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Automated conflict resolution for patients with multiple morbidity being treated using more than one set of single condition clinical guidance: A case study

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ABSTRACT

Background: The number of people in the UK with two or more conditions continues to grow and their clinical management is complicated by the reliance on guidance focused on a single condition. This leaves individual clinicians responsible for collating disparate information from patient management systems and care recommendations to manually manage the contradictions that exist in the simultaneous treatment of various conditions.

Methods/design: We have devised a modelling language based on BPMN that allows us to create computer interpretable representations of single condition guidance and incorporate patient data to detect the points of conflict between multiple conditions based on their transformation to logical constraints. This has been used to develop a prototype clinical decision support tool that we can use to highlight the causes of conflict between them in three main areas: medication, lifestyle and well-being, and appointment bookings.

Results: The prototype tool was used to discern contradictions in the care recommendations of chronic obstructive pulmonary disease and osteoarthritis. These were presented to a panel of clinicians who confirmed that the tool produced clinically relevant alerts that can advise clinicians of the presence of conflicts between guidelines relating to both clashes in medication or lifestyle advice.

Conclusions: The need for supporting general practitioners in their treatment of patients remains and this proof of concept has demonstrated that by converting this guidance into computer-interpretable pathways we can use constraint solvers to readily identify clinically relevant points of conflict between critical elements of the pathway.

1. Background

In the UK attempts to ensure consistent care have led to clinical evidence being collated by the National Institute for Health and Care Excellence (NICE) into more than 270 evidence-based medical guidelines [1,2]. This guidance is described as a stepwise progression of clinical decisions dependent upon the progression of the disease or condition [1]. The majority of these are based on randomised controlled trials (RCTs) and so tend to focus on single diseases or conditions [1,2]. The guidance documentation is lengthy and dense and so is also made available to clinicians as a series of flow charts containing links to the findings on which they were based and supporting information [3,4] yet these are seldom cross-referenced against other diseases and conditions [1].

General practitioners (GPs) attempting to treat patients with multiple morbidities are required to reconcile the conflicts that might occur between medication or lifestyle advice recommended by single condition guidelines using only their experience and their knowledge of the patient and the symptoms they describe. This places an enormous responsibility on the often discretionary decision making behaviour of GPs that even before the COVID-19 pandemic were accomodating unprecedented demands on their services and are now coping with fundamental changes to their working environment [5]. The growing pressure being placed on primary care has potentially serious implications for

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consistency of care, and patient safety [6] and has highlighted the need to improve the integration of existing guidelines and provide more timely, reliable and consistent decision support mechanisms [7].

Process modelling offers one promising solution to enabling clinicians to effectively navigate these various guidelines and the conflicts that can occur. Previously it has created systems for industry and finance that support interactions of similar sophistication to those encountered in healthcare [8,9]. It uses workflow languages such as Business Process Model and Notation (BPMN) which are capable of modelling the diverse interactions of environment, user, and system [10]. To ensure individual executions or actions within these models are compatible with others, algorithms have been created that detect and mitigate any conflicts between their composite elements [11–14]. These algorithms convert the modelled process into a series of logical statements [15,16], at which point constraint solvers can be used to detect conflict when creating or merging complex models (whose constituent components remain constant) [17–19]. The sophistication of these algorithms is increasing, and they can now account for more comprehensive models that include shifting variables such as time, resource, and cost. This means that constraint solvers can now recognise the more nuanced compromises necessitated by conflict resolution in dynamic circumstances, such as those observed in the modern healthcare environment [18,20].

To discover whether these same algorithms can be further developed to identify and mitigate the conflicts that occur when a single patient with multiple morbidities is treated using multiple sets of care recommendations, the Automated Conflict Resolution in Clinical Pathways (MITCON) study [21] applied automated methods of conflict detection to modelled care guidelines for two of the UK's most common chronic diseases; chronic obstructive pulmonary disease (COPD) and osteoarthritis (OA) where it's estimated that as many as 420,000 patients suffer with both [22,23]. Here we describe an overview of our approach and the results of the final phase of our work. The latter involved creating an excerpt of our composed care guidelines for COPD and OA relating specifically to primary care consultations and then applying our algorithms to automatically detect conflicts in medication and lifestyle advice before presenting them to a panel of clinicians to determine their validity and clinical relevance.

2. Methods

2.1. Study design

The Automated Conflict Resolution in Clinical Pathways or "MITCON" study was conducted in three phases [21]. The first phase involved the modelling of clinical pathways for a range of chronic conditions based on the NICE guidelines. The second phase involved the development of algorithms that automatically identified conflict between these pathways, and the third phase consisted of a validation of concept. These three phases are summarised below.

2.2. Phase 1: Modelling clinical pathways

The first phase of our work consisted of refining the graphical process modelling language BPMN to capture the key information of treatment guidelines. This included extending the language to ensure its expressiveness captured the nuance and ambiguities contained in clinical recommendations [24]. Through the development of BPMN + V the final models were able to capture the various characteristics of multiple guidelines including the temporal validity of certain parameters, for example the value of blood test results at a specific point in time or the prescription of a drug [25,26]. Ultimately, the expressiveness and formalism of the language allowed the compatibility of modelled guidelines to be explored, specifically COPD and OA [27]. These two guidelines are commonly experienced as discordant comorbidities with potential conflict between their discrete care recommendations. We explored within two domains: medication interactions informed by the British National Formulary [28], and behavioural or lifestyle advice informed by the National Institute for Health and Care Excellence [2].

2.3. Phase 2: Recognition of conflict

In the second phase, we used the automated constraint solver Z3 [29] to identify the root causes of conflict that arise from simultaneously following two single condition guidelines [27]. It utilises first order logic to discover inconsistencies between collections of logical statements [30–32]. It is a Satisfiability Modulo Theories (SMT) solver which means it is capable of incorporating both Boolean and integer variables [31] and enables identification of any conflicting logical constraints when merging several guidelines [20].

2.4. Phase 3: The proof of concept

In the third phase our prototype tool was used to identify possible conflicts between two excerpts of clinical guidance related specifically to primary care consultations. The conflicts identified were presented within an interface that mapped the conflicts back onto graphical representations of the original pathway models. The graphical interpretations of the guidelines and the sites of potential conflict were designed to enable clinicians to readily interpret the nature and location of the conflict. The excerpts of the clinical guidance used as an exemplar are related to OA, a degenerative bone disease [33] and COPD, a condition characterised by fixed airflow obstruction which encompasses several lung conditions that cause breathing difficulties including emphysema and chronic bronchitis [34]. The conflicts that were automatically discovered were presented to clinicians to confirm their validity and relevance to the clinical management of the patient.

3. Results

The results are described below using three figures that represent the evolution of our approach; the first describes BPMN + V by presenting excerpts of the guidelines modelled as pathways including the semantics of each pathway describing areas of parallel activity and potential conflict; the second shows the modelled pathways annotated with viable patient data; and the third identifies the conflicts between the guidelines as presented to a panel of clinicians.

3.1. Graphical representation of clinical guidance

BPMN's flexible, extensible and user-friendly graphical notation provides the facility to informally model the data in a process [29,35,36]. However, the semantics and details of how data interacts with the control-flow are not specified by the notation. We therefore created an extension to BPMN to provide this missing formalisation of the data semantics, and to specify the joint behaviour of the data-flow and control-flow [20]. This extension, BPMN + V, provides a data-driven formal model for care pathways. The control-flow of BPMN + V is restricted to the Workflow Graph subset [37], which imposes some further structure on the model such as requiring all splits (diamonds with multiple outgoing paths) to be matched with corresponding joins. BPMN + V formally specifies how data attributes are both constrained and modified by the activities that take place. Using free graphical tools such as bpmn.io (https://bpmn.io/), Camunda (https://camunda.com/download/modeler/) practitioners can easily create BPMN + V representations of care pathways including the associated data.

Fig. 1 shows excerpts of the OA and COPD pathways modelled using BPMN + V notation that incorporates the range of clinical variables described in the NICE guidelines [27]. Boxes indicate activities (such as prescription of medication) and arrows the sequence of activities. Diamonds with single input arrows and multiple output arrows indicate decision or split points: a cross within a diamond indicates that one only of the subsequent paths may be followed; a plus within a diamond that

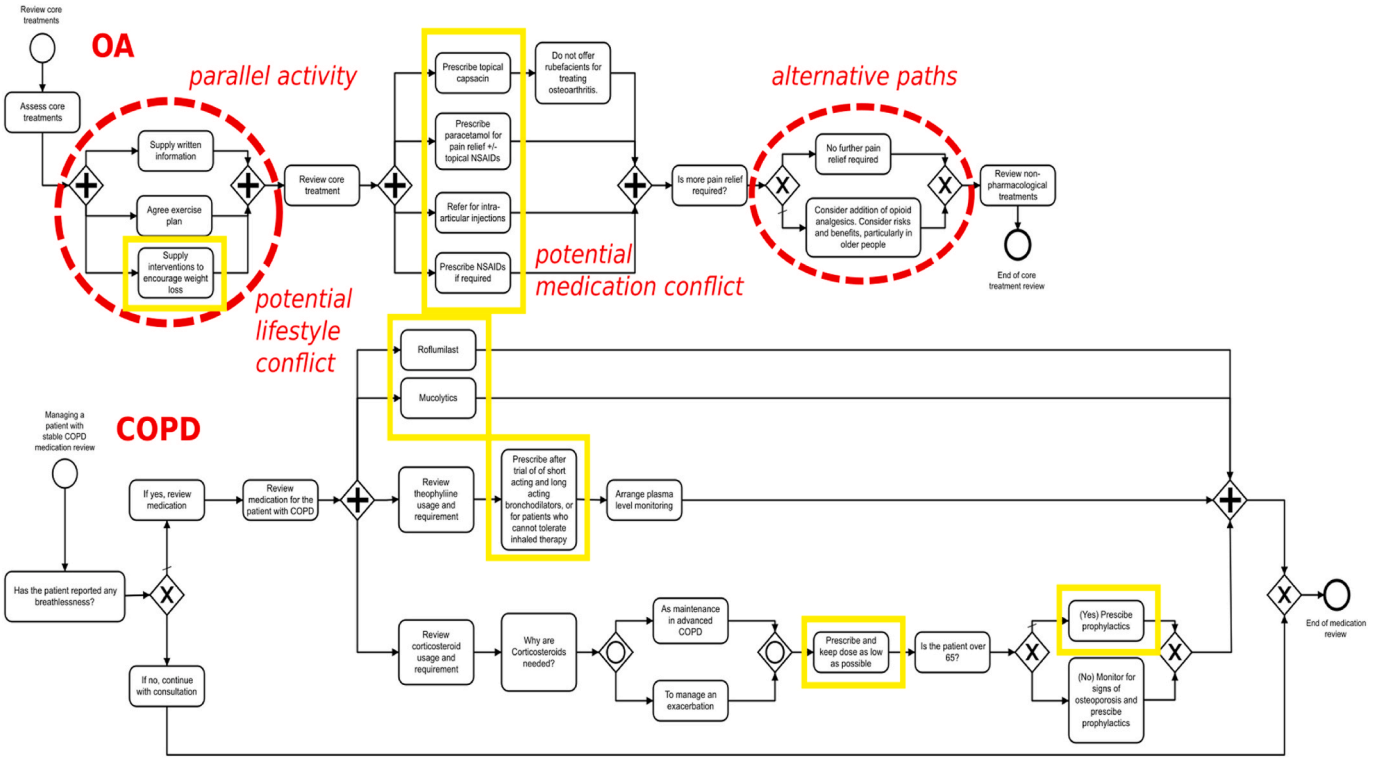

Fig. 1. Illustration of the pathway structures reflective of the guidance produced by NICE.

all subsequent paths will be followed; and a circle within a diamond that one or more of the paths will be followed. Diamonds with multiple input arrows and single output arrows indicate corresponding points at which multiple paths re-join.

Parallel activities are shown in the dashed red circle and alternative paths in the dashed red oval. We have manually annotated potential conflicts between the osteoarthritis and COPD pathways identified by yellow rectangles. These show a potential source of lifestyle conflict (recommendations for the pursuit of lifestyle choices that lead to weight loss in OA patients may 'conflict' with the breathlessness caused by

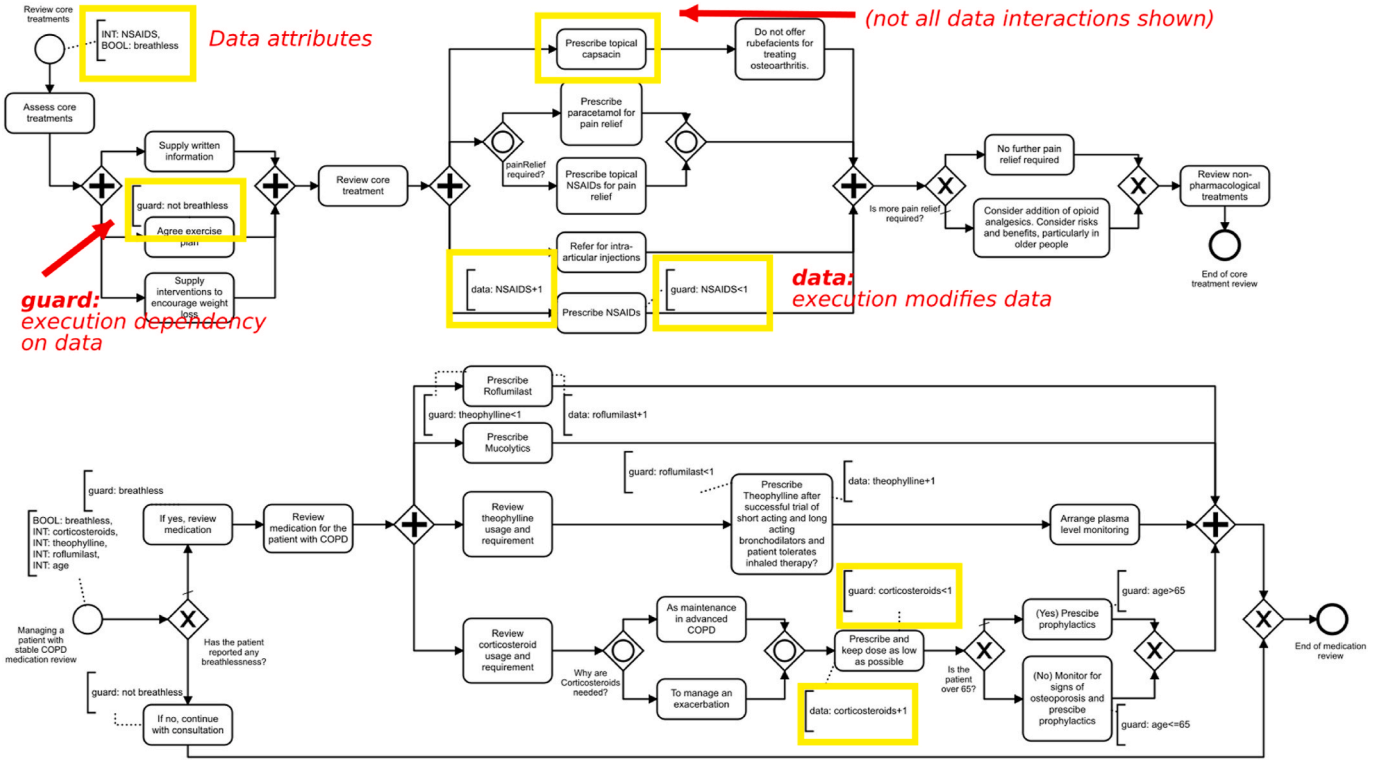

Fig. 2. Illustration of the extension of the BPMN models to the BPMN + V notation to annotate the guidelines with actionable data.

activity in COPD patients). We have also highlighted the conflict between the drugs prescribed for the two conditions, in this excerpt we draw attention to the conflict between prescribing roflumilast used in treating COPD to enhance the anti-inflammatory properties of corticosteroids and mucolytics (that thin mucus making it easier to expectorate) and Non-steroidal anti-inflammatory drugs (NSAID's) which are used to mitigate pain and swelling in those with OA [28,38].

3.2. Data annotation

The novel BPMN + V modelling tool also meant pathways could be readily populated with individual patient data critical to the precision of information around the potential conflict. We were able to link the various parts of the model with accurate and appropriate data for example attributes such as age, gender, and medication specific to each patient which help the clinician navigate a particular pathway. These attributes are in turn modified by the effects of the actions that take place. For example, the patient's age may restrict which treatments are appropriate, or the drugs prescribed for one condition might prevent prescription of certain other drugs for another. This data is categorised as either 'explicit' describing basic patient characteristics such as age, gender, and ethnicity or 'implicit' which is referenced but not modified by the model such as the characteristics of the drugs prescribed for that individual [28]. This is represented in Fig. 2 where we have annotated the model in the figure to highlight the BPMN + V extensions (yellow rectangles). For clarity, not all extensions are shown.

The annotation "guard" on an activity indicates a data constraint which must be met before the activity can take place. For example, "guard:NSAIDS<1" states that the integer variable NSAIDS (associated with a patient) must be less than 1. The annotation "data" describes how the data is modified when the activity takes place, e.g. "data:NSAIDS+1" states that the variable be incremented. These two annotations together might be used to prevent a prescription activity taking place if it were in conflict with this medication and/or setting the variable so that later activities "know" that the patient has now been prescribed with NSAIDS.

The next phase of the work consisted of the clinical guidance modelled as BPMN + V being transformed to sets of logical constraints. Formalisation as logical constraints allows us to describe the syntax and semantics of the composed excerpts of the pathways in a manner which facilitates detection of conflicts within them using the Z3 constraint solver(18). Z3 is a Satisfiability Modulo Theories (SMT) solver. SMT solvers address the problem of whether a "logical formula" (set of constraints) is satisfiable, i.e., that an allocation of variables can be found which results in no inconsistencies. They are used for analysis of systems or processes where communication, synchronisation and resource sharing are important [39]. Z3 employs built-in theories (such as for linear integer arithmetic) to allow a wide range of data to be represented. It allows extension with user-defined theories which allows us to model the syntax and semantics of BPMN + V, and to describe and analyse the behaviour of models in this notation. Finally, SMT provides specialised inference methods to find provably correct solutions. These inference methods allow solutions to be found more efficiently than through naïve exploration of the state space of the models, i.e., testing all possible evolutions of the control-flow and data attributes as the patient follows the model [18,20].

3.3. Conflict detection

We use Z3 to analyse the models to detect conflicts in the context of a given patient. To do so we first describe the characteristics of a patient as a set of data attributes. These characteristics are then also transformed to logical constraints and combined with the set of constraints describing the care pathway(s) relevant to the patient. Z3 then solves the combined model to identify inconsistencies brought about by the patient characteristics. Where the patient follows multiple care pathways these are similarly automatically checked for conflicts between the models brought about by the patient data. The model checking is dynamic, in the sense that it accounts for the evolution of the data attributes attached to both the patient and the models as the patient progresses through the pathways.

Once we have one or more care pathways modelled as BPMN + V, with data constraints, and a patient with given characteristics following the pathways, we have potential conflicts. We term conflicts between a patient and a single pathway as "inconsistencies". If we try to follow ("execute") the pathway according to the formal semantics, we will reach a point where we cannot proceed. This may indicate either a problem with the pathway or with the treatment being attempted. When a patient is following multiple pathways and a conflict occurs between the pathways, we use the term "conflict". Since we use the same method to discover both inconsistencies and conflicts, we henceforth consider potential conflicts between two BPMN + V models in the context of a patient with given characteristics.

To detect such conflicts, we compose (join) two pathways using a simple parallel composition. An example is presented in Fig. 3. Essentially this consists in adding a new start point, followed by a parallel split (plus symbol within a diamond). Following the parallel split activities in both models will be followed concurrently, according to the control-flow of each model. The final nodes in each model are joined with a corresponding parallel join.

Fig. 3 highlights a potential inconsistency brought about by data, and therefore a potential conflict in the treatment. If a patient is already prescribed with NSAIDS when they start this pathway, then the model will "block" at "prescribed NSAIDS" because all of these parallel activities must take place to continue following the model. This may indicate that the model should be changed to make this activity optional. The figure also highlights potential medication conflicts between NSAIDS and corticosteroids and the conflict in lifestyle recommendations between increasing physical activity and its moderation [28,40]. The models designed as illustrated will potentially block as either the patient will be prescribed with NSAIDS, preventing the prescription of corticosteroids, or vice versa. The NICE guidance information drawn from the BNF [28,40] and a shared set of exemplar fluid, patient specific variables were automatically interpreted by our bespoke software as a set of constraints deemed not to be violated. This resulted in a model which composed both pathways where all execution paths that violated a constraint were automatically identified and highlighted for the user. These were presented to senior and experienced clinicians that treated patients with multiple chronic conditions across primary, secondary and tertiary care settings.

4. Discussion

4.1. General findings

In the UK the increasing numbers of patients with multiple, long-term conditions present a challenge to existing models of care reliant on clinicians using guidelines developed for single conditions [40]. This means decisions are made about an individual's care without clinicians having the means to comprehensively identify, illustrate or understand the clinical consequences of that decision in relation to the treatment of any other condition. Our work demonstrates how our modified version of BPMN (BPMN + V) can translate clinical guidelines whilst still capturing their sophistication, and allows their transposition into logical constraints to successfully employ recognised constraint solvers to automatically identify clinically relevant conflicts.

4.2. Strengths and limitations

Alongside our partners in Edinburgh [41] we are the first to apply constraint solving software, that has proved so effective in financial and industrial settings, to the dynamic environment of healthcare. Though the example we present here consists of relatively small excerpts of the

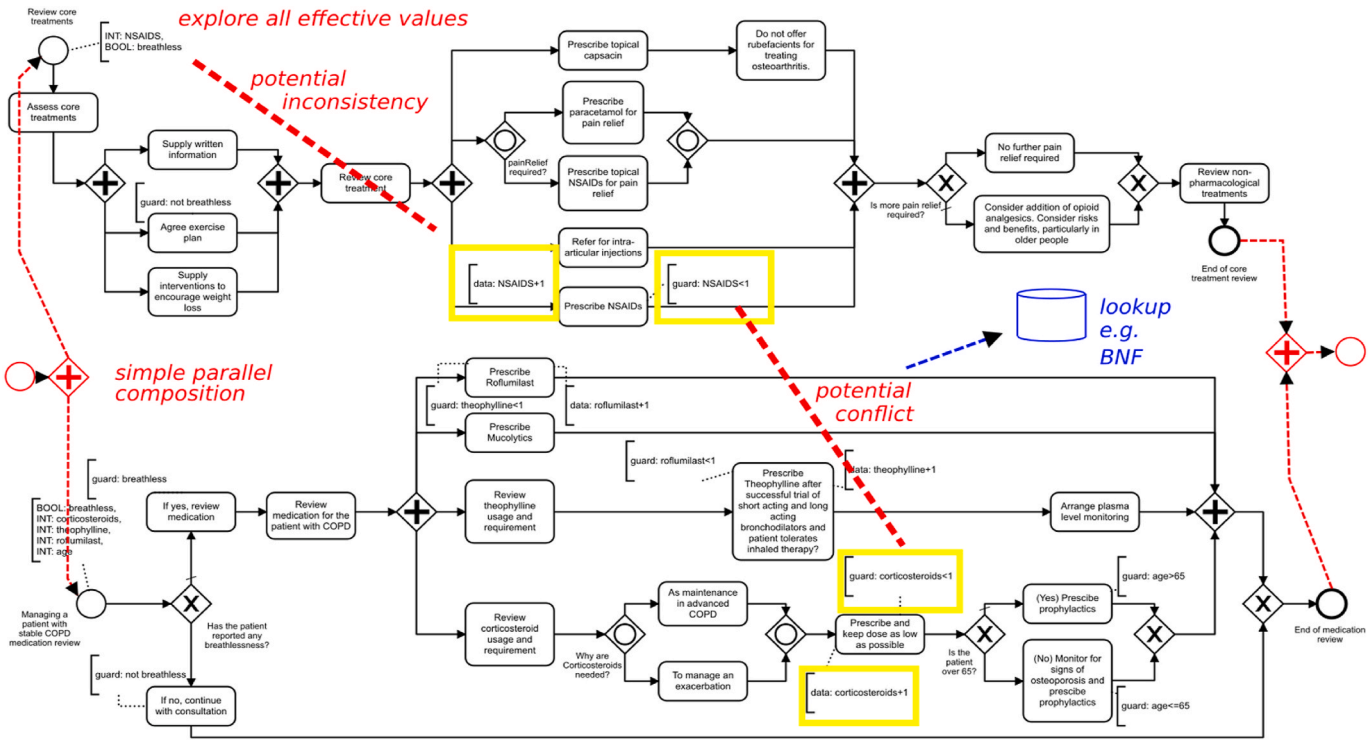

Fig. 3. Illustration of the composition of two pathways for automated detection of conflict highlighting the identified areas of conflict.

extended guidance for two chronic conditions it's apparent that the chosen methodology is capable of incorporating clinical pathways of extended length and additional conditions. Previous attempts to utilise software-based solutions to treat multi-morbid patients have focussed on the integration of clinical knowledge or patient data [42] to identify drug-drug interactions [43], though there is a growing awareness of the repercussions of conflicting lifestyle advice as we have identified here [43]. We acknowledge that there are computational hurdles that must still be overcome and though it is feasible for data to be semantically linked in real time this was beyond the scope of this prototype tool [44]. However, the clinical safety and effectiveness of integrating multiple guidance must be considered [45] therefore one possible solution is to create a library or database of conflicts between the most frequent combinations of conditions that can then be drawn on by the clinician.

Unfortunately, the ethical permissions for this work precluded the identification and presentation of attributable quotes from the clinicians involved in confirming the appropriateness of the conflicts in Phase 3 though their input was sufficient to confirm that we were successful in designing a readily interpretable interface [21,27].

4.3. Specific findings and comparison to existing literature

4.3.1. Modelling clinical guidance pathways

In treating patients with multiple morbidities clinicians frequently make independent decisions informed by an evidence-base limited by its reliance on Randomised Controlled Trials (RCTs) [24]. The applicability of this advice is further hindered by their representation as 'flat' flow charts containing only rudimentary hyperlinks to either fixed generic information or the original study [40]. This has meant that holistic consideration of interdependencies and conflicts between sets of recommendations is a difficult and involved proposition conducted within a complex and time-pressured environment [46,47].

Computer interpretable guidelines (CIGs) have long been considered the solution to improving the consistency of care for complex patients [48,49] and though there have been previous attempts to adopt formal software languages to supporting clinical decision making [50] only recently have they addressed the need to navigate multiple guidelines simultaneously as when treating patients with multiple morbidities [42,51]. The systems that have emerged have utilised CIGs such as PROforma [52] or GLIF [53] use their own notation and their semantics are not always made clear. The advantage of BPMN + V in this instance is that it is based on a widely used graphical notation that is clear and intuitive [54] with a track record of facilitating communication between non-specialists, [29,35,36] and outputs models in a standard XML structured text format [55].

The ability of our extension of BPMN to create interpretable pathways [46] that assimilated examples of the patient data held on the GPs' clinical management system alongside recommended guidance meant we could formally model procedural information. This meant the sequence of tasks and the roles of those fulfilling them could be presented in a format interpretable by constraint solvers allowing us to successfully detect and mitigate conflict between contrary elements of different pathways [56]. This integration meant that clinical guidance can be personalised for each individual patient [57] with both clinicians and patients now aware of the potential conflicts in clinical advice between conditions. It also creates opportunities for policymakers and commissioners to improve the way in which care of complex patients is delivered [58].

To maximise the potential of our system it would ideally link with multiple data sets from across primary, secondary and community settings. However, this process is hindered by the fractured environment of the NHS, the presence of multiple private software providers, and the constraints of the NHS Supply Chain [59,60]. NHS England (NHSE) is now prioritising interoperability of health information technology [61–63] and attempting to educate commissioners and care providers what this means in practice [64,65]. To achieve this NHSE now carefully define interoperability within two domains, technical interoperability relating solely to information exchange with no reference to its subsequent usability [66,67]; and semantic interoperability referring to the ability of systems to "understand the information received from others without ambiguity" and so being able to use it for the intended purpose [64].

4.3.2. Winning hearts and minds

The technological significance of our novel tool and others in this space is immaterial if those commissioning and practicing medicine fail to see the relevance of its impact on both the efficiency and effectiveness of clinical care. The growth of software use in the healthcare sector has been driven in part by meeting clinical need but also through the expansion of software providers looking to exploit new markets [68]. Sometimes these tools fail to meet the basic needs of utility and usability required by clinicians and support staff [69] and there has been a previous reluctance to engage end-users in the procurement of healthcare technologies leading to a reluctance to engage with digital solutions [70–74]. For example, there are a number of support tools available that address clashes in medication however the alerts they produce are not always apposite [68,69], frequently highlighting issues already recognised by clinicians and leading to high override rates [75],or their being disabled entirely [76]. The challenge of achieving true integration between people, data and work processes is estimated to be only 10% technical with more significant issues around engaging with the workforce in creating relevant tools [66]. The understanding of the impact of human factors on the design and implementation of health information technology is increasing [77] and offers a promising means of supporting a cultural shift in workforce attitudes towards it [78] facilitated by improving digital health education for undergraduates [79] and embedding concerted training opportunities for clinicians [80].

5. Conclusions

The acknowledgement of the pressure placed on GPs in dealing with patients with multiple morbidities during consultations that are growing shorter in duration was widely acknowledged pre-COVID 19 and is set be exacerbated by the surge in demand as the pandemic continues. A number of attempts have been made to bridge the gap between the static guidance provided by NICE and the dynamic reality of treating various patients with differing combinations of diseases. The successful use of automated constraint-solvers in detecting these conflicts described above means we can seek conflicts at scale and in a timely fashion and the prototype tool and methods we developed form the basis for better techniques for the automated composition of behavioural models for use elsewhere in healthcare. In its next iteration our prototype software tool will also be able to offer options for how these conflicts might be resolved, sympathetic to the economic priorities of care organisations by including data on cost.

Supporting data

As lead author using open source software I can confirm that associated data is available from the lead author upon reasonable request.

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Authors' contributions

Litchfield, and Turner were responsible for the conception of the work and the design of the study. Litchfield led the drafting of the article with input from Weber. Lee, Turner, Ferreira Filho all provided critical revisions. The final version was drafted by Litchfield and approved by Turner, Ferreira Filho, Weber, and Lee.

Declaration of competing interest

None declared.

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