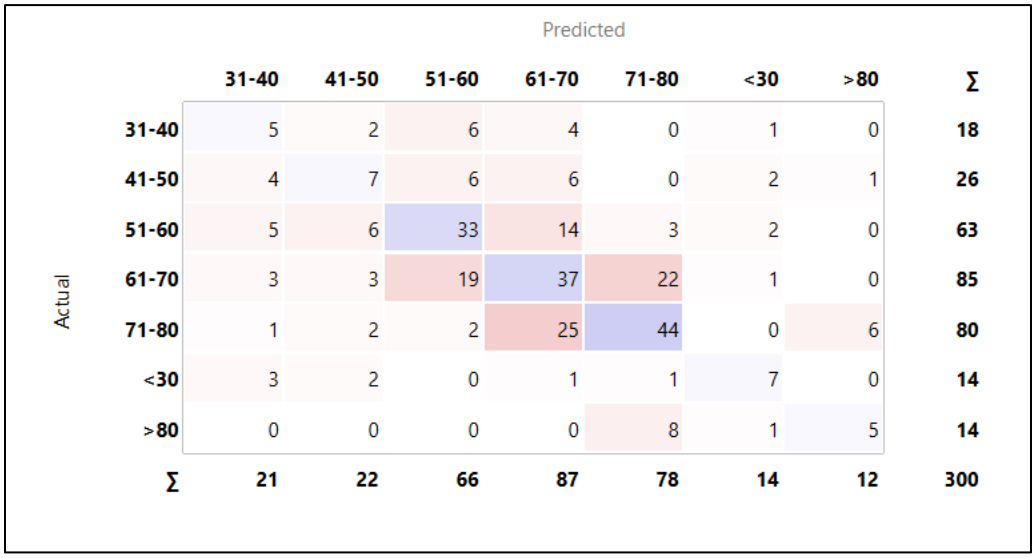


*Figure 7.5: Confusion matrix for gradient boosted classification model predictions for dataset with outliers removed of 'VA' group features for target 'VA at 12 months (categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80)'*

| Feature | Info. gain | Gain ratio | Gini | ANOVA | $\chi^2$ | ReliefF | FCBF |
|---|---|---|---|---|---|---|---|
| VA mean initial 2 visits post loading | 0.528 | 0.264 | 0.107 | 58.458 | 129.364 | 0.071 | 0.305 |
| VA post loading (VP) | 0.480 | 0.240 | 0.095 | 48.903 | 120.513 | 0.057 | 0.000 |
| VA baseline visit (V0) | 0.201 | 0.101 | 0.037 | 19.715 | 63.427 | 0.020 | 0.000 |
| Standard deviation of VA mean, post loading -12 months (VP-V12) | 0.124 | 0.062 | 0.020 | 11.989 | 35.180 | 0.042 | 0.058 |
| VA fellow eye (V0) | 0.073 | 0.037 | 0.017 | 3.059 | 17.115 | 0.012 | 0.033 |

*Table 7.9: Feature ranking in classification analyses of total dataset of 'VA_st_dev' group features for target 'VA at 12 months (categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80)'*

### 7.2.2 Regression analyses: VA at 12 months

The following regression analyses investigated the visual acuity at 12 months as a continuous variable using the devised feature groups.

#### 7.2.2.1 Feature group 'VA'

The feature group 'VA' was considered in relation to the VA at 12 months.

Target: VA at 12 months

Feature group: VA

- VA baseline visit (V0)
- VA fellow eye (V0)
- VA post loading (VP)
- VA mean of 2 visits immediately post loading

##### 7.2.2.1.1 ODM modelling

- On removing outlying data, the linear regression model showed improved performance ($R^2$ = 0.50, Pearson correlation = 0.711) (Table 7.10) . The scatterplot of the linear regression based model (Figure *7.6*) also began to suggest a degree of linearity but with the persistence of a significant degree of misestimation.

- Baseline visit VA was the most influential attribute according to the Rank widget, but the VA mean of 2 visits immediately post-loading shows a stronger relationship with VA at 12 months based on univariate regression and correlation results (Table 7.11). When additionally considering features most informative to the linear regression model (Figure 7.7), the VA mean of 2 visits immediately post loading again showed greater influence than the other attributes. The scatterplot of the VA mean of 2 visits immediately post loading plotted against VA at 12 months also suggests a linear relationship (figure 7.8) but with a significant degree of predictive error.
- Sub-analysis of the N1 group (no nAMD in the fellow eye) showed further improvement in the Linear Regression model performance ($R^2$ = 0.56, Pearson correlation = 0.749) after removing outliers (Table 7.12).

| Models | MSE | RMSE | MAE | $R^2$ | CVRMSE | Pearson correlation |
|---|---|---|---|---|---|---|
| Linear Regression | 110.94 | 10.53 | 7.51 | 0.50 | 17.15 | 0.711 |

*Table 7.10: Linear regression model performance with outliers removed for total dataset of 'VA' group features for target 'VA at 12 months'*

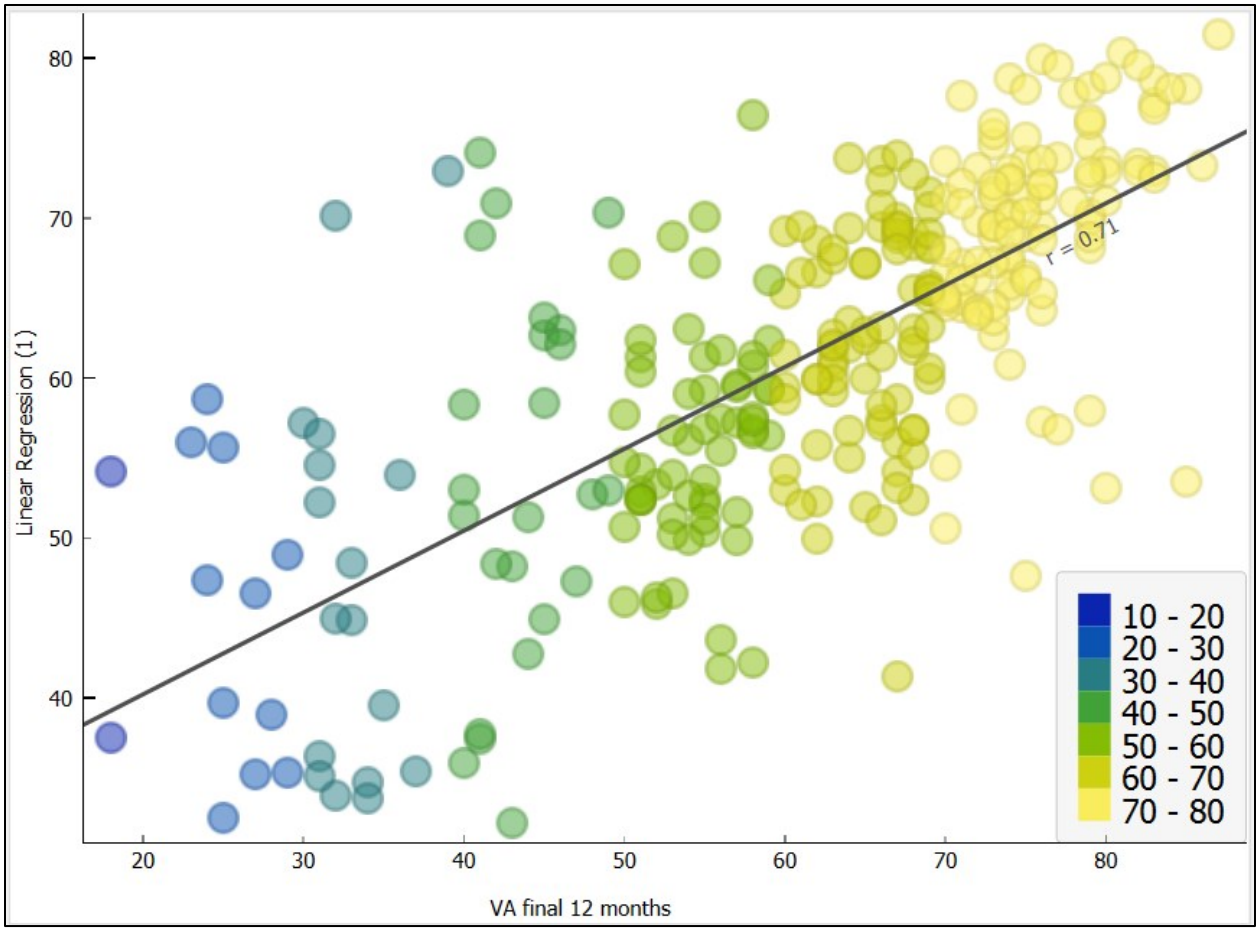


*Figure 7.6: Scatterplot of linear regression model predictions, with outliers removed, for total dataset of 'VA' group features for target 'VA at 12 months'*

| Feature | Univariate Regression | RReliefF | Spearman correlation |
|---|---|---|---|
| VA baseline visit (V0) | 114.170 | 0.091 | 0.514 |
| VA fellow eye (V0) | 7.448 | 0.106 | 0.222 |
| VA post loading (VP) | 295.823 | 0.065 | 0.694 |
| VA mean of 2 visits immediately post loading | 346.402 | 0.069 | 0.722 |

*Table 7.11: Feature ranking and Spearman correlation in regression analyses of total dataset of 'VA' group features for target 'VA at 12 months'*

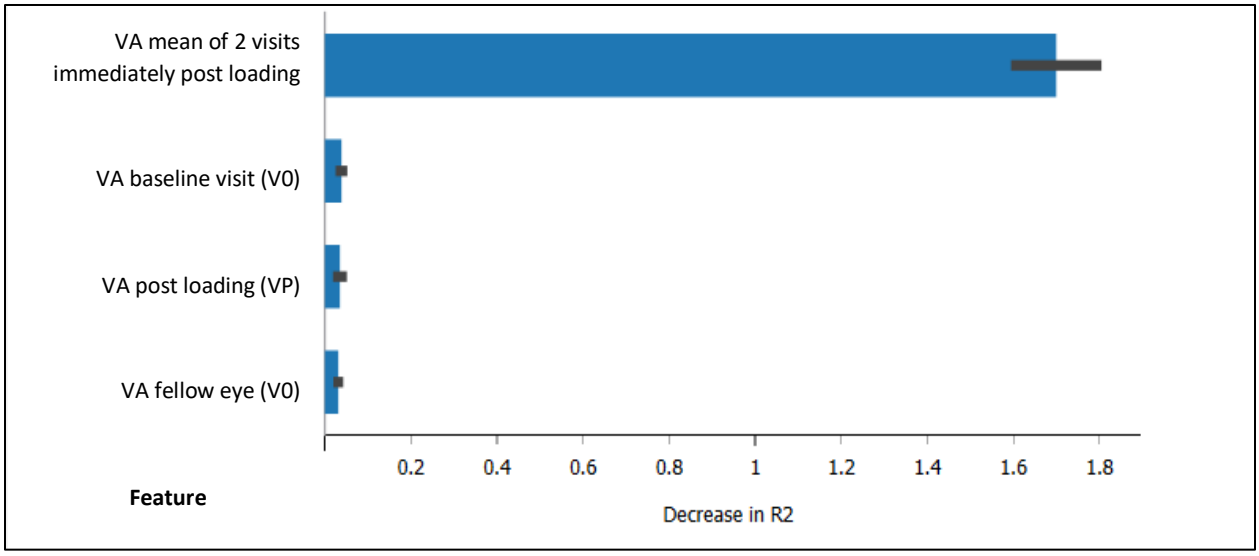


*Figure 7.7: Feature importance in linear regression model predictions, with outliers removed, for total dataset of 'VA' group features for target 'VA at 12 months' ranked by influence on $R^2$*

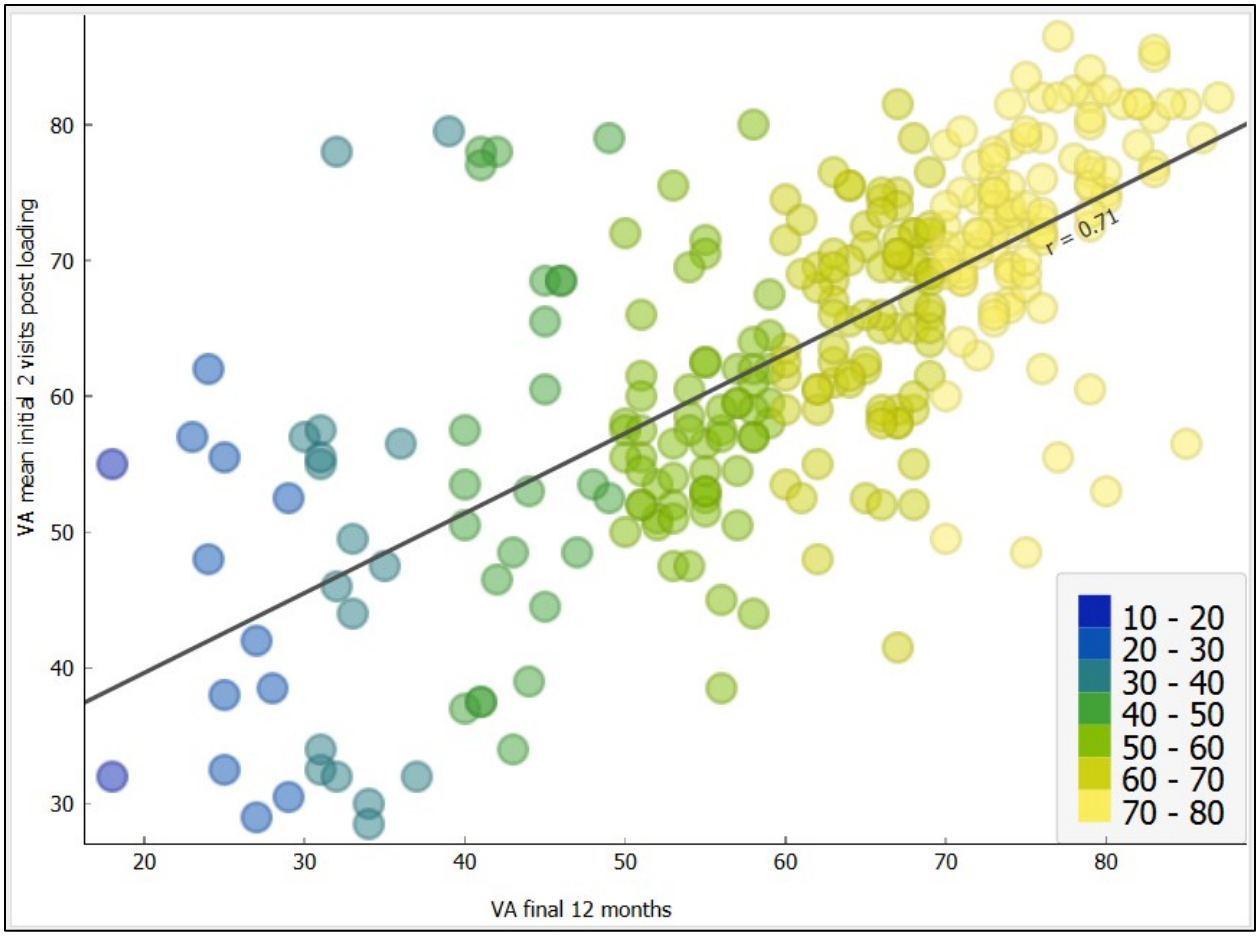


*Figure 7.8: Scatterplot of VA mean of 2 visits immediately post loading plotted against VA at 12 months*

| Models | MSE | RMSE | MAE | $R^2$ | CVRMSE | Pearson correlation |
|---|---|---|---|---|---|---|
| Linear Regression | 104.90 | 10.24 | 7.24 | 0.56 | 16.68 | 0.749 |

*Table 7.12: Linear regression model performance for N1 filtered dataset, with outliers removed, of 'VA' group features for target 'VA at 12 months'*

#### 7.2.2.2 Feature group 'VA_st dev'

The feature group 'VA_st dev' was considered in relation to the VA at 12 months.

Target: VA at 12 months

Feature group: VA_st dev

- VA baseline visit (V0)
- VA fellow eye (V0)
- VA post loading (VP)

- VA mean of 2 visits immediately post loading
- Standard deviation of VA mean, post loading -12 months (VP-V12)

7.2.2.2.1 ODM modelling

- After removing outliers, the Linear Regression model shows improved performance ($R^2$ = 0.59, Spearman correlation = 0.774) (Table 7.13). The scatterplot of the linear regression based model (Figure 7.9) also demonstrated linearity but with some degree of misestimation.
- VA mean of the 2 visits immediately post loading was ranked as the most influential attribute (Table 7.17).

| Models | MSE | RMSE | MAE | $R^2$ | CVRMSE | Spearman correlation |
|---|---|---|---|---|---|---|
| Linear Regression | 90.61 | 9.52 | 6.80 | 0.59 | 15.48 | 0.774 |

*Table 7.13: Linear regression model performance with outliers removed for total dataset of 'VA_st_dev' group features for target 'VA at 12 months'*

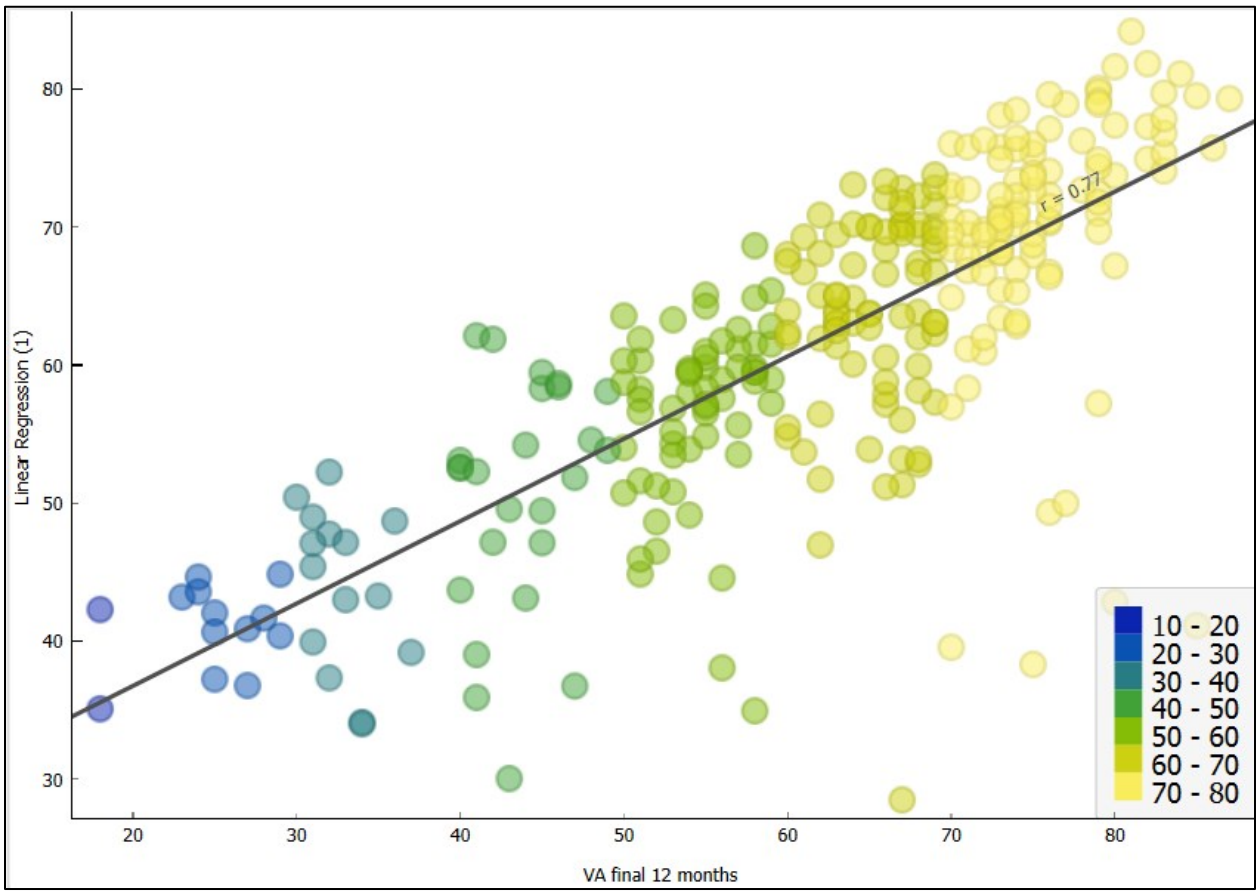


*Figure 7.9: Scatterplot of linear regression model predictions, with outliers removed, for total dataset of 'VA_st-dev' group features for target 'VA at 12 months'*

| Feature | Univariate Regression | RReliefF | Spearman correlation |
|---|---|---|---|
| VA mean of 2 visits immediately post loading | 346.402 | 0.074 | 0.722 |
| VA post loading (VP) | 295.823 | 0.074 | 0.694 |
| VA baseline visit (V0) | 114.170 | 0.081 | 0.514 |
| VA fellow eye (V0) | 7.448 | 0.124 | 0.222 |
| Standard deviation of VA mean, post loading -12 months (VP-V12) | 67.354 | 0.145 | -0.364 |

*Table 7.14: Feature ranking and Spearman correlation in regression analyses of total dataset of 'VA_st_dev' group features for target 'VA at 12 months'*

#### 7.2.2.3 Feature group 'VP_OCT'

The feature group 'VP_OCT' was considered in relation to the VA at 12 months.

Target: VA at 12 months

Feature group: VP_OCT

- 40 HEYEX OCT inputs from baseline visit (VP)

##### 7.2.2.3.1 ODM modelling

- After removing outliers, the Gradient Boosting model showed some improvement in performance ($R^2$ = 0.14, Gradient Boosting = 0.404), but the relationship remained weak (Table 7.15) with the scatterplot of the model predictions model showing significant dispersion around the best fit line (Figure 7.10).
- GCL volume over the central 3mm zone was ranked as the most influential feature (Table 7.16) however in view of the moderate model performance scores and relatively uniform RReliefF values, any conclusions drawn from these ranking results would however be guarded.

| Models | MSE | RMSE | MAE | $R^2$ | CVRMSE | Gradient Boosting |
|---|---|---|---|---|---|---|
| Gradient Boosting | 202.35 | 14.23 | 11.22 | 0.14 | 23.22 | 0.404 |

*Table 7.15: Gradient Boosting regression model performance with outliers removed for dataset of 'VP_OCT' group features for target 'VA at 12 months'*

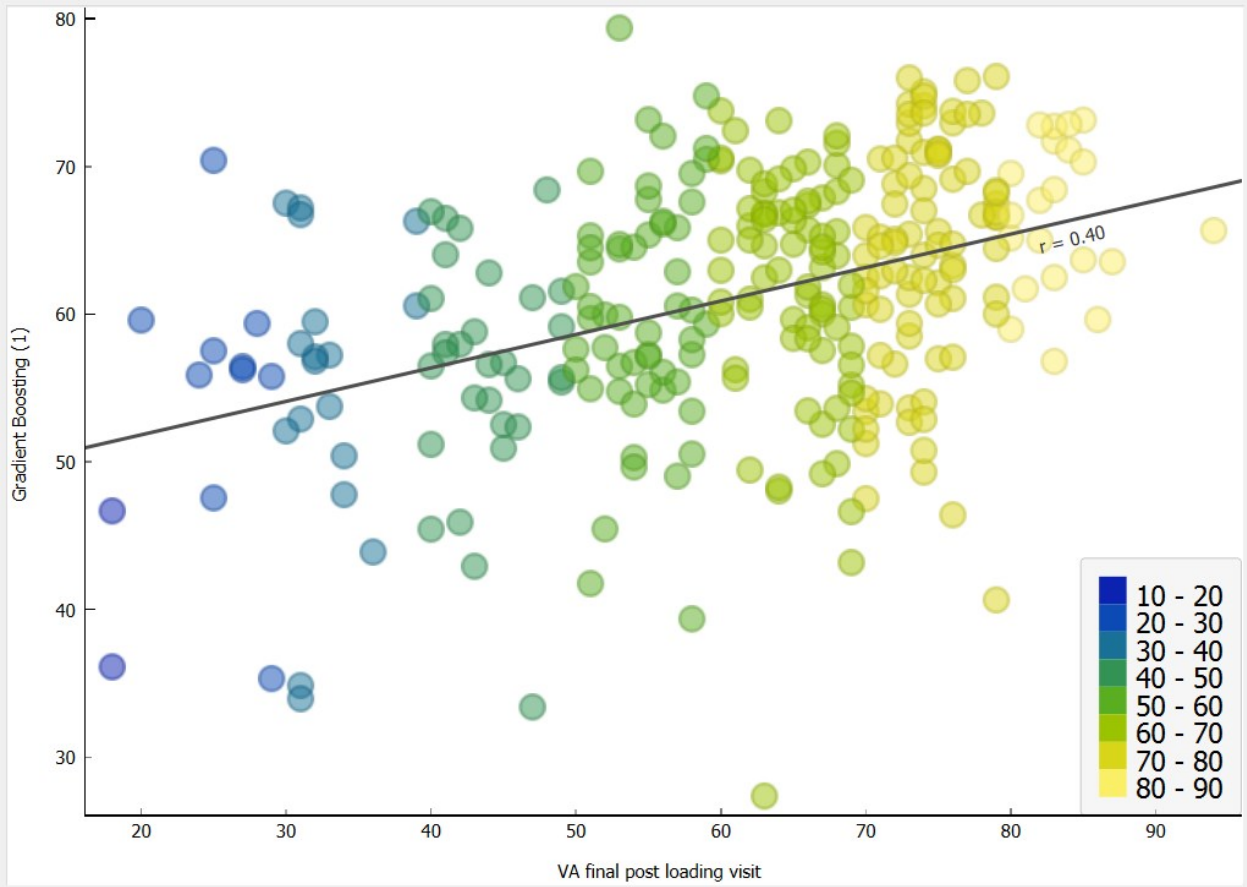


*Figure 7.10: Scatterplot of gradient boosting model predictions, with outliers removed, for total dataset of 'VP_OCT' group features for target 'VA at 12 months'*

| Feature | Univariate Regression | RReliefF |
|---|---|---|
| VP_GCL 3mm vol | 34.234 | 0.119 |
| VP_IPL 3mm vol | 30.866 | 0.085 |
| VP_IRLs 3mm vol | 16.066 | 0.103 |
| VP_IPL min CMT | 13.221 | 0.107 |
| VP_OPL 3mm vol | 8.081 | 0.114 |

*Table 7.16: Feature ranking in regression analyses of total dataset of 'VP_OCT' group features for target 'VA at 12 months'*

## 7.3 Mean of VA from final 2 visits in first year

Visual acuity was also considered at 12 months but as the mean of the letter score results from the final two visits in first year. The purpose of this was to account for fluctuation in VA and establish whether would have any bearing on modelling outcomes. The VA mean again formed a left skewed distribution around a mean of 61.24 letters (Table 7.17 and Figure 7.11) in a similar manner to the distribution of VA at 12 months. Classification and regression analyses were repeated using the mean VA of the final 2 visits in the first year, however, this approach did not significantly improve modelling outcomes or reveal new relationships. Modelling results are reported fully in appendices 6, 7 and 8.

| Distribution | Mean | Mode | Median | Dispersion | Standard deviation | Minimum | Maximum |
|---|---|---|---|---|---|---|---|
| VA at 12 months (mean of VA from final 2 visits) (letter score) | 61.24 | 72.5 | 61.24 | 0.24 | 14.76 | 20.50 | 94.0 |

*Table 7.17: VA at 12 months summary statistics (mean of VA from final 2 visits)*

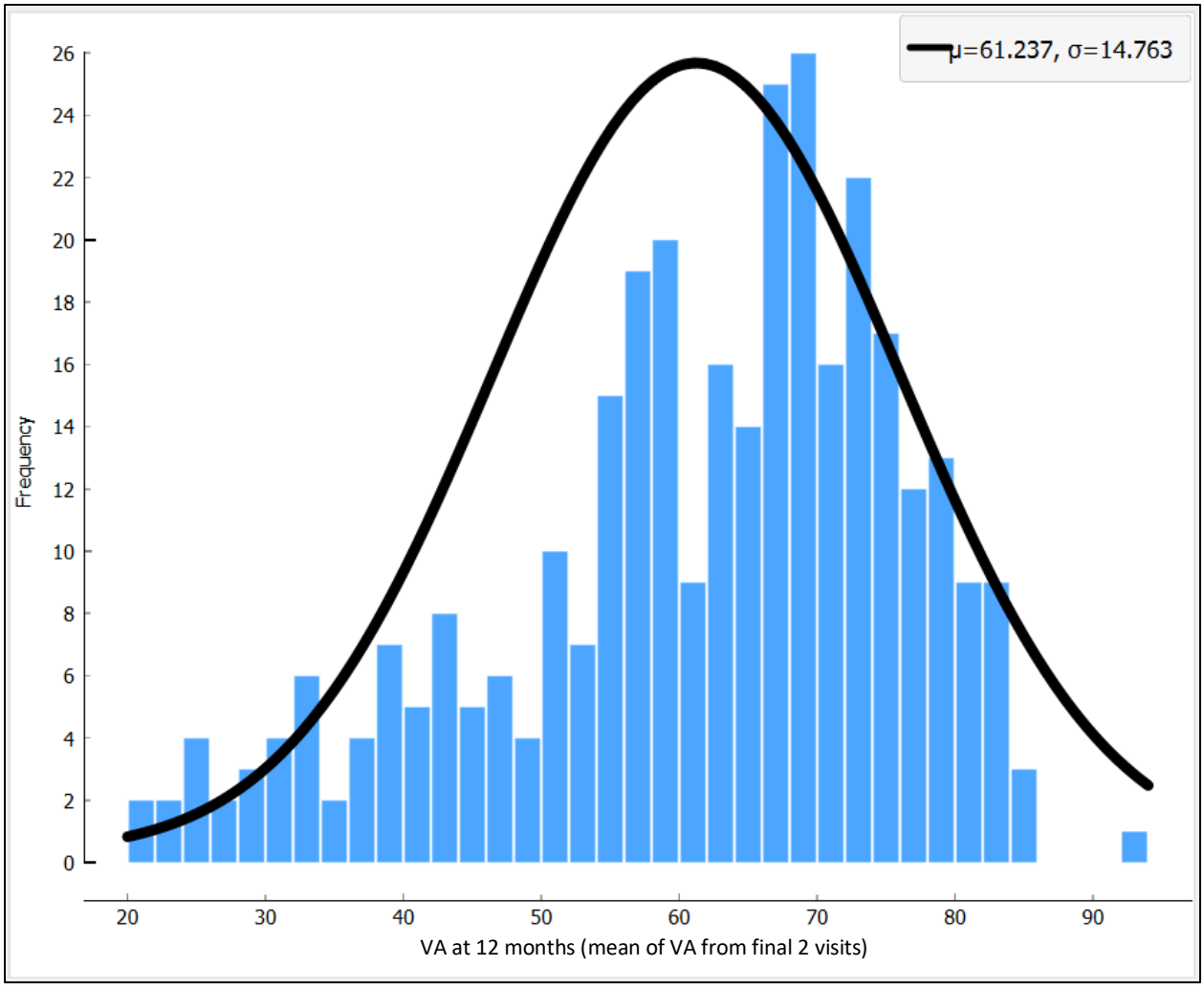


*Figure 7.11: Distribution of VA at 12 months (mean of VA from final 2 visits) (letter score)*

## 7.4 Change in visual acuity at 12 months from baseline

Visual acuity, recorded in letter score format, was available from baseline visits and at 12 months for all study eyes. Subtracting the two measures yielded the change in VA over the initial 12 months of management of those treated for nAMD. The 12 month VA change formed a slightly left skewed distribution (Figure 7.12) around a mean gain of 1.16 letters with a maximum gain of 37 letters and greatest loss found to be 49 letters (Table 7.18).

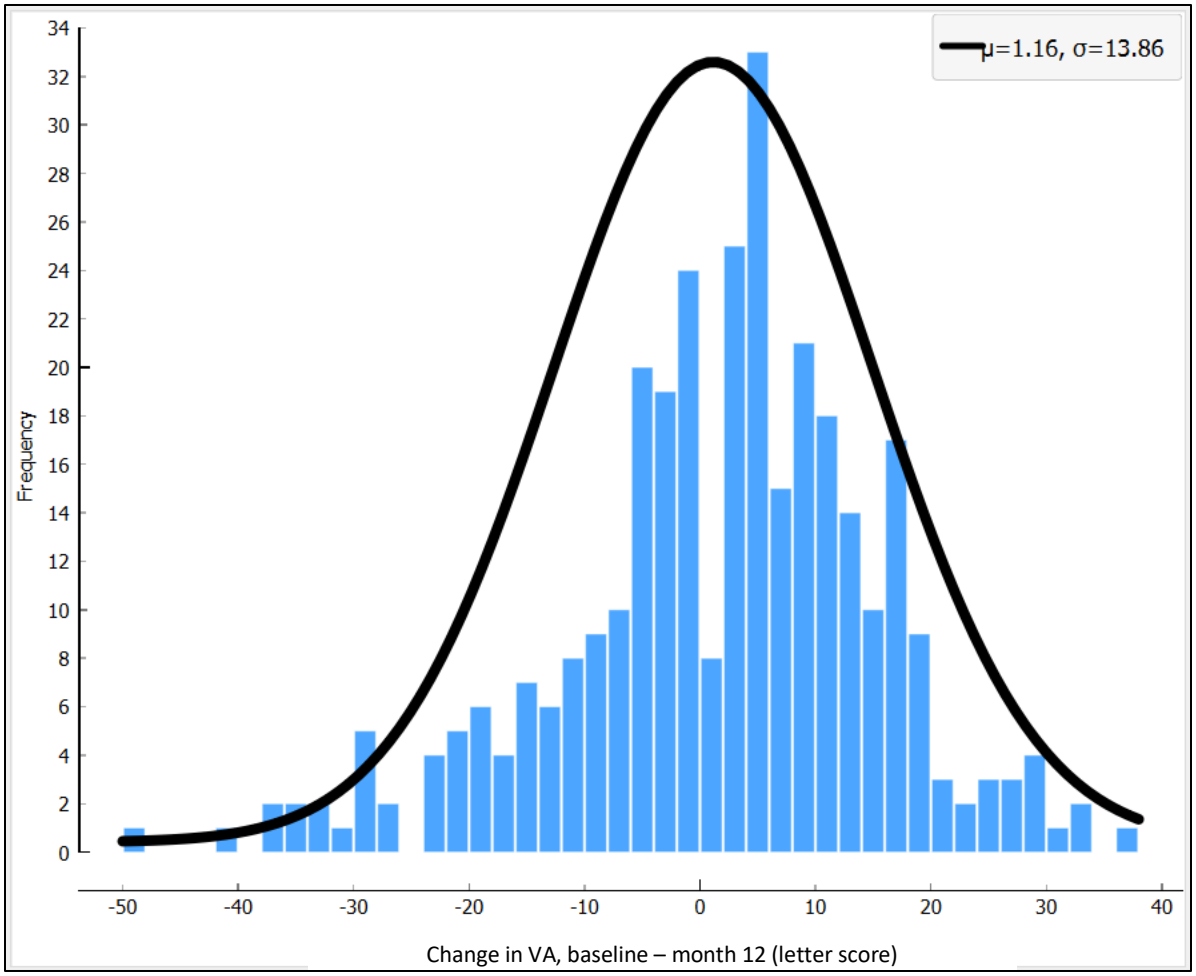


*Figure 7.12: Distribution of change in VA, baseline – month 12*

| Distribution | Mean | Mode | Median | Dispersion | Standard deviation | Minimum | Maximum |
|---|---|---|---|---|---|---|---|
| Change in VA, baseline – month 12 (letter score) | 1.16 | 5 | 3 | 11.99 | 13.86 | -49 | 37 |

*Table 7.18: Change in VA, baseline – month 12, summary statistics*

Change in VA was also sorted into two categories (Table 7.19 and Figure 7.13), those that did not lose or indeed gained VA (change ≥0 letters) and eyes that lost any degree of VA (change ≤-1 letters).

| Categories (VA) | Gained | Lost |
|---|---|---|
| VA change (letter score) | ≥0 | ≤-1 |
| Instances | 189 | 138 |

*Table 7.19: Categories of change in VA, baseline – month 12 and instances per group*

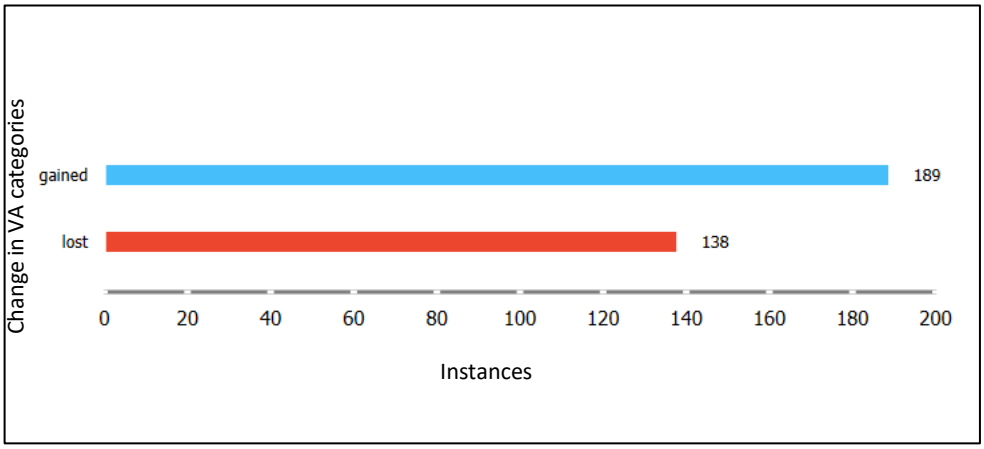


*Figure 7.13: Histogram of instances within two categories of change in VA, baseline – month 12*

### 7.4.1 Classification analyses: Change in VA, baseline - month 12 (categories: VA gained, lost)

The following classification analyses investigated the devised feature groups in relation to the change in visual acuity over 12 months within the classes VA gained or lost. The displayed results were averaged by ODM over the two groups. The results for each category were however viewed individually and if a significant correlation was identified or if the model behaviour was notably improved compared to the averaged results, such findings were reported.

#### 7.4.1.1 Feature group 'Demographic & qualitative'

The feature group 'Demographic & qualitative' was considered in relation to Change in VA, baseline - month 12.

Target: Change in VA, baseline - month 12 (categories: VA gained, lost)

Feature group: Demographic & qualitative

- Ethnicity
- Laterality
- Age At First Injection
- Sex
- Anti-VEGF drug type
- Interval 1st to 3rd injection
- Fellow eye activity

#### 7.4.1.1.1 ODM modelling

- Removal of outlying data in this series improved modelling accuracy to a level of significance (Table 7.20) with all learners except those based on Naïve Bayes, logistic regression and SVM returning adequate levels of performance across all indicators.
- The gradient boosting model displayed the highest accuracy however the confusion matrix for the model (Figure 7.14) continued to show a significant number of misclassifications.
- Sub-analysis of the N1 group showed improved accuracy for several models after removing outliers, with kNN showing the highest accuracy (table 7.21).
- The confusion matrix of the kNN based model (Figure 7.15) demonstrated the improved sensitivity of the model but the specificity remined relatively low.

| Model | AUC | CA | F1 | Precision | Recall | MCC | Specificity |
|---|---|---|---|---|---|---|---|
| Gradient Boosting | 0.60 | 0.57 | 0.57 | 0.56 | 0.57 | 0.11 | 0.53 |
| AdaBoost | 0.60 | 0.56 | 0.56 | 0.55 | 0.56 | 0.08 | 0.52 |
| Neural Network | 0.59 | 0.60 | 0.60 | 0.59 | 0.60 | 0.17 | 0.56 |
| kNN | 0.58 | 0.58 | 0.57 | 0.57 | 0.58 | 0.12 | 0.54 |
| Random Forest | 0.57 | 0.59 | 0.58 | 0.58 | 0.59 | 0.14 | 0.55 |
| Tree | 0.56 | 0.58 | 0.58 | 0.58 | 0.58 | 0.13 | 0.55 |
| Naïve Bayes | 0.55 | 0.56 | 0.54 | 0.54 | 0.56 | 0.06 | 0.49 |
| Logistic Regression | 0.55 | 0.55 | 0.51 | 0.52 | 0.55 | 0.01 | 0.46 |
| SVM | 0.52 | 0.55 | 0.54 | 0.54 | 0.55 | 0.05 | 0.50 |

*Table 7.20: Classification model performance with outliers removed of dataset of 'Demographic & qualitative' group features for target 'Change in VA, baseline - month 12 (categories: VA gained, lost)'*

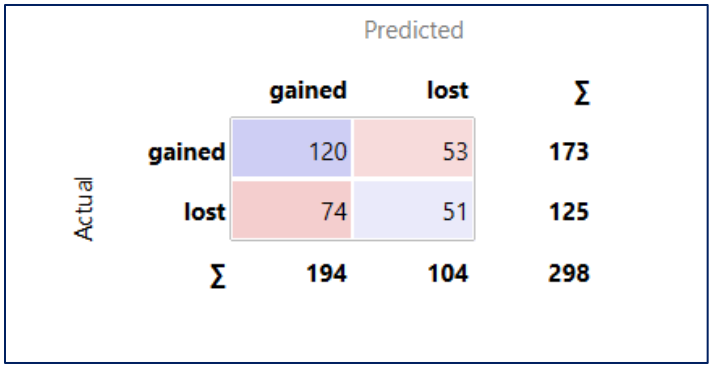


*Figure 7.14: Confusion matrix for gradient boosting classification model predictions for dataset with outliers removed for 'Demographic & qualitative' group features for target 'Change in VA, baseline - month 12 (categories: VA gained, lost)'*

| Model | AUC | CA | F1 | Precision | Recall | MCC | Specificity |
|---|---|---|---|---|---|---|---|
| kNN | 0.65 | 0.63 | 0.63 | 0.63 | 0.63 | 0.20 | 0.56 |
| Neural Network | 0.61 | 0.66 | 0.65 | 0.64 | 0.66 | 0.22 | 0.55 |
| Tree | 0.60 | 0.64 | 0.63 | 0.63 | 0.64 | 0.19 | 0.53 |
| Random Forest | 0.58 | 0.64 | 0.64 | 0.63 | 0.64 | 0.20 | 0.54 |
| AdaBoost | 0.57 | 0.60 | 0.59 | 0.59 | 0.60 | 0.10 | 0.51 |

*Table 7.21: Classification models demonstrating adequate level of performance for N1 filtered dataset with outliers removed of dataset of 'Demographic & qualitative' group features for target 'Change in VA, baseline - month 12 (categories: VA gained, lost)'*

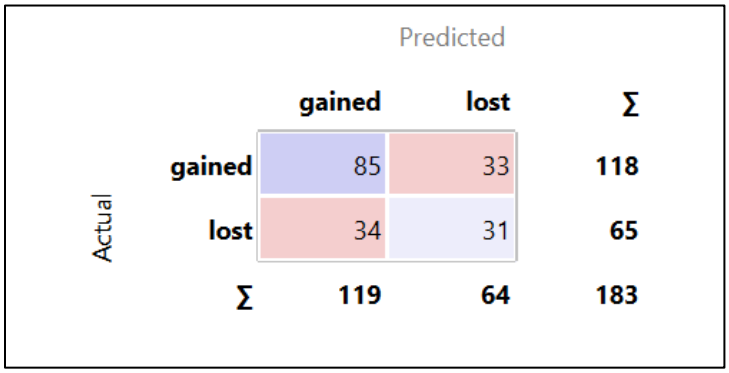


*Figure 7.15: Confusion matrix for kNN classification model predictions for N1 filtered dataset with outliers removed for 'Demographic & qualitative' group features for target 'Change in VA, baseline - month 12 (categories: VA gained, lost)'*

#### 7.4.1.2 Feature group 'VA'

The feature group 'VA' was considered in relation to Change in VA, baseline - month 12.

Target: Change in VA, baseline - month 12 (categories: VA gained, lost)

Feature group: VA

- VA baseline visit (V0)
- VA fellow eye (V0)
- VA post loading (VP)
- VA mean of 2 visits immediately post loading

##### 7.4.1.2.1 ODM modelling

- Removal of outlying data in this series improved modelling accuracy (Table 7.22) with all learners returning adequate levels of performance across all indicators.
- The model based on logistic regression displayed the highest levels of accuracy however confusion matrix for the model (Figure 7.16) did continue to show a significant number of misclassifications.
- Feature ranking scores found baseline VA of the treated eye to be the most influential feature (Table 7.23) with chi-squared scores indicating significance at the 0.05 α level and the other indicators being more elevated for baseline VA that the other attributes.
- Sub-analysis of the N1 group after outliers were removed showed improved accuracy for all models with logistic regression learner in achieving an AUC of 0.86 suggesting a relatively high level of predictive ability (Table 7.24).
- The confusion matrix for the logistic regression model however (Figure 7.17) did continue to show a significant number of misclassifications thus again questioning the model application.

| Model | AUC | CA | F1 | Precision | Recall | MCC | Specificity |
|---|---|---|---|---|---|---|---|
| Logistic Regression | 0.82 | 0.74 | 0.74 | 0.74 | 0.74 | 0.46 | 0.72 |
| Neural Network | 0.81 | 0.72 | 0.72 | 0.72 | 0.72 | 0.42 | 0.70 |
| SVM | 0.79 | 0.70 | 0.70 | 0.70 | 0.70 | 0.38 | 0.68 |
| Gradient Boosting | 0.73 | 0.66 | 0.66 | 0.66 | 0.66 | 0.30 | 0.63 |
| kNN | 0.70 | 0.64 | 0.64 | 0.64 | 0.64 | 0.26 | 0.61 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Random Forest | 0.69 | 0.63 | 0.63 | 0.63 | 0.63 | 0.23 | 0.59 |
| Tree | 0.68 | 0.64 | 0.63 | 0.64 | 0.64 | 0.25 | 0.59 |
| Naïve Bayes | 0.65 | 0.64 | 0.62 | 0.63 | 0.64 | 0.23 | 0.57 |
| AdaBoost | 0.59 | 0.60 | 0.60 | 0.60 | 0.60 | 0.18 | 0.58 |

*Table 7.22: Classification model performance with outliers removed of dataset of 'VA' group features for target 'Change in VA, baseline - month 12 (categories: VA gained, lost)'*

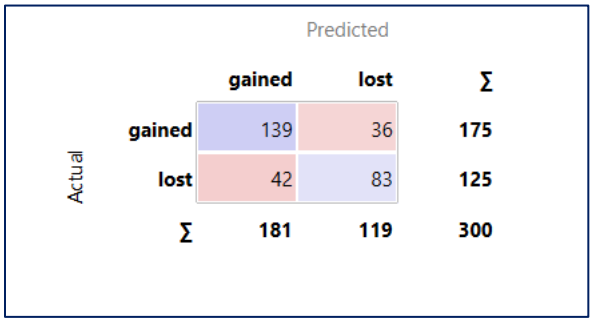


Figure 7.16: Confusion matrix for logistic regression classification model predictions for dataset with outliers removed for 'VA' group features for target 'Change in VA, baseline - month 12 (categories: VA gained, lost)'

| Feature | Info. gain | Gain ratio | Gini | ANOVA | $\chi^2$ | ReliefF | FCBF |
|---|---|---|---|---|---|---|---|
| VA baseline visit (V0) | 0.061 | 0.030 | 0.041 | 34.510 | 22.851 | 0.032 | 0.043 |
| VA fellow eye (V0) | 0.021 | 0.011 | 0.014 | 4.250 | 7.297 | 0.008 | 0.000 |
| VA mean initial 2 visits post loading | 0.008 | 0.004 | 0.006 | 1.421 | 1.776 | 0.005 | 0.000 |
| VA post loading (VP) | 0.008 | 0.004 | 0.006 | 0.525 | 0.227 | 0.005 | 0.000 |

*Table 7.23: Feature ranking in classification analyses of total dataset of 'VA' group features for target 'Change in VA, baseline - month 12 (categories: VA gained, lost)'*

| Model | AUC | | CA | F1 | Precision | Recall | MCC |
|---|---|---|---|---|---|---|---|
| Logistic Regression | 0.86 | 0.77 | 0.76 | 0.76 | 0.77 | 0.49 | 0.72 |
| Neural Network | 0.84 | 0.76 | 0.76 | 0.76 | 0.76 | 0.48 | 0.71 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| SVM | 0.80 | 0.73 | 0.72 | 0.73 | 0.73 | 0.41 | 0.64 |
| Gradient Boosting | 0.73 | 0.66 | 0.66 | 0.66 | 0.66 | 0.26 | 0.60 |
| kNN | 0.70 | 0.63 | 0.62 | 0.62 | 0.63 | 0.19 | 0.55 |
| Random Forest | 0.70 | 0.65 | 0.65 | 0.65 | 0.65 | 0.24 | 0.59 |
| Naïve Bayes | 0.68 | 0.63 | 0.61 | 0.61 | 0.63 | 0.16 | 0.52 |
| Tree | 0.66 | 0.66 | 0.64 | 0.64 | 0.66 | 0.23 | 0.56 |
| AdaBoost | 0.63 | 0.66 | 0.66 | 0.66 | 0.66 | 0.27 | 0.61 |

*Table 7.24: Classification model performance for N1 filtered dataset with outliers removed of dataset of 'VA' group features for target 'Change in VA, baseline - month 12 (categories: VA gained, lost)'*

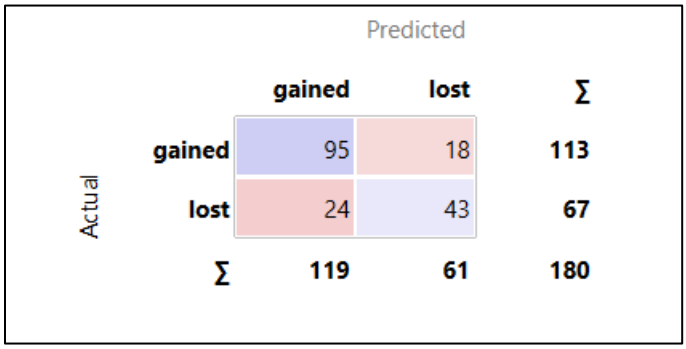


*Figure 7.17: Confusion matrix for logistic regression classification model predictions for N1 filtered dataset with outliers removed for 'VA' group features for target 'Change in VA, baseline - month 12 (categories: VA gained, lost)'*

#### 7.4.1.3 Feature group 'VA_st dev'

The feature group 'VA_st dev' was considered in relation to Change in VA, baseline - month 12.

Target: Change in VA, baseline - month 12 (categories: VA gained, lost)

Feature group: VA_st dev

- VA baseline visit (V0)
- VA fellow eye (V0)
- VA post loading (VP)
- VA mean of 2 visits immediately post loading
- Standard deviation of VA mean, post loading -12 months (VP-V12)

7.4.1.3.1 ODM modelling

- Removal of outlying data in this series improved modelling accuracy to a level of significance with all learners returning adequate levels of performance across all indicators (Table 7.25).
- The Neural Network based model displayed the highest levels of accuracy however the confusion matrix for the model (Figure 7.18) continued to show a significant number of misclassifications.
- Feature ranking scores found baseline VA of the treated eye and the standard deviation of VA mean, post loading -12 months, to be the most influential features (Table 7.26) with chi-squared scores indicating significance at the 0.05 α level.

| Model | AUC | CA | F1 | Precision | Recall | MCC | Specificity |
|---|---|---|---|---|---|---|---|
| Neural Network | 0.88 | 0.77 | 0.77 | 0.77 | 0.77 | 0.53 | 0.75 |
| Logistic Regression | 0.86 | 0.78 | 0.78 | 0.78 | 0.78 | 0.55 | 0.76 |
| SVM | 0.85 | 0.75 | 0.75 | 0.75 | 0.75 | 0.49 | 0.73 |
| Gradient Boosting | 0.78 | 0.70 | 0.70 | 0.70 | 0.70 | 0.38 | 0.67 |
| Random Forest | 0.74 | 0.68 | 0.68 | 0.68 | 0.68 | 0.34 | 0.65 |
| kNN | 0.74 | 0.68 | 0.68 | 0.68 | 0.68 | 0.34 | 0.64 |
| Naïve Bayes | 0.71 | 0.63 | 0.62 | 0.63 | 0.63 | 0.22 | 0.58 |
| Tree | 0.65 | 0.66 | 0.66 | 0.66 | 0.66 | 0.29 | 0.63 |
| AdaBoost | 0.63 | 0.64 | 0.64 | 0.64 | 0.64 | 0.25 | 0.61 |

*Table 7.25: Classification model performance with outliers removed of dataset of 'VA_st dev' group features for target 'Change in VA, baseline - month 12 (categories: VA gained, lost)'*

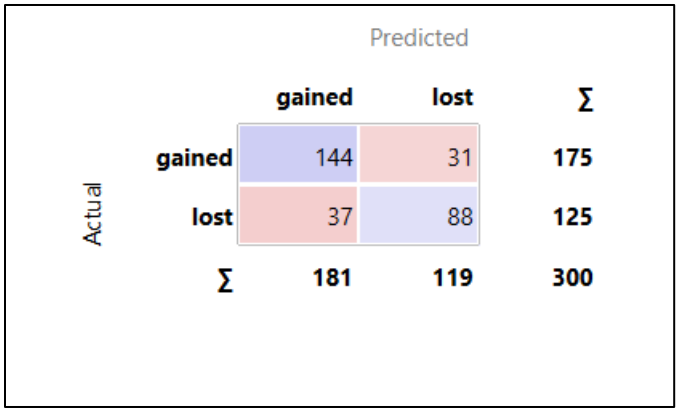


*Figure 7.18: Confusion matrix of neural network classification model predictions, with outliers removed, for 'VA_st dev' group features for target 'Change in VA, baseline - month 12 (categories: VA gained, lost)'*

| Feature | Info. gain | Gain ratio | Gini | ANOVA | $\chi^2$ | ReliefF | FCBF |
|---|---|---|---|---|---|---|---|
| VA baseline visit (V0) | 0.061 | 0.030 | 0.041 | 34.510 | 22.851 | 0.022 | 0.043 |
| Standard deviation of VA mean, post loading -12 months (VP-V12) | 0.061 | 0.030 | 0.041 | 28.966 | 21.094 | 0.026 | 0.042 |
| VA fellow eye (V0) | 0.021 | 0.011 | 0.014 | 4.250 | 7.297 | -0.008 | 0.000 |
| VA mean initial 2 visits post loading | 0.008 | 0.004 | 0.006 | 1.421 | 1.776 | 0.008 | 0.000 |
| VA post loading (VP) | 0.008 | 0.004 | 0.006 | 0.525 | 0.227 | 0.001 | 0.000 |

*Table 7.26: Feature ranking in classification analyses of total dataset of 'VA_st dev' group features for target 'Change in VA, baseline - month 12 (categories: VA gained, lost)'*

#### 7.4.1.4 Feature group 'V0_OCT'

The feature group 'V0_OCT' was considered in relation to Change in VA, baseline - month 12 (categories: VA gained, lost)

Target: Change in VA, baseline - month 12 (categories: VA gained, lost)

Feature group: V0_OCT

- 40 HEYEX OCT inputs from baseline visit (V0)

7.4.1.4.1 ODM modelling

- Modelling accuracy improved significantly on removing outliers in this analysis with all learners returning adequate levels of performance across all indicators (Table 7.27).
- The model based on Naïve Bayes displayed the highest levels of accuracy however confusion matrix for the model (Figure 7.19) did continue to show a significant number of misclassifications.

| Model | AUC | CA | F1 | Precision | Recall | MCC | Specificity |
|---|---|---|---|---|---|---|---|
| Naïve Bayes | 0.62 | 0.60 | 0.60 | 0.61 | 0.60 | 0.20 | 0.60 |
| SVM | 0.60 | 0.58 | 0.58 | 0.59 | 0.58 | 0.17 | 0.59 |
| Gradient Boosting | 0.60 | 0.60 | 0.60 | 0.60 | 0.60 | 0.17 | 0.56 |
| Random Forest | 0.59 | 0.60 | 0.60 | 0.60 | 0.60 | 0.17 | 0.57 |
| Neural Network | 0.58 | 0.58 | 0.58 | 0.58 | 0.58 | 0.14 | 0.55 |
| Tree | 0.56 | 0.57 | 0.57 | 0.57 | 0.57 | 0.12 | 0.55 |
| Logistic Regression | 0.55 | 0.55 | 0.54 | 0.54 | 0.55 | 0.06 | 0.51 |
| kNN | 0.54 | 0.55 | 0.55 | 0.55 | 0.55 | 0.08 | 0.53 |
| AdaBoost | 0.52 | 0.53 | 0.53 | 0.53 | 0.53 | 0.04 | 0.51 |

*Table 7.27: Classification model performance with outliers removed of dataset of 'V0_OCT' group features for target 'Change in VA, baseline - month 12 (categories: VA gained, lost)'*

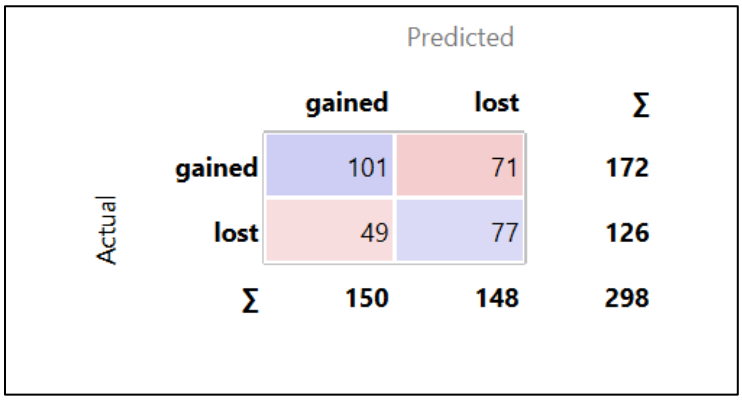


*Figure 7.19: Confusion matrix for Naïve Bayes classification model predictions for dataset with outliers removed for 'V0_OCT' group features for target 'Change in VA, baseline - month 12 (categories: VA gained, lost)'*

#### 7.4.1.5 Feature group 'VP_OCT'

The feature group 'VP_OCT' was considered in relation to Change in VA, baseline - month 12 (categories: VA gained, lost)

Target: Change in VA, baseline - month 12 (categories: VA gained, lost)

Feature group: VP_OCT

- 40 HEYEX OCT inputs from baseline visit (VP)

##### 7.4.1.5.1 ODM modelling

- Modelling accuracy improved slightly on removing outliers in this analysis with logistic regression, gradient boosting and adaptive boosting learners returning adequate levels of performance across all indicators (Table 7.28).
- The model based on logistic regression displayed the highest levels of accuracy however from the confusion matrix of the model (Figure 7.20) a high degree of misclassifications could be appreciated.

| Model | AUC | CA | F1 | Precision | Recall | MCC | Specificity |
|---|---|---|---|---|---|---|---|
| Logistic Regression | 0.53 | 0.60 | 0.57 | 0.58 | 0.60 | 0.11 | 0.50 |
| Naïve Bayes | 0.52 | 0.52 | 0.53 | 0.54 | 0.52 | 0.03 | 0.51 |
| AdaBoost | 0.52 | 0.52 | 0.53 | 0.53 | 0.52 | 0.03 | 0.51 |

*Table 7.28: Logistic Regression, Naïve Bayes and AdaBoost classification model performance with outliers removed of dataset of 'VP_OCT' group features for target 'Change in VA, baseline - month 12 (categories: VA gained, lost)'*

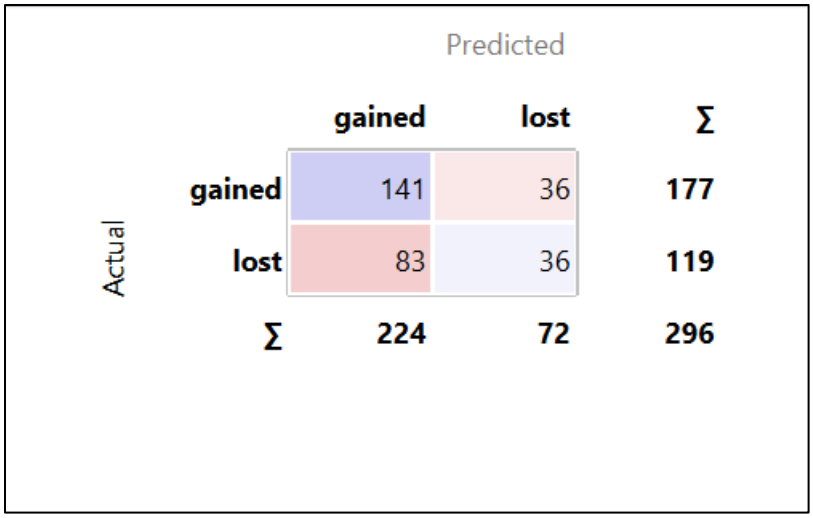


*Figure 7.20: Confusion matrix for logistic regression classification model predictions for dataset with outliers removed for 'VP_OCT' group features for target 'Change in VA, baseline - month 12 (categories: VA gained, lost)'*

#### 7.4.1.6 Feature group 'V0_OCTANE'

The feature group 'V0_OCTANE' was considered in relation to Change in VA, baseline - month 12 (categories: VA gained, lost)

Target: Change in VA, baseline - month 12 (categories: VA gained, lost)

Feature group: V0_OCTANE

- 12 OCTANE OCT inputs from baseline visit (V0)

##### 7.4.1.6.1 ODM modelling

- The Gradient Boosting model showed the highest accuracy among the models that reached significance across all metrics, but with a poor level of prognostication (Table 7.29) as can be appreciated from the misclassifications within the confusion matrix (Figure 7.21).

| Model | AUC | CA | F1 | Precision | Recall | MCC | Specificity |
|---|---|---|---|---|---|---|---|
| Gradient Boosting | 0.55 | 0.55 | 0.55 | 0.56 | 0.55 | 0.10 | 0.55 |
| Naïve Bayes | 0.55 | 0.53 | 0.52 | 0.57 | 0.53 | 0.11 | 0.58 |
| AdaBoost | 0.55 | 0.55 | 0.55 | 0.56 | 0.55 | 0.10 | 0.55 |
| Tree | 0.55 | 0.55 | 0.55 | 0.55 | 0.55 | 0.08 | 0.52 |
| Random Forest | 0.53 | 0.53 | 0.53 | 0.53 | 0.53 | 0.03 | 0.50 |

*Table 7.29: Classification model performance with outliers removed of dataset of 'V0_OCTANE' group features for target 'Change in VA, baseline - month 12 (categories: VA gained, lost)'*

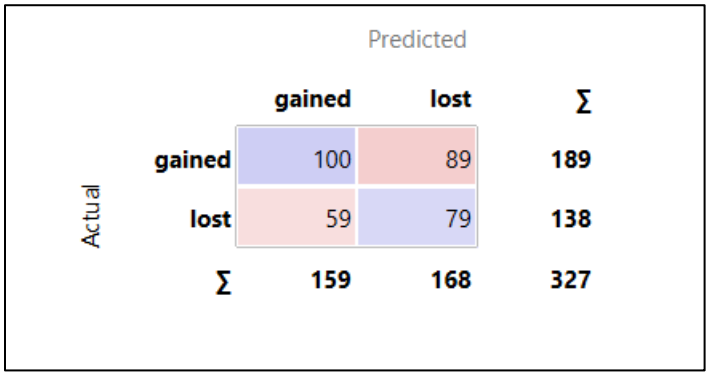


*Figure 7.21: Confusion matrix for logistic regression classification model predictions for dataset with outliers removed for 'V0_OCTANE' group features for target 'Change in VA, baseline - month 12 (categories: VA gained, lost)'*

### 7.4.2 Classification analyses: Change in VA, baseline - month 12 (categories: VA lost, maintained and gained)

Change in VA was further considered in three categories (Table 7.30 and Figure 7.22), those that lost five or more letters, those that gained 5 or more letters and those than had neither gain or lost more than 4 letters since base line measures were taken and had effectively maintained their level of VA over 12 months.

| Categories (VA) | Lost | Maintained | Gained |
|---|---|---|---|
| VA change (letter score) | ≤-5 | ≤±4 | ≥5 |
| Instances | 95 | 92 | 140 |

*Table 7.30: Categories of change in VA, baseline – month 12 and instances per group*

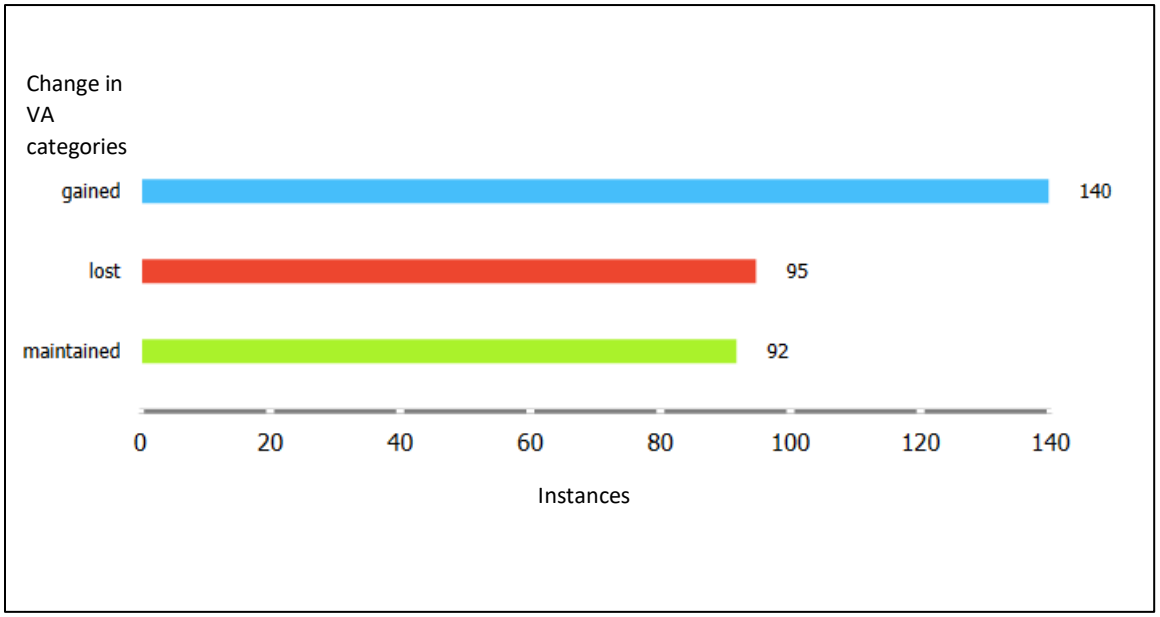


*Figure 7.22 Histogram of instances within three categories of change in VA, baseline – month 12*

#### 7.4.2.1 ODM modelling

Results were broadly similar to those reported when considering change in visual acuity as two categories (lost and gained), but with lower levels of modelling accuracy in all cases. Models able to separate eyes into the three classes, predicting whether VA was lost, gained or maintained from baseline over 12 months, could be developed to an acceptable level of accuracy in the feature groups 'VA_st dev', 'VA' and 'Demographic & qualitative' but not in the groups evaluating HEYEX or OCTANE

OCT outputs. Feature analysis again predicted baseline VA and standard deviation of VA mean, post loading -12 months, to have a strong predictive influence but in this series also determined fellow eye activity to have a somewhat weak, but statistically significant, prognostic influence. Results are fully reported in appendices 7 and 8.

### 7.4.3 Regression analyses: Change in VA, baseline - month 12

The following regression analyses attempted to predict the change in VA from baseline to 12 months as a continuous variable.

#### 7.4.3.1 Feature group 'VA'

The feature group 'VA' was considered in relation to Change in VA, baseline - month 12.

Target: Change in VA, baseline - month 12

Feature group: VA

- VA baseline visit (V0)
- VA fellow eye (V0)
- VA post loading (VP)
- VA mean of 2 visits immediately post loading

##### 7.4.3.1.1 ODM modelling

- Removing outliers significantly improved accuracy, with the best performing linear regression model returning an $R^2$ score of 0.46 (Table 7.19) and Spearman correlation of 0.712.
- The scatterplot of the linear regression based model (Figure 7.23) also suggested linearity but with a significant degree of misestimation.
- Baseline visit VA was the most influential attribute particularly based on univariate regression and Spearman correlation of -0.412 (Table 7.36). In terms of attributes which were most informative to the linear regression model however, baseline VA and the VA mean of 2 visits immediately post loading both seemed highly influential (Figure *7.24*).
- Sub-analysis of the N1 group showed improved $R^2$ (0.51) and Spearman correlation (0.747) for the Linear Regression model after removing outliers (Table 7.37).
- The scatterplot of the linear regression model again showed some misestimations but a linear relationship could be appreciated (Figure 7.25).

| Models | MSE | RMSE | MAE | $R^2$ | CVRMSE |
|---|---|---|---|---|---|
| Linear Regression | 96.57 | 9.83 | 7.09 | 0.46 | 835.17 |
| Random Forest | 125.63 | 11.21 | 8.34 | 0.29 | 952.56 |
| Gradient Boosting | 127.73 | 11.30 | 8.25 | 0.28 | 960.50 |
| SVM | 132.08 | 11.49 | 8.75 | 0.26 | 976.70 |
| kNN | 133.82 | 11.57 | 8.57 | 0.25 | 983.13 |
| AdaBoost | 134.48 | 11.60 | 8.56 | 0.24 | 985.55 |
| Tree | 209.02 | 14.46 | 10.57 | -0.18 | 1228.68 |

*Table 7.31: Regression model performance with outliers removed for total dataset of 'VA' group features for target 'Change in VA, baseline - month 12'*

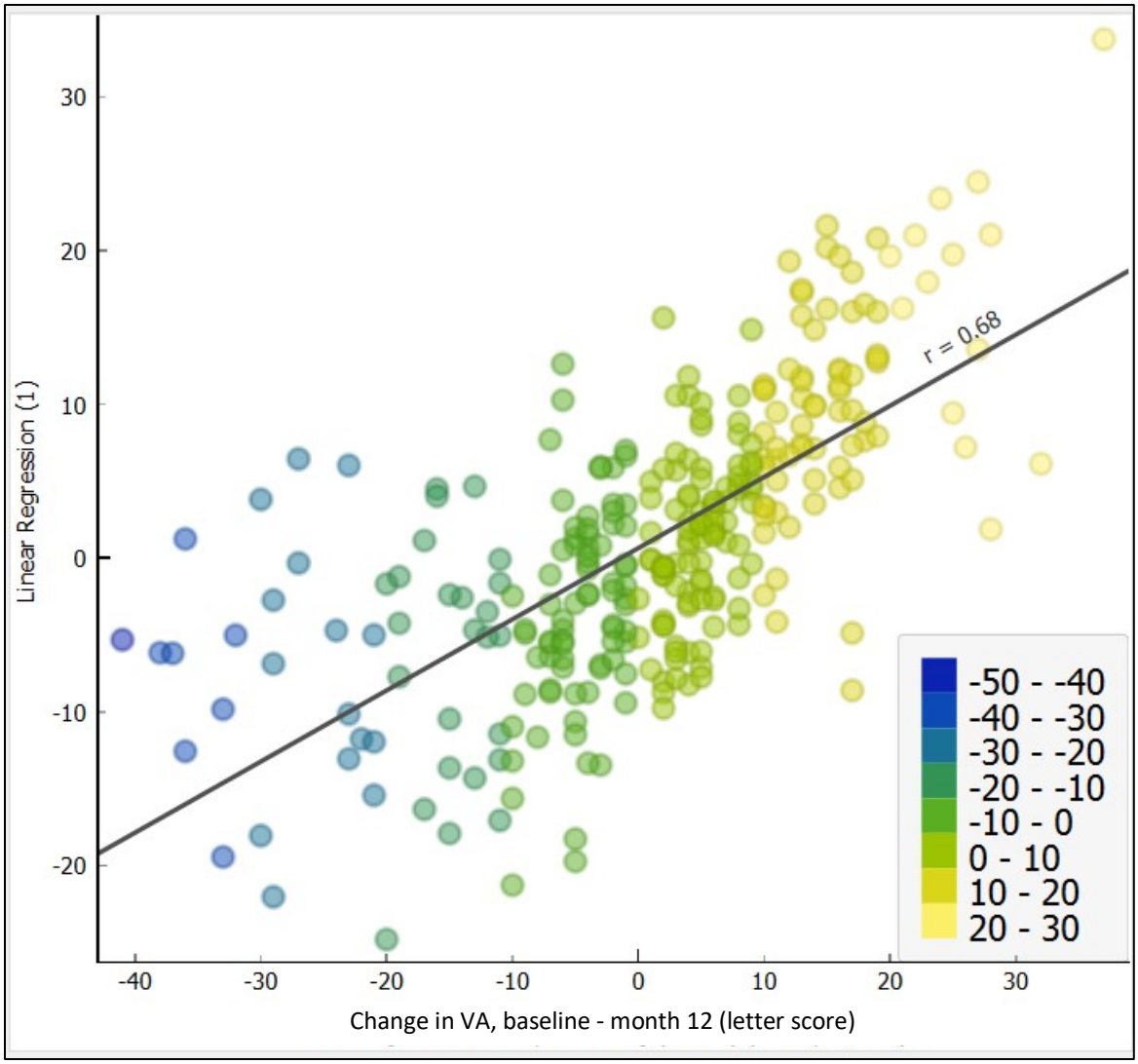


*Figure 7.23: Scatterplot of linear regression model predictions, with outliers removed, for total dataset of 'VA' group features for target 'Change in VA, baseline - month 12'*

| Feature | Univariate Regression | RReliefF | Spearman correlation |
|---|---|---|---|
| VA baseline visit (V0) | 60.685 | 0.123 | -0.412 |
| VA fellow eye (V0) | 2.947 | 0.100 | 0.162 |
| VA mean of 2 visits immediately post loading | 1.547 | 0.061 | 0.079 |
| VA post loading (VP) | 0.441 | 0.061 | 0.048 |

*Table 7.32: Feature ranking in regression analyses of total dataset of 'VA' group features for target 'Change in VA, baseline - month 12'*

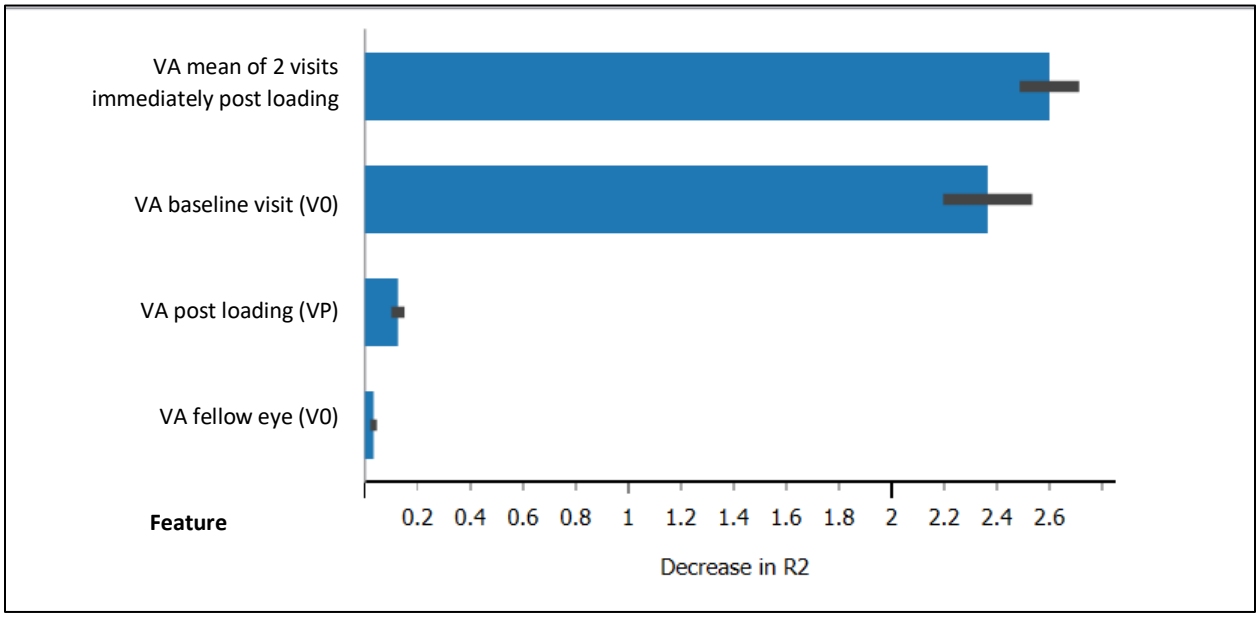


*Figure 7.24: Feature importance in linear regression model predictions, with outliers removed, for total dataset of 'VA' group features for target 'Change in VA, baseline - month 12' ranked by influence on $R^2$*

| Models | MSE | RMSE | MAE | $R^2$ | CVRMSE |
|---|---|---|---|---|---|
| Linear Regression | 91.13 | 9.55 | 6.74 | 0.51 | 333.65 |
| SVM | 135.68 | 11.65 | 8.27 | 0.27 | 407.12 |
| Random Forest | 139.79 | 11.82 | 8.77 | 0.25 | 413.25 |
| kNN | 144.21 | 12.01 | 8.59 | 0.23 | 419.72 |
| Gradient Boosting | 153.34 | 12.38 | 9.15 | 0.18 | 432.80 |
| AdaBoost | 166.68 | 12.91 | 9.02 | 0.11 | 451.24 |
| Tree | 174.54 | 13.21 | 9.47 | 0.07 | 461.76 |

*Table 7.33: Regression model performance for N1 filtered dataset, with outliers removed, of 'VA' group features for target 'Change in VA, baseline - month 12'*

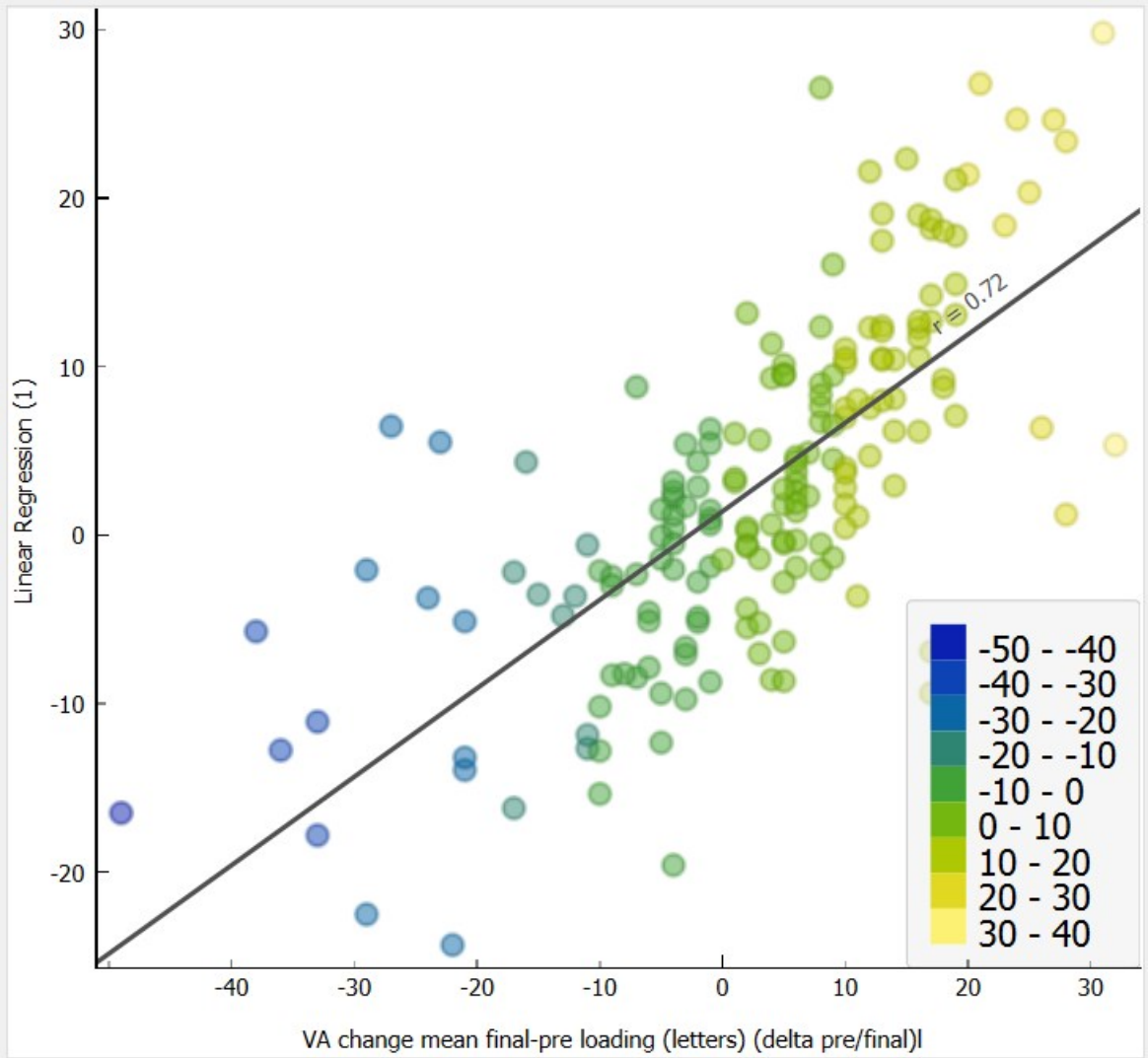


*Figure 7.25: Scatterplot of linear regression model predictions, with outliers removed, for N1 filtered dataset of 'VA' group features for target 'Change in VA, baseline - month 12'*

#### 7.4.3.2 Feature group 'VA_st dev'

The feature group 'VA_st dev' was considered in relation to Change in VA, baseline - month 12.

Target: Change in VA, baseline - month 12

Feature group: VA

- VA baseline visit (V0)
- VA fellow eye (V0)
- VA post loading (VP)
- VA mean of 2 visits immediately post loading

- Standard deviation of VA mean, post loading -12 months (VP-V12)

7.4.3.2.1 ODM modelling

- Removing outliers significantly improved linear regression modelling accuracy with $R^2$ = 0.57 (Table 7.34) and Spearman correlation of 0.761.
- The scatterplot of the linear regression based model (Figure 7.26) also showed linearity but with a moderate degree of misestimation persisting.
- Baseline visit VA and standard deviation of VA mean, post loading -12 months, were most influential attributes based on univariate regression and Spearman correlation (table 7.35). In terms of attributes which were most informative to the linear regression model however, baseline VA and the VA mean of 2 visits immediately post loading both were most influential (Figure *7.27*).

| Models | MSE | RMSE | MAE | $R^2$ | CVRMSE |
|---|---|---|---|---|---|
| Linear Regression | 74.62 | 8.64 | 6.19 | 0.57 | 702.32 |

*Table 7.34: Linear regression model performance with outliers removed for total dataset of 'VA_st dev' group features for target 'Change in VA, baseline - month 12'*

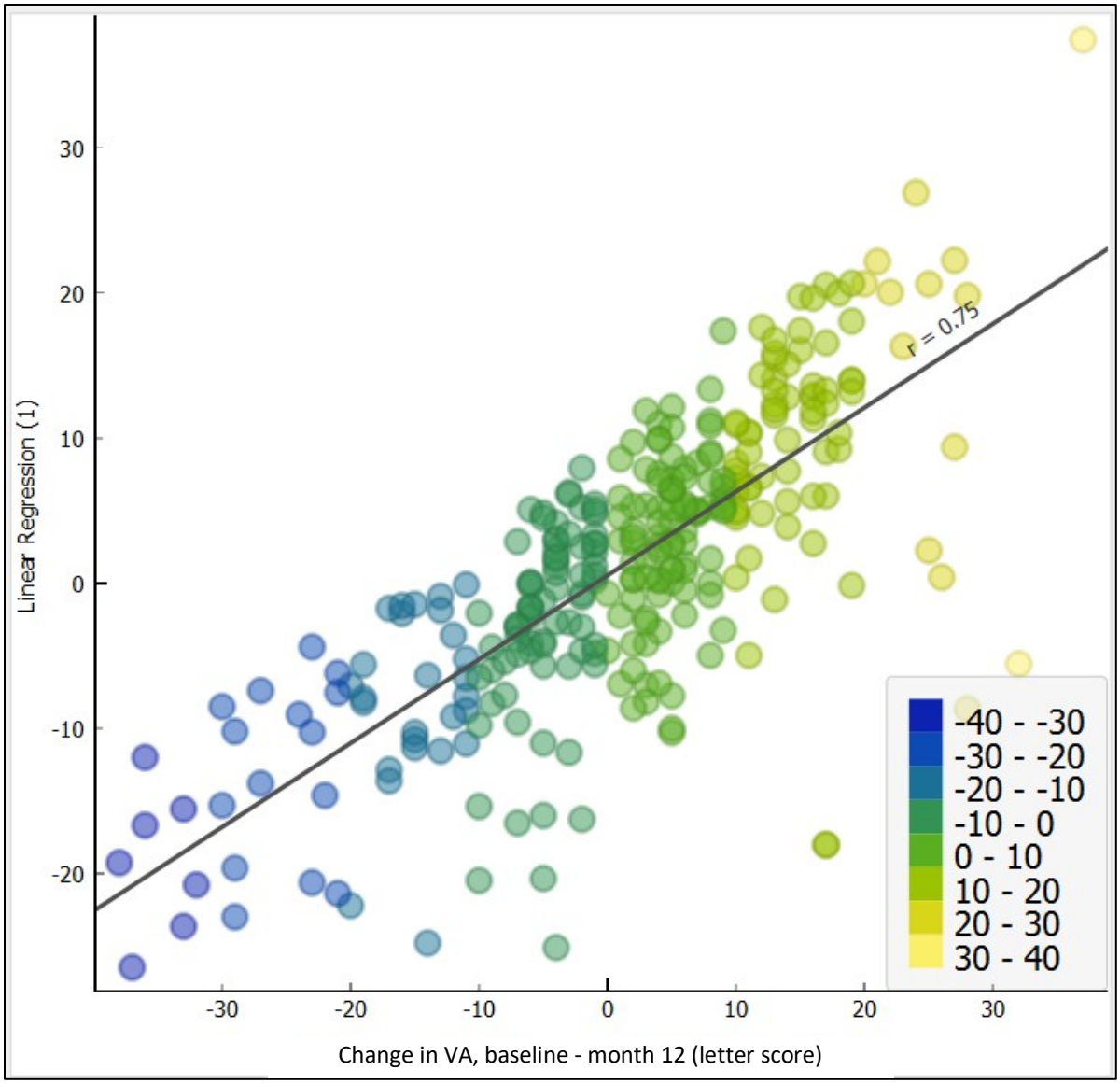


*Figure 7.26: Scatterplot of linear regression model predictions, with outliers removed, for total dataset of 'VA_st dev' group features for target 'Change in VA, baseline - month 12'*

| Feature | Univariate Regression | RReliefF | Spearman correlation |
|---|---|---|---|
| Standard deviation of VA mean, post loading -12 months (VP-V12) | 68.979 | 0.107 | -0.418 |
| VA baseline visit (V0) | 60.685 | 0.098 | -0.397 |
| VA fellow eye (V0) | 2.947 | 0.094 | 0.095 |

| | | | |
|---|---|---|---|
| VA mean of 2 visits immediately post loading | 1.547 | 0.064 | 0.069 |
| VA post loading (VP) | 0.441 | 0.065 | 0.037 |

*Table 7.35: Feature ranking in regression analyses of total dataset of 'VA_st dev' group features for target 'Change in VA, baseline - month 12'*

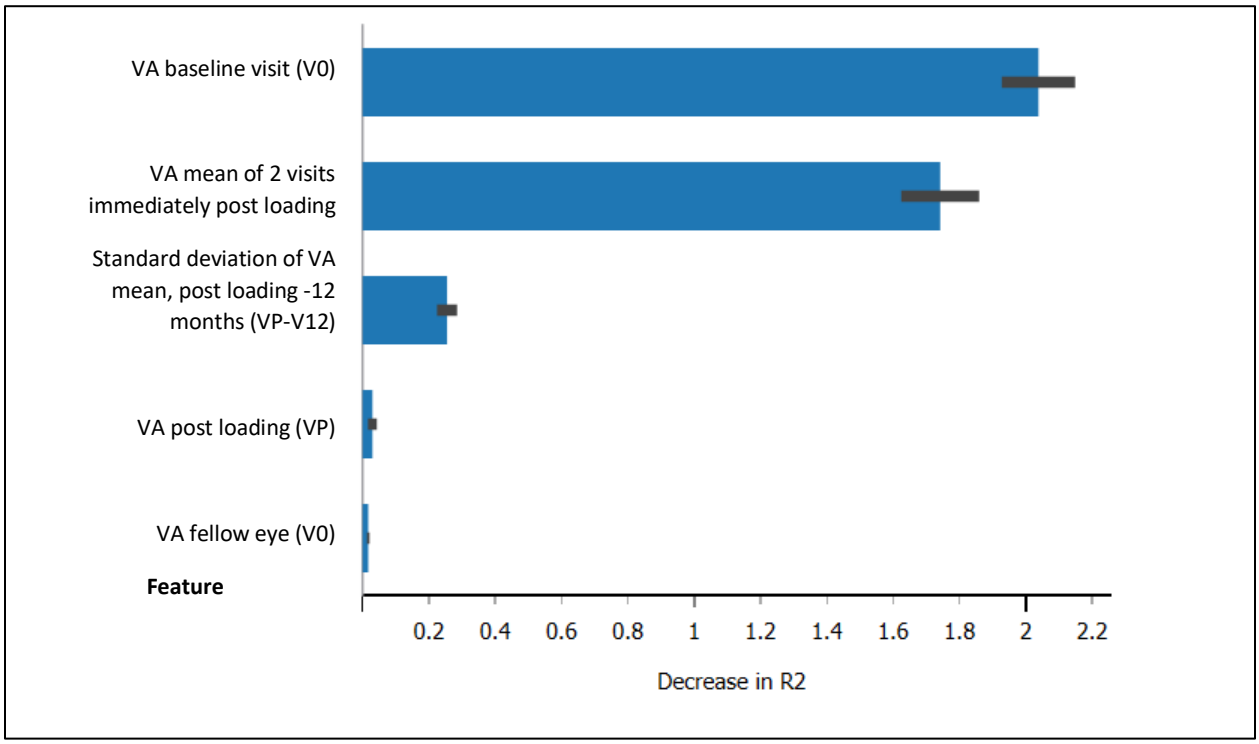


*Figure 7.27: Feature importance in linear regression model predictions, with outliers removed, for total dataset of 'VA_st dev' group features for target 'Change in VA, baseline - month 12' ranked by influence on $R^2$*

## 7.5 Visual acuity trend over 12 months

The trend in change in vision was also investigated in terms of whether this could be predicted. In doing so regression lines were plotted through letter score measures of VA obtained over the first year of visits of those with nAMD enrolled in the study (Figure 3.6). The slope of these lines of best fit were then added to the data pool for investigation. The slopes appeared normally distributed around a mean of -0.027 (standard deviation 1.052).

| Distribution | Mean | Mode | Median | Dispersion | Standard deviation | Minimum | Maximum |
|---|---|---|---|---|---|---|---|
| Change in VA trend (trend line slope) | -0.027 | 0.14 | 0.09 | -39.461 | 1.052 | -3.98 | 3.15 |

*Table 7.36: Year 1 VA trend (trend line slope) summary statistics*

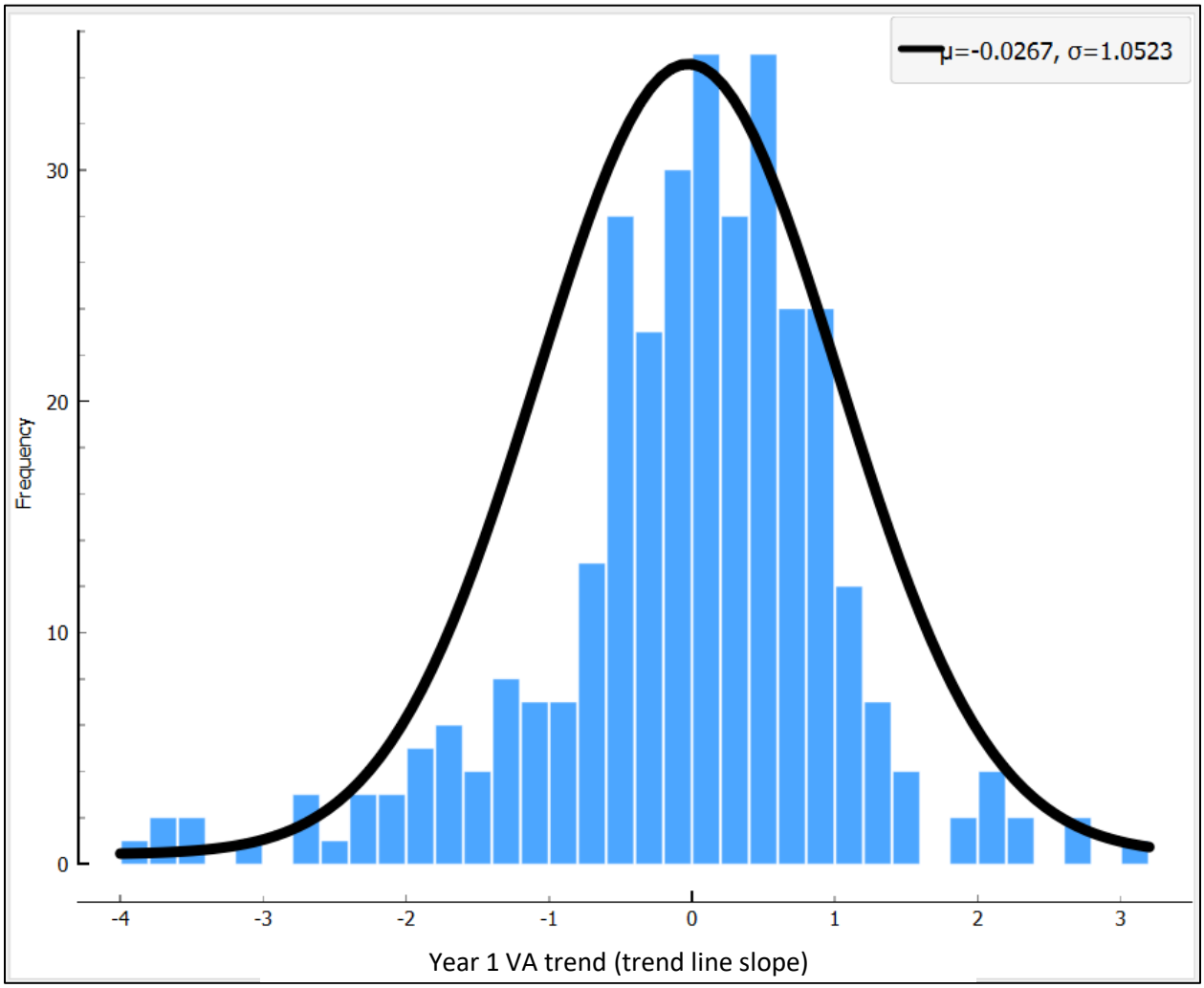


*Figure 7.28: Distribution of year 1 VA trend (trend line slope)*

As visual acuity measures gathered during the course of the study were used to determine the VA trend lines, standard deviation in VA means and compose feature groups, it was felt correlations may coincidentally be found. It was thus decided not to include feature groups developed around VA to establish associations with VA trend lines but rather use the remaining attributes as the independent

variables. A complete set of modelling and feature ranking outcomes, including those using the VA feature groups for the following series of analyses were however reported in appendices 6, 7 and 8.

### 7.5.1 Classification analyses: Year 1 VA trend (categories: gained, lost)

Categories were also formed based on the visual acuity trend line slope (Table 7.37 and Figure 7.29). The solitary eye with a neutral slope of 0.00 was placed in the gained class. Classification modelling was then performed on these groups.

| Categories | Gained | Lost |
|---|---|---|
| Slope of trend line | ≥ 0 | < 0 |
| Instances | 180 | 147 |

*Table 7.37: Categories of Year 1 VA trend and instances per group*

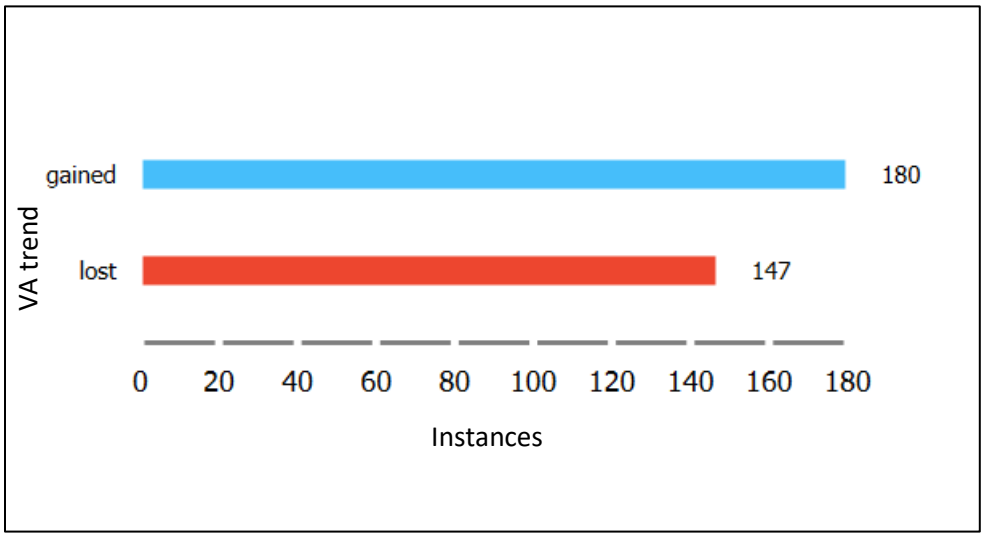


*Figure 7.29: Histogram of instances within Year 1 VA trend (categories: gained, lost)*

#### 7.5.1.1 Feature group 'Demographic & qualitative'

The feature group 'Demographic & qualitative' was considered in relation to Year 1 VA trend (categories: gained, lost).

Target: Year 1 VA trend (categories: gained, lost)

Feature group: Demographic & qualitative

- Ethnicity
- Laterality
- Age At First Injection
- Sex
- Anti-VEGF drug type
- Interval 1st to 3rd injection
- Fellow eye activity

#### 7.5.1.1.1 ODM modelling

- Removing outliers improved modelling accuracy, with the decision tree model showing the highest accuracy, but with low predictive performance (Table 7.38).

| Model | AUC | CA | F1 | Precision | Recall | MCC | Specificity |
|---|---|---|---|---|---|---|---|
| Tree | 0.57 | 0.59 | 0.59 | 0.59 | 0.59 | 0.17 | 0.57 |
| AdaBoost | 0.56 | 0.56 | 0.56 | 0.56 | 0.56 | 0.12 | 0.55 |
| Gradient Boosting | 0.56 | 0.55 | 0.55 | 0.55 | 0.55 | 0.09 | 0.54 |
| Random Forest | 0.55 | 0.55 | 0.55 | 0.55 | 0.55 | 0.09 | 0.54 |
| Naïve Bayes | 0.54 | 0.54 | 0.53 | 0.53 | 0.54 | 0.06 | 0.52 |
| kNN | 0.54 | 0.52 | 0.52 | 0.52 | 0.52 | 0.03 | 0.51 |
| Neural Network | 0.52 | 0.57 | 0.57 | 0.57 | 0.57 | 0.13 | 0.56 |
| Logistic Regression | 0.52 | 0.55 | 0.52 | 0.54 | 0.55 | 0.06 | 0.51 |
| SVM | 0.48 | 0.52 | 0.51 | 0.51 | 0.52 | 0.01 | 0.50 |

*Table 7.38: Classification model performance with outliers removed of dataset of 'Demographic & qualitative' group features for target 'Year 1 VA trend (categories: gained, lost)'*

### 7.5.1.2 Feature group 'V0_OCT'

The feature group 'V0_OCT' was considered in relation to Year 1 VA trend (categories: gained, lost)

Target: Year 1 VA trend (categories: gained, lost)

Feature group: V0_OCT

- 40 HEYEX OCT inputs from baseline visit (V0)

#### 7.5.1.2.1 ODM modelling

- Removing outliers improved modelling accuracy, with the gradient boosting model showing the highest accuracy, but with poor predictive performance (Table 7.39).

| Model | AUC | CA | F1 | Precision | Recall | MCC | Specificity |
|---|---|---|---|---|---|---|---|
| Gradient Boosting | 0.60 | 0.57 | 0.57 | 0.57 | 0.57 | 0.13 | 0.55 |
| Naïve Bayes | 0.58 | 0.57 | 0.57 | 0.58 | 0.57 | 0.14 | 0.57 |
| Logistic Regression | 0.57 | 0.55 | 0.55 | 0.55 | 0.55 | 0.09 | 0.54 |
| SVM | 0.56 | 0.58 | 0.58 | 0.59 | 0.58 | 0.16 | 0.58 |
| Random Forest | 0.55 | 0.56 | 0.56 | 0.56 | 0.56 | 0.11 | 0.54 |
| AdaBoost | 0.52 | 0.53 | 0.53 | 0.53 | 0.53 | 0.05 | 0.52 |
| Neural Network | 0.51 | 0.52 | 0.52 | 0.51 | 0.52 | 0.02 | 0.50 |
| Tree | 0.51 | 0.53 | 0.52 | 0.52 | 0.53 | 0.03 | 0.50 |
| kNN | 0.49 | 0.50 | 0.50 | 0.50 | 0.50 | -0.02 | 0.48 |

*Table 7.39: Classification model performance with outliers removed of dataset of 'V0_OCT' group features for target 'Year 1 VA trend (categories: gained, lost)'*

### 7.5.1.3 Feature group 'VP_OCT'

The feature group 'VP_OCT' was considered in relation to Year 1 VA trend (categories: gained, lost)

Target: Year 1 VA trend (categories: gained, lost)

Feature group: VP_OCT

- 40 HEYEX OCT inputs from baseline visit (VP)

#### 7.5.1.3.1 ODM modelling

- Removal of outlying data in this series improved modelling accuracy to a level of significance where the algorithms based on decision trees, Naïve Bayes, gradient boosting and neural network, returned models with adequate levels of performance (Table *7.40*).
- The model based on decision trees displayed the best levels of accuracy however predictive performance in this instance was deemed as poor.

- Sub-analysis of the N1 group shows that the gradient boosting model reaches acceptable performance after removing outliers (table 7.41).
- The confusion matrix for the N1 subgroup model (Figure 7.30) however showed a significant number of misclassifications thus predictions were deemed inadequate.

| Model | AUC | CA | F1 | Precision | Recall | MCC | Specificity |
|---|---|---|---|---|---|---|---|
| Tree | 0.57 | 0.56 | 0.56 | 0.56 | 0.56 | 0.10 | 0.53 |
| Naïve Bayes | 0.54 | 0.56 | 0.57 | 0.57 | 0.56 | 0.12 | 0.56 |
| Gradient Boosting | 0.54 | 0.53 | 0.53 | 0.52 | 0.53 | 0.03 | 0.50 |
| Neural Network | 0.51 | 0.53 | 0.53 | 0.53 | 0.53 | 0.04 | 0.51 |

*Table 7.40: Decision tree, Naïve Bayes, gradient boosting and neural network classification model performance with outliers removed of dataset of 'VP_OCT' group features for target 'Year 1 VA trend (categories: gained, lost)'*

| Model | AUC | CA | F1 | Precision | Recall | MCC | Specificity |
|---|---|---|---|---|---|---|---|
| Gradient Boosting | 0.60 | 0.64 | 0.63 | 0.63 | 0.64 | 0.20 | 0.54 |
| AdaBoost | 0.56 | 0.59 | 0.59 | 0.59 | 0.59 | 0.12 | 0.53 |
| Naïve Bayes | 0.55 | 0.50 | 0.51 | 0.54 | 0.50 | 0.01 | 0.51 |
| Tree | 0.54 | 0.58 | 0.58 | 0.58 | 0.58 | 0.09 | 0.52 |

*Table 7.41: Gradient boosting, AdaBoost, Naïve Bayes and Decision tree classification model performance with outliers removed in N1 filtered dataset of 'VP_OCT' group features for target 'Year 1 VA trend (categories: gained, lost)'*

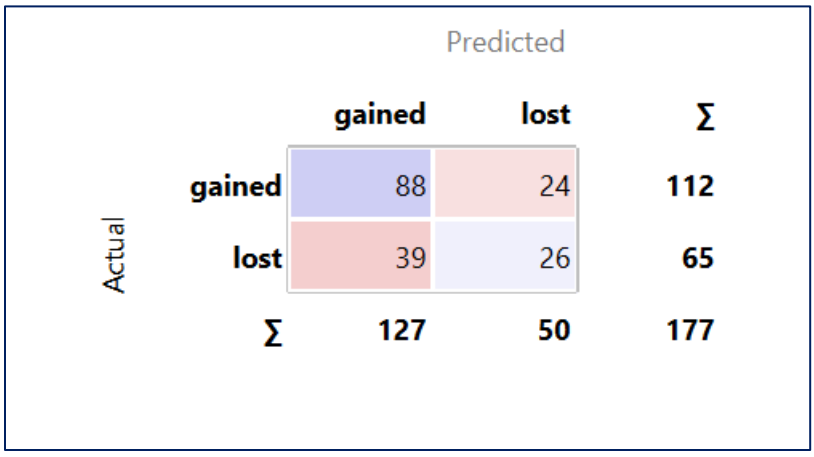


*Figure 7.30: Confusion matrix for gradient boosting classification model predictions for N1 filtered dataset with outliers removed for 'VP_OCT' group features for target 'Year 1 VA trend (categories: gained, lost)'*

#### 7.5.1.4 Feature group 'V0_OCTANE'

The feature group 'V0_OCTANE' was considered in relation to Year 1 VA trend (categories: gained, lost)

Target: Year 1 VA trend (categories: gained, lost)

Feature group: V0_OCTANE

- 12 OCTANE inputs from baseline visit (V0)

##### 7.5.1.4.1 ODM modelling

- Removal of outlying data in this series improved modelling accuracy to a level of significance where the learners based on random forests, adaptive boost and decision trees returned models with adequate levels of performance across all indicators (Table 7.42).
- The model based on random forests displayed the best levels of accuracy however in view of the relatively low scores, predictive performance in this instance was deemed as poor.

| Model | AUC | CA | F1 | Precision | Recall | MCC | Specificity |
|---|---|---|---|---|---|---|---|
| Random Forest | 0.55 | 0.55 | 0.55 | 0.56 | 0.55 | 0.12 | 0.56 |
| AdaBoost | 0.54 | 0.56 | 0.56 | 0.56 | 0.56 | 0.12 | 0.56 |
| Tree | 0.54 | 0.53 | 0.51 | 0.52 | 0.53 | 0.03 | 0.50 |

*Table 7.42: Random forests, adaptive boost and decision trees classification model performance with outliers removed of dataset of 'V0_OCTANE' group features for target 'Year 1 VA trend (categories: gained, lost)'*

#### 7.5.1.5 Feature group 'VP_OCTANE'

The feature group 'VP_OCTANE' was considered in relation to Year 1 VA trend (categories: gained, lost)

Target: Year 1 VA trend (categories: gained, lost)

Feature group: VP_OCTANE

- 12 OCTANE inputs from baseline visit (VP)

##### 7.5.1.5.1 ODM modelling

- Removal of outlying data in this series improved modelling accuracy with the neural networks model yielding the best levels of accuracy but with poor predictive performance (table 7.43).

| Model | AUC | CA | F1 | Precision | Recall | MCC | Specificity |
|---|---|---|---|---|---|---|---|
| Neural Network | 0.56 | 0.56 | 0.56 | 0.57 | 0.56 | 0.13 | 0.57 |
| Naïve Bayes | 0.55 | 0.57 | 0.50 | 0.58 | 0.57 | 0.11 | 0.50 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| AdaBoost | 0.52 | 0.55 | 0.55 | 0.56 | 0.55 | 0.11 | 0.56 |
| Random Forest | 0.51 | 0.52 | 0.52 | 0.53 | 0.52 | 0.04 | 0.52 |

*Table 7.43: Neural network, Naïve Bayes, AdaBoost and random forest classification model performance with outliers removed of dataset of 'VP_OCTANE' group features for target 'Year 1 VA trend (categories: gained, lost)'*

### 7.5.2 Classification analyses: Year 1 VA trend (categories: gained, lost, maintained)

Further categories were formed based on visual acuity trendline slope (Table 7.44). In this instance three classes were produced in an attempt to accurately predict which eyes trended towards gaining, loosing or maintaining vision.

| Categories | Gained | Lost | Maintained |
|---|---|---|---|
| Slope of trend line | ≥ 0.45 | ≤ -0.45 | > -0.44, < 0.44 |

*Table 7.44: Classifications of 3 categories of Year 1 VA trend: gained, lost and maintained*

In this series of classification analyses, no models were produced or features were identified with an adequate level of predictive ability.

### 7.5.3 Regression analyses: Year 1 VA trend

Regression analyses were also carried out in an attempt to establish any potential relationships. No models were however produced or features identified with an adequate level of predictive ability.

## 7.6 Visual acuity trend post loading

VA trendlines were also established from the first visit after the loading dose had been administered until the end of the first year of treatment. This was in order to account for the improvement that occurs on initiation of treatment of nAMD (Colquitt, 2008) and to determine if the change in vision thereafter could be predicted. The slopes of the regression lines again appeared normally distributed, this time, around a mean of -0.236 (Table 7.45 and Figure 7.31).

| Distribution | Mean | Mode | Median | Dispersion | Standard deviation | Minimum | Maximum |
|---|---|---|---|---|---|---|---|
| Year 1 VA trend post loading (trend line slope) | -0.236 | 0.13 | -0.08 | -5.06 | 1.186 | -5.06 | 4.96 |

*Table 7.45: Year 1 VA trend post loading (trend line slope) summary statistics*

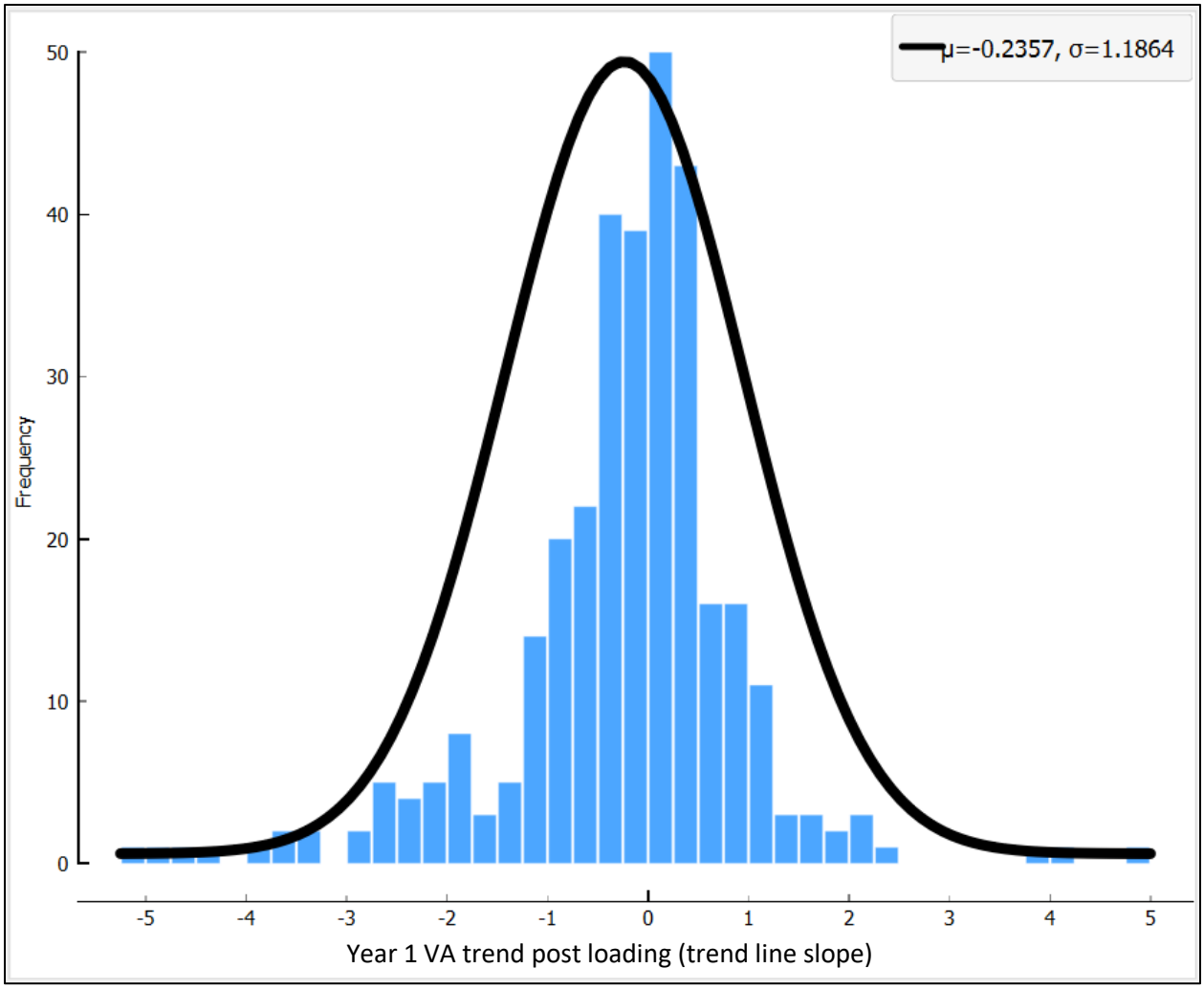


*Figure 7.31: Distribution of year 1 VA trend post loading (trend line slope)*

As was the case in the section 8.5 Year 1 VA trend analyses, visual acuity measures and standard deviation in VA means were not considered as attributes, as it was felt that relationships might inadvertently be found. A complete set of modelling and feature ranking outcomes, including those using the VA feature groups for the following series of analyses were however reported in appendices 6, 7 and 8.

### 7.6.1 Classification analyses: Year 1 VA trend post loading (categories: gained, lost)

Results were effectively in keeping with section 8.5.1 Year 1 VA trend analyses. Weak modelling relationships could be derived when considering the feature groups:

- Demographic & qualitative
- V0_OCT

- VP_OCT
- V0_OCTANE
- VP_OCTANE

In view of the relatively low accuracy scores however, predictive performance was deemed inadequate. Similarly no attributes from these analyses attained a level of significance across feature ranking metrics to suggest sufficient prognostic ability. Modelling and feature ranking outcomes are fully reported in appendices 6 and 7.

### 7.6.2 Classification analyses: Year 1 VA trend post loading (categories: gained, lost, maintained)

On considering year 1 VA trend, post loading, as three classifications, no models were produced or features were identified with an adequate level of predictive ability.

### 7.6.3 Regression analyses: Year 1 VA trend post loading

Regression analyses were also carried out in an attempt to establish any potential relationships. No models were however produced or features identified with an adequate level of predictive ability.

## 7.7 Standard deviation of VA mean, baseline - 12 months

The standard deviation of the VA mean, baseline - 12 months, was also investigated in terms of whether this could be predicted. Considering the standard deviation values from the instances, they appeared to form a right skewed distribution around a mean of 6.027 (Table 7.46 and Figure 7.32).

| Distribution | Mean | Mode | Median | Dispersion | Standard deviation | Minimum | Maximum |
|---|---|---|---|---|---|---|---|
| Standard deviation of VA mean (baseline - 12 months) | 6.027 | 2.67 | 5.08 | 0.552 | 3.325 | 0.79 | 19.56 |

*Table 7.46: Standard deviation of VA mean (baseline - 12 months) summary statistics*

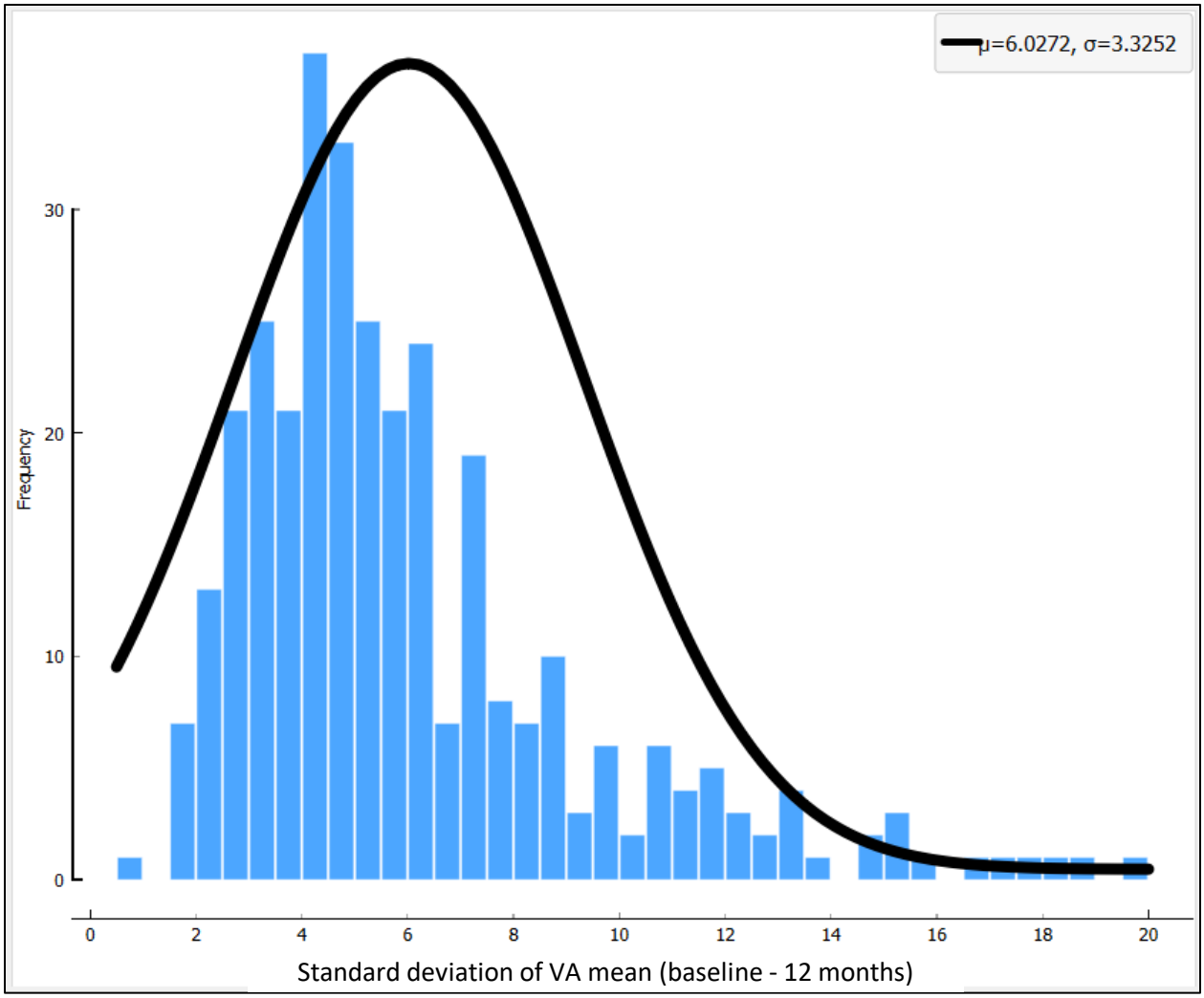


*Figure 7.32: Distribution of standard deviation of VA mean (baseline - 12 months)*

### 7.7.1 Regression analyses: Standard deviation of VA mean, baseline - 12 months

Regression analyses found no models were however produced or features identified with an adequate level of predictive ability.

## 7.8 Standard deviation of VA mean, post loading (post loading - month 12)

The standard deviation of the VA mean, post loading - 12 months, in addition to being used as an independent variable was also considered as an outcome variable. Considering the standard deviation values from the instances, they appeared to form a right skewed distribution around a mean of 5.295 (Table 7.47 and Figure 7.33).

| Distribution | Mean | Mode | Median | Dispersion | Standard deviation | Minimum | Maximum |
|---|---|---|---|---|---|---|---|
| Standard deviation of VA mean (post loading - month 12) | 5.295 | 4.00 | 4.31 | 0.645 | 3.418 | 0.41 | 20.31 |

*Table 7.47: Standard deviation of VA mean (post loading - 12 months) summary statistics*

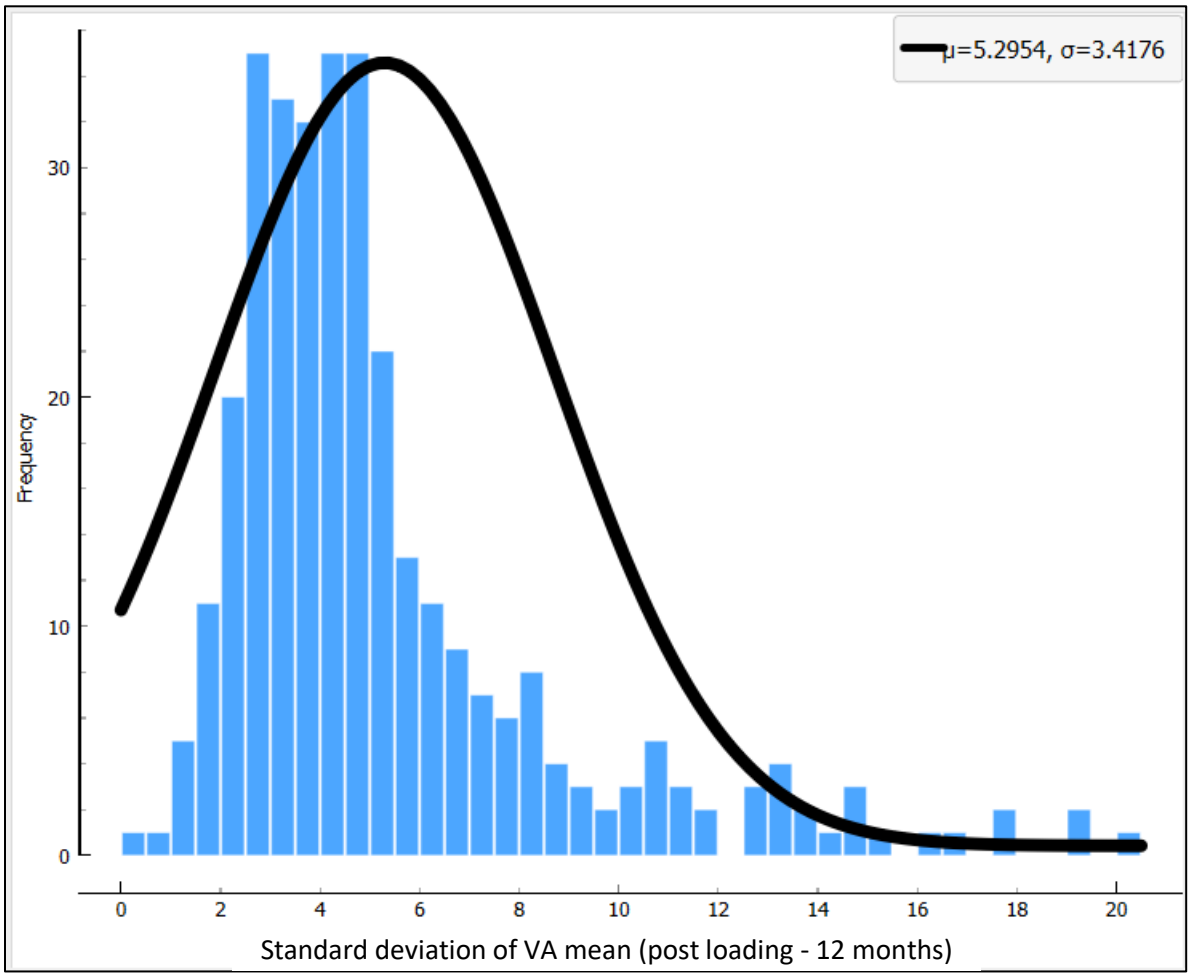


*Figure 7.33: Distribution of standard deviation of VA mean (post loading - 12 months)*

### 7.8.1 Regression analyses: Standard deviation of VA mean (post loading - 12 months)

Regression analyses of the standard deviation of VA mean (post loading - 12 months) however found that no models could be produced or features identified with an adequate level of predictive ability.

## 7.9 Discussion

This section aims to summarise previous studies which have attempted similar investigations, discuss the results from this body of work in predicting visual acuity and, in the cases of stronger relationships, to assess in more detail how individual features influence injection outcomes.

Bogunović et al. (2022), within their retrospective analysis of the TREND study, were also able to create models that could predict visual acuity outcomes with AUC of between 0.77 and 0.87. VA and IRF volume within the central 1mm region at baseline and after one month were the most important features in predicting VA after one year.

Prediction of VA at 12 months using baseline measures formed a regression model with $R^2$ of 0.36 with baseline BCVA, followed by IRC area and volume cited at the most influential features. The model accuracy improved to $R^2$ of 0.70 when considering input data from the four treatment initiation intervals: baseline and months 1, 2, and 3, with the last measured VA during the loading phase found to have the strongest predictive factor (Schmidt-Erfurth et al., 2018a).

VA at baseline and after 90 days were found to be the most informative measures in prediction models at one year with MAE 10 letters and RMSE 11 letters (Rohm et al., 2018) and a retrospective analysis of 154 eyes with nAMD found VA at three months to also be the best predictor of VA at four years (Chae et al., 2015).

Lower baseline VA, lower baseline age and higher injection number were independently associated with a higher VA change at year one and two by Fasler et al. (2019) and a review article of factors that predict nAMD visual outcomes found baseline VA, age and CNV lesion size to be the strongest indictors however that they did not display significant precision to guide patient management (Phan et al., 2021).

Within this study, in attempting to predict visual acuity at 12 months using classifications of VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80, modelling accuracy failed to reach an acceptable level when averaged across the categories using any of the devised feature groups. This was based on AUC, CA, precision, recall and specificity collectively all failing to reach a level above 50%. On considering individual categories however, it was found visual acuity could be predicted within the 71-80 letters class, at a statically significant level, by the SVM based model with AUC of 0.81 using the 'VA' variable group. Modelling with gradient boosting, considering the 'VA_st dev' group features, predicted VA with a similar level of accuracy in the 51-60 and 71-80 letter classes yielding an AUC of 0.82. The confusion

matrices for both the SVN and gradient boosted models (Figure *7.4* and Figure 7.5) however showed significant levels of misclassification thus rendering the clinical application of results from the models limited.

On assessing all the feature groups, several attributes (Table 7.48) yielded chi-squared values, at an α level of 0.05, suggesting they had some bearing in predicting between VA classes. The VA mean of the initial two post loading visits suggesting the strongest relationship based on elevated ranking scores within all indicators.

| |
|---|
| VA mean initial 2 visits post loading |
| VA post loading (VP) |
| VA baseline visit (V0) |
| Standard deviation of VA mean, post loading -12 months (VP-V12) |
| VA fellow eye (V0) |
| Age at first injection |

*Table 7.48: Features demonstrating significant relationship in predicting 'VA at 12 months (categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80)'*

Regression analyses were able to more successfully produce models in predicting VA at 12 months at a level of significance (Table 7.49). The linear regression models developed using the 'VA' and 'VA-st dev' group features in particular reached levels of $R^2$ and correlations suggesting strong relationships. In all cases the VA mean of the two visits post loading was the most informative attribute within the models. The linear regression model which considered the combined visual acuity and standard deviation variables, with outliers removed, had the highest degree of accuracy ($R^2$=0.59, Spearman correlation=0.774). The scatterplot of the linear regression model predictions (Figure 7.9) could be seen to show a relatively strong relationship with the regression line however the level of misestimation would continue to render the clinical application of these findings difficult. Using gradient boosting, post loading HEYEX OCT features could be modelled to predict VA at 12 months with $R^2$ of 0.18 and a Spearman correlation of 0.404 suggesting a weak relationship.

| Feature group | Best performing model | MAE | $R^2$ | Most informative attribute | Dataset |
|---|---|---|---|---|---|
| 'VA' | Linear Regression | 7.51 | 0.50 | VA mean of 2 visits post loading | Total with outliers removed |
| 'VA' | Linear Regression | 7.24 | 0.56 | VA mean of 2 visits post loading | N1 filtered with outliers removed |
| 'VA_st_dev' | Linear Regression | 6.80 | 0.59 | VA mean of 2 visits post loading | Total with outliers removed |
| 'VP_OCT' | Gradient Boosting | 11.22 | 0.14 | VP_ORLs 3mm vol | Total with outliers removed |

*Table 7.49: Regression models and features demonstrating significant relationships in predicting 'VA at 12 months'*

In considering the univariate regression and correlations between the individual features and visual acuity at 12 months, the VA mean of the two visits immediately post loading, VA post loading and baseline VA showed the presence of a strong relationship with VA at 12 months (Table 7.50). Indeed, the Spearman correlation (0.722) and the scatterplot of the VA mean of the two visits post loading predicting VA at 12 months, with outliers removed (Figure *7.8*), suggest a similar level of predictive accuracy to that of the linear regression models, thus is was perhaps not remarkable given that the VA mean of the 2 visits post loading had a strong influence within the models.

| Feature | Univariate Regression | Spearman correlation |
|---|---|---|
| VA mean of 2 visits immediately post loading | 346.402 | 0.722 |
| VA post loading (VP) | 295.823 | 0.694 |
| VA baseline visit (V0) | 114.170 | 0.514 |

*Table 7.50: Feature univariate regression and Spearman correlation scores*

Filtering to consider cases where there was no evidence of nAMD in the fellow eye produced a small improvement in modelling accuracy in the analyses considering the 'VA' feature group. This suggested fellow eye activity may have a subtle influence in visual outcomes of the study eye in this cohort but not to a degree where additional relationships were uncovered.

As measurement of VA has been shown to fluctuate (Siderov and Tiu, 1999, Patel et al., 2008, Aslam et al., 2014), some account of this was taken by attempting to model VA at 12 months taken as the mean of the letter score measures at the final two visits over the first year. In the repeated classification

analyses, again no learner produced a model with a significant level of accuracy and no features were identified implying a significant prognostic ability. Within regression analyses only the feature groups 'VA' and 'VA_st dev' models reached levels of significance with marginal improvement in $R^2$ to 0.54 and 0.64 respectively. No additional or stronger correlations were identified in considering the individual features. In view of these results it might be concluded that accounting for visual fluctuation by considering the mean of VA from final 2 visits over one year did not offer significant prognostic outcomes to the use of the solitary final VA measure.

The change in VA from baseline to the end of the first year of treatment was also considered as a dependent variable. In classification analyses, attempting to sort between eyes that lost or gained VA, several learners produced models with an appropriate degree of accuracy. The best performing model, based on AUC, in each category was summarised (Table 7.51).

| Feature group | Best performing model | AUC | Dataset | Most informative feature | *N1 filtering with outliers removed** | *N1 AUC** |
|---|---|---|---|---|---|---|
| Demographic & qualitative | Gradient Boosting | 0.60 | Outliers removed | Age at first injection | *kNN* | *0.65* |
| VA | Logistic Regression | 0.82 | Outliers removed | Baseline VA | *Logistic Regression* | *0.86* |
| VA_st dev | Neural Network | 0.88 | Outliers removed | Baseline VA | *Neural Network* | *0.88* |
| V0_OCT | Naïve Bayes | 0.62 | Outliers removed | V0_OPL 1mm CM vol | *No improvement* | - |
| VP_OCT | Logistic Regression | 0.53 | Outliers removed | VP retina 1mm CMT | *No improvement* | - |
| V0_OCTANE | Gradient Boosting | 0.55 | Outliers removed | V0 neurosensory retina vol | *No improvement* | - |

*Table 7.51: Feature groups considering VA at 12 months where accurate modelling was achieved; best performing algorithm, AUC, dataset, most informative attribute, N1 filtered model* and AUC* (*where accuracy improved)*

Post loading OCTANE OCT features did not yield an appropriate level of predictive ability however the remaining OCT derived groups did yield more successful modelling results. While the results of the post loading HEYEX OCT (VP_OCT) and baseline OCTANE OCT (V0_OCTANE) group models were barely above a level of significance, the Naïve Bayes algorithm produced a model predicting between eyes that lost or gained VA over 12 months with AUC of 0.62. ODM feature importance ranked baseline OPL volume within the central 1mm macular zone as the most informative attribute. However on considering the model nomogram (figure 7.34) both the central 1mm NFL volume and OPL volume appeared to convey roughly equal degrees of informedness. On interpreting the nomogram, it suggested that as baseline

NFL and OPL volume decreased, the odds of losing VA over 12 months increased. Conversely thus as NFL and OPL volume increased, the odds of gaining VA, compared to baseline, over 12 months increased. One could argue that this is perhaps contrary to conventional thinking where thicker baseline OCT measures would be associated with worse outcomes. It must also be stated that given the statistically significant but relatively low level of modelling accuracy and the fact NFL and OPL chi-squared scores were not at a level of significance at $\alpha = 0.05$, these findings may have limited application in real world situations.

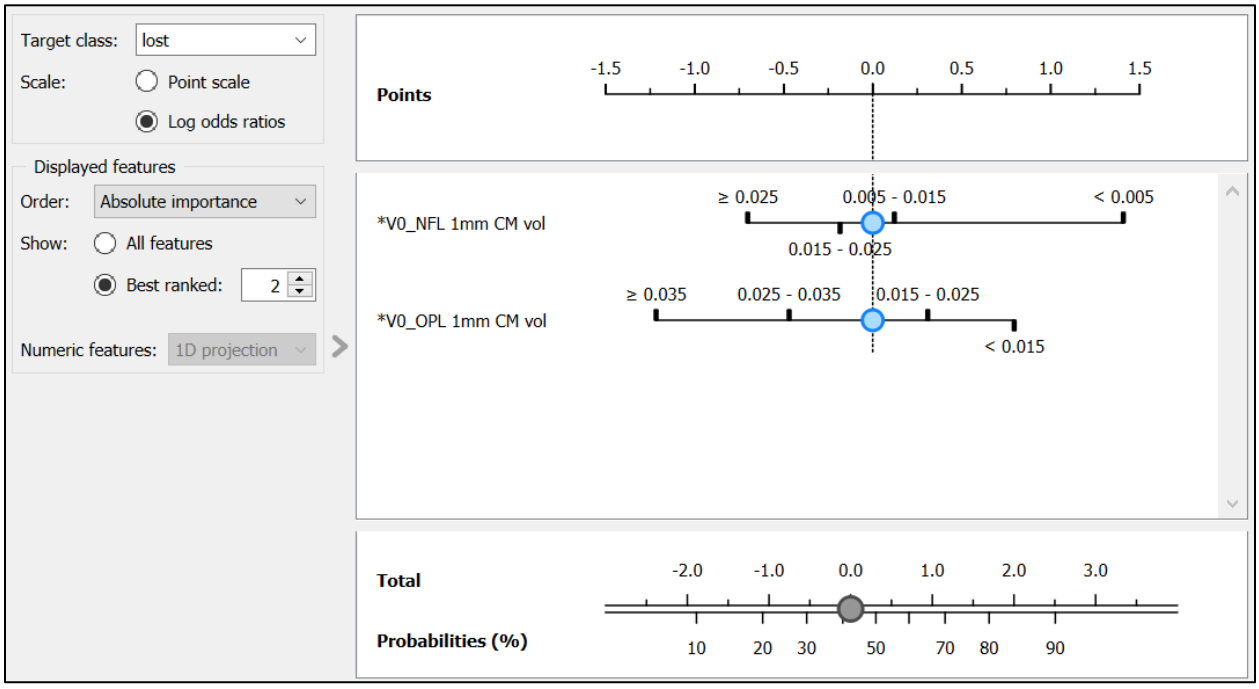


*Figure 7.34: Naïve Bayes nomogram demonstrating effect of baseline OPL and NFL volume on differentiating Change in VA, baseline - month 12 (categories: VA gained, lost)*

The finding that age at first injection was deemed by the kNN learner to be the most informative attribute, when developing models using the demographic & qualitative feature group, was not unexpected given this variable has previously been recognised as predictor of VA outcomes (Phan et al., 2021). Given also the kNN model AUC (0.60) suggested only a modest relationship, these results are not considered here in detail.

The nomogram of the logistic regression model (Figure 7.35), with AUC of 0.86, evaluating the combined VA and standard deviation features was however considered. This nomogram showed a similar pattern of behaviour when compared to modelling from the VA group features and was used in preference to neural network which was incompatible with ODM nomogram tools. The graph effectively described

that as baseline VA increased to a high level, if the either of the post loading VA features decreased to a low level, the resultant probability was that the patient would also show a sustained loss of vision at 12 months. Conversely, if the baseline VA was of a low magnitude and improved significantly post loading to a high value, the likelihood of this visual improvement being sustained was high. As standard deviation in the VA mean post loading increased, the favourability of the visual outcome declined. In relation to these aspects of prognostication, the model behaved with a high degree of certainty. The likelihood of loss or gain in vision showed a high level of uncertainty in cases where the baseline VA was close to the mean value and post loading VA was of a similar magnitude. This would perhaps explain the ongoing misclassifications within the confusion matrix (Figure 7.36). The finding that large changes from baseline to post loading were likely to sustained over 12 months, whether this outcome was favourable or adverse, are perhaps of clinical value and perhaps uses of the devised nomogram could also be helpful in real world setting provided moderate chnages in vision were interpreted carefully.

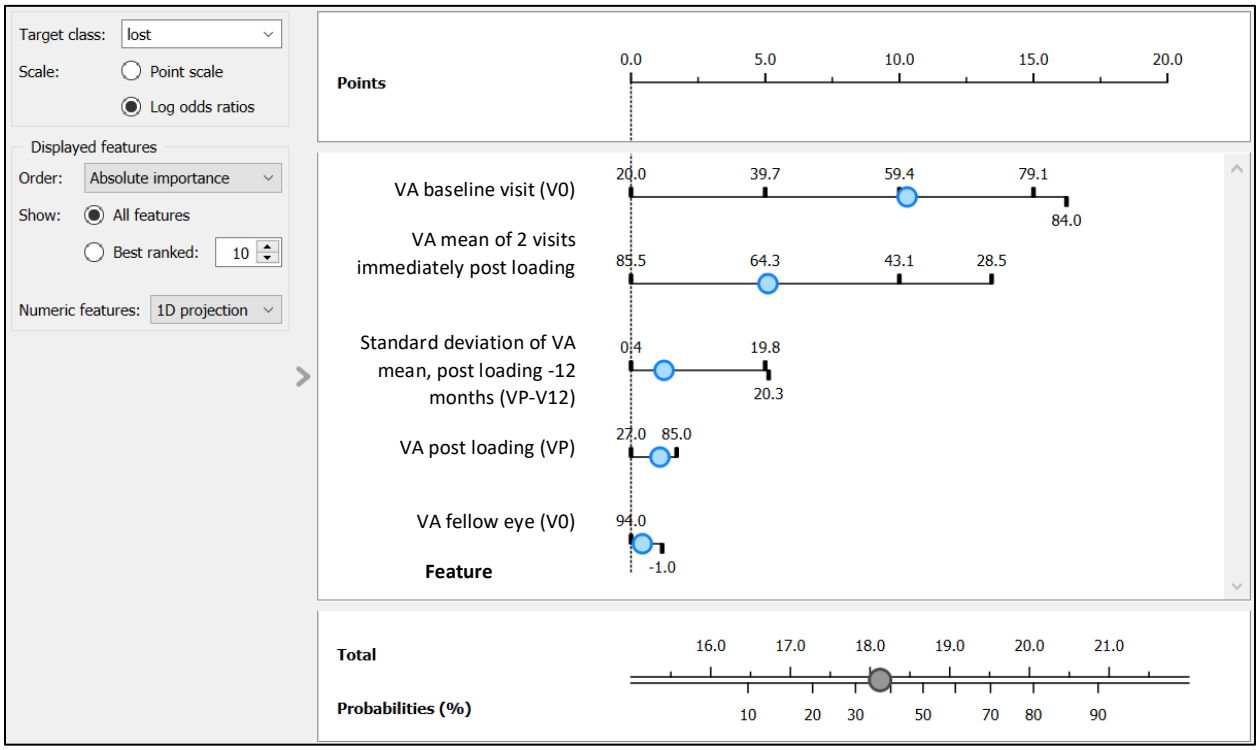


*Figure 7.35: Linear regression nomogram demonstrating effect of 'VA_st dev' group modelling, with outliers removed, on differentiating between the Change in VA, baseline - month 12 (categories: VA gained, lost)*

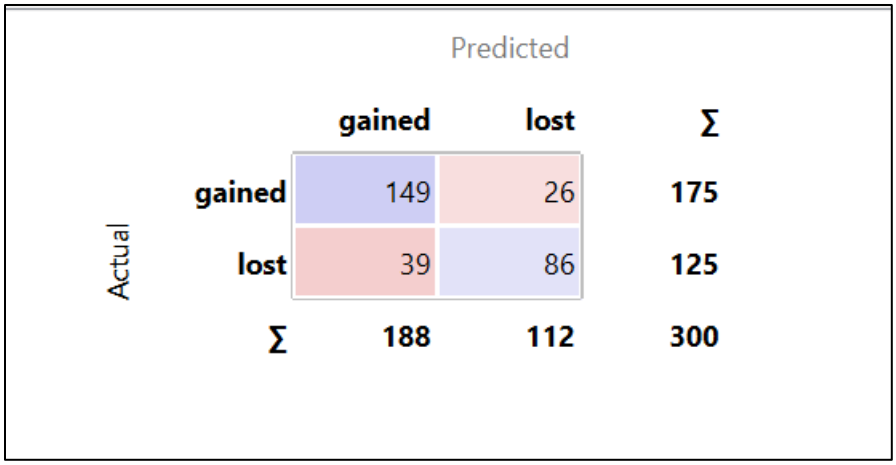


*Figure 7.36: Confusion matrix for logistic regression classification model predictions for dataset, with outliers removed, 'VA_st dev' group modelling for target Change in VA, baseline - month 12 (categories: VA gained, lost)*

Individual features determined as influential by classification analyses of change in VA, baseline - month 12 were baseline visit VA and the standard deviation of VA mean, post loading -12 months. Both of these have been considered within this body of work.

Filtering to consider cases where there was no evidence of nAMD in the fellow eye produced a modest improvement in modelling accuracy in the analyses consider the 'VA' feature group. This suggested fellow eye may have activity may have a subtle influence in visual outcomes of the study eye in this cohort but not to a degree where additional relationships were uncovered.

Change in VA over 12 months was further considered in three categories those that lost five or more letters, those that gained 5 or more letters and those than had neither gained or lost more than 4 letters since base line measures. Results were broadly similar to those reported when considering change in visual acuity as two categories (lost and gained), but with lower levels of modelling accuracy in all cases. It was therefore deemed that categorising VA change in this manner did not improve modelling prognostication or unveil any unknown relationships.

Change in VA from baseline to 12 months was also considered using regression analyses. Linear regression was found to be the most accurate method by which to create models (Table 7.52). Appropriate levels of accuracy were determined in considering the 'VA' group features, $R^2$ = 0.46, MAE = 7.09 letters, with this accuracy improving to $R^2$ = 0.51 and MAE of 6.74 letters when consider only those eyes where there was no fellow eye activity. In the linear regression model developed using the combined 'VA_st_dev' variable, accuracy improved further, R2 = 0.57 and MAE predicted to 6.19 letters.

In keeping with the classification results, baseline VA and the VA mean of 2 visits immediately post loading were the most influential attributes within models. Also in keeping with the classification results, but contrary to the regression analyses in predicting VA at 12 months, standard deviation of the VA mean post loading and baseline VA had a negative Spearman correlation with the change in VA over 12 months, -0.418 and 0.397 respectively. The correlation of the model prediction of the change in VA was also significantly higher of that of any individual attribute in this case suggesting attribute outcomes had to be combined to improve modelling projection.

| Feature group | Best performing model | MAE | $R^2$ | Most informative attribute | Dataset |
|---|---|---|---|---|---|
| 'VA' | Linear Regression | 7.09 | 0.46 | -baseline VA<br>-VA mean of 2 visits immediately post loading | Total with outliers removed |
| 'VA' | Linear Regression | 6.74 | 0.51 | -baseline VA<br>-VA mean of 2 visits immediately post loading | N1 filtered with outliers removed |
| 'VA_st_dev' | Linear Regression | 6.19 | 0.57 | -baseline VA<br>-VA mean of 2 visits immediately post loading | Total with outliers removed |

*Table 7.52: Regression models and features demonstrating significant relationships in predicting 'Change in VA, baseline - month 12'*

Filtering to consider cases where there was no evidence of nAMD in the fellow eye produced a modest improvement in modelling accuracy in the analyses considering the 'VA' feature group. This suggested fellow eye activity may have a subtle influence in visual outcomes of the study eye in this cohort but not to a degree where additional relationships were uncovered.

In the remaining analyses being reported; VA trend over 12 months, the standard deviation of VA mean, baseline - 12 months and Standard deviation of VA mean, post loading (post loading - month 12), the feature groups 'VA' and 'VA-st dev' were not considered within the discussion. This was because associations had already been determined in predicting VA outcomes with these independent variables by work within the study and reported in prior investigations (Chae et al., 2015, Rohm et al., 2018, Schmidt-Erfurth et al., 2018a, Fasler et al., 2019, Phan et al., 2021, Bogunović et al., 2022). Furthermore

as baseline VA, VA post loading, VA mean of the two visits immediately post loading and standard deviation of VA mean, were effectively components used to derive the VA trendlines and standard deviations, it was felt correlations may coincidentally be found.

Features and models that would predict the trendlines of VA change over 12 months were investigated. This was to again take even greater account of the fluctuation in VA to determine if more accurate predictions could be formed. The initial classification modelling involved attempting to group data instances between positive and negative trendline slopes, effectively differentiating those that had a trend suggesting loss of vision over 12 months and those that predicted a gain.

Modelling outcomes improved in that learners were able to make predictions at a statistically significant level using all feature groups (Table 7.53). AUC for all models was however ≤ 0.60 suggesting the strength of the prediction to be limited. Age at first injection, baseline average retinal thickness over the central 1mm zone, post loading minimum inner retinal layer thickness, post loading average outer retinal layer thickness over 1mm, baseline neurosensory retina volume and post loading RPE volume were the most informative attribute in devising models. In view of the accuracy indicators however, a clinical application of these results would be guarded.

No individual features were identified as producing a significant relationship in predicting the Year 1 VA trend. Filtering to consider cases where there was no evidence of nAMD in the fellow eye produced a modest improvement in modelling accuracy in the analyses consider the 'VP_OCT' feature group. This suggested fellow eye may have activity may have a subtle influence in visual outcomes of the study eye in this cohort but not to a degree where additional relationships were uncovered.

| Feature group | Best performing model | AUC | Dataset | Most informative feature | *N1 filtering with outliers removed** | *N1 AUC** | *Most informative feature* |
|---|---|---|---|---|---|---|---|
| Demographic & qualitative | Tree | 0.57 | Outliers removed | Age at first injection | - | - | - |
| V0_OCT | Gradient Boosting | 0.60 | Outliers removed | V0_retina 1mm CMT | - | - | - |
| VP_OCT | Tree | 0.57 | Outliers removed | VP_IRLs min CMT | Gradient Boosting | 0.60 | VP_ORL 1mm CMT |
| V0_OCTANE | Random Forest | 0.55 | Outliers removed | V0 Neurosensory Retina vol | - | - | - |
| VP_OCTANE | Neural Network | 0.56 | Outliers removed | VP RPE vol | - | - | - |

*Table 7.53: Feature groups considering Year 1 VA trend (categories: gained, lost) where accurate modelling was achieved; best performing algorithm, AUC, dataset, most informative attribute, N1 filtered model* and AUC* (*where accuracy improved)*

The visual acuity trendline slope was also considered between the intervals of immediately post loading and at 12 months. The purpose of this was to account for both the expected improvement in VA on initiation of treatment (Colquitt, 2008) and the fluctuation in VA measurement. The initial investigation again involved predicting between eyes with positive and negative slopes.

Results were effectively in keeping with Year 1 VA trend (categories: gained, lost) analyses but with generally slightly weaker relationships. Models could again be derived when considering the feature groups:

- Demographic & qualitative
- V0_OCT
- VP_OCT
- V0_OCTANE
- VP_OCTANE

Only the demographic & qualitative variables yielded a modelling improvement of AUC 0.61, but as this effective altered by 0.01, this was considered insignificant. In view of the continued low accuracy scoring however, predictive performance was deemed limited and no attributes from these analyses attained a level of significance across feature ranking metrics to suggest sufficient prognostic ability.

Further analyses were performed to predict the slope of the VA trendline in the categories; lost, gained and maintained. Regression analyses were also performed to predict the VA trendline slopes detailed above. In all such scenarios, no models were however produced or features identified with an adequate level of predictive ability.

Standard deviations of the VA mean from both baseline through to 12months and the post loading visit to 12 months were considered as outcome variables. The goal of this investigation was to determine if standard deviation of VA means, which had been shown to have a predictive influence in models created during this study, could be predicted by any input features. Standard deviation while able to describe the variance within the VA mean, could not be established until the end of the first year of treatment hence while producing an interesting relationship, would be of limited prognostic value until the later phases of treatment. In both series of regression analyses predicting standard deviation however, no models could be produced or features identified with an adequate level of predictive ability.

## 7.10 Key Findings

- Predicting VA at 12 months proved difficult, but models show improved accuracy for specific VA categories (51-60 and 71-80 letters) using the Gradient Boosting algorithm.
- The VA mean of the 2 visits immediately post loading was the most influential attribute in predicting VA at 12 months.
- Linear Regression models using baseline and post loading VA measures show strong relationships with VA at 12 months ($R^2$ = 0.59) and change in VA ($R^2$ = 0.57).
- OCT based features did not effectively predict VA at 12 months in regression analyses.
- Classification models accurately differentiated between eyes that lost or gained VA over 12 months, with Naïve Bayes (AUC = 0.62) and Neural Network (AUC = 0.88) showing the highest accuracy using OCT and visual acuity defined features respectively.
- Baseline OPL volume, post loading retina thickness, and baseline neurosensory retina volume are informative in predicting VA change.
- Large changes in VA from baseline to post-loading tend to be sustained over 12 months.
- Predicting the trend of VA change over 12 months is possible with moderate accuracy using various feature groups, but no individual features show strong predictive ability.
- Predicting the standard deviation of VA means over 12 months is not feasible with the available data.

# 8 Key findings, discussion and conclusion

## 8.1 Summary/introduction

This study aimed to evaluate OCT defined features in patients with nAMD and evaluate their bearing on visual prognosis and treatment frequency. Additionally the study would consider whether the findings could influence the tailoring of anti-VEGF treatment regimens and what role machine learning might play in managing nAMD.

The project considered changes within the individually segmented retinal layers and the fluid volumes and biomarkers typically used in the management of nAMD. This appears to be an innovative approach with prior work tending not to have studied as many retinal features collectively. Furthermore changes in visual acuity were evaluated in a number of novel methods which accounted for fluctuations in measurement. The study also took advantage of AI based tools, both in OCT image analysis and data modelling in determining relevant outcomes.

## 8.2 Can treatment frequency be predicted?

Anti-VEFG dosing frequency was considered in a number of classification and regression analyses. This included the application of ODM hierarchical clustering to sort studied eyes based on the pattern in which they received injections, a method which appeared to be unique to this study.

Classification models which predicted between eyes that received three or more than three injections reached the highest levels of accuracy. In considering baseline HEYEX OCT measures, the Naïve Bayes classifier was able to predict between the categories to an accuracy of AUC 0.63.

In forming models predicting between the categories; injections 3, >3, fellow eye visual acuity, baseline GCL 1mm central macular volume, post loading GCL 1mm central macular volume and post loading drusenoid PED volume were the most informative features.

Independent of the modelling, the standard deviation of the VA mean post loading was found to have a weak but statistically significant influence on predicting the number of injections with the likelihood of only requiring three injection increasing at the standard deviation reduced and the probability of needing more that three doses over 12 months increasing at the standard deviation increased.

Regression model outcomes were generally not at a viable level of predictive accuracy. If considering the univariate regression and correlation results of individual OCT based features, baseline HEYEX OCT results suggested retina$_t$ thicknesses and volumes had a weak, positive relationship with numbers of

injections administered (Spearman correlation in the range 0.251 - 0.285). Post loading HEYEX OCT data determined a slightly stronger relationship (Pearson correlation in the range 0.284-0.330) again with $retina_t$ thicknesses and volumes seemingly the most influential layer group.

In summary thus given the overall weak level of modelling and relationships developed in determining if anti-VEGF dosing can be predicted, it could be concluded that the findings within this study could not accurately predict injection frequency over one year to a degree that would be clinically relevant.

### 8.3 Can visual acuity outcomes be predicted?

As measurement of visual acuity has a strong subjective element and as discussed within section 4.4, despite applying rigorous methods to ensure the repeatability of measurement in a standardised method, is known to fluctuate due to reasons including patient related factors, change in refraction and variation in disease state. Furthermore VA is known to alter after the administration of anti-VEGF treatment, thus outcomes of VA over 12 months were considered in a number of methods which could be modelled most effectively.

Regression models were able to predict VA after 12 months of treatment and the change in visual acuity from baseline to 12 months using features related to baseline and post loading VA, to a reasonable level of accuracy. On considering the feature group comprising VA and standard deviation measures, linear regression of VA at 12 months resulted in a model with $R^2$=0.59 and Spearman correlation of 0.774 and in the case of change in visual acuity at 12 months from baseline, a model with $R^2$=0.57 and Spearman correlation of 0.761.

OCT determined features however were not able to model VA accurately in regression analyses with only the post loading HEYEX OCT inputs returning a model with positive $R^2$ of 0.14. Compared to strong correlations demonstrated by the models and VA related attributes, in the order of >0.7, the OCT related correlation scores were generally ≤0.2.

Classification analyses yielded the strongest predictive modelling performance in sorting between those that lost or gained VA over 12 months. In considering baseline and post loading VA inputs in cases where there was no evidence of nAMD in the fellow eye, logistic regression could categorise eyes with AUC of 0.86 and if adding the standard deviation of the VA mean, post loading – 12months, to the features, the neural network algorithm achieved modelling accuracy of AUC of 0.88. The models in this case could have a clinical application, particularly in cases where baseline and post loading VA was at the extremes of the scale as discussed in section 8.9.

Baseline HEYEX OCT, post loading HEYEX OCT and baseline OCTANE OCT measures were also able to be successfully modelled with ODM learners with AUC > 0.5. The baseline HEYEX OCT feature group in particular was used by Naïve Bayes to predict between the classed with AUC of 0.62. Baseline OPL 1mm central macular volume, post loading retina 1mm central macular thickness and baseline neurosensory retina volume were the most informative within the models. Whilst the OCT based models reached a level of predictive ability above random chance, their application within a clinical setting would remain inappropriate given an overall low level of accuracy.

Visual acuity outcomes were also considered in terms of whether eyes had lost gained or maintained VA over 12 months but without developing models with significant predictive ability. To account for potential post loading improvement in VA and fluctuation in VA measures, outcomes were also considered by taking the mean of the final 2 visits in the 12 month study period and the slope of visual trendlines over 12 months. No significant improvement in modelling ability was found and no significant relationship were observed.

In conclusion thus, VA at 12 months and change in VA over 12 months can be accurately modelled, and in the case of classification models of eyes that gained and lost VA over 12 months, to a degree where clinical applicability might be feasible. These predictions were however based on visual acuity measures with OCT features, based on these analyses, not rendering appropriate levels of predictive accuracy.

### 8.4 Is fellow eye activity significant?

In all models which reached a significant level of predictive ability, the dataset was filtered to consider cases where there was no evidence of nAMD in the fellow eye. The rationale behind this was due to a beneficial therapeutic effect of anti-VEGF agents in untreated fellow eyes having been described in several studies (section 3.8) and removing any potential effect this could have had on outcomes. Whilst in some cases repeating the modelling produced minor improvements in prognostication, removing the effect of fellow eye activity was considered negligible with no clinically relevant consequence identified.

### 8.5 Can OCT determined features help tailor anti-VEGF dosing?

From the modelling results of this study, it can be concluded that OCT determined features could not accurately predict the number of anti-VEGF doses that would be required over a year. An interesting finding was however that 106 of the 327 eyes enrolled within the study only required 3 anti-VEGF doses over the entire first year of management. This poses the issue that some eyes would effectively be overtreated under the treat and extend regimen now recommended by the Royal College of

Ophthalmologists. Without a means however to identify at baseline or early in nAMD therapy which patients would stabilise after the loading dose, some additional injections for such cases seems likely for the immediate future.

### 8.6 What role machine learning might play in managing nAMD?

Even within this project, ML was applied to several aspects of nAMD investigation. The convolutional neural network U-Net was applied to OCT images to develop AI based outputs of retinal fluid volumes and lesion thicknesses which were then used in further analyses. This allowed the accurate, rapid, repeatable determination of such features in close to 300 images without the need to have clinician validation as may have been the case if images were graded by an individual.

The ODM platform was used for data analysis to create classification and regression models, determine the influence of features within models and determine independent relationships between attributes and target variables. Furthermore unsupervised ML was able to apply hierarchical clustering to determine anti-VEGF treatment patterns. The combined volume of investigations carried out would have been unfeasible without ML.

From the work carried out in this study, a model to predict the change in VA over 12 months was developed with AUC of 0.88 which theoretically could have a clinical application. Additionally research being carried out by other groups considered within the project are developing similar models in attempt to predict outcomes in AMD with Mares et al. (2024) recently publishing real world results of their regulator approved, ML trained, fluid monitoring algorithm used in the active assessment of patients with nAMD.

It is the belief of the author that to tackle challenges including an aging population, expected increased prevalence of nAMD over time, workforce understaffing and training needs, the development and adoption of AI based tool will become common place in nAMD management. An additional benefit could be the ability of such system to digitise and automate the nAMD monitoring process which in turn could allow observation of active disease to be carried out outside of secondary care establishments, perhaps in optometric practices.

### 8.7 Limitations

During study enrolment, 724 eyes of 638 individuals were identified as having complete electronic medical records and HEYEX OCT scans available for review. Of these however only 327 eyes of 308 individuals were actually considered within the study. A potential consequence of application of

exclusion criteria in removal of poor quality images or images that could not be accurately segmented, as was most commonly the scenario, was the introduction of unintended selection bias.

As more disorganised, unsegmentable scans were more likely related to more complex disease states with features including SRF and RPE elevation more frequently acting to confuse segmentation algorithms (Sadda et al., 2006), this may have led to under representation of such groups within the study. Traits such as being male, non-white, older, having higher BMI and elevated blood pressure have also been reported to have statistically significant increased likelihood of being more prevalent in images excluded due to insufficient quality (Engelmann et al., 2023).

While a record of concurrent retinal therapy and surgical interventions was available and applied as exclusion criteria, further records of ocular and systemic co-morbidities were unfortunately not available and thus could not be studied as potential features and similarly could not be excluded thus introducing a further source of potential bias.

To maximise the study dataset, all eligible cases were included as this was felt to offer the best opportunity to train the algorithmics models. This had the effect to enrol all 327 eyes of 308 patients resulting in 19 individuals having both their eyes included in the study. While the potential effects of treatment crossover to the fellow eye were considered in section 3.8 and the project itself investigated and found the effect of fellow eye activity to be negligible, there are additional considerations including an underestimation of variance and bias in ocular comorbidities and systemic adverse events (Armstrong, 2013). While the benefits of studying both eyes of an individual in an effort to increase the size of a data pool have also been recognised, similarly have the potential risks and need to consider the implications carefully (Glassman and Melia, 2015).

The ethnic diversity within the Wirral study population was also largely homogenously British caucasian (n=300) with a further 23 eyes identified as ethnicity not stated. This may have led to further selection bias. Only 1 eye within the study was identified as being from an individual with non-caucasian ethnicity. Resolving this issue with the Wirral based dataset would however be difficult given the demographic make up of the local population.

Owing to the fact the project utilised real world data, there was a variation in the number of attendances for clinic appointments by patients over a 12 month period as discussed in section 3.7. and as not all patients attend appointments at monthly intervals, there was thus a further disparity in the interval between appointments when VA was recorded. This is hence a potential source of error

particularly affecting the analyses involving the mean of the VA form the 2 visits post loading and mean of the VA at 12 months. It is perhaps worth noting however that the no additional or stronger relationships were noted when predicting mean of VA from final 2 visits in first year when compared to the outcomes of VA at 12 months derived from a single integer.

## 8.8 Further work

During the course of the project it became obvious that the potential to carry out sub analyses from different cohorts within the data was vast. Some properties determined that could use further exploration however were the cohort that only received the three loading dose injection over the entire first year to stabilise the disease process. As discussed in thesis, such patients are likely to be managed under a treat and extend treatment pattern in future. Some of the benefits of PRN dosing will thus be lost over time with a lack of datasets also available in future to study the effects within the regimen. Further study on this subchohort perhaps by merging it with PRN data from another Trust to increase the population size may lead to some useful findings.

The standard deviation of the VA mean post loading did appear to have reasonable prognostic ability and equally could not be predicted during the loading phase of treatment. If indeed the standard deviation does describe the variability of VA and this correlates with worse visual outcomes over the course of therapy, this be useful piece of knowledge. One effect which was not examined during this body of work was whether the standard deviation was purely linked to disease state this hence additional investigation and indeed alternative properties of visual fluctuation may be investigated by the author in due course.

The study was able to exploit the computational capabilities of ODM to carry out vast numbers of analyses using large numbers of features which could easily be considered individually or in groups. Targets were manipulated to form a variety of classes and continuous data sets; outputs were readily visualised and scrutinised using the complement of accuracy and ranking tools. While the purpose of this project was to consider the outcomes of anti-VEGF therapy in nAMD, it is the belief of the author that with careful preparation of a dataset, that the methods and algorithmic pipelines developed in this study could be readily applied to undertakings in a variety of fields of research.

The capabilities of platforms such as ODM also extend far beyond those utilised in this body of work. Aspects which would be worth developing in future work include the furthered use of unsupervised machine learning and developing more customised tools by directly writing the code for the operation required although this was beyond the scope of this project.

Appendix 1: HRA approval



Dr Hannah Bartlett

Aston University

Aston Triangle

Birmingham

B4 7ETN/A

Email: approvals@hra.nhs.uk

11 May 2021

Dear Dr Bartlett

**HRA and Health and Care**

| | |
|---|---|
| **Study title:** | **Evaluating morphological changes seen on OCT in patients with wet AMD and their bearing on visual prognosis, lesion activity and treatment efficacy.** |
| **IRAS project ID:** | **289108** |
| **Protocol number:** | **N/A** |
| **Sponsor** | **Aston University** |

I am pleased to confirm that **HRA and Health and Care Research Wales (HCRW) Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

Please now work with participating NHS organisations to confirm capacity and capability, in line with the instructions provided in the "Information to support study set up" section towards the end of this letter.

**How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?**

HRA and HCRW Approval does not apply to NHS/HSC organisations within Northern Ireland and Scotland.

If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report (including this letter) have been sent to the coordinating centre of each participating nation. The relevant national coordinating function/s will contact you as appropriate.

Please see IRAS Help for information on working with NHS/HSC organisations in Northern Ireland and Scotland.

**How should I work with participating non-NHS organisations?**

HRA and HCRW Approval does not apply to non-NHS organisations. You should work with your non-NHS organisations to obtain local agreement in accordance with their procedures.

**What are my notification responsibilities during the study?**

The *"After HRA Approval – guidance for sponsors and investigators"* document on the HRA website gives detailed guidance on reporting expectations for studies with HRA and HCRW Approval, including:

- Registration of Research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics and is updated in the light of changes in reporting expectations or procedures.

**Who should I contact for further information?**

Please do not hesitate to contact me for assistance with this application. My contact details are below.

Your IRAS project ID is **289108**. Please quote this on all correspondence.

Yours sincerely,

Sarah Prothero

Approvals Specialist

Email: approvals@hra.nhs.uk

*Copy to:* *Mr Matthew Richards* **List of Documents**

The final document set assessed and approved by HRA and HCRW Approval is listed below.

| *Document* | *Version* | *Date* |
|---|---|---|
| IRAS Application Form [IRAS_Form_27042021] | | 27 April 2021 |
| Organisation Information Document [WUTH] | | 02 March 2021 |
| Organisation Information Document [Moorfields] | | 04 March 2021 |
| Other [Data collection template] | | |
| Other [Summary CV Principal investigator] | | 22 March 2021 |
| Other [Summary CV key collaborator] | | 31 March 2021 |
| Other [GCP certificate - student] | | 15 March 2021 |
| Referee's report or other scientific critique report [Proposal feedback] | | 30 November 2020 |

| | | |
|---|---|---|
| Referee's report or other scientific critique report [University Ethics Approval] | | 01 March 2021 |
| Research protocol or project proposal [Project proposal] | 1.0 | 13 November 2020 |
| Schedule of Events or SoECAT [WUTH] | 1.0 | 11 May 2021 |
| Schedule of Events or SoECAT [Moorfields] | 1.0 | 11 May 2021 |
| Summary CV for Chief Investigator (CI) [CI CV] | | 18 March 2021 |
| Summary CV for student | | 12 March 2021 |

| IRAS project ID | 289108 |
|---|---|

## Information to support study set up

The below provides all parties with information to support the arranging and confirming of capacity and capability with participating NHS organisations in England and Wales. This is intended to be an accurate reflection of the study at the time of issue of this letter.

| Types of participating NHS organisation | Expectations related to confirmation of capacity and capability | Agreement to be used | Funding arrangements | Oversight expectations | HR Good Practice Resource Pack expectations |
|---|---|---|---|---|---|
| 1) Site type 1 (Research site): Wirral University Hospital NHS Trust will be undertaking the following activities: Provision of pseudonymised dataset. | Research activities should not commence at participating NHS organisations in England or Wales prior to their formal confirmation of capacity and capability to deliver the study. | An Organisation Information Document has been submitted and the sponsor is not requesting and does not expect any other site agreement to be used. | No application for external funding has been made. | A Principal Investigator should be appointed at study sites. | No Honorary Research Contracts, Letters of Access or pre-engagement checks are expected for local staff employed by the participating NHS organisations. |

| | | | | | |
|---|---|---|---|---|---|
| 2) Site type 2 (Research site): Moorfields Eye Hospital NHS Foundation Trust will be undertaking the following activities: Processing of pseudonymised ocular scans. | Research activities should not commence at participating NHS organisations in England or Wales prior to their formal confirmation of capacity and capability to deliver the study. | An Organisation Information Document has been submitted and the sponsor is not requesting and does not expect any other site agreement to be used. | No application for external funding has been made. | A Principal Investigator should be appointed at study sites. | No Honorary Research Contracts, Letters of Access or pre-engagement checks are expected for local staff employed by the participating NHS organisations. |

**Other information to aid study set-up and delivery**

| *This details any other information that may be helpful to sponsors and participating NHS organisations in England and Wales in study set-up.* |
|---|
| The applicant has indicated they do not intend to apply for inclusion on the NIHRCRN Portfolio. |

Appendix 2: Data sharing agreement

Bevan Brittan

**Dated** **01/01/2021**

**Wirral University Teaching Hospital NHS Foundation Trust**
**(1)**

**MOORFIELDS EYE HOSPITAL NHS FOUNDATION TRUST**
**(2)**

# SERVICE AGREEMENT

**(Contract No: *[DN: please insert]*)**



Toronto Square – 7th Floor | Toronto Street | Leeds LS1 2HJ
T 0370 194 1000 F 0370 194 5465

Fleet Place House | 2 Fleet Place | Holborn Viaduct | London EC4M 7RF
T 0370 194 1000 F 0370 194 7800

Kings Orchard | 1 Queen Street | Bristol BS2 0HQ
T 0370 194 1000 F 0370 194 1001

Interchange Place | Edmund Street | Birmingham B3 2TA
T 0370 194 1000 F 0370 194 5001

Contents

**THIS AGREEMENT** is dated 01/01/2021

**BETWEEN**

(1) **Wirral University Teaching Hospital NHS Foundation Trust (WUTH)** whose address is Arrowe Park Road, Upton, Wirral, CH49 5PE **(University)** ***[DN: please confirm]*****; and**

(2) **MOORFIELDS EYE HOSPITAL NHS FOUNDATION TRUST** whose address is 162 City Road, London EC1V 2PD United Kingdom (**Institution**)

(together the "Parties")

**WHEREAS**

(A) The University is willing and able to perform its University Obligations on the terms and conditions as set forth below.

(B) The Institution is willing and able to perform its Institution Obligations on the terms and conditions as set forth below.

(C) The Parties agree that the Institution Obligations and University Obligations are being provided to the other respective Party by way of mutual consideration.

Therefore, University and the Institution agree as follows:

**1 DEFINITIONS**

**Affiliate** means any entity which directly or indirectly Controls, is Controlled by, or is under common Control with a Party. "Control" means direct or indirect ownership or control of more than 50% (fifty percent) of the voting interests of the Party or the power to direct or cause the direction of the management and policies of such Party whether by contract, through majority ownership of voting capital stock or otherwise. "Controlled" shall be **interpreted** accordingly.

**Change:** any change to this Agreement including to any of the Obligations.

**Change Control Note:** the written record of a Change agreed or to be agreed by the Parties pursuant to the Change Control Procedure.

**Change Control Procedure:** the procedure for changing this Agreement, as set out in Schedule 3.

**Cloud** means a third party data base, hosted by the Institution on an Institution server located in the European Union.

**Confidential Information** means all confidential information (however recorded or preserved) disclosed by a party or its Representatives to the other party and that party's Representatives in connection with this Agreement, including but not limited to:

(a) any information that would be regarded as confidential by a reasonable business person relating to: (i) the business, affairs, customers, suppliers or plans of the disclosing party; and (ii) the operations, processes, product information, know-how, designs, trade secrets or software of the disclosing party;

(b) any information developed by the parties in the course of carrying out this Agreement;

(c) Personal Data;

(d) any commercially sensitive information.

**Data** means the Shared Personal Data being transferred between the Parties under this Agreement as set out in Schedule 2.

**Data Protection Legislation** means, for the periods in which they are in force in the United Kingdom, the Data Protection Act 2018, the GDPR, the Electronic Communications Data Protection Directive 2002/58/EC, the Privacy and Electronic Communications (EC Directive) Regulations 2003 and all applicable Laws and regulations relating to Processing of Personal Data and privacy, including where applicable the guidance and codes of practice issued by the Information Commissioner, in each case as amended or substituted from time to time.

**Deadline** means any binding date or deadline agreed between the Parties in respect of the respective Party's Obligations.

**Documentation** means any document, record, report, presentation, data (including original and raw data) or other written material.

**EIR** means the Environmental Information Regulations 2004 and any subordinate legislation from time to time together with any guidance and/or codes of practice issued by the Information Commissioner or relevant government department in relation to the Environmental Information Regulations 2004.

**FOIA** means the Freedom of Information Act 2000 and any subordinate legislation (as defined in section 84 of the Freedom of Information Act 2000) made under the Freedom of Information Act 2000 from time to time together with any guidance and/or codes of practice issued by the Information Commissioner or relevant government department in relation to the Freedom of Information Act 2000.

**GDPR** means (a) the General Data Protection Regulation (Regulation (EU) 2016/679); and (b) any equivalent legislation amending or replacing the General Data Protection Regulation.

**Insolvency Event** means:

(a) the University is deemed unable to pay its debts within the meaning of section 123 of the Insolvency Act 1986

(b) the University commences negotiations with all or any class of its creditors with a view to rescheduling any of its debts, or makes a proposal for or enters into any compromise or arrangement with its creditors;

(c) a petition is filed, a notice is given, a resolution is passed, or an order is made, for or in connection with the winding up of the University;

(d) an application is made to court, or an order is made, for the appointment of an administrator, or a notice of intention to appoint an administrator is given or if an administrator is appointed, over the University;

(e) the holder of a qualifying floating charge over the assets of the University has become entitled to appoint or has appointed an administrative receiver;

(f) a person becomes entitled to appoint a receiver over the assets of the University or a receiver is appointed over the assets of the University;

(g) a creditor or encumbrancer of University attaches or takes possession of, or a distress, execution, sequestration or other such process is levied or enforced on or sued against, the whole or any part of the other Party's assets and such attachment or process is not discharged within 14 days;

(h) any event occurs, or proceeding is taken, with respect to the University in any jurisdiction to which it is subject that has an effect equivalent or similar to any of the events mentioned in (a) to (h) (inclusive); or

(i) the University suspends or ceases, or threatens to suspend or cease, carrying on all or a substantial part of its business.

**Institution Inventions** means the outputs generated as a result of the Octane API analysis of the Data.

**Institution Obligations** means those obligations to be fulfilled by the Institution in accordance with clause 4.

**Law** means any legal provision the parties must comply with including any law, statute, subordinate legislation within the meaning of section 21(1) of the Interpretation Act 1978, bye-law, enforceable right within the meaning of section 2 of the European Communities Act 1972, regulation, order, mandatory guidance or code of practice, judgment of a relevant court of law, or directives or requirements of any regulatory body, whether in the UK or elsewhere.

**Obligations** means University and Institution Obligations

**Octane API** means the algorithm and software to analyse the Data.

**OCT** means human eye scans from optical coherence tomography.

**Prohibited Act means** the following constitute Prohibited Acts:

(a) to directly or indirectly offer, promise or give any person working for or engaged by the Institution a financial or other advantage as an inducement or reward for any improper performance of a relevant function of activity in relation to obtaining this Agreement or any other contract with University;

(b) to directly or indirectly request, agree to receive or accept any financial or other advantage as an inducement or a reward for improper performance of a relevant function or activity in connection with this Agreement;

(c) committing any offence: (i) under the Bribery Act 2010; (ii) under legislation or common law concerning fraudulent acts; or (iii) of defrauding, attempting to defraud or conspiring to defraud the Authority;

(d) any activity, practice or conduct which would constitute one of the offences listed under (c) above, if such activity, practice or conduct had been carried out in the UK.

**Pseudonymised** means the processing of the Data in such a manner that the Data can no longer be attributed to a specific Data Subject without the use of additional information, provided that such additional information is kept separately and is subject to technical and organisational measures to ensure that the Data are not attributed to an identified or identifiable natural person.

**Purpose** means the activities that are undertaken by the Institution in which Data is used as described in Annex B. The activities that are undertaken by the University in which algorithms and software are used as described in Annex C to Schedule 1.

**Relevant Requirement** all applicable law relating to bribery, corruption and fraud, including the Bribery Act 2010 and any guidance issued by the Secretary of State for Justice pursuant to section 9 of the Bribery Act 2010.

**Representative** means, in relation to a party, its employees, officers, representatives and advisors.

**Subcontractor** means any service provider, supplier or subcontractor of the Institution.

**University Obligations** means those obligations to be fulfilled by the Institution in accordance with clause 4.

**Working Day** means Monday to Friday, excluding any public holidays in England and Wales.

Unless the context otherwise requires, words in the singular shall include the plural and in the plural shall include the singular.

## 2 PRINCIPLES OF THE AGREEMENT

2.1 The Appendices to the Agreement form an integral part of the Agreement. In case of inconsistencies between the Agreement and any Appendix, the terms of the Agreement shall prevail. The general terms and conditions of the Parties shall not apply, even if reference is made to them by either Party.

2.2 The University hereby nominates Mr Mandeep Gupta, Lead Optometrist, WUTH, phone number 07803923952 as the University's contact person for the Institution (the "University Project Manager"). The University may not exchange the University Project Manager without the Institution's written approval. Such approval shall not be unreasonably withheld.

2.3 Institution nominates Dr Siegfried Karl Wagner, Academic Clinical Fellow, NIHR Biomedical Research Centre at Moorfields Eye Hospital and UCL Institute of Ophthalmology, phone number 0207253341, as the Institution's contact person for the University (the "Institution Project Manager"). The Institution may not exchange the Institution Project Manager without the University's written approval. Such approval shall not be unreasonably withheld.

2.4 Both Parties shall nominate a deputy for each of the respective contact person/Project Manager, who shall be authorised to represent the contact person/Project Manager in the event of absence of the same.

## 3 SCOPE OF OBLIGATIONS

3.1 The Parties shall fulfil their Obligations as set out at Schedule 1.

3.2 Any requirement for a Change shall be subject to the Change Control Procedure.

## 4 OBLIGATIONS OF THE PARTIES

4.1 To the extent that the Parties have agreed or subsequently agree on specific deliverables, each Party shall provide the deliverables to the other Party as specified in or pursuant to the Agreement at the times set forth in or pursuant to the Agreement. The relevant Party shall make all reasonable modifications to such deliverables within a reasonable period after receipt of the other Party's written request.

4.2 The Institution shall report to the University any serendipitous findings that may be of direct and substantial consequence for the health or wellbeing of a patient and/or its family members. The University shall handle such serendipitous findings in accordance with its internal policies and applicable Law.

4.3 Each party represents and warrants that in carrying out its Obligations:

4.3.1 it will do so within the timelines and at the Deadlines agreed upon and with all reasonable care and skill in accordance with all applicable Laws and the provisions of this Agreement;

4.3.2 it shall use suitably qualified and trained employees capable of carrying out Institution Obligations;

4.3.3 its personnel is part of the Institution's own operations and is managed; and instructed by the Institution only;

4.3.4 any deliverables, Data, reports and other information provided to University pursuant hereto shall be prepared in accordance with best practices applicable to this Agreement;

4.3.5 it is in possession of (or will obtain prior to fulfilling Institution Obligations hereunder) and will comply with all necessary permits, approvals, licenses, consents and other authorizations required by applicable Law for the performance of Institution Obligations ("**Permits**").

4.4 All Data to be used for the performance of Institution Obligations and/or transferred to the Institution hereunder are collected in accordance with informed consents and fulfil besides possible other elements necessary at least the following requirements:

4.4.1 the informed consent complies with applicable Law and is given by the consenting person in compliance with applicable Law;

4.4.2 the consenting person, upon his/her clear comprehension and understanding of all facts, implications, and future consequences at the time the consent is given;

4.4.3 Data shall be Pseudonymised by the University before being provided to the Institution.

## 5 PRICE, PAYMENT AND TAXES

The Parties agree that Institution Obligations and University Obligations are being provided to the other respective Party by way of mutual consideration.

## 6 DELAY

6.1 The Institution shall fulfil Institution Obligations and any deliverables in accordance with the agreed Deadlines set forth in Schedule 1 or otherwise agreed upon between the Parties.

6.2 The University shall fulfil University Obligations and any deliverables in accordance with the agreed Deadlines set forth in Schedule 1 or otherwise agreed upon between the Parties.

6.3 Each Party shall keep the other Party informed about the progress of their respective Obligations. If either of the Parties are delayed in fulfilling their respective Obligations, they shall inform the other Party forthwith.

## 7 OWNERSHIP AND LICENCE OF OCTANE-API

7.1 The University will be granted a royalty-free perpetual non-exclusive license to use the research results resulting from the utilisation of Institution algorithms for its own purposes, as specified in Schedule 1 and in accordance with clause 12. [DN: please confirm whether the reference to Schedule 1 is intended to refer to details of the utilisation of algorithms, or the University's 'own purposes' I can confirm it is intended to refer to details of the utilisation of algorithms.

7.2 OCTANE-API is not licenced for clinical use.

## 8 CONFIDENTIALITY

8.1 Subject to clause 8.2, each Party shall keep the other Party's Confidential Information confidential and shall not:

8.1.1 use such Confidential Information except for the purpose of performing its rights and obligations under or in connection with this Agreement; or

8.1.2 disclose such Confidential Information in whole or in part to any third party, except as expressly permitted by this clause 0.

8.2 The obligation to maintain confidentiality of Confidential Information does not apply to any Confidential information:

8.2.1 which the other Party confirms in writing is not required to be treated as Confidential Information;

8.2.2 which is obtained from a third party who is lawfully authorised to disclose such information without any obligation of confidentiality;

8.2.3 which a Party is required to disclose by judicial, administrative, governmental or regulatory process in connection with any action, suit, proceedings or claim or otherwise by applicable Law, including the FOIA or the EIRs;

8.2.4 which is in or enters the public domain other than through any disclosure prohibited by this Agreement;

8.2.5 which a Party can demonstrate was lawfully in its possession prior to receipt from the other Party; or

8.2.6 which is disclosed by the Institution on a confidential basis to any central government or regulatory body.

8.3 A Party may disclose the other Party's Confidential information to those of its Representatives who need to know such Confidential Information for the purposes of performing or advising on the Party's obligations under this Agreement, provided that:

8.3.1 it informs such Representatives of the confidential nature of the Confidential Information before disclosure; and

8.3.2 it procures that its Representatives shall, in relation to any Confidential Information disclosed to them, comply with the obligations set out in this clause as if they were a party to this Agreement,

8.3.3 and at all times, it is liable for the failure of any Representatives to comply with the obligations set out in this clause 8.3.

8.4 The provisions of this clause 0 shall survive for a period of five years from the termination date.

## 9 FORCE MAJEURE

9.1 Force Majeure shall mean any event beyond the reasonable control of a Party, including but not limited to war, terrorist act, earthquake, hurricane, flooding and national strikes. A Party affected by Force Majeure shall forthwith notify the other Party of the nature and extent thereof.

9.2 Neither Party shall be deemed to be in breach of the Agreement, or otherwise be liable to the other, for delay in performance, or non-performance, of any of its obligations under the Agreement to the extent that such delay or non-performance is due to Force Majeure of which it has notified the other Party. The time for performance of the delayed obligation shall be extended accordingly. If the consequences of the Force Majeure event continue for a period of more than thirty (30) days, either Party shall be entitled to terminate the Agreement.

## 10 INSURANCE

10.1 The Parties are responsible for maintaining, at their own expense programs of insurance with reputable insurance companies in amounts which are reasonable and customary in the market for the respective activities they are carrying out under the Agreement and adequate to cover reasonable losses and damages caused by the Institution or the University, the Parties' personnel, Affiliates or Subcontractors in the course of its business and carrying out its Obligations under this Agreement.

10.2 The University shall give the Institution, on request, evidence of its policies referred to in this clause.

## 11 LIMITATION OF LIABILITY

11.1 Subject to clause 11.2, neither Party shall be liable to the other Party, whether in contract, tort (including negligence), breach of statutory duty, or otherwise, for any indirect or consequential loss arising under or in connection with this Agreement.

11.2 Each Party shall at all times take all reasonable steps to minimise and mitigate any loss or damage arising out of or in connection with this Agreement, including any losses for which the relevant Party is entitled to bring a claim against the other Party pursuant to the indemnities in this Agreement.

11.3 Subject to clause 11.1 and 11.4, each Party's liability to the other Party for all claims, losses or damages, whether arising from tort (including negligence), breach of statutory duty, or otherwise, arising under or in connection with this Agreement shall be limited to the Parties' respective insurance cover.

11.4 Notwithstanding any other provision of this Agreement neither Party limits or excludes its liability for:

11.4.1 fraud or fraudulent misrepresentation;

11.4.2 death or personal injury caused by its negligence (or the negligence of its personnel, agents or subcontractors);

11.4.3 breach of any obligation as to title implied by statute; or

11.4.4 any other liability for which may not be limited under any applicable law.

## 12 INTELLECTUAL PROPERTY

12.1 It is expressly agreed that neither Institution nor University transfers by operation of this Agreement to the other party any right in or license to any patents, copyrights, or other proprietary right owned as of the Effective Date of the Agreement or arising outside of the research conducted under this Agreement.

12.2 Any Background Intellectual Property Rights which may be contained in the Data and/or Material transferred to Institution for use in the Research Plan under this Agreement shall only be used for the Research Plan and University shall retain ownership in such Background Intellectual Property Rights.

12.3 Any improvements to a Party's Background generated in the conduct of the Research Project and all title and interest therein shall be owned exclusively by the Party owning such Background, and such Party shall be free to use and exploit the same at its discretion and the Background of the Party, as well as any improvements to a Party's Background, shall not be affected by terms and conditions of the present Agreement.

12.4 Unless specifically stated otherwise in this Agreement, all ownership rights to the Foreground arising from or in relation to the execution of the Agreement and Intellectual Property Rights thereto shall solely and exclusively belong to the University.

12.5 University reserve the right to request from the Institution for Institution Inventions during the Initial Term, or where relevant, the Extended Term of the Agreement.

12.6 The Institution grants University a world-wide, royalty free, perpetual, non-exclusive license to use Institution Inventions for internal research and educational purposes.

## 13 COMPLIANCE WITH LAWS

Both Parties warrant that they will perform their respective Obligations in strict compliance with all applicable Laws, including labour Laws, Data Protection Legislation and Laws relating to environment, health and safety.

## 14 DATA PROTECTION

Both Parties will comply with the Data Protection Legislation and the provisions of the Data Sharing Agreement at Schedule 2.

## 15 PUBLICATION

15.1 Both Parties agree, that the University and the Institution may have the wish to make research results publicly available in the form of articles in scientific journals, seminars, poster presentations, demonstrations, abstract books, etc. In the event of any intended scientific publication relating to the Purpose, the Parties shall safeguard each Party's interests and submit the manuscript to the other Party a minimum of 14 day prior to the proposed publication. Authorship will be dependent on the contribution of the generated research derived data to the paper as a whole. In principle, the Institution should be co-authors on each paper that results from this collaboration.

15.2 Each Party will provide any material for publication for review to the other Party at least thirty (30) days prior to submission for publication, public dissemination or review by a publication committee. If the other Party does not respond with this period, the publishing party will be free to proceed with the intended publication of the research results without further delay.

15.3 During the thirty (30) day period for review, the other Party shall be entitled to:

15.3.1 make a reasoned request to the publication party to delay the publication for an additional period of sixty (60) days (following the thirty (30) day period for review) in order to enable the other party to take steps to protects its proprietary information and/or intellectual property rights and know how, and the publication party shall not unreasonably withhold its consent to such a request; and

15.3.2 may cause the publication party to remove from the projected publication any confidential information from the other Party that are not research results resulting from the Purpose. The publication party will adapt the proposed publication in such a way that it will not publish the confidential information that is indicated by the other Party. The publication Party will only have the right to publish the adapted proposed publication after the written consent from the other Party.

15.4 In all oral presentations or written publications concerning the Purpose, each party will acknowledge the other Party's contribution to the Purpose, unless otherwise agreed in writing by the Parties.

15.5 Each Party shall promptly communicate in writing all results, data and developments resulting from the use of the Data ("Results") to the other Party. Each Party agrees not to use or disclose these Results to any third party without the written consent of the other party, which consent shall not be unreasonably withheld. Each Party shall be free to use these Results for its own educational, academic and research purposes, provided that no disclosure shall be made of any confidential information of the other Party.

## 16 FREEDOM OF INFORMATION

16.1 For the purposes of this clause 16, "**Information**" has the meaning given under section 84 of the FOIA and the meaning attached to "environmental information" contained in regulation 2 of the EIR as appropriate.

16.2 The University acknowledges that the Institution is subject to the requirements of the FOIA and the EIR.

16.3 The University shall provide all necessary assistance and cooperation as reasonably requested by the Institution to enable the Institution to comply with its obligations under the FOIA and EIR and transfer to the Institution all requests for Information under the FOIA and the EIR relating to this Agreement that it receives as soon as practicable and not respond directly to any such requests unless authorised in writing to do so by the Institution.

16.4 The University acknowledges that the Institution may be required under the FOIA and EIR to disclose Information without consulting or obtaining consent from UNIVERSITY. The Institution shall take reasonable steps to notify the University of a relevant request for Information (in accordance with the Secretary of State's section 45 Code of Practice on the Discharge of the Functions of Public Authorities under Part 1 of the FOIA) to the extent that it is permissible and reasonably practical for it to do so but (notwithstanding any other provision in this Agreement) the Institution shall be responsible for determining in its absolute discretion whether any Information is exempt from disclosure in accordance with the FOIA and/or the EIR.

## 17 PREVENTION OF BRIBERY

17.1 The University represents and warrants that neither it, nor its personnel:

17.1.1 has committed a Prohibited Act;

17.1.2 to the best of its knowledge has been or is subject to an investigation, inquiry or enforcement proceedings by a governmental, administrative or regulatory body regarding any Prohibited Act or alleged Prohibited Act; or

17.1.3 has been listed by any government department or agency as being debarred, suspended, proposed for suspension or debarment, or otherwise ineligible for participation in government procurement programmes or contracts on the grounds of a Prohibited Act.

17.2 The University shall notify the other promptly if, at any time during the Term, its circumstances, knowledge or awareness changes such that it would not be able to repeat the warranties set out in clause 17.1 at the relevant time.

17.3 The University represents and warrant shall (and shall procure that its University personnel shall):

17.3.1 not commit a Prohibited Act; and/or

17.3.2 not do or omit to do anything that would cause the Institution or any of the Institution's employees, consultants, contractors, sub-contractors or agents to contravene any of the Relevant Requirements or otherwise incur any liability in relation to the Relevant Requirements.

17.3.3 promptly report to the Institution any request or demand for any undue financial or other advantage of any kind received by the Supplier in connection with performance of this Agreement.

17.4 The University shall maintain appropriate and up to date records showing all payments made by the University in connection with this Agreement and the steps taken to comply with its obligations under clause 17.3.

17.5 The University shall allow the Institution and its third party representatives to audit any of the University's records and any other relevant documentation.

## 18 TERM AND TERMINATION

18.1 The Agreement shall become effective on the day of the last signature of the Agreement and shall continue for a period of two (2) years ("Initial Term"), after which the Parties may extend the Agreement by a further twelve (12) months ("Extended Term") by agreeing in writing to extend the Agreement at least three (3) months prior to the end of the Term.

**Voluntary termination**

18.2 Without affecting any other right or remedy available to the Parties, either Party may terminate this Agreement at any time by giving thirty (30) days' written notice to the other Party.

**Termination for breach**

18.3 Either Party may terminate this Agreement with immediate effect by service of written notice on the other Party in the following circumstances:

18.3.1 if either Party is in breach of any material obligation under this Agreement provided that if the breach is capable of remedy, the Party not in breach may only terminate this Agreement under this clause 18.3 if the Party in breach has failed to remedy such breach within 30 days of receipt of notice from the Party not in breach (a Remediation Notice) to do so;

18.3.2 if there is an Insolvency Event;

18.3.3 if the Institution reasonably believes that the circumstances set out in regulation 73(1) of the Public Contracts Regulations 2015 apply.

## 19 CONSEQUENCES OF TERMINATION

19.1 The Institution shall immediately cease and refrain from using Data on termination or expiry of the Agreement.

19.2 The Institution will destroy/delete the Data within the earlier of:

19.2.1 three (3) months after completion of the project in accordance with clause 19.3; or

19.2.2 expiry of the Initial Term or where relevant the Extended Term

unless agreed otherwise in writing.

19.3 For the avoidance of doubt, completion of the project shall be when:

19.3.1 Data has been processed by the University and provided to the Institution;

19.3.2 the Institution has delivered the Institution Inventions to the University; and

19.3.3 the Parties agree that the project is completed.

19.4 Any provision of this Agreement that expressly or by implication is intended to come into or continue force on or after termination or expiry, including clause 0(Confidentiality), clause 10 (Insurance), clause 10.2 (Limitation of Liability), clause 14 (Data Protection), clause 16 (Freedom of Information), clause 18.3 (Termination for Breach) and this clause 19 (Consequences of termination), shall remain in full force and effect.

19.5 Termination or expiry of this Agreement shall not affect any rights, remedies, obligations or liabilities of the parties that have accrued up to the date of termination or expiry, including the right to claim damages in respect of any breach of the agreement which existed at or before the termination date.

## 20 NOTICES

20.1 Any notice given to a Party under or in connection with this contract shall be in writing marked for the attention of the Party's Project Manager and shall be:

20.1.1 delivered by hand or by pre-paid first-class post or other next working day delivery service at its registered office (if a company) or its principal place of business (in any other case); or

20.1.2 sent by fax to its main fax number or sent by email to the address specified in clause 2.

20.2 Any notice shall be deemed to have been received:

20.2.1 if delivered by hand, on signature of a delivery receipt;

20.2.2 if sent by pre-paid first-class post or other next working day delivery service, at 9.00 am on the second Working Day after posting.

20.2.3 if sent by fax or email, at the time of transmission, or if this time falls outside working hours in the place of receipt, when working hours resume. In this clause 20.2.3, working hours means 9.00am to 5.00pm Monday to Friday on a day that is not a public holiday in the place of receipt.

20.3 This clause does not apply to the service of any proceedings or other documents in any legal action or, where applicable, any arbitration or other method of dispute resolution

**21 WAIVER**

No failure or delay by a Party to exercise any right or remedy provided under this Agreement or by law shall constitute a waiver of that or any other right or remedy, nor shall it prevent or restrict the further exercise of that or any other right or remedy. No single or partial exercise of such right or remedy shall prevent or restrict the further exercise of that or any other right or remedy.

**22 RIGHTS AND REMEDIES**

Except as expressly provided in this Agreement, the rights and remedies provided under this Agreement are in addition to, and not exclusive of, any rights or remedies provided by law.

**23 SEVERABILITY**

23.1 If any provision or part-provision of this Agreement is or becomes invalid, illegal or unenforceable, it shall be deemed deleted, but that shall not affect the validity and enforceability of the rest of this Agreement.

23.2 If any provision or part-provision of this Agreement is deemed deleted under clause 23.1, the parties shall negotiate in good faith to agree a replacement provision that, to the greatest extent possible, achieves the intended commercial result of the original provision.

**24 PARTNERSHIP OR AGENCY**

24.1 Nothing in this Agreement is intended to, or shall be deemed to, establish any partnership or joint venture between any of the Parties, constitute any Party the agent of another Party, or authorise any Party to make or enter into any commitments for or on behalf of any other Party.

24.2 Each Party confirms it is acting on its own behalf and not for the benefit of any other person.

**25 THIRD PARTY RIGHTS**

25.1 This Agreement does not give rise to any rights under the Contracts (Rights of Third Parties) Act 1999 to enforce any term of this Agreement.

## 26 PUBLICITY

26.1 The University shall not:

26.1.1 make any press announcements or publicise this Agreement or its contents in any way; or

26.1.2 use the Institution's name or logo in any promotion or marketing or announcement of orders,

except as required by law, any government or regulatory authority, any court or other authority of competent jurisdiction, without the prior written consent of the Institution, which shall not be unreasonably withheld or delayed.

## 27 ASSIGNEMENT

27.1 Neither Party shall assign this Agreement or any right granted hereunder without the prior written consent of the other Party.

## 28 ENTIRE AGREEMENT

28.1 This Agreement and the documents referred to in it constitutes the entire agreement between the parties and supersedes and extinguishes all previous agreements, promises, assurances, warranties, representations and understandings between them, whether written or oral, relating to its subject matter.

28.2 Each Party agrees that it shall have no remedies in respect of any statement, representation, assurance or warranty (whether made innocently or negligently) that is not set out in this Agreement. Each party agrees that it shall have no claim for innocent or negligent misrepresentation or negligent misstatement based on any statement in this Agreement.

## 29 VARIATION

No variation or amendment to this Agreement will be effective unless it is made in writing by mutual consent and signed by each Party's representative.

## 30 COUNTERPARTS

This Agreement may be executed in any number of counterparts, each of which when executed and delivered shall constitute an original of this Agreement, but all the counterparts shall together constitute the same agreement.

## 31 GOVERNING LAW

This Agreement and any dispute or claim arising out of or in connection with it or its subject matter or formation (including non-contractual disputes or claims) shall be governed by and construed in accordance with the law of England and Wales.

## 32 JURISDICTION

Each Party irrevocably agrees that the courts of England and Wales shall have exclusive jurisdiction to settle any dispute or claim arising out of or in connection with this Agreement or its subject matter or formation (including non-contractual disputes or claims).

This Agreement has been entered into on the date stated at the beginning of it.

**SIGNED ON BEHALF OF Wirral University Teaching Hospital NHS Foundation Trust :**

| Name | Position | Signature | Date |
|---|---|---|---|
| [redacted] | Dep-t, MS | | 3/11/21 |

**SIGNED ON BEHALF OF MOORFIELDS EYE HOSPITAL NHS FOUNDATION TRUST**

| Name | Position | Signature | Date |
|---|---|---|---|
| Declan Flanagan | Deputy Director of Researc | DocuSigned by: [redacted] D13CEDD15F1B4DD... | 2/14/2022 |

# SCHEDULE 1 – INSTITUTION AND UNIVERSITY OBLIGATIONS

## Annex A – Purpose MOORFIELDS (Research project MOORFIELDS using the Data)

**Project/Project Plan:**

- The Institution has developed a Deep Learning OCT segmentation algorithm in collaboration with DeepMind.
- The University will provide the Institution with a set of Data from the 'Evaluating the morphological changes seen on OCT in patients with wet AMD and their bearing on visual prognosis, lesion activity and treatment efficacy' Study which the Institution can use to test the algorithms.
- The Data will be managed through the Moorfields Research Informatics Strategy infrastructure.
- The Institution will use these OCT images for upload to OCTANE API and this will generate numerical and qualitative outputs. The Institution will not use the Data for any commercial activity.
- The Institution will destroy/delete the Data within the earlier of:
    - three (3) months after completion of the project
    - expiry of the Initial Term or where relevant the Extended Term

  unless agreed otherwise in writing.
- For the avoidance of doubt, completion of the project shall be when:
    - Data has been processed by the University and provided to the Institution;
    - the Institution has delivered the Institution Inventions to the University; and
    - the Parties agree that the project is completed.
- The University is entitled to use the Institution Inventions for its own projects.
- The Institution Inventions will be included in the data which the Institution will share with the University.

## Annex B – Measures taken by the Institution to prevent a data leak

- The Data will be uploaded to the Moorfields Research Informatics Strategy infrastructure.
- The Data will then be ephemerally processed by the Institution-DeepMind algorithm (this is a Cloud-based API).
- The Institution is required to produce audit logs demonstrating each stage of the process.
- The Institution shall only use the Data for the Agreed Purposes as set out in Schedule 2.

## SCHEDULE 2 – DATA SHARING AGREEMENT

### 1 INTENTION AND APPLICATION OF THIS AGREEMENT

1.1 The parties agree to share the Shared Personal Data for the Agreed Purposes as set out in this Data Sharing Agreement (**DSA**).

1.2 This DSA supersedes all prior agreements, negotiations and discussions between the parties in relation to the sharing of Personal Data.

### 2 DEFINITIONS AND INTERPRETATION

2.1 **Agreed Purposes** has the meaning set out in clause 4 of this DSA.

2.2 **Data Controller, Data Processor, Data Subject, Personal Data Breach, Processing** (including **"Process"** and **"Processed"**) **and Appropriate Technical and Organisational Measures** have the meaning set out in the Data Protection Legislation.

2.3 **Data Protection Impact Assessment** means an assessment by a Data Controller of the impact of the envisaged Processing on the protection of Personal Data.

2.4 **DPA 2018** means the Data Protection Act 2018.

2.5 **Information Commissioner's Office** means the UK's supervisory authority based at Information Commissioner's Office, Wycliffe House, Water Lane, Wilmslow, Cheshire, SK9 5AF.

2.6 **Joint Data Controllers** means where two or more Data Controllers jointly determine the purpose and means of Processing.

2.7 **Lawful Bases for Sharing** means the lawful bases on which the parties will share the Personal Data as set out in clause 7 of this DSA.

2.8 **Personal Data** means any data relating to an identified or identifiable natural person. An identifiable person is one who can be identified, directly or indirectly, in particular by reference to an identification number or to one or more factors specific to his physical, physiological, mental, economic, cultural or social identity. For the avoidance of doubt, Pseudonymised Data is also considered to be Personal Data.

2.9 **Shared Personal Data** means the Personal Data to be shared between the parties under clause 6 of this DSA.

2.10 **Special Categories of Personal Data** has the meaning set out in the Data Protection Legislation and for the purpose of this DSA shall include information relating to criminal convictions and offences.

### 3 THE DATA PROTECTION RELATIONSHIP

3.1 The parties acknowledge that for the purposes of the Data Protection Legislation the University and the Institution are acting as Joint Data Controllers in relation to any Processing of Personal Data as carried out under this DSA.

### 4 PURPOSE

4.1 This DSA sets out the framework for the sharing of Personal Data when one Data Controller discloses Personal Data to another Data Controller. It defines the principles and procedures that the parties shall adhere to and the responsibilities the parties owe to each other.

4.2 The parties consider this data sharing initiative is justifiable on the grounds that participants have consented to the use of their Personal Data for research purposes and their Personal Data will be shared with Institution in a pseudonymised format.

4.3 The parties agree to only share the Shared Personal Data for the purpose of inputting Pseudonymised retinal scans through the OCTane API for research purposes to obtain certain classification outputs (i.e. triage recommendation and disease classification), intermediate segmentation outputs and raw data to enable the development and use of AI algorithms.

4.4 The parties shall not Process Shared Personal Data in a way that is incompatible with the purposes described in this clause 4 of this DSA (**Agreed Purposes**).

## 5 SINGLE POINT OF CONTACT

5.1 Each party shall appoint a single point of contact (**SPoC**) who will work together to reach an agreement with regards to any issues arising from the data sharing and to actively improve the effectiveness of the data sharing initiative. The points of contact for each of the parties are:

| | |
|---|---|
| **University** | Mr Mandeep Gupta, Lead Optometrist, Ophthalmology department, Wirral University Teaching Hospital NHS Foundation Trust, Arrowe Park Road, Upton, Wirral, CH49 5PE, tel: +44 (0) 7803 923 952. |
| **Institution** | Dr Siegfried Wagner, Academic Clinical Fellow, NIHR Biomedical Research Centre at Moorfields Eye Hospital and UCL Institute of Ophthalmology, 162 City Road, London, EC1V 2PD, tel: +44 (0) 20 7253 3411. |

## 6 SHARED PERSONAL DATA

6.1 Shared Personal Data shall include the following types of Special Categories of Personal Data relevant to the following categories of Data Subject:

6.1.1 **WUTH Study Participants:** Pseudonymised health data, being images of the back of the eye from OCT scanning devices.

6.2 The Shared Personal Data must not be irrelevant or excessive with regard to the Agreed Purposes.

## 7 LAWFUL BASES FOR SHARING

7.1 The sharing of the Shared Personal Data between the parties will be carried out on the following lawful bases (**Lawful Bases for Sharing**):

7.1.1 Personal Data

*(a)* Article 6(1)(e) GDPR *processing is necessary for the performance of a task carried out in the public interest or in the exercise of official authority;*

7.1.2 Special Categories of Personal Data:

*(a)* Article 9(2)(j) GDPR *processing is necessary for archiving, scientific or historical research purposes;*

7.2 Each party will ensure that it only further Processes the Shared Personal Data fairly and lawfully and that it has legitimate grounds under the Data Protection Legislation for the Processing of Shared Personal Data.

## 8 COMPLIANCE WITH THE DATA PROTECTION LEGISLATION

8.1 Each party shall comply with all the obligations imposed on a Data Controller under the Data Protection Legislation.

8.2 Each party warrants and undertakes that it will:

8.2.1 Process the Shared Personal Data in compliance with all applicable laws, enactments, regulations, orders, standards and other similar instruments that apply to its Personal Data Processing operations.

8.2.2 Respond within a reasonable time and as far as reasonably possible to enquiries from the Information Commissioner's Office in relation to the Shared Personal Data.

8.2.3 Respond to a request from a Data Subject in accordance with the Data Protection Legislation.

8.2.4 Where applicable, pay the appropriate fees to the Information Commissioner's Office to Process all Shared Personal Data for the Agreed Purposes.

8.2.5 Maintain complete and accurate records and information to demonstrate its compliance with this DSA.

8.2.6 Take all appropriate steps to ensure compliance with the security measures set out in clause 12 of this DSA.

8.2.7 Not disclose or transfer Shared Personal Data outside the European Economic Area (**EEA**) unless it complies with the obligations set out in clause 14 of this DSA.

8.3 Any party sharing Shared Personal Data warrants and undertakes that it is entitled to provide the Shared Personal Data to the recipient party and will ensure that the Shared Personal Data are accurate.

8.4 The parties agree to use compatible technology, where possible, for the Processing of Shared Personal Data to ensure that there is no lack of accuracy resulting from Personal Data transfers.

8.5 The parties agree that, considering the nature of the Processing and the Data Subjects to which that Processing relates, the envisaged Processing under the DSA is likely to result in a high risk to the rights and freedoms of Data Subjects and as such, in accordance with Article 35 of the GDPR, each party agrees to conduct a Data Protection Impact Assessment prior to commencing any Processing, which shall include:

8.5.1 a systematic description of the envisaged Processing operations and the purpose of the Processing;

8.5.2 an assessment of the necessity and proportionality of the Processing operations in relation to the purposes;

8.5.3 an assessment of the risks to the rights and freedoms of Data Subjects; and

8.5.4 the measures envisaged to address the risks, including safeguards, security measures and mechanisms to ensure the protection of Personal Data.

## 9 LAWFUL, FAIR AND TRANSPARENT PROCESSING

9.1 Each party shall ensure that:

9.1.1 it Processes the Shared Personal Data fairly and lawfully during the term of this DSA;

9.1.2 it only shares the Shared Personal Data with the other parties on the Lawful Bases for Sharing;

9.1.3 it shall ensure the safekeeping and confidentiality of the Shared Personal Data and shall limit access to the Shared Personal Data to those employees or other authorised representatives who have a need to process them in accordance with this DSA and who are bound by written confidentiality obligations with respect to the Shared Personal Data;

9.1.4 it shall use prudence and reasonable care in the use, handling, storage, transportation, disposition and containment of the Shared Personal Data;

9.1.5 it shall adopt Appropriate Technical and Organisational Measures to prevent any Personal Data Breach, the minimum measures of which are specified in Annex C to Schedule 1. If either party identifies a Personal Data Breach, they will:

(a) inform the other party as soon as reasonably possible, though not later than twenty-four (24) hours after discovering the Personal Data Breach, the possible impact of the Personal Data Breach on the other party and/or the Data Subject(s), and also measures that is has taken or will take in order to correct the Personal Data Breach and/or limit its consequences;

(b) will immediately, at its own expense, take all measures to correct the shortcomings in security that resulted in the Personal Data Breach and to limit its consequences;

9.1.6 it only further Processes the Shared Personal Data on one or more of the legal bases set out in the Data Protection Legislation;

9.1.7 it provides clear and sufficient information to the Data Subjects, in respect of the Shared Personal Data, in accordance with the Data Protection Legislation, of the purposes for which it will Process their Personal Data, the legal basis for Processing their Personal Data and such other information as is required by Articles 13 and 14 of the GDPR including:

(a) if Shared Personal Data will be transferred to a third party, that fact and sufficient information about such transfer and the purpose of such transfer to enable the Data Subject to understand the purpose and risks of such transfer (including the sharing of Personal Data with the other parties to this DSA); and

(b) if Shared Personal Data will be transferred outside the EEA pursuant to clause 14.4 of this DSA, that fact and sufficient information about such transfer, the purpose of such transfer and the safeguards put in place by the Data Controller to enable the Data Subject to understand the purpose and risks of such transfer.

9.2 Where appropriate, each party shall ensure that it has all necessary consents in place to enable lawful transfer of the Shared Personal Data for the Agreed Purposes.

## 10 DATA QUALITY

10.1 The parties have developed a reliable means of converting Shared Personal Data to ensure compatibility with each party's respective datasets.

10.2 Each party shall ensure that before the date the Services Agreement is entered into, Shared Personal Data are accurate, and it will update the same if required prior to transferring the Shared Personal Data.

10.3 In the event that either party becomes aware of any changes to the Shared Personal Data, or aware or suspects that any of the Shared Personal Data contains inaccuracies, it shall notify the other party without undue delay.

## 11 DATA SUBJECTS' RIGHTS

11.1 The parties each agree to provide such assistance as is reasonably required to enable the other parties to comply with requests from Data Subjects to exercise their rights under the Data Protection Legislation within the time limits imposed by the Data Protection Legislation.

11.2 The SPoC for each party is responsible for maintaining a record of individual requests for information, the decisions made and any information that was exchanged. Records must include copies of the request for information, details of the data accessed and shared and where relevant, notes of any meeting, correspondence or phone calls relating to the request. The SPoC for each party are detailed in clause 5.

## 12 DATA SECURITY

12.1 The parties undertake to have in place throughout the term of the DSA Appropriate Technical and Organisational Measures (to comply with the obligations under Article 32 of the GDPR) to prevent unauthorised or unlawful Processing of the Shared Personal Data and the accidental loss or destruction of, or damage to, the Shared Personal Data to ensure a level of security appropriate to the harm that might result from such unauthorised or unlawful Processing or accidental loss, destruction or damage and the nature of the Shared Personal Data to be protected.

12.2 It is the responsibility of each party to ensure that its staff members are appropriately trained to handle and Process the Shared Personal Data in accordance with the Appropriate Technical and Organisational Measures noted in clause 12.1 of this DSA together with any other applicable national guidance and have entered into confidentiality agreements relating to the Processing of Personal Data.

12.3 The level, content and regularity of training referred to in clause 12.2 of this DSA shall be proportionate to the staff members' role, responsibility and frequency with respect to their handling and Processing of the Shared Personal Data.

## 13 DATA RETENTION AND DELETION

13.1 The parties shall not retain or Process Shared Personal Data for longer than is necessary to carry out the Agreed Purposes and shall only retain the Shared Personal Data for the period specified in the Service Agreement.

13.2 All Shared Personal Data must be stored appropriately by each party in accordance with that party's data storage and retention policies and procedures. No Personal Data should be stored by personnel on their own personal computer systems.

13.3 Each party shall ensure that once Shared Personal Data is no longer required and relevant retention periods have expired, Personal Data is securely and permanently deleted in accordance with that parties' retention and disposal policies or returned to the originating party as appropriate.

## 14 DATA TRANSFERS

14.1 For the purposes of this clause, transfers of Personal Data shall mean any sharing of Personal Data with a third party, and shall include, but is not limited to, the following:

14.1.1 subcontracting the Processing of Shared Personal Data;

14.1.2 granting a third-party Data Controller access to the Shared Personal Data.

14.2 If a party appoints a third-party Data Processor to Process the Shared Personal Data it shall comply with Article 28 and Article 30 of the GDPR.

14.3 If a party grants a third party Data Controller access to the Shared Personal Data, it shall comply with Article 26 of the GDPR (in the event the third party is a Joint Data Controller) and shall comply with the Information Commissioner's Data Sharing Code of Practice (as may be updated from time to time).

14.4 The parties shall not transfer any Shared Personal Data outside the EEA unless the transferor:

14.4.1 complies with the provisions of Article 26 of the GDPR (in the event the third party is a Joint Data Controller); and

14.4.2 ensures that (i) the transfer is to a country approved by the European Commission as providing adequate protection pursuant to Article 45 of the GDPR; (ii) there are appropriate safeguards in place pursuant to Article 46 of the GDPR; or (iii) one of the derogations for specific situations in Article 49 of the GDPR applies to the transfer.

## 15 PERSONAL DATA BREACHES

15.1 Each party shall comply with its obligation to report a Personal Data Breach to the Information Commissioner's Office under Article 33 of the GDPR and (where applicable) Data Subjects under Article 34 of the GDPR and shall each, promptly (and in any event within 24 hours) inform the SPoC of any party likely to be effected by the Personal Data Breach irrespective of whether there is a requirement to notify the Information Commissioner's Office or Data Subject(s).

15.2 The parties agree to provide reasonable assistance as is necessary to each other to facilitate the handling of any Personal Data Breach in an expeditious and compliant manner.

## 16 RESOLUTION OF DISPUTES WITH DATA SUBJECTS OR THE INFORMATION COMMISSIONER'S OFFICE

16.1 In the event of a dispute or claim brought by a Data Subject or the Information Commissioner's Office concerning the Processing of Shared Personal Data against one or a number of the parties, the parties will inform each other about any such disputes or claims and will cooperate with a view to settling them amicably in a timely fashion.

## 17 REVIEW AND TERMINATION OF THIS DSA

17.1 The parties shall review the effectiveness of this DSA every 12 months, having consideration to the Agreed Purposes and shall continue, amend or terminate this DSA depending on the outcome of this review. This review will involve:

17.1.1 assessing whether the purposes for which the Shared Personal Data is being Processed are still those listed in clause 4 of this DSA;

17.1.2 assessing whether the Shared Personal Data is still as listed in clause 6 of this DSA;

17.1.3 assessing whether the legal framework governing data quality, retention, and Data Subjects' rights are being complied with;

17.1.4 assessing whether Personal Data Breaches involving the Shared Personal Data have been handled in accordance with this DSA and the Data Protection Legislation; and

17.1.5 assessing whether this DSA needs to be updated to comply with any amendments to the Data Protection Legislation.

## 18 [INDEMNITY

18.1 Each party shall indemnify the other against all liabilities, costs, expenses, damages and losses (including but not limited to any direct, indirect or consequential losses, loss of profit, loss of reputation and all interest, penalties and legal costs (calculated on a full indemnity basis) and all other reasonable professional costs and expenses) suffered or incurred by the indemnified party arising out of or in connection with the breach of the Data Protection Legislation by the indemnifying party, its employees or agents, provided that the indemnified party gives to the indemnifier prompt notice of such claim, full information about the circumstances giving rise to it, reasonable assistance in dealing with the claim and sole authority to manage, defend and/or settle it.]

## 19 ALLOCATION OF COST

19.1 Each party shall perform its obligations under this DSA at its own cost.

## SCHEDULE 3- CHANGE CONTROL

### 1 GENERAL PRINCIPLES

1.1 Where either Party sees a need to change this Agreement, it may request such Change only in accordance with the Change Control Procedure set out in paragraph 2 of this Schedule 3.

1.2 Until such time as a Change is made in accordance with the Change Control Procedure, the Parties shall, unless otherwise agreed in writing, continue to perform this Agreement in compliance with its terms before such Change.

1.3 Any discussions which may take place between the Parties in connection with a request or recommendation before the authorisation of a resultant Change shall be without prejudice to the rights of either party.

1.4 Any work undertaken by either of the Parties which has not been authorised in advance by a Change, and which has not been otherwise agreed in accordance with the provisions of this Schedule 3, shall be undertaken entirely at the expense and liability of that Party.

### 2 PROCEDURE

2.1 Discussion between the Parties concerning a Change shall result in any one of the following:

2.1.1 no further action being taken; or

2.1.2 a request to change this Agreement by either Party.

2.2 Where a Party requests to Change this Agreement, that Party shall submit to the other Party a signed Change Control Note.

2.3 The receiving Party shall give its response to the Change Control Note within three (3) weeks.

2.4 Each Change Control Note shall contain:

2.4.1 the title of the Change;

2.4.2 the originator and date of the request or recommendation for the Change;

2.4.3 the reason for the Change;

2.4.4 full details of the Change, including any specifications;

2.4.5 the price, if any, of the Change;

2.4.6 a timetable for implementation, together with any proposals for acceptance of the Change;

2.4.7 a schedule of payments if appropriate;

2.4.8 details of the likely impact, if any, of the Change on other aspects of this Agreement including:

(a) the timetable for the provision of the Change;

(b) the personnel to be provided;

(c) the Charges;

(d) the documentation to be provided;

(e) the training to be provided;

(f) working arrangements;

(g) other contractual issues;

2.4.9 the date of expiry of validity of the Change Control Note; and

2.4.10 provision for signature by the Parties.

2.5 For each Change Control Note submitted by either Party, the other Party shall, within the period of the validity of the Change Control Note:

2.5.1 allocate a sequential number to the Change Control Note; and

2.5.2 evaluate the Change Control Note and, as appropriate:

(a) request further information;

(b) accept the Change Control Note by arranging for two copies of the Change Control Note to be signed and return one of the copies to the other Party; or

(c) notify the other Party of the rejection of the Change Control Note.

2.6 A Change Control Note signed by the Parties shall constitute an amendment to this Agreement.

Appendix 3: Treatment dose related classification models and model accuracy

| Target | Feature group | Dataset | Class results | Models | AUC | CA | F1 | Precision | Recall | MCC | Specificity |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Injections first year n=3, >3 | VA_st dev | full | averaged over classes | Tree | 0.53 | 0.57 | 0.57 | 0.57 | 0.57 | 0.01 | 0.45 |
| | | | | Logistic Regression | 0.51 | 0.66 | 0.54 | 0.45 | 0.66 | -0.08 | 0.32 |
| | | | | Gradient Boosting | 0.50 | 0.62 | 0.59 | 0.58 | 0.62 | 0.03 | 0.41 |
| | | | | Neural Network | 0.50 | 0.65 | 0.56 | 0.55 | 0.65 | -0.02 | 0.34 |
| | | | | AdaBoost | 0.49 | 0.55 | 0.55 | 0.55 | 0.55 | -0.02 | 0.43 |
| | | | | kNN | 0.48 | 0.60 | 0.57 | 0.56 | 0.60 | -0.01 | 0.39 |
| | | | | Naïve Bayes | 0.47 | 0.65 | 0.54 | 0.51 | 0.65 | -0.07 | 0.32 |
| | | | | Random Forest | 0.47 | 0.60 | 0.57 | 0.56 | 0.60 | -0.01 | 0.39 |
| | | | | SVM | 0.42 | 0.65 | 0.53 | 0.45 | 0.65 | -0.10 | 0.31 |
| Injections first year n=3, >3 | VA_st dev | outliers removed | averaged over classes | Logistic Regression | 0.63 | 0.67 | 0.58 | 0.60 | 0.67 | 0.06 | 0.37 |
| | | | | Neural Network | 0.62 | 0.67 | 0.60 | 0.62 | 0.67 | 0.10 | 0.39 |
| | | | | Gradient Boosting | 0.61 | 0.64 | 0.62 | 0.61 | 0.64 | 0.12 | 0.46 |
| | | | | Naïve Bayes | 0.58 | 0.62 | 0.57 | 0.55 | 0.62 | -0.02 | 0.37 |
| | | | | kNN | 0.58 | 0.62 | 0.60 | 0.60 | 0.62 | 0.08 | 0.45 |
| | | | | Random Forest | 0.58 | 0.66 | 0.64 | 0.63 | 0.66 | 0.16 | 0.49 |
| | | | | Tree | 0.57 | 0.61 | 0.62 | 0.62 | 0.61 | 0.13 | 0.52 |
| | | | | AdaBoost | 0.51 | 0.57 | 0.57 | 0.57 | 0.57 | 0.02 | 0.45 |
| | | | | SVM | 0.50 | 0.67 | 0.57 | 0.60 | 0.67 | 0.05 | 0.35 |
| Injections first year n=3, >3 | V0_OCT | full | averaged over classes | Random Forest | 0.54 | 0.63 | 0.59 | 0.57 | 0.63 | 0.03 | 0.39 |
| | | | | SVM | 0.53 | 0.68 | 0.58 | 0.65 | 0.68 | 0.11 | 0.36 |
| | | | | kNN | 0.53 | 0.61 | 0.58 | 0.57 | 0.61 | 0.01 | 0.40 |
| | | | | Logistic Regression | 0.52 | 0.66 | 0.55 | 0.55 | 0.66 | -0.01 | 0.33 |
| | | | | AdaBoost | 0.52 | 0.55 | 0.56 | 0.57 | 0.55 | 0.03 | 0.48 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Gradient Boosting | 0.51 | 0.60 | 0.57 | 0.55 | 0.60 | -0.02 | 0.38 |
| | | | | Tree | 0.50 | 0.54 | 0.55 | 0.56 | 0.54 | -0.01 | 0.44 |
| | | | | Naïve Bayes | 0.50 | 0.61 | 0.57 | 0.56 | 0.61 | -0.01 | 0.38 |
| | | | | Neural Network | 0.49 | 0.62 | 0.57 | 0.56 | 0.62 | 0.00 | 0.37 |
| Injections first year n=3, >3 | V0_OCT | outliers removed | averaged over classes | Naïve Bayes | 0.63 | 0.58 | 0.59 | 0.65 | 0.58 | 0.17 | 0.61 |
| | | | | kNN | 0.59 | 0.67 | 0.66 | 0.65 | 0.67 | 0.19 | 0.50 |
| | | | | Random Forest | 0.59 | 0.66 | 0.63 | 0.63 | 0.66 | 0.14 | 0.45 |
| | | | | Gradient Boosting | 0.58 | 0.66 | 0.64 | 0.63 | 0.66 | 0.15 | 0.47 |
| | | | | Neural Network | 0.57 | 0.62 | 0.60 | 0.59 | 0.62 | 0.05 | 0.42 |
| | | | | SVM | 0.57 | 0.68 | 0.56 | 0.57 | 0.68 | 0.00 | 0.32 |
| | | | | Logistic Regression | 0.55 | 0.62 | 0.57 | 0.55 | 0.62 | -0.04 | 0.36 |
| | | | | AdaBoost | 0.55 | 0.60 | 0.60 | 0.61 | 0.60 | 0.09 | 0.50 |
| | | | | Tree | 0.54 | 0.60 | 0.61 | 0.61 | 0.60 | 0.11 | 0.51 |
| Injections first year n=3, >3 | VP_OCT | full | averaged over classes | SVM | 0.59 | 0.68 | 0.57 | 0.62 | 0.68 | 0.07 | 0.35 |
| | | | | AdaBoost | 0.53 | 0.59 | 0.59 | 0.59 | 0.59 | 0.06 | 0.47 |
| | | | | Neural Network | 0.51 | 0.61 | 0.56 | 0.54 | 0.61 | -0.05 | 0.35 |
| | | | | Logistic Regression | 0.49 | 0.66 | 0.55 | 0.54 | 0.66 | -0.03 | 0.33 |
| | | | | Gradient Boosting | 0.49 | 0.60 | 0.56 | 0.54 | 0.60 | -0.05 | 0.36 |
| | | | | Naïve Bayes | 0.48 | 0.61 | 0.57 | 0.56 | 0.61 | -0.01 | 0.38 |
| | | | | Random Forest | 0.48 | 0.57 | 0.55 | 0.54 | 0.57 | -0.06 | 0.38 |
| | | | | kNN | 0.45 | 0.59 | 0.56 | 0.54 | 0.59 | -0.05 | 0.37 |
| | | | | Tree | 0.44 | 0.52 | 0.52 | 0.53 | 0.52 | -0.08 | 0.40 |
| Injections first year n=3, >3 | VP_OCT | outliers removed | averaged over classes | Naïve Bayes | 0.57 | 0.54 | 0.55 | 0.60 | 0.54 | 0.08 | 0.54 |
| | | | | Random Forest | 0.57 | 0.62 | 0.60 | 0.59 | 0.62 | 0.06 | 0.44 |
| | | | | SVM | 0.54 | 0.67 | 0.54 | 0.45 | 0.67 | 0.00 | 0.33 |
| | | | | Neural Network | 0.53 | 0.56 | 0.55 | 0.54 | 0.56 | -0.04 | 0.40 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Logistic Regression | 0.53 | 0.61 | 0.55 | 0.52 | 0.61 | -0.07 | 0.34 |
| | | | | Gradient Boosting | 0.50 | 0.59 | 0.57 | 0.55 | 0.59 | -0.01 | 0.40 |
| | | | | kNN | 0.49 | 0.60 | 0.57 | 0.55 | 0.60 | -0.02 | 0.39 |
| | | | | Tree | 0.48 | 0.55 | 0.56 | 0.56 | 0.55 | -0.01 | 0.44 |
| | | | | AdaBoost | 0.46 | 0.52 | 0.52 | 0.52 | 0.52 | -0.08 | 0.40 |
| Injections first year n=3, >3 | V0_OCTANE | full | averaged over classes | Random Forest | 0.49 | 0.63 | 0.57 | 0.55 | 0.63 | -0.01 | 0.36 |
| | | | | Naïve Bayes | 0.47 | 0.40 | 0.38 | 0.54 | 0.40 | -0.04 | 0.56 |
| | | | | AdaBoost | 0.46 | 0.50 | 0.51 | 0.53 | 0.50 | -0.08 | 0.41 |
| | | | | Tree | 0.46 | 0.48 | 0.50 | 0.53 | 0.48 | -0.07 | 0.44 |
| | | | | Neural Network | 0.45 | 0.62 | 0.55 | 0.52 | 0.62 | -0.07 | 0.33 |
| | | | | SVM (error) | | | | | | | |
| | | | | Gradient Boosting (error) | | | | | | | |
| | | | | kNN (error) | | | | | | | |
| | | | | Logistic Regression (error) | | | | | | | |
| Injections first year n=3, >3 | V0_OCTANE | outliers removed | averaged over classes | Tree | 0.55 | 0.63 | 0.60 | 0.59 | 0.63 | 0.05 | 0.41 |
| | | | | Naïve Bayes | 0.54 | 0.61 | 0.61 | 0.60 | 0.61 | 0.09 | 0.48 |
| | | | | SVM | 0.48 | 0.66 | 0.54 | 0.46 | 0.66 | -0.08 | 0.32 |
| | | | | Logistic Regression | 0.47 | 0.66 | 0.56 | 0.56 | 0.66 | -0.01 | 0.33 |
| | | | | Gradient Boosting | 0.46 | 0.63 | 0.57 | 0.56 | 0.63 | -0.01 | 0.36 |
| | | | | AdaBoost | 0.44 | 0.59 | 0.55 | 0.52 | 0.59 | -0.08 | 0.34 |
| | | | | kNN | 0.43 | 0.60 | 0.53 | 0.49 | 0.60 | -0.13 | 0.31 |
| | | | | Random Forest | 0.43 | 0.60 | 0.54 | 0.51 | 0.60 | -0.11 | 0.32 |
| | | | | Neural Network | 0.42 | 0.60 | 0.55 | 0.53 | 0.60 | -0.06 | 0.35 |
| Injections first year n=3, >3 | VP_OCTANE | full | averaged over classes | Neural Network | 0.56 | 0.55 | 0.56 | 0.60 | 0.55 | 0.09 | 0.55 |
| | | | | Naïve Bayes | 0.51 | 0.40 | 0.34 | 0.62 | 0.40 | 0.07 | 0.65 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | AdaBoost | 0.50 | 0.52 | 0.54 | 0.56 | 0.52 | 0.00 | 0.48 |
| | | | | Tree | 0.50 | 0.36 | 0.27 | 0.56 | 0.36 | -0.01 | 0.64 |
| | | | | Random Forest | 0.50 | 0.43 | 0.43 | 0.56 | 0.43 | 0.00 | 0.57 |
| | | | | SVM (error) | | | | | | | |
| | | | | Gradient Boosting (error) | | | | | | | |
| | | | | kNN (error) | | | | | | | |
| | | | | Logistic Regression (error) | | | | | | | |
| Injections first year n=3, >3 | VP_OCTANE | outliers removed | averaged over classes | Logistic Regression | 0.53 | 0.67 | 0.56 | 0.62 | 0.67 | 0.06 | 0.35 |
| | | | | SVM | 0.52 | 0.67 | 0.54 | 0.61 | 0.67 | 0.03 | 0.34 |
| | | | | Random Forest | 0.51 | 0.62 | 0.58 | 0.57 | 0.62 | 0.03 | 0.40 |
| | | | | kNN | 0.49 | 0.63 | 0.58 | 0.57 | 0.63 | 0.03 | 0.39 |
| | | | | Neural Network | 0.48 | 0.60 | 0.55 | 0.53 | 0.60 | -0.05 | 0.36 |
| | | | | AdaBoost | 0.47 | 0.60 | 0.56 | 0.54 | 0.60 | -0.02 | 0.38 |
| | | | | Gradient Boosting | 0.46 | 0.62 | 0.56 | 0.55 | 0.62 | -0.01 | 0.37 |
| | | | | Naïve Bayes | 0.46 | 0.51 | 0.52 | 0.52 | 0.51 | -0.09 | 0.40 |
| | | | | Tree | 0.44 | 0.58 | 0.53 | 0.51 | 0.58 | -0.09 | 0.35 |
| Injections first year n=3, >3 | VA | full | averaged over classes | AdaBoost | 0.55 | 0.60 | 0.60 | 0.60 | 0.60 | 0.10 | 0.50 |
| | | | | SVM | 0.54 | 0.65 | 0.54 | 0.48 | 0.65 | -0.09 | 0.32 |
| | | | | Random Forest | 0.52 | 0.63 | 0.60 | 0.59 | 0.63 | 0.07 | 0.42 |
| | | | | kNN | 0.52 | 0.61 | 0.59 | 0.58 | 0.61 | 0.04 | 0.43 |
| | | | | Neural Network | 0.51 | 0.67 | 0.57 | 0.59 | 0.67 | 0.04 | 0.35 |
| | | | | Gradient Boosting | 0.51 | 0.60 | 0.57 | 0.56 | 0.60 | -0.01 | 0.39 |
| | | | | Logistic Regression | 0.50 | 0.66 | 0.54 | 0.45 | 0.66 | -0.08 | 0.32 |
| | | | | Naïve Bayes | 0.49 | 0.66 | 0.55 | 0.54 | 0.66 | -0.03 | 0.33 |
| | | | | Tree | 0.49 | 0.55 | 0.55 | 0.55 | 0.55 | -0.02 | 0.43 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Injections first year n=3, >3 | VA | outliers removed | averaged over classes | Gradient Boosting | 0.60 | 0.64 | 0.61 | 0.61 | 0.64 | 0.11 | 0.45 |
| | | | | Random Forest | 0.57 | 0.63 | 0.61 | 0.60 | 0.63 | 0.09 | 0.45 |
| | | | | Logistic Regression | 0.56 | 0.67 | 0.56 | 0.60 | 0.67 | 0.04 | 0.35 |
| | | | | AdaBoost | 0.55 | 0.59 | 0.59 | 0.60 | 0.59 | 0.10 | 0.51 |
| | | | | Neural Network | 0.55 | 0.66 | 0.55 | 0.55 | 0.66 | -0.01 | 0.34 |
| | | | | kNN | 0.52 | 0.58 | 0.56 | 0.55 | 0.58 | -0.02 | 0.39 |
| | | | | Naïve Bayes | 0.52 | 0.63 | 0.56 | 0.54 | 0.63 | -0.03 | 0.35 |
| | | | | Tree | 0.50 | 0.53 | 0.54 | 0.56 | 0.53 | 0.01 | 0.47 |
| | | | | SVM | 0.49 | 0.66 | 0.55 | 0.56 | 0.66 | 0.00 | 0.34 |
| Injections first year n=3, >3 | Demographic & qualitative | full | averaged over classes | Naïve Bayes | 0.57 | 0.59 | 0.59 | 0.59 | 0.59 | 0.06 | 0.46 |
| | | | | Neural Network | 0.52 | 0.66 | 0.55 | 0.52 | 0.66 | -0.05 | 0.33 |
| | | | | SVM | 0.51 | 0.67 | 0.54 | 0.45 | 0.67 | -0.07 | 0.32 |
| | | | | Logistic Regression | 0.50 | 0.67 | 0.54 | 0.46 | 0.67 | -0.05 | 0.32 |
| | | | | AdaBoost | 0.48 | 0.55 | 0.54 | 0.53 | 0.55 | -0.07 | 0.38 |
| | | | | Gradient Boosting | 0.46 | 0.60 | 0.57 | 0.55 | 0.60 | -0.02 | 0.38 |
| | | | | Random Forest | 0.45 | 0.59 | 0.56 | 0.55 | 0.59 | -0.03 | 0.39 |
| | | | | Tree | 0.44 | 0.50 | 0.50 | 0.51 | 0.50 | -0.12 | 0.38 |
| | | | | kNN | 0.42 | 0.56 | 0.54 | 0.53 | 0.56 | -0.08 | 0.37 |
| Injections first year n=3, >3 | Demographic & qualitative | outliers removed | averaged over classes | SVM | 0.55 | 0.67 | 0.55 | 0.46 | 0.67 | -0.04 | 0.32 |
| | | | | kNN | 0.55 | 0.62 | 0.60 | 0.59 | 0.62 | 0.05 | 0.42 |
| | | | | Logistic Regression | 0.51 | 0.68 | 0.57 | 0.62 | 0.68 | 0.06 | 0.34 |
| | | | | AdaBoost | 0.50 | 0.58 | 0.57 | 0.56 | 0.58 | -0.01 | 0.41 |
| | | | | Tree | 0.50 | 0.54 | 0.55 | 0.56 | 0.54 | -0.02 | 0.44 |
| | | | | Random Forest | 0.49 | 0.60 | 0.57 | 0.56 | 0.60 | -0.01 | 0.39 |
| | | | | Naïve Bayes | 0.47 | 0.66 | 0.58 | 0.59 | 0.66 | 0.03 | 0.36 |
| | | | | Neural Network | 0.47 | 0.61 | 0.56 | 0.54 | 0.61 | -0.05 | 0.35 |
| | | | | Gradient Boosting | 0.47 | 0.60 | 0.56 | 0.54 | 0.60 | -0.05 | 0.36 |
| In | Vo | fu | av | Tree | 0.51 | 0.23 | 0.22 | 0.22 | 0.23 | 0.00 | 0.77 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | kNN | 0.51 | 0.28 | 0.24 | 0.22 | 0.28 | 0.02 | 0.75 |
| | | | | Gradient Boosting | 0.50 | 0.25 | 0.23 | 0.22 | 0.25 | 0.01 | 0.75 |
| | | | | Naïve Bayes | 0.50 | 0.00 | 0.01 | 0.11 | 0.00 | -0.02 | 0.99 |
| | | | | AdaBoost | 0.49 | 0.23 | 0.23 | 0.23 | 0.23 | 0.01 | 0.78 |
| | | | | Neural Network | 0.49 | 0.27 | 0.24 | 0.22 | 0.27 | 0.02 | 0.75 |
| | | | | Random Forest | 0.48 | 0.27 | 0.24 | 0.23 | 0.27 | 0.02 | 0.76 |
| | | | | Logistic Regression | 0.47 | 0.28 | 0.20 | 0.20 | 0.28 | -0.02 | 0.71 |
| | | | | SVM | 0.45 | 0.29 | 0.19 | 0.21 | 0.29 | -0.03 | 0.69 |
| Injections first year (categories 3, 4, 5, 6, 7, 8, 9, 10) | V0_OCT | outliers removed | averaged over classes | kNN | 0.55 | 0.32 | 0.27 | 0.26 | 0.32 | 0.08 | 0.76 |
| | | | | Tree | 0.55 | 0.28 | 0.27 | 0.26 | 0.28 | 0.07 | 0.79 |
| | | | | Neural Network | 0.53 | 0.30 | 0.27 | 0.26 | 0.30 | 0.07 | 0.78 |
| | | | | Naïve Bayes | 0.53 | 0.01 | 0.00 | 0.00 | 0.01 | 0.00 | 0.99 |
| | | | | Random Forest | 0.52 | 0.28 | 0.25 | 0.24 | 0.28 | 0.03 | 0.76 |
| | | | | AdaBoost | 0.52 | 0.24 | 0.24 | 0.25 | 0.24 | 0.04 | 0.80 |
| | | | | Gradient Boosting | 0.51 | 0.25 | 0.23 | 0.21 | 0.25 | 0.01 | 0.76 |
| | | | | Logistic Regression | 0.48 | 0.26 | 0.22 | 0.22 | 0.26 | 0.01 | 0.75 |
| | | | | SVM | 0.46 | 0.34 | 0.24 | 0.21 | 0.34 | 0.08 | 0.72 |
| Injections first year (categories 3, 4, 5, 6, 7, 8, 9, 10) | VP_OCT | full | averaged over classes | kNN | 0.50 | 0.28 | 0.24 | 0.22 | 0.28 | 0.02 | 0.74 |
| | | | | Naïve Bayes | 0.49 | 0.00 | 0.01 | 0.32 | 0.00 | -0.01 | 0.99 |
| | | | | Gradient Boosting | 0.48 | 0.25 | 0.22 | 0.21 | 0.25 | -0.01 | 0.74 |
| | | | | AdaBoost | 0.48 | 0.20 | 0.20 | 0.20 | 0.20 | -0.03 | 0.77 |
| | | | | Random Forest | 0.48 | 0.23 | 0.19 | 0.17 | 0.23 | -0.05 | 0.72 |
| | | | | Neural Network | 0.47 | 0.24 | 0.21 | 0.20 | 0.24 | -0.03 | 0.73 |
| | | | | Logistic Regression | 0.46 | 0.29 | 0.22 | 0.24 | 0.29 | 0.00 | 0.70 |
| | | | | Tree | 0.46 | 0.18 | 0.17 | 0.17 | 0.18 | -0.07 | 0.75 |
| | | | | SVM | 0.43 | 0.33 | 0.21 | 0.34 | 0.33 | 0.04 | 0.69 |
| Injections | VP_OCT | outliers | averaged | Random Forest | 0.56 | 0.30 | 0.27 | 0.27 | 0.30 | 0.05 | 0.75 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Neural Network | 0.54 | 0.26 | 0.24 | 0.24 | 0.26 | 0.01 | 0.75 |
| | | | | Tree | 0.53 | 0.28 | 0.27 | 0.27 | 0.28 | 0.05 | 0.78 |
| | | | | Gradient Boosting | 0.53 | 0.30 | 0.28 | 0.27 | 0.30 | 0.06 | 0.77 |
| | | | | Logistic Regression | 0.53 | 0.27 | 0.25 | 0.26 | 0.27 | 0.02 | 0.74 |
| | | | | Naïve Bayes | 0.53 | 0.01 | 0.01 | 0.15 | 0.01 | -0.02 | 0.99 |
| | | | | AdaBoost | 0.50 | 0.22 | 0.23 | 0.23 | 0.22 | 0.00 | 0.78 |
| | | | | kNN | 0.50 | 0.31 | 0.27 | 0.26 | 0.31 | 0.05 | 0.74 |
| | | | | SVM | 0.43 | 0.35 | 0.23 | 0.25 | 0.35 | 0.07 | 0.70 |
| Injections first year (categories 3, 4, 5, 6, 7, 8, 9, 10) | V0_OCTANE | full | averaged over classes | Tree | 0.50 | 0.27 | 0.20 | 0.17 | 0.27 | -0.02 | 0.71 |
| | | | | Naïve Bayes | 0.50 | 0.19 | 0.19 | 0.22 | 0.19 | 0.00 | 0.81 |
| | | | | Neural Network | 0.50 | 0.18 | 0.16 | 0.19 | 0.18 | -0.03 | 0.79 |
| | | | | SVM | 0.48 | 0.25 | 0.15 | 0.10 | 0.25 | -0.05 | 0.71 |
| | | | | Logistic Regression | 0.48 | 0.22 | 0.21 | 0.22 | 0.22 | 0.00 | 0.77 |
| | | | | AdaBoost | 0.47 | 0.20 | 0.19 | 0.19 | 0.20 | -0.04 | 0.76 |
| | | | | Gradient Boosting | 0.46 | 0.24 | 0.21 | 0.21 | 0.24 | -0.02 | 0.73 |
| | | | | Random Forest | 0.46 | 0.24 | 0.17 | 0.15 | 0.24 | -0.06 | 0.71 |
| | | | | kNN (error) | | | | | | | |
| Injections first year (categories 3, 4, 5, 6, 7, 8, 9, 10) | V0_OCTANE | outliers removed | averaged over classes | Naïve Bayes | 0.51 | 0.00 | 0.00 | 0.00 | 0.00 | -0.01 | 1.00 |
| | | | | Random Forest | 0.50 | 0.28 | 0.21 | 0.20 | 0.28 | -0.01 | 0.72 |
| | | | | AdaBoost | 0.48 | 0.27 | 0.22 | 0.21 | 0.27 | 0.01 | 0.74 |
| | | | | Tree | 0.47 | 0.26 | 0.20 | 0.19 | 0.26 | -0.02 | 0.72 |
| | | | | Gradient Boosting | 0.46 | 0.24 | 0.19 | 0.19 | 0.24 | -0.04 | 0.72 |
| | | | | Neural Network | 0.45 | 0.24 | 0.20 | 0.19 | 0.24 | -0.05 | 0.72 |
| | | | | kNN | 0.44 | 0.26 | 0.21 | 0.23 | 0.26 | -0.04 | 0.70 |
| | | | | Logistic Regression | 0.44 | 0.26 | 0.17 | 0.15 | 0.26 | -0.06 | 0.69 |
| | | | | SVM | 0.39 | 0.29 | 0.18 | 0.19 | 0.29 | -0.05 | 0.68 |
| Injections | VP_OCTANE | full | averaged | Random Forest | 0.50 | 0.18 | 0.13 | 0.10 | 0.18 | -0.02 | 0.80 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Neural Network | 0.50 | 0.17 | 0.14 | 0.11 | 0.17 | 0.01 | 0.84 |
| | | | | Tree | 0.50 | 0.28 | 0.15 | 0.10 | 0.28 | -0.02 | 0.70 |
| | | | | Naïve Bayes | 0.50 | 0.28 | 0.15 | 0.11 | 0.28 | 0.01 | 0.72 |
| | | | | AdaBoost | 0.50 | 0.14 | 0.12 | 0.10 | 0.14 | -0.01 | 0.85 |
| | | | | SVM (error) | | | | | | | |
| | | | | Gradient Boosting (error) | | | | | | | |
| | | | | kNN (error) | | | | | | | |
| | | | | Logistic Regression (error) | | | | | | | |
| Injections first year (categories 3, 4, 5, 6, 7, 8, 9, 10) | VP_OCTANE | outliers removed | averaged over classes | Naïve Bayes | 0.52 | 0.00 | 0.00 | 0.00 | 0.00 | -0.01 | 1.00 |
| | | | | kNN | 0.49 | 0.25 | 0.21 | 0.19 | 0.25 | -0.04 | 0.71 |
| | | | | AdaBoost | 0.49 | 0.28 | 0.23 | 0.22 | 0.28 | 0.00 | 0.72 |
| | | | | Logistic Regression | 0.48 | 0.29 | 0.20 | 0.20 | 0.29 | -0.03 | 0.69 |
| | | | | Random Forest | 0.48 | 0.26 | 0.21 | 0.20 | 0.26 | -0.05 | 0.70 |
| | | | | Neural Network | 0.47 | 0.26 | 0.21 | 0.21 | 0.26 | -0.04 | 0.70 |
| | | | | Tree | 0.46 | 0.33 | 0.23 | 0.26 | 0.33 | 0.04 | 0.69 |
| | | | | Gradient Boosting | 0.46 | 0.24 | 0.20 | 0.19 | 0.24 | -0.04 | 0.71 |
| | | | | SVM | 0.41 | 0.29 | 0.17 | 0.13 | 0.29 | -0.08 | 0.67 |
| Injections first year (categories 3, 4, 5, 6, 7, 8, 9, 10) | Demographic & qualitative | full | averaged over classes | Tree | 0.50 | 0.25 | 0.22 | 0.21 | 0.25 | -0.01 | 0.74 |
| | | | | AdaBoost | 0.49 | 0.22 | 0.21 | 0.21 | 0.22 | -0.02 | 0.76 |
| | | | | Naïve Bayes | 0.49 | 0.01 | 0.01 | 0.17 | 0.01 | -0.01 | 0.99 |
| | | | | kNN | 0.48 | 0.23 | 0.20 | 0.19 | 0.23 | -0.05 | 0.72 |
| | | | | Random Forest | 0.47 | 0.20 | 0.19 | 0.19 | 0.20 | -0.04 | 0.76 |
| | | | | Gradient Boosting | 0.47 | 0.22 | 0.21 | 0.21 | 0.22 | -0.02 | 0.75 |
| | | | | Neural Network | 0.46 | 0.31 | 0.22 | 0.22 | 0.31 | 0.03 | 0.71 |
| | | | | Logistic Regression | 0.44 | 0.31 | 0.17 | 0.18 | 0.31 | -0.02 | 0.68 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | SVM | 0.44 | 0.30 | 0.17 | 0.30 | 0.30 | -0.03 | 0.68 |
| Injections first year (categories 3, 4, 5, 6, 7, 8, 9, 10) | Demographic & qualitative | outliers removed | averaged over classes | Tree | 0.51 | 0.25 | 0.24 | 0.23 | 0.25 | 0.01 | 0.76 |
| | | | | AdaBoost | 0.50 | 0.24 | 0.24 | 0.24 | 0.24 | 0.02 | 0.77 |
| | | | | kNN | 0.50 | 0.23 | 0.20 | 0.19 | 0.23 | -0.04 | 0.73 |
| | | | | Random Forest | 0.49 | 0.20 | 0.20 | 0.19 | 0.20 | -0.04 | 0.75 |
| | | | | Gradient Boosting | 0.49 | 0.20 | 0.19 | 0.19 | 0.20 | -0.05 | 0.75 |
| | | | | Neural Network | 0.48 | 0.19 | 0.18 | 0.17 | 0.19 | -0.07 | 0.74 |
| | | | | Naïve Bayes | 0.48 | 0.19 | 0.19 | 0.21 | 0.19 | -0.01 | 0.80 |
| | | | | SVM | 0.47 | 0.33 | 0.21 | 0.18 | 0.33 | 0.06 | 0.71 |
| | | | | Logistic Regression | 0.46 | 0.29 | 0.21 | 0.19 | 0.29 | 0.01 | 0.72 |
| Injections first year (categories 3, 4, 5, 6, 7, 8, 9, 10) | VA | full | averaged over classes | Random Forest | 0.52 | 0.26 | 0.23 | 0.22 | 0.26 | 0.01 | 0.76 |
| | | | | kNN | 0.51 | 0.27 | 0.22 | 0.21 | 0.27 | 0.00 | 0.73 |
| | | | | AdaBoost | 0.50 | 0.23 | 0.23 | 0.23 | 0.23 | 0.01 | 0.78 |
| | | | | Naïve Bayes | 0.49 | 0.20 | 0.19 | 0.20 | 0.20 | -0.02 | 0.79 |
| | | | | Gradient Boosting | 0.49 | 0.24 | 0.22 | 0.21 | 0.24 | -0.01 | 0.75 |
| | | | | Tree | 0.48 | 0.23 | 0.21 | 0.20 | 0.23 | -0.02 | 0.76 |
| | | | | Neural Network | 0.45 | 0.24 | 0.18 | 0.18 | 0.24 | -0.07 | 0.70 |
| | | | | Logistic Regression | 0.45 | 0.28 | 0.18 | 0.14 | 0.28 | -0.07 | 0.68 |
| | | | | SVM | 0.45 | 0.29 | 0.19 | 0.15 | 0.29 | -0.03 | 0.69 |
| Injections first year (categories 3, 4, 5, 6, 7, 8, 9, 10) | VA | outliers removed | averaged over classes | Logistic Regression | 0.53 | 0.32 | 0.21 | 0.19 | 0.32 | 0.05 | 0.71 |
| | | | | Tree | 0.52 | 0.28 | 0.26 | 0.26 | 0.28 | 0.05 | 0.78 |
| | | | | Random Forest | 0.51 | 0.27 | 0.26 | 0.25 | 0.27 | 0.03 | 0.75 |
| | | | | Gradient Boosting | 0.51 | 0.26 | 0.25 | 0.24 | 0.26 | 0.03 | 0.77 |
| | | | | AdaBoost | 0.51 | 0.24 | 0.24 | 0.25 | 0.24 | 0.03 | 0.80 |
| | | | | Neural Network | 0.51 | 0.31 | 0.23 | 0.19 | 0.31 | 0.02 | 0.71 |
| | | | | kNN | 0.50 | 0.28 | 0.24 | 0.23 | 0.28 | 0.01 | 0.73 |
| | | | | SVM | 0.48 | 0.34 | 0.21 | 0.21 | 0.34 | 0.05 | 0.69 |
| | | | | Naïve Bayes | 0.47 | 0.13 | 0.14 | 0.16 | 0.13 | -0.03 | 0.83 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Injections first year (categories 3, 4, 5, 6, 7, 8, 9, 10) | VA_st dev | full | averaged over classes | kNN | 0.52 | 0.27 | 0.23 | 0.21 | 0.27 | 0.00 | 0.74 |
| | | | | Naïve Bayes | 0.50 | 0.11 | 0.14 | 0.22 | 0.11 | 0.00 | 0.89 |
| | | | | Random Forest | 0.49 | 0.26 | 0.23 | 0.22 | 0.26 | 0.00 | 0.74 |
| | | | | Tree | 0.47 | 0.22 | 0.21 | 0.20 | 0.22 | -0.02 | 0.76 |
| | | | | Gradient Boosting | 0.47 | 0.23 | 0.21 | 0.21 | 0.23 | -0.02 | 0.75 |
| | | | | AdaBoost | 0.47 | 0.18 | 0.18 | 0.19 | 0.18 | -0.05 | 0.77 |
| | | | | Neural Network | 0.46 | 0.24 | 0.19 | 0.18 | 0.24 | -0.07 | 0.70 |
| | | | | SVM | 0.44 | 0.28 | 0.18 | 0.16 | 0.28 | -0.05 | 0.69 |
| | | | | Logistic Regression | 0.43 | 0.26 | 0.17 | 0.15 | 0.26 | -0.10 | 0.68 |
| Injections first year (categories 3, 4, 5, 6, 7, 8, 9, 10) | VA_st dev | outliers removed | averaged over classes | Logistic Regression | 0.57 | 0.35 | 0.26 | 0.27 | 0.35 | 0.10 | 0.74 |
| | | | | SVM | 0.54 | 0.33 | 0.22 | 0.18 | 0.33 | 0.05 | 0.71 |
| | | | | Neural Network | 0.53 | 0.32 | 0.25 | 0.25 | 0.32 | 0.06 | 0.73 |
| | | | | Naïve Bayes | 0.50 | 0.10 | 0.13 | 0.21 | 0.10 | 0.00 | 0.90 |
| | | | | AdaBoost | 0.50 | 0.21 | 0.22 | 0.22 | 0.21 | -0.01 | 0.78 |
| | | | | Random Forest | 0.50 | 0.24 | 0.22 | 0.21 | 0.24 | -0.01 | 0.75 |
| | | | | Gradient Boosting | 0.49 | 0.24 | 0.23 | 0.21 | 0.24 | 0.00 | 0.76 |
| | | | | Tree | 0.48 | 0.22 | 0.21 | 0.20 | 0.22 | -0.02 | 0.76 |
| | | | | kNN | 0.48 | 0.29 | 0.23 | 0.22 | 0.29 | 0.02 | 0.73 |
| Injection pattern first year (categories: clusters 1, 2, 3, 4, 5, 6, 7, 8, 9, 10) | Demographic & qualitative | full | averaged over classes | Tree | 0.52 | 0.28 | 0.22 | 0.21 | 0.28 | 0.03 | 0.75 |
| | | | | Neural Network | 0.51 | 0.35 | 0.20 | 0.30 | 0.35 | 0.02 | 0.65 |
| | | | | AdaBoost | 0.51 | 0.26 | 0.21 | 0.20 | 0.26 | 0.01 | 0.74 |
| | | | | SVM | 0.50 | 0.36 | 0.19 | 0.13 | 0.36 | 0.00 | 0.64 |
| | | | | Gradient Boosting | 0.50 | 0.27 | 0.22 | 0.22 | 0.27 | 0.02 | 0.74 |
| | | | | Random Forest | 0.50 | 0.26 | 0.21 | 0.20 | 0.26 | 0.01 | 0.75 |
| | | | | Logistic Regression | 0.50 | 0.36 | 0.20 | 0.22 | 0.36 | 0.05 | 0.65 |
| | | | | Naïve Bayes | 0.49 | 0.17 | 0.17 | 0.16 | 0.17 | -0.01 | 0.82 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | kNN | 0.48 | 0.28 | 0.19 | 0.15 | 0.28 | -0.03 | 0.70 |
| Injection pattern first year (categories: clusters 1, 2, 3, 4, 5, 6, 7, 8, 9, 10) | Demographic & qualitative | outliers removed | averaged over classes | AdaBoost | 0.55 | 0.25 | 0.23 | 0.22 | 0.25 | 0.05 | 0.80 |
| | | | | Naïve Bayes | 0.54 | 0.30 | 0.22 | 0.19 | 0.30 | 0.03 | 0.73 |
| | | | | Logistic Regression | 0.54 | 0.37 | 0.23 | 0.19 | 0.37 | 0.09 | 0.68 |
| | | | | Tree | 0.53 | 0.24 | 0.21 | 0.20 | 0.24 | 0.02 | 0.77 |
| | | | | Gradient Boosting | 0.53 | 0.28 | 0.24 | 0.23 | 0.28 | 0.06 | 0.78 |
| | | | | kNN | 0.53 | 0.31 | 0.24 | 0.24 | 0.31 | 0.04 | 0.71 |
| | | | | SVM | 0.52 | 0.37 | 0.21 | 0.16 | 0.37 | 0.08 | 0.66 |
| | | | | Random Forest | 0.52 | 0.28 | 0.23 | 0.21 | 0.28 | 0.04 | 0.75 |
| | | | | Neural Network | 0.51 | 0.29 | 0.21 | 0.18 | 0.29 | 0.00 | 0.70 |
| Injection pattern first year (categories: clusters 1, 2, 3, 4, 5, 6, 7, 8, 9, 10) | VA | full | averaged over classes | AdaBoost | 0.52 | 0.20 | 0.20 | 0.20 | 0.20 | 0.03 | 0.83 |
| | | | | Random Forest | 0.51 | 0.25 | 0.19 | 0.16 | 0.25 | -0.01 | 0.74 |
| | | | | kNN | 0.51 | 0.29 | 0.20 | 0.17 | 0.29 | 0.01 | 0.72 |
| | | | | Neural Network | 0.50 | 0.35 | 0.19 | 0.13 | 0.35 | 0.01 | 0.66 |
| | | | | Logistic Regression | 0.49 | 0.36 | 0.20 | 0.17 | 0.36 | 0.05 | 0.65 |
| | | | | Gradient Boosting | 0.49 | 0.24 | 0.18 | 0.15 | 0.24 | -0.03 | 0.73 |
| | | | | Naïve Bayes | 0.48 | 0.27 | 0.18 | 0.17 | 0.27 | -0.03 | 0.71 |
| | | | | SVM | 0.48 | 0.36 | 0.19 | 0.13 | 0.36 | 0.00 | 0.64 |
| | | | | Tree | 0.47 | 0.17 | 0.16 | 0.15 | 0.17 | -0.03 | 0.80 |
| Injection pattern first year (categories: clusters 1, 2, 3, 4, 5, 6, 7, 8, 9, 10) | VA | outliers removed | averaged over classes | Logistic Regression | 0.53 | 0.36 | 0.21 | 0.16 | 0.36 | 0.03 | 0.65 |
| | | | | Neural Network | 0.53 | 0.37 | 0.21 | 0.16 | 0.37 | 0.05 | 0.65 |
| | | | | Random Forest | 0.51 | 0.28 | 0.22 | 0.20 | 0.28 | 0.03 | 0.75 |
| | | | | Gradient Boosting | 0.51 | 0.25 | 0.20 | 0.18 | 0.25 | 0.01 | 0.78 |
| | | | | Tree | 0.51 | 0.21 | 0.20 | 0.20 | 0.21 | 0.01 | 0.79 |
| | | | | AdaBoost | 0.49 | 0.16 | 0.16 | 0.17 | 0.16 | -0.02 | 0.81 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | kNN | 0.48 | 0.29 | 0.19 | 0.15 | 0.29 | -0.02 | 0.70 |
| | | | | Naïve Bayes | 0.47 | 0.30 | 0.21 | 0.16 | 0.30 | 0.03 | 0.72 |
| | | | | SVM | 0.46 | 0.37 | 0.20 | 0.14 | 0.37 | 0.00 | 0.63 |
| Injection pattern first year (categories: clusters 1, 2, 3, 4, 5, 6, 7, 8, 9, 10) | VA_st dev | full | averaged over classes | kNN | 0.51 | 0.30 | 0.21 | 0.17 | 0.30 | 0.01 | 0.71 |
| | | | | Neural Network | 0.50 | 0.32 | 0.18 | 0.13 | 0.32 | -0.02 | 0.67 |
| | | | | Tree | 0.50 | 0.20 | 0.19 | 0.19 | 0.20 | 0.01 | 0.81 |
| | | | | SVM | 0.50 | 0.36 | 0.19 | 0.13 | 0.36 | 0.01 | 0.64 |
| | | | | Naïve Bayes | 0.50 | 0.24 | 0.19 | 0.19 | 0.24 | -0.01 | 0.75 |
| | | | | Random Forest | 0.49 | 0.24 | 0.20 | 0.17 | 0.24 | 0.00 | 0.75 |
| | | | | AdaBoost | 0.48 | 0.14 | 0.14 | 0.15 | 0.14 | -0.04 | 0.82 |
| | | | | Gradient Boosting | 0.48 | 0.25 | 0.19 | 0.17 | 0.25 | -0.02 | 0.73 |
| | | | | Logistic Regression | 0.48 | 0.36 | 0.20 | 0.17 | 0.36 | 0.03 | 0.65 |
| Injection pattern first year (categories: clusters 1, 2, 3, 4, 5, 6, 7, 8, 9, 10) | VA_st dev | outliers removed | averaged over classes | Logistic Regression | 0.56 | 0.36 | 0.23 | 0.19 | 0.36 | 0.09 | 0.70 |
| | | | | Neural Network | 0.55 | 0.37 | 0.24 | 0.19 | 0.37 | 0.11 | 0.71 |
| | | | | Gradient Boosting | 0.54 | 0.31 | 0.26 | 0.23 | 0.31 | 0.09 | 0.79 |
| | | | | Random Forest | 0.52 | 0.29 | 0.22 | 0.20 | 0.29 | 0.03 | 0.74 |
| | | | | AdaBoost | 0.52 | 0.20 | 0.21 | 0.22 | 0.20 | 0.04 | 0.85 |
| | | | | SVM | 0.52 | 0.36 | 0.21 | 0.15 | 0.36 | 0.04 | 0.66 |
| | | | | Naïve Bayes | 0.51 | 0.24 | 0.20 | 0.17 | 0.24 | 0.00 | 0.77 |
| | | | | Tree | 0.49 | 0.20 | 0.19 | 0.18 | 0.20 | 0.00 | 0.81 |
| | | | | kNN | 0.49 | 0.31 | 0.21 | 0.18 | 0.31 | 0.02 | 0.70 |
| Injection pattern first year | V0_OCT | full | averaged over classes | Naïve Bayes | 0.52 | 0.15 | 0.17 | 0.21 | 0.15 | 0.02 | 0.87 |
| | | | | Logistic Regression | 0.51 | 0.37 | 0.22 | 0.26 | 0.37 | 0.08 | 0.67 |
| | | | | Tree | 0.51 | 0.18 | 0.17 | 0.17 | 0.18 | -0.01 | 0.81 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | AdaBoost | 0.51 | 0.19 | 0.19 | 0.19 | 0.19 | 0.01 | 0.83 |
| | | | | SVM | 0.50 | 0.36 | 0.19 | 0.13 | 0.36 | 0.00 | 0.64 |
| | | | | kNN | 0.50 | 0.29 | 0.21 | 0.19 | 0.29 | 0.01 | 0.72 |
| | | | | Gradient Boosting | 0.49 | 0.27 | 0.20 | 0.17 | 0.27 | 0.00 | 0.73 |
| | | | | Neural Network | 0.49 | 0.35 | 0.23 | 0.24 | 0.35 | 0.07 | 0.70 |
| | | | | Random Forest | 0.49 | 0.29 | 0.23 | 0.21 | 0.29 | 0.03 | 0.74 |
| Injection pattern first year (categories: clusters 1, 2, 3, 4, 5, 6, 7, 8, 9, 10) | V0_OCT | outliers removed | averaged over classes | Naïve Bayes | 0.56 | 0.14 | 0.15 | 0.26 | 0.14 | 0.05 | 0.92 |
| | | | | Neural Network | 0.54 | 0.25 | 0.20 | 0.17 | 0.25 | 0.01 | 0.77 |
| | | | | Random Forest | 0.53 | 0.29 | 0.23 | 0.20 | 0.29 | 0.04 | 0.76 |
| | | | | Gradient Boosting | 0.53 | 0.29 | 0.23 | 0.22 | 0.29 | 0.05 | 0.76 |
| | | | | kNN | 0.52 | 0.30 | 0.22 | 0.20 | 0.30 | 0.03 | 0.72 |
| | | | | Tree | 0.52 | 0.21 | 0.21 | 0.21 | 0.21 | 0.05 | 0.84 |
| | | | | SVM | 0.51 | 0.36 | 0.19 | 0.13 | 0.36 | 0.00 | 0.65 |
| | | | | Logistic Regression | 0.51 | 0.29 | 0.22 | 0.19 | 0.29 | 0.05 | 0.76 |
| | | | | AdaBoost | 0.50 | 0.16 | 0.17 | 0.18 | 0.16 | 0.01 | 0.84 |
| Injection pattern first year (categories: clusters 1, 2, 3, 4, 5, 6, 7, 8, 9, 10) | VP_OCT | full | averaged over classes | kNN | 0.54 | 0.30 | 0.22 | 0.19 | 0.30 | 0.03 | 0.73 |
| | | | | Neural Network | 0.54 | 0.34 | 0.22 | 0.21 | 0.34 | 0.06 | 0.70 |
| | | | | Logistic Regression | 0.53 | 0.35 | 0.20 | 0.16 | 0.35 | 0.04 | 0.67 |
| | | | | Naïve Bayes | 0.53 | 0.14 | 0.16 | 0.20 | 0.14 | 0.01 | 0.88 |
| | | | | Random Forest | 0.49 | 0.24 | 0.18 | 0.15 | 0.24 | -0.03 | 0.73 |
| | | | | Tree | 0.49 | 0.17 | 0.16 | 0.15 | 0.17 | -0.03 | 0.81 |
| | | | | Gradient Boosting | 0.48 | 0.29 | 0.21 | 0.18 | 0.29 | 0.02 | 0.73 |
| | | | | AdaBoost | 0.48 | 0.13 | 0.13 | 0.14 | 0.13 | -0.04 | 0.82 |
| | | | | SVM | 0.45 | 0.36 | 0.19 | 0.13 | 0.36 | 0.00 | 0.64 |
| Injection pattern | VP_OCT | outliers removed | averaged over classes | Random Forest | 0.55 | 0.28 | 0.21 | 0.18 | 0.28 | 0.01 | 0.73 |
| | | | | kNN | 0.54 | 0.29 | 0.22 | 0.19 | 0.29 | 0.02 | 0.72 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Naïve Bayes | 0.53 | 0.10 | 0.09 | 0.26 | 0.10 | 0.04 | 0.93 |
| | | | | Gradient Boosting | 0.53 | 0.31 | 0.24 | 0.23 | 0.31 | 0.06 | 0.75 |
| | | | | SVM | 0.52 | 0.37 | 0.20 | 0.14 | 0.37 | 0.00 | 0.63 |
| | | | | Tree | 0.50 | 0.19 | 0.19 | 0.19 | 0.19 | 0.00 | 0.81 |
| | | | | Neural Network | 0.49 | 0.30 | 0.25 | 0.22 | 0.30 | 0.07 | 0.78 |
| | | | | Logistic Regression | 0.49 | 0.30 | 0.22 | 0.19 | 0.30 | 0.04 | 0.74 |
| | | | | AdaBoost | 0.49 | 0.15 | 0.16 | 0.16 | 0.15 | -0.03 | 0.82 |
| Injection pattern first year (categories: clusters 1, 2, 3, 4, 5, 6, 7, 8, 9, 10) | V0_OCTANE | full | averaged over classes | Gradient Boosting | 0.52 | 0.21 | 0.17 | 0.16 | 0.21 | 0.02 | 0.81 |
| | | | | Logistic Regression | 0.52 | 0.18 | 0.16 | 0.16 | 0.18 | 0.02 | 0.83 |
| | | | | Neural Network | 0.51 | 0.10 | 0.09 | 0.16 | 0.10 | 0.02 | 0.91 |
| | | | | Naïve Bayes | 0.51 | 0.09 | 0.09 | 0.15 | 0.09 | -0.01 | 0.90 |
| | | | | Random Forest | 0.50 | 0.31 | 0.19 | 0.14 | 0.31 | -0.02 | 0.67 |
| | | | | Tree | 0.50 | 0.21 | 0.17 | 0.14 | 0.21 | 0.01 | 0.80 |
| | | | | kNN | 0.50 | 0.37 | 0.20 | 0.13 | 0.37 | 0.00 | 0.63 |
| | | | | SVM | 0.50 | 0.31 | 0.19 | 0.14 | 0.31 | 0.00 | 0.69 |
| | | | | AdaBoost | 0.50 | 0.15 | 0.14 | 0.14 | 0.15 | -0.01 | 0.84 |
| Injection pattern first year (categories: clusters 1, 2, 3, 4, 5, 6, 7, 8, 9, 10) | V0_OCTANE | outliers removed | averaged over classes | Logistic Regression | 0.55 | 0.38 | 0.23 | 0.20 | 0.38 | 0.04 | 0.63 |
| | | | | Naïve Bayes | 0.53 | 0.13 | 0.10 | 0.10 | 0.13 | 0.08 | 0.94 |
| | | | | Neural Network | 0.53 | 0.30 | 0.23 | 0.21 | 0.30 | 0.01 | 0.70 |
| | | | | Random Forest | 0.52 | 0.30 | 0.20 | 0.15 | 0.30 | -0.03 | 0.68 |
| | | | | AdaBoost | 0.51 | 0.21 | 0.21 | 0.21 | 0.21 | 0.02 | 0.80 |
| | | | | Gradient Boosting | 0.49 | 0.30 | 0.23 | 0.21 | 0.30 | 0.02 | 0.72 |
| | | | | Tree | 0.49 | 0.30 | 0.23 | 0.21 | 0.30 | -0.01 | 0.69 |
| | | | | SVM | 0.45 | 0.39 | 0.21 | 0.15 | 0.39 | 0.00 | 0.61 |
| | | | | kNN | 0.44 | 0.30 | 0.23 | 0.20 | 0.30 | 0.01 | 0.70 |
| Injection | VP_OCTANE | full | averaged | Neural Network | 0.50 | 0.27 | 0.18 | 0.14 | 0.27 | 0.00 | 0.74 |

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| | | | | AdaBoost | 0.50 | 0.24 | 0.17 | 0.14 | 0.24 | 0.00 | 0.75 |
| | | | | Naïve Bayes | 0.50 | 0.33 | 0.20 | 0.15 | 0.33 | 0.03 | 0.69 |
| | | | | Random Forest | 0.50 | 0.27 | 0.18 | 0.14 | 0.27 | -0.01 | 0.72 |
| | | | | Tree | 0.50 | 0.33 | 0.20 | 0.14 | 0.33 | -0.01 | 0.66 |
| | | | | SVM (error) | | | | | | | |
| | | | | Gradient Boosting (error) | | | | | | | |
| | | | | kNN (error) | | | | | | | |
| | | | | Logistic Regression (error) | | | | | | | |
| Injection pattern first year (categories: clusters 1, 2, 3, 4, 5, 6, 7, 8, 9, 10) | VP_OCTANE | outliers removed | averaged over classes | Gradient Boosting | 0.52 | 0.31 | 0.24 | 0.24 | 0.31 | 0.04 | 0.72 |
| | | | | Random Forest | 0.52 | 0.32 | 0.25 | 0.23 | 0.32 | 0.06 | 0.73 |
| | | | | Tree | 0.51 | 0.25 | 0.21 | 0.21 | 0.25 | 0.00 | 0.74 |
| | | | | Naïve Bayes | 0.51 | 0.06 | 0.03 | 0.08 | 0.06 | -0.01 | 0.94 |
| | | | | AdaBoost | 0.50 | 0.20 | 0.19 | 0.19 | 0.20 | 0.01 | 0.81 |
| | | | | Neural Network | 0.50 | 0.33 | 0.26 | 0.24 | 0.33 | 0.08 | 0.73 |
| | | | | Logistic Regression | 0.49 | 0.35 | 0.21 | 0.18 | 0.35 | 0.01 | 0.65 |
| | | | | SVM | 0.48 | 0.37 | 0.20 | 0.14 | 0.37 | 0.00 | 0.63 |
| | | | | kNN | 0.47 | 0.28 | 0.19 | 0.15 | 0.28 | -0.02 | 0.70 |

Appendix 4: Treatment dose related classification model feature ranking

| Target | Feature group | Dataset | Class results | Feature | Info. gain | Gain ratio | Gini | ANOVA | $\chi^2$ | ReliefF | FCBF |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Injections first year n=3, >3 | VA_st dev | full | averaged over classes | Standard deviation of VA mean, post loading -12 months (VP-V12) | 0.028 | 0.014 | 0.017 | 13.870 | 8.294 | 0.020 | 0.020 |
| | | | | VA fellow eye (V0) | 0.006 | 0.003 | 0.004 | 0.941 | 0.572 | 0.013 | 0.000 |
| | | | | VA baseline visit (V0) | 0.006 | 0.003 | 0.003 | 2.266 | 1.446 | 0.005 | 0.000 |
| | | | | VA post loading (VP) | 0.004 | 0.002 | 0.002 | 0.984 | 0.619 | 0.001 | 0.000 |
| | | | | VA mean initial 2 visits post loading | 0.004 | 0.002 | 0.002 | 0.248 | 0.140 | 0.002 | 0.000 |
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| Injections first year n=3, >3 | VA_st dev | outliers removed | averaged over classes | Standard deviation of VA mean, post loading -12 months (VP-V12) | 0.026 | 0.013 | 0.015 | 13.613 | 6.619 | 0.006 | 0.018 |
| | | | | VA baseline visit (V0) | 0.009 | 0.005 | 0.006 | 2.341 | 0.877 | 0.002 | 0.000 |
| | | | | VA post loading (VP) | 0.006 | 0.003 | 0.004 | 2.958 | 1.707 | -0.004 | 0.000 |
| | | | | VA fellow eye (V0) | 0.005 | 0.003 | 0.003 | 1.150 | 1.002 | 0.008 | 0.000 |
| | | | | VA mean initial 2 visits post loading | 0.005 | 0.002 | 0.003 | 1.257 | 0.393 | 0.001 | 0.000 |
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| Injections first year n=3, >3 | V0_OCT | full | averaged over classes | V0_GCL 1mm CM vol | 0.036 | 0.022 | 0.018 | 7.514 | 7.233 | 0.011 | 0.029 |
| | | | | V0_RPE 3mm vol | 0.035 | 0.018 | 0.021 | 1.006 | 10.323 | 0.004 | 0.025 |
| | | | | V0_retina 3mm vol | 0.035 | 0.017 | 0.022 | 8.585 | 11.494 | 0.007 | 0.000 |
| | | | | V0_RPE 1mm CMT | 0.032 | 0.016 | 0.019 | 1.565 | 5.837 | 0.005 | 0.000 |
| | | | | V0_ORLs 1mm CM vol | 0.029 | 0.015 | 0.018 | 2.993 | 3.696 | 0.007 | 0.000 |
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| Injections first year n=3, >3 | V0_OCT | outliers removed | averaged over classes | V0_retina 3mm vol | 0.043 | 0.022 | 0.026 | 14.103 | 13.808 | 0.004 | 0.000 |
| | | | | V0_RPE 3mm vol | 0.037 | 0.019 | 0.022 | 3.501 | 12.063 | 0.000 | 0.000 |
| | | | | V0_retina min CMT | 0.034 | 0.017 | 0.020 | 14.070 | 10.881 | 0.011 | 0.000 |
| | | | | V0_retina 1mm CM vol | 0.027 | 0.014 | 0.016 | 12.346 | 9.710 | 0.003 | 0.000 |
| | | | | V0_GCL 1mm CM vol | 0.038 | 0.024 | 0.019 | 8.680 | 8.874 | 0.020 | 0.032 |
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| Injections first year n=3, >3 | VP_OCT | full | averaged over classes | VP_NFL 1mm CM vol | 0.014 | 0.026 | 0.007 | 3.347 | 0.588 | 0.000 | 0.000 |
| | | | | VP_RPE 1mm CMT | 0.033 | 0.016 | 0.020 | 2.019 | 3.963 | 0.003 | 0.023 |
| | | | | VP_retina 3mm vol | 0.031 | 0.015 | 0.018 | 6.053 | 6.803 | 0.005 | 0.000 |
| | | | | VP_RPE 3mm vol | 0.026 | 0.013 | 0.015 | 1.811 | 6.008 | 0.001 | 0.000 |
| | | | | VP_retina 1mm CMT | 0.025 | 0.012 | 0.015 | 6.423 | 7.161 | 0.010 | 0.000 |
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| Injections first year n=3, >3 | VP_OCT | outliers removed | averaged over classes | VP_RPE 1mm CM vol | 0.022 | 0.011 | 0.013 | 4.032 | 8.254 | 0.010 | 0.000 |
| | | | | VP_RPE 3mm vol | 0.022 | 0.011 | 0.013 | 3.825 | 4.156 | 0.004 | 0.000 |
| | | | | VP_ORLs min CMT | 0.026 | 0.013 | 0.015 | 4.384 | 3.753 | 0.005 | 0.000 |
| | | | | VP_ORLs 3mm vol | 0.021 | 0.011 | 0.012 | 4.532 | 3.417 | 0.006 | 0.000 |
| | | | | VP_OPL 1mm CMT | 0.011 | 0.006 | 0.007 | 1.594 | 3.133 | 0.005 | 0.000 |
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| Injections first year n=3, >3 | V0_OCTANE | full | averaged over classes | V0_vol_serous_ped | 0.040 | 0.020 | 0.020 | 1.041 | 0.304 | 0.035 | 0.029 |
| | | | | V0_vol_posterior_hyaloid | 0.030 | 0.015 | 0.015 | 0.115 | 0.029 | 0.029 | 0.000 |
| | | | | V0_vol_subretinal_hyper_reflect | 0.027 | 0.013 | 0.016 | 0.192 | 0.058 | 0.007 | 0.000 |
| | | | | V0_vol_epiretinal_membrane | 0.019 | 0.009 | 0.012 | 0.624 | 0.039 | 0.005 | 0.000 |
| | | | | V0_vol_subretinal_fluid | 0.019 | 0.009 | 0.011 | 0.866 | 0.000 | 0.002 | 0.000 |
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| Injections first year n=3, >3 | V0_OCTANE | outliers removed | averaged over classes | V0_vol_fibrovascular_ped | 0.020 | 0.010 | 0.012 | 5.954 | 2.852 | 0.012 | 0.000 |
| | | | | V0_vol_subretinal_fluid | 0.017 | 0.009 | 0.010 | 1.014 | 0.711 | 0.040 | 0.000 |
| | | | | V0_vol_neurosensory_retina | 0.010 | 0.005 | 0.006 | 1.867 | 0.593 | 0.003 | 0.000 |
| | | | | V0_vol_intraretinal_fluid | 0.005 | 0.003 | 0.003 | 0.159 | 0.573 | -0.004 | 0.000 |
| | | | | V0_vol_drusenoid_ped | 0.010 | 0.005 | 0.006 | 0.704 | 0.435 | -0.021 | 0.000 |
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| Injections first year n=3, >3 | VP_OCTANE | full | averaged over classes | VP_vol_serous_ped | 0.093 | 0.046 | 0.025 | 0.032 | 0.000 | -0.004 | 0.076 |
| | | | | VP_vol_subretinal_hyper_reflect | 0.034 | 0.017 | 0.022 | 1.679 | 0.591 | 0.040 | 0.000 |
| | | | | VP_vol_epiretinal_membrane | 0.023 | 0.012 | 0.015 | 0.376 | 0.620 | -0.023 | 0.000 |
| | | | | VP_vol_vitreous_and_subhyaloid | 0.009 | 0.005 | 0.006 | 1.462 | 2.427 | 0.001 | 0.000 |
| | | | | VP_vol_neurosensory_retina | 0.009 | 0.005 | 0.006 | 1.320 | 0.477 | -0.002 | 0.000 |
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| Injections first year n=3, >3 | VP_OCTANE | outliers removed | averaged over classes | VP_vol_vitreous_and_subhyaloid | 0.012 | 0.006 | 0.007 | 2.592 | 4.918 | 0.004 | 0.000 |
| | | | | VP_vol_rpe | 0.009 | 0.005 | 0.006 | 1.222 | 2.061 | -0.007 | 0.000 |
| | | | | VP_vol_neurosensory_retina | 0.009 | 0.004 | 0.006 | 3.814 | 0.806 | 0.000 | 0.000 |
| | | | | VP_vol_subretinal_fluid | 0.011 | 0.006 | 0.007 | 2.256 | 0.546 | 0.016 | 0.000 |
| | | | | VP_vol_intraretinal_fluid | 0.007 | 0.003 | 0.004 | 0.187 | 0.546 | -0.010 | 0.000 |
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| Injections first year n=3, >3 | VA | full | averaged over classes | VA fellow eye (V0) | 0.006 | 0.003 | 0.004 | 0.941 | 0.572 | 0.004 | 0.004 |
| | | | | VA baseline visit (V0) | 0.006 | 0.003 | 0.003 | 2.266 | 1.446 | 0.004 | 0.000 |
| | | | | VA post loading (VP) | 0.004 | 0.002 | 0.002 | 0.984 | 0.619 | 0.002 | 0.000 |
| | | | | VA mean initial 2 visits post loading | 0.004 | 0.002 | 0.002 | 0.248 | 0.140 | 0.002 | 0.000 |
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| Injections first year n=3, >3 | VA | outliers removed | averaged over classes | | 0.008 | 0.004 | 0.005 | 1.919 | 0.615 | 0.011 | 0.005 |
| | | | | | 0.005 | 0.003 | 0.003 | 2.509 | 1.558 | 0.005 | 0.000 |
| | | | | | 0.005 | 0.003 | 0.003 | 1.033 | 0.425 | 0.003 | 0.000 |
| | | | | | 0.005 | 0.003 | 0.003 | 1.406 | 1.103 | 0.023 | 0.000 |
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| Injections first year n=3, >3 | Demographic & qualitative | full | averaged over classes | Anti-VEGF drug type | 0.025 | 0.026 | 0.010 | NA | 0.005 | 0.000 | 0.028 |
| | | | | Ethnicity | 0.005 | 0.011 | 0.003 | NA | 0.010 | 0.006 | 0.000 |
| | | | | Age At First Injection | 0.015 | 0.008 | 0.009 | NA | 3.722 | 0.010 | 0.000 |
| | | | | Laterality | 0.004 | 0.004 | 0.002 | NA | 0.834 | -0.012 | 0.004 |
| | | | | Time interval 1st to 3rd injection | 0.006 | 0.004 | 0.003 | NA | 0.604 | 0.000 | 0.000 |
| | | | | Fellow eye activity | 0.003 | 0.002 | 0.002 | NA | 2.070 | -0.026 | 0.000 |
| | | | | Sex | 0.001 | 0.001 | 0.001 | NA | 0.386 | 0.004 | 0.000 |
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| Injections first year n=3, >3 | Demographic & qualitative | outliers removed | averaged over classes | Age At First Injection | 0.009 | 0.005 | 0.006 | NA | 2.921 | 0.037 | 0.000 |
| | | | | Fellow eye activity | 0.002 | 0.001 | 0.001 | NA | 1.263 | 0.010 | 0.000 |
| | | | | Laterality | 0.003 | 0.003 | 0.002 | NA | 0.575 | -0.012 | 0.003 |
| | | | | Sex | 0.001 | 0.001 | 0.001 | NA | 0.360 | -0.006 | 0.000 |
| | | | | Time interval 1st to 3rd injection | 0.004 | 0.003 | 0.003 | NA | 0.083 | -0.002 | 0.000 |
| | | | | Ethnicity | 0.006 | 0.012 | 0.003 | NA | 0.017 | 0.002 | 0.000 |
| | | | | Anti-VEGF drug type | 0.024 | 0.026 | 0.009 | NA | 0.000 | 0.016 | 0.027 |
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| Injections first year (categories 3, 4, 5, 6, 7, 8, 9, 10) | V0_OCT | full | averaged over classes | V0_retina 3mm vol | 0.100 | 0.050 | 0.018 | 2.827 | 21.343 | 0.000 | 0.048 |
| | | | | V0_IPL 3mm vol | 0.098 | 0.049 | 0.020 | 4.962 | 24.363 | -0.002 | 0.000 |
| | | | | V0_GCL 1mm CM vol | 0.079 | 0.049 | 0.016 | 1.746 | 11.791 | -0.003 | 0.000 |
| | | | | V0_OPL 3mm vol | 0.083 | 0.042 | 0.017 | 3.846 | 17.192 | 0.003 | 0.000 |
| | | | | V0_retina 1mm CMT | 0.081 | 0.040 | 0.013 | 1.670 | 15.472 | 0.002 | 0.000 |
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| Injections first year (categories 3, 4, 5, 6, 7, 8, 9, 10) | V0_OCT | outliers removed | averaged over classes | V0_retina 3mm vol | 0.116 | 0.058 | 0.022 | 4.195 | 24.295 | 0.000 | 0.056 |
| | | | | V0_IPL 3mm vol | 0.090 | 0.045 | 0.018 | 3.752 | 19.423 | 0.004 | 0.000 |
| | | | | V0_retina 1mm CM vol | 0.097 | 0.049 | 0.016 | 2.759 | 18.164 | 0.007 | 0.000 |
| | | | | V0_NFL min CMT | 0.050 | 0.038 | 0.009 | 1.180 | 17.490 | 0.000 | 0.000 |
| | | | | V0_GCL min CMT | 0.070 | 0.041 | 0.013 | 1.348 | 17.237 | 0.005 | 0.035 |
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| Injections first year (categories 3, 4, 5, 6, 7, 8, 9, 10) | VP_OCT | full | averaged over classes | VP_NFL 1mm CM vol | 0.049 | 0.088 | 0.009 | 1.604 | 1.908 | 0.002 | 0.000 |
| | | | | VP_retina 3mm vol | 0.138 | 0.069 | 0.021 | 9.644 | 35.902 | 0.011 | 0.067 |
| | | | | VP_INL 1mm CM vol | 0.091 | 0.055 | 0.012 | 6.328 | 12.755 | 0.008 | 0.000 |
| | | | | VP_RPE 1mm CMT | 0.108 | 0.054 | 0.020 | 1.732 | 12.210 | 0.005 | 0.000 |
| | | | | VP_IPL 1mm CM vol | 0.064 | 0.052 | 0.011 | 3.016 | 10.917 | 0.003 | 0.000 |
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| Injections first year (categories 3, 4, 5, 6, 7, 8, 9, 10) | VP_OCT | outliers removed | averaged over classes | VP_retina 3mm vol | 0.097 | 0.049 | 0.015 | 9.215 | 23.894 | 0.012 | NA |
| | | | | VP_IPL 3mm vol | 0.068 | 0.034 | 0.015 | 3.325 | 17.356 | 0.001 | NA |
| | | | | VP_ORLs 3mm vol | 0.081 | 0.041 | 0.013 | 13.165 | 15.858 | 0.013 | NA |
| | | | | VP_RPE 3mm vol | 0.077 | 0.038 | 0.013 | 9.793 | 15.113 | 0.010 | NA |
| | | | | VP_RPE 1mm CM vol | 0.087 | 0.045 | 0.016 | 5.774 | 14.210 | 0.011 | NA |
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| Injections first year (categories 3, 4, 5, 6, 7, 8, 9, 10) | V0_OCTANE | full | averaged over classes | V0_vol_serous_ped | 0.215 | 0.107 | 0.032 | 0.890 | 2.174 | 0.010 | 0.104 |
| | | | | V0_vol_posterior_hyaloid | 0.184 | 0.092 | 0.029 | 0.325 | 1.566 | 0.035 | 0.000 |
| | | | | V0_vol_epiretinal_membrane | 0.111 | 0.056 | 0.019 | 0.552 | 0.844 | -0.021 | NA |
| | | | | V0_vol_choroid_and_outer_layers | 0.091 | 0.046 | 0.011 | 1.039 | 7.098 | 0.004 | 0.000 |
| | | | | V0_vol_subretinal_fluid | 0.086 | 0.043 | 0.012 | 4.732 | 10.017 | 0.006 | 0.000 |
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| Injections first year (categories 3, 4, 5, 6, 7, 8, 9, 10) | V0_OCTANE | outliers removed | averaged over classes | V0_vol_vitreous_and_subhyaloid | 0.069 | 0.034 | 0.011 | 1.665 | 10.303 | 0.002 | 0.000 |
| | | | | V0_vol_subretinal_fluid | 0.107 | 0.054 | 0.014 | 4.997 | 10.027 | 0.012 | 0.000 |
| | | | | V0_vol_fibrovascular_ped | 0.085 | 0.043 | 0.017 | 1.330 | 6.822 | 0.018 | 0.040 |
| | | | | V0_vol_neurosensory_retina | 0.076 | 0.038 | 0.014 | 1.164 | 6.607 | 0.019 | 0.000 |
| | | | | V0_vol_choroid_and_outer_layers | 0.102 | 0.051 | 0.013 | 1.040 | 6.423 | -0.001 | 0.049 |
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| Injections first year (categories 3, 4, 5, 6, 7, 8, 9, 10) | VP_OCTANE | full | averaged over classes | VP_vol_serous_ped | 0.450 | 0.225 | 0.053 | 1.405 | 2.302 | 0.030 | 0.231 |
| | | | | VP_vol_epiretinal_membrane | 0.297 | 0.148 | 0.049 | 1.554 | 2.949 | 0.016 | 0.000 |
| | | | | VP_vol_posterior_hyaloid | 0.165 | 0.083 | 0.023 | 0.631 | 2.670 | -0.010 | 0.000 |
| | | | | VP_vol_subretinal_hyper_reflect | 0.119 | 0.059 | 0.020 | 1.354 | 5.280 | -0.007 | 0.000 |
| | | | | VP_vol_drusenoid_ped | 0.114 | 0.057 | 0.016 | 1.027 | 5.967 | 0.014 | 0.000 |
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| Injections first year (categories 3, 4, 5, 6, 7, 8, 9, 10) | VP_OCTANE | outliers removed | averaged over classes | VP_vol_vitreous_and_subhyaloid | 0.105 | 0.052 | 0.014 | 1.474 | 10.191 | 0.014 | 0.000 |
| | | | | VP_vol_fibrovascular_ped | 0.100 | 0.050 | 0.016 | 1.839 | 10.134 | 0.004 | 0.000 |
| | | | | VP_vol_intraretinal_fluid | 0.111 | 0.056 | 0.016 | 0.999 | 8.444 | 0.000 | 0.000 |
| | | | | VP_vol_choroid_and_outer_layers | 0.067 | 0.033 | 0.009 | 0.536 | 6.289 | 0.019 | 0.000 |
| | | | | VP_vol_rpe | 0.066 | 0.033 | 0.012 | 2.337 | 5.985 | 0.006 | 0.000 |
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| Injections first year (categories 3, 4, 5, 6, 7, 8, 9, 10) | Demographic & qualitative | full | averaged over classes | Anti-VEGF drug type | 0.171 | 0.181 | 0.020 | NA | 6.072 | 0.010 | 0.115 |
| | | | | Ethnicity | 0.017 | 0.037 | 0.003 | NA | 0.095 | -0.010 | 0.000 |
| | | | | Time interval 1st to 3rd injection | 0.054 | 0.035 | 0.009 | NA | 3.236 | 0.002 | 0.028 |
| | | | | Fellow eye activity | 0.051 | 0.030 | 0.008 | NA | 12.858 | -0.016 | 0.000 |
| | | | | Age At First Injection | 0.051 | 0.026 | 0.009 | NA | 7.374 | -0.006 | 0.024 |

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| | | | | Laterality | 0.013 | 0.013 | 0.002 | NA | 2.670 | 0.044 | 0.008 |
| | | | | Sex | 0.009 | 0.010 | 0.001 | NA | 2.756 | 0.027 | 0.000 |
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| Injections first year (categories 3, 4, 5, 6, 7, 8, 9, 10) | Demographic & qualitative | outliers removed | averaged over classes | Fellow eye activity | 0.055 | 0.032 | 0.009 | NA | 11.062 | 0.009 | 0.000 |
| | | | | Age At First Injection | 0.037 | 0.019 | 0.005 | NA | 7.129 | 0.023 | 0.017 |
| | | | | Anti-VEGF drug type | 0.189 | 0.201 | 0.023 | NA | 6.244 | 0.022 | 0.128 |
| | | | | Sex | 0.010 | 0.011 | 0.001 | NA | 2.764 | -0.027 | 0.000 |
| | | | | Time interval 1st to 3rd injection | 0.047 | 0.031 | 0.007 | NA | 2.527 | -0.001 | 0.025 |
| | | | | Laterality | 0.013 | 0.013 | 0.002 | NA | 2.506 | -0.027 | 0.008 |
| | | | | Ethnicity | 0.018 | 0.037 | 0.004 | NA | 0.115 | 0.002 | 0.000 |
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| Injections first year (categories 3, 4, 5, 6, 7, 8, 9, 10) | VA | full | averaged over classes | VA fellow eye (V0) | 0.051 | 0.026 | 0.007 | 0.410 | 2.028 | 0.014 | 0.024 |
| | | | | VA post loading (VP) | 0.047 | 0.024 | 0.004 | 0.681 | 7.648 | -0.001 | 0.022 |
| | | | | VA mean initial 2 visits post loading | 0.047 | 0.023 | 0.004 | 0.307 | 3.882 | -0.001 | 0.000 |
| | | | | VA baseline visit (V0) | 0.037 | 0.018 | 0.006 | 0.676 | 4.926 | 0.001 | 0.000 |
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| Injections first year (categories 3, 4, 5, 6, 7, 8, 9, 10) | VA | outliers removed | averaged over classes | VA post loading (VP) | 0.057 | 0.029 | 0.005 | 1.108 | 8.575 | 0.011 | 0.027 |
| | | | | VA baseline visit (V0) | 0.056 | 0.028 | 0.008 | 0.876 | 7.918 | 0.006 | 0.000 |
| | | | | VA mean initial 2 visits post loading | 0.050 | 0.025 | 0.004 | 0.459 | 5.076 | 0.005 | 0.000 |
| | | | | VA fellow eye (V0) | 0.048 | 0.024 | 0.008 | 0.446 | 1.905 | -0.002 | 0.022 |
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| Injections first year (categories 3, 4, 5, 6, 7, 8, 9, 10) | VA_st dev | full | averaged over classes | Standard deviation of VA mean, post loading -12 months (VP-V12) | 0.077 | 0.039 | 0.017 | 3.701 | 14.641 | -0.003 | 0.037 |
| | | | | VA fellow eye (V0) | 0.051 | 0.026 | 0.007 | 0.410 | 2.028 | 0.007 | 0.024 |
| | | | | VA post loading (VP) | 0.047 | 0.024 | 0.004 | 0.681 | 7.648 | 0.006 | 0.022 |
| | | | | VA mean initial 2 visits post loading | 0.047 | 0.023 | 0.004 | 0.307 | 3.882 | 0.004 | 0.000 |

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| | | | | VA baseline visit (V0) | 0.037 | 0.018 | 0.006 | 0.676 | 4.926 | -0.007 | 0.000 |
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| Injections first year (categories 3, 4, 5, 6, 7, 8, 9, 10) | VA_st dev | outliers removed | averaged over classes | Standard deviation of VA mean, post loading -12 months (VP-V12) | 0.077 | 0.039 | 0.016 | 3.974 | 11.269 | 0.007 | 0.037 |
| | | | | VA post loading (VP) | 0.058 | 0.029 | 0.005 | 1.171 | 8.629 | 0.009 | 0.027 |
| | | | | VA baseline visit (V0) | 0.057 | 0.029 | 0.008 | 0.864 | 7.898 | 0.004 | 0.000 |
| | | | | VA mean initial 2 visits post loading | 0.051 | 0.025 | 0.004 | 0.491 | 5.409 | 0.009 | 0.000 |
| | | | | VA fellow eye (V0) | 0.049 | 0.024 | 0.008 | 0.417 | 1.850 | -0.001 | 0.023 |
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| Injection pattern first year (categories: clusters 1, 2, 3, 4, 5, 6, 7, 8, 9, 10) | Demographic & qualitative | full | averaged over classes | Anti-VEGF drug type | 0.101 | 0.111 | 0.017 | NA | 5.887 | 0.027 | 0.055 |
| | | | | Ethnicity | 0.030 | 0.065 | 0.004 | NA | 0.309 | 0.014 | 0.000 |
| | | | | Time interval 1st to 3rd injection | 0.100 | 0.064 | 0.012 | NA | 12.449 | 0.004 | 0.046 |
| | | | | Fellow eye activity | 0.091 | 0.053 | 0.008 | NA | 17.121 | 0.019 | 0.000 |
| | | | | Age At First Injection | 0.076 | 0.038 | 0.012 | NA | 13.389 | 0.004 | 0.032 |
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| Injection pattern first year (categories: clusters 1, 2, 3, 4, 5, 6, 7, 8, 9, 10) | Demographic & qualitative | outliers removed | averaged over classes | Age At First Injection | 0.109 | 0.055 | 0.012 | NA | 16.119 | 0.011 | 0.046 |
| | | | | Fellow eye activity | 0.099 | 0.057 | 0.009 | NA | 16.033 | 0.016 | 0.000 |
| | | | | Time interval 1st to 3rd injection | 0.102 | 0.069 | 0.012 | NA | 8.948 | 0.016 | 0.048 |
| | | | | Sex | 0.022 | 0.025 | 0.002 | NA | 5.828 | 0.071 | 0.000 |
| | | | | Anti-VEGF drug type | 0.108 | 0.119 | 0.018 | NA | 5.457 | 0.047 | 0.059 |
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| Injection pattern first year (categories: clusters 1, 2, 3, 4, 5, 6, 7, 8, 9, 10) | VA | full | averaged over classes | VA fellow eye (V0) | 0.077 | 0.039 | 0.009 | 1.269 | 10.276 | 0.018 | 0.032 |
| | | | | VA initial post loading | 0.051 | 0.026 | 0.005 | 0.740 | 5.526 | 0.018 | 0.021 |
| | | | | TW0OperVABestMeasure | 0.043 | 0.021 | 0.005 | 0.730 | 6.012 | 0.012 | 0.000 |
| | | | | VA mean initial 2 visits post loading | 0.040 | 0.020 | 0.005 | 0.550 | 4.017 | 0.015 | 0.000 |
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| Injection pattern first year (categories: clusters 1, 2, 3, 4, 5, 6, 7, 8, 9, 10) | VA | outliers removed | averaged over classes | VA fellow eye (V0) | 0.081 | 0.040 | 0.010 | 1.573 | 12.810 | 0.023 | 0.034 |
| | | | | TW0OperVABestMeasure | 0.044 | 0.022 | 0.004 | 1.063 | 7.064 | 0.024 | 0.000 |
| | | | | VA initial post loading | 0.046 | 0.023 | 0.005 | 0.738 | 4.800 | 0.023 | 0.000 |
| | | | | VA mean initial 2 visits post loading | 0.046 | 0.023 | 0.006 | 0.346 | 3.682 | 0.019 | 0.019 |
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| Injection pattern first year (categories: clusters 1, 2, 3, 4, 5, 6, 7, 8, 9, 10) | VA_st dev | full | averaged over classes | Standard deviation of VA mean, post loading -12 months (VP-V12) | 0.084 | 0.042 | 0.018 | 2.855 | 17.670 | 0.002 | 0.035 |
| | | | | VA fellow eye (V0) | 0.077 | 0.039 | 0.009 | 1.269 | 10.276 | 0.014 | 0.032 |
| | | | | VA post loading (VP) | 0.051 | 0.026 | 0.005 | 0.740 | 5.526 | 0.003 | 0.021 |
| | | | | VA baseline visit (V0) | 0.043 | 0.021 | 0.005 | 0.730 | 6.012 | 0.004 | 0.000 |
| | | | | VA mean initial 2 visits post loading | 0.040 | 0.020 | 0.005 | 0.550 | 4.017 | 0.005 | 0.000 |
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| Injection pattern | VA_st dev | outliers | averaged | Standard deviation of VA mean, post loading -12 months (VP-V12) | 0.092 | 0.046 | 0.019 | 3.005 | 17.787 | 0.005 | 0.039 |

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| | | | | VA fellow eye (V0) | 0.078 | 0.039 | 0.009 | 1.446 | 11.572 | 0.010 | 0.033 |
| | | | | VA baseline visit (V0) | 0.049 | 0.025 | 0.005 | 1.371 | 8.970 | 0.023 | 0.020 |
| | | | | VA post loading (VP) | 0.048 | 0.024 | 0.006 | 0.836 | 5.262 | 0.018 | 0.000 |
| | | | | VA mean initial 2 visits post loading | 0.049 | 0.025 | 0.007 | 0.410 | 3.972 | 0.019 | 0.000 |
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| Injection pattern first year (categories: clusters 1, 2, 3, 4, 5, 6, 7, 8, 9, 10) | V0_OCT | full | averaged over classes | V0_GCL 1mm CM vol | 0.114 | 0.071 | 0.017 | 2.765 | 26.604 | 0.008 | 0.053 |
| | | | | V0_NFL 1mm CM vol | 0.078 | 0.063 | 0.008 | 1.166 | 6.334 | 0.002 | 0.000 |
| | | | | V0_IPL 1mm CM vol | 0.099 | 0.060 | 0.014 | 0.401 | 8.522 | 0.001 | 0.000 |
| | | | | V0_RPE 1mm CM vol | 0.111 | 0.056 | 0.016 | 1.486 | 18.906 | 0.009 | 0.047 |
| | | | | V0_RPE 1mm CMT | 0.107 | 0.054 | 0.016 | 1.461 | 15.231 | 0.009 | 0.000 |
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| Injection pattern first year (categories: clusters 1, 2, 3, 4, 5, 6, 7, 8, 9, 10) | V0_OCT | outliers removed | averaged over classes | V0_GCL 1mm CM vol | 0.116 | 0.073 | 0.018 | 2.795 | 27.184 | 0.003 | 0.000 |
| | | | | V0_retina 3mm vol | 0.104 | 0.052 | 0.023 | 2.830 | 23.150 | 0.004 | 0.000 |
| | | | | V0_retina min CMT | 0.096 | 0.048 | 0.020 | 3.188 | 22.581 | 0.006 | 0.000 |
| | | | | V0_IPL 3mm vol | 0.095 | 0.048 | 0.015 | 3.050 | 22.418 | 0.002 | 0.000 |
| | | | | V0_GCL 1mm CMT | 0.106 | 0.053 | 0.015 | 2.871 | 21.031 | 0.002 | 0.000 |
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| Injection pattern first year (categories: clusters 1, 2, 3, 4, 5, 6, 7, 8, 9, 10) | VP_OCT | full | averaged over classes | VP_NFL 1mm CM vol | 0.055 | 0.099 | 0.010 | 1.476 | 1.664 | 0.000 | 0.000 |
| | | | | VP_NFL min CMT | 0.073 | 0.080 | 0.009 | 1.338 | 21.135 | -0.008 | 0.000 |
| | | | | VP_retina 3mm vol | 0.138 | 0.069 | 0.025 | 2.654 | 29.654 | 0.001 | 0.059 |
| | | | | VP_IPL 1mm CM vol | 0.081 | 0.066 | 0.013 | 2.448 | 11.428 | -0.006 | 0.000 |
| | | | | VP_OPL 1mm CM vol | 0.085 | 0.062 | 0.013 | 1.477 | 5.090 | 0.009 | 0.000 |
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| Injection pattern first year (categories: clusters 1, 2, 3, 4, 5, 6, 7, 8, 9, 10) | VP_OCT | outliers removed | averaged over classes | VP_RPE 1mm CM vol | 0.103 | 0.053 | 0.018 | 2.962 | 23.851 | 0.010 | 0.000 |
| | | | | VP_retina 3mm vol | 0.122 | 0.061 | 0.018 | 3.614 | 23.787 | 0.009 | 0.052 |
| | | | | VP_retina 1mm CM vol | 0.088 | 0.044 | 0.013 | 3.965 | 19.423 | 0.012 | 0.000 |
| | | | | VP_RPE 1mm CMT | 0.117 | 0.059 | 0.022 | 2.931 | 18.493 | 0.010 | 0.000 |
| | | | | VP_retina 1mm CMT | 0.088 | 0.044 | 0.013 | 3.971 | 17.962 | 0.012 | 0.000 |
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| Injection pattern first year (categories: clusters 1, 2, 3, 4, 5, 6, 7, 8, 9, 10) | V0_OCTANE | full | averaged over classes | V0_vol__um3_serous_ped | 0.457 | 0.229 | 0.052 | 1.562 | 9.509 | 0.006 | 0.223 |
| | | | | V0_vol__um3_epiretinal_membrane | 0.354 | 0.177 | 0.043 | 0.804 | 3.968 | 0.008 | 0.168 |
| | | | | V0_vol__um3_posterior_hyaloid | 0.204 | 0.102 | 0.027 | 0.647 | 4.453 | 0.033 | 0.000 |
| | | | | V0_vol__um3_rpe | 0.139 | 0.070 | 0.013 | 1.072 | 6.986 | 0.015 | 0.060 |
| | | | | V0_vol__um3_drusenoid_ped | 0.132 | 0.066 | 0.013 | 0.855 | 8.743 | 0.003 | 0.056 |
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| Injection pattern first year (categories: clusters 1, 2, 3, 4, 5, 6, 7, 8, 9, 10) | V0_OCTANE | outliers removed | averaged over classes | V0_vol__um3_drusenoid_ped | 0.166 | 0.083 | 0.016 | 1.202 | 12.940 | 0.016 | 0.072 |
| | | | | V0_vol__um3_neurosensory_retina | 0.128 | 0.064 | 0.012 | 1.961 | 12.652 | 0.003 | 0.000 |
| | | | | V0_vol__um3_serous_ped | 0.572 | 0.286 | 0.075 | 2.032 | 10.453 | 0.007 | 0.305 |
| | | | | V0_vol__um3_vitreous_and_subhyaloid | 0.078 | 0.039 | 0.011 | 0.971 | 9.137 | -0.005 | 0.000 |
| | | | | V0_vol__um3_rpe | 0.149 | 0.075 | 0.014 | 1.196 | 7.688 | 0.006 | 0.065 |
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|---|---|---|---|---|---|---|---|---|---|---|---|
| Injection pattern first year (categories: clusters 1, 2, 3, 4, 5, 6, 7, 8, 9, 10) | VP_OCTANE | full | averaged over classes | VP_vol_um3_serous_ped | 0.518 | 0.259 | 0.047 | 0.552 | 0.951 | -0.002 | 0.252 |
| | | | | VP_vol_um3_epiretinal_membrane | 0.339 | 0.170 | 0.041 | 0.546 | 1.878 | 0.009 | 0.000 |
| | | | | VP_vol_um3_posterior_hyaloid | 0.286 | 0.143 | 0.028 | 0.633 | 3.237 | -0.040 | 0.000 |
| | | | | VP_vol_um3_subretinal_hyper_reflect | 0.183 | 0.091 | 0.020 | 0.935 | 6.280 | -0.006 | 0.000 |
| | | | | VP_vol_um3_subretinal_fluid | 0.133 | 0.067 | 0.015 | 1.019 | 5.453 | 0.000 | 0.000 |
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| Injection pattern first year (categories: clusters 1, 2, 3, 4, 5, 6, 7, 8, 9, 10) | VP_OCTANE | outliers removed | averaged over classes | VP_vol_um3_rpe | 0.111 | 0.055 | 0.015 | 2.063 | 14.107 | -0.004 | 0 |
| | | | | VP_vol_um3_neurosensory_retina | 0.143 | 0.071 | 0.019 | 2.047 | 12.902 | -0.005 | 0 |
| | | | | VP_vol_um3_choroid_and_outer_layers | 0.091 | 0.046 | 0.01 | 0.892 | 7.783 | 0.005 | 0 |
| | | | | VP_vol_um3_posterior_hyaloid | 0.358 | 0.179 | 0.041 | 1.084 | 6.732 | -0.022 | 0 |
| | | | | VP_vol_um3_subretinal_fluid | 0.123 | 0.062 | 0.013 | 0.973 | 6.641 | -0.006 | 0 |
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Appendix 5: Treatment dose related regression models, model accuracy and feature ranking

| Target | Feature group | Dataset | Models | MSE | RMSE | MAE | R2 | CVRMSE | Feature | Univar. reg. | RReliefF |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Injections First Year | V0_OCTANE | full | Random Forest | 2.48 | 1.57 | 1.32 | -0.09 | 34.49 | V0_vol_subretinal_fluid | 8.647 | 0.221 |
| | | | SVM | 2.55 | 1.60 | 1.33 | -0.12 | 34.99 | V0_vol_neurosensory_retina | 3.838 | 0.155 |
| | | | Tree | 3.51 | 1.87 | 1.49 | -0.54 | 41.04 | V0_vol_rpe | 2.665 | 0.221 |
| | | | AdaBoost | 3.56 | 1.89 | 1.45 | -0.57 | 41.33 | V0_vol_fibrovascular_ped | 1.783 | 0.188 |
| | | | Gradient Boosting | 4.18 | 2.04 | 1.61 | -0.84 | 44.80 | V0_vol_vitreous_and_subhyaloid | 1.637 | 0.193 |
| | | | Linear Regression | 8.03 | 2.83 | 1.89 | -2.54 | 62.10 | | | |
| | | | kNN (error) | | | | | | | | |
| Injections First Year | V0_OCTANE | outliers removed | Linear Regression | 2.36 | 1.54 | 1.28 | -0.04 | 33.66 | V0_vol_subretinal_fluid | 9.544 | 0.320 |
| | | | Gradient Boosting | 2.36 | 1.54 | 1.27 | -0.04 | 33.68 | V0_vol_neurosensory_retina | 4.470 | 0.176 |
| | | | Random Forest | 2.41 | 1.55 | 1.30 | -0.06 | 34.06 | V0_vol_subretinal_hyper_reflect | 2.155 | 0.371 |
| | | | kNN | 2.61 | 1.61 | 1.34 | -0.15 | 35.40 | V0_vol_rpe | 1.798 | 0.260 |
| | | | AdaBoost | 2.62 | 1.62 | 1.31 | -0.15 | 35.47 | V0_vol_intraretinal_fluid | 1.720 | 0.276 |
| | | | SVM | 2.78 | 1.67 | 1.31 | -0.22 | 36.57 | | | |
| | | | Tree | 2.79 | 1.67 | 1.35 | -0.23 | 36.65 | | | |
| Injections First Year | VP_OCTANE | full | AdaBoost | 7.58 | 2.75 | 1.97 | -2.34 | 60.35 | VP_vol_subretinal_fluid | 5.546 | 0.292 |
| | | | SVM | 8.36 | 2.89 | 2.37 | -2.68 | 63.38 | VP_vol_subretinal_hyper_reflect | 3.150 | 0.369 |
| | | | Tree | 8.92 | 2.99 | 2.55 | -2.93 | 65.44 | VP_vol_rpe | 2.388 | 0.278 |
| | | | Random Forest | 10.16 | 3.19 | 2.66 | -3.47 | 69.85 | VP_vol_drusenoid_ped | 1.059 | 0.317 |
| | | | Gradient Boosting | 19.40 | 4.40 | 3.66 | -7.54 | 96.53 | VP_vol_neurosensory_retina | 0.746 | 0.109 |
| | | | Linear Regression | 20.66 | 4.55 | 3.46 | -8.10 | 99.61 | | | |
| | | | kNN (error) | | | | | | | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| Injections First Year | VP_OCTANE | outliers removed | Linear Regression | 2.28 | 1.51 | 1.27 | -0.06 | 33.53 | VP_vol_neurosensory_retina | 8.716 | 0.182 |
| | | | Random Forest | 2.40 | 1.55 | 1.28 | -0.11 | 34.38 | VP_vol_rpe | 3.626 | 0.240 |
| | | | kNN | 2.42 | 1.56 | 1.26 | -0.12 | 34.55 | VP_vol_subretinal_fluid | 2.935 | 0.371 |
| | | | Gradient Boosting | 2.52 | 1.59 | 1.32 | -0.16 | 35.22 | VP_vol_drusenoid_ped | 1.554 | 0.275 |
| | | | AdaBoost | 2.56 | 1.60 | 1.29 | -0.18 | 35.47 | VP_vol_intraretinal_fluid | 1.073 | 0.357 |
| | | | SVM | 2.72 | 1.65 | 1.28 | -0.26 | 36.60 | | | |
| | | | Tree | 2.86 | 1.69 | 1.39 | -0.32 | 37.51 | | | |
| Injections First Year | Demographic & qualitative | full | Linear Regression | 2.41 | 1.55 | 1.31 | -0.06 | 34.04 | Fellow eye activity | NA | 0.234 |
| | | | kNN | 2.83 | 1.68 | 1.36 | -0.24 | 36.84 | Anti-VEGF drug type | NA | 0.161 |
| | | | Gradient Boosting | 2.85 | 1.69 | 1.36 | -0.26 | 37.02 | Age At First Injection | NA | 0.131 |
| | | | SVM | 2.86 | 1.69 | 1.30 | -0.26 | 37.04 | Sex | NA | 0.103 |
| | | | Random Forest | 2.97 | 1.72 | 1.40 | -0.31 | 37.79 | Laterality | NA | 0.078 |
| | | | AdaBoost | 3.27 | 1.81 | 1.43 | -0.44 | 39.63 | | | |
| | | | Tree | 3.64 | 1.91 | 1.50 | -0.60 | 41.81 | | | |
| Injections First Year | Demographic & qualitative | outliers removed | Linear Regression | 2.00 | 1.42 | 1.19 | 0.13 | 30.94 | Fellow eye activity | NA | 0.220 |
| | | | Gradient Boosting | 2.23 | 1.49 | 1.26 | 0.03 | 32.63 | Anti-VEGF drug type | NA | 0.192 |
| | | | Random Forest | 2.32 | 1.52 | 1.26 | -0.01 | 33.28 | Age At First Injection | NA | 0.171 |
| | | | SVM | 2.53 | 1.59 | 1.29 | -0.10 | 34.77 | Sex | NA | 0.120 |
| | | | kNN | 2.60 | 1.61 | 1.30 | -0.13 | 35.26 | Laterality | NA | 0.091 |
| | | | AdaBoost | 2.64 | 1.63 | 1.28 | -0.15 | 35.55 | | | |
| | | | Tree | 2.89 | 1.70 | 1.36 | -0.26 | 37.15 | | | |
| Injections First Year | VA | full | Linear Regression | 2.36 | 1.54 | 1.30 | -0.04 | 33.69 | VA fellow eye (V0) | 0.751 | 0.103 |
| | | | Gradient Boosting | 2.71 | 1.65 | 1.34 | -0.19 | 36.08 | VA baseline visit (V0) | 2.474 | 0.086 |
| | | | kNN | 2.80 | 1.67 | 1.33 | -0.23 | 36.65 | VA mean of 2 visits immediately post loading | 0.009 | 0.059 |
| | | | Random Forest | 2.80 | 1.67 | 1.37 | -0.23 | 36.67 | VA post loading (VP) | 0.227 | 0.059 |
| | | | SVM | 2.88 | 1.70 | 1.33 | -0.27 | 37.21 | | | |
| | | | AdaBoost | 3.09 | 1.76 | 1.35 | -0.36 | 38.52 | | | |
| | | | Tree | 3.80 | 1.95 | 1.53 | -0.67 | 42.72 | | | |
| Injec tions | VA | outli ers | Linear Regression | 2.22 | 1.49 | 1.24 | 0.00 | 32.83 | VA fellow eye (V0) | 1.836 | 0.095 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Gradient Boosting | 2.40 | 1.55 | 1.26 | -0.09 | 34.13 | VA baseline visit (V0) | 1.341 | 0.080 |
| | | | Random Forest | 2.59 | 1.61 | 1.31 | -0.17 | 35.47 | VA post loading (VP) | 1.113 | 0.065 |
| | | | SVM | 2.68 | 1.64 | 1.26 | -0.21 | 36.11 | VA mean of 2 visits immediately post loading | 0.174 | 0.059 |
| | | | kNN | 2.88 | 1.70 | 1.40 | -0.30 | 37.40 | | | |
| | | | AdaBoost | 3.47 | 1.86 | 1.41 | -0.57 | 41.04 | | | |
| | | | Tree | 4.18 | 2.04 | 1.57 | -0.89 | 45.07 | | | |
| Injections First Year | VA_st dev | full | Linear Regression | 2.43 | 1.56 | 1.31 | -0.07 | 34.18 | Standard deviation of VA mean, post loading -12 months (VP-V12) | 14.454 | 0.083 |
| | | | SVM | 2.63 | 1.62 | 1.30 | -0.16 | 35.52 | VA baseline visit (V0) | 2.474 | 0.072 |
| | | | kNN | 2.70 | 1.64 | 1.33 | -0.19 | 36.03 | VA fellow eye (V0) | 0.751 | 0.109 |
| | | | Random Forest | 2.72 | 1.65 | 1.36 | -0.20 | 36.13 | VA post loading (VP) | 0.227 | 0.060 |
| | | | Gradient Boosting | 2.97 | 1.72 | 1.43 | -0.31 | 37.80 | VA mean of 2 visits immediately post loading | 0.009 | 0.056 |
| | | | AdaBoost | 3.10 | 1.76 | 1.39 | -0.36 | 38.58 | | | |
| | | | Tree | 4.87 | 2.21 | 1.74 | -1.14 | 48.36 | | | |
| Injections First Year | VA_st dev | outliers removed | Linear Regression | 2.19 | 1.48 | 1.24 | 0.01 | 32.55 | Standard deviation of VA mean, post loading -12 months (VP-V12) | 12.760 | 0.106 |
| | | | Gradient Boosting | 2.54 | 1.59 | 1.33 | -0.14 | 35.07 | VA fellow eye (V0) | 1.635 | 0.100 |
| | | | SVM | 2.62 | 1.62 | 1.30 | -0.18 | 35.58 | VA baseline visit (V0) | 1.550 | 0.073 |
| | | | Random Forest | 2.67 | 1.63 | 1.36 | -0.20 | 35.91 | VA post loading (VP) | 1.128 | 0.061 |
| | | | kNN | 2.90 | 1.70 | 1.41 | -0.31 | 37.48 | VA mean of 2 visits immediately post loading | 0.168 | 0.062 |
| | | | AdaBoost | 3.30 | 1.82 | 1.42 | -0.49 | 39.97 | | | |
| | | | Tree | 4.14 | 2.03 | 1.62 | -0.86 | 44.75 | | | |
| Injections First Year | V0_OCT | full | Linear Regression | 2.37 | 1.54 | 1.30 | -0.05 | 33.77 | V0_OPL 3mm vol | 15.600 | 0.132 |
| | | | SVM | 2.54 | 1.59 | 1.26 | -0.12 | 34.96 | V0_retina 3mm vol | 14.398 | 0.071 |
| | | | Random Forest | 2.63 | 1.62 | 1.34 | -0.16 | 35.52 | V0_IRLs 3mm vol | 8.207 | 0.060 |
| | | | Gradient Boosting | 2.67 | 1.63 | 1.35 | -0.17 | 35.78 | V0_retina min CMT | 8.069 | 0.081 |
| | | | kNN | 2.79 | 1.67 | 1.39 | -0.23 | 36.58 | V0_IPL 3mm vol | 7.732 | 0.067 |
| | | | AdaBoost | 2.81 | 1.68 | 1.34 | -0.24 | 36.74 | | | |
| | | | Tree | 3.62 | 1.90 | 1.46 | -0.59 | 41.69 | | | |
| Injec tions | V0_O CT | outli ers | Gradient Boosting | 2.40 | 1.55 | 1.27 | -0.03 | 33.80 | V0_retina 3mm vol | 24.072 | 0.086 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | AdaBoost | 2.49 | 1.58 | 1.21 | -0.07 | 34.40 | V0_OPL 3mm vol | 14.349 | 0.154 |
| | | | SVM | 2.50 | 1.58 | 1.25 | -0.07 | 34.48 | V0_retina min CMT | 13.265 | 0.106 |
| | | | Random Forest | 2.56 | 1.60 | 1.33 | -0.09 | 34.86 | V0_retina 1mm CMT | 13.258 | 0.091 |
| | | | kNN | 2.69 | 1.64 | 1.33 | -0.15 | 35.76 | V0_retina 1mm CM vol | 13.058 | 0.090 |
| | | | Linear Regression | 2.84 | 1.68 | 1.35 | -0.21 | 36.71 | | | |
| | | | Tree | 3.71 | 1.93 | 1.47 | -0.59 | 41.98 | | | |
| Injections First Year | VP_OCT | full | Linear Regression | 2.31 | 1.52 | 1.28 | -0.02 | 33.35 | VP_retina 3mm vol | 39.657 | 0.058 |
| | | | SVM | 2.61 | 1.61 | 1.30 | -0.15 | 35.38 | VP_retina 1mm CMT | 34.611 | 0.061 |
| | | | kNN | 2.70 | 1.64 | 1.35 | -0.19 | 36.02 | VP_retina 1mm CM vol | 33.624 | 0.06 |
| | | | Random Forest | 2.71 | 1.65 | 1.35 | -0.19 | 36.08 | VP_retina min CMT | 28.417 | 0.061 |
| | | | Gradient Boosting | 2.73 | 1.65 | 1.34 | -0.20 | 36.23 | VP_NFL 3mm vol | 24.401 | 0.063 |
| | | | AdaBoost | 2.86 | 1.69 | 1.31 | -0.26 | 37.08 | | | |
| | | | Tree | 4.55 | 2.13 | 1.70 | -1.01 | 46.78 | | | |
| Injections First Year | VP_OCT | outliers removed | Random Forest | 2.01 | 1.42 | 1.18 | 0.00 | 31.59 | VP_retina 3mm vol | 32.986 | 0.076 |
| | | | SVM | 2.09 | 1.45 | 1.18 | -0.04 | 32.24 | VP_ORLs 3mm vol | 28.777 | 0.041 |
| | | | Linear Regression | 2.12 | 1.46 | 1.19 | -0.06 | 32.51 | VP_ORLs min CMT | 26.062 | 0.038 |
| | | | kNN | 2.23 | 1.49 | 1.21 | -0.11 | 33.28 | VP_retina 1mm CMT | 21.456 | 0.066 |
| | | | Gradient Boosting | 2.28 | 1.51 | 1.23 | -0.14 | 33.65 | VP_ORLs 1mm CMT | 21.424 | 0.066 |
| | | | AdaBoost | 2.42 | 1.56 | 1.23 | -0.21 | 34.72 | | | |
| | | | Tree | 3.53 | 1.88 | 1.47 | -0.77 | 41.91 | | | |

Appendix 6: Visual acuity related classification models, model accuracy

| Target | Feature group | Dataset | Class results | Models | AUC | CA | F1 | Precision | Recall | MCC | Specificity |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints | VA_st dev | full | averaged over classes | Logistic Regression | 0.54 | 0.55 | 0.52 | 0.55 | 0.55 | 0.08 | 0.51 |
| | | | | Neural Network | 0.54 | 0.56 | 0.54 | 0.55 | 0.56 | 0.09 | 0.53 |
| | | | | SVM | 0.52 | 0.54 | 0.52 | 0.53 | 0.54 | 0.06 | 0.51 |
| | | | | Random Forest | 0.51 | 0.50 | 0.50 | 0.50 | 0.50 | -0.01 | 0.49 |
| | | | | kNN | 0.51 | 0.53 | 0.52 | 0.52 | 0.53 | 0.04 | 0.51 |
| | | | | Tree | 0.49 | 0.50 | 0.50 | 0.50 | 0.50 | 0.00 | 0.50 |
| | | | | Naïve Bayes | 0.49 | 0.50 | 0.49 | 0.49 | 0.50 | -0.03 | 0.47 |
| | | | | AdaBoost | 0.48 | 0.48 | 0.48 | 0.48 | 0.48 | -0.05 | 0.48 |
| | | | | Gradient Boosting | 0.46 | 0.48 | 0.47 | 0.47 | 0.48 | -0.06 | 0.46 |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints | VA_st dev | outliers removed | averaged over classes | Logistic Regression | 0.66 | 0.61 | 0.60 | 0.60 | 0.61 | 0.20 | 0.60 |
| | | | | Neural Network | 0.65 | 0.59 | 0.59 | 0.59 | 0.59 | 0.18 | 0.59 |
| | | | | SVM | 0.64 | 0.60 | 0.60 | 0.60 | 0.60 | 0.19 | 0.59 |
| | | | | Naïve Bayes | 0.64 | 0.59 | 0.59 | 0.60 | 0.59 | 0.19 | 0.60 |
| | | | | Gradient Boosting | 0.58 | 0.55 | 0.55 | 0.55 | 0.55 | 0.09 | 0.54 |
| | | | | kNN | 0.58 | 0.56 | 0.56 | 0.56 | 0.56 | 0.12 | 0.56 |
| | | | | Random Forest | 0.58 | 0.58 | 0.58 | 0.58 | 0.58 | 0.15 | 0.57 |
| | | | | AdaBoost | 0.49 | 0.49 | 0.49 | 0.49 | 0.49 | -0.02 | 0.49 |
| | | | | Tree | 0.48 | 0.52 | 0.52 | 0.52 | 0.52 | 0.04 | 0.52 |
| Change in VA post loading (month 4 - | VP_OCT | full | averaged over classes | Tree | 0.55 | 0.54 | 0.54 | 0.54 | 0.54 | 0.08 | 0.53 |
| | | | | Random Forest | 0.52 | 0.50 | 0.49 | 0.49 | 0.50 | -0.02 | 0.48 |
| | | | | Neural Network | 0.51 | 0.51 | 0.51 | 0.51 | 0.51 | 0.01 | 0.49 |
| | | | | AdaBoost | 0.50 | 0.50 | 0.50 | 0.50 | 0.50 | 0.00 | 0.50 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Naïve Bayes | 0.50 | 0.49 | 0.49 | 0.49 | 0.49 | -0.03 | 0.48 |
| | | | | Gradient Boosting | 0.49 | 0.52 | 0.52 | 0.52 | 0.52 | 0.03 | 0.51 |
| | | | | kNN | 0.48 | 0.47 | 0.46 | 0.46 | 0.47 | -0.08 | 0.45 |
| | | | | Logistic Regression | 0.48 | 0.51 | 0.49 | 0.50 | 0.51 | 0.00 | 0.48 |
| | | | | SVM | 0.44 | 0.54 | 0.53 | 0.53 | 0.54 | 0.05 | 0.51 |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints | VP_OCT | outliers removed | averaged over classes | Logistic Regression | 0.53 | 0.51 | 0.51 | 0.51 | 0.51 | 0.01 | 0.50 |
| | | | | Neural Network | 0.50 | 0.51 | 0.51 | 0.51 | 0.51 | 0.02 | 0.50 |
| | | | | Tree | 0.50 | 0.51 | 0.51 | 0.51 | 0.51 | 0.03 | 0.51 |
| | | | | Random Forest | 0.47 | 0.46 | 0.46 | 0.46 | 0.46 | -0.08 | 0.46 |
| | | | | kNN | 0.46 | 0.46 | 0.46 | 0.46 | 0.46 | -0.08 | 0.45 |
| | | | | AdaBoost | 0.45 | 0.46 | 0.46 | 0.45 | 0.46 | -0.10 | 0.45 |
| | | | | SVM | 0.45 | 0.53 | 0.51 | 0.52 | 0.53 | 0.03 | 0.50 |
| | | | | Naïve Bayes | 0.42 | 0.44 | 0.44 | 0.44 | 0.44 | -0.12 | 0.44 |
| | | | | Gradient Boosting | 0.42 | 0.47 | 0.47 | 0.47 | 0.47 | -0.06 | 0.46 |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints | V0_OCT | full | averaged over classes | AdaBoost | 0.54 | 0.54 | 0.54 | 0.54 | 0.54 | 0.08 | 0.54 |
| | | | | Tree | 0.53 | 0.53 | 0.53 | 0.53 | 0.53 | 0.06 | 0.53 |
| | | | | Logistic Regression | 0.52 | 0.56 | 0.53 | 0.55 | 0.56 | 0.09 | 0.52 |
| | | | | kNN | 0.50 | 0.51 | 0.51 | 0.51 | 0.51 | 0.01 | 0.50 |
| | | | | Random Forest | 0.49 | 0.52 | 0.52 | 0.52 | 0.52 | 0.03 | 0.51 |
| | | | | Naïve Bayes | 0.48 | 0.48 | 0.47 | 0.47 | 0.48 | -0.07 | 0.46 |
| | | | | Neural Network | 0.47 | 0.50 | 0.49 | 0.49 | 0.50 | -0.03 | 0.48 |
| | | | | SVM | 0.44 | 0.52 | 0.49 | 0.50 | 0.52 | 0.00 | 0.48 |
| | | | | Gradient Boosting | 0.44 | 0.43 | 0.43 | 0.42 | 0.43 | -0.16 | 0.41 |
| Change in VA post loading (month 4 - month 12), when | V0_OCT | outliers removed | averaged over classes | Random Forest | 0.57 | 0.55 | 0.55 | 0.55 | 0.55 | 0.09 | 0.54 |
| | | | | Naïve Bayes | 0.56 | 0.54 | 0.54 | 0.55 | 0.54 | 0.09 | 0.54 |
| | | | | Gradient Boosting | 0.50 | 0.52 | 0.51 | 0.51 | 0.52 | 0.02 | 0.51 |
| | | | | SVM | 0.49 | 0.53 | 0.50 | 0.51 | 0.53 | 0.02 | 0.49 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | kNN | 0.48 | 0.49 | 0.49 | 0.49 | 0.49 | -0.03 | 0.48 |
| | | | | AdaBoost | 0.47 | 0.48 | 0.48 | 0.48 | 0.48 | -0.05 | 0.47 |
| | | | | Neural Network | 0.46 | 0.52 | 0.51 | 0.51 | 0.52 | 0.02 | 0.50 |
| | | | | Tree | 0.46 | 0.48 | 0.48 | 0.48 | 0.48 | -0.04 | 0.48 |
| | | | | Logistic Regression | 0.45 | 0.50 | 0.48 | 0.49 | 0.50 | -0.03 | 0.47 |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints | Demographic & qualitative | full | averaged over classes | kNN | 0.53 | 0.51 | 0.51 | 0.51 | 0.51 | 0.02 | 0.50 |
| | | | | AdaBoost | 0.50 | 0.51 | 0.51 | 0.51 | 0.51 | 0.01 | 0.50 |
| | | | | Gradient Boosting | 0.49 | 0.51 | 0.51 | 0.51 | 0.51 | 0.01 | 0.50 |
| | | | | SVM | 0.53 | 0.51 | 0.48 | 0.49 | 0.51 | -0.03 | 0.47 |
| | | | | Random Forest | 0.49 | 0.49 | 0.49 | 0.49 | 0.49 | -0.03 | 0.48 |
| | | | | Tree | 0.49 | 0.48 | 0.48 | 0.49 | 0.48 | -0.03 | 0.49 |
| | | | | Naïve Bayes | 0.45 | 0.48 | 0.48 | 0.48 | 0.48 | -0.05 | 0.47 |
| | | | | Neural Network | 0.46 | 0.48 | 0.46 | 0.46 | 0.48 | -0.07 | 0.45 |
| | | | | Logistic Regression | 0.42 | 0.51 | 0.40 | 0.43 | 0.51 | -0.09 | 0.44 |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints | Demographic & qualitative | outliers removed | averaged over classes | Gradient Boosting | 0.61 | 0.57 | 0.57 | 0.57 | 0.57 | 0.14 | 0.57 |
| | | | | Random Forest | 0.57 | 0.56 | 0.56 | 0.56 | 0.56 | 0.11 | 0.55 |
| | | | | Naïve Bayes | 0.57 | 0.54 | 0.53 | 0.53 | 0.54 | 0.06 | 0.52 |
| | | | | AdaBoost | 0.56 | 0.57 | 0.57 | 0.57 | 0.57 | 0.13 | 0.56 |
| | | | | Tree | 0.55 | 0.55 | 0.55 | 0.56 | 0.55 | 0.11 | 0.56 |
| | | | | Logistic Regression | 0.55 | 0.54 | 0.53 | 0.54 | 0.54 | 0.07 | 0.52 |
| | | | | Neural Network | 0.54 | 0.53 | 0.53 | 0.53 | 0.53 | 0.05 | 0.52 |
| | | | | SVM | 0.54 | 0.53 | 0.53 | 0.53 | 0.53 | 0.05 | 0.53 |
| | | | | kNN | 0.54 | 0.55 | 0.54 | 0.54 | 0.55 | 0.08 | 0.53 |
| Change in VA post loading (month 4 - month 12), when | V0_OCTANE | full | averaged over classes | Neural Network | 0.51 | 0.44 | 0.37 | 0.44 | 0.44 | -0.08 | 0.50 |
| | | | | SVM | 0.51 | 0.46 | 0.29 | 0.21 | 0.46 | 0.00 | 0.54 |
| | | | | AdaBoost | 0.51 | 0.50 | 0.51 | 0.51 | 0.50 | 0.01 | 0.51 |
| | | | | Random Forest | 0.51 | 0.47 | 0.37 | 0.51 | 0.47 | 0.00 | 0.53 |
| | | | | Gradient Boosting | 0.50 | 0.51 | 0.51 | 0.51 | 0.51 | 0.01 | 0.50 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Logistic Regression | 0.50 | 0.44 | 0.43 | 0.45 | 0.44 | -0.09 | 0.47 |
| | | | | Naïve Bayes | 0.47 | 0.48 | 0.48 | 0.48 | 0.48 | -0.05 | 0.47 |
| | | | | Tree | 0.47 | 0.50 | 0.50 | 0.50 | 0.50 | -0.01 | 0.49 |
| | | | | kNN (error) | | | | | | | |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints | V0_OCTANE | outliers removed | averaged over classes | Random Forest | 0.54 | 0.57 | 0.56 | 0.57 | 0.57 | 0.12 | 0.54 |
| | | | | Gradient Boosting | 0.52 | 0.54 | 0.52 | 0.52 | 0.54 | 0.03 | 0.49 |
| | | | | AdaBoost | 0.50 | 0.56 | 0.55 | 0.55 | 0.56 | 0.08 | 0.52 |
| | | | | kNN | 0.49 | 0.47 | 0.47 | 0.49 | 0.47 | -0.03 | 0.49 |
| | | | | Neural Network | 0.48 | 0.56 | 0.55 | 0.55 | 0.56 | 0.09 | 0.53 |
| | | | | Naïve Bayes | 0.47 | 0.44 | 0.30 | 0.44 | 0.44 | -0.04 | 0.54 |
| | | | | Tree | 0.47 | 0.51 | 0.48 | 0.48 | 0.51 | -0.04 | 0.46 |
| | | | | SVM | 0.45 | 0.51 | 0.49 | 0.49 | 0.51 | -0.03 | 0.47 |
| | | | | Logistic Regression | 0.40 | 0.52 | 0.43 | 0.45 | 0.52 | -0.08 | 0.43 |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints (categories: VA gained, lost) | VP_OCTANE | full | averaged over classes | Naïve Bayes | 0.49 | 0.47 | 0.40 | 0.50 | 0.47 | -0.01 | 0.52 |
| | | | | Neural Network | 0.50 | 0.50 | 0.50 | 0.50 | 0.50 | 0.00 | 0.50 |
| | | | | Tree | 0.50 | 0.47 | 0.37 | 0.51 | 0.47 | 0.00 | 0.53 |
| | | | | Random Forest | 0.50 | 0.50 | 0.50 | 0.50 | 0.50 | 0.00 | 0.50 |
| | | | | AdaBoost | 0.52 | 0.53 | 0.53 | 0.53 | 0.53 | 0.05 | 0.52 |
| | | | | SVM (error) | | | | | | | |
| | | | | Gradient Boosting (error) | | | | | | | |
| | | | | kNN (error) | | | | | | | |
| | | | | Logistic Regression (error) | | | | | | | |
| Change in VA post loading | VP_OCTANE | outliers removed | averaged over classes | SVM | 0.56 | 0.54 | 0.52 | 0.54 | 0.54 | 0.06 | 0.51 |
| | | | | Naïve Bayes | 0.52 | 0.46 | 0.32 | 0.46 | 0.46 | -0.03 | 0.53 |
| | | | | Tree | 0.50 | 0.54 | 0.48 | 0.53 | 0.54 | 0.04 | 0.49 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Gradient Boosting | 0.50 | 0.56 | 0.55 | 0.55 | 0.56 | 0.10 | 0.53 |
| | | | | Logistic Regression | 0.48 | 0.53 | 0.48 | 0.51 | 0.53 | 0.01 | 0.48 |
| | | | | Random Forest | 0.47 | 0.54 | 0.53 | 0.54 | 0.54 | 0.07 | 0.52 |
| | | | | AdaBoost | 0.46 | 0.51 | 0.50 | 0.50 | 0.51 | 0.00 | 0.49 |
| | | | | Neural Network | 0.45 | 0.52 | 0.51 | 0.52 | 0.52 | 0.02 | 0.50 |
| | | | | kNN | 0.40 | 0.43 | 0.43 | 0.43 | 0.43 | -0.14 | 0.43 |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints | VA | full | averaged over classes | SVM | 0.55 | 0.56 | 0.52 | 0.56 | 0.56 | 0.09 | 0.52 |
| | | | | Logistic Regression | 0.53 | 0.56 | 0.52 | 0.56 | 0.56 | 0.10 | 0.52 |
| | | | | Neural Network | 0.53 | 0.53 | 0.51 | 0.52 | 0.53 | 0.03 | 0.50 |
| | | | | kNN | 0.51 | 0.53 | 0.52 | 0.52 | 0.53 | 0.04 | 0.51 |
| | | | | Naïve Bayes | 0.49 | 0.50 | 0.49 | 0.49 | 0.50 | -0.03 | 0.48 |
| | | | | Tree | 0.49 | 0.48 | 0.48 | 0.49 | 0.48 | -0.03 | 0.48 |
| | | | | Random Forest | 0.48 | 0.50 | 0.49 | 0.49 | 0.50 | -0.02 | 0.48 |
| | | | | AdaBoost | 0.48 | 0.48 | 0.48 | 0.48 | 0.48 | -0.05 | 0.47 |
| | | | | Gradient Boosting | 0.47 | 0.47 | 0.47 | 0.47 | 0.47 | -0.07 | 0.46 |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints | VA | outliers removed | averaged over classes | Logistic Regression | 0.64 | 0.57 | 0.57 | 0.57 | 0.57 | 0.13 | 0.55 |
| | | | | Neural Network | 0.61 | 0.59 | 0.59 | 0.59 | 0.59 | 0.17 | 0.58 |
| | | | | Naïve Bayes | 0.61 | 0.60 | 0.60 | 0.60 | 0.60 | 0.20 | 0.60 |
| | | | | kNN | 0.61 | 0.59 | 0.59 | 0.59 | 0.59 | 0.18 | 0.58 |
| | | | | SVM | 0.59 | 0.58 | 0.57 | 0.58 | 0.58 | 0.15 | 0.56 |
| | | | | Random Forest | 0.56 | 0.55 | 0.55 | 0.55 | 0.55 | 0.09 | 0.54 |
| | | | | Gradient Boosting | 0.56 | 0.55 | 0.55 | 0.55 | 0.55 | 0.09 | 0.54 |
| | | | | Tree | 0.50 | 0.49 | 0.49 | 0.49 | 0.49 | -0.03 | 0.49 |
| | | | | AdaBoost | 0.50 | 0.51 | 0.51 | 0.51 | 0.51 | 0.01 | 0.50 |
| Change in VA post loading (month 4 - | VA_st dev | full | averaged over classes | Random Forest | 0.52 | 0.41 | 0.39 | 0.38 | 0.41 | 0.03 | 0.63 |
| | | | | SVM | 0.51 | 0.49 | 0.39 | 0.54 | 0.49 | 0.14 | 0.59 |
| | | | | kNN | 0.49 | 0.34 | 0.34 | 0.35 | 0.34 | -0.03 | 0.62 |
| | | | | Tree | 0.48 | 0.33 | 0.33 | 0.34 | 0.33 | -0.03 | 0.64 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Gradient Boosting | 0.48 | 0.36 | 0.35 | 0.34 | 0.36 | -0.04 | 0.60 |
| | | | | AdaBoost | 0.48 | 0.34 | 0.34 | 0.34 | 0.34 | -0.04 | 0.62 |
| | | | | Logistic Regression | 0.47 | 0.45 | 0.33 | 0.38 | 0.45 | 0.01 | 0.56 |
| | | | | Naïve Bayes | 0.47 | 0.35 | 0.31 | 0.32 | 0.35 | -0.11 | 0.54 |
| | | | | Neural Network | 0.46 | 0.41 | 0.36 | 0.38 | 0.41 | -0.02 | 0.57 |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints | VA_st dev | outliers removed | averaged over classes | Neural Network | 0.76 | 0.60 | 0.59 | 0.59 | 0.60 | 0.35 | 0.74 |
| | | | | Logistic Regression | 0.76 | 0.59 | 0.56 | 0.58 | 0.59 | 0.34 | 0.72 |
| | | | | SVM | 0.73 | 0.56 | 0.52 | 0.56 | 0.56 | 0.28 | 0.68 |
| | | | | Naïve Bayes | 0.72 | 0.52 | 0.52 | 0.54 | 0.52 | 0.27 | 0.75 |
| | | | | Gradient Boosting | 0.72 | 0.57 | 0.56 | 0.56 | 0.57 | 0.31 | 0.76 |
| | | | | Random Forest | 0.70 | 0.55 | 0.55 | 0.54 | 0.55 | 0.28 | 0.73 |
| | | | | Tree | 0.63 | 0.48 | 0.49 | 0.49 | 0.48 | 0.20 | 0.72 |
| | | | | kNN | 0.61 | 0.41 | 0.41 | 0.42 | 0.41 | 0.09 | 0.67 |
| | | | | AdaBoost | 0.57 | 0.46 | 0.46 | 0.46 | 0.46 | 0.15 | 0.69 |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints | V0_OCT | full | averaged over classes | Random Forest | 0.56 | 0.44 | 0.42 | 0.41 | 0.44 | 0.08 | 0.64 |
| | | | | Neural Network | 0.53 | 0.40 | 0.37 | 0.37 | 0.40 | 0.00 | 0.59 |
| | | | | SVM | 0.52 | 0.43 | 0.33 | 0.30 | 0.43 | -0.01 | 0.56 |
| | | | | Gradient Boosting | 0.52 | 0.39 | 0.37 | 0.36 | 0.39 | 0.00 | 0.61 |
| | | | | AdaBoost | 0.51 | 0.38 | 0.38 | 0.38 | 0.38 | 0.02 | 0.65 |
| | | | | kNN | 0.51 | 0.38 | 0.38 | 0.39 | 0.38 | 0.04 | 0.66 |
| | | | | Logistic Regression | 0.51 | 0.40 | 0.33 | 0.37 | 0.40 | -0.06 | 0.55 |
| | | | | Tree | 0.50 | 0.37 | 0.37 | 0.37 | 0.37 | 0.02 | 0.65 |
| | | | | Naïve Bayes | 0.48 | 0.35 | 0.34 | 0.34 | 0.35 | -0.04 | 0.62 |
| Change in VA post loading (month 4 - | V0_OCT | outliers removed | averaged over classes | Gradient Boosting | 0.58 | 0.45 | 0.43 | 0.42 | 0.45 | 0.11 | 0.67 |
| | | | | Neural Network | 0.54 | 0.41 | 0.41 | 0.41 | 0.41 | 0.08 | 0.67 |
| | | | | Naïve Bayes | 0.54 | 0.39 | 0.38 | 0.42 | 0.39 | 0.09 | 0.70 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Random Forest | 0.53 | 0.43 | 0.41 | 0.41 | 0.43 | 0.08 | 0.66 |
| | | | | AdaBoost | 0.52 | 0.39 | 0.38 | 0.38 | 0.39 | 0.04 | 0.65 |
| | | | | Tree | 0.52 | 0.38 | 0.38 | 0.39 | 0.38 | 0.05 | 0.68 |
| | | | | Logistic Regression | 0.51 | 0.38 | 0.36 | 0.35 | 0.38 | 0.00 | 0.62 |
| | | | | kNN | 0.50 | 0.40 | 0.39 | 0.39 | 0.40 | 0.06 | 0.66 |
| | | | | SVM | 0.46 | 0.46 | 0.40 | 0.46 | 0.46 | 0.10 | 0.63 |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints | VP_OCT | full | averaged over classes | Neural Network | 0.54 | 0.46 | 0.43 | 0.43 | 0.46 | 0.10 | 0.64 |
| | | | | SVM | 0.52 | 0.44 | 0.35 | 0.33 | 0.44 | 0.01 | 0.56 |
| | | | | Random Forest | 0.52 | 0.40 | 0.38 | 0.37 | 0.40 | 0.01 | 0.61 |
| | | | | Gradient Boosting | 0.52 | 0.39 | 0.37 | 0.37 | 0.39 | 0.00 | 0.60 |
| | | | | Naïve Bayes | 0.52 | 0.43 | 0.42 | 0.42 | 0.43 | 0.08 | 0.64 |
| | | | | Tree | 0.51 | 0.36 | 0.37 | 0.37 | 0.36 | 0.01 | 0.65 |
| | | | | Logistic Regression | 0.51 | 0.46 | 0.40 | 0.43 | 0.46 | 0.07 | 0.59 |
| | | | | kNN | 0.50 | 0.37 | 0.37 | 0.37 | 0.37 | 0.02 | 0.64 |
| | | | | AdaBoost | 0.49 | 0.36 | 0.36 | 0.36 | 0.36 | -0.01 | 0.63 |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints | VP_OCT | outliers removed | averaged over classes | kNN | 0.54 | 0.40 | 0.40 | 0.40 | 0.40 | 0.06 | 0.66 |
| | | | | AdaBoost | 0.51 | 0.38 | 0.38 | 0.38 | 0.38 | 0.02 | 0.64 |
| | | | | Naïve Bayes | 0.50 | 0.38 | 0.39 | 0.40 | 0.38 | 0.05 | 0.68 |
| | | | | Neural Network | 0.50 | 0.41 | 0.39 | 0.38 | 0.41 | 0.04 | 0.63 |
| | | | | Tree | 0.50 | 0.35 | 0.35 | 0.35 | 0.35 | -0.01 | 0.63 |
| | | | | Logistic Regression | 0.50 | 0.44 | 0.41 | 0.42 | 0.44 | 0.05 | 0.60 |
| | | | | Gradient Boosting | 0.49 | 0.35 | 0.34 | 0.33 | 0.35 | -0.05 | 0.59 |
| | | | | Random Forest | 0.49 | 0.36 | 0.34 | 0.32 | 0.36 | -0.06 | 0.59 |
| | | | | SVM | 0.42 | 0.46 | 0.36 | 0.36 | 0.46 | 0.04 | 0.57 |
| Change in VA post loading (month 4 - month 12), when | V0_OCTANE | full | averaged over classes | Neural Network | 0.52 | 0.43 | 0.40 | 0.41 | 0.43 | 0.05 | 0.61 |
| | | | | Random Forest | 0.48 | 0.46 | 0.30 | 0.27 | 0.46 | 0.01 | 0.55 |
| | | | | Naïve Bayes | 0.48 | 0.30 | 0.30 | 0.36 | 0.30 | 0.01 | 0.70 |
| | | | | AdaBoost | 0.46 | 0.32 | 0.32 | 0.31 | 0.32 | -0.08 | 0.60 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Tree | 0.44 | 0.26 | 0.22 | 0.21 | 0.26 | -0.13 | 0.63 |
| | | | | SVM (error) | | | | | | | |
| | | | | Gradient Boosting (error) | | | | | | | |
| | | | | kNN (error) | | | | | | | |
| | | | | Logistic Regression (error) | | | | | | | |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints | V0_OCTANE | outliers removed | averaged over classes | Random Forest | 0.53 | 0.44 | 0.40 | 0.41 | 0.44 | 0.07 | 0.62 |
| | | | | kNN | 0.53 | 0.39 | 0.37 | 0.37 | 0.39 | 0.00 | 0.61 |
| | | | | AdaBoost | 0.52 | 0.46 | 0.42 | 0.42 | 0.46 | 0.09 | 0.62 |
| | | | | Gradient Boosting | 0.52 | 0.44 | 0.39 | 0.40 | 0.44 | 0.05 | 0.60 |
| | | | | Naïve Bayes | 0.50 | 0.20 | 0.09 | 0.32 | 0.20 | -0.02 | 0.79 |
| | | | | Tree | 0.49 | 0.45 | 0.37 | 0.40 | 0.45 | 0.03 | 0.58 |
| | | | | Neural Network | 0.49 | 0.41 | 0.37 | 0.37 | 0.41 | 0.02 | 0.60 |
| | | | | SVM | 0.49 | 0.47 | 0.35 | 0.48 | 0.47 | 0.07 | 0.56 |
| | | | | Logistic Regression | 0.47 | 0.43 | 0.34 | 0.34 | 0.43 | -0.01 | 0.57 |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints (categories: VA gained, maintained, lost) | VP_OCTANE | full | averaged over classes | Random Forest | 0.50 | 0.39 | 0.34 | 0.32 | 0.39 | 0.01 | 0.62 |
| | | | | AdaBoost | 0.50 | 0.39 | 0.35 | 0.32 | 0.39 | 0.00 | 0.61 |
| | | | | Naïve Bayes | 0.50 | 0.37 | 0.30 | 0.34 | 0.37 | 0.03 | 0.65 |
| | | | | Tree | 0.50 | 0.34 | 0.23 | 0.32 | 0.34 | 0.00 | 0.66 |
| | | | | Neural Network | 0.49 | 0.39 | 0.35 | 0.31 | 0.39 | -0.01 | 0.59 |
| | | | | SVM (error) | | | | | | | |
| | | | | Gradient Boosting (error) | | | | | | | |
| | | | | kNN (error) | | | | | | | |
| | | | | Logistic Regression (error) | | | | | | | |

| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints | VP_OCTANE | outliers removed | averaged over classes | Random Forest | 0.52 | 0.41 | 0.36 | 0.35 | 0.41 | 0.01 | 0.60 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | SVM | 0.50 | 0.43 | 0.31 | 0.35 | 0.43 | 0.00 | 0.57 |
| | | | | Logistic Regression | 0.50 | 0.43 | 0.34 | 0.34 | 0.43 | 0.01 | 0.58 |
| | | | | Naïve Bayes | 0.49 | 0.22 | 0.09 | 0.44 | 0.22 | 0.01 | 0.78 |
| | | | | AdaBoost | 0.49 | 0.41 | 0.37 | 0.38 | 0.41 | 0.03 | 0.62 |
| | | | | Neural Network | 0.49 | 0.38 | 0.34 | 0.34 | 0.38 | -0.03 | 0.59 |
| | | | | Gradient Boosting | 0.48 | 0.40 | 0.36 | 0.36 | 0.40 | 0.00 | 0.60 |
| | | | | kNN | 0.46 | 0.31 | 0.29 | 0.28 | 0.31 | -0.10 | 0.60 |
| | | | | Tree | 0.46 | 0.39 | 0.35 | 0.34 | 0.39 | -0.01 | 0.61 |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints | Demographic & qualitative | full | averaged over classes | Tree | 0.51 | 0.36 | 0.36 | 0.37 | 0.36 | 0.01 | 0.65 |
| | | | | SVM | 0.50 | 0.44 | 0.30 | 0.28 | 0.44 | -0.04 | 0.54 |
| | | | | Random Forest | 0.49 | 0.37 | 0.37 | 0.36 | 0.37 | 0.00 | 0.63 |
| | | | | Gradient Boosting | 0.49 | 0.38 | 0.36 | 0.35 | 0.38 | -0.02 | 0.61 |
| | | | | Logistic Regression | 0.48 | 0.45 | 0.32 | 0.54 | 0.45 | 0.00 | 0.55 |
| | | | | Naïve Bayes | 0.48 | 0.33 | 0.33 | 0.33 | 0.33 | -0.05 | 0.62 |
| | | | | kNN | 0.48 | 0.33 | 0.33 | 0.34 | 0.33 | -0.04 | 0.62 |
| | | | | AdaBoost | 0.48 | 0.35 | 0.33 | 0.33 | 0.35 | -0.05 | 0.61 |
| | | | | Neural Network | 0.47 | 0.40 | 0.32 | 0.32 | 0.40 | -0.06 | 0.56 |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints | Demographic & qualitative | outliers removed | averaged over classes | Gradient Boosting | 0.53 | 0.37 | 0.36 | 0.35 | 0.37 | -0.01 | 0.61 |
| | | | | kNN | 0.53 | 0.37 | 0.37 | 0.37 | 0.37 | 0.02 | 0.65 |
| | | | | Random Forest | 0.53 | 0.40 | 0.39 | 0.38 | 0.40 | 0.03 | 0.63 |
| | | | | AdaBoost | 0.51 | 0.40 | 0.39 | 0.39 | 0.40 | 0.05 | 0.65 |
| | | | | Logistic Regression | 0.51 | 0.41 | 0.36 | 0.39 | 0.41 | 0.00 | 0.58 |
| | | | | Tree | 0.50 | 0.34 | 0.34 | 0.35 | 0.34 | -0.01 | 0.65 |
| | | | | Neural Network | 0.49 | 0.37 | 0.35 | 0.35 | 0.37 | -0.03 | 0.60 |
| | | | | Naïve Bayes | 0.48 | 0.37 | 0.33 | 0.35 | 0.37 | -0.06 | 0.57 |
| | | | | SVM | 0.47 | 0.42 | 0.34 | 0.33 | 0.42 | 0.00 | 0.57 |
| C h | V A | f u | a v | Tree | 0.53 | 0.38 | 0.38 | 0.39 | 0.38 | 0.05 | 0.67 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | SVM | 0.53 | 0.45 | 0.34 | 0.44 | 0.45 | 0.01 | 0.55 |
| | | | | Random Forest | 0.53 | 0.42 | 0.40 | 0.40 | 0.42 | 0.05 | 0.62 |
| | | | | kNN | 0.51 | 0.37 | 0.37 | 0.37 | 0.37 | 0.01 | 0.64 |
| | | | | Gradient Boosting | 0.49 | 0.39 | 0.37 | 0.36 | 0.39 | 0.00 | 0.61 |
| | | | | AdaBoost | 0.49 | 0.35 | 0.35 | 0.35 | 0.35 | -0.02 | 0.62 |
| | | | | Neural Network | 0.46 | 0.42 | 0.34 | 0.37 | 0.42 | -0.03 | 0.56 |
| | | | | Naïve Bayes | 0.45 | 0.39 | 0.33 | 0.31 | 0.39 | -0.07 | 0.56 |
| | | | | Logistic Regression | 0.45 | 0.45 | 0.32 | 0.37 | 0.45 | 0.00 | 0.55 |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints | VA | outliers removed | averaged over classes | Logistic Regression | 0.62 | 0.44 | 0.39 | 0.41 | 0.44 | 0.05 | 0.60 |
| | | | | Neural Network | 0.60 | 0.41 | 0.37 | 0.38 | 0.41 | 0.00 | 0.59 |
| | | | | Gradient Boosting | 0.57 | 0.45 | 0.45 | 0.44 | 0.45 | 0.12 | 0.67 |
| | | | | Naïve Bayes | 0.57 | 0.40 | 0.38 | 0.40 | 0.40 | 0.09 | 0.67 |
| | | | | Tree | 0.56 | 0.39 | 0.40 | 0.40 | 0.39 | 0.06 | 0.66 |
| | | | | SVM | 0.55 | 0.43 | 0.36 | 0.39 | 0.43 | 0.01 | 0.57 |
| | | | | Random Forest | 0.55 | 0.40 | 0.40 | 0.39 | 0.40 | 0.04 | 0.63 |
| | | | | AdaBoost | 0.53 | 0.40 | 0.40 | 0.40 | 0.40 | 0.06 | 0.66 |
| | | | | kNN | 0.53 | 0.34 | 0.34 | 0.35 | 0.34 | -0.02 | 0.62 |
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints (categories: | V0_OCT | full | averaged over classes | Naïve Bayes | 0.54 | 0.40 | 0.40 | 0.40 | 0.40 | 0.09 | 0.69 |
| | | | | Random Forest | 0.53 | 0.39 | 0.38 | 0.38 | 0.39 | 0.06 | 0.68 |
| | | | | Tree | 0.52 | 0.38 | 0.38 | 0.38 | 0.38 | 0.06 | 0.68 |
| | | | | AdaBoost | 0.50 | 0.35 | 0.35 | 0.35 | 0.35 | 0.01 | 0.66 |
| | | | | SVM | 0.50 | 0.38 | 0.34 | 0.33 | 0.38 | 0.01 | 0.63 |
| | | | | kNN | 0.49 | 0.31 | 0.31 | 0.32 | 0.31 | -0.03 | 0.66 |
| | | | | Neural Network | 0.49 | 0.36 | 0.36 | 0.36 | 0.36 | 0.02 | 0.65 |
| | | | | Logistic Regression | 0.49 | 0.41 | 0.37 | 0.39 | 0.41 | 0.07 | 0.65 |
| | | | | Gradient Boosting | 0.48 | 0.34 | 0.33 | 0.33 | 0.34 | -0.01 | 0.65 |
| Change | V0_OCT | outliers | averaged | Logistic Regression | 0.55 | 0.37 | 0.36 | 0.36 | 0.37 | 0.03 | 0.66 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Neural Network | 0.55 | 0.37 | 0.37 | 0.37 | 0.37 | 0.04 | 0.67 |
| | | | | Gradient Boosting | 0.55 | 0.38 | 0.37 | 0.38 | 0.38 | 0.04 | 0.66 |
| | | | | Random Forest | 0.55 | 0.35 | 0.35 | 0.35 | 0.35 | 0.01 | 0.65 |
| | | | | Naïve Bayes | 0.52 | 0.33 | 0.31 | 0.32 | 0.33 | 0.01 | 0.68 |
| | | | | Tree | 0.52 | 0.37 | 0.37 | 0.37 | 0.37 | 0.04 | 0.67 |
| | | | | AdaBoost | 0.51 | 0.35 | 0.35 | 0.36 | 0.35 | 0.02 | 0.67 |
| | | | | kNN | 0.48 | 0.32 | 0.33 | 0.33 | 0.32 | -0.02 | 0.66 |
| | | | | SVM | 0.46 | 0.40 | 0.35 | 0.38 | 0.40 | 0.04 | 0.64 |
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints (categories: | VP_OCT | full | averaged over classes | SVM | 0.53 | 0.41 | 0.33 | 0.45 | 0.41 | 0.06 | 0.63 |
| | | | | Neural Network | 0.53 | 0.40 | 0.40 | 0.41 | 0.40 | 0.08 | 0.66 |
| | | | | Logistic Regression | 0.52 | 0.39 | 0.34 | 0.37 | 0.39 | 0.02 | 0.63 |
| | | | | kNN | 0.50 | 0.33 | 0.33 | 0.34 | 0.33 | -0.01 | 0.66 |
| | | | | Naïve Bayes | 0.50 | 0.38 | 0.37 | 0.37 | 0.38 | 0.05 | 0.67 |
| | | | | Tree | 0.49 | 0.31 | 0.31 | 0.32 | 0.31 | -0.03 | 0.65 |
| | | | | Random Forest | 0.49 | 0.33 | 0.32 | 0.32 | 0.33 | -0.03 | 0.64 |
| | | | | Gradient Boosting | 0.48 | 0.36 | 0.35 | 0.35 | 0.36 | 0.01 | 0.65 |
| | | | | AdaBoost | 0.46 | 0.29 | 0.29 | 0.29 | 0.29 | -0.09 | 0.63 |
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints (categories: | VP_OCT | outliers removed | averaged over classes | Neural Network | 0.55 | 0.36 | 0.35 | 0.35 | 0.36 | 0.01 | 0.65 |
| | | | | Logistic Regression | 0.54 | 0.39 | 0.38 | 0.38 | 0.39 | 0.06 | 0.66 |
| | | | | AdaBoost | 0.50 | 0.34 | 0.34 | 0.34 | 0.34 | -0.01 | 0.65 |
| | | | | kNN | 0.49 | 0.35 | 0.34 | 0.35 | 0.35 | 0.01 | 0.66 |
| | | | | SVM | 0.49 | 0.39 | 0.31 | 0.30 | 0.39 | 0.01 | 0.62 |
| | | | | Gradient Boosting | 0.49 | 0.33 | 0.32 | 0.32 | 0.33 | -0.04 | 0.63 |
| | | | | Tree | 0.48 | 0.32 | 0.33 | 0.33 | 0.32 | -0.02 | 0.65 |
| | | | | Naïve Bayes | 0.47 | 0.31 | 0.31 | 0.31 | 0.31 | -0.04 | 0.65 |
| | | | | Random Forest | 0.45 | 0.31 | 0.31 | 0.30 | 0.31 | -0.06 | 0.63 |
| Change in visual | V0_OCTANE | full | averaged over | Naïve Bayes | 0.53 | 0.35 | 0.28 | 0.27 | 0.35 | 0.01 | 0.66 |
| | | | | AdaBoost | 0.52 | 0.42 | 0.32 | 0.32 | 0.42 | 0.07 | 0.63 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Tree | 0.52 | 0.40 | 0.26 | 0.27 | 0.40 | 0.02 | 0.60 |
| | | | | Random Forest | 0.51 | 0.40 | 0.23 | 0.16 | 0.40 | 0.00 | 0.60 |
| | | | | Neural Network | 0.47 | 0.40 | 0.25 | 0.26 | 0.40 | -0.01 | 0.60 |
| | | | | SVM (error) | | | | | | | |
| | | | | Gradient Boosting (error) | | | | | | | |
| | | | | kNN (error) | | | | | | | |
| | | | | Logistic Regression (error) | | | | | | | |
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints (categories: | V0_OCTANE | outliers removed | averaged over classes | kNN | 0.55 | 0.38 | 0.37 | 0.40 | 0.38 | 0.08 | 0.69 |
| | | | | Naïve Bayes | 0.53 | 0.33 | 0.20 | 0.24 | 0.33 | -0.01 | 0.67 |
| | | | | Random Forest | 0.52 | 0.39 | 0.37 | 0.38 | 0.39 | 0.06 | 0.66 |
| | | | | Gradient Boosting | 0.51 | 0.38 | 0.35 | 0.36 | 0.38 | 0.04 | 0.65 |
| | | | | SVM | 0.50 | 0.35 | 0.28 | 0.38 | 0.35 | -0.05 | 0.61 |
| | | | | Tree | 0.50 | 0.38 | 0.29 | 0.31 | 0.38 | 0.01 | 0.63 |
| | | | | Neural Network | 0.46 | 0.32 | 0.30 | 0.31 | 0.32 | -0.06 | 0.63 |
| | | | | Logistic Regression | 0.45 | 0.32 | 0.27 | 0.28 | 0.32 | -0.09 | 0.61 |
| | | | | AdaBoost | 0.45 | 0.34 | 0.30 | 0.30 | 0.34 | -0.05 | 0.62 |
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA | VP_OCTANE | full | averaged over classes | AdaBoost | 0.51 | 0.35 | 0.28 | 0.25 | 0.35 | 0.04 | 0.68 |
| | | | | Random Forest | 0.50 | 0.34 | 0.28 | 0.24 | 0.34 | 0.01 | 0.67 |
| | | | | Tree | 0.50 | 0.28 | 0.18 | 0.24 | 0.28 | 0.01 | 0.72 |
| | | | | Naïve Bayes | 0.49 | 0.31 | 0.24 | 0.23 | 0.31 | -0.01 | 0.69 |
| | | | | Neural Network | 0.48 | 0.31 | 0.25 | 0.22 | 0.31 | -0.03 | 0.66 |
| | | | | SVM (error) | | | | | | | |
| | | | | Gradient Boosting (error) | | | | | | | |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | kNN (error) | | | | | | | |
| | | | | Logistic Regression (error) | | | | | | | |
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints (categories: VA gained, maintained, lost) | VP_OCTANE | outliers removed | averaged over classes | Neural Network | 0.55 | 0.42 | 0.40 | 0.42 | 0.42 | 0.10 | 0.67 |
| | | | | Naïve Bayes | 0.53 | 0.37 | 0.32 | 0.34 | 0.37 | 0.04 | 0.66 |
| | | | | Tree | 0.52 | 0.39 | 0.37 | 0.38 | 0.39 | 0.05 | 0.65 |
| | | | | Gradient Boosting | 0.50 | 0.39 | 0.36 | 0.36 | 0.39 | 0.04 | 0.65 |
| | | | | Random Forest | 0.50 | 0.38 | 0.35 | 0.36 | 0.38 | 0.03 | 0.64 |
| | | | | Logistic Regression | 0.49 | 0.37 | 0.32 | 0.34 | 0.37 | -0.01 | 0.62 |
| | | | | SVM | 0.48 | 0.40 | 0.34 | 0.37 | 0.40 | 0.04 | 0.63 |
| | | | | AdaBoost | 0.48 | 0.36 | 0.33 | 0.33 | 0.36 | -0.01 | 0.63 |
| | | | | kNN | 0.45 | 0.28 | 0.26 | 0.27 | 0.28 | -0.10 | 0.63 |
| | | | | | | | | | | | |
| | | | | | | | | | | | |
| | | | | | | | | | | | |
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints (categories: | Demographic & qualitative | full | averaged over classes | Logistic Regression | 0.55 | 0.40 | 0.31 | 0.33 | 0.40 | 0.02 | 0.62 |
| | | | | SVM | 0.53 | 0.39 | 0.32 | 0.33 | 0.39 | 0.02 | 0.63 |
| | | | | Neural Network | 0.50 | 0.36 | 0.33 | 0.33 | 0.36 | 0.00 | 0.63 |
| | | | | kNN | 0.50 | 0.33 | 0.32 | 0.34 | 0.33 | 0.00 | 0.67 |
| | | | | AdaBoost | 0.50 | 0.35 | 0.34 | 0.34 | 0.35 | 0.00 | 0.65 |
| | | | | Random Forest | 0.48 | 0.34 | 0.34 | 0.34 | 0.34 | -0.01 | 0.65 |
| | | | | Naïve Bayes | 0.48 | 0.31 | 0.31 | 0.31 | 0.31 | -0.05 | 0.64 |
| | | | | Gradient Boosting | 0.48 | 0.36 | 0.36 | 0.35 | 0.36 | 0.02 | 0.67 |
| | | | | Tree | 0.48 | 0.31 | 0.32 | 0.33 | 0.31 | -0.03 | 0.66 |
| Change in visual acuity over 12 months when | Demographic & qualitative | outliers removed | averaged over classes | kNN | 0.58 | 0.40 | 0.40 | 0.41 | 0.40 | 0.10 | 0.70 |
| | | | | Naïve Bayes | 0.56 | 0.41 | 0.40 | 0.41 | 0.41 | 0.08 | 0.67 |
| | | | | AdaBoost | 0.54 | 0.39 | 0.39 | 0.39 | 0.39 | 0.07 | 0.68 |
| | | | | Random Forest | 0.53 | 0.39 | 0.39 | 0.39 | 0.39 | 0.07 | 0.68 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Gradient Boosting | 0.53 | 0.38 | 0.38 | 0.38 | 0.38 | 0.05 | 0.67 |
| | | | | Logistic Regression | 0.52 | 0.42 | 0.40 | 0.40 | 0.42 | 0.10 | 0.68 |
| | | | | Neural Network | 0.51 | 0.37 | 0.36 | 0.36 | 0.37 | 0.03 | 0.66 |
| | | | | Tree | 0.51 | 0.36 | 0.36 | 0.37 | 0.36 | 0.03 | 0.67 |
| | | | | SVM | 0.50 | 0.36 | 0.35 | 0.35 | 0.36 | 0.01 | 0.65 |
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints (categories: | VA | full | averaged over classes | kNN | 0.52 | 0.37 | 0.37 | 0.37 | 0.37 | 0.05 | 0.68 |
| | | | | Naïve Bayes | 0.51 | 0.40 | 0.37 | 0.38 | 0.40 | 0.06 | 0.65 |
| | | | | Tree | 0.51 | 0.36 | 0.36 | 0.36 | 0.36 | 0.03 | 0.67 |
| | | | | AdaBoost | 0.51 | 0.35 | 0.35 | 0.35 | 0.35 | 0.01 | 0.66 |
| | | | | Gradient Boosting | 0.50 | 0.34 | 0.33 | 0.33 | 0.34 | -0.01 | 0.65 |
| | | | | Random Forest | 0.50 | 0.33 | 0.32 | 0.32 | 0.33 | -0.03 | 0.64 |
| | | | | Neural Network | 0.50 | 0.38 | 0.35 | 0.37 | 0.38 | 0.02 | 0.64 |
| | | | | Logistic Regression | 0.49 | 0.41 | 0.32 | 0.35 | 0.41 | 0.05 | 0.62 |
| | | | | SVM | 0.48 | 0.38 | 0.30 | 0.30 | 0.38 | -0.01 | 0.62 |
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints (categories: | VA | outliers removed | averaged over classes | Logistic Regression | 0.72 | 0.55 | 0.55 | 0.55 | 0.55 | 0.31 | 0.74 |
| | | | | Neural Network | 0.69 | 0.50 | 0.50 | 0.51 | 0.50 | 0.23 | 0.72 |
| | | | | SVM | 0.67 | 0.44 | 0.42 | 0.43 | 0.44 | 0.13 | 0.67 |
| | | | | Gradient Boosting | 0.64 | 0.46 | 0.46 | 0.46 | 0.46 | 0.17 | 0.71 |
| | | | | Random Forest | 0.63 | 0.44 | 0.43 | 0.43 | 0.44 | 0.13 | 0.69 |
| | | | | kNN | 0.60 | 0.43 | 0.42 | 0.42 | 0.43 | 0.13 | 0.70 |
| | | | | Naïve Bayes | 0.59 | 0.43 | 0.41 | 0.44 | 0.43 | 0.12 | 0.68 |
| | | | | Tree | 0.59 | 0.46 | 0.46 | 0.46 | 0.46 | 0.18 | 0.71 |
| | | | | AdaBoost | 0.54 | 0.40 | 0.40 | 0.40 | 0.40 | 0.08 | 0.68 |
| Change in visual acuity over 12 months when | VA_st dev | full | averaged over classes | Tree | 0.51 | 0.35 | 0.35 | 0.36 | 0.35 | 0.02 | 0.67 |
| | | | | Tree | 0.51 | 0.35 | 0.35 | 0.36 | 0.35 | 0.02 | 0.67 |
| | | | | Naïve Bayes | 0.50 | 0.35 | 0.34 | 0.34 | 0.35 | -0.01 | 0.63 |
| | | | | kNN | 0.50 | 0.34 | 0.34 | 0.34 | 0.34 | 0.00 | 0.66 |
| | | | | AdaBoost | 0.49 | 0.33 | 0.33 | 0.33 | 0.33 | -0.01 | 0.65 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Neural Network | 0.49 | 0.37 | 0.34 | 0.34 | 0.37 | 0.00 | 0.63 |
| | | | | Gradient Boosting | 0.48 | 0.33 | 0.32 | 0.32 | 0.33 | -0.03 | 0.64 |
| | | | | Logistic Regression | 0.48 | 0.43 | 0.34 | 0.42 | 0.43 | 0.08 | 0.63 |
| | | | | Random Forest | 0.46 | 0.34 | 0.34 | 0.34 | 0.34 | -0.01 | 0.65 |
| | | | | SVM | 0.46 | 0.38 | 0.31 | 0.34 | 0.38 | 0.00 | 0.62 |
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints (categories: | VA_st dev | outliers removed | averaged over classes | Neural Network | 0.80 | 0.63 | 0.63 | 0.63 | 0.63 | 0.43 | 0.79 |
| | | | | Logistic Regression | 0.79 | 0.62 | 0.62 | 0.63 | 0.62 | 0.42 | 0.79 |
| | | | | SVM | 0.78 | 0.57 | 0.56 | 0.59 | 0.57 | 0.34 | 0.74 |
| | | | | Gradient Boosting | 0.72 | 0.53 | 0.53 | 0.53 | 0.53 | 0.29 | 0.75 |
| | | | | Random Forest | 0.70 | 0.54 | 0.54 | 0.54 | 0.54 | 0.29 | 0.75 |
| | | | | Naïve Bayes | 0.69 | 0.50 | 0.50 | 0.50 | 0.50 | 0.24 | 0.73 |
| | | | | kNN | 0.65 | 0.48 | 0.47 | 0.48 | 0.48 | 0.21 | 0.72 |
| | | | | Tree | 0.59 | 0.44 | 0.44 | 0.45 | 0.44 | 0.15 | 0.70 |
| | | | | AdaBoost | 0.56 | 0.43 | 0.43 | 0.43 | 0.43 | 0.13 | 0.70 |
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints (categories: | V0_OCT | full | averaged over classes | Logistic Regression | 0.53 | 0.51 | 0.48 | 0.48 | 0.51 | -0.04 | 0.46 |
| | | | | kNN | 0.52 | 0.53 | 0.53 | 0.53 | 0.53 | 0.04 | 0.51 |
| | | | | Neural Network | 0.51 | 0.50 | 0.50 | 0.50 | 0.50 | -0.01 | 0.49 |
| | | | | SVM | 0.50 | 0.50 | 0.50 | 0.50 | 0.50 | -0.01 | 0.49 |
| | | | | Naïve Bayes | 0.50 | 0.47 | 0.47 | 0.47 | 0.47 | -0.08 | 0.45 |
| | | | | Random Forest | 0.49 | 0.50 | 0.49 | 0.49 | 0.50 | -0.03 | 0.47 |
| | | | | AdaBoost | 0.48 | 0.49 | 0.48 | 0.48 | 0.49 | -0.04 | 0.47 |
| | | | | Gradient Boosting | 0.47 | 0.50 | 0.49 | 0.49 | 0.50 | -0.03 | 0.47 |
| | | | | Tree | 0.43 | 0.44 | 0.44 | 0.44 | 0.44 | -0.13 | 0.43 |
| Change in visual acuity over 12 months when | V0_OCT | outliers removed | averaged over classes | Gradient Boosting | 0.60 | 0.57 | 0.57 | 0.57 | 0.57 | 0.13 | 0.55 |
| | | | | Naïve Bayes | 0.58 | 0.57 | 0.57 | 0.58 | 0.57 | 0.14 | 0.57 |
| | | | | Logistic Regression | 0.57 | 0.55 | 0.55 | 0.55 | 0.55 | 0.09 | 0.54 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | SVM | 0.56 | 0.58 | 0.58 | 0.59 | 0.58 | 0.16 | 0.58 |
| | | | | Random Forest | 0.55 | 0.56 | 0.56 | 0.56 | 0.56 | 0.11 | 0.54 |
| | | | | AdaBoost | 0.52 | 0.53 | 0.53 | 0.53 | 0.53 | 0.05 | 0.52 |
| | | | | Neural Network | 0.51 | 0.52 | 0.52 | 0.51 | 0.52 | 0.02 | 0.50 |
| | | | | Tree | 0.51 | 0.53 | 0.52 | 0.52 | 0.53 | 0.03 | 0.50 |
| | | | | kNN | 0.49 | 0.50 | 0.50 | 0.50 | 0.50 | -0.02 | 0.48 |
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints (categories: | VP_OCT | full | averaged over classes | Logistic Regression | 0.53 | 0.54 | 0.51 | 0.52 | 0.54 | 0.03 | 0.49 |
| | | | | Naïve Bayes | 0.53 | 0.51 | 0.51 | 0.51 | 0.51 | 0.00 | 0.49 |
| | | | | AdaBoost | 0.51 | 0.52 | 0.52 | 0.52 | 0.52 | 0.03 | 0.50 |
| | | | | Neural Network | 0.51 | 0.51 | 0.50 | 0.50 | 0.51 | -0.01 | 0.48 |
| | | | | SVM | 0.50 | 0.53 | 0.53 | 0.53 | 0.53 | 0.06 | 0.53 |
| | | | | Gradient Boosting | 0.49 | 0.52 | 0.51 | 0.51 | 0.52 | 0.01 | 0.49 |
| | | | | Tree | 0.47 | 0.49 | 0.49 | 0.49 | 0.49 | -0.04 | 0.47 |
| | | | | Random Forest | 0.46 | 0.50 | 0.49 | 0.49 | 0.50 | -0.03 | 0.47 |
| | | | | kNN | 0.43 | 0.44 | 0.43 | 0.43 | 0.44 | -0.15 | 0.42 |
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints (categories: | VP_OCT | outliers removed | averaged over classes | Tree | 0.57 | 0.56 | 0.56 | 0.56 | 0.56 | 0.10 | 0.53 |
| | | | | Random Forest | 0.55 | 0.53 | 0.52 | 0.51 | 0.53 | 0.01 | 0.48 |
| | | | | Naïve Bayes | 0.54 | 0.56 | 0.57 | 0.57 | 0.56 | 0.12 | 0.56 |
| | | | | Gradient Boosting | 0.54 | 0.53 | 0.53 | 0.52 | 0.53 | 0.03 | 0.50 |
| | | | | Neural Network | 0.51 | 0.53 | 0.53 | 0.53 | 0.53 | 0.04 | 0.51 |
| | | | | AdaBoost | 0.50 | 0.50 | 0.50 | 0.51 | 0.50 | -0.01 | 0.49 |
| | | | | Logistic Regression | 0.49 | 0.50 | 0.48 | 0.47 | 0.50 | -0.07 | 0.44 |
| | | | | SVM | 0.47 | 0.54 | 0.54 | 0.54 | 0.54 | 0.05 | 0.51 |
| | | | | kNN | 0.46 | 0.53 | 0.51 | 0.51 | 0.53 | 0.01 | 0.48 |
| Change in visual acuity over 12 months when considered | V0_OCTANE | full | averaged over classes | Neural Network | 0.54 | 0.53 | 0.41 | 0.45 | 0.53 | -0.06 | 0.44 |
| | | | | AdaBoost | 0.54 | 0.55 | 0.54 | 0.55 | 0.55 | 0.08 | 0.52 |
| | | | | Naïve Bayes | 0.53 | 0.49 | 0.46 | 0.53 | 0.49 | 0.04 | 0.54 |
| | | | | Random Forest | 0.51 | 0.55 | 0.39 | 0.30 | 0.55 | 0.00 | 0.45 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Tree | 0.51 | 0.52 | 0.52 | 0.52 | 0.52 | 0.03 | 0.51 |
| | | | | SVM (error) | | | | | | | |
| | | | | Gradient Boosting (error) | | | | | | | |
| | | | | kNN (error) | | | | | | | |
| | | | | Logistic Regression (error) | | | | | | | |
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints (categories: | V0_OCTANE | outliers removed | averaged over classes | Random Forest | 0.55 | 0.55 | 0.55 | 0.56 | 0.55 | 0.12 | 0.56 |
| | | | | AdaBoost | 0.54 | 0.56 | 0.56 | 0.56 | 0.56 | 0.12 | 0.56 |
| | | | | Tree | 0.54 | 0.53 | 0.51 | 0.52 | 0.53 | 0.03 | 0.50 |
| | | | | Naïve Bayes | 0.52 | 0.54 | 0.38 | 0.44 | 0.54 | -0.03 | 0.46 |
| | | | | Neural Network | 0.48 | 0.52 | 0.51 | 0.53 | 0.52 | 0.05 | 0.53 |
| | | | | kNN | 0.48 | 0.50 | 0.49 | 0.49 | 0.50 | -0.03 | 0.47 |
| | | | | Logistic Regression | 0.46 | 0.47 | 0.41 | 0.42 | 0.47 | -0.15 | 0.42 |
| | | | | Gradient Boosting | 0.45 | 0.48 | 0.48 | 0.49 | 0.48 | -0.03 | 0.49 |
| | | | | SVM | 0.44 | 0.50 | 0.50 | 0.51 | 0.50 | 0.02 | 0.51 |
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints (categories: VA gained, lost) | VP_OCTANE | full | averaged over classes | Neural Network | 0.52 | 0.45 | 0.28 | 0.20 | 0.45 | 0.00 | 0.55 |
| | | | | Naïve Bayes | 0.50 | 0.45 | 0.28 | 0.20 | 0.45 | 0.00 | 0.55 |
| | | | | Random Forest | 0.50 | 0.45 | 0.28 | 0.20 | 0.45 | 0.00 | 0.55 |
| | | | | Tree | 0.50 | 0.45 | 0.28 | 0.20 | 0.45 | 0.00 | 0.55 |
| | | | | AdaBoost | 0.50 | 0.45 | 0.28 | 0.20 | 0.45 | 0.00 | 0.55 |
| | | | | SVM (error) | | | | | | | |
| | | | | Gradient Boosting (error) | | | | | | | |
| | | | | kNN (error) | | | | | | | |
| | | | | Logistic Regression (error) | | | | | | | |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints (categories: | VP_OCTANE | outliers removed | averaged over classes | Neural Network | 0.56 | 0.56 | 0.56 | 0.57 | 0.56 | 0.13 | 0.57 |
| | | | | Naïve Bayes | 0.55 | 0.57 | 0.50 | 0.58 | 0.57 | 0.11 | 0.50 |
| | | | | AdaBoost | 0.52 | 0.55 | 0.55 | 0.56 | 0.55 | 0.11 | 0.56 |
| | | | | Random Forest | 0.51 | 0.52 | 0.52 | 0.53 | 0.52 | 0.04 | 0.52 |
| | | | | Logistic Regression | 0.50 | 0.54 | 0.49 | 0.52 | 0.54 | 0.02 | 0.48 |
| | | | | kNN | 0.50 | 0.50 | 0.48 | 0.48 | 0.50 | -0.05 | 0.46 |
| | | | | SVM | 0.50 | 0.56 | 0.56 | 0.58 | 0.56 | 0.15 | 0.58 |
| | | | | Gradient Boosting | 0.50 | 0.52 | 0.52 | 0.53 | 0.52 | 0.06 | 0.53 |
| | | | | Tree | 0.49 | 0.51 | 0.44 | 0.45 | 0.51 | -0.08 | 0.44 |
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints (categories: | Demographic & qualitative | full | averaged over classes | SVM | 0.58 | 0.51 | 0.50 | 0.50 | 0.51 | -0.01 | 0.48 |
| | | | | Random Forest | 0.58 | 0.57 | 0.56 | 0.57 | 0.57 | 0.12 | 0.54 |
| | | | | AdaBoost | 0.58 | 0.57 | 0.56 | 0.56 | 0.57 | 0.12 | 0.55 |
| | | | | Logistic Regression | 0.56 | 0.55 | 0.48 | 0.54 | 0.55 | 0.05 | 0.48 |
| | | | | Tree | 0.55 | 0.56 | 0.55 | 0.55 | 0.56 | 0.10 | 0.54 |
| | | | | kNN | 0.54 | 0.55 | 0.54 | 0.54 | 0.55 | 0.07 | 0.53 |
| | | | | Neural Network | 0.53 | 0.52 | 0.49 | 0.50 | 0.52 | -0.01 | 0.47 |
| | | | | Gradient Boosting | 0.52 | 0.54 | 0.53 | 0.53 | 0.54 | 0.06 | 0.51 |
| | | | | Naïve Bayes | 0.52 | 0.51 | 0.51 | 0.51 | 0.51 | 0.00 | 0.49 |
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints (categories: | Demographic & qualitative | outliers removed | averaged over classes | Tree | 0.57 | 0.59 | 0.59 | 0.59 | 0.59 | 0.17 | 0.57 |
| | | | | AdaBoost | 0.56 | 0.56 | 0.56 | 0.56 | 0.56 | 0.12 | 0.55 |
| | | | | Gradient Boosting | 0.56 | 0.55 | 0.55 | 0.55 | 0.55 | 0.09 | 0.54 |
| | | | | Random Forest | 0.55 | 0.55 | 0.55 | 0.55 | 0.55 | 0.09 | 0.54 |
| | | | | Naïve Bayes | 0.54 | 0.54 | 0.53 | 0.53 | 0.54 | 0.06 | 0.52 |
| | | | | kNN | 0.54 | 0.52 | 0.52 | 0.52 | 0.52 | 0.03 | 0.51 |
| | | | | Neural Network | 0.52 | 0.57 | 0.57 | 0.57 | 0.57 | 0.13 | 0.56 |
| | | | | Logistic Regression | 0.52 | 0.55 | 0.52 | 0.54 | 0.55 | 0.06 | 0.51 |
| | | | | SVM | 0.48 | 0.52 | 0.51 | 0.51 | 0.52 | 0.01 | 0.50 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints (categories: | VA | full | averaged over classes | Logistic Regression | 0.58 | 0.55 | 0.48 | 0.53 | 0.55 | 0.04 | 0.48 |
| | | | | SVM | 0.55 | 0.47 | 0.47 | 0.47 | 0.47 | -0.06 | 0.46 |
| | | | | Random Forest | 0.54 | 0.55 | 0.55 | 0.55 | 0.55 | 0.09 | 0.53 |
| | | | | Gradient Boosting | 0.53 | 0.53 | 0.52 | 0.52 | 0.53 | 0.03 | 0.50 |
| | | | | Naïve Bayes | 0.51 | 0.51 | 0.49 | 0.50 | 0.51 | -0.01 | 0.47 |
| | | | | Tree | 0.50 | 0.52 | 0.52 | 0.52 | 0.52 | 0.02 | 0.50 |
| | | | | AdaBoost | 0.48 | 0.49 | 0.49 | 0.48 | 0.49 | -0.04 | 0.47 |
| | | | | Neural Network | 0.48 | 0.50 | 0.49 | 0.49 | 0.50 | -0.03 | 0.47 |
| | | | | kNN | 0.46 | 0.48 | 0.48 | 0.49 | 0.48 | -0.04 | 0.48 |
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints (categories: | VA | outliers removed | averaged over classes | Logistic Regression | 0.80 | 0.73 | 0.73 | 0.73 | 0.73 | 0.44 | 0.72 |
| | | | | Neural Network | 0.79 | 0.72 | 0.72 | 0.72 | 0.72 | 0.43 | 0.71 |
| | | | | SVM | 0.77 | 0.70 | 0.70 | 0.70 | 0.70 | 0.38 | 0.68 |
| | | | | Gradient Boosting | 0.73 | 0.67 | 0.67 | 0.67 | 0.67 | 0.34 | 0.66 |
| | | | | kNN | 0.71 | 0.65 | 0.65 | 0.65 | 0.65 | 0.29 | 0.64 |
| | | | | Random Forest | 0.69 | 0.64 | 0.64 | 0.64 | 0.64 | 0.26 | 0.63 |
| | | | | Tree | 0.67 | 0.66 | 0.66 | 0.66 | 0.66 | 0.31 | 0.64 |
| | | | | Naïve Bayes | 0.66 | 0.65 | 0.64 | 0.64 | 0.65 | 0.28 | 0.62 |
| | | | | AdaBoost | 0.60 | 0.61 | 0.61 | 0.61 | 0.61 | 0.21 | 0.60 |
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints (categories: | VA_st dev | full | averaged over classes | Logistic Regression | 0.53 | 0.54 | 0.48 | 0.52 | 0.54 | 0.02 | 0.47 |
| | | | | Random Forest | 0.53 | 0.53 | 0.52 | 0.52 | 0.53 | 0.04 | 0.51 |
| | | | | SVM | 0.52 | 0.45 | 0.45 | 0.45 | 0.45 | -0.10 | 0.45 |
| | | | | AdaBoost | 0.51 | 0.52 | 0.52 | 0.52 | 0.52 | 0.03 | 0.51 |
| | | | | Naïve Bayes | 0.50 | 0.53 | 0.51 | 0.51 | 0.53 | 0.01 | 0.49 |
| | | | | Neural Network | 0.49 | 0.50 | 0.49 | 0.49 | 0.50 | -0.03 | 0.47 |
| | | | | kNN | 0.48 | 0.49 | 0.49 | 0.49 | 0.49 | -0.04 | 0.47 |
| | | | | Gradient Boosting | 0.46 | 0.48 | 0.47 | 0.47 | 0.48 | -0.08 | 0.45 |
| | | | | Tree | 0.41 | 0.44 | 0.43 | 0.43 | 0.44 | -0.15 | 0.41 |

| Ch | VP_fu | av | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints (categories: | VA_st dev | outliers removed | averaged over classes | Neural Network | 0.84 | 0.75 | 0.75 | 0.75 | 0.75 | 0.50 | 0.74 |
| | | | | Logistic Regression | 0.83 | 0.75 | 0.75 | 0.75 | 0.75 | 0.49 | 0.74 |
| | | | | SVM | 0.80 | 0.70 | 0.70 | 0.70 | 0.70 | 0.38 | 0.69 |
| | | | | Random Forest | 0.74 | 0.67 | 0.66 | 0.66 | 0.67 | 0.32 | 0.65 |
| | | | | Gradient Boosting | 0.74 | 0.67 | 0.67 | 0.66 | 0.67 | 0.32 | 0.65 |
| | | | | kNN | 0.73 | 0.67 | 0.67 | 0.67 | 0.67 | 0.33 | 0.66 |
| | | | | Naïve Bayes | 0.69 | 0.65 | 0.64 | 0.65 | 0.65 | 0.28 | 0.62 |
| | | | | AdaBoost | 0.62 | 0.63 | 0.63 | 0.63 | 0.63 | 0.25 | 0.61 |
| | | | | Tree | 0.60 | 0.60 | 0.60 | 0.60 | 0.60 | 0.18 | 0.58 |
| Change in VA, baseline - month 12 (categories: VA gained, maintained, lost) | V0_OCT | full | averaged over classes | Neural Network | 0.49 | 0.38 | 0.37 | 0.37 | 0.38 | 0.03 | 0.65 |
| | | | | Gradient Boosting | 0.49 | 0.37 | 0.36 | 0.35 | 0.37 | 0.01 | 0.64 |
| | | | | SVM | 0.47 | 0.40 | 0.29 | 0.34 | 0.40 | -0.03 | 0.58 |
| | | | | Naïve Bayes | 0.47 | 0.34 | 0.33 | 0.33 | 0.34 | -0.02 | 0.64 |
| | | | | AdaBoost | 0.47 | 0.31 | 0.31 | 0.31 | 0.31 | -0.06 | 0.63 |
| | | | | kNN | 0.47 | 0.36 | 0.33 | 0.34 | 0.36 | -0.02 | 0.62 |
| | | | | Random Forest | 0.47 | 0.34 | 0.33 | 0.33 | 0.34 | -0.03 | 0.63 |
| | | | | Tree | 0.47 | 0.32 | 0.32 | 0.32 | 0.32 | -0.05 | 0.63 |
| | | | | Logistic Regression | 0.45 | 0.34 | 0.28 | 0.28 | 0.34 | -0.10 | 0.58 |
| Change in VA, baseline - month 12 (categories: VA gained, maintained, lost) | V0_OCT | outliers removed | averaged over classes | Neural Network | 0.58 | 0.39 | 0.39 | 0.39 | 0.39 | 0.06 | 0.67 |
| | | | | SVM | 0.57 | 0.45 | 0.39 | 0.39 | 0.45 | 0.12 | 0.67 |
| | | | | kNN | 0.56 | 0.42 | 0.41 | 0.43 | 0.42 | 0.09 | 0.66 |
| | | | | Random Forest | 0.56 | 0.41 | 0.41 | 0.40 | 0.41 | 0.09 | 0.68 |
| | | | | Gradient Boosting | 0.56 | 0.38 | 0.36 | 0.36 | 0.38 | 0.03 | 0.65 |
| | | | | Naïve Bayes | 0.55 | 0.38 | 0.36 | 0.37 | 0.38 | 0.05 | 0.68 |
| | | | | Logistic Regression | 0.54 | 0.38 | 0.37 | 0.37 | 0.38 | 0.04 | 0.66 |
| | | | | AdaBoost | 0.53 | 0.38 | 0.38 | 0.39 | 0.38 | 0.06 | 0.68 |
| | | | | Tree | 0.52 | 0.39 | 0.38 | 0.38 | 0.39 | 0.06 | 0.67 |
| | | | | AdaBoost | 0.54 | 0.40 | 0.40 | 0.40 | 0.40 | 0.08 | 0.68 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | kNN | 0.52 | 0.41 | 0.36 | 0.37 | 0.41 | 0.05 | 0.64 |
| | | | | Neural Network | 0.52 | 0.36 | 0.35 | 0.34 | 0.36 | 0.00 | 0.64 |
| | | | | SVM | 0.52 | 0.41 | 0.30 | 0.35 | 0.41 | 0.00 | 0.59 |
| | | | | Logistic Regression | 0.50 | 0.41 | 0.33 | 0.37 | 0.41 | 0.02 | 0.60 |
| | | | | Gradient Boosting | 0.50 | 0.36 | 0.35 | 0.35 | 0.36 | 0.01 | 0.64 |
| | | | | Naïve Bayes | 0.49 | 0.36 | 0.35 | 0.34 | 0.36 | 0.00 | 0.64 |
| | | | | Random Forest | 0.49 | 0.36 | 0.36 | 0.35 | 0.36 | 0.01 | 0.65 |
| | | | | Tree | 0.49 | 0.33 | 0.33 | 0.33 | 0.33 | -0.02 | 0.64 |
| Change in VA, baseline - month 12 (categories: VA gained, maintained, lost) | VP_OCT | outliers removed | averaged over classes | Neural Network | 0.53 | 0.42 | 0.41 | 0.41 | 0.42 | 0.08 | 0.66 |
| | | | | Gradient Boosting | 0.51 | 0.40 | 0.39 | 0.38 | 0.40 | 0.05 | 0.65 |
| | | | | Logistic Regression | 0.51 | 0.37 | 0.35 | 0.34 | 0.37 | -0.02 | 0.61 |
| | | | | Random Forest | 0.51 | 0.37 | 0.34 | 0.34 | 0.37 | -0.02 | 0.62 |
| | | | | Tree | 0.49 | 0.36 | 0.36 | 0.35 | 0.36 | 0.01 | 0.65 |
| | | | | AdaBoost | 0.49 | 0.33 | 0.33 | 0.33 | 0.33 | -0.03 | 0.64 |
| | | | | kNN | 0.48 | 0.39 | 0.36 | 0.36 | 0.39 | 0.00 | 0.61 |
| | | | | Naïve Bayes | 0.47 | 0.29 | 0.29 | 0.31 | 0.29 | -0.07 | 0.65 |
| | | | | SVM | 0.44 | 0.43 | 0.30 | 0.39 | 0.43 | -0.02 | 0.56 |
| Change in VA, baseline - month 12 (categories: VA gained, maintained, lost) | V0_OCTANE | full | averaged over classes | AdaBoost | 0.55 | 0.42 | 0.36 | 0.33 | 0.42 | 0.12 | 0.70 |
| | | | | Tree | 0.55 | 0.41 | 0.34 | 0.32 | 0.41 | 0.11 | 0.69 |
| | | | | Gradient Boosting | 0.54 | 0.42 | 0.36 | 0.33 | 0.42 | 0.13 | 0.70 |
| | | | | Naïve Bayes | 0.53 | 0.35 | 0.29 | 0.28 | 0.35 | 0.03 | 0.67 |
| | | | | Random Forest | 0.53 | 0.38 | 0.32 | 0.30 | 0.38 | 0.06 | 0.68 |
| | | | | Neural Network | 0.52 | 0.39 | 0.31 | 0.27 | 0.39 | -0.01 | 0.60 |
| | | | | Logistic Regression | 0.50 | 0.33 | 0.28 | 0.24 | 0.33 | -0.06 | 0.61 |
| | | | | SVM | 0.47 | 0.41 | 0.34 | 0.29 | 0.41 | 0.07 | 0.65 |
| | | | | kNN (error) | | | | | | | |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Change in VA, baseline - month 12 (categories: VA gained, maintained, lost) | V0_OCTANE | outliers removed | averaged over classes | Gradient Boosting | 0.55 | 0.40 | 0.40 | 0.40 | 0.40 | 0.09 | 0.70 |
| | | | | kNN | 0.54 | 0.38 | 0.34 | 0.35 | 0.38 | 0.03 | 0.66 |
| | | | | Tree | 0.52 | 0.37 | 0.33 | 0.35 | 0.37 | -0.03 | 0.61 |
| | | | | AdaBoost | 0.51 | 0.35 | 0.35 | 0.35 | 0.35 | 0.00 | 0.66 |
| | | | | Naïve Bayes | 0.51 | 0.42 | 0.24 | 0.17 | 0.42 | 0.00 | 0.58 |
| | | | | SVM | 0.50 | 0.37 | 0.34 | 0.33 | 0.37 | 0.02 | 0.66 |
| | | | | Logistic Regression | 0.50 | 0.36 | 0.29 | 0.30 | 0.36 | -0.06 | 0.60 |
| | | | | Neural Network | 0.49 | 0.31 | 0.31 | 0.32 | 0.31 | -0.05 | 0.66 |
| | | | | Random Forest | 0.48 | 0.32 | 0.32 | 0.33 | 0.32 | -0.03 | 0.66 |
| Change in VA, baseline - month 12 (categories: VA gained, maintained, lost) | VP_OCTANE | full | averaged over classes | Naïve Bayes | 0.50 | 0.29 | 0.13 | 0.08 | 0.29 | 0.00 | 0.71 |
| | | | | Random Forest | 0.50 | 0.29 | 0.13 | 0.08 | 0.29 | 0.00 | 0.71 |
| | | | | Tree | 0.50 | 0.29 | 0.13 | 0.08 | 0.29 | 0.00 | 0.71 |
| | | | | AdaBoost | 0.50 | 0.29 | 0.13 | 0.08 | 0.29 | 0.00 | 0.71 |
| | | | | Neural Network | 0.50 | 0.29 | 0.13 | 0.08 | 0.29 | 0.00 | 0.71 |
| | | | | SVM (error) | | | | | | | |
| | | | | Gradient Boosting (error) | | | | | | | |
| | | | | kNN (error) | | | | | | | |
| | | | | Logistic Regression (error) | | | | | | | |
| Change in VA, baseline - month 12 (categories: VA gained, maintained, lost) | VP_OCTANE | outliers removed | averaged over classes | Neural Network | 0.55 | 0.42 | 0.40 | 0.41 | 0.42 | 0.12 | 0.71 |
| | | | | Random Forest | 0.55 | 0.39 | 0.37 | 0.36 | 0.39 | 0.06 | 0.68 |
| | | | | Naïve Bayes | 0.54 | 0.40 | 0.30 | 0.27 | 0.40 | 0.00 | 0.60 |
| | | | | kNN | 0.53 | 0.39 | 0.36 | 0.37 | 0.39 | 0.06 | 0.66 |
| | | | | Gradient Boosting | 0.53 | 0.36 | 0.36 | 0.37 | 0.36 | 0.03 | 0.67 |
| | | | | Logistic Regression | 0.52 | 0.37 | 0.30 | 0.32 | 0.37 | -0.04 | 0.60 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | AdaBoost | 0.52 | 0.37 | 0.36 | 0.37 | 0.37 | 0.05 | 0.68 |
| | | | | SVM | 0.50 | 0.41 | 0.34 | 0.30 | 0.41 | 0.07 | 0.66 |
| | | | | Tree | 0.49 | 0.36 | 0.30 | 0.32 | 0.36 | -0.05 | 0.60 |
| Change in VA, baseline - month 12 (categories: VA gained, maintained, lost) | Demographic & qualitative | full | averaged over classes | kNN | 0.52 | 0.41 | 0.37 | 0.39 | 0.41 | 0.05 | 0.63 |
| | | | | Neural Network | 0.52 | 0.39 | 0.31 | 0.32 | 0.39 | -0.02 | 0.60 |
| | | | | Random Forest | 0.51 | 0.34 | 0.34 | 0.34 | 0.34 | -0.02 | 0.63 |
| | | | | Gradient Boosting | 0.51 | 0.35 | 0.33 | 0.33 | 0.35 | -0.03 | 0.62 |
| | | | | Naïve Bayes | 0.51 | 0.34 | 0.34 | 0.34 | 0.34 | 0.00 | 0.66 |
| | | | | AdaBoost | 0.49 | 0.34 | 0.34 | 0.34 | 0.34 | -0.02 | 0.64 |
| | | | | Tree | 0.49 | 0.36 | 0.35 | 0.35 | 0.36 | 0.00 | 0.63 |
| | | | | Logistic Regression | 0.49 | 0.42 | 0.29 | 0.34 | 0.42 | 0.01 | 0.59 |
| | | | | SVM | 0.47 | 0.42 | 0.30 | 0.38 | 0.42 | 0.02 | 0.59 |
| Change in VA, baseline - month 12 (categories: VA gained, maintained, lost) | Demographic & qualitative | outliers removed | averaged over classes | AdaBoost | 0.60 | 0.42 | 0.42 | 0.42 | 0.42 | 0.11 | 0.69 |
| | | | | kNN | 0.59 | 0.45 | 0.43 | 0.43 | 0.45 | 0.12 | 0.67 |
| | | | | Random Forest | 0.59 | 0.45 | 0.44 | 0.44 | 0.45 | 0.15 | 0.69 |
| | | | | Gradient Boosting | 0.59 | 0.45 | 0.44 | 0.44 | 0.45 | 0.14 | 0.69 |
| | | | | Naïve Bayes | 0.58 | 0.46 | 0.44 | 0.44 | 0.46 | 0.14 | 0.68 |
| | | | | Logistic Regression | 0.56 | 0.46 | 0.43 | 0.43 | 0.46 | 0.14 | 0.67 |
| | | | | Tree | 0.54 | 0.43 | 0.42 | 0.42 | 0.43 | 0.10 | 0.67 |
| | | | | SVM | 0.54 | 0.42 | 0.38 | 0.37 | 0.42 | 0.07 | 0.64 |
| | | | | Neural Network | 0.52 | 0.40 | 0.38 | 0.36 | 0.40 | 0.05 | 0.66 |
| Change in VA, baseline - month 12 (categories: VA gained, maintained, lost) | VA | full | averaged over classes | kNN | 0.53 | 0.42 | 0.38 | 0.39 | 0.42 | 0.07 | 0.65 |
| | | | | SVM | 0.53 | 0.38 | 0.28 | 0.26 | 0.38 | -0.05 | 0.59 |
| | | | | Neural Network | 0.50 | 0.35 | 0.30 | 0.28 | 0.35 | -0.06 | 0.60 |
| | | | | AdaBoost | 0.50 | 0.34 | 0.34 | 0.35 | 0.34 | 0.00 | 0.65 |
| | | | | Naïve Bayes | 0.50 | 0.35 | 0.32 | 0.32 | 0.35 | -0.04 | 0.60 |
| | | | | Tree | 0.50 | 0.36 | 0.36 | 0.36 | 0.36 | 0.00 | 0.63 |
| | | | | Logistic Regression | 0.49 | 0.41 | 0.29 | 0.33 | 0.41 | -0.03 | 0.58 |
| | | | | Random Forest | 0.49 | 0.34 | 0.33 | 0.33 | 0.34 | -0.03 | 0.63 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Gradient Boosting | 0.48 | 0.36 | 0.35 | 0.35 | 0.36 | -0.01 | 0.63 |
| Change in VA, baseline - month 12 (categories: VA gained, maintained, lost) | VA | outliers removed | averaged over classes | Logistic Regression | 0.80 | 0.61 | 0.60 | 0.59 | 0.61 | 0.40 | 0.79 |
| | | | | Neural Network | 0.79 | 0.57 | 0.56 | 0.55 | 0.57 | 0.34 | 0.77 |
| | | | | SVM | 0.75 | 0.55 | 0.54 | 0.53 | 0.55 | 0.30 | 0.75 |
| | | | | Gradient Boosting | 0.74 | 0.59 | 0.59 | 0.59 | 0.59 | 0.37 | 0.79 |
| | | | | Random Forest | 0.72 | 0.53 | 0.53 | 0.52 | 0.53 | 0.28 | 0.75 |
| | | | | kNN | 0.68 | 0.54 | 0.51 | 0.51 | 0.54 | 0.27 | 0.73 |
| | | | | Tree | 0.62 | 0.50 | 0.50 | 0.50 | 0.50 | 0.23 | 0.74 |
| | | | | Naïve Bayes | 0.62 | 0.45 | 0.42 | 0.41 | 0.45 | 0.13 | 0.68 |
| | | | | AdaBoost | 0.61 | 0.49 | 0.49 | 0.49 | 0.49 | 0.21 | 0.73 |
| Change in VA, baseline - month 12 (categories: VA gained, maintained, lost) | VA_st dev | full | averaged over classes | kNN | 0.53 | 0.40 | 0.37 | 0.37 | 0.40 | 0.04 | 0.64 |
| | | | | SVM | 0.53 | 0.40 | 0.30 | 0.31 | 0.40 | -0.02 | 0.59 |
| | | | | Gradient Boosting | 0.52 | 0.41 | 0.39 | 0.39 | 0.41 | 0.06 | 0.65 |
| | | | | AdaBoost | 0.50 | 0.35 | 0.35 | 0.35 | 0.35 | 0.01 | 0.65 |
| | | | | Random Forest | 0.50 | 0.36 | 0.35 | 0.35 | 0.36 | 0.00 | 0.65 |
| | | | | Naïve Bayes | 0.49 | 0.36 | 0.33 | 0.33 | 0.36 | -0.03 | 0.61 |
| | | | | Neural Network | 0.49 | 0.35 | 0.32 | 0.31 | 0.35 | -0.04 | 0.62 |
| | | | | Logistic Regression | 0.49 | 0.40 | 0.30 | 0.33 | 0.40 | -0.01 | 0.59 |
| | | | | Tree | 0.47 | 0.33 | 0.32 | 0.32 | 0.33 | -0.04 | 0.63 |
| Change in VA, baseline - month 12 (categories: VA gained, maintained, lost) | VA_st dev | outliers removed | averaged over classes | Neural Network | 0.86 | 0.69 | 0.69 | 0.69 | 0.69 | 0.53 | 0.84 |
| | | | | Logistic Regression | 0.84 | 0.66 | 0.65 | 0.65 | 0.66 | 0.47 | 0.81 |
| | | | | SVM | 0.83 | 0.65 | 0.64 | 0.64 | 0.65 | 0.45 | 0.80 |
| | | | | Random Forest | 0.78 | 0.57 | 0.57 | 0.57 | 0.57 | 0.34 | 0.77 |
| | | | | Gradient Boosting | 0.77 | 0.60 | 0.59 | 0.59 | 0.60 | 0.38 | 0.79 |
| | | | | kNN | 0.73 | 0.56 | 0.54 | 0.55 | 0.56 | 0.32 | 0.74 |
| | | | | Tree | 0.68 | 0.55 | 0.55 | 0.55 | 0.55 | 0.30 | 0.76 |
| | | | | Naïve Bayes | 0.68 | 0.49 | 0.48 | 0.48 | 0.49 | 0.20 | 0.71 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | AdaBoost | 0.67 | 0.58 | 0.58 | 0.58 | 0.58 | 0.35 | 0.78 |
| Change in VA, baseline - month 12 (categories: VA gained, lost) | V0_OCT | full | averaged over classes | kNN | 0.55 | 0.57 | 0.57 | 0.57 | 0.57 | 0.11 | 0.54 |
| | | | | Gradient Boosting | 0.53 | 0.52 | 0.51 | 0.51 | 0.52 | -0.01 | 0.47 |
| | | | | Random Forest | 0.53 | 0.55 | 0.55 | 0.55 | 0.55 | 0.08 | 0.53 |
| | | | | Neural Network | 0.52 | 0.53 | 0.53 | 0.53 | 0.53 | 0.03 | 0.50 |
| | | | | Naïve Bayes | 0.51 | 0.53 | 0.53 | 0.53 | 0.53 | 0.03 | 0.50 |
| | | | | Tree | 0.49 | 0.52 | 0.51 | 0.51 | 0.52 | 0.00 | 0.48 |
| | | | | SVM | 0.49 | 0.47 | 0.47 | 0.48 | 0.47 | -0.07 | 0.45 |
| | | | | Logistic Regression | 0.49 | 0.54 | 0.50 | 0.51 | 0.54 | 0.00 | 0.45 |
| | | | | AdaBoost | 0.46 | 0.48 | 0.48 | 0.48 | 0.48 | -0.07 | 0.45 |
| Change in VA, baseline - month 12 (categories: VA gained, lost) | V0_OCT | outliers removed | averaged over classes | Naïve Bayes | 0.62 | 0.60 | 0.60 | 0.61 | 0.60 | 0.20 | 0.60 |
| | | | | SVM | 0.60 | 0.58 | 0.58 | 0.59 | 0.58 | 0.17 | 0.59 |
| | | | | Gradient Boosting | 0.60 | 0.60 | 0.60 | 0.60 | 0.60 | 0.17 | 0.56 |
| | | | | Random Forest | 0.59 | 0.60 | 0.60 | 0.60 | 0.60 | 0.17 | 0.57 |
| | | | | Neural Network | 0.58 | 0.58 | 0.58 | 0.58 | 0.58 | 0.14 | 0.55 |
| | | | | Tree | 0.56 | 0.57 | 0.57 | 0.57 | 0.57 | 0.12 | 0.55 |
| | | | | Logistic Regression | 0.55 | 0.55 | 0.54 | 0.54 | 0.55 | 0.06 | 0.51 |
| | | | | kNN | 0.54 | 0.55 | 0.55 | 0.55 | 0.55 | 0.08 | 0.53 |
| | | | | AdaBoost | 0.52 | 0.53 | 0.53 | 0.53 | 0.53 | 0.04 | 0.51 |
| Change in VA, baseline - month 12 (categories: VA gained, lost) | VP_OCT | full | averaged over classes | Naïve Bayes | 0.51 | 0.55 | 0.54 | 0.54 | 0.55 | 0.05 | 0.50 |
| | | | | kNN | 0.51 | 0.52 | 0.51 | 0.51 | 0.52 | -0.01 | 0.47 |
| | | | | SVM | 0.51 | 0.52 | 0.50 | 0.50 | 0.52 | -0.02 | 0.46 |
| | | | | AdaBoost | 0.51 | 0.51 | 0.51 | 0.52 | 0.51 | 0.01 | 0.50 |
| | | | | Logistic Regression | 0.48 | 0.54 | 0.49 | 0.50 | 0.54 | -0.01 | 0.44 |
| | | | | Gradient Boosting | 0.48 | 0.53 | 0.52 | 0.51 | 0.53 | 0.00 | 0.47 |
| | | | | Random Forest | 0.48 | 0.51 | 0.50 | 0.49 | 0.51 | -0.04 | 0.45 |
| | | | | Tree | 0.45 | 0.46 | 0.46 | 0.45 | 0.46 | -0.12 | 0.42 |
| | | | | Neural Network | 0.41 | 0.50 | 0.48 | 0.47 | 0.50 | -0.08 | 0.43 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Change in VA, baseline - month 12 (categories: VA gained, lost) | VP_OCT | outliers removed | averaged over classes | Logistic Regression | 0.53 | 0.60 | 0.57 | 0.58 | 0.60 | 0.11 | 0.50 |
| | | | | Gradient Boosting | 0.52 | 0.57 | 0.55 | 0.55 | 0.57 | 0.06 | 0.49 |
| | | | | Naïve Bayes | 0.52 | 0.52 | 0.53 | 0.54 | 0.52 | 0.03 | 0.51 |
| | | | | Tree | 0.52 | 0.54 | 0.53 | 0.53 | 0.54 | 0.02 | 0.48 |
| | | | | AdaBoost | 0.52 | 0.52 | 0.53 | 0.53 | 0.52 | 0.03 | 0.51 |
| | | | | Neural Network | 0.51 | 0.54 | 0.53 | 0.53 | 0.54 | 0.01 | 0.48 |
| | | | | Random Forest | 0.51 | 0.55 | 0.53 | 0.53 | 0.55 | 0.03 | 0.47 |
| | | | | SVM | 0.48 | 0.57 | 0.54 | 0.54 | 0.57 | 0.05 | 0.48 |
| | | | | kNN | 0.48 | 0.53 | 0.51 | 0.50 | 0.53 | -0.03 | 0.45 |
| Change in VA, baseline - month 12 (categories: VA gained, lost) | V0_OCTANE | full | averaged over classes | Logistic Regression | 0.56 | 0.54 | 0.53 | 0.52 | 0.54 | 0.02 | 0.49 |
| | | | | Gradient Boosting | 0.55 | 0.55 | 0.55 | 0.56 | 0.55 | 0.10 | 0.55 |
| | | | | Naïve Bayes | 0.55 | 0.53 | 0.52 | 0.57 | 0.53 | 0.11 | 0.58 |
| | | | | AdaBoost | 0.55 | 0.55 | 0.55 | 0.56 | 0.55 | 0.10 | 0.55 |
| | | | | Tree | 0.55 | 0.55 | 0.55 | 0.55 | 0.55 | 0.08 | 0.52 |
| | | | | Random Forest | 0.53 | 0.53 | 0.53 | 0.53 | 0.53 | 0.03 | 0.50 |
| | | | | Neural Network | 0.52 | 0.55 | 0.49 | 0.50 | 0.55 | -0.02 | 0.44 |
| | | | | SVM | 0.51 | 0.55 | 0.53 | 0.53 | 0.55 | 0.04 | 0.48 |
| | | | | kNN (error) | | | | | | | |
| Change in VA, baseline - month 12 (categories: VA gained, lost) | V0_OCTANE | outliers removed | averaged over classes | SVM | 0.53 | 0.54 | 0.48 | 0.50 | 0.54 | -0.01 | 0.45 |
| | | | | kNN | 0.51 | 0.52 | 0.50 | 0.50 | 0.52 | -0.01 | 0.47 |
| | | | | AdaBoost | 0.51 | 0.50 | 0.47 | 0.47 | 0.50 | -0.07 | 0.44 |
| | | | | Tree | 0.50 | 0.53 | 0.50 | 0.51 | 0.53 | -0.01 | 0.47 |
| | | | | Naïve Bayes | 0.49 | 0.53 | 0.48 | 0.49 | 0.53 | -0.03 | 0.45 |
| | | | | Gradient Boosting | 0.49 | 0.51 | 0.48 | 0.48 | 0.51 | -0.05 | 0.45 |
| | | | | Neural Network | 0.48 | 0.48 | 0.47 | 0.46 | 0.48 | -0.09 | 0.44 |
| | | | | Random Forest | 0.46 | 0.48 | 0.47 | 0.47 | 0.48 | -0.08 | 0.44 |
| | | | | Logistic Regression | 0.41 | 0.50 | 0.41 | 0.40 | 0.50 | -0.15 | 0.40 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Change in VA, baseline - month 12 (categories: VA gained, lost) | VP_OCTANE | full | averaged over classes | Neural Network | 0.53 | 0.42 | 0.25 | 0.18 | 0.42 | 0.00 | 0.58 |
| | | | | Naïve Bayes | 0.50 | 0.42 | 0.25 | 0.18 | 0.42 | 0.00 | 0.58 |
| | | | | Random Forest | 0.50 | 0.42 | 0.25 | 0.18 | 0.42 | 0.00 | 0.58 |
| | | | | Tree | 0.50 | 0.42 | 0.25 | 0.18 | 0.42 | 0.00 | 0.58 |
| | | | | AdaBoost | 0.50 | 0.42 | 0.25 | 0.18 | 0.42 | 0.00 | 0.58 |
| | | | | SVM (error) | | | | | | | |
| | | | | Gradient Boosting (error) | | | | | | | |
| | | | | kNN (error) | | | | | | | |
| | | | | Logistic Regression (error) | | | | | | | |
| Change in VA, baseline - month 12 (categories: VA gained, lost) | VP_OCTANE | outliers removed | averaged over classes | Tree | 0.58 | 0.59 | 0.53 | 0.58 | 0.59 | 0.10 | 0.48 |
| | | | | Neural Network | 0.56 | 0.56 | 0.54 | 0.55 | 0.56 | 0.06 | 0.49 |
| | | | | Random Forest | 0.54 | 0.55 | 0.53 | 0.53 | 0.55 | 0.04 | 0.49 |
| | | | | Naïve Bayes | 0.53 | 0.49 | 0.49 | 0.52 | 0.49 | 0.01 | 0.52 |
| | | | | AdaBoost | 0.53 | 0.56 | 0.51 | 0.53 | 0.56 | 0.03 | 0.46 |
| | | | | Gradient Boosting | 0.53 | 0.57 | 0.51 | 0.54 | 0.57 | 0.04 | 0.47 |
| | | | | Logistic Regression | 0.49 | 0.56 | 0.49 | 0.53 | 0.56 | 0.02 | 0.45 |
| | | | | kNN | 0.48 | 0.53 | 0.48 | 0.48 | 0.53 | -0.05 | 0.43 |
| | | | | SVM | 0.48 | 0.60 | 0.55 | 0.59 | 0.60 | 0.13 | 0.50 |
| Change in VA, baseline - month 12 (categories: VA gained, lost) | Demographic & qualitative | full | averaged over classes | SVM | 0.52 | 0.55 | 0.52 | 0.53 | 0.55 | 0.03 | 0.48 |
| | | | | Random Forest | 0.50 | 0.52 | 0.52 | 0.51 | 0.52 | 0.01 | 0.49 |
| | | | | kNN | 0.47 | 0.48 | 0.48 | 0.47 | 0.48 | -0.08 | 0.44 |
| | | | | Neural Network | 0.47 | 0.52 | 0.46 | 0.47 | 0.52 | -0.08 | 0.42 |
| | | | | AdaBoost | 0.47 | 0.50 | 0.50 | 0.50 | 0.50 | -0.03 | 0.46 |
| | | | | Gradient Boosting | 0.47 | 0.52 | 0.51 | 0.51 | 0.52 | 0.00 | 0.48 |
| | | | | Logistic Regression | 0.46 | 0.57 | 0.43 | 0.46 | 0.57 | -0.04 | 0.42 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Tree | 0.46 | 0.48 | 0.47 | 0.47 | 0.48 | -0.09 | 0.43 |
| | | | | Naïve Bayes | 0.43 | 0.47 | 0.47 | 0.46 | 0.47 | -0.10 | 0.43 |
| Change in VA, baseline - month 12 (categories: VA gained, lost) | Demographic & qualitative | outliers removed | averaged over classes | Gradient Boosting (1) | 0.60 | 0.57 | 0.57 | 0.56 | 0.57 | 0.11 | 0.53 |
| | | | | AdaBoost | 0.60 | 0.56 | 0.56 | 0.55 | 0.56 | 0.08 | 0.52 |
| | | | | Neural Network | 0.59 | 0.60 | 0.60 | 0.59 | 0.60 | 0.17 | 0.56 |
| | | | | kNN | 0.58 | 0.58 | 0.57 | 0.57 | 0.58 | 0.12 | 0.54 |
| | | | | Random Forest | 0.57 | 0.59 | 0.58 | 0.58 | 0.59 | 0.14 | 0.55 |
| | | | | Tree | 0.56 | 0.58 | 0.58 | 0.58 | 0.58 | 0.13 | 0.55 |
| | | | | Naïve Bayes | 0.55 | 0.56 | 0.54 | 0.54 | 0.56 | 0.06 | 0.49 |
| | | | | Logistic Regression (2) | 0.55 | 0.55 | 0.51 | 0.52 | 0.55 | 0.01 | 0.46 |
| | | | | SVM | 0.52 | 0.55 | 0.54 | 0.54 | 0.55 | 0.05 | 0.50 |
| Change in VA, baseline - month 12 (categories: VA gained, lost) | VA | full | averaged over classes | Random Forest | 0.56 | 0.55 | 0.55 | 0.54 | 0.55 | 0.06 | 0.51 |
| | | | | Logistic Regression | 0.56 | 0.57 | 0.47 | 0.52 | 0.57 | 0.00 | 0.44 |
| | | | | Naïve Bayes | 0.53 | 0.55 | 0.53 | 0.53 | 0.55 | 0.03 | 0.48 |
| | | | | Tree | 0.53 | 0.54 | 0.53 | 0.53 | 0.54 | 0.04 | 0.50 |
| | | | | Neural Network | 0.52 | 0.57 | 0.53 | 0.54 | 0.57 | 0.06 | 0.48 |
| | | | | kNN | 0.50 | 0.53 | 0.53 | 0.53 | 0.53 | 0.03 | 0.50 |
| | | | | Gradient Boosting | 0.50 | 0.52 | 0.51 | 0.51 | 0.52 | -0.01 | 0.47 |
| | | | | SVM | 0.49 | 0.53 | 0.52 | 0.52 | 0.53 | 0.02 | 0.49 |
| | | | | AdaBoost | 0.48 | 0.50 | 0.50 | 0.49 | 0.50 | -0.04 | 0.47 |
| Change in VA, baseline - month 12 (categories: VA gained, lost) | VA | outliers removed | averaged over classes | Logistic Regression | 0.82 | 0.74 | 0.74 | 0.74 | 0.74 | 0.46 | 0.72 |
| | | | | Neural Network | 0.81 | 0.72 | 0.72 | 0.72 | 0.72 | 0.42 | 0.70 |
| | | | | SVM | 0.79 | 0.70 | 0.70 | 0.70 | 0.70 | 0.38 | 0.68 |
| | | | | Gradient Boosting | 0.73 | 0.66 | 0.66 | 0.66 | 0.66 | 0.30 | 0.63 |
| | | | | kNN | 0.70 | 0.64 | 0.64 | 0.64 | 0.64 | 0.26 | 0.61 |
| | | | | Random Forest | 0.69 | 0.63 | 0.63 | 0.63 | 0.63 | 0.23 | 0.59 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Tree | 0.68 | 0.64 | 0.63 | 0.64 | 0.64 | 0.25 | 0.59 |
| | | | | Naïve Bayes | 0.65 | 0.64 | 0.62 | 0.63 | 0.64 | 0.23 | 0.57 |
| | | | | AdaBoost | 0.59 | 0.60 | 0.60 | 0.60 | 0.60 | 0.18 | 0.58 |
| Change in VA, baseline - month 12 (categories: VA gained, lost) | VA_st dev | full | averaged over classes | Logistic Regression | 0.56 | 0.58 | 0.50 | 0.57 | 0.58 | 0.07 | 0.46 |
| | | | | Tree | 0.52 | 0.55 | 0.54 | 0.54 | 0.55 | 0.06 | 0.51 |
| | | | | Naïve Bayes | 0.52 | 0.56 | 0.53 | 0.54 | 0.56 | 0.05 | 0.48 |
| | | | | Random Forest | 0.52 | 0.56 | 0.56 | 0.56 | 0.56 | 0.09 | 0.52 |
| | | | | AdaBoost | 0.50 | 0.51 | 0.51 | 0.51 | 0.51 | -0.01 | 0.49 |
| | | | | Gradient Boosting | 0.50 | 0.53 | 0.52 | 0.51 | 0.53 | 0.01 | 0.48 |
| | | | | SVM | 0.49 | 0.53 | 0.52 | 0.52 | 0.53 | 0.02 | 0.49 |
| | | | | Neural Network | 0.49 | 0.55 | 0.53 | 0.53 | 0.55 | 0.03 | 0.48 |
| | | | | kNN | 0.47 | 0.52 | 0.52 | 0.52 | 0.52 | 0.01 | 0.49 |
| Change in VA, baseline - month 12 (categories: VA gained, lost) | VA_st dev | outliers removed | averaged over classes | Neural Network | 0.88 | 0.77 | 0.77 | 0.77 | 0.77 | 0.53 | 0.75 |
| | | | | Logistic Regression | 0.86 | 0.78 | 0.78 | 0.78 | 0.78 | 0.55 | 0.76 |
| | | | | SVM | 0.85 | 0.75 | 0.75 | 0.75 | 0.75 | 0.49 | 0.73 |
| | | | | Gradient Boosting | 0.78 | 0.70 | 0.70 | 0.70 | 0.70 | 0.38 | 0.67 |
| | | | | Random Forest | 0.74 | 0.68 | 0.68 | 0.68 | 0.68 | 0.34 | 0.65 |
| | | | | kNN | 0.74 | 0.68 | 0.68 | 0.68 | 0.68 | 0.34 | 0.64 |
| | | | | Naïve Bayes | 0.71 | 0.63 | 0.62 | 0.63 | 0.63 | 0.22 | 0.58 |
| | | | | Tree | 0.65 | 0.66 | 0.66 | 0.66 | 0.66 | 0.29 | 0.63 |
| | | | | AdaBoost | 0.63 | 0.64 | 0.64 | 0.64 | 0.64 | 0.25 | 0.61 |
| VA at 12 months (mean of VA from final 2 visits categories: letter score VA <30, 31- | V0_OCT | full | averaged over classes | Naïve Bayes | 0.54 | 0.22 | 0.24 | 0.28 | 0.22 | 0.08 | 0.86 |
| | | | | Logistic Regression | 0.53 | 0.26 | 0.23 | 0.21 | 0.26 | 0.02 | 0.76 |
| | | | | Random Forest | 0.53 | 0.27 | 0.24 | 0.22 | 0.27 | 0.04 | 0.78 |
| | | | | AdaBoost | 0.51 | 0.21 | 0.21 | 0.21 | 0.21 | 0.02 | 0.80 |
| | | | | Neural Network | 0.51 | 0.23 | 0.20 | 0.22 | 0.23 | -0.02 | 0.76 |
| | | | | kNN | 0.51 | 0.20 | 0.19 | 0.18 | 0.20 | -0.02 | 0.78 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Gradient Boosting | 0.50 | 0.25 | 0.23 | 0.21 | 0.25 | 0.02 | 0.78 |
| | | | | Tree | 0.49 | 0.19 | 0.20 | 0.20 | 0.19 | 0.00 | 0.81 |
| | | | | SVM | 0.49 | 0.25 | 0.21 | 0.19 | 0.25 | 0.00 | 0.75 |
| VA at 12 months (mean of VA from final 2 visits categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80) | V0_OCT | outliers removed | averaged over classes | Tree | 0.54 | 0.24 | 0.24 | 0.25 | 0.24 | 0.06 | 0.81 |
| | | | | Logistic Regression | 0.53 | 0.25 | 0.24 | 0.24 | 0.25 | 0.04 | 0.79 |
| | | | | Gradient Boosting | 0.53 | 0.20 | 0.19 | 0.19 | 0.20 | -0.02 | 0.77 |
| | | | | Neural Network | 0.52 | 0.24 | 0.23 | 0.24 | 0.24 | 0.03 | 0.78 |
| | | | | SVM | 0.51 | 0.26 | 0.20 | 0.18 | 0.26 | 0.01 | 0.75 |
| | | | | AdaBoost | 0.51 | 0.22 | 0.22 | 0.22 | 0.22 | 0.03 | 0.81 |
| | | | | Naïve Bayes | 0.51 | 0.07 | 0.05 | 0.11 | 0.07 | 0.01 | 0.93 |
| | | | | kNN | 0.49 | 0.20 | 0.19 | 0.18 | 0.20 | -0.02 | 0.79 |
| | | | | Random Forest | 0.48 | 0.22 | 0.20 | 0.19 | 0.22 | -0.02 | 0.76 |
| VA at 12 months (mean of VA from final 2 visits categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80) | VP_OCT | full | averaged over classes | kNN | 0.50 | 0.21 | 0.20 | 0.19 | 0.21 | 0.00 | 0.79 |
| | | | | Gradient Boosting | 0.50 | 0.23 | 0.21 | 0.20 | 0.23 | 0.00 | 0.77 |
| | | | | Naïve Bayes | 0.49 | 0.14 | 0.15 | 0.17 | 0.14 | -0.02 | 0.84 |
| | | | | Random Forest | 0.49 | 0.20 | 0.19 | 0.19 | 0.20 | -0.04 | 0.76 |
| | | | | Neural Network | 0.49 | 0.21 | 0.19 | 0.18 | 0.21 | -0.04 | 0.75 |
| | | | | AdaBoost | 0.49 | 0.18 | 0.18 | 0.18 | 0.18 | -0.03 | 0.80 |
| | | | | SVM | 0.48 | 0.23 | 0.18 | 0.17 | 0.23 | -0.03 | 0.74 |
| | | | | Tree | 0.48 | 0.17 | 0.17 | 0.17 | 0.17 | -0.04 | 0.80 |
| | | | | Logistic Regression | 0.48 | 0.23 | 0.19 | 0.25 | 0.23 | -0.03 | 0.74 |
| VA at 12 months (mean of VA from final 2 visits categories: letter score VA <30, 31- | VP_OCT | outliers removed | averaged over classes | SVM | 0.58 | 0.25 | 0.19 | 0.17 | 0.25 | -0.01 | 0.74 |
| | | | | AdaBoost | 0.52 | 0.24 | 0.23 | 0.23 | 0.24 | 0.05 | 0.81 |
| | | | | Tree | 0.52 | 0.23 | 0.24 | 0.24 | 0.23 | 0.05 | 0.81 |
| | | | | Neural Network | 0.52 | 0.21 | 0.20 | 0.19 | 0.21 | -0.01 | 0.78 |
| | | | | Naïve Bayes | 0.51 | 0.09 | 0.06 | 0.18 | 0.09 | 0.03 | 0.93 |
| | | | | kNN | 0.51 | 0.20 | 0.20 | 0.19 | 0.20 | -0.01 | 0.79 |
| | | | | Logistic Regression | 0.51 | 0.24 | 0.22 | 0.22 | 0.24 | 0.02 | 0.78 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Random Forest | 0.51 | 0.20 | 0.18 | 0.18 | 0.20 | -0.04 | 0.76 |
| | | | | Gradient Boosting | 0.47 | 0.17 | 0.15 | 0.14 | 0.17 | -0.07 | 0.76 |
| VA at 12 months (mean of VA from final 2 visits categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80) | V0_OCTANE | full | averaged over classes | Logistic Regression | 0.51 | 0.24 | 0.21 | 0.20 | 0.24 | 0.02 | 0.78 |
| | | | | SVM | 0.51 | 0.25 | 0.16 | 0.12 | 0.25 | 0.00 | 0.75 |
| | | | | Neural Network | 0.51 | 0.26 | 0.22 | 0.21 | 0.26 | 0.03 | 0.77 |
| | | | | AdaBoost | 0.50 | 0.21 | 0.18 | 0.19 | 0.21 | -0.01 | 0.78 |
| | | | | Gradient Boosting | 0.50 | 0.22 | 0.19 | 0.20 | 0.22 | 0.00 | 0.78 |
| | | | | Tree | 0.49 | 0.22 | 0.16 | 0.13 | 0.22 | -0.01 | 0.77 |
| | | | | Random Forest | 0.49 | 0.26 | 0.16 | 0.13 | 0.26 | 0.01 | 0.74 |
| | | | | Naïve Bayes | 0.49 | 0.17 | 0.15 | 0.17 | 0.17 | -0.02 | 0.80 |
| | | | | kNN (error) | | | | | | | |
| VA at 12 months (mean of VA from final 2 visits categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80) | V0_OCTANE | outliers removed | averaged over classes | SVM | 0.53 | 0.26 | 0.18 | 0.15 | 0.26 | 0.00 | 0.74 |
| | | | | Logistic Regression | 0.52 | 0.28 | 0.21 | 0.20 | 0.28 | 0.03 | 0.75 |
| | | | | kNN | 0.51 | 0.26 | 0.23 | 0.23 | 0.26 | 0.06 | 0.80 |
| | | | | Tree | 0.51 | 0.28 | 0.25 | 0.25 | 0.28 | 0.06 | 0.79 |
| | | | | Naïve Bayes | 0.50 | 0.04 | 0.02 | 0.29 | 0.04 | 0.00 | 0.96 |
| | | | | AdaBoost | 0.49 | 0.24 | 0.20 | 0.19 | 0.24 | 0.00 | 0.76 |
| | | | | Random Forest | 0.49 | 0.26 | 0.22 | 0.24 | 0.26 | 0.02 | 0.76 |
| | | | | Gradient Boosting | 0.48 | 0.24 | 0.20 | 0.20 | 0.24 | 0.01 | 0.77 |
| | | | | Neural Network | 0.47 | 0.25 | 0.21 | 0.21 | 0.25 | 0.02 | 0.77 |
| VA at 12 months (mean of VA from final 2 visits categories: letter score VA <30, 31- | VP_OCTANE | full | averaged over classes | AdaBoost | 0.50 | 0.12 | 0.07 | 0.05 | 0.12 | 0.01 | 0.88 |
| | | | | Naïve Bayes | 0.50 | 0.18 | 0.08 | 0.05 | 0.18 | -0.02 | 0.80 |
| | | | | Tree | 0.50 | 0.20 | 0.08 | 0.05 | 0.20 | 0.00 | 0.80 |
| | | | | Random Forest | 0.50 | 0.13 | 0.07 | 0.05 | 0.13 | -0.01 | 0.87 |
| | | | | Neural Network | 0.49 | 0.12 | 0.07 | 0.05 | 0.12 | -0.01 | 0.87 |
| | | | | SVM (error) | | | | | | | |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Gradient Boosting (error) | | | | | | | |
| | | | | kNN (error) | | | | | | | |
| | | | | Logistic Regression (error) | | | | | | | |
| VA at 12 months (mean of VA from final 2 visits categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80) | VP_OCTANE | outliers removed | averaged over classes | Naïve Bayes | 0.51 | 0.07 | 0.03 | 0.26 | 0.07 | 0.04 | 0.95 |
| | | | | Tree | 0.51 | 0.23 | 0.20 | 0.21 | 0.23 | 0.00 | 0.77 |
| | | | | kNN | 0.49 | 0.21 | 0.19 | 0.20 | 0.21 | 0.00 | 0.78 |
| | | | | AdaBoost | 0.49 | 0.23 | 0.19 | 0.19 | 0.23 | -0.01 | 0.76 |
| | | | | Neural Network | 0.48 | 0.23 | 0.19 | 0.18 | 0.23 | 0.00 | 0.76 |
| | | | | Random Forest | 0.48 | 0.24 | 0.20 | 0.19 | 0.24 | 0.00 | 0.76 |
| | | | | Gradient Boosting | 0.48 | 0.24 | 0.21 | 0.23 | 0.24 | 0.01 | 0.76 |
| | | | | Logistic Regression | 0.46 | 0.22 | 0.14 | 0.11 | 0.22 | -0.06 | 0.73 |
| | | | | SVM | 0.43 | 0.24 | 0.17 | 0.14 | 0.24 | -0.03 | 0.74 |
| VA at 12 months (mean of VA from final 2 visits categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80) | Demographic & qualitative | full | averaged over classes | Gradient Boosting | 0.52 | 0.24 | 0.23 | 0.23 | 0.24 | 0.03 | 0.79 |
| | | | | Random Forest | 0.50 | 0.26 | 0.25 | 0.24 | 0.26 | 0.05 | 0.79 |
| | | | | Neural Network | 0.50 | 0.29 | 0.25 | 0.26 | 0.29 | 0.06 | 0.76 |
| | | | | AdaBoost | 0.50 | 0.25 | 0.24 | 0.23 | 0.25 | 0.04 | 0.79 |
| | | | | Tree | 0.50 | 0.20 | 0.20 | 0.20 | 0.20 | 0.00 | 0.80 |
| | | | | Logistic Regression | 0.49 | 0.28 | 0.22 | 0.20 | 0.28 | 0.03 | 0.75 |
| | | | | kNN | 0.49 | 0.19 | 0.18 | 0.23 | 0.19 | -0.04 | 0.78 |
| | | | | Naïve Bayes | 0.48 | 0.11 | 0.12 | 0.16 | 0.11 | -0.04 | 0.86 |
| | | | | SVM | 0.48 | 0.28 | 0.22 | 0.20 | 0.28 | 0.03 | 0.75 |
| VA at 12 months (mean of VA from final 2 visits | Demographic & qualitative | outliers removed | averaged over classes | SVM | 0.54 | 0.32 | 0.25 | 0.23 | 0.32 | 0.08 | 0.76 |
| | | | | AdaBoost | 0.54 | 0.26 | 0.25 | 0.26 | 0.26 | 0.05 | 0.80 |
| | | | | kNN | 0.53 | 0.21 | 0.19 | 0.18 | 0.21 | -0.02 | 0.77 |
| | | | | Gradient Boosting | 0.51 | 0.23 | 0.23 | 0.23 | 0.23 | 0.03 | 0.80 |
| | | | | Neural Network | 0.50 | 0.28 | 0.25 | 0.23 | 0.28 | 0.06 | 0.77 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Tree | 0.50 | 0.18 | 0.18 | 0.19 | 0.18 | -0.02 | 0.79 |
| | | | | Logistic Regression | 0.50 | 0.27 | 0.23 | 0.20 | 0.27 | 0.02 | 0.76 |
| | | | | Random Forest | 0.49 | 0.22 | 0.21 | 0.21 | 0.22 | -0.01 | 0.77 |
| | | | | Naïve Bayes | 0.49 | 0.22 | 0.20 | 0.19 | 0.22 | -0.01 | 0.77 |
| VA at 12 months (mean of VA from final 2 visits categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80) | VA | full | averaged over classes | Logistic Regression | 0.55 | 0.29 | 0.23 | 0.21 | 0.29 | 0.06 | 0.76 |
| | | | | kNN | 0.55 | 0.25 | 0.25 | 0.25 | 0.25 | 0.05 | 0.80 |
| | | | | Gradient Boosting | 0.54 | 0.28 | 0.26 | 0.25 | 0.28 | 0.06 | 0.79 |
| | | | | Neural Network | 0.54 | 0.29 | 0.25 | 0.23 | 0.29 | 0.06 | 0.77 |
| | | | | Random Forest | 0.53 | 0.25 | 0.23 | 0.22 | 0.25 | 0.03 | 0.78 |
| | | | | Tree | 0.53 | 0.21 | 0.21 | 0.22 | 0.21 | 0.01 | 0.81 |
| | | | | Naïve Bayes | 0.51 | 0.24 | 0.22 | 0.22 | 0.24 | 0.01 | 0.77 |
| | | | | SVM | 0.51 | 0.28 | 0.23 | 0.20 | 0.28 | 0.03 | 0.75 |
| | | | | AdaBoost | 0.50 | 0.20 | 0.20 | 0.20 | 0.20 | 0.00 | 0.80 |
| VA at 12 months (mean of VA from final 2 visits categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80) | VA | outliers removed | averaged over classes | Neural Network | 0.78 | 0.47 | 0.43 | 0.40 | 0.47 | 0.31 | 0.83 |
| | | | | Logistic Regression | 0.78 | 0.47 | 0.45 | 0.45 | 0.47 | 0.31 | 0.84 |
| | | | | SVM | 0.77 | 0.49 | 0.45 | 0.41 | 0.49 | 0.34 | 0.84 |
| | | | | Random Forest | 0.74 | 0.40 | 0.40 | 0.39 | 0.40 | 0.23 | 0.83 |
| | | | | Gradient Boosting | 0.74 | 0.42 | 0.42 | 0.41 | 0.42 | 0.26 | 0.85 |
| | | | | Naïve Bayes | 0.74 | 0.37 | 0.37 | 0.39 | 0.37 | 0.22 | 0.86 |
| | | | | kNN | 0.71 | 0.40 | 0.39 | 0.39 | 0.40 | 0.23 | 0.82 |
| | | | | Tree | 0.66 | 0.40 | 0.40 | 0.40 | 0.40 | 0.24 | 0.85 |
| | | | | AdaBoost | 0.61 | 0.38 | 0.38 | 0.38 | 0.38 | 0.22 | 0.84 |
| VA at 12 months (mean of VA from final 2 visits | VA_st dev | full | averaged over classes | Logistic Regression | 0.56 | 0.30 | 0.24 | 0.21 | 0.30 | 0.07 | 0.76 |
| | | | | Random Forest | 0.56 | 0.25 | 0.22 | 0.21 | 0.25 | 0.02 | 0.77 |
| | | | | kNN | 0.54 | 0.26 | 0.24 | 0.24 | 0.26 | 0.05 | 0.79 |
| | | | | Gradient Boosting | 0.54 | 0.25 | 0.23 | 0.23 | 0.25 | 0.03 | 0.78 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Neural Network | 0.53 | 0.28 | 0.25 | 0.23 | 0.28 | 0.06 | 0.77 |
| | | | | Naïve Bayes | 0.53 | 0.24 | 0.22 | 0.23 | 0.24 | 0.02 | 0.78 |
| | | | | Tree | 0.53 | 0.24 | 0.24 | 0.25 | 0.24 | 0.06 | 0.82 |
| | | | | SVM | 0.51 | 0.27 | 0.22 | 0.19 | 0.27 | 0.03 | 0.75 |
| | | | | AdaBoost | 0.50 | 0.19 | 0.19 | 0.19 | 0.19 | 0.00 | 0.80 |
| VA at 12 months (mean of VA from final 2 visits categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80) | VA_st dev | outliers removed | averaged over classes | Neural Network | 0.84 | 0.47 | 0.45 | 0.45 | 0.47 | 0.32 | 0.85 |
| | | | | SVM | 0.83 | 0.48 | 0.45 | 0.44 | 0.48 | 0.33 | 0.85 |
| | | | | Logistic Regression | 0.81 | 0.47 | 0.46 | 0.46 | 0.47 | 0.32 | 0.84 |
| | | | | Gradient Boosting | 0.78 | 0.45 | 0.45 | 0.44 | 0.45 | 0.30 | 0.85 |
| | | | | Random Forest | 0.78 | 0.43 | 0.42 | 0.42 | 0.43 | 0.27 | 0.84 |
| | | | | Naïve Bayes | 0.75 | 0.38 | 0.39 | 0.42 | 0.38 | 0.24 | 0.87 |
| | | | | kNN | 0.72 | 0.40 | 0.39 | 0.38 | 0.40 | 0.23 | 0.82 |
| | | | | Tree | 0.65 | 0.39 | 0.39 | 0.39 | 0.39 | 0.23 | 0.84 |
| | | | | AdaBoost | 0.65 | 0.45 | 0.45 | 0.45 | 0.45 | 0.30 | 0.85 |
| VA at 12 months (categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80) | V0_OCT | full | averaged over classes | Random Forest | 0.53 | 0.27 | 0.24 | 0.22 | 0.27 | 0.05 | 0.78 |
| | | | | Tree | 0.52 | 0.22 | 0.22 | 0.23 | 0.22 | 0.04 | 0.82 |
| | | | | kNN | 0.51 | 0.24 | 0.23 | 0.24 | 0.24 | 0.04 | 0.80 |
| | | | | AdaBoost | 0.51 | 0.23 | 0.22 | 0.22 | 0.23 | 0.03 | 0.80 |
| | | | | Neural Network | 0.50 | 0.23 | 0.20 | 0.18 | 0.23 | -0.01 | 0.76 |
| | | | | Logistic Regression | 0.50 | 0.28 | 0.23 | 0.29 | 0.28 | 0.04 | 0.76 |
| | | | | Naïve Bayes | 0.50 | 0.17 | 0.19 | 0.21 | 0.17 | 0.01 | 0.84 |
| | | | | SVM | 0.50 | 0.26 | 0.20 | 0.18 | 0.26 | 0.01 | 0.74 |
| | | | | Gradient Boosting | 0.49 | 0.23 | 0.21 | 0.22 | 0.23 | 0.00 | 0.77 |
| VA at 12 months (categories: letter score VA | V0_OCT | outliers removed | averaged over classes | Neural Network | 0.57 | 0.26 | 0.24 | 0.24 | 0.26 | 0.04 | 0.79 |
| | | | | Gradient Boosting | 0.57 | 0.27 | 0.24 | 0.24 | 0.27 | 0.05 | 0.78 |
| | | | | SVM | 0.56 | 0.32 | 0.24 | 0.21 | 0.32 | 0.08 | 0.76 |
| | | | | Logistic Regression | 0.56 | 0.26 | 0.25 | 0.24 | 0.26 | 0.05 | 0.79 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Naïve Bayes | 0.56 | 0.13 | 0.11 | 0.20 | 0.13 | 0.06 | 0.91 |
| | | | | Random Forest | 0.54 | 0.23 | 0.22 | 0.21 | 0.23 | 0.01 | 0.78 |
| | | | | Tree | 0.53 | 0.25 | 0.25 | 0.25 | 0.25 | 0.06 | 0.82 |
| | | | | kNN | 0.53 | 0.24 | 0.23 | 0.22 | 0.24 | 0.03 | 0.79 |
| | | | | AdaBoost | 0.52 | 0.23 | 0.23 | 0.22 | 0.23 | 0.03 | 0.80 |
| VA at 12 months (categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80) | VP_OCT | full | averaged over classes | Neural Network | 0.52 | 0.27 | 0.23 | 0.21 | 0.27 | 0.04 | 0.77 |
| | | | | Tree | 0.50 | 0.19 | 0.19 | 0.19 | 0.19 | -0.01 | 0.80 |
| | | | | Random Forest | 0.50 | 0.24 | 0.22 | 0.20 | 0.24 | 0.02 | 0.77 |
| | | | | Logistic Regression | 0.50 | 0.27 | 0.22 | 0.21 | 0.27 | 0.03 | 0.76 |
| | | | | Gradient Boosting | 0.49 | 0.22 | 0.20 | 0.19 | 0.22 | -0.01 | 0.77 |
| | | | | kNN | 0.48 | 0.18 | 0.17 | 0.16 | 0.18 | -0.04 | 0.78 |
| | | | | AdaBoost | 0.48 | 0.17 | 0.17 | 0.17 | 0.17 | -0.04 | 0.79 |
| | | | | SVM | 0.48 | 0.28 | 0.21 | 0.17 | 0.28 | 0.03 | 0.75 |
| | | | | Naïve Bayes | 0.47 | 0.13 | 0.14 | 0.17 | 0.13 | -0.02 | 0.85 |
| VA at 12 months (categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80) | VP_OCT | outliers removed | averaged over classes | SVM | 0.57 | 0.30 | 0.24 | 0.21 | 0.30 | 0.06 | 0.76 |
| | | | | Neural Network | 0.56 | 0.26 | 0.25 | 0.24 | 0.26 | 0.06 | 0.80 |
| | | | | Naïve Bayes | 0.56 | 0.10 | 0.08 | 0.19 | 0.10 | 0.02 | 0.92 |
| | | | | Logistic Regression | 0.56 | 0.30 | 0.27 | 0.25 | 0.30 | 0.09 | 0.80 |
| | | | | Random Forest | 0.54 | 0.25 | 0.22 | 0.21 | 0.25 | 0.02 | 0.78 |
| | | | | Tree | 0.54 | 0.23 | 0.24 | 0.24 | 0.23 | 0.06 | 0.82 |
| | | | | kNN | 0.53 | 0.24 | 0.23 | 0.23 | 0.24 | 0.03 | 0.79 |
| | | | | Gradient Boosting | 0.52 | 0.22 | 0.20 | 0.19 | 0.22 | -0.01 | 0.77 |
| | | | | AdaBoost | 0.50 | 0.20 | 0.20 | 0.20 | 0.20 | 0.00 | 0.79 |
| VA at 12 months (categories: letter score VA | V0_OCTANE | full | averaged over classes | Naïve Bayes | 0.51 | 0.20 | 0.18 | 0.18 | 0.20 | 0.01 | 0.80 |
| | | | | Neural Network | 0.51 | 0.24 | 0.20 | 0.19 | 0.24 | 0.01 | 0.77 |
| | | | | AdaBoost | 0.51 | 0.22 | 0.19 | 0.21 | 0.22 | 0.02 | 0.80 |
| | | | | Random Forest | 0.51 | 0.23 | 0.16 | 0.24 | 0.23 | 0.00 | 0.77 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Logistic Regression | 0.51 | 0.23 | 0.19 | 0.19 | 0.23 | 0.01 | 0.78 |
| | | | | Gradient Boosting | 0.51 | 0.22 | 0.18 | 0.21 | 0.22 | 0.01 | 0.79 |
| | | | | SVM | 0.50 | 0.26 | 0.16 | 0.12 | 0.26 | 0.02 | 0.76 |
| | | | | Tree | 0.49 | 0.23 | 0.17 | 0.18 | 0.23 | -0.01 | 0.76 |
| | | | | kNN (error) | | | | | | | |
| VA at 12 months (categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80) | V0_OCTANE | outliers removed | averaged over classes | Tree | 0.57 | 0.30 | 0.28 | 0.29 | 0.30 | 0.09 | 0.78 |
| | | | | AdaBoost | 0.53 | 0.26 | 0.22 | 0.21 | 0.26 | 0.02 | 0.76 |
| | | | | Naïve Bayes | 0.53 | 0.05 | 0.01 | 0.00 | 0.05 | -0.01 | 0.95 |
| | | | | Logistic Regression | 0.52 | 0.27 | 0.21 | 0.22 | 0.27 | 0.02 | 0.74 |
| | | | | kNN | 0.52 | 0.22 | 0.21 | 0.21 | 0.22 | 0.00 | 0.78 |
| | | | | Gradient Boosting | 0.51 | 0.24 | 0.22 | 0.24 | 0.24 | 0.00 | 0.75 |
| | | | | Random Forest | 0.49 | 0.24 | 0.21 | 0.21 | 0.24 | 0.00 | 0.76 |
| | | | | SVM | 0.49 | 0.26 | 0.19 | 0.19 | 0.26 | -0.01 | 0.73 |
| | | | | Neural Network | 0.47 | 0.19 | 0.18 | 0.17 | 0.19 | -0.05 | 0.75 |
| VA at 12 months (categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80) | VP_OCTANE | full | averaged over classes | Random Forest | 0.50 | 0.11 | 0.06 | 0.04 | 0.11 | -0.01 | 0.89 |
| | | | | Tree | 0.50 | 0.18 | 0.07 | 0.04 | 0.18 | -0.01 | 0.81 |
| | | | | AdaBoost | 0.50 | 0.12 | 0.06 | 0.04 | 0.12 | -0.01 | 0.88 |
| | | | | Naïve Bayes | 0.49 | 0.17 | 0.07 | 0.04 | 0.17 | -0.02 | 0.82 |
| | | | | Neural Network | 0.49 | 0.11 | 0.06 | 0.04 | 0.11 | -0.02 | 0.87 |
| | | | | Logistic Regression (error) | | | | | | | |
| | | | | kNN (error) | | | | | | | |
| | | | | Gradient Boosting (error) | | | | | | | |
| | | | | SVM (error) | | | | | | | |
| VA at 12 months | VP_OCTANE | outliers removed | averaged over | Naïve Bayes | 0.53 | 0.07 | 0.03 | 0.02 | 0.07 | 0.02 | 0.94 |
| | | | | Tree | 0.51 | 0.26 | 0.24 | 0.25 | 0.26 | 0.04 | 0.77 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Logistic Regression | 0.49 | 0.25 | 0.17 | 0.15 | 0.25 | -0.02 | 0.74 |
| | | | | kNN | 0.48 | 0.19 | 0.17 | 0.17 | 0.19 | -0.03 | 0.78 |
| | | | | AdaBoost | 0.48 | 0.19 | 0.18 | 0.19 | 0.19 | -0.06 | 0.75 |
| | | | | Neural Network | 0.47 | 0.19 | 0.17 | 0.16 | 0.19 | -0.05 | 0.75 |
| | | | | Random Forest | 0.47 | 0.22 | 0.19 | 0.18 | 0.22 | -0.02 | 0.76 |
| | | | | Gradient Boosting | 0.46 | 0.18 | 0.15 | 0.14 | 0.18 | -0.08 | 0.75 |
| | | | | SVM | 0.45 | 0.23 | 0.16 | 0.13 | 0.23 | -0.06 | 0.72 |
| VA at 12 months (categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80) | Demographic & qualitative | full | averaged over classes | Random Forest | 0.52 | 0.23 | 0.21 | 0.20 | 0.23 | 0.01 | 0.78 |
| | | | | Naïve Bayes | 0.51 | 0.18 | 0.19 | 0.23 | 0.18 | 0.03 | 0.85 |
| | | | | kNN | 0.51 | 0.19 | 0.19 | 0.20 | 0.19 | -0.03 | 0.79 |
| | | | | SVM | 0.51 | 0.28 | 0.19 | 0.19 | 0.28 | 0.02 | 0.74 |
| | | | | Tree | 0.50 | 0.21 | 0.21 | 0.22 | 0.21 | 0.01 | 0.81 |
| | | | | Neural Network | 0.49 | 0.27 | 0.21 | 0.20 | 0.27 | 0.02 | 0.75 |
| | | | | AdaBoost | 0.48 | 0.20 | 0.19 | 0.18 | 0.20 | -0.03 | 0.78 |
| | | | | Logistic Regression | 0.48 | 0.26 | 0.19 | 0.16 | 0.26 | 0.00 | 0.74 |
| | | | | Gradient Boosting | 0.48 | 0.20 | 0.19 | 0.18 | 0.20 | -0.02 | 0.78 |
| VA at 12 months (categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80) | Demographic & qualitative | outliers removed | averaged over classes | Tree | 0.53 | 0.23 | 0.23 | 0.24 | 0.23 | 0.04 | 0.82 |
| | | | | kNN | 0.52 | 0.25 | 0.24 | 0.23 | 0.25 | 0.04 | 0.79 |
| | | | | AdaBoost | 0.52 | 0.20 | 0.20 | 0.20 | 0.20 | 0.00 | 0.80 |
| | | | | Neural Network | 0.51 | 0.28 | 0.25 | 0.23 | 0.28 | 0.05 | 0.77 |
| | | | | Logistic Regression | 0.51 | 0.28 | 0.23 | 0.20 | 0.28 | 0.04 | 0.75 |
| | | | | Gradient Boosting | 0.51 | 0.24 | 0.23 | 0.22 | 0.24 | 0.03 | 0.79 |
| | | | | Random Forest | 0.51 | 0.29 | 0.27 | 0.25 | 0.29 | 0.07 | 0.79 |
| | | | | SVM | 0.50 | 0.33 | 0.27 | 0.25 | 0.33 | 0.10 | 0.76 |
| | | | | Naïve Bayes | 0.48 | 0.26 | 0.22 | 0.21 | 0.26 | 0.02 | 0.77 |
| VA at 12 months | VA | full | averaged over | Naïve Bayes | 0.52 | 0.26 | 0.23 | 0.21 | 0.26 | 0.04 | 0.78 |
| | | | | AdaBoost | 0.50 | 0.20 | 0.20 | 0.21 | 0.20 | 0.01 | 0.81 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Random Forest | 0.50 | 0.24 | 0.23 | 0.21 | 0.24 | 0.02 | 0.78 |
| | | | | Tree | 0.50 | 0.22 | 0.22 | 0.23 | 0.22 | 0.03 | 0.81 |
| | | | | Neural Network | 0.50 | 0.27 | 0.22 | 0.20 | 0.27 | 0.03 | 0.76 |
| | | | | kNN | 0.49 | 0.21 | 0.20 | 0.19 | 0.21 | 0.00 | 0.79 |
| | | | | Logistic Regression | 0.49 | 0.26 | 0.20 | 0.22 | 0.26 | 0.00 | 0.74 |
| | | | | Gradient Boosting | 0.49 | 0.24 | 0.22 | 0.20 | 0.24 | 0.02 | 0.78 |
| | | | | SVM | 0.44 | 0.29 | 0.22 | 0.21 | 0.29 | 0.04 | 0.75 |
| VA at 12 months (categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80) | VA | outliers removed | averaged over classes | Neural Network | 0.76 | 0.45 | 0.41 | 0.38 | 0.45 | 0.28 | 0.83 |
| | | | | Logistic Regression | 0.76 | 0.44 | 0.40 | 0.40 | 0.44 | 0.27 | 0.82 |
| | | | | SVM | 0.76 | 0.46 | 0.41 | 0.39 | 0.46 | 0.29 | 0.83 |
| | | | | Naïve Bayes | 0.74 | 0.39 | 0.39 | 0.41 | 0.39 | 0.25 | 0.87 |
| | | | | Random Forest | 0.72 | 0.40 | 0.39 | 0.39 | 0.40 | 0.23 | 0.83 |
| | | | | Gradient Boosting | 0.71 | 0.41 | 0.40 | 0.40 | 0.41 | 0.24 | 0.83 |
| | | | | kNN | 0.67 | 0.34 | 0.33 | 0.32 | 0.34 | 0.16 | 0.81 |
| | | | | Tree | 0.61 | 0.34 | 0.33 | 0.34 | 0.34 | 0.16 | 0.82 |
| | | | | AdaBoost | 0.60 | 0.37 | 0.37 | 0.37 | 0.37 | 0.21 | 0.83 |
| VA at 12 months (categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80) | VA_st dev | full | averaged over classes | AdaBoost | 0.51 | 0.21 | 0.22 | 0.22 | 0.21 | 0.03 | 0.82 |
| | | | | Naïve Bayes | 0.51 | 0.23 | 0.22 | 0.21 | 0.23 | 0.02 | 0.80 |
| | | | | Logistic Regression | 0.51 | 0.26 | 0.20 | 0.20 | 0.26 | 0.01 | 0.75 |
| | | | | Tree | 0.49 | 0.21 | 0.21 | 0.21 | 0.21 | 0.02 | 0.81 |
| | | | | kNN | 0.49 | 0.22 | 0.20 | 0.19 | 0.22 | 0.00 | 0.78 |
| | | | | Random Forest | 0.49 | 0.23 | 0.21 | 0.19 | 0.23 | 0.00 | 0.77 |
| | | | | Neural Network | 0.48 | 0.24 | 0.19 | 0.17 | 0.24 | -0.01 | 0.75 |
| | | | | Gradient Boosting | 0.48 | 0.22 | 0.20 | 0.19 | 0.22 | -0.01 | 0.78 |
| | | | | SVM | 0.46 | 0.26 | 0.20 | 0.18 | 0.26 | 0.01 | 0.74 |
| VA at 12 months | VA_st dev | outliers removed | averaged over | Neural Network | 0.81 | 0.45 | 0.43 | 0.42 | 0.45 | 0.30 | 0.84 |
| | | | | SVM | 0.81 | 0.46 | 0.44 | 0.43 | 0.46 | 0.31 | 0.84 |

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| | | | | Logistic Regression | 0.79 | 0.44 | 0.41 | 0.42 | 0.44 | 0.27 | 0.83 |
| | | | | Random Forest | 0.79 | 0.45 | 0.44 | 0.44 | 0.45 | 0.29 | 0.85 |
| | | | | Gradient Boosting | 0.78 | 0.46 | 0.46 | 0.46 | 0.46 | 0.31 | 0.85 |
| | | | | Naïve Bayes | 0.75 | 0.40 | 0.40 | 0.41 | 0.40 | 0.26 | 0.87 |
| | | | | kNN | 0.69 | 0.35 | 0.34 | 0.34 | 0.35 | 0.16 | 0.81 |
| | | | | AdaBoost | 0.63 | 0.41 | 0.41 | 0.42 | 0.41 | 0.25 | 0.85 |
| | | | | Tree | 0.61 | 0.35 | 0.35 | 0.35 | 0.35 | 0.18 | 0.83 |

Appendix 7: Visual acuity related classification model feature ranking

| Target | Feature group | dataset | class results | Feature | Info. gain | Gain ratio | Gini | ANOVA | $\chi^2$ | ReliefF | FCBF |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit | VA_st dev | full | averaged over classes | VA baseline visit (V0) | 0.037 | 0.019 | 0.025 | 18.653 | 12.562 | -0.006 | 0.025 |
| | | | | VA post loading (VP) | 0.037 | 0.018 | 0.025 | 16.245 | 13.595 | 0.010 | 0.000 |
| | | | | VA mean initial 2 visits post loading | 0.027 | 0.013 | 0.018 | 13.169 | 8.934 | 0.012 | 0.000 |
| | | | | Standard deviation of VA mean, post loading -12 months (VP-V12) | 0.025 | 0.013 | 0.017 | 8.783 | 8.029 | 0.014 | 0.017 |
| | | | | VA fellow eye (V0) | 0.007 | 0.003 | 0.005 | 0.196 | 1.070 | -0.005 | 0.000 |
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| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit | VA_st dev | outliers removed | averaged over classes | TW0OperVABestMeasure | 0.036 | 0.018 | 0.024 | 14.945 | 10.600 | 0.001 | 0.024 |
| | | | | VA initial post loading | 0.034 | 0.017 | 0.023 | 12.384 | 11.594 | 0.006 | 0.000 |
| | | | | Standard deviation of VA mean, post loading -12 months (VP-V12) | 0.029 | 0.015 | 0.020 | 10.780 | 7.973 | 0.012 | 0.020 |
| | | | | VA mean initial 2 visits post loading | 0.024 | 0.012 | 0.016 | 9.323 | 7.015 | 0.008 | 0.000 |
| | | | | VA fellow eye (V0) | 0.010 | 0.005 | 0.007 | 0.845 | 2.493 | -0.010 | 0.000 |
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| Change in VA post loading (month 4 - month 12), when considered as slope of line of best | VP_OCT | full | averaged over classes | VP_NFL 1mm CMT | 0.009 | 0.005 | 0.006 | 1.813 | 3.021 | 0.000 | 0.000 |
| | | | | VP_NFL 3mm vol | 0.007 | 0.004 | 0.005 | 1.046 | 1.793 | -0.002 | 0.000 |
| | | | | VP_RPE 3mm vol | 0.005 | 0.003 | 0.004 | 1.452 | 1.521 | 0.001 | 0.000 |
| | | | | VP_IPL 1mm CM vol | 0.008 | 0.006 | 0.005 | 2.650 | 1.423 | 0.001 | 0.000 |
| | | | | VP_ONL 1mm CMT | 0.007 | 0.003 | 0.005 | 0.727 | 1.401 | -0.003 | 0.000 |
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| Ch an | VP _ | ou ti | av er | VP_NFL 1mm CMT | 0.021 | 0.011 | 0.014 | 2.506 | 2.832 | 0.010 | 0.000 |

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| | | | | VP_ONL 1mm CMT | 0.007 | 0.004 | 0.005 | 2.519 | 1.661 | 0.002 | 0.000 |
| | | | | VP_NFL 3mm vol | 0.010 | 0.005 | 0.007 | 2.271 | 1.647 | 0.004 | 0.000 |
| | | | | VP_ONL 1mm CM vol | 0.006 | 0.003 | 0.004 | 1.928 | 1.401 | -0.005 | 0.000 |
| | | | | VP_IPL 1mm CM vol | 0.009 | 0.008 | 0.005 | 2.587 | 1.296 | 0.000 | 0.000 |
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| Change in VA post loading (month 4 - month 12), when considered as slope of line of best | V0_OCT | full | averaged over classes | V0_NFL 1mm CMT | 0.021 | 0.011 | 0.014 | 1.320 | 0.844 | 0.003 | 0.014 |
| | | | | V0_NFL 3mm vol | 0.020 | 0.010 | 0.014 | 1.194 | 3.649 | 0.003 | 0.000 |
| | | | | V0_OPL 1mm CM vol | 0.014 | 0.009 | 0.010 | 1.771 | 1.603 | -0.002 | 0.000 |
| | | | | V0_retina min CMT | 0.017 | 0.009 | 0.012 | 2.149 | 1.432 | 0.004 | 0.000 |
| | | | | V0_IPL 3mm vol | 0.015 | 0.008 | 0.010 | 1.216 | 1.906 | 0.005 | 0.000 |
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| Change in VA post loading (month 4 - month 12), when considered as slope of line of best | V0_OCT | outliers removed | averaged over classes | V0_retina 1mm CM vol | 0.017 | 0.008 | 0.012 | 2.847 | 4.409 | 0.000 | 0.000 |
| | | | | V0_NFL 3mm vol | 0.018 | 0.009 | 0.013 | 0.348 | 3.321 | 0.001 | 0.000 |
| | | | | V0_retina 1mm CMT | 0.026 | 0.013 | 0.018 | 2.579 | 2.488 | 0.000 | 0.018 |
| | | | | V0_retina 3mm vol | 0.009 | 0.005 | 0.006 | 2.443 | 1.785 | -0.002 | 0.000 |
| | | | | V0_retina min CMT | 0.012 | 0.006 | 0.008 | 2.797 | 1.764 | 0.005 | 0.000 |
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| Change in VA post loading (month 4 - month 12), when considered as slope | Demographic & qualitative | full | averaged over classes | Anti-VEGF drug type | 0.014 | 0.015 | 0.010 | NA | 0.211 | -0.008 | 0.015 |
| | | | | Time interval 1st to 3rd injection | 0.016 | 0.011 | 0.011 | NA | 0.342 | 0.003 | 0.000 |
| | | | | Ethnicity | 0.005 | 0.011 | 0.003 | NA | 0.012 | 0.012 | 0.000 |
| | | | | Age At First Injection | 0.017 | 0.009 | 0.012 | NA | 2.111 | 0.006 | 0.000 |
| | | | | Fellow eye activity | 0.013 | 0.008 | 0.009 | NA | 8.744 | -0.036 | 0.000 |
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| Change in VA post | Demographic & | outliers removed | averaged over | Fellow eye activity | 0.019 | 0.011 | 0.013 | NA | 11.328 | 0.100 | 0.000 |
| | | | | Age At First Injection | 0.019 | 0.010 | 0.013 | NA | 1.693 | -0.004 | 0.013 |
| | | | | Anti-VEGF drug type | 0.018 | 0.019 | 0.012 | NA | 0.345 | -0.020 | 0.019 |

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| | | | | Time interval 1st to 3rd injection | 0.020 | 0.013 | 0.013 | NA | 0.331 | -0.009 | 0.000 |
| | | | | Sex | 0.000 | 0.000 | 0.000 | NA | 0.100 | -0.016 | 0.000 |
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| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit | V0_OCTANE | full | averaged over classes | | Info. gain | Gain ratio | Gini | ANOVA | $\chi^2$ | ReliefF | FCBF |
| | | | | V0_vol_posterior_hyaloid | 0.039 | 0.019 | 0.026 | 3.648 | 3.321 | 0.020 | 0.026 |
| | | | | V0_vol_neurosensory_retina | 0.024 | 0.012 | 0.017 | 0.651 | 3.125 | 0.000 | 0.000 |
| | | | | V0_vol_epiretinal_membrane | 0.011 | 0.005 | 0.008 | 0.331 | 0.075 | 0.002 | 0.000 |
| | | | | V0_vol_subretinal_fluid | 0.011 | 0.005 | 0.007 | 0.937 | 0.439 | -0.011 | 0.000 |
| | | | | V0_vol_serous_ped | 0.009 | 0.005 | 0.006 | 0.093 | 0.029 | 0.007 | 0.000 |
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| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit | V0_OCTANE | outliers removed | averaged over classes | | Info. gain | Gain ratio | Gini | ANOVA | $\chi^2$ | ReliefF | FCBF |
| | | | | V0_vol_neurosensory_retina | 0.021 | 0.010 | 0.014 | 0.155 | 2.944 | -0.006 | 0.000 |
| | | | | V0_vol_fibrovascular_ped | 0.009 | 0.004 | 0.006 | 1.140 | 2.543 | -0.005 | 0.000 |
| | | | | V0_vol_posterior_hyaloid | 0.028 | 0.014 | 0.019 | 1.207 | 1.900 | -0.009 | 0.019 |
| | | | | V0_vol_drusenoid_ped | 0.007 | 0.004 | 0.005 | 0.308 | 1.214 | -0.009 | 0.000 |
| | | | | V0_vol_choroid_and_outer_layers | 0.002 | 0.001 | 0.001 | 0.112 | 0.424 | 0.015 | 0.000 |
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| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA | VP_OCTANE | full | averaged over classes | | Info. gain | Gain ratio | Gini | ANOVA | $\chi^2$ | ReliefF | FCBF |
| | | | | VP_vol_serous_ped | 0.047 | 0.024 | 0.032 | 0.331 | 0.001 | 0.005 | 0.033 |
| | | | | VP_vol_subretinal_fluid | 0.041 | 0.020 | 0.028 | 2.513 | 2.955 | 0.006 | 0.000 |
| | | | | VP_vol_posterior_hyaloid | 0.023 | 0.011 | 0.015 | 0.486 | 0.034 | 0.055 | 0.000 |
| | | | | VP_vol_intraretinal_fluid | 0.019 | 0.010 | 0.013 | 0.920 | 0.602 | -0.001 | 0.000 |
| | | | | VP_vol_neurosensory_retina | 0.012 | 0.006 | 0.008 | 3.788 | 3.725 | 0.004 | 0.000 |
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| Ch | VP | out | av | VP_vol_subretinal_fluid | 0.053 | 0.027 | 0.036 | 1.059 | 3.930 | -0.033 | 0.000 |

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| | | | | VP_vol_intraretinal_fluid | 0.034 | 0.017 | 0.023 | 2.399 | 2.351 | -0.007 | 0.000 |
| | | | | VP_vol_neurosensory_retina | 0.009 | 0.004 | 0.006 | 1.202 | 1.531 | -0.004 | 0.000 |
| | | | | VP_vol_drusenoid_ped | 0.022 | 0.011 | 0.015 | 0.136 | 0.878 | -0.007 | 0.000 |
| | | | | VP_vol_fibrovascular_ped | 0.007 | 0.004 | 0.005 | 1.671 | 0.633 | -0.025 | 0.000 |
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| Change in VA post loading (month 4 - month 12), when considered as slope | VA | full | averaged over classes | VA baseline visit (V0) | 0.037 | 0.019 | 0.025 | 18.653 | 12.562 | 0.006 | 0.025 |
| | | | | VA post loading (VP) | 0.037 | 0.018 | 0.025 | 16.245 | 13.595 | 0.010 | 0.000 |
| | | | | VA mean initial 2 visits post loading | 0.027 | 0.013 | 0.018 | 13.169 | 8.934 | 0.009 | 0.000 |
| | | | | VA fellow eye (V0) | 0.007 | 0.003 | 0.005 | 0.196 | 1.070 | 0.012 | 0.000 |
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| Change in VA post loading (month 4 - month 12), when considered as slope | VA | outliers removed | averaged over classes | VA baseline visit (V0) | 0.039 | 0.020 | 0.026 | 16.090 | 11.554 | -0.004 | 0.027 |
| | | | | VA post loading (VP) | 0.034 | 0.017 | 0.023 | 12.605 | 11.447 | 0.004 | 0.000 |
| | | | | VA mean initial 2 visits post loading | 0.028 | 0.014 | 0.019 | 9.677 | 7.794 | -0.001 | 0.000 |
| | | | | VA fellow eye (V0) | 0.011 | 0.005 | 0.008 | 1.041 | 2.924 | 0.003 | 0.000 |
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| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through | VA_st dev | full | averaged over classes | | Info. gain | Gain ratio | Gini | ANOVA | $\chi^2$ | ReliefF | FCBF |
| | | | | Standard deviation of VA mean, post loading -12 months (VP-V12) | 0.215 | 0.107 | 0.104 | 45.412 | 69.563 | 0.017 | 0.139 |
| | | | | VA post loading (VP) | 0.069 | 0.035 | 0.023 | 17.242 | 24.354 | 0.001 | 0.041 |
| | | | | VA mean initial 2 visits post loading | 0.057 | 0.029 | 0.020 | 17.502 | 20.583 | 0.004 | 0.000 |
| | | | | VA baseline visit (V0) | 0.056 | 0.028 | 0.018 | 13.935 | 19.850 | 0.009 | 0.000 |
| | | | | VA fellow eye (V0) | 0.023 | 0.011 | 0.008 | 0.892 | 3.760 | -0.001 | 0.000 |
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| Change in VA post | VA_st dev | outliers removed | averaged over classes | Standard deviation of VA mean, post loading -12 months (VP-V12) | 0.188 | 0.094 | 0.093 | 41.013 | 56.621 | 0.019 | 0.120 |
| | | | | VA post loading (VP) | 0.065 | 0.033 | 0.022 | 13.181 | 20.905 | 0.003 | 0.038 |

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| | | | | VA baseline visit (V0) | 0.059 | 0.030 | 0.020 | 13.505 | 19.041 | 0.004 | 0.000 |
| | | | | VA mean initial 2 visits post loading | 0.055 | 0.028 | 0.020 | 13.947 | 17.706 | 0.004 | 0.000 |
| | | | | VA fellow eye (V0) | 0.025 | 0.013 | 0.009 | 1.460 | 5.336 | 0.011 | 0.000 |
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| Change in VA post loading (month 4 - month 12), when considered as slope of line of best | V0_OCT | full | averaged over classes | V0_ONL min CMT | 0.032 | 0.016 | 0.012 | 0.474 | 0.480 | 0.011 | 0.018 |
| | | | | V0_NFL 1mm CMT | 0.031 | 0.015 | 0.015 | 1.720 | 1.425 | 0.001 | 0.018 |
| | | | | V0_INL min CMT | 0.030 | 0.015 | 0.013 | 1.169 | 0.092 | 0.003 | 0.000 |
| | | | | V0_RPE min CMT | 0.029 | 0.014 | 0.015 | 1.823 | 5.891 | 0.001 | 0.017 |
| | | | | V0_NFL min CMT | 0.019 | 0.014 | 0.007 | 1.146 | 4.119 | 0.000 | 0.000 |
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| Change in VA post loading (month 4 - month 12), when considered as slope of line of best | V0_OCT | outliers removed | averaged over classes | V0_ seg ERROR (2) | 0.019 | 0.012 | 0.008 | 3.554 | 8.090 | 0.010 | 0.013 |
| | | | | V0_IPL 3mm vol | 0.018 | 0.009 | 0.010 | 1.927 | 4.452 | -0.001 | 0.000 |
| | | | | V0_RPE min CMT | 0.026 | 0.013 | 0.013 | 0.679 | 4.447 | 0.007 | 0.015 |
| | | | | V0_retina 1mm CM vol | 0.016 | 0.008 | 0.007 | 1.628 | 4.347 | -0.003 | 0.000 |
| | | | | V0_OPL 3mm vol | 0.013 | 0.007 | 0.007 | 2.708 | 4.083 | -0.009 | 0.000 |
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| Change in VA post loading (month 4 - month 12), when considered as slope of line of best | VP_OCT | full | averaged over classes | VP_GCL min CMT | 0.017 | 0.011 | 0.009 | 2.358 | 7.107 | 0.003 | 0.000 |
| | | | | VP_NFL min CMT | 0.041 | 0.044 | 0.020 | 1.650 | 5.361 | 0.009 | 0.035 |
| | | | | VP_NFL 3mm vol | 0.027 | 0.014 | 0.013 | 0.339 | 3.676 | 0.001 | 0.000 |
| | | | | VP_IPL 3mm vol | 0.012 | 0.006 | 0.007 | 2.680 | 3.623 | 0.005 | 0.000 |
| | | | | VP_ORLs 1mm CM vol | 0.020 | 0.010 | 0.008 | 1.479 | 3.232 | 0.006 | 0.000 |
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| Change in VA post | VP_OCT | outliers removed | averaged over | VP_NFL min CMT | 0.037 | 0.045 | 0.018 | 1.943 | 6.917 | 0.004 | 0.032 |
| | | | | VP_GCL min CMT | 0.016 | 0.010 | 0.008 | 1.358 | 4.808 | -0.001 | 0.000 |
| | | | | VP_NFL 3mm vol | 0.029 | 0.015 | 0.014 | 0.467 | 4.389 | 0.003 | 0.000 |

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| | | | | VP_IPL 3mm vol | 0.011 | 0.005 | 0.006 | 1.840 | 3.087 | 0.004 | 0.000 |
| | | | | VP_IRLs 3mm vol | 0.021 | 0.010 | 0.010 | 1.051 | 2.704 | -0.005 | 0.000 |
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| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through | V0_OCTANE | full | averaged over classes | V0_vol_neurosensory_retina | 0.038 | 0.019 | 0.015 | 0.008 | 7.574 | 0.000 | 0.000 |
| | | | | V0_vol_vitreous_and_subhyaloid | 0.013 | 0.007 | 0.006 | 1.193 | 2.953 | -0.008 | 0.000 |
| | | | | V0_vol_intraretinal_fluid | 0.026 | 0.013 | 0.012 | 1.975 | 2.238 | -0.003 | 0.000 |
| | | | | V0_vol_fibrovascular_ped | 0.018 | 0.009 | 0.008 | 0.522 | 1.886 | -0.002 | 0.000 |
| | | | | V0_vol_posterior_hyaloid | 0.034 | 0.017 | 0.014 | 0.989 | 1.589 | 0.010 | 0.000 |
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| Change in VA post loading (month 4 - month 12), when considered as slope of line of best | V0_OCTANE | outliers removed | averaged over classes | V0_vol_neurosensory_retina | 0.032 | 0.016 | 0.014 | 0.005 | 4.241 | 0.003 | 0.000 |
| | | | | V0_vol_vitreous_and_subhyaloid | 0.022 | 0.011 | 0.009 | 1.511 | 3.812 | -0.004 | 0.000 |
| | | | | V0_vol_intraretinal_fluid | 0.032 | 0.016 | 0.015 | 2.010 | 2.380 | 0.002 | 0.000 |
| | | | | V0_vol_fibrovascular_ped | 0.024 | 0.012 | 0.010 | 0.308 | 1.440 | -0.013 | 0.000 |
| | | | | V0_vol_posterior_hyaloid | 0.055 | 0.028 | 0.024 | 0.559 | 1.164 | 0.005 | 0.000 |
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| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through | VP_OCTANE | full | averaged over classes | VP_vol_subretinal_fluid | 0.064 | 0.032 | 0.029 | 4.324 | 5.251 | 0.002 | 0.000 |
| | | | | VP_vol_rpe | 0.031 | 0.016 | 0.015 | 1.941 | 5.239 | 0.010 | 0.000 |
| | | | | VP_vol_neurosensory_retina | 0.024 | 0.012 | 0.010 | 2.291 | 4.868 | -0.001 | 0.000 |
| | | | | VP_vol_vitreous_and_subhyaloid | 0.037 | 0.019 | 0.018 | 0.364 | 1.148 | -0.001 | 0.000 |
| | | | | VP_vol_drusenoid_ped | 0.013 | 0.006 | 0.006 | 0.673 | 0.829 | -0.013 | 0.000 |
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| Change in VA post loading (month 4 - month 12), when considered as slope of line of best | VP_OCTANE | outliers removed | averaged over classes | VP_vol_rpe | 0.029 | 0.014 | 0.013 | 1.738 | 4.846 | 0.005 | 0.000 |
| | | | | VP_vol_subretinal_fluid | 0.082 | 0.041 | 0.036 | 3.286 | 4.073 | -0.009 | 0.000 |
| | | | | VP_vol_neurosensory_retina | 0.018 | 0.009 | 0.008 | 0.626 | 2.578 | 0.007 | 0.000 |
| | | | | VP_vol_drusenoid_ped | 0.018 | 0.009 | 0.009 | 0.507 | 1.375 | 0.009 | 0.000 |
| | | | | VP_vol_subretinal_hyper_reflect | 0.050 | 0.025 | 0.021 | 0.650 | 1.027 | 0.005 | 0.000 |
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| Change in VA post loading (month 4 - month 12), when considered as slope | Demographic & qualitative | full | averaged over classes | Ethnicity | 0.020 | 0.043 | 0.009 | NA | 0.267 | -0.037 | 0.021 |
| | | | | Fellow eye activity | 0.030 | 0.018 | 0.012 | NA | 12.883 | 0.063 | 0.000 |
| | | | | Anti-VEGF drug type | 0.014 | 0.015 | 0.006 | NA | 0.144 | 0.023 | 0.000 |
| | | | | Time interval 1st to 3rd injection | 0.019 | 0.012 | 0.006 | NA | 1.485 | 0.002 | 0.000 |
| | | | | Age At First Injection | 0.014 | 0.007 | 0.007 | NA | 1.638 | 0.013 | 0.000 |
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| Change in VA post loading (month 4 - month 12), when considered as slope | Demographic & qualitative | outliers removed | averaged over classes | Fellow eye activity | 0.031 | 0.018 | 0.013 | NA | 13.735 | -0.030 | 0.000 |
| | | | | Time interval 1st to 3rd injection | 0.018 | 0.012 | 0.007 | NA | 0.902 | 0.006 | 0.000 |
| | | | | Sex | 0.002 | 0.002 | 0.001 | NA | 0.625 | 0.007 | 0.000 |
| | | | | Age At First Injection | 0.012 | 0.006 | 0.006 | NA | 0.502 | 0.007 | 0.000 |
| | | | | Laterality | 0.002 | 0.002 | 0.001 | NA | 0.342 | -0.028 | 0.000 |
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| Change in VA post loading (month 4 - month 12), when considered as slope of line of best | VA | full | averaged over classes | VA post loading (VP) | 0.069 | 0.035 | 0.023 | 17.242 | 24.354 | 0.006 | 0.041 |
| | | | | VA mean initial 2 visits post loading | 0.057 | 0.029 | 0.020 | 17.502 | 20.583 | 0.005 | 0.000 |
| | | | | VA baseline visit (V0) | 0.056 | 0.028 | 0.018 | 13.935 | 19.850 | 0.016 | 0.000 |
| | | | | VA fellow eye (V0) | 0.023 | 0.011 | 0.008 | 0.892 | 3.760 | 0.012 | 0.013 |
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| Change in VA post | VA | outliers removed | averaged over | VA baseline visit (V0) | 0.062 | 0.031 | 0.019 | 13.127 | 19.695 | 0.012 | 0.037 |
| | | | | VA post loading (VP) | 0.059 | 0.030 | 0.019 | 11.409 | 18.819 | 0.007 | 0.000 |
| | | | | VA mean initial 2 visits post loading | 0.045 | 0.023 | 0.016 | 11.773 | 13.680 | 0.004 | 0.000 |

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| | | | | VA fellow eye (V0) | 0.027 | 0.014 | 0.010 | 1.660 | 6.223 | 0.011 | 0.000 |
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| Change in visual acuity over 12 months when considered as slope of line of best fit through | V0_OCT | full | averaged over classes | V0_OPL 1mm CM vol | 0.048 | 0.030 | 0.019 | 3.639 | 5.498 | 0.014 | 0.031 |
| | | | | V0_NFL min CMT | 0.034 | 0.026 | 0.015 | 2.563 | 15.890 | 0.001 | 0.000 |
| | | | | V0_GCL 1mm CM vol | 0.033 | 0.021 | 0.009 | 2.753 | 4.764 | -0.003 | 0.000 |
| | | | | V0_OPL 1mm CMT | 0.037 | 0.019 | 0.015 | 2.922 | 9.410 | 0.007 | 0.000 |
| | | | | V0_retina min CMT | 0.035 | 0.017 | 0.014 | 4.933 | 8.067 | 0.001 | 0.000 |
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| Change in visual acuity over 12 months when considered as slope of line of best fit | V0_OCT | outliers removed | averaged over classes | V0_NFL min CMT | 0.040 | 0.030 | 0.017 | 3.825 | 14.499 | 0.009 | 0.000 |
| | | | | V0_GCL min CMT | 0.022 | 0.013 | 0.010 | 3.440 | 9.981 | 0.000 | 0.000 |
| | | | | V0_OPL 1mm CMT | 0.037 | 0.018 | 0.015 | 2.599 | 8.493 | -0.004 | 0.000 |
| | | | | V0_retina 1mm CM vol | 0.018 | 0.009 | 0.007 | 2.806 | 5.884 | 0.003 | 0.000 |
| | | | | V0_OPL 1mm CM vol | 0.045 | 0.029 | 0.018 | 3.613 | 5.384 | 0.008 | 0.029 |
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| Change in visual acuity over 12 months when considered as slope of line of best fit through | VP_OCT | full | averaged over classes | VP_NFL 1mm CM vol | 0.018 | 0.032 | 0.006 | 0.530 | 0.201 | 0.001 | 0.017 |
| | | | | VP_NFL min CMT | 0.012 | 0.014 | 0.005 | 0.343 | 1.296 | 0.001 | 0.000 |
| | | | | VP_OPL 1mm CM vol | 0.018 | 0.013 | 0.008 | 3.281 | 2.511 | 0.005 | 0.000 |
| | | | | VP_RPE 3mm vol | 0.026 | 0.013 | 0.010 | 1.439 | 6.881 | -0.001 | 0.000 |
| | | | | VP_ONL 1mm CM vol | 0.025 | 0.013 | 0.010 | 0.801 | 0.446 | 0.000 | 0.000 |
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| Change in visual acuity over 12 | VP_OCT | outliers removed | averaged over classes | VP_RPE 3mm vol | 0.028 | 0.014 | 0.011 | 2.207 | 5.945 | 0.005 | 0.016 |
| | | | | VP_IRLs 3mm vol | 0.020 | 0.010 | 0.009 | 3.344 | 5.115 | 0.008 | 0.000 |
| | | | | VP_OPL 1mm CMT | 0.015 | 0.008 | 0.008 | 3.882 | 4.483 | 0.003 | 0.000 |
| | | | | VP_OPL min CMT | 0.015 | 0.007 | 0.007 | 2.022 | 4.213 | -0.004 | 0.000 |

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| | | | | VP_ORLs 3mm vol | 0.019 | 0.010 | 0.008 | 2.232 | 3.644 | 0.007 | 0.000 |
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| Change in visual acuity over 12 months when considered as slope of line of best fit through VA | V0_OCTANE | full | averaged over classes | V0_vol_serous_ped | 0.131 | 0.066 | 0.055 | 2.291 | 1.054 | -0.014 | 0.080 |
| | | | | V0_vol_epiretinal_membrane | 0.050 | 0.025 | 0.023 | 0.799 | 0.736 | 0.003 | 0.000 |
| | | | | V0_vol_intraretinal_fluid | 0.042 | 0.021 | 0.019 | 0.570 | 1.735 | 0.003 | 0.000 |
| | | | | V0_vol_neurosensory_retina | 0.036 | 0.018 | 0.017 | 0.334 | 5.583 | -0.002 | 0.000 |
| | | | | V0_vol_subretinal_hyper_reflect | 0.025 | 0.013 | 0.011 | 1.468 | 2.892 | -0.021 | 0.000 |
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| Change in visual acuity over 12 months when considered as slope of line of best fit through | V0_OCTANE | outliers removed | averaged over classes | V0_vol_neurosensory_retina | 0.031 | 0.015 | 0.014 | 0.120 | 4.755 | -0.003 | 0.000 |
| | | | | V0_vol_subretinal_hyper_reflect | 0.031 | 0.016 | 0.014 | 1.732 | 4.613 | 0.000 | 0.000 |
| | | | | V0_vol_vitreous_and_subhyaloid | 0.055 | 0.027 | 0.028 | 0.802 | 2.627 | -0.011 | 0.000 |
| | | | | V0_vol_intraretinal_fluid | 0.051 | 0.026 | 0.024 | 0.815 | 1.983 | -0.011 | 0.000 |
| | | | | V0_vol_rpe | 0.019 | 0.010 | 0.008 | 0.458 | 0.782 | -0.007 | 0.000 |
| | | | | V0_vol_choroid_and_outer_layers | 0.015 | 0.007 | 0.006 | 0.733 | 0.626 | 0.023 | 0.000 |
| | | | | V0_vol_fibrovascular_ped | 0.026 | 0.013 | 0.013 | 0.580 | 0.606 | 0.005 | 0.000 |
| | | | | V0_vol_serous_ped | 0.113 | 0.057 | 0.044 | 0.659 | 0.524 | -0.015 | 0.067 |
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| Change in visual acuity over 12 months when considered as slope of line of best fit through VA | VP_OCTANE | full | averaged over classes | VP_vol_serous_ped | 0.073 | 0.037 | 0.033 | 0.277 | 0.003 | 0.005 | 0.043 |
| | | | | VP_vol_drusenoid_ped | 0.037 | 0.018 | 0.016 | 1.184 | 5.003 | -0.004 | 0.000 |
| | | | | VP_vol_subretinal_fluid | 0.035 | 0.018 | 0.016 | 2.212 | 2.633 | 0.025 | 0.000 |
| | | | | VP_vol_neurosensory_retina | 0.028 | 0.014 | 0.011 | 3.810 | 4.726 | 0.001 | 0.000 |
| | | | | VP_vol_posterior_hyaloid | 0.028 | 0.014 | 0.013 | 0.076 | 0.788 | -0.027 | 0.000 |
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| Change in | VP_OCTANE | outliers | averaged | VP_vol_rpe | 0.015 | 0.007 | 0.007 | 2.396 | 4.953 | -0.009 | 0.000 |
| | | | | VP_vol_drusenoid_ped | 0.038 | 0.019 | 0.017 | 1.088 | 4.901 | -0.002 | 0.000 |

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| | | | | VP_vol_choroid_and_outer_layers | 0.026 | 0.013 | 0.011 | 0.569 | 2.249 | 0.002 | 0.000 |
| | | | | VP_vol_neurosensory_retina | 0.018 | 0.009 | 0.007 | 1.348 | 1.862 | 0.004 | 0.000 |
| | | | | VP_vol_intraretinal_fluid | 0.041 | 0.020 | 0.018 | 0.227 | 1.600 | -0.004 | 0.000 |
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| Change in visual acuity over 12 months when considered as slope of line of best fit through | Demographic & qualitative | full | averaged over classes | Fellow eye activity | 0.054 | 0.031 | 0.024 | NA | 12.820 | 0.044 | 0.034 |
| | | | | Time interval 1st to 3rd injection | 0.049 | 0.031 | 0.018 | NA | 4.638 | -0.004 | 0.032 |
| | | | | Ethnicity | 0.011 | 0.023 | 0.005 | NA | 0.052 | -0.004 | 0.000 |
| | | | | Age At First Injection | 0.025 | 0.012 | 0.010 | NA | 4.557 | -0.008 | 0.000 |
| | | | | Anti-VEGF drug type | 0.011 | 0.012 | 0.004 | NA | 0.030 | 0.013 | 0.000 |
| | | | | Laterality | 0.005 | 0.005 | 0.002 | NA | 1.169 | 0.011 | 0.000 |
| | | | | Sex | 0.001 | 0.002 | 0.001 | NA | 0.462 | 0.024 | 0.000 |
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| Change in visual acuity over 12 months when considered as slope of line of best fit through | Demographic & qualitative | outliers removed | averaged over classes | Fellow eye activity | 0.055 | 0.032 | 0.024 | NA | 14.657 | -0.011 | 0.034 |
| | | | | Age At First Injection | 0.018 | 0.009 | 0.008 | NA | 3.006 | -0.007 | 0.000 |
| | | | | Time interval 1st to 3rd injection | 0.044 | 0.029 | 0.017 | NA | 2.701 | -0.004 | 0.029 |
| | | | | Sex | 0.005 | 0.006 | 0.002 | NA | 1.399 | 0.005 | 0.000 |
| | | | | Laterality | 0.006 | 0.006 | 0.003 | NA | 1.259 | 0.008 | 0.000 |
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| Change in visual acuity over 12 months when considered as slope of line of best fit through | VA | full | averaged over classes | VA baseline visit (V0) | 0.113 | 0.056 | 0.047 | 28.070 | 39.263 | 0.017 | 0.068 |
| | | | | VA fellow eye (V0) | 0.026 | 0.013 | 0.012 | 0.833 | 4.138 | 0.007 | 0.000 |
| | | | | VA post loading (VP) | 0.017 | 0.009 | 0.008 | 2.573 | 4.023 | -0.002 | 0.000 |
| | | | | VA mean initial 2 visits post loading | 0.010 | 0.005 | 0.005 | 2.062 | 1.937 | -0.003 | 0.000 |
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| Change in visual acuity over 12 months when considered as slope of line of best fit | VA | outliers removed | averaged over classes | VA baseline visit (V0) | 0.095 | 0.048 | 0.039 | 20.808 | 29.668 | 0.023 | 0.056 |
| | | | | VA fellow eye (V0) | 0.031 | 0.016 | 0.013 | 1.738 | 7.535 | 0.003 | 0.000 |
| | | | | VA post loading (VP) | 0.013 | 0.006 | 0.006 | 1.053 | 2.748 | -0.001 | 0.000 |
| | | | | VA mean initial 2 visits post loading | 0.012 | 0.006 | 0.005 | 0.933 | 1.817 | -0.004 | 0.000 |
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| Change in visual acuity over 12 months when considered as slope of line of best fit through VA | VA_st dev | full | averaged over classes | Standard deviation of VA mean, post loading -12 months (VP-V12) | 0.147 | 0.073 | 0.064 | 36.338 | 46.304 | 0.026 | 0.090 |
| | | | | VA baseline visit (V0) | 0.113 | 0.056 | 0.047 | 28.070 | 39.263 | 0.027 | 0.068 |
| | | | | VA fellow eye (V0) | 0.026 | 0.013 | 0.012 | 0.833 | 4.138 | 0.010 | 0.000 |
| | | | | VA post loading (VP) | 0.017 | 0.009 | 0.008 | 2.573 | 4.023 | -0.003 | 0.000 |
| | | | | VA mean initial 2 visits post loading | 0.010 | 0.005 | 0.005 | 2.062 | 1.937 | 0.004 | 0.000 |
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| Change in visual acuity over 12 months when considered as slope of line of best fit through | VA_st dev | outliers removed | averaged over classes | Standard deviation of VA mean, post loading -12 months (VP-V12) | 0.159 | 0.079 | 0.070 | 39.496 | 45.310 | 0.013 | 0.098 |
| | | | | VA baseline visit (V0) | 0.098 | 0.049 | 0.041 | 22.739 | 30.967 | 0.025 | 0.058 |
| | | | | VA fellow eye (V0) | 0.027 | 0.013 | 0.012 | 1.322 | 5.498 | 0.008 | 0.000 |
| | | | | VA mean initial 2 visits post loading | 0.015 | 0.007 | 0.007 | 1.461 | 1.585 | 0.009 | 0.000 |
| | | | | VA post loading (VP) | 0.013 | 0.006 | 0.006 | 1.426 | 2.961 | 0.009 | 0.000 |
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| Change in visual acuity over 12 months when considered as slope | V0_OCT | full | averaged over classes | V0_OPL 1mm CM vol | 0.030 | 0.019 | 0.020 | 7.752 | 5.036 | 0.008 | 0.024 |
| | | | | V0_retina 1mm CM vol | 0.035 | 0.017 | 0.024 | 3.876 | 11.499 | -0.005 | 0.000 |
| | | | | V0_OPL 1mm CMT | 0.033 | 0.017 | 0.022 | 6.307 | 6.135 | 0.001 | 0.000 |
| | | | | V0_retina 1mm CMT | 0.033 | 0.017 | 0.023 | 3.651 | 10.123 | -0.006 | 0.000 |
| | | | | V0_retina min CMT | 0.030 | 0.015 | 0.020 | 6.490 | 8.371 | -0.004 | 0.000 |
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| Change in visual acuity over 12 months when considered as slope of line of best fit | V0_OCT | outliers removed | averaged over classes | V0_retina 1mm CM vol | 0.033 | 0.017 | 0.023 | 6.936 | 11.689 | 0.006 | 0.000 |
| | | | | V0_NFL min CMT | 0.019 | 0.015 | 0.013 | 5.163 | 10.755 | 0.005 | 0.000 |
| | | | | V0_retina min CMT | 0.026 | 0.013 | 0.018 | 7.899 | 7.353 | 0.006 | 0.000 |
| | | | | V0_retina 1mm CMT | 0.037 | 0.018 | 0.025 | 6.511 | 6.318 | 0.003 | 0.000 |
| | | | | V0_GCL min CMT | 0.011 | 0.006 | 0.007 | 7.361 | 6.001 | 0.000 | 0.000 |
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| Change in visual acuity over 12 months when considered as slope of line of best fit through | VP_OCT | full | averaged over classes | VP_NFL min CMT | 0.016 | 0.017 | 0.010 | 0.245 | 0.976 | 0.007 | 0.017 |
| | | | | VP_RPE 3mm vol | 0.019 | 0.009 | 0.013 | 3.393 | 3.203 | -0.003 | 0.000 |
| | | | | VP_IRLs min CMT | 0.018 | 0.009 | 0.013 | 3.128 | 2.105 | -0.005 | 0.000 |
| | | | | VP_IRLs 1mm CM vol | 0.016 | 0.008 | 0.011 | 0.686 | 1.387 | 0.002 | 0.000 |
| | | | | VP_ONL 1mm CM vol | 0.016 | 0.008 | 0.011 | 0.560 | 0.067 | 0.001 | 0.000 |
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| Change in visual acuity over 12 months when considered as slope of line of best fit | VP_OCT | outliers removed | averaged over classes | VP_INL 1mm CMT | 0.012 | 0.006 | 0.008 | 4.986 | 4.262 | 0.001 | 0.000 |
| | | | | VP_IPL min CMT | 0.010 | 0.005 | 0.007 | 5.172 | 3.528 | -0.007 | 0.000 |
| | | | | VP_INL min CMT | 0.009 | 0.004 | 0.006 | 2.078 | 3.303 | 0.006 | 0.000 |
| | | | | VP_GCL min CMT | 0.005 | 0.004 | 0.004 | 0.268 | 2.921 | -0.001 | 0.000 |
| | | | | VP_IRLs min CMT | 0.017 | 0.008 | 0.011 | 4.347 | 2.916 | 0.005 | 0.000 |
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| Change in visual acuity over 12 months when considered as slope of | V0_OCTANE | full | averaged over classes | V0_vol_neurosensory_retina | 0.050 | 0.025 | 0.031 | 0.629 | 3.880 | 0.001 | 0.035 |
| | | | | V0_vol_posterior_hyaloid | 0.017 | 0.008 | 0.011 | 0.832 | 0.636 | 0.035 | 0.000 |
| | | | | V0_vol_serous_ped | 0.013 | 0.007 | 0.009 | 0.575 | 0.147 | -0.021 | 0.000 |
| | | | | V0_vol_vitreous_and_subhyaloid | 0.011 | 0.005 | 0.007 | 0.965 | 0.605 | -0.013 | 0.007 |
| | | | | V0_vol_intraretinal_fluid | 0.011 | 0.005 | 0.007 | 0.495 | 0.112 | -0.007 | 0.000 |
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| Change in visual acuity over 12 months when considered as slope of line of best fit through | V0_OCTANE | outliers removed | averaged over classes | V0_vol_neurosensory_retina | 0.036 | 0.018 | 0.023 | 0.258 | 4.526 | 0.004 | 0.025 |
| | | | | V0_vol_subretinal_fluid | 0.007 | 0.004 | 0.005 | 0.922 | 1.275 | 0.007 | 0.000 |
| | | | | V0_vol_subretinal_hyper_reflect | 0.004 | 0.002 | 0.003 | 0.004 | 0.795 | 0.015 | 0.000 |
| | | | | V0_vol_vitreous_and_subhyaloid | 0.015 | 0.007 | 0.010 | 0.986 | 0.742 | 0.008 | 0.010 |
| | | | | V0_vol_fibrovascular_ped | 0.002 | 0.001 | 0.001 | 0.067 | 0.499 | 0.003 | 0.000 |
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| Change in visual acuity over 12 months when considered as slope of line of best fit through VA | VP_OCTANE | full | averaged over classes | VP_vol_serous_ped | 0.164 | 0.082 | 0.105 | 0.687 | 0.092 | -0.014 | 0.123 |
| | | | | VP_vol_vitreous_and_subhyaloid | 0.024 | 0.012 | 0.016 | 0.326 | 0.090 | -0.012 | 0.000 |
| | | | | VP_vol_drusenoid_ped | 0.024 | 0.012 | 0.016 | 0.013 | 1.685 | 0.005 | 0.000 |
| | | | | VP_vol_subretinal_fluid | 0.015 | 0.007 | 0.010 | 2.172 | 2.348 | 0.029 | 0.000 |
| | | | | VP_vol_neurosensory_retina | 0.015 | 0.007 | 0.010 | 4.966 | 3.297 | -0.002 | 0.000 |
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| Change in visual acuity over 12 months when considered as slope of line of best fit | VP_OCTANE | outliers removed | averaged over classes | VP_vol_rpe | 0.018 | 0.009 | 0.012 | 3.415 | 5.329 | 0.017 | 0.000 |
| | | | | VP_vol_intraretinal_fluid | 0.013 | 0.006 | 0.009 | 0.896 | 2.236 | 0.009 | 0.000 |
| | | | | VP_vol_neurosensory_retina | 0.011 | 0.005 | 0.007 | 1.941 | 2.046 | 0.010 | 0.000 |
| | | | | VP_vol_subretinal_fluid | 0.021 | 0.011 | 0.014 | 0.830 | 1.730 | 0.008 | 0.000 |
| | | | | VP_vol_drusenoid_ped | 0.024 | 0.012 | 0.017 | 0.000 | 1.639 | 0.008 | 0.000 |
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| Change in visual acuity over 12 months when | Demographic & qualitative | full | averaged over classes | Ethnicity | 0.012 | 0.026 | 0.007 | NA | 0.163 | -0.006 | 0.000 |
| | | | | Fellow eye activity | 0.027 | 0.016 | 0.018 | NA | 6.259 | -0.046 | 0.020 |
| | | | | Time interval 1st to 3rd injection | 0.020 | 0.013 | 0.012 | NA | 2.235 | 0.003 | 0.016 |
| | | | | Age At First Injection | 0.019 | 0.010 | 0.013 | NA | 5.747 | 0.003 | 0.000 |
| | | | | Anti-VEGF drug type | 0.004 | 0.004 | 0.003 | NA | 0.020 | 0.038 | 0.000 |
| | | | | Sex | 0.000 | 0.000 | 0.000 | NA | 0.136 | 0.010 | 0.000 |

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| | | | | Laterality | 0.000 | 0.000 | 0.000 | NA | 0.007 | -0.006 | 0.000 |
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| Change in visual acuity over 12 months when considered as slope of line of best fit through | Demographic & qualitative | outliers removed | averaged over classes | Fellow eye activity | 0.021 | 0.012 | 0.014 | NA | 4.221 | -0.008 | 0.015 |
| | | | | Age At First Injection | 0.009 | 0.005 | 0.006 | NA | 1.889 | 0.010 | 0.000 |
| | | | | Time interval 1st to 3rd injection | 0.024 | 0.016 | 0.014 | NA | 1.206 | 0.000 | 0.019 |
| | | | | Ethnicity | 0.011 | 0.022 | 0.007 | NA | 0.125 | 0.004 | 0.000 |
| | | | | Laterality | 0.000 | 0.000 | 0.000 | NA | 0.053 | -0.002 | 0.000 |
| | | | | Anti-VEGF drug type | 0.005 | 0.005 | 0.003 | NA | 0.052 | -0.018 | 0.000 |
| | | | | Sex | 0.000 | 0.000 | 0.000 | NA | 0.015 | 0.014 | 0.000 |
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| Change in visual acuity over 12 months when considered as slope of line of best fit | VA | full | averaged over classes | VA baseline visit (V0) | 0.052 | 0.026 | 0.035 | 27.851 | 18.787 | 0.015 | 0.036 |
| | | | | VA fellow eye (V0) | 0.029 | 0.014 | 0.020 | 6.249 | 9.083 | 0.012 | 0.019 |
| | | | | VA post loading (VP) | 0.004 | 0.002 | 0.003 | 0.394 | 0.229 | 0.000 | 0.000 |
| | | | | VA mean initial 2 visits post loading | 0.001 | 0.001 | 0.001 | 0.016 | 0.291 | 0.006 | 0.000 |
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| Change in visual acuity over 12 months when considered as slope of line of best fit | VA | outliers removed | averaged over classes | VA baseline visit (V0) | 0.055 | 0.027 | 0.037 | 27.070 | 18.240 | 0.019 | 0.038 |
| | | | | VA fellow eye (V0) | 0.038 | 0.019 | 0.026 | 8.891 | 11.483 | 0.003 | 0.026 |
| | | | | VA post loading (VP) | 0.002 | 0.001 | 0.001 | 0.359 | 0.460 | 0.002 | 0.000 |
| | | | | VA mean initial 2 visits post loading | 0.001 | 0.000 | 0.001 | 0.056 | 0.182 | 0.003 | 0.000 |
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| Change in visual acuity over 12 months when | VA_st dev | full | averaged over classes | VA baseline visit (V0) | 0.052 | 0.026 | 0.035 | 27.851 | 18.787 | 0.015 | 0.036 |
| | | | | Standard deviation of VA mean, post loading -12 months (VP-V12) | 0.048 | 0.024 | 0.032 | 18.548 | 17.243 | 0.020 | 0.033 |
| | | | | VA fellow eye (V0) | 0.029 | 0.014 | 0.020 | 6.249 | 9.083 | 0.013 | 0.019 |
| | | | | VA post loading (VP) | 0.004 | 0.002 | 0.003 | 0.394 | 0.229 | 0.011 | 0.000 |
| | | | | VA mean initial 2 visits post loading | 0.001 | 0.001 | 0.001 | 0.016 | 0.291 | 0.012 | 0.000 |

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| Change in visual acuity over 12 months when considered as slope of line of best fit through | VA_st dev | outliers removed | averaged over classes | VA baseline visit (V0) | 0.055 | 0.027 | 0.037 | 27.008 | 18.240 | 0.021 | 0.038 |
| | | | | Standard deviation of VA mean, post loading -12 months (VP-V12) | 0.048 | 0.024 | 0.032 | 22.222 | 15.524 | 0.020 | 0.033 |
| | | | | VA fellow eye (V0) | 0.033 | 0.017 | 0.023 | 7.392 | 9.319 | 0.014 | 0.023 |
| | | | | VA mean initial 2 visits post loading | 0.002 | 0.001 | 0.001 | 0.197 | 0.278 | 0.003 | 0.000 |
| | | | | VA post loading (VP) | 0.001 | 0.001 | 0.001 | 0.206 | 0.272 | 0.001 | 0.000 |
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| Change in VA, baseline - month 12 (categories: VA gained, maintained, lost) | V0_OCT | full | averaged over classes | V0_OPL 1mm CM vol | 0.050 | 0.032 | 0.024 | 5.549 | 6.886 | 0.004 | 0.033 |
| | | | | V0_GCL 1mm CM vol | 0.040 | 0.025 | 0.014 | 4.981 | 8.367 | 0.000 | 0.000 |
| | | | | V0_OPL 1mm CMT | 0.048 | 0.024 | 0.021 | 5.106 | 13.722 | 0.001 | 0.000 |
| | | | | V0_IPL 1mm CM vol | 0.037 | 0.023 | 0.016 | 4.652 | 7.623 | 0.002 | 0.000 |
| | | | | V0_retina 1mm CM vol | 0.045 | 0.022 | 0.022 | 4.978 | 14.708 | 0.001 | 0.000 |
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| Change in VA, baseline - month 12 (categories: VA gained, maintained, lost) | V0_OCT | outliers removed | averaged over classes | V0_OPL 1mm CMT | 0.052 | 0.026 | 0.023 | 5.013 | 13.750 | 0.007 | 0.000 |
| | | | | V0_NFL min CMT | 0.036 | 0.027 | 0.017 | 2.874 | 13.066 | 0.004 | 0.000 |
| | | | | V0_retina 1mm CM vol | 0.037 | 0.019 | 0.018 | 6.856 | 12.499 | 0.006 | 0.000 |
| | | | | V0_GCL min CMT | 0.031 | 0.018 | 0.015 | 5.160 | 10.708 | 0.005 | 0.000 |
| | | | | V0_retina min CMT | 0.034 | 0.017 | 0.016 | 7.570 | 10.531 | 0.004 | 0.000 |
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| Change in VA, baseline - month 12 | VP_OCT | full | averaged over classes | VP_NFL 1mm CM vol | 0.026 | 0.046 | 0.010 | 0.006 | 0.359 | 0.001 | 0.025 |
| | | | | VP_RPE 3mm vol | 0.040 | 0.020 | 0.019 | 2.800 | 10.633 | 0.001 | 0.000 |
| | | | | VP_IRLs min CMT | 0.032 | 0.016 | 0.014 | 3.703 | 6.262 | 0.009 | 0.000 |
| | | | | VP_ONL 1mm CM vol | 0.030 | 0.015 | 0.014 | 2.031 | 3.086 | 0.009 | 0.000 |
| | | | | VP_NFL min CMT | 0.012 | 0.013 | 0.005 | 0.048 | 0.041 | 0.002 | 0.000 |

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| Change in VA, baseline - month 12 (categories: VA gained, maintained, lost) | VP_OCT | outliers removed | averaged over classes | VP_RPE 3mm vol | 0.041 | 0.020 | 0.019 | 2.787 | 8.664 | 0.000 | 0.023 |
| | | | | VP_IRLs min CMT | 0.030 | 0.015 | 0.013 | 4.116 | 5.922 | 0.000 | 0.000 |
| | | | | VP_ORLs 3mm vol | 0.023 | 0.011 | 0.010 | 2.748 | 5.288 | -0.002 | 0.000 |
| | | | | VP_IPL min CMT | 0.021 | 0.011 | 0.010 | 3.818 | 4.686 | 0.012 | 0.000 |
| | | | | VP_ORLs min CMT | 0.010 | 0.005 | 0.004 | 0.871 | 2.674 | 0.000 | 0.000 |
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| Change in VA, baseline - month 12 (categories: VA gained, maintained, lost) | V0_OCTANE | full | averaged over classes | V0_vol_serous_ped | 0.086 | 0.043 | 0.033 | 0.711 | 0.417 | -0.006 | 0.051 |
| | | | | V0_vol_epiretinal_membrane | 0.041 | 0.021 | 0.018 | 0.631 | 0.285 | 0.017 | 0.000 |
| | | | | V0_vol_intraretinal_fluid | 0.037 | 0.019 | 0.018 | 1.934 | 1.411 | -0.004 | 0.000 |
| | | | | V0_vol_subretinal_hyper_reflect | 0.028 | 0.014 | 0.015 | 1.807 | 7.027 | 0.007 | 0.000 |
| | | | | V0_vol_neurosensory_retina | 0.028 | 0.014 | 0.013 | 1.432 | 2.302 | 0.003 | 0.000 |
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| Change in VA, baseline - month 12 (categories: VA gained, maintained, lost) | V0_OCTANE | outliers removed | averaged over classes | V0_vol_subretinal_hyper_reflect | 0.033 | 0.016 | 0.017 | 1.661 | 8.152 | 0.014 | 0.000 |
| | | | | V0_vol_neurosensory_retina | 0.023 | 0.011 | 0.010 | 1.054 | 3.404 | 0.007 | 0.000 |
| | | | | V0_vol_vitreous_and_subhyaloid | 0.016 | 0.008 | 0.008 | 0.559 | 2.954 | -0.007 | 0.000 |
| | | | | V0_vol_rpe | 0.024 | 0.012 | 0.010 | 1.297 | 2.403 | 0.000 | 0.000 |
| | | | | V0_vol_drusenoid_ped | 0.020 | 0.010 | 0.009 | 2.380 | 1.693 | 0.006 | 0.000 |
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| Change in VA, baseline - month 12 | VP_OCTANE | full | averaged over classes | VP_vol_serous_ped | 0.230 | 0.115 | 0.091 | 0.319 | 0.049 | 0.002 | 0.150 |
| | | | | VP_vol_fibrovascular_ped | 0.041 | 0.020 | 0.018 | 1.058 | 2.845 | 0.021 | 0.000 |
| | | | | VP_vol_intraretinal_fluid | 0.039 | 0.020 | 0.016 | 1.966 | 5.092 | -0.004 | 0.000 |
| | | | | VP_vol_neurosensory_retina | 0.038 | 0.019 | 0.013 | 3.638 | 2.961 | 0.005 | 0.000 |
| | | | | VP_vol_epiretinal_membrane | 0.037 | 0.018 | 0.015 | 0.125 | 0.259 | 0.030 | 0.000 |

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| Change in VA, baseline - month 12 (categories: VA gained, maintained, lost) | VP_OCTANE | outliers removed | averaged over classes | VP_vol_rpe | 0.016 | 0.008 | 0.008 | 1.940 | 8.343 | 0.004 | 0.000 |
| | | | | VP_vol_intraretinal_fluid | 0.058 | 0.029 | 0.024 | 1.464 | 4.147 | 0.019 | 0.000 |
| | | | | VP_vol_fibrovascular_ped | 0.038 | 0.019 | 0.016 | 1.422 | 3.743 | 0.010 | 0.000 |
| | | | | VP_vol_drusenoid_ped | 0.027 | 0.013 | 0.012 | 0.495 | 3.474 | 0.003 | 0.000 |
| | | | | VP_vol_vitreous_and_subhyaloid | 0.026 | 0.013 | 0.010 | 0.414 | 3.119 | 0.003 | 0.000 |
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| Change in VA, baseline - month 12 (categories: VA gained, maintained, lost) | Demographic & qualitative | full | averaged over classes | Fellow eye activity | 0.072 | 0.042 | 0.035 | NA | 22.308 | 0.039 | 0.046 |
| | | | | Time interval 1st to 3rd injection | 0.059 | 0.038 | 0.022 | NA | 5.911 | 0.000 | 0.039 |
| | | | | Ethnicity | 0.012 | 0.025 | 0.005 | NA | 0.108 | 0.007 | 0.000 |
| | | | | Age At First Injection | 0.022 | 0.011 | 0.011 | NA | 4.391 | 0.002 | 0.000 |
| | | | | Anti-VEGF drug type | 0.010 | 0.011 | 0.004 | NA | 0.086 | -0.007 | 0.000 |
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| Change in VA, baseline - month 12 (categories: VA gained, maintained, lost) | Demographic & qualitative | outliers removed | averaged over classes | Fellow eye activity | 0.065 | 0.038 | 0.032 | NA | 19.355 | 0.018 | 0.041 |
| | | | | Time interval 1st to 3rd injection | 0.049 | 0.033 | 0.017 | NA | 3.401 | -0.004 | 0.033 |
| | | | | Age At First Injection | 0.016 | 0.008 | 0.008 | NA | 1.764 | -0.001 | 0.000 |
| | | | | Sex | 0.002 | 0.002 | 0.001 | NA | 0.576 | 0.035 | 0.000 |
| | | | | Laterality | 0.003 | 0.003 | 0.001 | NA | 0.531 | 0.000 | 0.000 |
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| Change in VA, baseline - | VA | full | averaged over classes | VA baseline visit (V0) | 0.109 | 0.055 | 0.053 | 29.100 | 39.660 | 0.029 | 0.065 |
| | | | | VA fellow eye (V0) | 0.038 | 0.019 | 0.017 | 1.951 | 9.219 | 0.006 | 0.022 |
| | | | | VA post loading (VP) | 0.007 | 0.003 | 0.003 | 1.362 | 1.248 | 0.000 | 0.000 |
| | | | | VA mean initial 2 visits post loading | 0.007 | 0.003 | 0.003 | 2.419 | 1.971 | 0.008 | 0.000 |

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| Change in VA, baseline - month 12 (categories: VA gained, maintained, lost) | VA | outliers removed | averaged over classes | VA baseline visit (V0) | 0.089 | 0.044 | 0.043 | 20.711 | 29.401 | 0.034 | 0.053 |
| | | | | VA fellow eye (V0) | 0.047 | 0.024 | 0.022 | 3.289 | 11.754 | -0.005 | 0.027 |
| | | | | VA mean initial 2 visits post loading | 0.009 | 0.005 | 0.004 | 0.872 | 1.207 | 0.012 | 0.000 |
| | | | | VA post loading (VP) | 0.003 | 0.002 | 0.001 | 0.195 | 0.191 | 0.007 | 0.000 |
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| Change in VA, baseline - month 12 (categories: VA gained, maintained, lost) | VA_st dev | full | averaged over classes | VA baseline visit (V0) | 0.109 | 0.055 | 0.053 | 29.100 | 39.660 | 0.016 | 0.065 |
| | | | | Standard deviation of VA mean, post loading -12 months (VP-V12) | 0.100 | 0.050 | 0.042 | 27.891 | 33.490 | 0.023 | 0.059 |
| | | | | VA fellow eye (V0) | 0.038 | 0.019 | 0.017 | 1.951 | 9.219 | 0.006 | 0.022 |
| | | | | VA post loading (VP) | 0.007 | 0.003 | 0.003 | 1.362 | 1.248 | 0.004 | 0.000 |
| | | | | VA mean initial 2 visits post loading | 0.007 | 0.003 | 0.003 | 2.419 | 1.971 | 0.005 | 0.000 |
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| Change in VA, baseline - month 12 (categories: VA gained, maintained, lost) | VA_st dev | outliers removed | averaged over classes | Standard deviation of VA mean, post loading -12 months (VP-V12) | 0.103 | 0.052 | 0.043 | 26.776 | 32.548 | 0.023 | 0.062 |
| | | | | VA baseline visit (V0) | 0.094 | 0.047 | 0.046 | 22.841 | 30.959 | 0.034 | 0.056 |
| | | | | VA fellow eye (V0) | 0.043 | 0.022 | 0.020 | 2.386 | 9.008 | 0.007 | 0.025 |
| | | | | VA mean initial 2 visits post loading | 0.011 | 0.005 | 0.005 | 0.981 | 1.072 | 0.013 | 0.000 |
| | | | | VA post loading (VP) | 0.005 | 0.002 | 0.002 | 0.210 | 0.289 | 0.010 | 0.000 |
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| Change in | V0_OCT | full | averaged | V0_OPL 1mm CM vol | 0.044 | 0.028 | 0.028 | 12.087 | 7.161 | -0.001 | 0.035 |
| | | | | V0_retina 1mm CM vol | 0.045 | 0.023 | 0.030 | 9.704 | 15.656 | 0.002 | 0.000 |

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| | | | | V0_IPL 1mm CM vol | 0.037 | 0.023 | 0.023 | 9.994 | 7.978 | 0.003 | 0.000 |
| | | | | V0_retina 1mm CMT | 0.045 | 0.022 | 0.030 | 9.466 | 13.150 | 0.001 | 0.000 |
| | | | | V0_retina min CMT | 0.044 | 0.022 | 0.029 | 13.907 | 12.993 | 0.003 | 0.000 |
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| Change in VA, baseline - month 12 (categories: VA gained, lost) | V0_OCT | outliers removed | averaged over classes | V0_retina 1mm CM vol | 0.041 | 0.021 | 0.028 | 10.913 | 13.407 | 0.013 | 0.000 |
| | | | | V0_NFL min CMT | 0.023 | 0.018 | 0.015 | 4.980 | 10.874 | 0.009 | 0.000 |
| | | | | V0_OPL 1mm CMT | 0.039 | 0.020 | 0.026 | 9.274 | 9.887 | 0.004 | 0.000 |
| | | | | V0_GCL min CMT | 0.021 | 0.012 | 0.014 | 9.080 | 9.716 | 0.005 | 0.000 |
| | | | | V0_retina min CMT | 0.033 | 0.016 | 0.022 | 12.662 | 9.387 | 0.013 | 0.000 |
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| Change in VA, baseline - month 12 (categories: VA gained, lost) | VP_OCT | full | averaged over classes | VP_NFL min CMT | 0.012 | 0.013 | 0.008 | 0.728 | 0.544 | -0.011 | 0.000 |
| | | | | VP_IRLs min CMT | 0.020 | 0.010 | 0.014 | 2.750 | 2.298 | 0.003 | 0.014 |
| | | | | VP_RPE 3mm vol | 0.018 | 0.009 | 0.012 | 5.165 | 4.049 | 0.002 | 0.000 |
| | | | | VP_OPL 1mm CM vol | 0.011 | 0.008 | 0.007 | 4.002 | 1.539 | 0.005 | 0.000 |
| | | | | VP_ORLs 3mm vol | 0.016 | 0.008 | 0.010 | 5.494 | 2.082 | 0.000 | 0.000 |
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| Change in VA, baseline - month 12 (categories: VA gained, lost) | VP_OCT | outliers removed | averaged over classes | VP_IRLs min CMT | 0.023 | 0.011 | 0.015 | 5.694 | 4.233 | 0.011 | 0.000 |
| | | | | VP_IPL min CMT | 0.011 | 0.006 | 0.007 | 6.149 | 3.493 | -0.009 | 0.000 |
| | | | | VP_OPL 1mm CMT | 0.009 | 0.005 | 0.006 | 5.493 | 2.860 | 0.000 | 0.000 |
| | | | | VP_RPE 3mm vol | 0.015 | 0.008 | 0.010 | 1.191 | 2.850 | 0.006 | 0.000 |
| | | | | VP_IRLs 1mm CM vol | 0.013 | 0.007 | 0.009 | 1.750 | 1.843 | 0.002 | 0.000 |
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| Change in VA, | V0_OCT ANE | full | averaged over | V0_vol_serous_ped | 0.035 | 0.017 | 0.024 | 1.566 | 0.367 | -0.031 | 0.024 |
| | | | | V0_vol_neurosensory_retina | 0.031 | 0.016 | 0.020 | 0.984 | 2.665 | -0.001 | 0.000 |

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| | | | | V0_vol_posterior_hyaloid | 0.020 | 0.010 | 0.013 | 0.474 | 0.278 | 0.008 | 0.000 |
| | | | | V0_vol_vitreous_and_subhyaloid | 0.017 | 0.009 | 0.011 | 0.087 | 0.086 | 0.003 | 0.000 |
| | | | | V0_vol_epiretinal_membrane | 0.017 | 0.008 | 0.011 | 0.166 | 0.074 | 0.003 | 0.000 |
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| Change in VA, baseline - month 12 (categories: VA gained, lost) | V0_OCTANE | outliers removed | averaged over classes | V0_vol_neurosensory_retina | 0.024 | 0.012 | 0.016 | 0.786 | 4.099 | -0.005 | 0.016 |
| | | | | V0_vol_subretinal_hyper_reflect | 0.009 | 0.005 | 0.006 | 0.251 | 1.210 | 0.006 | 0.000 |
| | | | | V0_vol_subretinal_fluid | 0.003 | 0.001 | 0.002 | 0.702 | 0.953 | 0.007 | 0.000 |
| | | | | V0_vol_fibrovascular_ped | 0.003 | 0.002 | 0.002 | 0.142 | 0.449 | -0.013 | 0.000 |
| | | | | V0_vol_posterior_hyaloid | 0.017 | 0.009 | 0.011 | 0.201 | 0.326 | 0.012 | 0.000 |
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| Change in VA, baseline - month 12 (categories: VA gained, lost) | VP_OCTANE | full | averaged over classes | VP_vol_serous_ped | 0.152 | 0.076 | 0.097 | 0.237 | 0.030 | 0.003 | 0.113 |
| | | | | VP_vol_epiretinal_membrane | 0.034 | 0.017 | 0.022 | 0.092 | 0.349 | -0.004 | 0.000 |
| | | | | VP_vol_drusenoid_ped | 0.030 | 0.015 | 0.020 | 0.028 | 0.933 | 0.008 | 0.000 |
| | | | | VP_vol_vitreous_and_subhyaloid | 0.020 | 0.010 | 0.013 | 1.718 | 1.210 | -0.018 | 0.000 |
| | | | | VP_vol_neurosensory_retina | 0.017 | 0.008 | 0.011 | 5.908 | 3.763 | 0.002 | 0.000 |
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| Change in VA, baseline - month 12 (categories: VA gained, lost) | VP_OCTANE | outliers removed | averaged over classes | VP_vol_rpe | 0.017 | 0.009 | 0.011 | 1.912 | 5.547 | -0.010 | 0.000 |
| | | | | VP_vol_intraretinal_fluid | 0.019 | 0.009 | 0.013 | 2.703 | 2.665 | 0.002 | 0.000 |
| | | | | VP_vol_neurosensory_retina | 0.011 | 0.006 | 0.007 | 2.418 | 2.015 | 0.002 | 0.000 |
| | | | | VP_vol_drusenoid_ped | 0.029 | 0.014 | 0.019 | 0.016 | 1.126 | -0.003 | 0.000 |
| | | | | VP_vol_posterior_hyaloid | 0.024 | 0.012 | 0.015 | 0.355 | 0.423 | -0.019 | 0.000 |
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| Change in VA, baseline - month 12 (categories: VA gained, lost) | Demographics | outliers removed | averaged over classes | Ethnicity | 0.013 | 0.027 | 0.008 | NA | 0.086 | -0.002 | 0.000 |

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| | | | | Time interval 1st to 3rd injection | 0.023 | 0.015 | 0.015 | NA | 3.727 | 0.001 | 0.019 |
| | | | | Fellow eye activity | 0.023 | 0.013 | 0.015 | NA | 7.967 | 0.006 | 0.017 |
| | | | | Age At First Injection | 0.023 | 0.012 | 0.015 | NA | 5.876 | 0.022 | 0.000 |
| | | | | Anti-VEGF drug type | 0.003 | 0.003 | 0.002 | NA | 0.010 | 0.028 | 0.000 |
| | | | | Sex | 0.000 | 0.000 | 0.000 | NA | 0.037 | -0.006 | 0.000 |
| | | | | Laterality | 0.000 | 0.000 | 0.000 | NA | 0.020 | 0.002 | 0.000 |
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| Change in VA, baseline - month 12 (categories: VA gained, lost) | Demographic & qualitative | outliers removed | averaged over classes | Fellow eye activity | 0.015 | 0.008 | 0.010 | NA | 4.869 | 0.018 | 0.000 |
| | | | | Time interval 1st to 3rd injection | 0.024 | 0.016 | 0.014 | NA | 2.116 | 0.010 | 0.020 |
| | | | | Age At First Injection | 0.017 | 0.009 | 0.011 | NA | 1.325 | -0.002 | 0.000 |
| | | | | Sex | 0.000 | 0.000 | 0.000 | NA | 0.108 | 0.016 | 0.000 |
| | | | | Ethnicity | 0.011 | 0.023 | 0.006 | NA | 0.056 | 0.010 | 0.000 |
| | | | | Laterality | 0.000 | 0.000 | 0.000 | NA | 0.049 | 0.014 | 0.000 |
| | | | | Anti-VEGF drug type | 0.004 | 0.005 | 0.003 | NA | 0.029 | -0.004 | 0.000 |
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| Change in VA, baseline - month 12 (categories: VA gained, lost) | VA | full | averaged over classes | VA baseline visit (V0) | 0.061 | 0.030 | 0.041 | 34.510 | 22.851 | 0.032 | 0.043 |
| | | | | VA fellow eye (V0) | 0.021 | 0.011 | 0.014 | 4.250 | 7.297 | 0.008 | 0.000 |
| | | | | VA mean initial 2 visits post loading | 0.008 | 0.004 | 0.006 | 1.421 | 1.776 | 0.005 | 0.000 |
| | | | | VA post loading (VP) | 0.008 | 0.004 | 0.006 | 0.525 | 0.227 | 0.005 | 0.000 |
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| Change in VA, baseline - month 12 (categories: VA gained, lost) | VA | outliers removed | averaged over classes | VA baseline visit (V0) | 0.050 | 0.025 | 0.033 | 24.461 | 16.933 | 0.035 | 0.035 |
| | | | | VA fellow eye (V0) | 0.026 | 0.013 | 0.018 | 5.348 | 8.038 | 0.017 | 0.000 |
| | | | | VA mean initial 2 visits post loading | 0.007 | 0.003 | 0.005 | 1.924 | 1.922 | 0.010 | 0.000 |
| | | | | VA post loading (VP) | 0.002 | 0.001 | 0.001 | 0.713 | 0.205 | 0.009 | 0.000 |
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| Change in VA, baseline - month 12 (categories: VA gained, lost) | VA_st dev | full | averaged over classes | VA baseline visit (V0) | 0.061 | 0.030 | 0.041 | 34.510 | 22.851 | 0.022 | 0.043 |
| | | | | Standard deviation of VA mean, post loading -12 months (VP-V12) | 0.061 | 0.030 | 0.041 | 28.966 | 21.094 | 0.026 | 0.042 |
| | | | | VA fellow eye (V0) | 0.021 | 0.011 | 0.014 | 4.250 | 7.297 | -0.008 | 0.000 |
| | | | | VA mean initial 2 visits post loading | 0.008 | 0.004 | 0.006 | 1.421 | 1.776 | 0.008 | 0.000 |
| | | | | VA post loading (VP) | 0.008 | 0.004 | 0.006 | 0.525 | 0.227 | 0.001 | 0.000 |
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| Change in VA, baseline - month 12 (categories: VA gained, lost) | VA_st dev | outliers removed | averaged over classes | Standard deviation of VA mean, post loading -12 months (VP-V12) | 0.060 | 0.030 | 0.040 | 29.639 | 18.983 | 0.016 | 0.042 |
| | | | | VA baseline visit (V0) | 0.050 | 0.025 | 0.033 | 24.413 | 16.933 | 0.039 | 0.035 |
| | | | | VA fellow eye (V0) | 0.022 | 0.011 | 0.015 | 4.182 | 6.176 | 0.004 | 0.000 |
| | | | | VA mean initial 2 visits post loading | 0.010 | 0.005 | 0.007 | 2.609 | 2.140 | 0.002 | 0.000 |
| | | | | VA post loading (VP) | 0.002 | 0.001 | 0.001 | 1.009 | 0.386 | 0.001 | 0.000 |
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| VA at 12 months (mean of VA from final 2 visits categories: letter score VA <30, 31-40, | V0_OCT | full | averaged over classes | V0_IPL 3mm vol | 0.077 | 0.039 | 0.009 | 1.336 | 8.974 | 0.007 | 0.035 |
| | | | | V0_NFL 1mm CMT | 0.074 | 0.037 | 0.014 | 0.937 | 11.450 | -0.002 | 0.000 |
| | | | | V0_GCL 1mm CM vol | 0.055 | 0.034 | 0.010 | 1.748 | 9.549 | 0.004 | 0.000 |
| | | | | V0_GCL 3mm vol | 0.061 | 0.031 | 0.009 | 2.332 | 12.816 | 0.008 | 0.000 |
| | | | | V0_ONL 1mm CMT | 0.059 | 0.030 | 0.010 | 2.179 | 8.778 | 0.008 | 0.000 |
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| VA at 12 months (mean of VA from final 2 visits categories: letter score VA | V0_OCT | outliers removed | averaged over classes | V0_GCL min CMT | 0.042 | 0.025 | 0.007 | 1.268 | 15.821 | 0.000 | 0.000 |
| | | | | V0_NFL 1mm CMT | 0.095 | 0.048 | 0.018 | 1.358 | 13.749 | -0.002 | 0.044 |
| | | | | V0_NFL min CMT | 0.051 | 0.038 | 0.008 | 1.224 | 12.136 | 0.003 | 0.000 |
| | | | | V0_GCL 3mm vol | 0.050 | 0.025 | 0.008 | 2.044 | 11.572 | 0.013 | 0.000 |
| | | | | V0_GCL 1mm CM vol | 0.067 | 0.042 | 0.012 | 2.045 | 10.560 | 0.008 | 0.000 |
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| VA at 12 months (mean of VA from final 2 visits categories: letter score VA <30, 31-40, | VP_OCT | full | averaged over classes | VP_NFL 1mm CM vol | 0.039 | 0.071 | 0.006 | 1.057 | 1.194 | -0.001 | 0.026 |
| | | | | VP_IPL 3mm vol | 0.117 | 0.059 | 0.013 | 5.982 | 24.985 | 0.002 | 0.055 |
| | | | | VP_OPL 1mm CM vol | 0.067 | 0.049 | 0.012 | 2.102 | 4.797 | 0.007 | 0.000 |
| | | | | VP_GCL 1mm CM vol | 0.047 | 0.044 | 0.006 | 0.753 | 4.734 | -0.007 | 0.000 |
| | | | | VP_GCL 3mm vol | 0.083 | 0.042 | 0.011 | 6.598 | 24.095 | -0.001 | 0.000 |
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| VA at 12 months (mean of VA from final 2 visits categories: letter score VA <30, 31-40, | VP_OCT | outliers removed | averaged over classes | VP_IPL 3mm vol | 0.127 | 0.064 | 0.016 | 6.591 | 31.527 | 0.006 | 0.060 |
| | | | | VP_GCL 3mm vol | 0.105 | 0.052 | 0.013 | 7.509 | 25.638 | 0.006 | 0.000 |
| | | | | VP_IRLs 3mm vol | 0.105 | 0.053 | 0.011 | 4.694 | 23.277 | 0.010 | 0.000 |
| | | | | VP_ONL 1mm CMT | 0.096 | 0.048 | 0.015 | 3.637 | 21.373 | 0.016 | 0.044 |
| | | | | VP_ONL 1mm CM vol | 0.083 | 0.042 | 0.012 | 3.615 | 18.160 | 0.016 | 0.000 |
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| VA at 12 months (mean of VA from final 2 visits categories: letter score VA <30, 31-40, | V0_OCTANE | full | averaged over classes | V0_vol_epiretinal_membrane | 0.251 | 0.126 | 0.033 | 0.759 | 1.840 | 0.021 | 0.124 |
| | | | | V0_vol_posterior_hyaloid | 0.244 | 0.122 | 0.035 | 1.973 | 4.431 | -0.012 | 0.000 |
| | | | | V0_vol_serous_ped | 0.203 | 0.101 | 0.027 | 0.418 | 1.013 | -0.002 | 0.000 |
| | | | | V0_vol_choroid_and_outer_layers | 0.082 | 0.041 | 0.015 | 2.901 | 13.828 | -0.009 | 0.038 |
| | | | | V0_vol_neurosensory_retina | 0.076 | 0.038 | 0.009 | 0.668 | 8.332 | 0.001 | 0.000 |
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| VA at 12 months (mean of VA from final 2 visits categories: letter score VA | V0_OCTANE | outliers removed | averaged over classes | V0_vol_choroid_and_outer_layers | 0.131 | 0.066 | 0.030 | 3.057 | 17.295 | -0.005 | 0.000 |
| | | | | V0_vol_subretinal_fluid | 0.059 | 0.030 | 0.012 | 1.268 | 11.023 | 0.019 | 0.000 |
| | | | | V0_vol_neurosensory_retina | 0.067 | 0.033 | 0.009 | 1.003 | 7.070 | 0.019 | 0.000 |
| | | | | V0_vol_vitreous_and_subhyaloid | 0.058 | 0.029 | 0.009 | 1.110 | 6.124 | -0.002 | 0.000 |
| | | | | V0_vol_drusenoid_ped | 0.057 | 0.029 | 0.009 | 0.684 | 5.365 | 0.010 | 0.000 |
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| VA at 12 months (mean of VA from final 2 visits categories: letter score VA <30, 31-40, 41-50, 51- | VP_OCTANE | full | averaged over classes | VP_vol_serous_ped | 0.465 | 0.233 | 0.073 | 1.071 | 0.592 | 0.018 | 0.254 |
| | | | | VP_vol_epiretinal_membrane | 0.271 | 0.136 | 0.038 | 0.577 | 1.522 | 0.003 | 0.000 |
| | | | | VP_vol_subretinal_hyper_reflect | 0.137 | 0.069 | 0.030 | 1.455 | 7.084 | 0.007 | 0.000 |
| | | | | VP_vol_intraretinal_fluid | 0.118 | 0.059 | 0.016 | 1.517 | 4.485 | -0.003 | 0.000 |
| | | | | VP_vol_choroid_and_outer_layers | 0.106 | 0.053 | 0.019 | 0.617 | 3.585 | 0.025 | 0.000 |
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| VA at 12 months (mean of VA from final 2 visits categories: letter score VA <30, 31-40, | VP_OCTANE | outliers removed | averaged over classes | VP_vol_neurosensory_retina | 0.075 | 0.038 | 0.008 | 2.174 | 8.722 | 0.003 | 0.000 |
| | | | | VP_vol_subretinal_hyper_reflect | 0.148 | 0.074 | 0.032 | 1.412 | 7.381 | 0.007 | 0.000 |
| | | | | VP_vol_subretinal_fluid | 0.122 | 0.061 | 0.014 | 2.206 | 5.329 | 0.015 | 0.000 |
| | | | | VP_vol_drusenoid_ped | 0.083 | 0.042 | 0.012 | 0.894 | 4.912 | -0.005 | 0.000 |
| | | | | VP_vol_choroid_and_outer_layers | 0.126 | 0.063 | 0.023 | 0.537 | 4.572 | 0.005 | 0.000 |
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| VA at 12 months (mean of VA from final 2 visits categories: letter score VA <30, 31-40, | Demographic & qualitative | full | averaged over classes | Ethnicity | 0.030 | 0.065 | 0.007 | NA | 0.174 | -0.006 | 0.000 |
| | | | | Age At First Injection | 0.074 | 0.037 | 0.008 | NA | 20.845 | 0.017 | 0.034 |
| | | | | Anti-VEGF drug type | 0.032 | 0.033 | 0.005 | NA | 0.540 | -0.030 | 0.000 |
| | | | | Sex | 0.027 | 0.030 | 0.005 | NA | 8.219 | -0.012 | 0.016 |
| | | | | Fellow eye activity | 0.045 | 0.027 | 0.007 | NA | 9.594 | -0.013 | 0.022 |
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| VA at 12 months (mean of VA from final 2 visits categories: | Demographic & qualitative | outliers removed | averaged over classes | Age At First Injection | 0.076 | 0.038 | 0.009 | NA | 15.376 | 0.014 | 0.035 |
| | | | | Fellow eye activity | 0.042 | 0.024 | 0.007 | NA | 10.017 | -0.046 | 0.000 |
| | | | | Sex | 0.028 | 0.031 | 0.007 | NA | 8.050 | -0.001 | 0.017 |
| | | | | Laterality | 0.014 | 0.014 | 0.005 | NA | 2.898 | 0.001 | 0.008 |
| | | | | Time interval 1st to 3rd injection | 0.037 | 0.025 | 0.005 | NA | 2.546 | -0.006 | 0.019 |
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| VA at 12 months (mean of VA from final 2 visits categories: letter score VA <30, 31-40, | VA | full | averaged over classes | VA mean initial 2 visits post loading | 0.581 | 0.291 | 0.117 | 65.456 | 138.506 | 0.073 | 0.347 |
| | | | | VA post loading (VP) | 0.484 | 0.242 | 0.096 | 53.771 | 126.022 | 0.065 | 0.000 |
| | | | | VA baseline visit (V0) | 0.225 | 0.112 | 0.040 | 21.143 | 69.173 | 0.022 | 0.000 |
| | | | | VA fellow eye (V0) | 0.059 | 0.029 | 0.014 | 2.319 | 13.058 | 0.013 | 0.027 |
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| VA at 12 months (mean of VA from final 2 visits categories: letter score VA <30, 31-40, | VA | outliers removed | averaged over classes | VA mean initial 2 visits post loading | 0.559 | 0.280 | 0.118 | 53.547 | 120.873 | 0.090 | 0.334 |
| | | | | VA post loading (VP) | 0.438 | 0.219 | 0.091 | 43.697 | 108.184 | 0.084 | 0.000 |
| | | | | VA baseline visit (V0) | 0.215 | 0.108 | 0.040 | 18.062 | 61.004 | 0.035 | 0.000 |
| | | | | VA fellow eye (V0) | 0.069 | 0.035 | 0.017 | 2.486 | 14.863 | 0.034 | 0.032 |
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| VA at 12 months (mean of VA from final 2 visits categories: letter score VA <30, 31-40, 41-50, | VA_st dev | full | averaged over classes | VA mean initial 2 visits post loading | 0.581 | 0.291 | 0.117 | 65.456 | 138.506 | 0.071 | 0.347 |
| | | | | VA post loading (VP) | 0.484 | 0.242 | 0.096 | 53.771 | 126.022 | 0.070 | 0.000 |
| | | | | VA baseline visit (V0) | 0.225 | 0.112 | 0.040 | 21.143 | 69.173 | 0.030 | 0.000 |
| | | | | Standard deviation of VA mean, post loading -12 months (VP-V12) | 0.142 | 0.071 | 0.024 | 12.800 | 41.265 | 0.055 | 0.067 |
| | | | | VA fellow eye (V0) | 0.059 | 0.029 | 0.014 | 2.319 | 13.058 | 0.028 | 0.027 |
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| VA at 12 months (mean of VA from final 2 visits categories: | VA_st dev | outliers removed | averaged over classes | VA mean initial 2 visits post loading | 0.547 | 0.274 | 0.113 | 56.989 | 123.881 | 0.075 | 0.325 |
| | | | | VA post loading (VP) | 0.441 | 0.220 | 0.090 | 45.202 | 111.397 | 0.059 | 0.000 |
| | | | | VA baseline visit (V0) | 0.214 | 0.107 | 0.038 | 18.353 | 60.748 | 0.020 | 0.000 |
| | | | | Standard deviation of VA mean, post loading -12 months (VP-V12) | 0.152 | 0.076 | 0.022 | 13.744 | 41.949 | 0.036 | 0.073 |
| | | | | VA fellow eye (V0) | 0.071 | 0.036 | 0.017 | 2.637 | 15.129 | 0.018 | 0.033 |
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| VA at 12 months (categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80) | V0_OCT | full | averaged over classes | V0_IPL 1mm CM vol | 0.073 | 0.045 | 0.009 | 1.301 | 8.575 | 0.004 | 0.000 |
| | | | | V0_ONL 1mm CMT | 0.089 | 0.045 | 0.016 | 3.095 | 15.763 | 0.016 | 0.041 |
| | | | | V0_NFL 1mm CMT | 0.089 | 0.044 | 0.016 | 1.760 | 13.696 | 0.003 | 0.041 |
| | | | | V0_GCL 1mm CM vol | 0.070 | 0.043 | 0.012 | 2.002 | 10.743 | 0.005 | 0.000 |
| | | | | V0_ONL min CMT | 0.083 | 0.042 | 0.014 | 2.259 | 11.166 | 0.005 | 0.000 |
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| VA at 12 months (categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80) | V0_OCT | outliers removed | averaged over classes | V0_ONL 1mm CMT | 0.091 | 0.045 | 0.017 | 3.032 | 17.418 | 0.005 | 0.042 |
| | | | | V0_NFL 1mm CMT | 0.113 | 0.057 | 0.020 | 2.784 | 16.830 | 0.005 | 0.053 |
| | | | | V0_IPL 1mm CMT | 0.080 | 0.040 | 0.013 | 2.761 | 15.736 | 0.002 | 0.000 |
| | | | | V0_INL 3mm vol | 0.073 | 0.037 | 0.007 | 2.976 | 14.984 | 0.003 | 0.000 |
| | | | | V0_IPL 3mm vol | 0.083 | 0.041 | 0.009 | 3.007 | 14.971 | 0.005 | 0.000 |
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| VA at 12 months (categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80) | VP_OCT | full | averaged over classes | VP_NFL 1mm CM vol | 0.046 | 0.083 | 0.006 | 1.015 | 1.290 | -0.002 | 0.000 |
| | | | | VP_IPL 3mm vol | 0.137 | 0.069 | 0.018 | 5.778 | 25.665 | 0.012 | 0.065 |
| | | | | VP_IRLs 1mm CM vol | 0.109 | 0.055 | 0.021 | 1.894 | 11.832 | 0.003 | 0.000 |
| | | | | VP_GCL 3mm vol | 0.096 | 0.048 | 0.016 | 6.457 | 23.314 | 0.015 | 0.000 |
| | | | | VP_IRLs 1mm CMT | 0.092 | 0.046 | 0.018 | 1.572 | 10.546 | 0.004 | 0.000 |
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| VA at 12 months (categories: letter score VA <30, 31-40, 41-50, | VP_OCT | outliers removed | averaged over classes | VP_IPL 3mm vol | 0.170 | 0.086 | 0.025 | 6.965 | 31.501 | 0.011 | 0.082 |
| | | | | VP_GCL 3mm vol | 0.125 | 0.063 | 0.018 | 7.691 | 26.050 | 0.016 | 0.000 |
| | | | | VP_IRLs 3mm vol | 0.109 | 0.055 | 0.014 | 4.905 | 21.442 | 0.007 | 0.000 |
| | | | | VP_ONL min CMT | 0.060 | 0.030 | 0.012 | 3.594 | 16.673 | 0.013 | 0.000 |
| | | | | VP_IPL min CMT | 0.068 | 0.034 | 0.015 | 2.500 | 16.079 | 0.008 | 0.031 |
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| VA at 12 months (categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80) | V0_OCTANE | full | averaged over classes | V0_vol_epiretinal_membrane | 0.256 | 0.128 | 0.037 | 0.875 | 2.134 | 0.009 | 0.125 |
| | | | | V0_vol_serous_ped | 0.215 | 0.108 | 0.028 | 0.749 | 1.823 | -0.033 | 0.000 |
| | | | | V0_vol_posterior_hyaloid | 0.213 | 0.107 | 0.031 | 1.847 | 3.247 | 0.029 | 0.000 |
| | | | | V0_vol_choroid_and_outer_layers | 0.080 | 0.040 | 0.015 | 2.634 | 12.267 | 0.004 | 0.036 |
| | | | | V0_vol_vitreous_and_subhyaloid | 0.073 | 0.037 | 0.013 | 1.158 | 6.942 | -0.011 | 0.000 |
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| VA at 12 months (categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80) | V0_OCTANE | outliers removed | averaged over classes | V0_vol_choroid_and_outer_layers | 0.141 | 0.070 | 0.030 | 2.903 | 16.485 | 0.005 | 0.066 |
| | | | | V0_vol_drusenoid_ped | 0.071 | 0.035 | 0.012 | 1.640 | 9.651 | 0.003 | 0.000 |
| | | | | V0_vol_subretinal_fluid | 0.063 | 0.032 | 0.010 | 1.336 | 6.551 | 0.048 | 0.000 |
| | | | | V0_vol_neurosensory_retina | 0.073 | 0.037 | 0.009 | 0.788 | 5.721 | 0.021 | 0.033 |
| | | | | V0_vol_vitreous_and_subhyaloid | 0.064 | 0.032 | 0.012 | 1.015 | 5.685 | 0.010 | 0.000 |
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| VA at 12 months (categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80) | VP_OCTANE | full | averaged over classes | VP_vol_serous_ped | 0.551 | 0.276 | 0.093 | 0.663 | 0.344 | 0.000 | 0.315 |
| | | | | VP_vol_epiretinal_membrane | 0.220 | 0.110 | 0.032 | 1.056 | 1.995 | 0.015 | 0.000 |
| | | | | VP_vol_subretinal_hyper_reflect | 0.136 | 0.068 | 0.033 | 1.537 | 8.697 | 0.005 | 0.000 |
| | | | | VP_vol_posterior_hyaloid | 0.132 | 0.066 | 0.026 | 0.930 | 2.029 | -0.022 | 0.000 |
| | | | | VP_vol_subretinal_fluid | 0.124 | 0.062 | 0.026 | 1.978 | 6.508 | 0.053 | 0.000 |
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| VA at 12 months (categories: letter score VA | VP_OCTANE | outliers removed | averaged over classes | VP_vol_neurosensory_retina | 0.090 | 0.045 | 0.015 | 2.716 | 12.159 | -0.027 | 0.000 |
| | | | | VP_vol_subretinal_hyper_reflect | 0.099 | 0.050 | 0.022 | 1.104 | 6.875 | -0.031 | 0.000 |
| | | | | VP_vol_subretinal_fluid | 0.133 | 0.067 | 0.022 | 1.858 | 5.936 | -0.003 | 0.000 |
| | | | | VP_vol_choroid_and_outer_layers | 0.108 | 0.054 | 0.014 | 0.441 | 5.860 | -0.019 | 0.000 |
| | | | | VP_vol_drusenoid_ped | 0.105 | 0.053 | 0.016 | 0.976 | 4.920 | -0.012 | 0.000 |
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| VA at 12 months (categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80) | Demographic & qualitative | full | averaged over classes | Ethnicity | 0.035 | 0.075 | 0.008 | NA | 0.284 | 0.002 | 0.000 |
| | | | | Time interval 1st to 3rd injection | 0.061 | 0.039 | 0.008 | NA | 1.432 | 0.002 | 0.031 |
| | | | | Anti-VEGF drug type | 0.031 | 0.033 | 0.005 | NA | 0.684 | 0.014 | 0.000 |
| | | | | Age At First Injection | 0.066 | 0.033 | 0.009 | NA | 16.374 | 0.005 | 0.030 |
| | | | | Fellow eye activity | 0.050 | 0.030 | 0.011 | NA | 9.407 | 0.023 | 0.024 |
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| VA at 12 months (categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80) | Demographic & qualitative | outliers removed | averaged over classes | Fellow eye activity | 0.056 | 0.033 | 0.012 | NA | 9.936 | 0.000 | 0.027 |
| | | | | Age At First Injection | 0.056 | 0.028 | 0.007 | NA | 9.638 | 0.010 | 0.000 |
| | | | | Sex | 0.023 | 0.025 | 0.005 | NA | 6.429 | -0.007 | 0.014 |
| | | | | Laterality | 0.013 | 0.013 | 0.004 | NA | 2.572 | -0.008 | 0.000 |
| | | | | Time interval 1st to 3rd injection | 0.051 | 0.034 | 0.007 | NA | 2.270 | 0.000 | 0.026 |
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| VA at 12 months (categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80) | VA | full | averaged over classes | VA mean initial 2 visits post loading | 0.528 | 0.264 | 0.107 | 58.458 | 129.364 | 0.037 | 0.305 |
| | | | | VA post loading (VP) | 0.480 | 0.240 | 0.095 | 48.903 | 120.513 | 0.030 | 0.000 |
| | | | | VA baseline visit (V0) | 0.201 | 0.101 | 0.037 | 19.715 | 63.427 | 0.015 | 0.000 |
| | | | | VA fellow eye (V0) | 0.073 | 0.037 | 0.017 | 3.059 | 17.115 | 0.010 | 0.033 |
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| VA at 12 months (categories: letter score VA <30, 31-40, 41- | VA | outliers removed | averaged over classes | VA mean initial 2 visits post loading | 0.503 | 0.251 | 0.108 | 49.088 | 112.177 | 0.065 | 0.290 |
| | | | | VA post loading (VP) | 0.435 | 0.217 | 0.088 | 40.692 | 104.453 | 0.050 | 0.000 |
| | | | | VA baseline visit (V0) | 0.188 | 0.094 | 0.036 | 16.772 | 54.626 | 0.020 | 0.000 |
| | | | | VA fellow eye (V0) | 0.077 | 0.039 | 0.016 | 2.900 | 15.736 | 0.023 | 0.036 |
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| VA at 12 months (categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80) | VA_st dev | full | averaged over classes | VA mean initial 2 visits post loading | 0.528 | 0.264 | 0.107 | 58.458 | 129.364 | 0.071 | 0.305 |
| | | | | VA post loading (VP) | 0.480 | 0.240 | 0.095 | 48.903 | 120.513 | 0.057 | 0.000 |
| | | | | VA baseline visit (V0) | 0.201 | 0.101 | 0.037 | 19.715 | 63.427 | 0.020 | 0.000 |
| | | | | Standard deviation of VA mean, post loading -12 months (VP-V12) | 0.124 | 0.062 | 0.020 | 11.989 | 35.180 | 0.042 | 0.058 |
| | | | | VA fellow eye (V0) | 0.073 | 0.037 | 0.017 | 3.059 | 17.115 | 0.012 | 0.033 |
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| VA at 12 months (categories: letter score VA <30, 31-40, 41-50, 51-60, 61-70, 71-80, >80) | VA_st dev | outliers removed | averaged over classes | VA mean initial 2 visits post loading | 0.513 | 0.257 | 0.111 | 51.604 | 118.428 | 0.074 | 0.299 |
| | | | | VA post loading (VP) | 0.441 | 0.221 | 0.089 | 41.782 | 108.297 | 0.054 | 0.000 |
| | | | | VA baseline visit (V0) | 0.188 | 0.094 | 0.036 | 17.058 | 54.807 | 0.017 | 0.000 |
| | | | | Standard deviation of VA mean, post loading -12 months (VP-V12) | 0.122 | 0.061 | 0.019 | 11.652 | 34.609 | 0.038 | 0.058 |
| | | | | VA fellow eye (V0) | 0.081 | 0.041 | 0.017 | 3.130 | 16.749 | 0.000 | 0.038 |
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Appendix 8: Visual acuity related regression models, model accuracy and feature ranking

| Target | Feature group | Dataset | Models | MSE | RMSE | MAE | R2 | CVRMSE | Feature | Univariate regression | RRelieff |
|---|---|---|---|---|---|---|---|---|---|---|---|
| VA at 12 months | V0_OCTANE | full | SVM | 252.19 | 15.88 | 12.99 | -0.06 | 26.04 | V0_vol_fibrovascular_ped | 3.670 | 0.220 |
| | | | Random Forest | 268.58 | 16.39 | 13.65 | -0.13 | 26.87 | V0_vol_choroid_and_outer_layers | 2.354 | 0.265 |
| | | | Gradient Boosting | 350.15 | 18.71 | 14.81 | -0.47 | 30.68 | V0_vol_epiretinal_membrane | 2.099 | 0.457 |
| | | | AdaBoost | 362.27 | 19.03 | 15.10 | -0.52 | 31.21 | V0_vol_rpe | 0.949 | 0.234 |
| | | | Tree | 371.02 | 19.26 | 15.34 | -0.56 | 31.58 | V0_vol_subretinal_fluid | 0.684 | 0.245 |
| | | | Linear Regression | 772.91 | 27.80 | 20.86 | -2.24 | 45.58 | | | |
| | | | kNN (error) | | | | | | | | |
| VA at 12 months | V0_OCTANE | outliers removed | SVM | 242.75 | 15.58 | 12.46 | -0.02 | 25.54 | V0_vol_choroid_and_outer_layers | 2.437 | 0.298 |
| | | | Linear Regression | 253.77 | 15.93 | 12.89 | -0.07 | 26.12 | V0_vol_fibrovascular_ped | 1.987 | 0.210 |
| | | | Random Forest | 267.62 | 16.36 | 13.32 | -0.13 | 26.82 | V0_vol_epiretinal_membrane | 1.780 | 0.503 |
| | | | Gradient Boosting | 279.41 | 16.72 | 13.36 | -0.18 | 27.40 | V0_vol_rpe | 1.204 | 0.238 |
| | | | kNN | 284.17 | 16.86 | 13.26 | -0.20 | 27.64 | V0_vol_posterior_hyaloid | 0.919 | 0.455 |
| | | | AdaBoost | 300.17 | 17.33 | 14.18 | -0.26 | 28.40 | | | |
| | | | Tree | 340.78 | 18.46 | 14.17 | -0.43 | 30.26 | | | |
| VA at 12 months | VP_OCTANE | full | AdaBoost | 398.27 | 19.96 | 16.36 | -0.67 | 32.72 | VP_vol_neurosensory_retina | 6.779 | 0.102 |
| | | | Random Forest | 700.49 | 26.47 | 23.11 | -1.94 | 43.39 | VP_vol_epiretinal_membrane | 2.038 | 0.495 |
| | | | SVM | 717.91 | 26.79 | 23.51 | -2.01 | 43.93 | VP_vol_subretinal_hyper_reflect | 1.407 | 0.392 |
| | | | Linear Regression | 828.94 | 28.79 | 24.27 | -2.48 | 47.21 | VP_vol_choroid_and_outer_layers | 1.306 | 0.240 |
| | | | Gradient Boosting | 933.31 | 30.55 | 25.76 | -2.92 | 50.09 | VP_vol_subretinal_fluid | 1.089 | 0.282 |
| | | | Tree | 1343.18 | 36.65 | 30.75 | -4.64 | 60.09 | | | |
| | | | kNN error | | | | | | | | |

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| VA at 12 months | VP_OCTANE | outliers removed | SVM | 246.67 | 15.71 | 12.65 | 0.00 | 25.88 | VP_vol_neurosensory_retina | 13.592 | 0.212 |
| | | | Linear Regression | 253.41 | 15.92 | 13.03 | -0.03 | 26.23 | VP_vol_epiretinal_membrane | 2.152 | 0.489 |
| | | | Random Forest | 272.50 | 16.51 | 13.44 | -0.11 | 27.20 | VP_vol_subretinal_hyper_reflect | 1.708 | 0.387 |
| | | | Gradient Boosting | 278.18 | 16.68 | 13.75 | -0.13 | 27.48 | VP_vol_fibrovascular_ped | 1.547 | 0.225 |
| | | | AdaBoost | 299.29 | 17.30 | 14.44 | -0.21 | 28.50 | VP_vol_subretinal_fluid | 1.522 | 0.428 |
| | | | kNN | 301.24 | 17.36 | 13.83 | -0.22 | 28.60 | | | |
| | | | Tree | 317.12 | 17.81 | 14.27 | -0.29 | 29.34 | | | |
| VA at 12 months | VA_st dev | full | Linear Regression | 235.63 | 15.35 | 12.41 | 0.01 | 25.17 | VA mean of 2 visits immediately post loading | 346.402 | 0.074 |
| | | | Gradient Boosting | 241.79 | 15.55 | 12.59 | -0.01 | 25.49 | VA post loading (VP) | 295.823 | 0.074 |
| | | | SVM | 245.28 | 15.66 | 12.73 | -0.03 | 25.68 | VA baseline visit (V0) | 114.170 | 0.081 |
| | | | Random Forest | 262.69 | 16.21 | 13.02 | -0.10 | 26.57 | VA fellow eye (V0) | 7.448 | 0.124 |
| | | | AdaBoost | 271.11 | 16.47 | 13.00 | -0.14 | 27.00 | Standard deviation of VA mean, post loading -12 months (VP-V12) | 67.354 | 0.145 |
| | | | kNN | 286.15 | 16.92 | 13.55 | -0.20 | 27.74 | | | |
| | | | Tree | 452.04 | 21.26 | 16.95 | -0.90 | 34.86 | | | |
| VA at 12 months | VA_st dev | outliers removed | Linear Regression | 90.61 | 9.52 | 6.80 | 0.59 | 15.48 | VA mean of 2 visits immediately post loading | 305.213 | 0.080 |
| | | | Random Forest | 106.50 | 10.32 | 7.19 | 0.52 | 16.78 | VA post loading (VP) | 253.945 | 0.083 |
| | | | kNN | 110.68 | 10.52 | 7.69 | 0.50 | 17.11 | VA baseline visit (V0) | 99.841 | 0.077 |
| | | | SVM | 113.05 | 10.63 | 8.01 | 0.49 | 17.29 | Standard deviation of VA mean, post loading -12 months (VP-V12) | 66.359 | 0.160 |
| | | | Gradient Boosting | 115.54 | 10.75 | 7.25 | 0.47 | 17.48 | VA fellow eye (V0) | 5.582 | 0.116 |
| | | | AdaBoost | 121.41 | 11.02 | 7.51 | 0.45 | 17.92 | | | |
| | | | Tree | 170.54 | 13.06 | 9.07 | 0.22 | 21.23 | | | |
| VA at 12 months | VA | full | Linear Regression | 237.19 | 15.40 | 12.45 | 0.00 | 25.25 | VA baseline visit (V0) | 114.170 | 0.091 |
| | | | SVM | 243.35 | 15.60 | 12.72 | -0.02 | 25.58 | VA fellow eye (V0) | 7.448 | 0.106 |
| | | | Gradient Boosting | 260.60 | 16.14 | 12.84 | -0.09 | 26.47 | VA post loading (VP) | 295.823 | 0.065 |
| | | | Random Forest | 261.90 | 16.18 | 13.19 | -0.10 | 26.53 | VA mean of 2 visits immediately post loading | 346.402 | 0.069 |
| | | | AdaBoost | 281.61 | 16.78 | 13.31 | -0.18 | 27.51 | | | |
| | | | kNN | 284.88 | 16.88 | 13.59 | -0.20 | 27.67 | | | |

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| | | | Tree | 435.57 | 20.87 | 16.18 | -0.83 | 34.22 | | | |
| VA at 12 months | VA | outliers removed | Linear Regression | 110.94 | 10.53 | 7.51 | 0.50 | 17.15 | VA fellow eye (V0) | 5.878 | 0.100 |
| | | | kNN | 136.20 | 11.67 | 8.71 | 0.39 | 19.00 | VA baseline visit (V0) | 98.957 | 0.073 |
| | | | SVM | 137.46 | 11.72 | 8.93 | 0.39 | 19.09 | VA mean of 2 visits immediately post loading | 295.440 | 0.063 |
| | | | Random Forest | 138.81 | 11.78 | 8.70 | 0.38 | 19.18 | VA post loading (VP) | 250.012 | 0.059 |
| | | | Gradient Boosting | 144.19 | 12.01 | 8.66 | 0.36 | 19.55 | | | |
| | | | AdaBoost | 156.07 | 12.49 | 8.87 | 0.30 | 20.34 | | | |
| | | | Tree | 174.82 | 13.22 | 9.80 | 0.22 | 21.53 | | | |
| VA at 12 months | Demographic & qualitative | full | Linear Regression | 243.00 | 15.59 | 12.64 | -0.02 | 25.56 | Fellow eye activity | NA | 0.229 |
| | | | Random Forest | 281.12 | 16.77 | 13.38 | -0.18 | 27.49 | Ethnicity | NA | 0.035 |
| | | | kNN | 290.23 | 17.04 | 13.78 | -0.22 | 27.93 | Anti-VEGF drug type | NA | 0.193 |
| | | | AdaBoost | 301.25 | 17.36 | 13.75 | -0.26 | 28.46 | Sex | NA | 0.058 |
| | | | Gradient Boosting | 301.51 | 17.36 | 13.87 | -0.27 | 28.47 | Laterality | NA | 0.072 |
| | | | SVM | 327.78 | 18.10 | 15.53 | -0.38 | 29.68 | Time interval 1st to 3rd injection | NA | 0.031 |
| | | | Tree | 355.00 | 18.84 | 14.70 | -0.49 | 30.89 | Age At First Injection | NA | 0.145 |
| VA at 12 months | Demographic & qualitative | outliers removed | Linear Regression | 230.21 | 15.17 | 12.20 | -0.02 | 24.86 | Fellow eye activity | NA | 0.278 |
| | | | SVM | 230.85 | 15.19 | 12.56 | -0.03 | 24.90 | Age At First Injection | NA | 0.174 |
| | | | kNN | 257.17 | 16.04 | 12.69 | -0.14 | 26.28 | Anti-VEGF drug type | NA | 0.124 |
| | | | Gradient Boosting | 268.89 | 16.40 | 13.17 | -0.20 | 26.87 | Laterality | NA | 0.088 |
| | | | Random Forest | 276.84 | 16.64 | 13.62 | -0.23 | 27.27 | Sex | NA | 0.075 |
| | | | AdaBoost | 287.57 | 16.96 | 13.65 | -0.28 | 27.79 | Time interval 1st to 3rd injection | NA | 0.063 |
| | | | Tree | 364.77 | 19.10 | 15.35 | -0.62 | 31.30 | Ethnicity | NA | 0.053 |
| VA at 12 months | V0_OCT | full | SVM | 220.01 | 14.83 | 11.77 | -0.01 | 24.22 | V0_GCL 3mm vol | 10.470 | 0.112 |
| | | | Linear Regression | 225.36 | 15.01 | 12.07 | -0.03 | 24.51 | V0_OPL 3mm vol | 9.688 | 0.123 |
| | | | Gradient Boosting | 239.80 | 15.49 | 12.29 | -0.10 | 25.29 | V0_ONL 3mm vol | 6.434 | 0.109 |
| | | | AdaBoost | 249.72 | 15.80 | 12.15 | -0.15 | 25.81 | V0_RPE 3mm vol | 5.080 | 0.073 |
| | | | Random Forest | 254.07 | 15.94 | 12.75 | -0.17 | 26.03 | V0_ONL 1mm CMT | 4.943 | 0.097 |
| | | | kNN | 265.51 | 16.29 | 12.91 | -0.22 | 26.61 | | | |
| | | | Tree | 396.56 | 19.91 | 15.47 | -0.82 | 32.52 | | | |
| VA a | V0 | out | SVM | 206.23 | 14.36 | 11.31 | 0.04 | 23.35 | V0_RPE 3mm vol | 14.387 | 0.101 |

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| | | | AdaBoost | 211.28 | 14.54 | 11.45 | 0.01 | 23.64 | V0_OPL 3mm vol | 10.216 | 0.125 |
| | | | Random Forest | 212.06 | 14.56 | 11.79 | 0.01 | 23.68 | V0_GCL 3mm vol | 10.164 | 0.109 |
| | | | Gradient Boosting | 227.23 | 15.07 | 12.25 | -0.06 | 24.51 | V0_RPE 1mm CM vol | 7.680 | 0.103 |
| | | | Linear Regression | 236.30 | 15.37 | 12.30 | -0.10 | 25.00 | V0_RPE 1mm CMT | 7.271 | 0.105 |
| | | | kNN | 243.11 | 15.59 | 12.36 | -0.14 | 25.35 | | | |
| | | | Tree | 371.63 | 19.28 | 15.43 | -0.74 | 31.35 | | | |
| VA at 12 months | VP_OCT | full | Linear Regression | 218.55 | 14.78 | 11.87 | 0.00 | 24.14 | VP_GCL 3mm vol | 36.979 | 0.097 |
| | | | SVM | 221.95 | 14.90 | 11.91 | -0.02 | 24.33 | VP_IPL 3mm vol | 32.526 | 0.071 |
| | | | Random Forest | 241.14 | 15.53 | 12.53 | -0.11 | 25.36 | VP_IPL min CMT | 15.312 | 0.112 |
| | | | AdaBoost | 249.81 | 15.81 | 12.53 | -0.15 | 25.81 | VP_IRLs 3mm vol | 15.099 | 0.098 |
| | | | kNN | 251.73 | 15.87 | 12.68 | -0.16 | 25.91 | VP_OPL 1mm CM vol | 6.685 | 0.081 |
| | | | Gradient Boosting | 257.84 | 16.06 | 13.05 | -0.18 | 26.22 | | | |
| | | | Tree | 393.33 | 19.83 | 15.36 | -0.80 | 32.39 | | | |
| VA at 12 months | VP_OCT | outliers removed | Gradient Boosting | 175.80 | 13.26 | 10.55 | 0.18 | 21.53 | VP_GCL 3mm vol | 44.907 | 0.133 |
| | | | Random Forest | 180.86 | 13.45 | 10.84 | 0.16 | 21.84 | VP_IPL 3mm vol | 40.408 | 0.085 |
| | | | AdaBoost | 189.97 | 13.78 | 11.11 | 0.12 | 22.38 | VP_IRLs 3mm vol | 30.978 | 0.127 |
| | | | SVM | 197.95 | 14.07 | 11.23 | 0.08 | 22.85 | VP_IPL min CMT | 12.262 | 0.151 |
| | | | Linear Regression | 202.71 | 14.24 | 11.50 | 0.06 | 23.12 | VP_OPL 1mm CM vol | 12.132 | 0.092 |
| | | | kNN | 238.15 | 15.43 | 12.23 | -0.11 | 25.06 | | | |
| | | | Tree | 318.09 | 17.84 | 14.00 | -0.48 | 28.96 | | | |
| VA at 12 months (mean of VA from final 2 visits) | V0_OCTANE | full | Random Forest | 230.29 | 15.18 | 12.18 | -0.06 | 24.78 | V0_vol_fibrovascular_ped | 4.124 | 0.222 |
| | | | SVM | 235.55 | 15.35 | 12.48 | -0.08 | 25.06 | V0_vol_choroid_and_outer_layers | 2.491 | 0.275 |
| | | | Tree | 286.02 | 16.91 | 13.54 | -0.31 | 27.62 | V0_vol_epiretinal_membrane | 1.765 | 0.455 |
| | | | AdaBoost | 293.09 | 17.12 | 13.71 | -0.34 | 27.96 | V0_vol_rpe | 1.421 | 0.246 |
| | | | Gradient Boosting | 293.27 | 17.13 | 13.90 | -0.35 | 27.97 | V0_vol_subretinal_fluid | 1.314 | 0.261 |
| | | | Linear Regression | 511.62 | 22.62 | 17.13 | -1.35 | 36.94 | | | |
| | | | kNN (error) | | | | | | | | |
| VA at 12 months (mean of | V0_OCTANE | outliers removed | SVM | 222.87 | 14.93 | 11.80 | -0.02 | 24.43 | V0_vol_choroid_and_outer_layers | 2.521 | 0.320 |
| | | | Linear Regression | 229.74 | 15.16 | 12.18 | -0.05 | 24.80 | V0_vol_fibrovascular_ped | 2.107 | 0.208 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Random Forest | 248.04 | 15.75 | 12.46 | -0.14 | 25.77 | V0_vol_rpe | 1.617 | 0.267 |
| | | | kNN | 254.70 | 15.96 | 12.51 | -0.17 | 26.12 | V0_vol_epiretinal_membrane | 1.418 | 0.490 |
| | | | Gradient Boosting | 260.58 | 16.14 | 12.82 | -0.19 | 26.42 | V0_vol_subretinal_fluid | 1.312 | 0.276 |
| | | | AdaBoost | 278.57 | 16.69 | 13.47 | -0.27 | 27.31 | | | |
| | | | Tree | 312.82 | 17.69 | 13.77 | -0.43 | 28.94 | | | |
| VA at 12 months (mean of VA from final 2 visits) | VP_OCTANE | full | AdaBoost | 411.39 | 20.28 | 16.51 | -0.89 | 33.12 | VP_vol_neurosensory_retina | 9.831 | 0.089 |
| | | | SVM | 779.41 | 27.92 | 24.52 | -2.58 | 45.59 | VP_vol_subretinal_fluid | 1.771 | 0.276 |
| | | | Random Forest | 798.60 | 28.26 | 24.80 | -2.66 | 46.15 | VP_vol_drusenoid_ped | 1.513 | 0.286 |
| | | | Linear Regression | 901.39 | 30.02 | 25.40 | -3.14 | 49.03 | VP_vol_subretinal_hyper_reflect | 1.167 | 0.373 |
| | | | Gradient Boosting | 1019.43 | 31.93 | 26.98 | -3.68 | 52.14 | VP_vol_epiretinal_membrane | 1.162 | 0.505 |
| | | | Tree | 1388.07 | 37.26 | 31.59 | -5.37 | 60.84 | | | |
| | | | kNN (error) | | | | | | | | |
| VA at 12 months (mean of VA from final 2 visits) | VP_OCTANE | outliers removed | SVM | 226.73 | 15.06 | 12.09 | -0.01 | 24.71 | VP_vol_neurosensory_retina | 13.122 | 0.190 |
| | | | Linear Regression | 230.32 | 15.18 | 12.35 | -0.02 | 24.90 | VP_vol_subretinal_hyper_reflect | 1.760 | 0.401 |
| | | | Random Forest | 241.82 | 15.55 | 12.73 | -0.07 | 25.52 | VP_vol_subretinal_fluid | 1.535 | 0.403 |
| | | | Gradient Boosting | 246.60 | 15.70 | 12.85 | -0.10 | 25.77 | VP_vol_fibrovascular_ped | 1.354 | 0.200 |
| | | | AdaBoost | 269.39 | 16.41 | 13.66 | -0.20 | 26.93 | VP_vol_epiretinal_membrane | 1.233 | 0.486 |
| | | | kNN | 273.96 | 16.55 | 13.20 | -0.22 | 27.16 | | | |
| | | | Tree | 305.35 | 17.47 | 14.08 | -0.36 | 28.67 | | | |
| VA at 12 months (mean of VA from final 2 visits) | Demographic & qualitative | full | Linear Regression | 224.98 | 15.00 | 12.12 | -0.03 | 24.49 | Fellow eye activity | NA | 0.168 |
| | | | kNN | 264.03 | 16.25 | 13.05 | -0.21 | 26.53 | Age At First Injection | NA | 0.141 |
| | | | Gradient Boosting | 267.46 | 16.35 | 12.93 | -0.23 | 26.71 | Anti-VEGF drug type | NA | 0.128 |
| | | | Random Forest | 279.59 | 16.72 | 13.31 | -0.28 | 27.31 | Sex | NA | 0.082 |
| | | | SVM | 296.78 | 17.23 | 14.80 | -0.36 | 28.13 | Laterality | NA | 0.065 |
| | | | AdaBoost | 300.66 | 17.34 | 13.52 | -0.38 | 28.32 | | | |
| | | | Tree | 327.83 | 18.11 | 14.21 | -0.50 | 29.57 | | | |
| VA at 12 months (mean of VA from | Demographic & qualitative | outliers removed | Linear Regression | 207.46 | 14.40 | 11.61 | 0.00 | 23.47 | Fellow eye activity | NA | 0.294 |
| | | | SVM | 215.96 | 14.70 | 12.03 | -0.04 | 23.94 | Age At First Injection | NA | 0.163 |
| | | | kNN | 234.76 | 15.32 | 12.20 | -0.13 | 24.96 | Anti-VEGF drug type | NA | 0.140 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Gradient Boosting | 245.75 | 15.68 | 12.46 | -0.18 | 25.54 | Sex | NA | 0.106 |
| | | | Random Forest | 248.81 | 15.77 | 12.82 | -0.20 | 25.70 | Laterality | NA | 0.084 |
| | | | AdaBoost | 287.39 | 16.95 | 13.34 | -0.39 | 27.62 | | | |
| | | | Tree | 329.05 | 18.14 | 14.54 | -0.59 | 29.55 | | | |
| VA at 12 months (mean of VA from final 2 visits) | VA | full | Linear Regression | 218.16 | 14.77 | 11.85 | 0.00 | 24.12 | VA fellow eye (V0) | 7.110 | 0.109 |
| | | | SVM | 226.55 | 15.05 | 12.17 | -0.04 | 24.58 | VA baseline visit (V0) | 124.745 | 0.073 |
| | | | Random Forest | 243.21 | 15.60 | 12.50 | -0.12 | 25.47 | VA mean of 2 visits immediately post loading | 404.341 | 0.068 |
| | | | Gradient Boosting | 244.47 | 15.64 | 12.33 | -0.12 | 25.53 | VA post loading (VP) | 334.226 | 0.068 |
| | | | AdaBoost | 257.47 | 16.05 | 12.69 | -0.18 | 26.20 | | | |
| | | | kNN | 269.12 | 16.40 | 13.13 | -0.23 | 26.79 | | | |
| | | | Tree | 377.07 | 19.42 | 15.16 | -0.73 | 31.71 | | | |
| VA at 12 months (mean of VA from final 2 visits) | VA | outliers removed | Linear Regression | 93.79 | 9.68 | 6.95 | 0.54 | 15.69 | VA mean of 2 visits immediately post loading | 344.578 | 0.085 |
| | | | kNN | 115.84 | 10.76 | 7.94 | 0.44 | 17.44 | VA post loading (VP) | 280.414 | 0.079 |
| | | | SVM | 116.67 | 10.80 | 8.13 | 0.43 | 17.50 | VA baseline visit (V0) | 108.635 | 0.083 |
| | | | Gradient Boosting | 118.28 | 10.88 | 7.75 | 0.43 | 17.62 | VA fellow eye (V0) | 5.119 | 0.105 |
| | | | Random Forest | 123.33 | 11.11 | 8.09 | 0.40 | 18.00 | | | |
| | | | AdaBoost | 140.51 | 11.85 | 8.27 | 0.32 | 19.21 | | | |
| | | | Tree | 162.53 | 12.75 | 9.18 | 0.21 | 20.66 | | | |
| VA at 12 months (mean of VA from final 2 visits) | VA_st dev | full | Linear Regression | 216.99 | 14.73 | 11.79 | 0.00 | 24.05 | VA mean of 2 visits immediately post loading | 404.341 | 0.081 |
| | | | SVM | 226.33 | 15.04 | 12.07 | -0.04 | 24.57 | VA post loading (VP) | 334.226 | 0.078 |
| | | | Gradient Boosting | 227.74 | 15.09 | 12.14 | -0.04 | 24.64 | VA baseline visit (V0) | 124.745 | 0.094 |
| | | | Random Forest | 234.21 | 15.30 | 12.20 | -0.07 | 24.99 | Standard deviation of VA mean, post loading -12 months (VP-V12) | 71.357 | 0.173 |
| | | | AdaBoost | 254.39 | 15.95 | 12.59 | -0.17 | 26.05 | VA fellow eye (V0) | 7.110 | 0.134 |
| | | | kNN | 267.29 | 16.35 | 13.02 | -0.23 | 26.70 | | | |
| | | | Tree | 387.89 | 19.69 | 15.55 | -0.78 | 32.16 | | | |
| VA at 12 months (mean of VA from final 2 visits) | VA_st dev | outliers removed | Linear Regression | 72.28 | 8.50 | 6.06 | 0.64 | 13.76 | VA mean of 2 visits immediately post loading | 363.603 | 0.070 |
| | | | Random Forest | 79.11 | 8.89 | 6.23 | 0.61 | 14.39 | VA post loading (VP) | 289.351 | 0.070 |
| | | | Gradient Boosting | 80.65 | 8.98 | 6.27 | 0.60 | 14.54 | VA baseline visit (V0) | 111.472 | 0.074 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | kNN | 89.70 | 9.47 | 6.82 | 0.56 | 15.33 | Standard deviation of VA mean, post loading -12 months (VP-V12) | 75.171 | 0.182 |
| | | | AdaBoost | 90.42 | 9.51 | 6.43 | 0.55 | 15.39 | VA fellow eye (V0) | 4.953 | 0.106 |
| | | | SVM | 97.36 | 9.87 | 7.31 | 0.52 | 15.97 | | | |
| | | | Tree | 132.89 | 11.53 | 8.04 | 0.34 | 18.66 | | | |
| VA at 12 months (mean of VA from final 2 visits) | V0_OCT | full | SVM | 1.46 | 1.21 | 0.84 | -0.04 | | V0_OPL 3mm vol | 8.667 | 0.137 |
| | | | Linear Regression | 1.47 | 1.21 | 0.84 | -0.05 | | V0_retina min CMT | 5.297 | 0.068 |
| | | | AdaBoost | 1.61 | 1.27 | 0.87 | -0.14 | | V0_GCL min CMT | 5.165 | 0.101 |
| | | | kNN | 1.72 | 1.31 | 0.96 | -0.22 | | V0_GCL 1mm CMT | 3.430 | 0.072 |
| | | | Gradient Boosting | 1.72 | 1.31 | 0.93 | -0.22 | | V0_IPL 3mm vol | 3.158 | 0.061 |
| | | | Random Forest | 1.79 | 1.34 | 0.94 | -0.27 | | | | |
| | | | Tree | 2.56 | 1.60 | 1.21 | -0.82 | | | | |
| VA at 12 months (mean of VA from final 2 visits) | V0_OCT | outliers removed | SVM | 1.57 | 1.25 | 0.86 | -0.05 | | V0_OPL 3mm vol | 9.550 | 0.139 |
| | | | AdaBoost | 1.61 | 1.27 | 0.88 | -0.08 | | V0_GCL min CMT | 4.972 | 0.140 |
| | | | Gradient Boosting | 1.62 | 1.27 | 0.92 | -0.09 | | V0_retina min CMT | 4.773 | 0.099 |
| | | | Linear Regression | 1.67 | 1.29 | 0.95 | -0.12 | | V0_ORLs min CMT | 4.075 | 0.084 |
| | | | Random Forest | 1.70 | 1.30 | 0.94 | -0.14 | | V0_GCL 1mm CMT | 3.705 | 0.099 |
| | | | kNN | 1.80 | 1.34 | 0.97 | -0.21 | | | | |
| | | | Tree | 2.88 | 1.70 | 1.25 | -0.93 | | | | |
| VA at 12 months (mean of VA from final 2 visits) | VP_OCT | full | Linear Regression | 1.47 | 1.21 | 0.84 | -0.04 | | VP_IPL 3mm vol | 3.513 | 0.071 |
| | | | SVM | 1.48 | 1.21 | 0.84 | -0.05 | | VP_IPL 1mm CM vol | 3.498 | 0.062 |
| | | | kNN | 1.57 | 1.25 | 0.92 | -0.12 | | VP_IRLs 3mm vol | 3.173 | 0.084 |
| | | | AdaBoost | 1.66 | 1.29 | 0.88 | -0.18 | | VP_OPL 3mm vol | 2.829 | 0.123 |
| | | | Random Forest | 1.84 | 1.36 | 0.95 | -0.31 | | VP_IPL min CMT | 2.761 | 0.113 |
| | | | Gradient Boosting | 1.93 | 1.39 | 0.96 | -0.37 | | | | |
| | | | Tree | 2.94 | 1.71 | 1.24 | -1.09 | | | | |
| VA at 12 months (mean of VA from final 2 visits) | VP_OCT | outliers removed | SVM | 1.43 | 1.19 | 0.81 | -0.04 | | VP_IRLs 3mm vol | 6.221 | 0.097 |
| | | | AdaBoost | 1.47 | 1.21 | 0.82 | -0.07 | | VP_IPL 3mm vol | 3.517 | 0.078 |
| | | | Linear Regression | 1.57 | 1.25 | 0.88 | -0.15 | | VP_IPL 1mm CM vol | 2.977 | 0.077 |
| | | | kNN | 1.63 | 1.28 | 0.87 | -0.19 | | VP_GCL 3mm vol | 2.831 | 0.121 |
| | | | Random Forest | 1.86 | 1.36 | 0.94 | -0.36 | | VP_NFL 1mm CM vol | 2.742 | 0.007 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Gradient Boosting | 1.89 | 1.37 | 0.98 | -0.38 | | | | |
| | | | Tree | 2.68 | 1.64 | 1.19 | -0.95 | | | | |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints | V0_OCTANE | full | SVM | 1.61 | 1.27 | 0.84 | -0.14 | | V0_vol_choroid_and_outer_layers | 2.081 | 0.250 |
| | | | Random Forest | 1.65 | 1.28 | 0.86 | -0.17 | | V0_vol_drusenoid_ped | 2.003 | 0.261 |
| | | | Tree | 1.66 | 1.29 | 0.91 | -0.18 | | V0_vol_neurosensory_retina | 1.352 | 0.172 |
| | | | AdaBoost | 1.67 | 1.29 | 0.91 | -0.19 | | V0_vol_fibrovascular_ped | 1.096 | 0.170 |
| | | | Gradient Boosting | 1.72 | 1.31 | 0.90 | -0.22 | | V0_vol_rpe | 0.954 | 0.217 |
| | | | Linear Regression | 2.88 | 1.70 | 1.18 | -1.04 | | | | |
| | | | kNN (error) | | | | | | | | |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints | V0_OCTANE | outliers removed | SVM | 1.45 | 1.20 | 0.81 | -0.01 | | V0_vol_drusenoid_ped | 2.618 | 0.281 |
| | | | Random Forest | 1.58 | 1.26 | 0.88 | -0.09 | | V0_vol_choroid_and_outer_layers | 1.827 | 0.282 |
| | | | Gradient Boosting | 1.58 | 1.26 | 0.89 | -0.10 | | V0_vol_neurosensory_retina | 1.517 | 0.167 |
| | | | Linear Regression | 1.59 | 1.26 | 0.87 | -0.10 | | V0_vol_epiretinal_membrane | 0.903 | 0.442 |
| | | | kNN | 1.63 | 1.28 | 0.92 | -0.13 | | V0_vol_serous_ped | 0.566 | 0.488 |
| | | | Tree | 2.07 | 1.44 | 0.99 | -0.44 | | | | |
| | | | AdaBoost | 2.14 | 1.46 | 1.13 | -0.48 | | | | |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints | VP_OCTANE | full | AdaBoost | 2.44 | 1.56 | 1.02 | -0.73 | | VP_vol_neurosensory_retina | 4.778 | 0.087 |
| | | | Tree | 3.25 | 1.80 | 1.54 | -1.31 | | VP_vol_subretinal_fluid | 4.104 | 0.276 |
| | | | SVM | 4.20 | 2.05 | 1.76 | -1.98 | | VP_vol_vitreous_and_subhyaloid | 2.091 | 0.185 |
| | | | Random Forest | 4.36 | 2.09 | 1.79 | -2.10 | | VP_vol_rpe | 1.456 | 0.222 |
| | | | Gradient Boosting | 7.12 | 2.67 | 2.14 | -4.06 | | VP_vol_intraretinal_fluid | 1.060 | 0.326 |
| | | | Linear Regression | 7.24 | 2.69 | 2.11 | -4.14 | | | | |
| | | | kNN (error) | | | | | | | | |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of | VP_OCTANE | outliers removed | kNN | 1.88 | 1.37 | 0.99 | -0.27 | | VP_vol_neurosensory_retina | 4.531 | 0.204 |
| | | | SVM | 1.47 | 1.21 | 0.83 | 0.00 | | VP_vol_subretinal_fluid | 3.279 | 0.357 |
| | | | Gradient Boosting | 1.90 | 1.38 | 0.98 | -0.29 | | VP_vol_vitreous_and_subhyaloid | 1.875 | 0.252 |
| | | | AdaBoost | 2.25 | 1.50 | 1.18 | -0.53 | | VP_vol_epiretinal_membrane | 1.412 | 0.483 |
| | | | Tree | 2.03 | 1.43 | 1.01 | -0.38 | | VP_vol_rpe | 1.124 | 0.235 |
| | | | Linear Regression | 1.60 | 1.26 | 0.87 | -0.08 | | | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Random Forest | 1.81 | 1.34 | 0.95 | -0.22 | | | | |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints | Demographic & qualitative | full | Linear Regression | 1.46 | 1.21 | 0.84 | -0.04 | | Fellow eye activity | NA | 0.286 |
| | | | SVM | 1.80 | 1.34 | 1.02 | -0.28 | | Anti-VEGF drug type | NA | 0.153 |
| | | | kNN | 1.90 | 1.38 | 0.97 | -0.35 | | Age At First Injection | NA | 0.136 |
| | | | Gradient Boosting | 2.02 | 1.42 | 0.99 | -0.44 | | Ethnicity | NA | 0.109 |
| | | | Random Forest | 2.03 | 1.43 | 1.01 | -0.44 | | Sex | NA | 0.069 |
| | | | AdaBoost | 2.28 | 1.51 | 1.06 | -0.62 | | | | |
| | | | Tree | 2.35 | 1.53 | 1.12 | -0.67 | | | | |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints | Demographic & qualitative | outliers removed | kNN | 1.52 | 1.23 | 0.90 | -0.06 | | Fellow eye activity | NA | 0.212 |
| | | | Linear Regression | 1.52 | 1.23 | 0.86 | -0.07 | | Anti-VEGF drug type | NA | 0.182 |
| | | | SVM | 1.57 | 1.25 | 0.88 | -0.10 | | Age At First Injection | NA | 0.168 |
| | | | Gradient Boosting | 1.65 | 1.29 | 0.92 | -0.16 | | Sex | NA | 0.124 |
| | | | Random Forest | 1.69 | 1.30 | 0.93 | -0.19 | | Time interval 1st to 3rd injection | NA | 0.085 |
| | | | AdaBoost | 2.01 | 1.42 | 1.00 | -0.41 | | | | |
| | | | Tree | 2.07 | 1.44 | 1.04 | -0.45 | | | | |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints | VA | full | Linear Regression | 1.48 | 1.22 | 0.84 | -0.05 | | VA fellow eye (V0) | 1.727 | 0.090 |
| | | | SVM | 1.62 | 1.27 | 0.88 | -0.15 | | VA baseline visit (V0) | 19.571 | 0.083 |
| | | | AdaBoost | 1.66 | 1.29 | 0.91 | -0.18 | | VA post loading (VP) | 23.528 | 0.061 |
| | | | kNN | 1.76 | 1.33 | 0.94 | -0.25 | | VA mean of 2 visits immediately post loading | 18.775 | 0.058 |
| | | | Gradient Boosting | 1.85 | 1.36 | 0.95 | -0.32 | | | | |
| | | | Random Forest | 1.89 | 1.37 | 0.98 | -0.34 | | | | |
| | | | Tree | 2.82 | 1.68 | 1.23 | -1.01 | | | | |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints | VA | outliers removed | Linear Regression | 1.29 | 1.14 | 0.80 | 0.06 | | VA baseline visit (V0) | 16.981 | 0.080 |
| | | | SVM | 1.36 | 1.17 | 0.79 | 0.00 | | VA post loading (VP) | 15.123 | 0.065 |
| | | | kNN | 1.51 | 1.23 | 0.88 | -0.10 | | VA mean of 2 visits immediately post loading | 11.156 | 0.066 |
| | | | Gradient Boosting | 1.65 | 1.29 | 0.91 | -0.21 | | VA fellow eye (V0) | 4.957 | 0.108 |
| | | | Random Forest | 1.70 | 1.30 | 0.94 | -0.24 | | | | |
| | | | AdaBoost | 1.84 | 1.36 | 0.94 | -0.35 | | | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Tree | 2.56 | 1.60 | 1.16 | -0.87 | | | | |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints | VA_st dev | full | Linear Regression | 1.46 | 1.21 | 0.83 | -0.04 | | Standard deviation of VA mean, post loading -12 months (VP-V12) | 44.587 | 0.179 |
| | | | SVM | 1.51 | 1.23 | 0.84 | -0.08 | | VA post loading (VP) | 23.528 | 0.057 |
| | | | AdaBoost | 1.59 | 1.26 | 0.90 | -0.13 | | VA baseline visit (V0) | 19.571 | 0.080 |
| | | | kNN | 1.75 | 1.32 | 0.92 | -0.24 | | VA mean of 2 visits immediately post loading | 18.775 | 0.053 |
| | | | Gradient Boosting | 1.78 | 1.33 | 0.94 | -0.27 | | VA fellow eye (V0) | 1.727 | 0.123 |
| | | | Random Forest | 1.82 | 1.35 | 0.97 | -0.29 | | | | |
| | | | Tree | 2.45 | 1.56 | 1.22 | -0.74 | | | | |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints | VA_st dev | outliers removed | Linear Regression | 1.04 | 1.02 | 0.70 | 0.20 | | Standard deviation of VA mean, post loading -12 months (VP-V12) | 59.316 | 0.121 |
| | | | Random Forest | 1.09 | 1.05 | 0.70 | 0.17 | | VA post loading (VP) | 14.992 | 0.068 |
| | | | SVM | 1.12 | 1.06 | 0.71 | 0.15 | | VA baseline visit (V0) | 14.821 | 0.094 |
| | | | Gradient Boosting | 1.16 | 1.08 | 0.71 | 0.12 | | VA mean of 2 visits immediately post loading | 10.457 | 0.071 |
| | | | kNN | 1.21 | 1.10 | 0.76 | 0.08 | | VA fellow eye (V0) | 4.125 | 0.103 |
| | | | AdaBoost | 1.29 | 1.14 | 0.73 | 0.01 | | | | |
| | | | Tree | 1.54 | 1.24 | 0.83 | -0.17 | | | | |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints | V0_OCT | full | SVM | 1.13 | 1.07 | 0.78 | -0.02 | | V0_retina min CMT | 9.107 | 0.081 |
| | | | Linear Regression | 1.16 | 1.08 | 0.80 | -0.05 | | V0_OPL 3mm vol | 6.674 | 0.137 |
| | | | Random Forest | 1.30 | 1.14 | 0.86 | -0.18 | | V0_retina 1mm CM vol | 5.379 | 0.074 |
| | | | AdaBoost | 1.31 | 1.15 | 0.85 | -0.19 | | V0_retina 1mm CMT | 5.212 | 0.074 |
| | | | Gradient Boosting | 1.35 | 1.16 | 0.87 | -0.22 | | V0_GCL min CMT | 4.981 | 0.063 |
| | | | kNN | 1.38 | 1.18 | 0.90 | -0.25 | | | | |
| | | | Tree | 2.03 | 1.43 | 1.10 | -0.84 | | | | |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints | V0_OCT | outliers removed | SVM | 1.20 | 1.09 | 0.79 | -0.04 | | V0_retina min CMT | 7.438 | 0.096 |
| | | | Gradient Boosting | 1.24 | 1.11 | 0.84 | -0.08 | | V0_OPL 3mm vol | 7.425 | 0.149 |
| | | | AdaBoost | 1.25 | 1.12 | 0.82 | -0.09 | | V0_OPL 1mm CM vol | 5.230 | 0.088 |
| | | | Random Forest | 1.28 | 1.13 | 0.85 | -0.12 | | V0_GCL min CMT | 5.025 | 0.055 |
| | | | Linear Regression | 1.31 | 1.15 | 0.87 | -0.14 | | V0_retina 1mm CM vol | 4.727 | 0.078 |
| | | | kNN | 1.40 | 1.18 | 0.90 | -0.22 | | | | |
| | | | Tree | 2.02 | 1.42 | 1.07 | -0.76 | | | | |
| Cha | VP | fu | SVM | 1.13 | 1.06 | 0.79 | -0.02 | | VP_GCL min CMT | 3.333 | 0.037 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Linear Regression | 1.14 | 1.07 | 0.80 | -0.03 | | VP_IPL min CMT | 3.010 | 0.102 |
| | | | kNN | 1.22 | 1.10 | 0.85 | -0.10 | | VP_IPL 3mm vol | 2.329 | 0.082 |
| | | | AdaBoost | 1.23 | 1.11 | 0.83 | -0.11 | | VP_GCL 3mm vol | 2.128 | 0.113 |
| | | | Random Forest | 1.34 | 1.16 | 0.87 | -0.21 | | VP_NFL 3mm vol | 1.922 | 0.056 |
| | | | Gradient Boosting | 1.35 | 1.16 | 0.87 | -0.22 | | | | |
| | | | Tree | 1.99 | 1.41 | 1.09 | -0.80 | | | | |
| Change in VA post loading (month 4 - month 12), when considered as slope of line of best fit through VA datapoints | VP_OCT | outliers removed | SVM | 1.14 | 1.07 | 0.79 | -0.06 | | VP_RPE 3mm vol | 4.811 | 0.060 |
| | | | Linear Regression | 1.21 | 1.10 | 0.82 | -0.13 | | VP_IRLs 3mm vol | 3.550 | 0.110 |
| | | | AdaBoost | 1.26 | 1.12 | 0.81 | -0.17 | | VP_IPL 3mm vol | 3.194 | 0.081 |
| | | | Random Forest | 1.30 | 1.14 | 0.83 | -0.21 | | VP_GCL 3mm vol | 3.007 | 0.125 |
| | | | kNN | 1.30 | 1.14 | 0.83 | -0.21 | | VP_ORLs 3mm vol | 2.938 | 0.058 |
| | | | Gradient Boosting | 1.32 | 1.15 | 0.84 | -0.23 | | | | |
| | | | Tree | 2.09 | 1.45 | 1.10 | -0.95 | | | | |
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints | V0_OCTANE | full | AdaBoost | 1.12 | 1.06 | 0.78 | -0.01 | | V0_vol_drusenoid_ped | 4.885 | 0.320 |
| | | | SVM | 1.12 | 1.06 | 0.76 | -0.01 | | V0_vol_fibrovascular_ped | 1.364 | 0.202 |
| | | | Random Forest | 1.13 | 1.06 | 0.77 | -0.02 | | V0_vol_neurosensory_retina | 1.046 | 0.167 |
| | | | Tree | 1.16 | 1.08 | 0.78 | -0.04 | | V0_vol_epiretinal_membrane | 0.974 | 0.470 |
| | | | Gradient Boosting | 1.18 | 1.09 | 0.80 | -0.06 | | V0_vol_subretinal_hyper_reflect | 0.821 | 0.313 |
| | | | Linear Regression | 1.37 | 1.17 | 0.83 | -0.24 | | | | |
| | | | kNN (error) | | | | | | | | |
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints | V0_OCTANE | outliers removed | SVM | 1.14 | 1.07 | 0.80 | -0.02 | | V0_vol_drusenoid_ped | 5.125 | 0.277 |
| | | | Linear Regression | 1.21 | 1.10 | 0.82 | -0.07 | | V0_vol_subretinal_hyper_reflect | 1.353 | 0.329 |
| | | | Random Forest | 1.23 | 1.11 | 0.83 | -0.09 | | V0_vol_neurosensory_retina | 1.056 | 0.142 |
| | | | Gradient Boosting | 1.24 | 1.12 | 0.85 | -0.11 | | V0_vol_epiretinal_membrane | 1.003 | 0.490 |
| | | | kNN | 1.25 | 1.12 | 0.81 | -0.11 | | V0_vol_serous_ped | 0.787 | 0.482 |
| | | | AdaBoost | 1.27 | 1.13 | 0.85 | -0.13 | | | | |
| | | | Tree | 1.55 | 1.25 | 0.93 | -0.38 | | | | |
| Change in visual acuity | VP_OCTANE | full | AdaBoost | 1.56 | 1.25 | 0.94 | -0.41 | | VP_vol_neurosensory_retina | 5.998 | 0.096 |
| | | | Tree | 2.20 | 1.48 | 1.26 | -0.99 | | VP_vol_subretinal_fluid | 3.068 | 0.315 |
| | | | SVM | 2.61 | 1.62 | 1.39 | -1.36 | | VP_vol_vitreous_and_subhyaloid | 2.731 | 0.176 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Random Forest | 2.71 | 1.65 | 1.42 | -1.45 | | VP_vol_choroid_and_outer_layers | 1.456 | 0.216 |
| | | | Linear Regression | 3.42 | 1.85 | 1.50 | -2.09 | | VP_vol_rpe | 1.427 | 0.224 |
| | | | Gradient Boosting | 3.46 | 1.86 | 1.55 | -2.13 | | | | |
| | | | kNN (error) | | | | | | | | |
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints | VP_OCTANE | outliers removed | SVM | 1.19 | 1.09 | 0.78 | -0.02 | | VP_vol_neurosensory_retina | 3.206 | 0.194 |
| | | | Linear Regression | 1.26 | 1.12 | 0.83 | -0.08 | | VP_vol_vitreous_and_subhyaloid | 2.001 | 0.236 |
| | | | Random Forest | 1.35 | 1.16 | 0.87 | -0.16 | | VP_vol_subretinal_fluid | 1.486 | 0.422 |
| | | | Gradient Boosting | 1.39 | 1.18 | 0.85 | -0.19 | | VP_vol_rpe | 1.376 | 0.237 |
| | | | AdaBoost | 1.41 | 1.19 | 0.88 | -0.21 | | VP_vol_choroid_and_outer_layers | 1.359 | 0.249 |
| | | | kNN | 1.46 | 1.21 | 0.91 | -0.25 | | | | |
| | | | Tree | 1.81 | 1.34 | 1.00 | -0.55 | | | | |
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints | Demographic & qualitative | full | Linear Regression | 1.15 | 1.07 | 0.78 | -0.04 | | Fellow eye activity | NA | 0.213 |
| | | | kNN | 1.50 | 1.22 | 0.92 | -0.35 | | Anti-VEGF drug type | NA | 0.151 |
| | | | Gradient Boosting | 1.52 | 1.23 | 0.90 | -0.37 | | Age At First Injection | NA | 0.122 |
| | | | SVM | 1.54 | 1.24 | 0.96 | -0.39 | | Sex | NA | 0.082 |
| | | | Random Forest | 1.58 | 1.26 | 0.95 | -0.42 | | Laterality | NA | 0.064 |
| | | | Tree | 1.72 | 1.31 | 0.99 | -0.56 | | | | |
| | | | AdaBoost | 1.77 | 1.33 | 0.97 | -0.60 | | | | |
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints | Demographic & qualitative | outliers removed | kNN | 1.12 | 1.06 | 0.82 | -0.02 | | Fellow eye activity | NA | 0.237 |
| | | | Linear Regression | 1.13 | 1.06 | 0.78 | -0.03 | | Age At First Injection | NA | 0.191 |
| | | | SVM | 1.20 | 1.09 | 0.81 | -0.09 | | Anti-VEGF drug type | NA | 0.163 |
| | | | Gradient Boosting | 1.21 | 1.10 | 0.83 | -0.10 | | Sex | NA | 0.103 |
| | | | Random Forest | 1.23 | 1.11 | 0.85 | -0.12 | | Laterality | NA | 0.081 |
| | | | AdaBoost | 1.40 | 1.18 | 0.90 | -0.28 | | | | |
| | | | Tree | 1.56 | 1.25 | 0.96 | -0.42 | | | | |
| Change in visual acuity over 12 | VA | full | Linear Regression | 1.14 | 1.07 | 0.78 | -0.03 | | VA fellow eye (V0) | 2.574 | 0.111 |
| | | | SVM | 1.17 | 1.08 | 0.80 | -0.05 | | VA baseline visit (V0) | 48.674 | 0.108 |
| | | | kNN | 1.39 | 1.18 | 0.86 | -0.26 | | VA post loading (VP) | 3.984 | 0.067 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Random Forest | 1.40 | 1.18 | 0.87 | -0.27 | | VA mean of 2 visits immediately post loading | 1.581 | 0.063 |
| | | | Gradient Boosting | 1.41 | 1.19 | 0.87 | -0.27 | | | | |
| | | | AdaBoost | 1.44 | 1.20 | 0.88 | -0.30 | | | | |
| | | | Tree | 2.23 | 1.49 | 1.13 | -1.02 | | | | |
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints | VA | outliers removed | Linear Regression | 0.81 | 0.90 | 0.64 | 0.23 | | VA baseline visit (V0) | 34.362 | 0.085 |
| | | | SVM | 0.88 | 0.94 | 0.66 | 0.16 | | VA fellow eye (V0) | 5.850 | 0.112 |
| | | | kNN | 1.01 | 1.01 | 0.73 | 0.03 | | VA post loading (VP) | 2.065 | 0.065 |
| | | | Gradient Boosting | 1.05 | 1.02 | 0.74 | 0.00 | | VA mean of 2 visits immediately post loading | 0.406 | 0.071 |
| | | | Random Forest | 1.10 | 1.05 | 0.76 | -0.05 | | | | |
| | | | AdaBoost | 1.23 | 1.11 | 0.80 | -0.17 | | | | |
| | | | Tree | 1.49 | 1.22 | 0.91 | -0.43 | | | | |
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints | VA_st dev | full | Linear Regression | 1.13 | 1.06 | 0.78 | -0.02 | | Standard deviation of VA mean, post loading -12 months (VP-V12) | 64.576 | 0.141 |
| | | | SVM | 1.18 | 1.09 | 0.80 | -0.06 | | VA baseline visit (V0) | 48.674 | 0.099 |
| | | | AdaBoost | 1.28 | 1.13 | 0.84 | -0.15 | | VA post loading (VP) | 3.984 | 0.065 |
| | | | Gradient Boosting | 1.29 | 1.14 | 0.85 | -0.17 | | VA fellow eye (V0) | 2.574 | 0.121 |
| | | | Random Forest | 1.31 | 1.15 | 0.85 | -0.19 | | VA mean of 2 visits immediately post loading | 1.581 | 0.063 |
| | | | kNN | 1.37 | 1.17 | 0.85 | -0.24 | | | | |
| | | | Tree | 2.04 | 1.43 | 1.12 | -0.85 | | | | |
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints | VA_st dev | outliers removed | Linear Regression | 0.63 | 0.79 | 0.56 | 0.37 | | Standard deviation of VA mean, post loading -12 months (VP-V12) | 72.945 | 0.141 |
| | | | Random Forest | 0.70 | 0.84 | 0.59 | 0.30 | | VA baseline visit (V0) | 33.411 | 0.098 |
| | | | Gradient Boosting | 0.70 | 0.84 | 0.58 | 0.30 | | VA fellow eye (V0) | 4.623 | 0.115 |
| | | | SVM | 0.73 | 0.86 | 0.57 | 0.27 | | VA post loading (VP) | 1.802 | 0.070 |
| | | | kNN | 0.80 | 0.90 | 0.64 | 0.20 | | VA mean of 2 visits immediately post loading | 0.184 | 0.070 |
| | | | AdaBoost | 0.90 | 0.95 | 0.64 | 0.11 | | | | |
| | | | Tree | 1.19 | 1.09 | 0.79 | -0.18 | | | | |
| Change in visual acuity over 12 months when | V0_OCT | full | Linear Regression | 12.47 | 3.53 | 2.53 | -0.07 | 66.68 | V0_ONL 1mm CMT | 3.846 | 0.090 |
| | | | SVM | 13.29 | 3.65 | 2.29 | -0.14 | 68.85 | V0_ONL 1mm CM vol | 3.800 | 0.086 |
| | | | AdaBoost | 14.08 | 3.75 | 2.52 | -0.21 | 70.86 | V0_INL min CMT | 2.065 | 0.074 |
| | | | kNN | 14.38 | 3.79 | 2.69 | -0.23 | 71.61 | V0_RPE min CMT | 1.937 | 0.043 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Random Forest | 14.40 | 3.80 | 2.74 | -0.23 | 71.67 | V0_ORLs min CMT | 1.894 | 0.058 |
| | | | Gradient Boosting | 15.19 | 3.90 | 2.79 | -0.30 | 73.59 | | | |
| | | | Tree | 24.96 | 5.00 | 3.45 | -1.14 | 94.35 | | | |
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints | V0_OCT | outliers removed | Random Forest | 12.82 | 3.58 | 2.59 | -0.09 | 66.67 | V0_ONL 1mm CMT | 3.102 | 0.104 |
| | | | SVM | 13.33 | 3.65 | 2.32 | -0.14 | 68.00 | V0_ONL 1mm CM vol | 2.838 | 0.107 |
| | | | AdaBoost | 13.42 | 3.66 | 2.47 | -0.14 | 68.21 | V0_INL min CMT | 2.825 | 0.078 |
| | | | Gradient Boosting | 13.52 | 3.68 | 2.64 | -0.15 | 68.47 | V0_ONL min CMT | 2.756 | 0.119 |
| | | | kNN | 14.00 | 3.74 | 2.72 | -0.19 | 69.68 | V0_IPL 3mm vol | 2.221 | 0.091 |
| | | | Linear Regression | 18.28 | 4.28 | 2.78 | -0.56 | 79.60 | | | |
| | | | Tree | 19.85 | 4.46 | 3.23 | -0.69 | 82.96 | | | |
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints | VP_OCT | full | Linear Regression | 12.06 | 3.47 | 2.47 | -0.03 | 65.59 | VP_GCL min CMT | 6.198 | 0.077 |
| | | | AdaBoost | 13.08 | 3.62 | 2.44 | -0.12 | 68.29 | VP_NFL min CMT | 4.612 | 0.057 |
| | | | Random Forest | 13.27 | 3.64 | 2.67 | -0.14 | 68.78 | VP_INL 1mm CMT | 3.323 | 0.041 |
| | | | SVM | 13.27 | 3.64 | 2.33 | -0.14 | 68.80 | VP_IRLs 1mm CMT | 2.875 | 0.046 |
| | | | kNN | 13.43 | 3.66 | 2.59 | -0.15 | 69.21 | VP_IRLs 1mm CM vol | 2.868 | 0.039 |
| | | | Gradient Boosting | 14.97 | 3.87 | 2.82 | -0.28 | 73.06 | | | |
| | | | Tree | 21.62 | 4.65 | 3.30 | -0.85 | 87.80 | | | |
| Change in visual acuity over 12 months when considered as slope of line of best fit through VA datapoints | VP_OCT | outliers removed | SVM | 12.65 | 3.56 | 2.27 | -0.10 | 67.24 | VP_IPL 3mm vol | 5.069 | 0.081 |
| | | | Linear Regression | 12.68 | 3.56 | 2.57 | -0.10 | 67.31 | VP_NFL min CMT | 5.044 | 0.053 |
| | | | Random Forest | 13.42 | 3.66 | 2.59 | -0.17 | 69.24 | VP_GCL 3mm vol | 4.420 | 0.124 |
| | | | kNN | 13.49 | 3.67 | 2.58 | -0.17 | 69.43 | VP_GCL min CMT | 3.286 | 0.062 |
| | | | AdaBoost | 13.51 | 3.68 | 2.47 | -0.17 | 69.48 | VP_RPE 3mm vol | 2.582 | 0.074 |
| | | | Gradient Boosting | 16.18 | 4.02 | 2.86 | -0.41 | 76.04 | | | |
| | | | Tree | 21.01 | 4.58 | 3.25 | -0.83 | 86.64 | | | |
| Standard deviation of VA mean, post loading (post loading - month 12) | V0_OCTANE | full | Random Forest | 15.47 | 3.93 | 3.05 | -0.32 | 74.28 | V0_vol_epiretinal_membrane | 7.389 | 0.471 |
| | | | SVM | 17.38 | 4.17 | 2.65 | -0.49 | 78.72 | V0_vol_neurosensory_retina | 1.999 | 0.158 |
| | | | AdaBoost | 26.95 | 5.19 | 3.33 | -1.31 | 98.04 | V0_vol_posterior_hyaloid | 1.757 | 0.412 |
| | | | Tree | 28.35 | 5.32 | 4.10 | -1.43 | 100.54 | V0_vol_rpe | 1.498 | 0.203 |
| | | | Gradient Boosting | 33.21 | 5.76 | 4.11 | -1.84 | 108.83 | V0_vol_serous_ped | 1.404 | 0.494 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Linear Regression | 131.97 | 11.49 | 7.22 | -10.30 | 216.94 | | | |
| | | | kNN (error) | | | | | | | | |
| Standard deviation of VA mean, post loading (post loading - month 12) | V0_OCTANE | outliers removed | Linear Regression | 12.76 | 3.57 | 2.49 | -0.05 | 66.86 | V0_vol_epiretinal_membrane | 5.447 | 0.501 |
| | | | SVM | 13.49 | 3.67 | 2.31 | -0.11 | 68.74 | V0_vol_neurosensory_retina | 2.802 | 0.236 |
| | | | Random Forest | 13.83 | 3.72 | 2.68 | -0.14 | 69.60 | V0_vol_posterior_hyaloid | 1.615 | 0.430 |
| | | | Gradient Boosting | 14.41 | 3.80 | 2.65 | -0.19 | 71.04 | V0_vol_intraretinal_fluid | 1.473 | 0.230 |
| | | | kNN | 14.74 | 3.84 | 2.75 | -0.21 | 71.85 | V0_vol_rpe | 1.351 | 0.239 |
| | | | Tree | 16.14 | 4.02 | 2.82 | -0.33 | 75.20 | | | |
| | | | AdaBoost | 19.89 | 4.46 | 3.33 | -0.64 | 83.48 | | | |
| Standard deviation of VA mean, post loading (post loading - month 12) | VP_OCTANE | full | Tree | 23.52 | 4.85 | 4.22 | -1.01 | 91.58 | VP_vol_subretinal_fluid | 4.707 | 0.301 |
| | | | SVM | 27.31 | 5.23 | 4.42 | -1.34 | 98.70 | VP_vol_neurosensory_retina | 3.102 | 0.098 |
| | | | AdaBoost | 28.88 | 5.37 | 3.82 | -1.47 | 101.48 | VP_vol_choroid_and_outer_layers | 2.547 | 0.242 |
| | | | Random Forest | 31.52 | 5.61 | 4.77 | -1.70 | 106.02 | VP_vol_rpe | 2.013 | 0.252 |
| | | | Gradient Boosting | 59.32 | 7.70 | 6.42 | -4.08 | 145.45 | VP_vol_drusenoid_ped | 1.049 | 0.269 |
| | | | Linear Regression | 65.63 | 8.10 | 6.28 | -4.62 | 152.98 | | | |
| | | | kNN (error) | | | | | | | | |
| Standard deviation of VA mean, post loading (post loading - month 12) | VP_OCTANE | outliers removed | Linear Regression | 13.25 | 3.64 | 2.63 | -0.08 | 67.91 | VP_vol_subretinal_fluid | 3.268 | 0.353 |
| | | | SVM | 13.91 | 3.73 | 2.34 | -0.13 | 69.58 | VP_vol_choroid_and_outer_layers | 2.447 | 0.258 |
| | | | Random Forest | 14.91 | 3.86 | 2.84 | -0.21 | 72.05 | VP_vol_serous_ped | 1.903 | 0.502 |
| | | | kNN | 15.17 | 3.89 | 2.96 | -0.23 | 72.67 | VP_vol_rpe | 1.294 | 0.269 |
| | | | Tree | 15.29 | 3.91 | 2.79 | -0.24 | 72.96 | VP_vol_neurosensory_retina | 0.845 | 0.187 |
| | | | Gradient Boosting | 16.16 | 4.02 | 2.89 | -0.32 | 75.01 | | | |
| | | | AdaBoost | 19.33 | 4.40 | 3.40 | -0.57 | 82.04 | | | |
| Standard deviation of VA mean, post loading (post loading - month 12) | Demographic & qualitative | full | Linear Regression | 12.24 | 3.50 | 2.49 | -0.05 | 66.08 | Fellow eye activity | NA | 0.230 |
| | | | kNN | 14.55 | 3.81 | 2.83 | -0.25 | 72.02 | Anti-VEGF drug type | NA | 0.170 |
| | | | Gradient Boosting | 14.63 | 3.83 | 2.67 | -0.25 | 72.24 | Age At First Injection | NA | 0.119 |
| | | | Random Forest | 15.39 | 3.92 | 2.77 | -0.32 | 74.09 | Sex | NA | 0.097 |
| | | | SVM | 15.87 | 3.98 | 2.51 | -0.36 | 75.24 | Laterality | NA | 0.068 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Tree | 18.19 | 4.26 | 2.98 | -0.56 | 80.54 | | | |
| | | | AdaBoost | 19.46 | 4.41 | 3.07 | -0.67 | 83.31 | | | |
| Standard deviation of VA mean, post loading (post loading - month 12) | Demographic & qualitative | outliers removed | Linear Regression | 13.18 | 3.63 | 2.55 | -0.15 | 68.46 | Fellow eye activity | NA | 0.264 |
| | | | SVM | 13.92 | 3.73 | 2.39 | -0.21 | 70.37 | Age At First Injection | NA | 0.179 |
| | | | kNN | 14.30 | 3.78 | 2.68 | -0.24 | 71.33 | Anti-VEGF drug type | NA | 0.130 |
| | | | Gradient Boosting | 14.73 | 3.84 | 2.78 | -0.28 | 72.38 | Sex | NA | 0.122 |
| | | | Random Forest | 15.76 | 3.97 | 2.82 | -0.37 | 74.87 | Laterality | NA | 0.077 |
| | | | AdaBoost | 17.90 | 4.23 | 2.89 | -0.56 | 79.79 | | | |
| | | | Tree | 18.87 | 4.34 | 3.13 | -0.64 | 81.93 | | | |
| Standard deviation of VA mean, post loading (post loading - month 12) | VA | full | Linear Regression | 11.85 | 3.44 | 2.43 | -0.01 | 65.02 | VA fellow eye (V0) | 3.786 | 0.106 |
| | | | SVM | 13.26 | 3.64 | 2.27 | -0.13 | 68.76 | VA baseline visit (V0) | 0.520 | 0.091 |
| | | | kNN | 13.58 | 3.69 | 2.65 | -0.16 | 69.59 | VA post loading (VP) | 8.256 | 0.065 |
| | | | Gradient Boosting | 13.94 | 3.73 | 2.64 | -0.19 | 70.51 | VA mean of 2 visits immediately post loading | 11.621 | 0.063 |
| | | | Random Forest | 14.18 | 3.77 | 2.77 | -0.21 | 71.12 | | | |
| | | | AdaBoost | 14.79 | 3.85 | 2.56 | -0.27 | 72.62 | | | |
| | | | Tree | 23.25 | 4.82 | 3.60 | -0.99 | 91.06 | | | |
| Standard deviation of VA mean, post loading (post loading - month 12) | VA | outliers removed | Linear Regression | 10.65 | 3.26 | 2.31 | 0.02 | 62.43 | VA mean of 2 visits immediately post loading | 6.627 | 0.067 |
| | | | kNN | 10.81 | 3.29 | 2.34 | 0.01 | 62.89 | VA post loading (VP) | 4.134 | 0.069 |
| | | | Gradient Boosting | 10.92 | 3.30 | 2.39 | 0.00 | 63.20 | VA fellow eye (V0) | 2.766 | 0.130 |
| | | | AdaBoost | 11.33 | 3.37 | 2.32 | -0.04 | 64.38 | VA baseline visit (V0) | 0.948 | 0.090 |
| | | | Random Forest | 11.53 | 3.40 | 2.44 | -0.06 | 64.95 | | | |
| | | | SVM | 12.39 | 3.52 | 2.27 | -0.14 | 67.33 | | | |
| | | | Tree | 16.70 | 4.09 | 2.85 | -0.53 | 78.18 | | | |
| Standard deviation of VA mean, post loading (post loading - month 12) | V0_OCT | full | Linear Regression | 11.66 | 3.42 | 2.55 | -0.05 | 56.66 | V0_IPL 3mm vol | 3.977 | 0.060 |
| | | | SVM | 12.43 | 3.53 | 2.38 | -0.12 | 58.49 | V0_GCL 3mm vol | 3.227 | 0.096 |
| | | | AdaBoost | 12.87 | 3.59 | 2.57 | -0.16 | 59.52 | V0_ONL 1mm CM vol | 1.717 | 0.082 |
| | | | kNN | 13.20 | 3.63 | 2.72 | -0.19 | 60.28 | V0_ONL 1mm CMT | 1.576 | 0.085 |
| | | | Random Forest | 13.25 | 3.64 | 2.75 | -0.20 | 60.40 | V0_INL min CMT | 1.521 | 0.070 |
| | | | Gradient Boosting | 14.89 | 3.86 | 2.86 | -0.35 | 64.02 | | | |
| | | | Tree | 19.31 | 4.39 | 3.26 | -0.75 | 72.91 | | | |
| Sta | V0 | out | SVM | 12.38 | 3.52 | 2.39 | -0.10 | 58.29 | V0_IPL 3mm vol | 0.085 | |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Gradient Boosting | 12.45 | 3.53 | 2.60 | -0.11 | 58.45 | V0_GCL 3mm vol | 0.106 | |
| | | | AdaBoost | 12.54 | 3.54 | 2.44 | -0.12 | 58.67 | V0_INL min CMT | 0.089 | |
| | | | Random Forest | 12.71 | 3.57 | 2.65 | -0.13 | 59.06 | V0_OPL 3mm vol | 0.127 | |
| | | | kNN | 13.39 | 3.66 | 2.75 | -0.19 | 60.63 | V0_RPE 3mm vol | 0.074 | |
| | | | Linear Regression | 15.70 | 3.96 | 2.78 | -0.40 | 65.64 | | | |
| | | | Tree | 20.08 | 4.48 | 3.27 | -0.79 | 74.25 | | | |
| Standard deviation of VA mean, post loading (post loading - month 12) | VP_OCT | full | Linear Regression | 11.30 | 3.36 | 2.51 | -0.02 | 55.78 | VP_GCL min CMT | 5.917 | 0.061 |
| | | | AdaBoost | 12.37 | 3.52 | 2.44 | -0.12 | 58.36 | VP_INL min CMT | 4.007 | 0.086 |
| | | | SVM | 12.37 | 3.52 | 2.43 | -0.12 | 58.36 | VP_NFL 1mm CM vol | 3.539 | 0.007 |
| | | | Random Forest | 12.80 | 3.58 | 2.63 | -0.16 | 59.35 | VP_IPL 3mm vol | 3.316 | 0.084 |
| | | | kNN | 13.02 | 3.61 | 2.64 | -0.18 | 59.86 | VP_NFL min CMT | 2.994 | 0.067 |
| | | | Gradient Boosting | 13.77 | 3.71 | 2.70 | -0.25 | 61.58 | | | |
| | | | Tree | 19.91 | 4.46 | 3.37 | -0.80 | 74.03 | | | |
| Standard deviation of VA mean, post loading (post loading - month 12) | VP_OCT | outliers removed | SVM | 11.89 | 3.45 | 2.41 | -0.10 | 57.50 | VP_NFL min CMT | 4.850 | 0.048 |
| | | | Linear Regression | 12.21 | 3.49 | 2.60 | -0.13 | 58.28 | VP_IPL 3mm vol | 4.748 | 0.085 |
| | | | AdaBoost | 12.62 | 3.55 | 2.57 | -0.17 | 59.25 | VP_GCL min CMT | 4.160 | 0.053 |
| | | | kNN | 12.78 | 3.58 | 2.62 | -0.18 | 59.62 | VP_GCL 3mm vol | 4.095 | 0.134 |
| | | | Random Forest | 12.84 | 3.58 | 2.74 | -0.19 | 59.75 | VP_RPE 3mm vol | 3.788 | 0.054 |
| | | | Gradient Boosting | 13.71 | 3.70 | 2.75 | -0.27 | 61.73 | | | |
| | | | Tree | 20.28 | 4.50 | 3.51 | -0.88 | 75.09 | | | |
| Standard deviation of VA mean, baseline - 12 months | V0_OCT | full | Random Forest | 12.30 | 3.51 | 2.57 | -0.11 | 58.18 | V0_vol_epiretinal_membrane | 5.378 | 0.473 |
| | | | SVM | 16.49 | 4.06 | 2.74 | -0.49 | 67.38 | V0_vol_serous_ped | 2.897 | 0.500 |
| | | | AdaBoost | 25.41 | 5.04 | 3.48 | -1.30 | 83.63 | V0_vol_neurosensory_retina | 1.729 | 0.180 |
| | | | Tree | 27.93 | 5.28 | 4.18 | -1.53 | 87.68 | V0_vol_fibrovascular_ped | 1.249 | 0.252 |
| | | | Gradient Boosting | 30.41 | 5.51 | 4.13 | -1.75 | 91.50 | V0_vol_vitreous_and_subhyaloid | 0.889 | 0.230 |
| | | | Linear Regression | 118.86 | 10.90 | 6.89 | -9.75 | 180.88 | | | |
| | | | kNN (error) | | | | | | | | |
| Standard deviation | V0_OCT | outliers | Linear Regression | 11.78 | 3.43 | 2.55 | -0.05 | 56.34 | V0_vol_epiretinal_membrane | 3.994 | 0.482 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Random Forest | 12.37 | 3.52 | 2.68 | -0.10 | 57.74 | V0_vol_neurosensory_retina | 3.282 | 0.185 |
| | | | SVM | 12.39 | 3.52 | 2.40 | -0.10 | 57.79 | V0_vol_fibrovascular_ped | 1.833 | 0.207 |
| | | | Gradient Boosting | 13.33 | 3.65 | 2.74 | -0.18 | 59.93 | V0_vol_serous_ped | 1.342 | 0.476 |
| | | | kNN | 13.64 | 3.69 | 2.73 | -0.21 | 60.63 | V0_vol_rpe | 0.974 | 0.219 |
| | | | Tree | 13.65 | 3.69 | 2.73 | -0.21 | 60.66 | | | |
| | | | AdaBoost | 17.43 | 4.18 | 3.18 | -0.55 | 68.55 | | | |
| Standard deviation of VA mean, baseline - 12 months | VP_OCTANE | full | SVM | 21.12 | 4.60 | 3.79 | -0.91 | 76.25 | VP_vol_subretinal_fluid | 4.524 | 0.309 |
| | | | Tree | 21.76 | 4.66 | 3.90 | -0.97 | 77.40 | VP_vol_choroid_and_outer_layers | 3.298 | 0.244 |
| | | | Random Forest | 22.77 | 4.77 | 3.91 | -1.06 | 79.18 | VP_vol_neurosensory_retina | 3.111 | 0.102 |
| | | | AdaBoost | 25.60 | 5.06 | 3.71 | -1.32 | 83.95 | VP_vol_drusenoid_ped | 2.290 | 0.302 |
| | | | Gradient Boosting | 45.31 | 6.73 | 5.64 | -3.10 | 111.69 | VP_vol_subretinal_hyper_reflect | 1.464 | 0.411 |
| | | | Linear Regression | 51.84 | 7.20 | 5.55 | -3.69 | 119.45 | | | |
| | | | kNN (error) | | | | | | | | |
| Standard deviation of VA mean, baseline - 12 months | VP_OCTANE | outliers removed | Linear Regression | 12.24 | 3.50 | 2.62 | -0.06 | 57.05 | VP_vol_choroid_and_outer_layers | 3.129 | 0.261 |
| | | | SVM | 12.50 | 3.54 | 2.41 | -0.08 | 57.64 | VP_vol_subretinal_fluid | 2.846 | 0.420 |
| | | | Random Forest | 12.61 | 3.55 | 2.72 | -0.09 | 57.90 | VP_vol_fibrovascular_ped | 1.314 | 0.208 |
| | | | kNN | 13.80 | 3.71 | 2.90 | -0.19 | 60.56 | VP_vol_serous_ped | 1.249 | 0.519 |
| | | | AdaBoost | 14.01 | 3.74 | 2.96 | -0.21 | 61.02 | VP_vol_drusenoid_ped | 1.045 | 0.294 |
| | | | Gradient Boosting | 14.46 | 3.80 | 2.84 | -0.25 | 62.01 | | | |
| | | | Tree | 17.12 | 4.14 | 3.05 | -0.48 | 67.46 | | | |
| Standard deviation of VA mean, baseline - 12 months | Demographic & qualitative | full | Linear Regression | 11.91 | 3.45 | 2.55 | -0.08 | 57.25 | Fellow eye activity | NA | 0.299 |
| | | | kNN | 13.68 | 3.70 | 2.86 | -0.24 | 61.36 | Anti-VEGF drug type | NA | 0.134 |
| | | | Gradient Boosting | 14.61 | 3.82 | 2.83 | -0.32 | 63.41 | Age At First Injection | NA | 0.125 |
| | | | SVM | 15.38 | 3.92 | 2.64 | -0.39 | 65.07 | Sex | NA | 0.083 |
| | | | Random Forest | 15.63 | 3.95 | 2.95 | -0.41 | 65.60 | Laterality | NA | 0.068 |
| | | | AdaBoost | 18.83 | 4.34 | 3.16 | -0.70 | 72.00 | | | |
| | | | Tree | 20.13 | 4.49 | 3.31 | -0.82 | 74.44 | | | |
| Standard deviation of VA | Demographic & | outliers removed | Linear Regression | 12.18 | 3.49 | 2.54 | -0.13 | 58.13 | Fellow eye activity | NA | 0.240 |
| | | | SVM | 13.35 | 3.65 | 2.44 | -0.24 | 60.86 | Anti-VEGF drug type | NA | 0.187 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Gradient Boosting | 13.41 | 3.66 | 2.73 | -0.25 | 61.00 | Age At First Injection | NA | 0.163 |
| | | | kNN | 13.81 | 3.72 | 2.76 | -0.29 | 61.90 | Laterality | NA | 0.084 |
| | | | Random Forest | 14.49 | 3.81 | 2.85 | -0.35 | 63.40 | Sex | NA | 0.082 |
| | | | Tree | 16.95 | 4.12 | 3.10 | -0.58 | 68.58 | | | |
| | | | AdaBoost | 17.23 | 4.15 | 3.04 | -0.60 | 69.14 | | | |
| Standard deviation of VA mean, baseline - 12 months | VA_st dev | full | Linear Regression | 11.23 | 3.35 | 2.47 | -0.02 | 55.60 | VA fellow eye (V0) | 1.724 | 0.096 |
| | | | SVM | 11.80 | 3.44 | 2.26 | -0.07 | 57.00 | VA baseline visit (V0) | 8.539 | 0.081 |
| | | | Random Forest | 12.29 | 3.51 | 2.64 | -0.11 | 58.16 | VA post loading (VP) | 7.484 | 0.055 |
| | | | kNN | 12.53 | 3.54 | 2.64 | -0.13 | 58.74 | VA mean of 2 visits immediately post loading | 10.993 | 0.055 |
| | | | Gradient Boosting | 12.85 | 3.58 | 2.66 | -0.16 | 59.46 | | | |
| | | | AdaBoost | 13.09 | 3.62 | 2.57 | -0.18 | 60.04 | | | |
| | | | Tree | 20.06 | 4.48 | 3.32 | -0.81 | 74.31 | | | |
| Standard deviation of VA mean, baseline - 12 months | VA_st dev | outliers removed | Random Forest | 9.37 | 3.06 | 2.23 | 0.07 | 52.12 | VA baseline visit (V0) | 7.496 | 0.083 |
| | | | Gradient Boosting | 9.45 | 3.07 | 2.24 | 0.06 | 52.33 | VA mean of 2 visits immediately post loading | 6.451 | 0.067 |
| | | | AdaBoost | 9.49 | 3.08 | 2.14 | 0.06 | 52.45 | VA post loading (VP) | 3.880 | 0.066 |
| | | | Linear Regression | 9.90 | 3.15 | 2.28 | 0.02 | 53.58 | VA fellow eye (V0) | 2.225 | 0.109 |
| | | | kNN | 9.97 | 3.16 | 2.24 | 0.01 | 53.76 | | | |
| | | | SVM | 10.71 | 3.27 | 2.13 | -0.06 | 55.73 | | | |
| | | | Tree | 14.88 | 3.86 | 2.73 | -0.47 | 65.69 | | | |
| Standard deviation of VA mean, baseline - 12 months | V0_OCT | full | SVM | 191.37 | 13.83 | 10.66 | 0.00 | 1196.72 | V0_retina min CMT | 11.533 | 0.064 |
| | | | Linear Regression | 202.36 | 14.23 | 10.87 | -0.05 | 1230.62 | V0_IPL 1mm CM vol | 8.965 | 0.021 |
| | | | AdaBoost | 231.26 | 15.21 | 11.67 | -0.20 | 1315.54 | V0_IPL 1mm CMT | 7.968 | 0.034 |
| | | | Random Forest | 233.11 | 15.27 | 11.86 | -0.21 | 1320.81 | V0_INL 3mm vol | 7.268 | 0.072 |
| | | | Gradient Boosting | 238.90 | 15.46 | 11.86 | -0.24 | 1337.11 | V0_retina 1mm CM vol | 6.775 | 0.065 |
| | | | kNN | 246.45 | 15.70 | 12.32 | -0.28 | 1358.05 | | | |
| | | | Tree | 375.57 | 19.38 | 14.98 | -0.95 | 1676.49 | | | |
| Standard deviation of VA mean, baseline - 12 | V0_OCT | outliers removed | SVM | 189.03 | 13.75 | 10.28 | 0.02 | 1317.41 | V0_retina min CMT | 11.379 | 0.098 |
| | | | AdaBoost | 198.49 | 14.09 | 10.46 | -0.03 | 1349.97 | V0_retina 1mm CM vol | 7.584 | 0.088 |
| | | | Gradient Boosting | 206.25 | 14.36 | 10.84 | -0.07 | 1376.10 | V0_OPL 1mm CM vol | 7.379 | 0.070 |
| | | | kNN | 229.52 | 15.15 | 11.78 | -0.19 | 1451.66 | V0_IPL 1mm CM vol | 7.363 | 0.023 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Random Forest | 232.68 | 15.25 | 11.59 | -0.20 | 1461.63 | V0_retina 1mm CMT | 7.287 | 0.089 |
| | | | Linear Regression | 277.44 | 16.66 | 11.87 | -0.44 | 1596.02 | | | |
| | | | Tree | 380.52 | 19.51 | 15.45 | -0.97 | 1869.14 | | | |
| Standard deviation of VA mean, baseline - 12 months | VP_OCT | full | SVM | 190.56 | 13.80 | 10.63 | 0.01 | 1194.17 | VP_ORLs 3mm vol | 4.908 | 0.020 |
| | | | Linear Regression | 196.17 | 14.01 | 10.95 | -0.02 | 1211.64 | VP_RPE 3mm vol | 4.259 | 0.020 |
| | | | AdaBoost | 203.54 | 14.27 | 11.08 | -0.06 | 1234.18 | VP_GCL min CMT | 4.018 | 0.067 |
| | | | kNN | 214.95 | 14.66 | 11.55 | -0.12 | 1268.31 | VP_NFL 3mm vol | 3.396 | 0.072 |
| | | | Random Forest | 215.86 | 14.69 | 11.17 | -0.12 | 1271.00 | VP_IPL min CMT | 3.358 | 0.107 |
| | | | Gradient Boosting | 225.60 | 15.02 | 11.69 | -0.17 | 1299.34 | | | |
| | | | Tree | 360.79 | 18.99 | 14.73 | -0.88 | 1643.18 | | | |
| Standard deviation of VA mean, baseline - 12 months | VP_OCT | outliers removed | SVM | 184.81 | 13.59 | 10.31 | -0.01 | 898.20 | VP_RPE 3mm vol | 5.462 | 0.060 |
| | | | AdaBoost | 214.58 | 14.65 | 10.86 | -0.17 | 967.85 | VP_IPL min CMT | 4.547 | 0.162 |
| | | | Linear Regression | 217.32 | 14.74 | 11.58 | -0.19 | 974.02 | VP_ORLs 3mm vol | 4.018 | 0.057 |
| | | | kNN | 224.95 | 15.00 | 11.38 | -0.23 | 990.96 | VP_IRLs min CMT | 3.168 | 0.096 |
| | | | Random Forest | 229.35 | 15.14 | 11.60 | -0.26 | 1000.60 | VP_GCL 3mm vol | 3.140 | 0.124 |
| | | | Gradient Boosting | 232.02 | 15.23 | 11.47 | -0.27 | 1006.42 | | | |
| | | | Tree | 364.09 | 19.08 | 14.53 | -0.99 | 1260.72 | | | |
| Change in visual acuity at 12 months from baseline | V0_OCTANE | full | Random Forest | 199.26 | 14.12 | 11.02 | -0.04 | 1221.14 | V0_vol_drusenoid_ped | 5.771 | 0.259 |
| | | | SVM | 203.15 | 14.25 | 11.11 | -0.06 | 1233.02 | V0_vol_subretinal_hyper_reflect | 1.912 | 0.282 |
| | | | Tree | 245.55 | 15.67 | 12.24 | -0.28 | 1355.58 | V0_vol_epiretinal_membrane | 1.675 | 0.456 |
| | | | AdaBoost | 246.17 | 15.69 | 11.89 | -0.28 | 1357.29 | V0_vol_fibrovascular_ped | 1.567 | 0.181 |
| | | | Gradient Boosting | 246.93 | 15.71 | 12.22 | -0.29 | 1359.39 | V0_vol_neurosensory_retina | 1.044 | 0.140 |
| | | | Linear Regression | 389.71 | 19.74 | 15.17 | -1.03 | 1707.76 | | | |
| | | | kNN (error) | | | | | | | | |
| Change in visual acuity at 12 months from baseline | V0_OCTANE | outliers removed | SVM | 195.38 | 13.98 | 10.79 | -0.01 | 1509.21 | V0_vol_drusenoid_ped | 5.546 | 0.262 |
| | | | Linear Regression | 202.54 | 14.23 | 11.09 | -0.05 | 1536.61 | V0_vol_subretinal_hyper_reflect | 2.546 | 0.290 |
| | | | AdaBoost | 212.15 | 14.57 | 11.26 | -0.10 | 1572.62 | V0_vol_epiretinal_membrane | 1.450 | 0.481 |
| | | | kNN | 213.29 | 14.60 | 11.16 | -0.11 | 1576.85 | V0_vol_subretinal_fluid | 1.321 | 0.260 |
| | | | Random Forest | 216.53 | 14.71 | 11.62 | -0.12 | 1588.79 | V0_vol_serous_ped | 0.965 | 0.481 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Gradient Boosting | 233.86 | 15.29 | 11.72 | -0.21 | 1651.13 | | | |
| | | | Tree | 275.06 | 16.58 | 12.77 | -0.43 | 1790.68 | | | |
| Change in visual acuity at 12 months from baseline | VP_OCTANE | full | AdaBoost | 315.94 | 17.77 | 14.29 | -0.64 | 1537.65 | VP_vol_neurosensory_retina | 7.080 | 0.125 |
| | | | Tree | 445.44 | 21.11 | 18.12 | -1.32 | 1825.79 | VP_vol_vitreous_and_subhyaloid | 2.787 | 0.219 |
| | | | Random Forest | 522.28 | 22.85 | 19.71 | -1.72 | 1977.00 | VP_vol_subretinal_fluid | 2.015 | 0.327 |
| | | | SVM | 526.74 | 22.95 | 19.98 | -1.74 | 1985.43 | VP_vol_epiretinal_membrane | 1.652 | 0.490 |
| | | | Linear Regression | 607.81 | 24.65 | 20.69 | -2.16 | 2132.74 | VP_vol_posterior_hyaloid | 1.420 | 0.421 |
| | | | Gradient Boosting | 639.35 | 25.29 | 21.50 | -2.33 | 2187.38 | | | |
| | | | kNN (error) | | | | | | | | |
| Change in visual acuity at 12 months from baseline | VP_OCTANE | outliers removed | SVM | 202.02 | 14.21 | 10.92 | 0.00 | 1307.28 | VP_vol_neurosensory_retina | 2.654 | 0.213 |
| | | | Linear Regression | 216.96 | 14.73 | 11.42 | -0.07 | 1354.75 | VP_vol_epiretinal_membrane | 2.327 | 0.491 |
| | | | Random Forest | 227.15 | 15.07 | 11.53 | -0.12 | 1386.20 | VP_vol_vitreous_and_subhyaloid | 1.751 | 0.273 |
| | | | Gradient Boosting | 237.24 | 15.40 | 11.57 | -0.17 | 1416.67 | VP_vol_rpe | 1.367 | 0.275 |
| | | | AdaBoost | 242.56 | 15.57 | 11.88 | -0.20 | 1432.46 | VP_vol_posterior_hyaloid | 1.330 | 0.439 |
| | | | kNN | 246.54 | 15.70 | 12.31 | -0.22 | 1444.17 | | | |
| | | | Tree | 294.84 | 17.17 | 12.78 | -0.46 | 1579.30 | | | |
| Change in visual acuity at 12 months from baseline | Demographic & qualitative | full | Linear Regression | 196.60 | 14.02 | 10.68 | -0.02 | 1212.96 | Fellow eye activity | NA | 0.267 |
| | | | Gradient Boosting | 242.55 | 15.57 | 11.86 | -0.26 | 1347.27 | Age At First Injection | NA | 0.144 |
| | | | Random Forest | 244.13 | 15.62 | 11.88 | -0.27 | 1351.65 | Anti-VEGF drug type | NA | 0.106 |
| | | | kNN | 246.91 | 15.71 | 12.21 | -0.28 | 1359.32 | Ethnicity | NA | 0.097 |
| | | | SVM | 253.16 | 15.91 | 13.00 | -0.32 | 1376.42 | Sex | NA | 0.074 |
| | | | Tree | 283.98 | 16.85 | 13.12 | -0.48 | 1457.81 | | | |
| | | | AdaBoost | 291.71 | 17.08 | 13.35 | -0.52 | 1477.52 | | | |
| Change in visual acuity at 12 months from baseline | Demographic & qualitative | outliers removed | Linear Regression | 193.63 | 13.92 | 10.65 | -0.03 | 1047.16 | Fellow eye activity | NA | 0.271 |
| | | | kNN | 202.83 | 14.24 | 11.14 | -0.08 | 1071.75 | Age At First Injection | NA | 0.162 |
| | | | SVM | 202.84 | 14.24 | 11.22 | -0.08 | 1071.76 | Anti-VEGF drug type | NA | 0.126 |
| | | | Random Forest | 203.57 | 14.27 | 11.19 | -0.08 | 1073.70 | Sex | NA | 0.081 |
| | | | Gradient Boosting | 217.36 | 14.74 | 11.50 | -0.15 | 1109.47 | Time interval 1st to 3rd injection | NA | 0.077 |
| | | | AdaBoost | 231.98 | 15.23 | 11.84 | -0.23 | 1146.16 | | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Tree | 258.78 | 16.09 | 12.60 | -0.37 | 1210.56 | | | |
| Change in visual acuity at 12 months from baseline | VA | full | SVM | 194.09 | 13.93 | 10.88 | -0.01 | 1205.18 | VA baseline visit (V0) | 60.685 | 0.123 |
| | | | Linear Regression | 198.43 | 14.09 | 10.82 | -0.03 | 1218.60 | VA fellow eye (V0) | 2.947 | 0.100 |
| | | | Gradient Boosting | 232.22 | 15.24 | 11.71 | -0.21 | 1318.26 | VA mean of 2 visits immediately post loading | 1.547 | 0.061 |
| | | | Random Forest | 239.38 | 15.47 | 11.97 | -0.25 | 1338.44 | VA post loading (VP) | 0.441 | 0.061 |
| | | | AdaBoost | 242.24 | 15.56 | 12.12 | -0.26 | 1346.41 | | | |
| | | | kNN | 242.75 | 15.58 | 11.83 | -0.26 | 1347.84 | | | |
| | | | Tree | 393.14 | 19.83 | 15.55 | -1.05 | 1715.27 | | | |
| Change in visual acuity at 12 months from baseline | VA | outliers removed | Linear Regression | 96.57 | 9.83 | 7.09 | 0.46 | 835.17 | VA baseline visit (V0) | 41.942 | 0.108 |
| | | | Random Forest | 125.63 | 11.21 | 8.34 | 0.29 | 952.56 | VA fellow eye (V0) | 5.311 | 0.124 |
| | | | Gradient Boosting | 127.73 | 11.30 | 8.25 | 0.28 | 960.50 | VA mean of 2 visits immediately post loading | 2.149 | 0.064 |
| | | | SVM | 132.08 | 11.49 | 8.75 | 0.26 | 976.70 | VA post loading (VP) | 0.733 | 0.067 |
| | | | kNN | 133.82 | 11.57 | 8.57 | 0.25 | 983.13 | | | |
| | | | AdaBoost | 134.48 | 11.60 | 8.56 | 0.24 | 985.55 | | | |
| | | | Tree | 209.02 | 14.46 | 10.57 | -0.18 | 1228.68 | | | |
| Change in visual acuity at 12 months from baseline | VA_st dev | full | SVM | 195.57 | 13.98 | 10.84 | -0.02 | 1209.77 | Standard deviation of VA mean, post loading -12 months (VP-V12) | 68.979 | 0.107 |
| | | | Linear Regression | 196.43 | 14.02 | 10.78 | -0.02 | 1212.43 | VA baseline visit (V0) | 60.685 | 0.098 |
| | | | AdaBoost | 225.66 | 15.02 | 11.72 | -0.17 | 1299.52 | VA fellow eye (V0) | 2.947 | 0.094 |
| | | | Random Forest | 228.68 | 15.12 | 11.62 | -0.19 | 1308.20 | VA mean of 2 visits immediately post loading | 1.547 | 0.064 |
| | | | Gradient Boosting | 237.82 | 15.42 | 11.60 | -0.24 | 1334.08 | VA post loading (VP) | 0.441 | 0.065 |
| | | | kNN | 238.89 | 15.46 | 11.79 | -0.24 | 1337.08 | | | |
| | | | Tree | 405.12 | 20.13 | 15.54 | -1.11 | 1741.20 | | | |
| Change in visual acuity at 12 months from baseline | VA_st dev | outliers removed | Linear Regression | 74.62 | 8.64 | 6.19 | 0.57 | 702.32 | Standard deviation of VA mean, post loading -12 months (VP-V12) | 61.515 | 0.150 |
| | | | Random Forest | 95.95 | 9.80 | 6.99 | 0.45 | 796.37 | VA baseline visit (V0) | 42.590 | 0.103 |
| | | | Gradient Boosting | 98.98 | 9.95 | 7.05 | 0.43 | 808.85 | VA fellow eye (V0) | 3.880 | 0.119 |
| | | | kNN | 106.40 | 10.32 | 7.55 | 0.39 | 838.63 | VA mean of 2 visits immediately post loading | 2.916 | 0.069 |
| | | | AdaBoost | 107.56 | 10.37 | 7.38 | 0.38 | 843.17 | VA post loading (VP) | 0.968 | 0.073 |
| | | | SVM | 120.63 | 10.98 | 8.23 | 0.30 | 892.94 | | | |
| | | | Tree | 162.45 | 12.75 | 9.17 | 0.06 | 1036.22 | | | |

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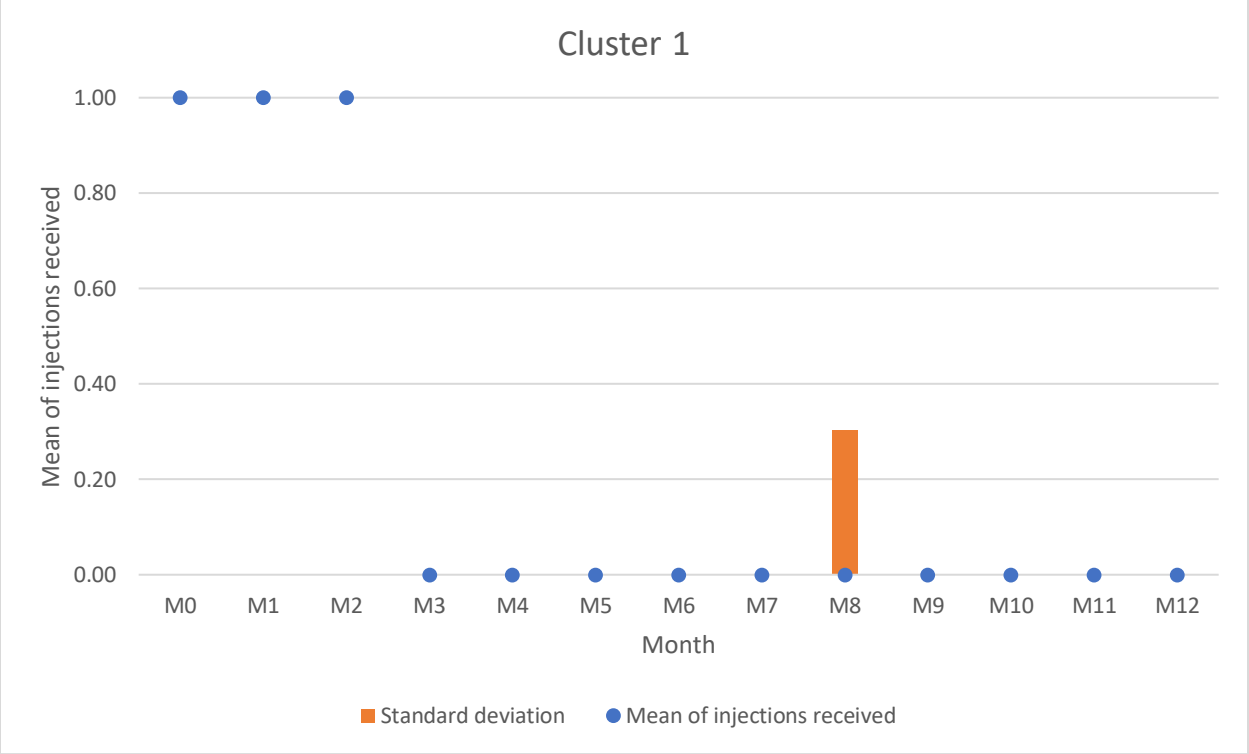
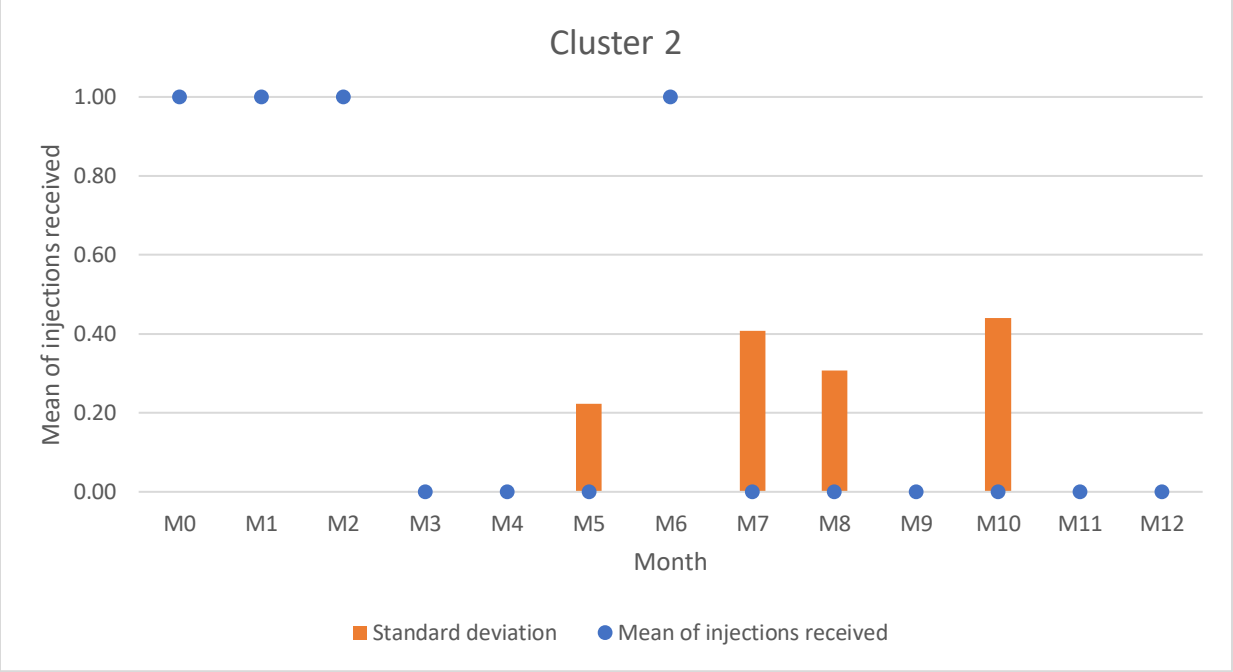
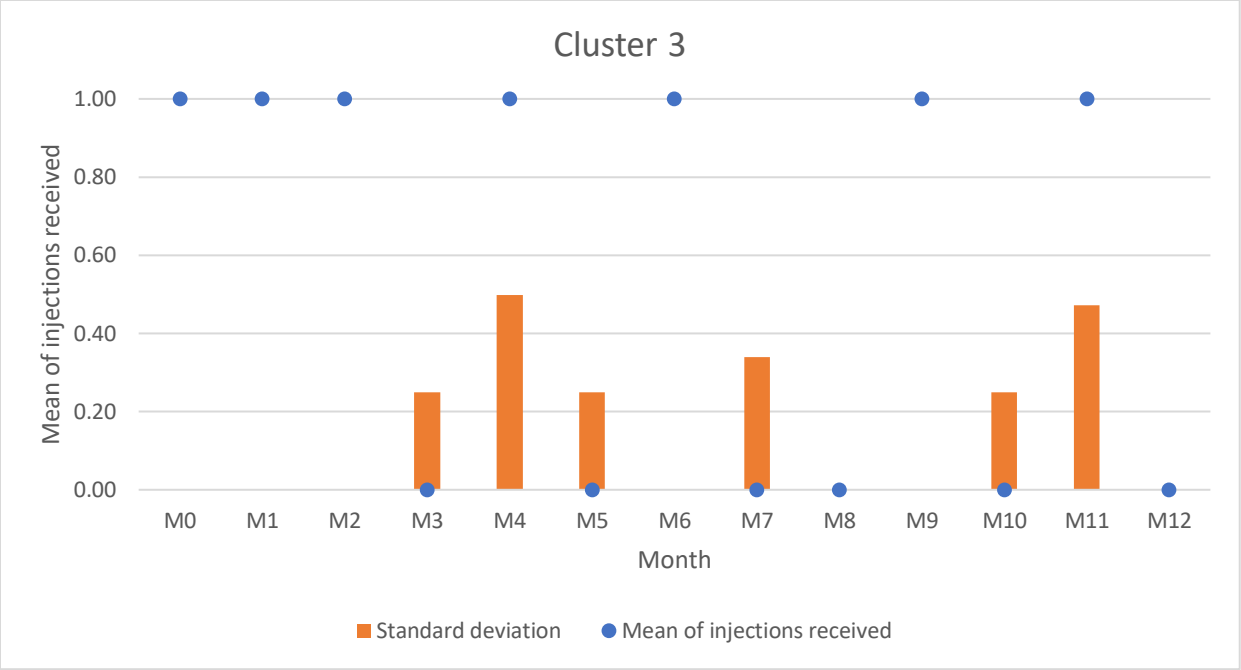
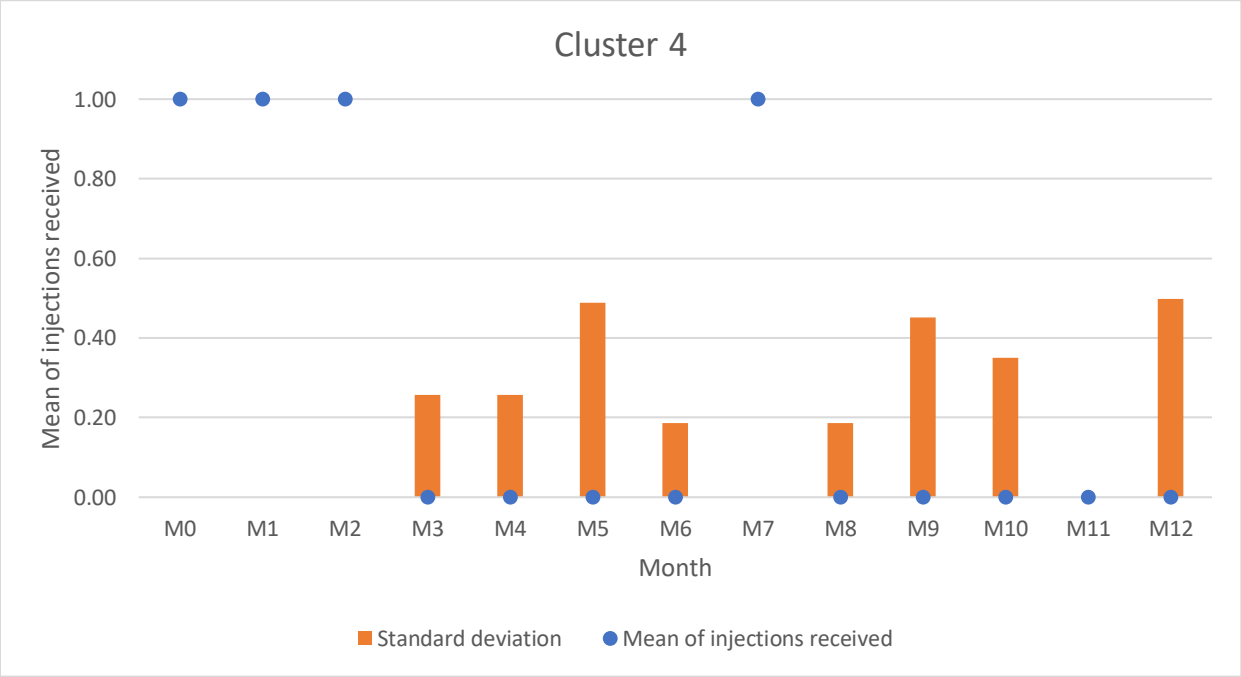
|---|---|---|---|---|---|---|---|---|---|---|---|
| Change in visual acuity at 12 months from baseline | V0_OCT | full | Linear Regression | 334.84 | 18.30 | 15.39 | -0.01 | 32.00 | V0_OPL 3mm vol | 10.625 | 0.136 |
| | | | SVM | 340.69 | 18.46 | 14.90 | -0.03 | 32.28 | V0_GCL 3mm vol | 7.830 | 0.153 |
| | | | Random Forest | 375.01 | 19.37 | 16.03 | -0.14 | 33.86 | V0_IRLs min CMT | 3.776 | 0.105 |
| | | | kNN | 383.86 | 19.59 | 16.18 | -0.16 | 34.26 | V0_IPL 3mm vol | 3.569 | 0.107 |
| | | | AdaBoost | 425.44 | 20.63 | 16.85 | -0.29 | 36.07 | V0_IPL min CMT | 3.555 | 0.144 |
| | | | Gradient Boosting | 437.64 | 20.92 | 17.05 | -0.32 | 36.58 | | | |
| | | | Tree | 669.44 | 25.87 | 20.34 | -1.03 | 45.24 | | | |
| Change in visual acuity at 12 months from baseline | V0_OCT | outliers removed | Gradient Boosting | 313.55 | 17.71 | 14.25 | 0.08 | 30.79 | V0_OPL 3mm vol | 9.698 | 0.166 |
| | | | Random Forest | 316.48 | 17.79 | 14.39 | 0.07 | 30.93 | V0_GCL 3mm vol | 8.106 | 0.164 |
| | | | SVM | 350.29 | 18.72 | 15.14 | -0.03 | 32.54 | V0_IPL 3mm vol | 4.480 | 0.109 |
| | | | AdaBoost | 367.27 | 19.16 | 15.38 | -0.08 | 33.32 | V0_IPL min CMT | 3.820 | 0.114 |
| | | | kNN | 379.21 | 19.47 | 15.85 | -0.11 | 33.86 | V0_IRLs min CMT | 3.409 | 0.115 |
| | | | Tree | 558.78 | 23.64 | 19.00 | -0.64 | 41.10 | | | |
| | | | Linear Regression | 561.81 | 23.70 | 18.47 | -0.65 | 41.21 | | | |
| Change in visual acuity at 12 months from baseline | VP_OCT | full | Linear Regression | 332.81 | 18.24 | 15.36 | -0.01 | 31.90 | VP_retina 3mm vol | 1.568 | 0.055 |
| | | | SVM | 344.73 | 18.57 | 15.02 | -0.04 | 32.47 | VP_retina 1mm CMT | 0.654 | 0.064 |
| | | | Random Forest | 381.26 | 19.53 | 16.03 | -0.15 | 34.14 | VP_retina 1mm CM vol | 0.561 | 0.064 |
| | | | kNN | 394.53 | 19.86 | 15.94 | -0.19 | 34.73 | VP_retina min CMT | 0.628 | 0.067 |
| | | | Gradient Boosting | 423.02 | 20.57 | 16.25 | -0.28 | 35.97 | VP_NFL 3mm vol | 0.727 | 0.110 |
| | | | AdaBoost | 426.23 | 20.65 | 16.34 | -0.29 | 36.10 | | | |
| | | | Tree | 598.76 | 24.47 | 19.83 | -0.81 | 42.79 | | | |
| Change in visual acuity at 12 months from baseline | VP_OCT | outliers removed | AdaBoost | 325.68 | 18.05 | 13.90 | 0.01 | 31.30 | VP_GCL 3mm vol | 17.652 | 0.160 |
| | | | SVM | 330.41 | 18.18 | 14.38 | -0.01 | 31.53 | VP_IRLs 3mm vol | 16.852 | 0.164 |
| | | | Random Forest | 354.75 | 18.83 | 15.28 | -0.08 | 32.67 | VP_IPL 3mm vol | 15.605 | 0.105 |
| | | | Gradient Boosting | 366.53 | 19.15 | 15.29 | -0.12 | 33.21 | VP_OPL 3mm vol | 7.691 | 0.156 |
| | | | kNN | 382.27 | 19.55 | 15.51 | -0.16 | 33.91 | VP_retina 3mm vol | 6.191 | 0.113 |
| | | | Linear Regression | 423.41 | 20.58 | 16.34 | -0.29 | 35.69 | | | |
| | | | Tree | 529.88 | 23.02 | 18.17 | -0.61 | 39.93 | | | |

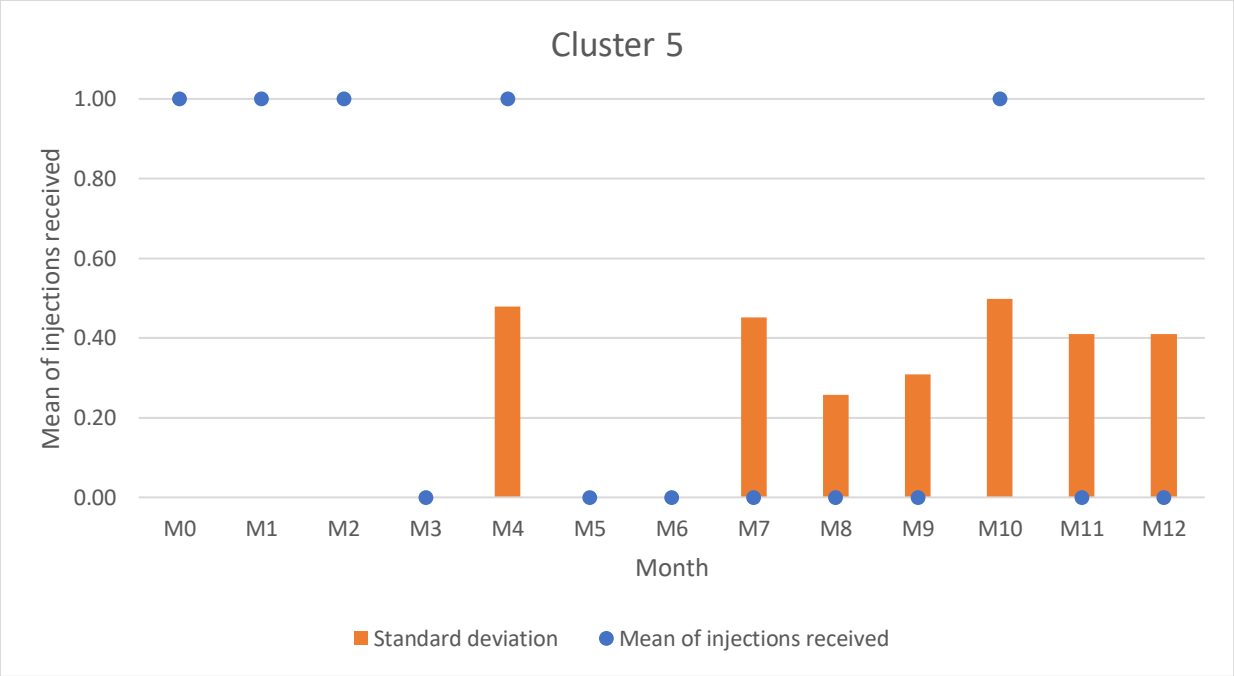
Appendix 9: Combined cluster and column charts of clustering showing distribution of injections received per month

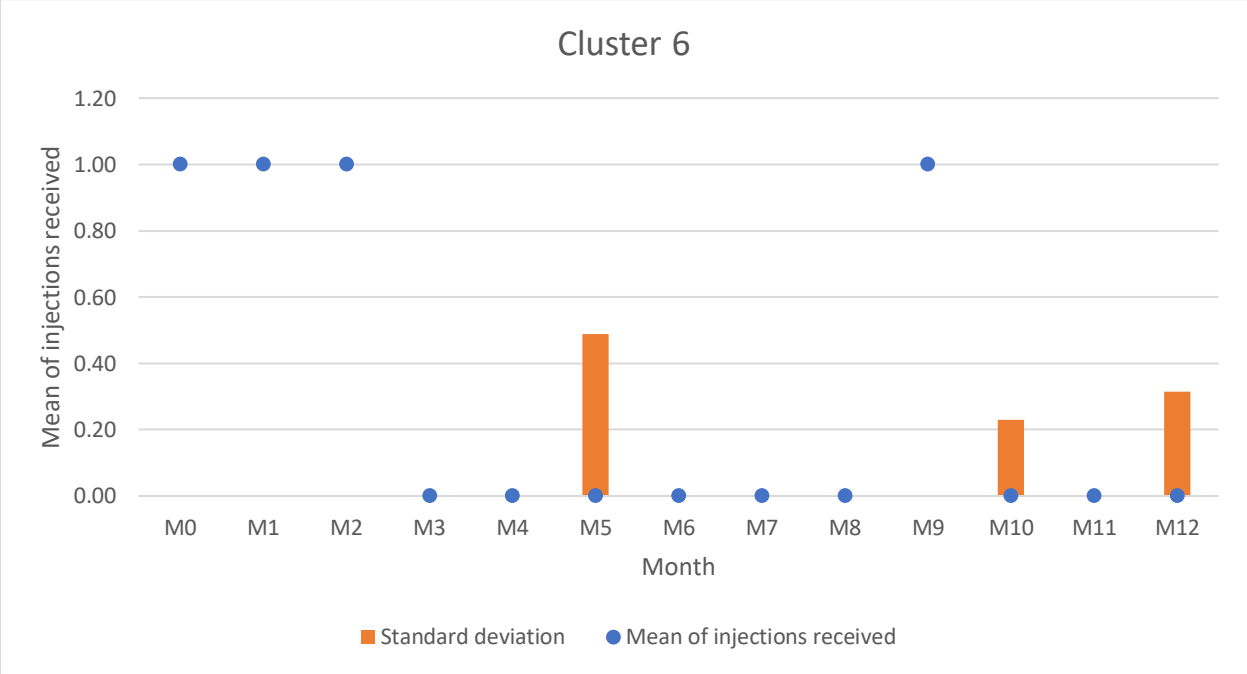


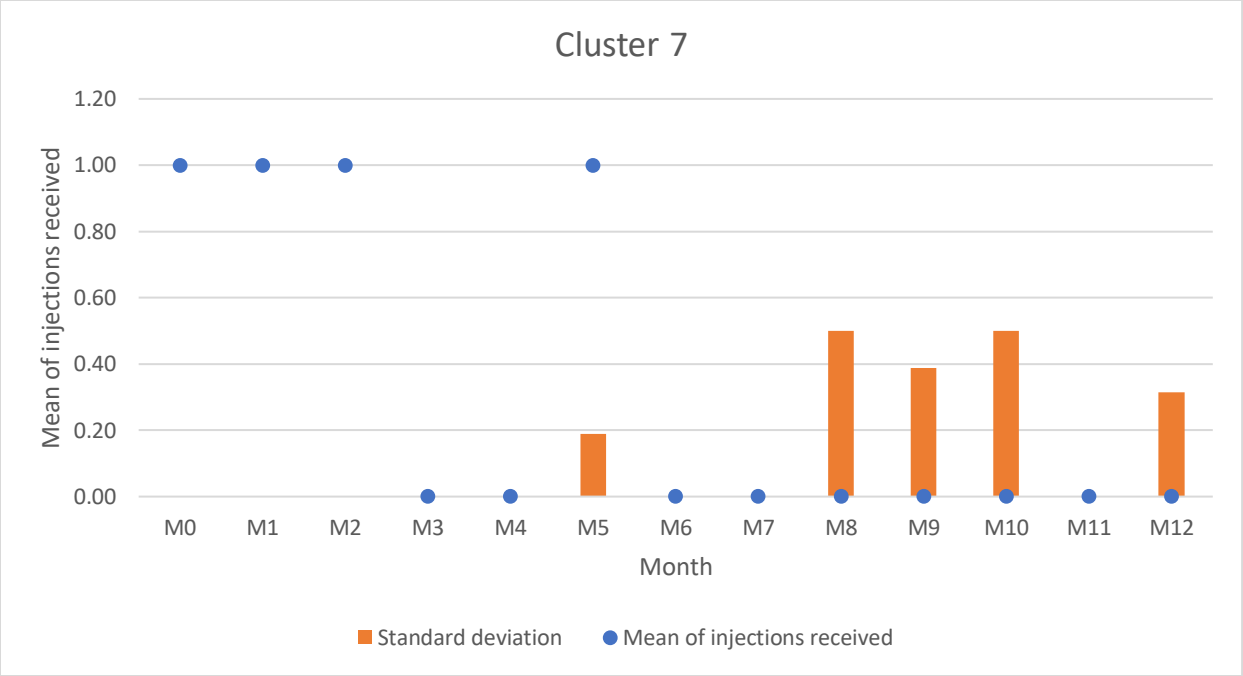



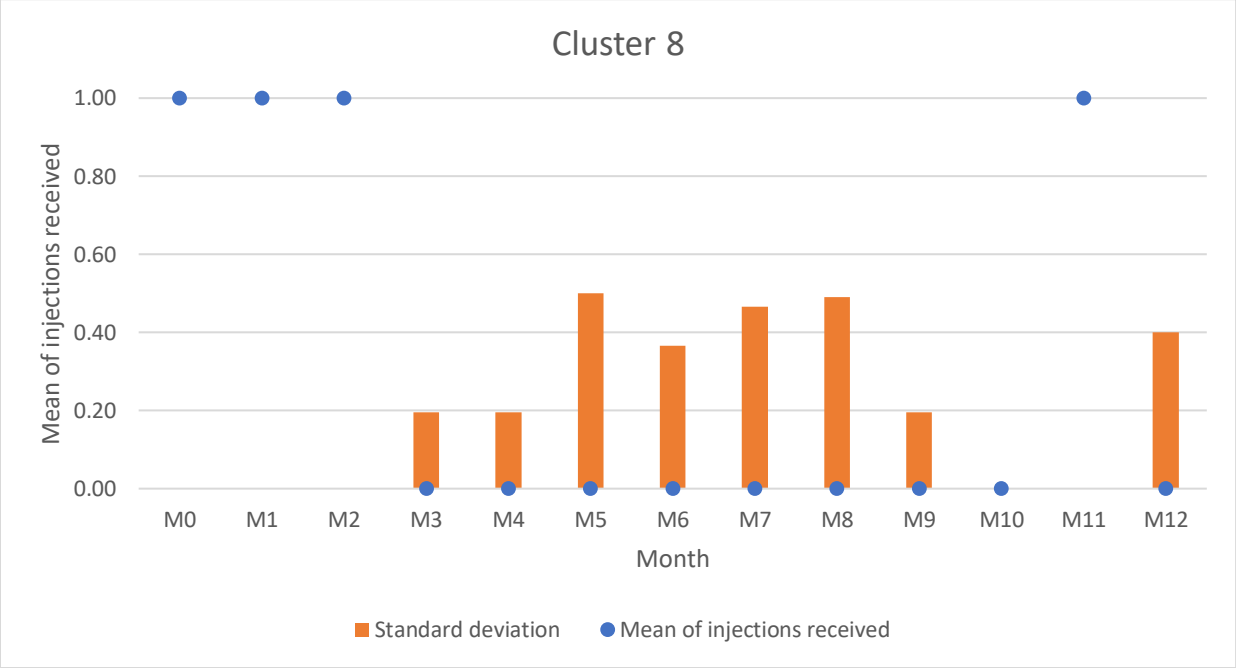

Cluster 3
1.00
0.80
0.60
0.40
0.20
0.00
Mean of injections received
M0
M1
M2
M3
M4
M5
M6
M7
M8
M9
M10
M11
M12
Month
Standard deviation
Mean of injections received

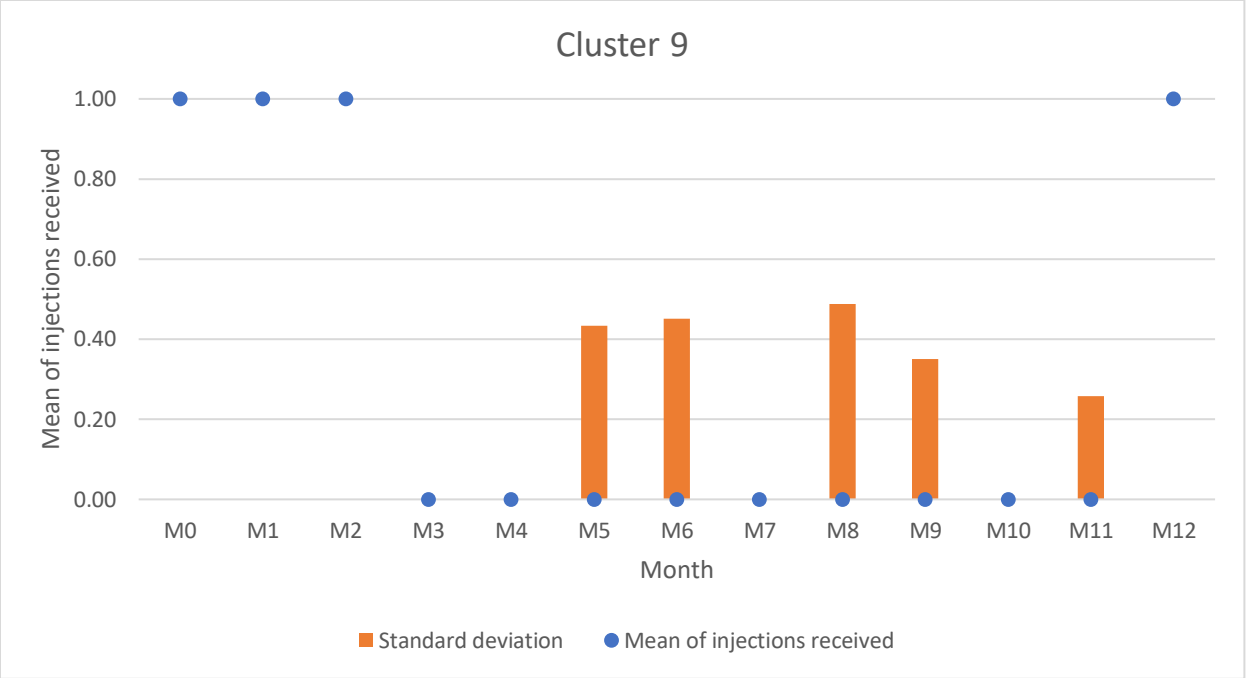

Cluster 4
1.00
0.80
0.60
0.40
0.20
0.00
Mean of injections received
M0
M1
M2
M3
M4
M5
M6
M7
M8
M9
M10
M11
M12
Month
Standard deviation
Mean of injections received

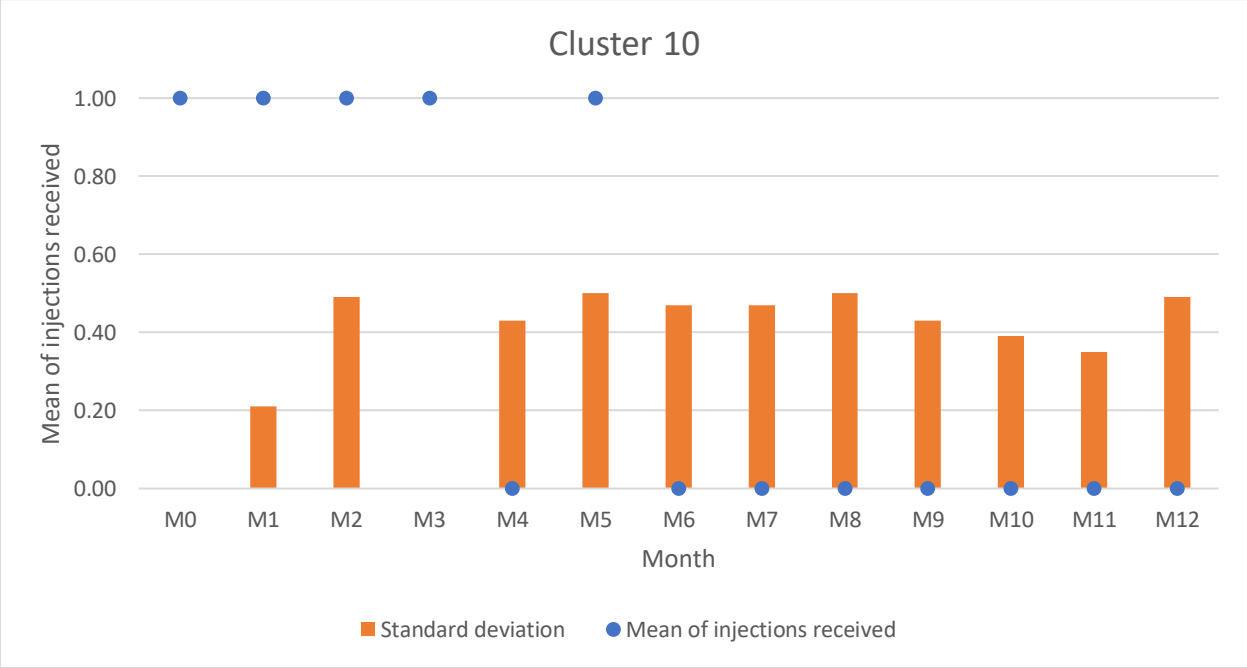

Cluster 5
1.00
0.80
0.60
0.40
0.20
0.00
Mean of injections received
M0
M1
M2
M3
M4
M5
M6
M7
M8
M9
M10
M11
M12
Month
Standard deviation
Mean of injections received


Cluster 6
1.20
1.00
0.80
0.60
0.40
0.20
0.00
Mean of injections received
M0
M1
M2
M3
M4
M5
M6
M7
M8
M9
M10
M11
M12
Month
Standard deviation
Mean of injections received


Cluster 7
1.20
1.00
0.80
0.60
0.40
0.20
0.00
Mean of injections received
M0
M1
M2
M3
M4
M5
M6
M7
M8
M9
M10
M11
M12
Month
Standard deviation
Mean of injections received


Cluster 8
1.00
0.80
0.60
0.40
0.20
0.00
Mean of injections received
M0
M1
M2
M3
M4
M5
M6
M7
M8
M9
M10
M11
M12
Month
Standard deviation
Mean of injections received


Cluster 9
1.00
0.80
0.60
0.40
0.20
0.00
Mean of injections received
M0
M1
M2
M3
M4
M5
M6
M7
M8
M9
M10
M11
M12
Month
Standard deviation
Mean of injections received


Cluster 10
1.00
0.80
0.60
0.40
0.20
0.00
Mean of injections received
M0
M1
M2
M3
M4
M5
M6
M7
M8
M9
M10
M11
M12
Month
Standard deviation
Mean of injections received

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