AN EXPLORATION OF QUALITY OF LIFE AND MENTAL HEALTH IN ADULTS WITH ATOPIC DERMATITIS

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Atopic dermatitis (AD) is a common, often persistent skin disease that is characterised by severe itching and inflammation of the skin. Although it is most common in children, AD in adults is often a serious condition and poses a significant social issue, with a number of studies suggesting a significant negative impact of AD on quality of life (QoL) and mental health in adults. This multi-method thesis aimed to explore QoL and mental well-being in adults living within the UK. After conducting a systematic review and meta-analysis of studies investigating QoL in adults, the first empirical study (chapter 4) qualitatively explored the daily experiences and perceptions of adults with AD. Additionally, in order to measure quality of life and mental health, psychometric questionnaires were completed by a large UK sample (chapter 5). Finally, this research aimed to measure the temporal relationship between psychological stress and AD severity over time in a feasibility study (chapter 6). The qualitative study found that participants with the condition experienced many challenges such as living with the visibility of AD, physical and psychological distress, and lack of support from others. The quantitative study built on these findings and established that AD patients reported lower health-related QoL and higher levels of anxiety compared to healthy adults. Several psychological, clinical and demographic variables also significantly predicted QoL in this study. Finally, the feasibility study found that psychological stress experienced one week significantly predicted disease severity the following week. The opposite was also found where AD severity measured one week significantly predicted stress the following week. The findings of this thesis will facilitate better understanding of living with the condition and enables recommendations for clinical practice which include support from health care professionals and increased public awareness of the condition.

Keywords: atopic dermatitis, quality of life, mental health, health psychology, long-term conditions

Dedication

Dedicated to all women who have been deprived of, discouraged and disheartened from furthering their education. May we grow in wisdom, self-belief and number.

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“When you are on my side, Lord, what do I need to worry about?”
Sri Guru Granth Sahib Ji, Ang 1096

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Abbreviations and specialist terminology

AD- Atopic Dermatitis

ANOVA- Analysis Of Variance

APPG- All Party Parliamentary Groups

CNS- Central Nervous System

CRD- Centre for Reviews and Dissemination

DFI- Dermatitis Family Index

DLQI- Dermatology Life Quality Index

DOH- Department Of Health

EASI- Eczema Area and Severity Index

EU- European Union

F- f ratio: ratio of two mean square values

GP- General Practitioner

HADS- Hospital Anxiety and Depression Scale

HCP- Health Care Professional

HPA- Hypothalamic Pituitary Adrenal

HRQoL- Health Related Quality Of Life

IgE- Immunoglobin-E

IPA- Interpretative Phenomenological Analysis

LTC- Long Term Condition

MMAT- Mixed Methods Appraisal Tool

NHS- National Health Service

NICE- National Institute for Health and Care Excellence

ONS- Office for National Statistics

p- probability

PCDS- Primary Care Dermatology Society

POEM- Patient Oriented Eczema Measure

POMS- Profile Of Mood States

PRISMA- Preferred Reporting Items for Systematic Reviews and Meta-analyses

PROM- Patient Reported Outcome Measure

PSS- Perceived Stress Scale

QoL- Quality of Life

RCT- Randomised Controlled Trial

SCORAD- Score for atopic dermatitis extent

SF-36- Short Form survey

SIGN- Scottish Intercollegiate Guidelines Network

SSRI- Selective Serotonin Reuptake Inhibitor

STROBE- Strengthening the Reporting of Observational Studies in Epidemiology

TA- Thematic Analysis

UK- United Kingdom

WHO- World Health Organisation

WHOQoL- World Health Organisation Quality of Life

Chapter 1: Introduction

This chapter provides a background to atopic dermatitis (AD), its' symptoms, aetiology, prognosis and treatment. The impact of AD on quality of life (QoL) as well as the association between AD and mental health determinants with a focus on anxiety, depression and psychological stress are then discussed. Gaps in current literature and rationale for this thesis are considered, and finally, the outline of the thesis is discussed.

1.1. Long-term conditions

When diagnosed with a long-term condition/illness, an individual can change from being healthy to living with long-term illness in a world of health (Radley, 2004). Approximately half of the UK population reports having a long-term illness, with the most commonly occurring long-term illnesses being hypertension, asthma, and depression (ONS, 2015). A long-term condition (LTC) is any medical condition that cannot currently be cured but can be managed with the use of medication and/or other therapies (De Ridder, Fournier & Bensing, 2004).

According to George and Martin (2016), approximately thirty percent of the UK population with LTCs account for seventy percent of the health spend. Over fifteen million people in England are estimated to have at least one LTC (George & Martin, 2016) and it is estimated to increase to approximately eighteen million in another five years. Individuals with long-term conditions are frequent users of health care services and are estimated to account for 77% of all inpatients, 68% of A&E and hospital appointments and 55% of primary care appointments in the UK (George & Martin, 2014). There are different types of LTCS, some may be life-threatening whereas others such as atopic dermatitis are not considered to be (Radley, 2004). The terms long-term condition and chronic condition have been used interchangeably in literature, however the UK Government (DOH, 2015), and the National Health Service (NHS, 2016) in the

UK use the terminology, long-term condition. Thus, in this thesis, the term long-term conditions will be used throughout.

1.2 Atopic dermatitis

Atopic dermatitis (AD) is a chronic inflammatory skin disease characterised by intense and unrelenting pruritus (itch), lesions, dry skin and water loss through the skin. The lifetime prevalence of AD is 10-20% in children and 1-3% in adults worldwide (Larsen & Hannifin, 2002), with almost 90% of AD patients being diagnosed with the condition younger than the age of five (Krakowski, Eichenfield, & Dohil, 2008). Although majority of AD patients grow out of it, the disease may persist into adulthood and may even present for the first time during adulthood (Novak, Leung, & Bieber, 2003). Indeed, AD in adults tends to be more severe and debilitating (Kapoor et al., 2008). There are two main forms of AD that have been identified: an 'extrinsic' form which is associated to Immunoglobin-E (IgE) -mediated sensitisation involving 70-80% of patients, and an 'intrinsic' form of AD without IgE-mediated sensitisation which involves 20-30% of patients. IgE is an antibody found in the blood that is a marker for allergic diseases and people who have elevated IgE levels can have one or more allergies. A number of clinical studies propose that AD is the cutaneous manifestation of a systemic condition that can give rise to allergic rhinitis, food allergy and asthmas, all of which are distinguished by high serum IgE levels. This is a phenomenon defined as 'atopic march' (Spergel & Paller, 2003).

The concept of 'atopy' which originated form the Greek atopic meaning 'different' or 'out of place', was proposed by Coca and Cooke in 1923 (Coca & Cooke, 1923), and referred to abnormal levels of sensitiveness, the cause of which was uncertain. The original definition did not include AD in its' definition, it included allergic rhinitis and asthma. Many years of research in dermatology have introduced considerable developments to the management and understanding of the condition (Ring, 2016). Nonetheless, the cause of AD remains somewhat elusive. AD is considered to be a complex association between

the environment, genetics, skin-barrier dysfunction, immunological defects and cutaneous infections (Otsuka, Rerknimitr, Seidel, Honda, & Kabashima, 2017).

1.2.1 Clinical presentation

There are several major features of the disease that help in its' identification; a typical illustration of the condition is one that is characterised by dry, itchy skin with lesions of a typical appearance and distribution (Leung & Bieber, 2003). Pruritus (itch) is present in all patients with AD and is exacerbated by numerous factors such as changes in humidity, allergen presence and psychological stress (Leung & Bieber, 2003). Although it occurs throughout the day, it is often perceived more severe during the night (Leung & Bieber, 2003). Scratching the skin over prolonged periods of time results in lichenification (thickening) of the skin.

The distribution of AD is mainly determined by a patient's age and disease severity (Leung & Bieber, 2003). AD symptoms are largely present on exterior surfaces of the hands and legs. . The involvement of the face and neck is most prevalent in adult AD, also known as head-and-neck dermatitis, (Salvador, Romero-Pérez, & Encabo-Durán, 2017). Chronic inflammation of the area surrounding the mouth is also common in young women (Hello, Aubert, Bernier, Néel, & Barbarot, 2016). Hyperpigmentation of the neck is present in severe cases of AD; this is a phenomenon called 'dirty neck' as a result of its' unclean appearance. Skin lesions in AD may be patchy and a large number of patients report suffering from complications such as bacterial and viral infections of their skin (Cho, Strickland, Boguniewicz, & Leung, 2001). To put in context, more than 80% of patients with AD have colonisation with staphylococcus aureus on their skin (Breuer, Haussler, Kapp, & Werfe, 2002), compared to less than a quarter of the healthy population.

1.2.2 Diagnostic criteria

The diagnosis of AD is based on the clinical presentation of the disease as opposed to laboratory tests. A clinician may look out for essential features of AD e.g. pruritus, and genetic factors such as family history of the condition (Leung et al., 2004). However, it is challenging to determine a defined set of criteria for a condition that is so variable in time, distribution, and morphology (Williams, 2000). Hanifin and Rajka (1980) defined a set of minor and major diagnostic criteria based on the most commonly occurring symptoms of AD in patients. These diagnostic criteria are highly suited for use in hospital settings, but unsuitable for use as a tool in primary care or population-based studies (Schultz & Hanifin, 1992). This is because the features in the criteria have been derived largely from hospital patients from a white ethnic group, and some of the features are relatively poorly defined themselves while some, such as food intolerance are prevalent in people with other types of condition. The Hanifin and Rajka criteria serves as a foundation for a more streamlined set of criteria defined as the UK Working Party's Diagnostic criteria for Atopic Dermatitis (table 1) (Hanifin & Rajka, 1980). With sensitivity of 85% and 96% specificity, it is a reasonably good diagnostic tool for atopic dermatitis in both tertiary and primary care settings and is the criteria used in the UK for diagnosing AD (Kanwar & Handa, 2006).

Table 1.1 UK Working Party Criteria for diagnosing AD

An itchy skin condition plus three or more of the following:
• Onset below the age of 2 years
• History of skin crease involvement
• History of a generally dry skin
• Personal history of other atopic disease
• Visual flexural dermatitis

1.2.3 Epidemiology

The prevalence of AD is estimated to have increased in the past forty years in Europe, despite there not being strong evidence to support this (Williams, Stewart, von Mutius,

Cookson, & Anderson, 2008). This is due to the majority of data being comprised of patient-reported outcomes using questionnaires, which results in difficulty interpreting and comparing due to variations in the methodology used and data collected (e.g. socio-demographic characteristics). Nonetheless, a number of conclusions can be ascertained from published literature. Trends in Europe and globally reflect one another and include the notion that AD is more prevalent in overcrowded urban areas and symptoms are worsened in cold or temperate climates (Nutten, 2015). Additionally, higher socio-economic status, family education, family history, being female and a smaller family size are associated with development of AD (DaVeiga, 2012).

With regards to AD in adults, there are little differences between Europe, Japan and America for the prevalence of the disease (2.1%-4.1%), although there are different rates of prevalence within and between countries. AD diagnosis using the UK Working Party criteria ranges from 4.3% (Japan) to 16.7% (Italy) and is higher than the proportion of patients who reported being diagnosed by a physician. AD prevalence among older age groups is found to be lower than younger ages, with the peak prevalence estimated in the 25 to 34 age groups. after the age of 45 (Barbaot et al., 2018). Southern Europe has higher proportions of mild AD relative to the UK and Germany, which have lower proportions of mild AD using various severity scales (Barbaot et al., 2018).

1.2.4 Pathogenesis of AD

Despite the number of people who suffer from AD, the pathogenesis of the condition remains unclear. There are two major hypotheses surrounding the pathogenesis of the condition: the ‘outside-inside hypothesis’ and the ‘inside-outside hypothesis’. The ‘outside-inside’ (Elias, Wood, & Feingold, 1999) hypothesis suggests that a skin-barrier dysfunction Is the main cause of AD and as a result microbes can penetrate the skin and affect the immune system.. The skin inflammation that occurs as a result causes an increase in AD severity and compromised barrier function. In contrast, the ‘inside-outside’ hypothesis (Hatano, Terashi, Arakawa, & Katagiri, 2005) suggests the opposite;

the abnormally sensitive immune system responds more than it should to a small amount of microbes and the resulting skin inflammation is unable to serve as an effective barrier, which as a result allows more microbes to penetrate the skin (Elias & Schmuth, 2009). Skin barrier defects were first proposed by Elias, Wood, and Feingold (1999) and Taieb (1999).

The complicated immunopathology of AD comprises various types pathways and inflammatory cells (Fiset, Leung, & Hamid, 2006). Interestingly, when compared to other skin conditions such as psoriasis, it is only AD which results in frequent skin infections due to the fact that those with AD present down regulation of the genes responsible for the immune defence system (Nomura et al., 2003). AD onset is also strongly influenced by genetic and environmental factors. A number of empirical findings suggest a stronger association of AD with maternal atopy compared to paternal (Cookson et al., 1992; Diepgen & Blettner,1996; Moffatt & Cookson, 1998). However, conflicting evidence for this exists with some studies (Purvis et al., 2005; Wadonda-Kabondo, Sterne, Golding, Kennedy, & Archer, 2004) showing no parent-of-origin effect in AD. Generally, compared to allergic asthma and rhinitis, parental AD causes a higher transmission risk to offspring (Leung & Bieber, 2003). A recently conducted systematic review of population-based twin studies of the concordance and heritability of AD reported concordance rates for AD ranged from 0.15 to 0.86 for monozygotic and from 0.05 to 0.41 for dizygotic twins, with an overall ratio of monozygotic: dizygotic twins of approximately three. The heritability of AD is estimated to be approximately 75% (Elmose &Thomson, 2015) suggesting the presence of AD specific genes.

Many however, suggest that the increase in AD coupled with its' strong association with socio-economic status and urbanisation indicates that AD develops as a result of environmental factors. The decrease in family size, improved personal hygiene and a reduction in infections have resulted in the development of the so-called hygiene hypothesis (Strachan, 1989) which helps explain the increased incidence of AD. A large

body of literature supports the hypothesis (El-Zein, Parent, Benedetti, & Rousseau, 2010). Debarry et al. (2007) and Ege et al. (2011) found that children exposed to animals in farms during early childhood has lower incidence of atopic conditions Nevertheless, a number of studies have shown that some infections can increase a person's risk of atopic dermatitis (Cramer et al., 2012).

1.2.5 Management of atopic dermatitis

An approach that involves many steps or stages is required in the treatment and maintenance of AD.. An effective treatment regime should aim to alleviate AD symptoms and reduce the frequency of exacerbations and inflammation of the skin. Hoare, Po, and Williams (2000) proposed that an effective management strategy for AD should involve restoring the skin-barrier function, eliminate factors that trigger symptoms, reduce skin inflammation and the use of antibiotics in case of skin infection. A 2011 Scottish Intercollegiate Guidelines Network (SIGN) guideline proposes guidelines for the management of AD which are similar for children and adults with the condition AD (Scottish Intercollegiate Guidelines Network, 2011), although the current NICE guidelines only apply to children. In 2014, the American Academy of Dermatology proposed approaches for the management of AD in children and adults (Eichenfield et al., 2014; Sidbury et al., 2014). The Primary Care Dermatology Society (PCDS) stepwise approach updated in July 2016, characterizes updates guidance on managing AD in the UK (Table 1.2). According to these guidelines, patients with AD flares should be treated with copious amounts of emollients and the short-term use of steroid to alleviate symptoms .

Table 1.2 Summary of the Primary Care Dermatology Society recommendations for the management of AD (as relevant to adults)

Step 1	General measures	Assessment Patient education and signposting Develop a management plan	Copious use of emollients at each step
Step 2	Initial management for patients presenting with a flare-up	"Hit hard" for a few days with a moderate to potent topical steroid once daily until settled	e.g. Betnovate (betamethasone valerate_ or Elocon (mometasone)
		Skin infection- widespread	Add a systemic antibiotic i.e. flucloxacillin or erythromycin, for one week
		Skin infection- localised	Consider Betnovate cream or Fucibet (fusidic acid/ betamethasone valerate) cream without a systemic antibiotic
		Marked sleep disturbance	Consider a sedating antihistamine (hydroxyzine, chlorpheniramine)
		take a skin swab if not settling; review after -2 weeks to discuss long-term management	
Step 3	Long-term management	Emollients (mainstay of therapy) Allow 15-20 minutes to dry before application of topical steroid	Moisturisers: use patient preference, prescribe generously Bath/shower preparations: those with antiseptic properties for frequent flares; antipruritic such as Balnuem-plus bath oil for itchy skin Soap substitutes: one of the prescribed moisturisers can be used
		Topical steroids Use lowest appropriate potency for age, site, and severity, and apply thinly Extra care needed o the face and around the yes Avoid use on lower legs of alder patients and others at risk of leg ulcers	Adult face: mild or moderate potency e.g. Eumovate (clobestasone butyrate 0.05%) Adult trunk and limbs: potent e.g. Betnovate 0.1% or Elocon Palms and soles: potent or very potent e.g. Dermovate (clobestasol propionate 0.05%)
		Bandages and dressings can be sued to top of emollients or topical corticosteroids (but not on wet, infected AD)	As per step 2
Step 4	Management of flare-up's	Infrequent flare ups (every 4-8 weeks)	• Limited prophylaxis with topical steroid (Betnovate or Elocon): "weekend regimen" • Consider topical tacrolimus as steroid alternative • Consider alternative diagnosis such as contact allergic dermatitis
		Frequent flare-ups • Check adherence • Swab for infection	
Step 5	Topical immunomodulator treatment	Consider topical calcineurin inhibitors when: • Eczema involves the eyelids and periorbital skin • Regular topical steroid use on the face	• Pimecrolimus for milder cases • Tacrolimus for more severe cases

		• Regular topical steroids use on the lower legs (elderly patients) and others at risk of leg ulcers • Any signs of skin atrophy	
Step 6	Scalp eczema	• Mild tar-based shampoo • Water-based topical steroid scalp application once or twice daily until settled •Remove thick scale before applying a topical	• e.g. Betacap (betamethasone valerate) • e.g. with Sebco ointment (coal tar/salicylic acid/sulfur)
Step 7	Referral	Refer in cases of: • Diagnostic uncertainty • Severe eczema • Moderate to severe eczema only partially responding to steps 1–5 • Steroid atrophy or concerns regarding the amount of topical steroids/immunomodulators being used • Possible contact allergic dermatitis	

1.3 Atopic dermatitis in adults

Although AD often starts in infancy and early childhood, it can progress to adulthood. Approximately ten percent of patients diagnosed as children continue to suffer with AD in adulthood (Bruin Weller, Rockmann, Knulst, & Bruijnzeel-Koomen, 2013). According to research exploring the prevalence of AD, 3-17% of adults self-report having the condition (Harrop et al., 2007; Kim et al., 2010; Muto et al., 2003) The reported prevalence of people reporting long-term or lifetime AD ranges more widely, from 3% to 40%. Most sufferers of AD have had it through childhood or had a family history of the condition (Harrop et al., 2007; Muto et al., 2003).

AD in adults is often severe and in many cases involves chronic, red, thick, lichenified plaques (raised areas on skin), sometimes with isolated pruritic papules (itchy raised areas) (Bruin Weller, Rockmann, Knulst, & Bruijnzeel-Komeen, 2013) In adulthood, itching is often severe and has effects on patients' daily lives, sleep and activity (e.g.

Kelsay, 2006; Kong, Han, Lee, & Son, 2016; Sherry, Attarian, Zee, & Silverberg, 2016). As discussed earlier, different parts of the body are affected in adults compared to children; visible areas of the body such as the neck and face are often more affected (Zeppa, Bellini, & Lisi, 2011). These often serious symptoms can give rise to infections and metabolic disorders and can result in hospitalization. Adult AD has significant social implications with approximately 30% of affected adults being unable to keep their jobs due to flare-up of the condition (Shum, Lawton, Williams, Docherty, & Jones, 2000).A reddened face is one of the most problematic but common symptom of AD in adults can gives rise to stigmatisation (Tada, Yasamati, Toi, Akiyama, & Tarata, 1999). Hyperpigmentation of the neck is also a frequently occurring symptom unique to adults AD. T It has been suggested that children with AD 'grow out' of the condition but, by young adulthood, 80% of those who have not grown out of it have persistent symptoms (Abuabara, Hoffstad, Troxel, Gelfand, & Margolis, 2015).

Two large (n=833, n=955) studies which followed a cohort for over 24 years, recruited patients with AD who were dermatology clinic patients as children. AD was present in 62% of participants who were admitted to hospital as children and in 40% of those who had not., AD symptoms were more prevalent on the hands (Rystedt, 1985) and neck (Sandstrom & Fergemann, 2004) These findings suggest that AD in adults may be the result of persistent AD through childhood through to adulthood, with a small group of patients presenting late-onset of the disease (Garmhausen et al., 2013; Tanei & Katsuoka, 2008). The above discussed factors taken together can have a significant impact on quality of life in adults

1.4 Quality of life

Quality of life (QoL) is a broad multidimensional concept that considers both positive and negative subjective evaluations of life (The WHOQoL Group, 1998). The World Health Organisation (WHO) defines quality of life as "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to

their goals, expectations, standards and concerns. It is a broad ranging concept affected in a complex way by the person's physical health, psychological state, level of independence, social relationships, and their relationships to salient features of the environment" (p.5, WHOQoL Group, 1994). Early QoL measurements in relation to health relied on assessments of physical abilities, for example, the ability of a patient to walk a certain distance or walk without the need of a walking aid or assistance. However, in the last ten years, the concept of health related quality of life has encompassed how an individual's actual situation is different to their expectations.

Because many life domains are related to health, HRQoL is used to differentiate and specify health related issues from the general issues of quality of life. The term HRQoL was developed by psychological and sociological researchers primarily to help measure the health domains that influence an individual's physical and mental health status (Cella et al., 2005). HRQoL as a concept, therefore, is more appropriate in that it can be measured within distinct components which can be interpreted separately (Kolotkin et al., 2003). Health-related quality of life is broadly defined as "quality of life relative to one's health or disease status" (Bakas et al., 2012, p.1). It is associated with "optimal levels of mental, physical, role, and social functioning, including relationships, and perceptions of health, fitness, life satisfaction and well-being including assessment of patients' level of satisfaction with treatment, outcome, and health status with future prospects" (Bowling, 1995, p.6). According to Both, Essink-Bot, Busschbach & Nijsten (2007), incorporating HRQoL in AD patient assessments has become significant due to the increased prevalence of skin conditions. Whilst there is a large pool of instruments and psychometric techniques to measure HRQoL, there is often uncertainty over which HRQoL instruments should be used in dermatology. Both QoL and HRQoL concepts represent patients' own satisfaction with life and can be influenced by how they perceive the physical, mental, and social effects of long-term conditions such as AD on their daily living (Fivenson, 2002). This suggests that QoL and HRQoL are individualised concepts

and AD may be considered as an irritation for one patient but may be severely frustrating for others (Mozaffari et al., 2007).

Studies that have examined QoL and HRQoL in patients with AD of different ethnicities and religious beliefs have found significant differences in their perceptions about factors that make up their overall QoL (Jobanputra & Bachmann, 2008). Assessing QoL and HRQoL therefore, using measures that can capture patients' individualised experiences of health becomes a vital and often required part of health outcomes appraisal (Anderson & Burckhardt, 2003).

1.4.1 Measuring QoL in Dermatology

There are numerous reasons why quality of life should be measured in those with skin diseases. In places that have a lack of dermatology services, it is imperative that health care professionals emphasise the effect of skin disease on their patients and this effect is in place equivalent, or even greater than the effect of some systemic diseases. This evidence may be used to inform the development of dermatology services (APPG, 2009). Clinical trials and research do not typically consider the view of patients with skin disease, rather they focus on traditional outcomes such as measuring skin lesions. When developing new therapies, QoL measurement in addition to clinical measurements provides added perspective, and these is increased interest in such outcome measures. Many health care professionals consider QoL of their patients when making critical decisions about their care and treatment, for example starting azathioprine in AD patients (Hermansen, Helland & Finlay, 2002). Similarly, in places where clinical audit activities are required, QoL measures may be used. Some of the components of generic health questionnaires may be redundant in assessing quality of life in skin disease. For example, in AD, an instrument that does not contain a question about the effect of itching may underestimate the impact of the condition on a patient's life. Many generic measures of QoL also do not include many of the salient factors known to be associated with skin diseases, which may respond to treatment. Therefore, several questionnaires

have been the outcome of the growing interest in QoL e.g. the Dermatology Life Quality Index (DLQI) (Finlay & Khan, 1994), Skindex (Chren et al., 1996) and the Dermatitis Family Impact (DFI) questionnaire (Lawson, Lewis-Jones, Finlay, Reid, & Owens, 1998).

1.5 Quality of life and atopic dermatitis in adults

Health professionals commonly discount atopic dermatitis and tend to perceive it as a trivial condition of the skin that resolves itself in time (Noerreslet, Jemec, & Traulsen, 2009). Those who do comprehend the seriousness and chronic nature of AD are often not aware of the implications the disease has, despite patients with AD being impacted by the visibility attached to AD and living with the condition itself (Finlay, 2001). Furthermore, with an increasing incidence in developing countries, and it being regarded as one of the most common long-term conditions in Western countries, AD is a global public health concern. Although it is not life-threatening, AD has an impact on patients' QoL due to the disfiguring and irritating characteristics of the condition . Indeed, skin diseases were recently found to be the one of the most troublesome non-life threatening disease according to a global survey (Hay et al., 2014). This burden includes the significant social and economic costs related not only to the direct cost of treatment, but also additional indirect costs such as impact on employment and productivity, and the substantially reduced HRQoL of patients with AD (Dalgard et al., 2015).

Emotional impact and symptoms surrounding the condition are regarded to be aspects of QoL most affected compared to factors such as social functioning which has less of an impact on patients (Holm, Wulf, Stegmann, & Jemec, 2006). Nonetheless, Roosta, Black, Peng and Riley (2010) found that more than a quarter of college students perceived a significant impact of AD on their social lives. Daily activities have also been found to be affected in more than 35% of participants in a community-based survey and approximately the same amount of participants were limited in self-care such as wearing makeup and shaving (Anderson & Rajagopalan, 2001). Decreased QoL in AD is correlated with disease severity and increased itch and sleep disturbances, as reported

in numerous studies (Beikert et al., 2014; Chrostowska-Plak, Reich, & Szepietowski, 2013; Holm et al., 2006; Misery et al., 2007; Sanchez-Perez, Dauden-Tello, More, & Lara, 2013; Wittkowski, Richards, Griffiths, & Main, 2004). Notably however the correlation of QoL with objective measures of disease severity such as Scoring Atopic Dermatitis (SCORAD) is often not strong (Chrostowka-Plak et al., 2013; Haeck et al., 2012; Wittkowski et al., 2004).

AD symptoms that are present on visible areas of the body and genital areas have been found to predict impaired QoL in adult patients with AD (Beikert et al., 2014; Holm et al., 2004; Misery et al., 2007).Thus factors aside from objectively measured AD severity appear to impact quality of life. Kiebert et al. (2002) explored quality of life in 107 adult AD patients using generic quality of life questionnaire (SF-36) and compared these findings to SF-36 scores collected in the past on healthy people. The authors found that AD patients had worse mental QoL compared to those with other conditions such as type 2 diabetes.

However, as with other studies mentioned above, recruitment was limited to outpatient dermatology clinics, which tends to see more severe patients (Basarab, Munn, & Jones, 1996). Additionally, the authors did not consider socio-demographic characteristics such as gender and age when comparing the QoL scores of the AD group with the general population and people with other diseases. The impact of AD on QoL has been found to differ by age and gender (Chernyshov, 2012; Holm et al., 2004; Hon, Wong, Leung, Chow, & Ng, 2008). Despite these limitations, AD does appear to be associated with quality of life and mental health issues.

It is not surprising that AD has a great impact on HRQoL in patients partly due to the chronic clinical course of the condition. Further, since it has no definitive cure, patients with AD not only suffer with the symptoms caused by the disease but also from compromised and life-long psychosocial and economic burden (Dalgard et al., 2015;

Hay et al., 2014). Since HRQoL encompasses both QoL that is independent of, but possibly affected by the disease (Lifschitz, 2015), the burden of the illness, and functional impairments in completing daily tasks are common factors impacting HRQoL (Lifschitz, 2015). Although these studies demonstrate the extent to which AD impacts QoL in adults, they are not without their limitations such as small sample sizes.. This thesis will address some of the issues uncovered in the literature such as small sample sizes and methodological weaknesses and inconsistencies in the measurement of QoL in adults with AD.

1.6 Atopic dermatitis and mental health

Atopic dermatitis is significantly related to mental health determinants such as anxiety, depression and psychological stress. This section provides evidence surrounding the relationship between AD and these mental health determinants, and gaps in current literature.

1.6.1 Atopic dermatitis and psychological stress

Complex psycho-neuro-immunological interactions are involved in AD (Arndt, Smith, & Tausk, 2008). Stress is found to alter the skin barrier, antimicrobial immunity and t-cell immune responses, which in turn gives rise to pruritus and increased skin damage from scratching (Arndt, Smith, & Tausk, 2008). Stress-related severity is one of the most significant triggers of AD symptoms (Morren et al., 1994). The resulting itch-scratch cycle causes high levels of stress and anxiety in patients, decreasing overall QoL (Arck & Paus, 2006).

The central nervous system (CNS) can initiate and/or aggravate atopic inflammation through release of pro-inflammatory neuropeptides (Misery, 1997). On the other hand, these neuropeptides that are released in the skin when exacerbated impact the CNS, disturbing perception and recognition networks of patients with AD (Fitzpatrick, Eisen, Wolf, Freedberg, & Austen, 1993), suggestive of a bi-directional relationship between

stress and AD. Early clinical observations first proposed the notion that psychology stress related to a traumatic life event is associated to the development of atopic dermatitis (Brown, 1972; Greenhill & Finesinger,1942; Wittkower & Russel, 1953). Psychological stress and AD severity in these studies were mainly explored using questionnaires or interviews with patients and these events included death in the family, problems during childhood and parental divorce. Notably however the accuracy of adults' abilities to recall childhood events is questionable and unreliable. Nonetheless, the association between AD severity and stress in more recently published literature shows that interpersonal and daily stressors are also highly related to AD severity in adults (Oh et al., 2010; Arndt, Smith, & Tausk, 2008).

The only known longitudinal study used daily diaries to assess stress in 40 adults over a period of two weeks. The authors found that stress on day X predicted AD severity on day X+1 and this prediction was reciprocal. Patients with AD may suffer from generally elevated stress levels due to living with the condition. For example, Buske-Kirschbaum, Gierens, Höllig, and Hellhammer, (2002) found that adults with AD report higher levels of distress due to their condition, and the amount of stress is positively related to the severity of the condition, medication taken and intensity of priorities. Social skill deficits have also been reported by others, whereby adults with AD when engaging in discussions with their parents and partners, showed less willingness to discuss their condition, showed less self-acceptance and displayed less self-disclosure compared to a nonatopic control group. Thus, AD patients appear to have more problematic relationships with their families and significant others which could result in increased interpersonal stress levels (Carroll, Balkrishnan, Feldman, Fleischer & Manuel, 2005).

A cross-sectional study (Benea, Muresian, Manolache, Robu, & Diaconu, 2001) looking at the relationship between stress and severity of AD found that stress alone is not the most important trigger factor of AD exacerbation (only 5.83% of patients), but it is a very important factor in maintaining the AD (45.42%) and the disease itself could be a stressor

for the patient, resulting in a vicious circle (17 of 50 patients who were reviewed by a Psychologist reported that the duration of the disease induced stress; 34%). The causal relationship between stress and AD is poorly understood due to the lack of longitudinal studies, and many existing studies focus on self-reported perceptions of stress, not taking in to account objective measures such as salivary cortisol, which is a biological indicator of stress.

Cortisol is secreted from the adrenal cortex in the Hypothalamic-Pituitary-Adrenal(HPA) axis, with elevated levels due to both acute and chronic stressors resulting from for example, discrimination, social isolation and feelings of stigmatisation in relation to AD (Steptoe, Cropley, Griffith, & Kirschbaum, 2000) and situations giving rise to acute stress such as earthquakes (Kodama et al., 1999). Salivary cortisol levels are found to reflect psychological stress, thus are reliable and accurate indicators of chronic stress. . Mizawa, Yamaguchi, Ueda, Makino, & Shimizu, (2013) compared psychological stress in AD patients to healthy participants through the measurement of cortisol levels in saliva. The SCORAD severity measure was also used to assess disease severity in adults with AD. The findings illustrated significantly higher salivary cortisol levels in AD patients compared to healthy participants ($p<0.001$). Furthermore, cortisol levels in the saliva were also significantly correlated with objective disease severity ($r=0.42$, $p<0.05$). This leads to speculation that higher AD severity is related to increase in psychological stress compared to mild or moderate severity and also suggests that patients with AD might be suffering from chronic stress.

Overall, findings of published literature suggest that AD is a cause of stress in patients and symptoms of AD may be exacerbated by stress. Hence, it should be viewed as a chronic inflammatory skin condition that has a strong psycho-dermatological component. As a result of the cross-sectional design used in the majority of the studies exploring stress and AD, a temporal relationship between AD and psychological stress cannot be determined. Additionally, most studies exploring stress and AD rely on self-reported

assessments of stress levels, which may not relate to physiological changes such as cortisol levels, which can result in an exacerbation of AD symptoms. However, it could be argued that self-reporting of perceived stress allows for an appropriate measure of the actual levels of stress experienced by patients (Nielsen et al., 2005). In an ideal world, it would be beneficial to measure stress using both objective measures and self-report.

1.6.2 Atopic Dermatitis, anxiety and depression

Although there is acknowledgement of physical comorbidities such as asthma and food allergy alongside AD, there is a lack of appreciation for the psychological impact it may have on the patient, in particular anxiety and depression (Park et al., 2016; Radtke, Schafer, Glaeske, Jacobi, & Augustin, 2016). Mental health comorbidities such as anxiety and depression are present in a number of skin conditions, however five decades ago, AD patients were noted to have a unique psychological profile, high in anxiety and depression, which is unlike the case for patients with other cutaneous conditions (Ahmar & Kurban, 1976). Adults with AD experience relentless pruritus, the main source of morbidity in this condition. Even mild disease negatively affects a patient's life, and more generalised disease can affect a patient to a similar degree as having diabetes (Kiebert et al., 2002). Through the studies done so far, a strong association is found between dermatological conditions and psychological problems (Shenoi, Prabhu, Nirmal, & Petrolwala, 2013).

The incidence of mental health comorbidities among dermatology patients has been found to be approximately between 30% and 40% (Ghosh, Behere, Sharma, & Sreejayan, 2013). The presence of a concomitant compromised mental well-being is predominantly observed in patients with various dermatological disorders like atopic dermatitis, acne, pruritus, urticaria, alopecia, psoriasis or vitiligo (Picardi, Abeni, Melchi, Puddu, & Pasquini, 2000) of which AD is the most common skin disease observed in general practice. Various mechanisms have been proposed to understand this

association, both forming a vicious cycle (Hashizume & Takigawa, 2006). Most frequent symptoms reported as a basis for distress are disfigurement and itching causing significant insomnia, and sleep deprivation leads to fatigue, mood lability, impaired functioning and suicide in a few cases (Gilchrest, 1982; Dieris-Hirche, Gieler, Kupfer, & Milch, 2009; Rønnstad et al., 2018). Furthermore, frequent bullying and embarrassment due to disfigurement leads to social stigma and social isolation. Disfigurement caused by AD can lower patients' self-esteem, in turn increasing the propensity to suffer from anxiety and depression (Koo & Lebwohl, 2001).

Studies investigating the relationship between AD and depression or anxiety disorders in adults are very limited, and findings are equivocal across studies (e.g. Ginsburg, Prytowsky, Kornfeld, & Wollland, 1993; Dieris-Hirche, Gieler, Kupfer, & Milch ,2009; Slattery & Essex, 2011). It is not clear if a severity-dependent relationship is present between AD and anxiety or depression. A nationwide Danish cohort study found no relationship between the likelihood of using antidepressants and mild AD, however moderate-severe patients with AD had increased risk of antidepressant and anxiolytic medication use (Thyssen et al., 2018). In contrast, a US cross-sectional study found no difference between patients with moderate-to-severe AD and depression and anxiety compared with patients with mild AD (Whiteley, Emir, Seitzman, & Makinson, 2016), however, the AD cohort had a significantly higher prevalence of anxiety and depression compared to healthy controls.

There are very few randomised controlled trials (RCT) exploring the impact of anxiety and depression treatment on AD but one methodologically sound study explored anxiety after treatment with either an antidepressant or placebo drug. Thirty-seven adults with AD took part in a double-blind clinical trial and were randomised to either receive daily anxiolytic/antidepressants or placebos for a month. Significant improvements were noted in mood and disease severity in those who received antidepressants/anxiolytics but this improvement was not seen in the placebo group (Kawana, Kato, & Omi,

2010).Interestingly, significant positive correlated between anxiety and disease severity were also noted showing that as anxiety reduced so did reported severity. Adults with AD reported an association between emotional distress, itch, and scratching; 81% of patients reported that anxiety and stress exacerbated their itch (Wahlgren, 1992). In two randomized controlled trials and several case series, the selective serotonin reuptake inhibitors (SSRIs) paroxetine, sertraline, and fluoxetine which are antidepressants, improved pruritus (itch) which were the result of a number of medical conditions (Browning, Combes, & Mayo, 2003; Mayo et al., 2007; Zylicz, Smits, & Krajnik, 1998; Zylicz, Krajnik, & Sorge, 2003). Another RCT used treatment for AD as opposed to anxiety/depression as above. Trial results from a clinical trial of dupilumab, a medicine used in the treatment of AD, found that the number of adults with severe AD who also suffered with anxiety or depression showed significantly more improvement in their anxiety/depression in the active arm compared to those who received placebos (Simpson et al., 2016).

Kim et al (2015) found a greater relationship with depressive symptoms in adults who had moderate or severe AD compared to mild AD, although this difference was not significant. The researchers used a sample of 1517 men with dermatologist-diagnosed AD for their study. A 2013 survey of 428 US adult patients showed higher rates of depressive symptoms in those with moderate or severe disease (40%) compared to mild AD (34.6%), although this difference was not statistically significant.

Based on the above findings, there are contradictory findings surrounding the severity-dependent relationship between AD and mental health comorbidities (Holm et al., 2016). Dieris-Hirche, Gieler, Kupfer, and Milch (2009) found significantly higher levels of anxiety, depression and suicidal thoughts in patients with atopic dermatitis, however increase in suicide risk and severity of depression were not significantly correlated with clinical severity of the condition. A further study found an association between AD severity and suicidal ideation, however after adjusting for depression and other factors,

this association was non-significant (Dalgard et al., 2015). The finding above supports the notion that suicidal ideation occurs as a result of mental health issues and not just due to AD (Hawton, Casanas, Haw, & Saunder, 2013).

it is likely that the combination of anxiety, depression, psychological stress and disease severity form a vicious cycle in patients with AD (Oh et al., 2010) and in severe cases, may result in suicidal ideation, attempts and actual suicide. The inconsistencies in the findings between AD and psychological variables may be as a result of various study methodologies, including varying anxiety/depression scales and limitations in previous studies including the use of non-validated symptom questionnaire instead of validated measures. Furthermore, not all studies have adjusted for atopic comorbidities and demographic characteristics in their analyses, therefore one cannot deduce the lone effect of AD in the development of depression and anxiety disorders.

Unfortunately, there is a lack of psychological support available to patients. A report compiled by the officers of the All Party Parliamentary Group on Skin (APPGS) in 2011 consisting of dermatologists, GPs, and patient groups reported there is a lack of appropriate psychological support for patients with AD amongst other skin conditions, with AD being trivialised and thought of as a minor skin ailment. A life-long AD patient reported how her condition played a part in her decision to stop practising as a commercial lawyer; issues such as dress code and frequent absences due to the condition or hospital appointments were poorly appreciated by work colleagues. . Dermatologists, nurses, and patients acknowledged the lack of psychologists and other professionals specialising in mental health , and only three out of 127 hospitals had a dedicated psycho-dermatology service. Health care professionals also emphasised their concerns about patients not being referred to psychologists due to referrals falling on ‘deaf ears’(p. 25). This emphasises the notion of mental health needs being viewed as largely separate to that of physical needs, despite the significant impact of these AD and other related skin conditions on patients’ quality of life and psychological well-being.

1.7 Chapter summary

The fact that AD is not a fatal condition should not make it less attractive from research funding point of view. As discussed above, AD has a significant impact of QoL and is associated with anxiety, depression and in some severe cases, suicidal ideation and suicide. It can also have an impact on family members and poses a huge burden to the healthcare system. As detailed above, QoL research looking at AD in adults is also relatively scarce; most research focuses on children with the condition. Inconsistencies in measurements used for QoL and disease severity may result in conflicted findings. Moreover, most current research is cross-sectional, has small sample sizes and does not differentiate between clinically diagnosed and self-diagnosed AD. There is also lack of research on AD in the United Kingdom, despite the UK having one of the highest prevalence rates of the condition in adults (5%) (Harrop et al., 2007). The majority of previous research on QoL and mental health in AD has been conducted in France, Germany, Spain, Sweden and the USA; prevalence rates in these countries are lower (2-3%) than the UK (Harrop et al., 2007). All research to date on the impact of AD on QoL in adults has been quantitative and much is cross-sectional rather than longitudinal. In-depth qualitative research could help explore issues which are not fully addressed in quantitative studies and allow a more detailed participant exploration of living with the condition. people's lives. In order to address some of the limitations of the research to date, this thesis aims to explore in detail the impact AD has on quality of life and mental health of adults through a systematic review of published literature, a qualitative study using one-to-one interviews, a quantitative study to investigate QoL and mental health in adults with AD using a large sample of people living in the UK and a longitudinal study to investigate the causal impact of stress, anxiety and depression on AD.

1.8 Brief overview of thesis main studies

This thesis seeks to explore quality of life and mental well-being in adults with atopic dermatitis in the UK. Using both qualitative and quantitative methods, it is hoped that this

research will inform better health care provision and support for patients with AD, as well as a richer information base for health care professionals dealing with these patients.

Chapter 2: General methodology

This chapter discusses the researcher's epistemological stance, methodological decisions made throughout the research process and justification for the choice of analyses for each study in thesis.

Chapter 3: systematic review and meta-analysis

This chapter provides the first systematic review exploring QoL in adults with AD. It includes a rigorous narrative synthesis and critical review of studies conducted in the area so far as well as methodological and general recommendations. Seven studies included in the review are included in a meta-analysis.

Chapter 4: Qualitative exploration into adults' experiences of living with AD

This chapter explores participants' accounts of living with AD and issues that have been uncovered through the systematic review are explored in further detail. Participant interviews are analysed using thematic analysis (Braun & Clarke, 2006) and novel issues not found in previous literature are uncovered in this chapter.

Chapter 5: A quantitative exploration on the impact of AD on QoL and mental health in adults

This chapter uses validated questionnaires to compare QoL, anxiety, depression, and psychological stress in adults with AD compared to healthy controls. Participants in this study include adults with clinically diagnosed AD living in the UK. Data in this study have been analysed to explore differences between groups as well as to explore predictors of QoL.

Chapter 6: A longitudinal analysis of the impact that psychological stress plays on AD exacerbation

The final empirical chapter makes use of daily diaries and validated questionnaires to explore the bidirectional relationship between psychological stress and AD severity. It is a 12 week-long feasibility study which required participants to record stressful events and flare-ups. Data for this study have been analysed using cross-lagged panel analysis and Pearson's correlations. Implications and recommendations are discussed.

Chapter 7: General discussion

This chapter discusses the findings and contributions of each study detailed in the thesis. It employs a critical view of how the thesis has contributed to existing knowledge in the field of dermatology. It also provides recommendations for clinical practice and finally the researcher provides a general reflection on experiences throughout the PhD.

Chapter 2: Methodology

This chapter provides justification for methodological decisions and the researcher's epistemological position. Additionally, decisions surrounding study designs, participant recruitment, data collection and data analyses are presented.

Using a range of research methods collectively is referred to as 'mixed methods'. Mixed methods designs have become increasingly popular in the health sciences (O' Cathain, 2009). There has been a view that both methods are incompatible with each other because they are underpinned by fundamentally different assumptions about reality (ontology) and understanding(epistemology). This incompatible paradigm debate exists due to the differences in theoretical perspectives of these methods, for example between quantitative and qualitative research. For this thesis a multiple-method approach has been used as opposed to a mixed-method. Multi-method research involves using more than one method of data collection in a study, whereas mixed-methods research includes the mixing of both quantitative and qualitative methods or paradigms in one study (Ivankova, Creswell, & Plano Clark, 2007). Mixed-methods research may indeed be perceived as a type of multi-method research. This thesis uses both quantitative and qualitative methods to explore quality of life and mental health in adults with atopic dermatitis, with the use of a cross-sectional survey, daily diaries over a period and semi-structured interviews together.

2.1 Epistemology

The philosophical assumptions underpinned by quantitative and qualitative research are often perceived as holding opposing paradigms (Todd, Nerlich, McKeown, & Clarke, 2004). According to Hall (2013), the use of multiple methods in one study is often referred to being incompatible due to the opposing paradigms. Thus it is important for researchers to be aware of and discuss what assumptions they make about knowledge as it shapes the method of inquiry and overall research process (Creswell & Plano-Clark,

2011). The over-simplistic belief is that qualitative research is associated with 'interpretive' or 'constructivist' paradigms and quantitative research focusses on 'scientific' or 'positivist' paradigms despite significant overlap between these methods. It is important to be aware of these differences, although this chapter asserts that these differences are overstated and can be overcome. If the differences in aims and assumptions between the two approaches are not identified and acknowledged, research that incorporates both methods is likely to violate the assumptions of one or other of these approaches.

Quantitative methods propose an objective reality and the notion that absolute knowledge can be obtained (Scotland, 2012); these approaches are based on positivism. Indeed, from the quantitative perspective, an investigator and the phenomena investigated are separate entities. Thus, a phenomenon can be studied with being influenced or influencing it, "inquiry takes place as through a one-way mirror" (Guba & Lincoln, 1994, p. 110). Qualitative approaches on the other hand reject the notion of a single correct definition of knowledge or reality; these approaches are rooted in the interpretivist paradigm (Braun & Clarke, 2013; Mcevoy & Richards, 2006). They assume a number of realities and aim to explore in depth how individuals perceive the world and experience events (Braun & Clarke, 2013; Willig, 2013). Thus, interpretive researchers argue that attaining 'objective knowledge' is not possible (Yardley & Bishop, 2008) and acknowledge the role they play in knowledge construction and thus practise reflectivity.

Some researchers argue that focussing on certain types of methods is in itself unhelpful. According to Hiles (2014), emphasizing on the differences between quantitative and qualitative approaches is problematic; placing this importance does not account for the importance of impact of the strategy on the research design. Hiles (2014) also argued that the terms 'qualitative' and 'quantitative' methods should be abandoned, and that all research makes paradigm assumptions and decisions about research design, data

collection, data analysis and critical evaluations. Instead, three logics on inquiry have been proposed by Hiles (2014): induction, abduction, and deduction. Induction is a data-driven approach which aims to use data to generate new theories. Qualitative research tends to take an inductive approach. On the other hand, deductive approaches are concerned with testing data from theories, and quantitative research tends to be deductive. Finally, abduction begins with several observations from which the simplest and most likely conclusion is derived. Unlike deductive reasoning, this process results in a reasonable conclusion, but it does not positively verify it. According to Hiles (2014) abductive reasoning employs 'mixed measures' or what is commonly referred to as 'mixed methods' research.

2.2 Mixed methods research

Both qualitative and quantitative methods uniquely contribute to research thus incorporating them both in research has the ability to explore and reveal different areas of a topic under study (Harper &Thompson, 2012). Qualitative approaches may identify experiences or concepts that are not easily captured using questionnaires or response categories whereas quantitative approaches are able to test pre-existing theories and provide comparisons and patterns. (Creswell & Plano-Clark, 2011). It is however imperative for researchers to be aware of the differences in assumptions and aims between these two types of approaches, in order to avoid applying inappropriate or inaccurate criteria for validity assessments of, for example qualitative research (e.g. use of a large sample, objectivity) and as a result proposing irrelevant conclusions (e.g. causality between variables). Equally, lack of knowledge surrounding quantitative approaches could also result in inaccurate criteria (e.g. small, unrepresentative sample, inappropriate statistical tests). Sale, Lohfield, and Brazil (2002) argue that regardless of the debate surrounding incompatible paradigms, a mixed approach permits for greater insight of complicated issues than if either approach was used alone. Triangulation is

another advantage that is proposed to improve the integrity of results (Merterns & Hesse-Biber, 2012).

Both qualitative and quantitative approaches study different phenomena thus distinguishing between the two is vital (Sale, Lohfeld, & Brazil, 2002). Although the 'involvement' may appear similar across the two approaches, the distinction is between the 'lived experience' and 'measure'. Distinction between both methods encourages clarity and links the phenomenon to its corresponding paradigm and method. Positioning the study as multi-method helps to determine if any approach takes precedence within the research and minimises undermining one aspect. Within this thesis, the qualitative element is deemed equally as important as the quantitative element although quantitative approach encompasses a larger volume of the findings; both approaches are awarded equal weighting.

When using different types of methods, a researcher needs to contemplate and focus on differences in paradigms (Harper & Thompson, 2012). For example, in this thesis daily diaries and online surveys were used and aligning with positivism, assumes that that data collected represents a factual truth which is autonomous from participant effects. Additionally the qualitative study in this thesis used semi-structured interviews which were analysed thematically; the focus here is on individual experiences and perceptions of living with AD and it was assumed these experiences may share common themes. The section below details the rationale for study design, sampling, recruitment methods, and data analysis for each empirical study in this thesis.

2.3 Systematic review and meta-analysis

2.3.1 Study design

For many years, numerous studies focussing on the psychological and social impacts of skin conditions have been published (Al-ahmar & Kurban, 1976; Baughman & Sobel, 1971;Coles, 1975; Gupta, Gupta, & Ellis, 1987; Ramsay & O'Reagan, 1988; Stankler,

1981; Susskind & McGuire, 1959; Wittkower, 1946; Wittkower & Hunt, 1958). Nonetheless, only recently have these studies have become increasingly consistent in their methodology (de Korte, Mombers, Bos, & Sprangers, 2004).This increase is partly due to the recent development and use of QoL questionnaires which allow for comparisons across AD patients as well as other patients groups and healthy controls.

Research into the impact of AD on patients' QoL is carried out worldwide and specialist journals are produced, informing readers about new developments. However, with over 200 journals in dermatology alone (Delamere & Williams, 2001), it is near impossible for anyone to keep informed about this vast quantity of research. Reviews aim to address this problem by summarising studies that focus on similar/same questions. Cook, Mulrow and Haynes (1997) define a systematic review as a summary current literature that makes the use of reproducible methodology to critically evaluate, systematically search and effectively synthesize data on a specific area. A systematic review synthesizes findings of empirical studies that are related to one another by using bias and error reducing strategies (Cook, Mulrow, & Haynes, 1997).The systematic review conducted for this thesis included studies that explored QoL in relation to AD in adults.

In healthcare settings where evidence is evolving frequently, systematic reviews have become increasingly valuable. Health care professionals use these reviews to keep informed of the evidence in their field and these reviews are frequently used as a starting point in developing clinical guidelines in practice (Moher, Liberati, Tetzlaff, & Altman, 2009). The researcher carried out a systematic review to identify what is currently known, where knowledge is lacking, as well as guide future research. By developing a coding protocol in which all the categories of data extracted from empirical studies were listed and defined, the review revealed various gaps in current QoL literature in relation to AD. These will be discussed in detail within the next chapter. This is the first systematic review to explore QoL in adults with AD. A meta-analysis of homogenous studies was also conducted. The systematic review and meta-analysis within this thesis focuses on

quality of life specifically as opposed to quality of life and mental health. This was due to a number of reasons such as the presence of existing reviews focusing on mental health and atopic dermatitis in adults (Ronnstad et al., 2018) and the intention for a succinct and focused review which not have been possible when considering the wide-ranging definition of mental health. Mental health, although highly related to quality of life, is a factor that affects AD separately, with or without an impact to QoL.

Systematic reviews provide a wide range of topics within a given subject; may be useful in understanding new concepts, but are rarely comprehensive; rarely give details about the methods; are likely to be written in line with the opinions of the author; quality differences between the studies are rarely considered; and as a result, can be misinterpreted and lead to inadvertent bias (Selcuk, 2019). To avoid these issues in systematic review writing, the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) group, which mainly consists of Cochrane authors, has developed the PRISMA guidelines in 2009 (Moher, Liberati, Tetzlaff, & Altman, 2009). The review in this thesis followed the PRISMA guidelines for several reasons. A systematic review will extensively scan published literature on a certain subject and seek answers to a succinctly detailed research enquiry, whilst using a variety of inclusion and exclusion criteria to identify studies for the review and then synthesize the findings. The PRISMA statement which consists of a 27-item checklist and a four phase flow diagram, aims to improve the reporting of systematic reviews and meta-analyses. Full compliance with the checklist items facilitate clarity and transparency in reporting; thus ensuring a well-structed report that well-defines the study question, clearly states its' title and objectives, clearly and justifiably indicates inclusion and exclusion criteria, critically and accurately prioritizes the reviewed study reports, and provides a clear analysis of the eligible study reports.

2.4 Qualitative study using semi-structured interviews

In this section further information on rationale for study design, sampling, recruitment methods, and data analysis are discussed for the qualitative study.

2.4.1 Study design

The systematic review revealed that QoL in relation to AD was measured using only cross-sectional methods, and although the findings illustrated a profound effect of AD in QoL, the review highlighted areas that warranted further exploratory research, such as sleep disturbances and personal relationships. Thus, this study employed a qualitative inductive approach to explore lived experiences of adults with AD using semi-structured interviews.

Interviewing is the most common method of data collection for qualitative research (Barriball & While,1994; DiCicco-Bloom & Crabtree, 2006, King, 2004). The purpose of a qualitative research interview is to gain an understanding of the interviewee's perspective of the research topic (King, 2004). Several advantages of the semi-structured approach to collecting data were considered for this study. First, a semi structured interview is a useful method for exploratory research topics that are complex or where little is known about the research area. Since this is the first study exploring adults' experiences of living with AD, this method of data collection was considered most appropriate. Second, semi-structured interviews are considered a useful approach to answer questions from the perspective of subjective experience, enabling the individuals to be participants in meaning-generation and interpreters of their experiences as opposed to sources of information (DiCicco-Bloom & Crabtree, 2006; Saks & Allsop, 2012). This was considered very useful for the present study as it sought to explore the experiences of AD patients. Third, by adopting a semi-structured approach, the interviews allow flexibility in collecting data by enabling the interviewer to probe the

participant for more information and clarification of answers and pursue emergent themes (Barriball & While, 1994, Saks & Allsop, 2012).

Face-to-face interviewing is thought to be the most effective way of gathering data during interviews (Hold, 2010) and is assumed superior than other methods in ensuring high quality of data. However Norvick (2008) found that when interviews are conducted via telephone, there is little compromise on quality depth of findings. Moreover, Hold(2010) identified a number of advantages of conducting interviews via telephone, such as less cost of travel, practicality and increased articulation due to lack of non-verbal communication. These are benefits that also apply to video-conferencing software such as Zoom, with the added advantage of being able to visually communicate with participants (Hanna, 2012). In order to effectively manage the research budget and practically collect a range of responses, face-to-face, Zoom and telephone interviews were deemed feasible to collect data for this study. Participants in the study were offered these options prior to arranging interviews.

2.4.2 Sampling and recruitment methods

Recruitment of all participants was achieved through purposive sampling. This is a extensively used non-probability method which is utilised when aspects are chosen through the judgement of the researcher (Patton, 2002). Purposive sampling identifies people who have knowledge of or are experienced with a chosen phenomenon of interest (Creswell & Plano-Clark, 2011). According to Palinkas et al (2015), using purposive sampling for a multi-method study adheres to the similar principles that regulate other forms of sampling.

Within qualitative research, the sample size is often determined when data saturation has occurred; this is a notion rooted in grounded theory analysis (Bowen, 2008). Although there is no universally accepted approach for reaching data saturation, it is said to transpire when the collection of further data does not create new meaningful

information and the study can be replicated (Guest, Bunce, & Johnson, 2006; Morse, 1995), deeming it ambiguous as there are currently no pragmatic guidelines (Fusch & Ness, 2015). As a result, in the vast majority of qualitative studies, the notion of saturation is introduced but how it is relevant in the context of the study is often not discussed (Bowen, 2008).

Is beneficial to consider sample sizes with regards to data sufficiency i.e. “are the amount if interviews I have conducted enough to answer my research question?” Data sufficiency was sought through frequent research supervision and via a reflective diary. For example, a quote from the reflexive diary following the 16th interview reads: “I am satisfied with the interviews so far, and can see similar discussion topics cropping up in the interviews”. Further, although discussions during supervisory meetings confirmed a range of participants’ experiences and narrative,, there was a large sense of consistency between interviews, with the remaining interviews conducted with the confidence that data sufficiency had been attained.. Sample for this study falls within the ‘moderate’ criteria as recommended by Braun & Clarke (2013)- a small sample size would include six to ten participants with moderate samples ranging from 10-20 participants.

Participants for the study were recruited using various platforms on social media and via Aston University using posters and e-mail circulations. One application of social media in research settings is the ability to facilitate recruitment in studies. Traditionally, snowball sampling is a process of recruiting participants who may be challenging to recruit using other means (Faugier & Sargeant, 1997). In health and clinical research, this may comprise those who feel socially isolated, stigmatised or have specific demographic characteristics, such as areas where there is cultural diversity or where literacy or language barriers may exist (Sadler, Lee, Lim, & Fullerton, 2010). As social isolation has been found in adults with AD (Blome, Radtke, Eissing, & Augustin, 2016; Chamlin, 2006; Zuberbie et al., 2006), it is essential to apply data collection strategies that can be easily accessed, such as online data collection strategies (Lyons, 2015).

According to Slamons (2016), such data collection can occur through any means that are used as communication devices, for example, computers and mobile devices. The use of internet-mediated research methods can enable access to a diverse sample of the general population. Indeed Facebook use in the UK is one of the highest penetration rate in the EU (O'Dea, 2019). Additionally, this social networking site is used multiple times a day by approximately half the UK population and only 20% of UK adults that use the internet do not use Facebook (O'Dea, 2019).

It is also important however to acknowledge a number of challenges with online data collection that apply to the studies in this PhD thesis, for example the issue of 'representativeness' (Coulson, 2015, p.14) where participants who are recruited using online methods may not be representative of the AD population as the internet may not be equally available across the population. However this may change as the use of internet grows (Hewson, 2003). Hewson (2016) suggests that although 'in the early days of internet mediated research, there were widespread concerns about biases inherent in the internet-user population' (p.71), there is no evidence of bias regarding some groups of users (White, upper-class, well-educated males). Additionally, data collection using traditional methods such as pen and paper have been found to be consistent with online data collection (Gosling, Vazire, Srivastava, and John, 2004) thus the discrepancies between the two may be slight. According to Hewson (2003), participants recruited online may indeed be more representative than those recruited using traditional methods..

2.4.3 Rationale for method of analysis

The chosen method of analysis for this study is thematic analysis (TA). This widely used method is used to identify, analyse and interpret patterns or themes in qualitative data (Braun & Clarke, 2006). It is a unique form of qualitative analysis as it can be applied to numerous theoretical contexts whereby the researcher embraces a systematic approach and undertakes several steps in order to generate initial codes and develop themes

which embody patterns of meaning. According to Braun and Clarke (2013), TA was developed due to its' flexibility and usability as a technique to recognize themes within and across data with regard to participants' feelings, perspectives, views and experiences (Braun & Clarke, 2013).Although its' flexibility is considered a strength, TA has also been criticised for this flexible approach due to lack of transparency and its undefined nature(Antaki, Billig, & Potter, 2003). Willig (2013) states that using TA as a tool does not offer a clear theoretical base for research. In order to overcome these limitations, a number of decisions are required by the research and these need to be explicit, including approach of data, generation of codes, interpretation of data beyond spoken word and the researcher's epistemological stance. The researcher has identified critical realism epistemological stance, thus the two remaining issues will be discussed.

A deductive or 'bottom up' approach is determined by the researcher's theoretical interest and uses a pre-existing theory to understand the data. On the other hand, an inductive or 'top down' approach is data driven therefore not influenced by the researcher's analytic preconceptions (Willig, 2013). In order to explore participants' experiences of living with AD, an inductive thematic analysis approach was employed. The findings are therefore grounded in participant's accounts as opposed to pre-conceptual framework. TA also has the ability to identify different kinds of meaning. These include the explicit content of participant discussions, or latent meanings which rely on the researcher's interpretation of participant discussions (Willig, 2013), For this study, a latent approach was employed as the researcher was interested in 'unspoken' information during the interview. Participant quotes were included in the write-up of this chapter to enhance credibility of the researcher's interpretation and demonstrate how conclusions were derived.

It could be argued that Interpretative Phenomenological analysis (IPA) might be a better method of analysis to explore experiences of adults with AD. It is a qualitative approach

that takes an idiographic focus i.e. it aims to offer insight into how an individual, in a certain situation, makes sense of a given phenomenon (Smith & Shinebourne, 2012).Both IPA and TA analyses involve coding and theme development, however both processed differ somewhat for each method. Coding within IPA involves initial notes or comments whereby the researcher writes their initial analytic observations about the data, whereby coding in TA occurs after data familiarisation where the researcher notes initial analytic observations surrounding the entire data set and each data item. This is followed by codes across all data items. IPA is recommended when working with a smaller sample and maintains a more idiographic focus, and thematic analysis is recommended when working with a larger sample with a focus more on patterned meaning across the dataset (Braun & Clarke, 2006). There is sometimes the assumption that if one is conducting phenomenological research, IPA must be used. Therefore, it is important to note that there is a long and diverse history of phenomenological research in the social and health sciences (Langdridge, 2007). Thematic analysis has a long history as a phenomenological method that predates the development of IPA. As a result of its theoretical freedom, TA offers a highly flexible approach which can be modified for the requirements of many studies, providing complex, rich and detailed account of data (Braun & Clarke, 2006; King, 2004). The usefulness of TA in exploring research participants' perspective, generating unanticipated insights and highlighting differences and similarities are amongst the purposes proposed by Braun and Clarke (2006) and King (2004). Thematic analysis is also ideal for use in large data sets for summarising key features, as in this thesis, due to it forcing the researcher to implement a well-structured approach to handling data and in turn generate a clear, organised report. Additionally, as there were no qualitative studies focusing on adults with AD at the time of writing, a large, diverse set of participants best allowed for initial qualitative exploration of living with the condition. For these reasons, thematic analysis was chosen.

2.4.4 Reflexivity

Coyle (2016) discusses the importance of reflexivity in qualitative research, defining it as an acknowledgement of the researcher's personal understanding, experiences and theoretical commitments have in their analysis. Reflexivity allows the researcher to determine their influence on the research process and analysis (Willig, 2013). According to her, reflexivity involves 'reflecting upon the ways in which our own values, experiences, interests, beliefs, political commitments, wider aims in life and social identities' have shaped the research process (Willig, 2013, p.10). In order to be reflexive, the researcher needs to consider the ways that the ways that they may have/can influence the data. The remainder of this section-which will be written in first person- will discuss the researcher's impact of the research process, the data and how personal experiences could influence the analytical process (Coyle, 2016).

. As I was diagnosed with and have suffered from AD since childhood, this experience was the most important aspect for reflection. Living with the condition could impact my interpretation of the data through consideration of my personal experiences of having AD. I was however diagnosed at a very young age and have been able to manage my AD through pharmacological interventions and dietary changes; my condition is classed moderate to severe. My participants' experiences, were largely different to my own and this allowed interpretation to be grounded in the participants' experiences, as opposed to my own experiences or assumptions. I also had regular meetings with my supervision team to discuss the findings of the analysis and kept a reflective diary throughout this process in order to further ensure that my analyses were grounded in participants' experiences and perceptions. .

2.5 Quantitative study using questionnaires

In this section further information on decisions made regarding study design, sampling, and recruitment methods are discussed for the cross-sectional survey study.

2.5.1 Study design

An online quantitative survey was used with the aim of collecting data from a large sample in order to maximise representativeness of adults with AD. The systematic review highlighted the paucity of large-scale quantitative studies in the UK, with most large-scale studies being conducted outside the country where the prevalence, management of AD and health-care system may be very different to the UK (Kowalska-Olędzka, Czarnecka, & Baran, 2019).

Survey methods use a systematic method to collect data directly from respondents using standardised questionnaires for the purpose of quantitatively analysing a target population (Callegaro, Manfreda, & Vehovar, 2015; Shi, 2007). Surveys can be considered a useful approach to explore factors associated with phenomenon of interest and test hypotheses (Shi, 2007). As a research method, surveys, particularly cross-sectional surveys, are considered the most used method of data collection (Shi, 2007). Cross-sectional surveys capture response data from a sample of a target population at one point in time (Shi, 2007). Previous research has widely adopted cross-sectional survey methodology to explore quality of life in adults with AD (Lee et al., 2018; Misery et al., 2007; Misery et al., 2018; Silverberg et al., 2018).

Online surveys fall within the broader category of survey methods. Whilst retaining the same principles of general survey methodology, online surveys can offer several additional advantages. In addition to being deemed efficient and cost-effective, online surveys reduce the demand placed on study subjects, as they have the flexibility of completing the questionnaires in their own time and can opt out without feeling obliged to continue (Murdoch et al., 2014). Hewson (2014) also suggests that online surveys can yield reliable and valid data, whilst also extending the geographical sampling area and maximising chances of recruiting a representative sample.

Using online survey panels to recruit participants also helps optimise recruitment of healthy people when they are used as a comparison group in health research. For the present study, conducting an online survey allowed all adults with AD in the UK take part in the survey if they wished to do so whilst giving respondents the flexibility to complete the survey at their convenience (Shi, 2007). An additional advantage that online surveys can offer is that data entry is not a separate process, therefore errors associated with data entry are reduced (Wright, 2005).

However, disadvantages associated with online surveys were also considered. Self-selection bias is a major limitation of online survey research (Bethlehem, 2010; Eysenbach, & Wyatt, 2002; Thompson, Surface, Martin, & Sanders, 2003). Undoubtedly, there would be some individuals more likely than others to complete the online survey and a tendency for some individuals to respond to a study invitation whereas others might ignore it, resulting in a systematic bias. However, for the quantitative study, participants were recruited both online and via an outpatients Dermatology clinic.

2.5.2 Sampling and recruitment methods

Recruitment of all participants was achieved through opportunity sampling. As this was an online survey, anyone who met the inclusion criteria was eligible to take part. A number of recruitment methods were used to achieve this, including recruitment via an outpatients Dermatology clinic in Birmingham and recruitment using social media platforms such as Facebook and Twitter. The decision to use social media to complement the dermatology clinic was based upon findings of the systematic review. The majority of the studies in the review had recruited through clinics and typically patients referred to tertiary care tend to represent a more severe sub-set of cases and/or need hospital facilities that are not available at general practices (Basarab, Munn, & Jones, 1996).

Inclusion criteria were adults aged 18 or above with clinically diagnosed atopic dermatitis. The exclusion criteria were participants living outside the UK. Within the control sample, participants had to be aged 18 and above with no long-term conditions as these could affect their QoL ratings and undermine differences between healthy groups and AD patients. Further, adults with AD were excluded if they had any other skin condition or diagnosed long-term condition apart from asthma, hay fever or food allergy as these conditions are commonly experienced by patients with AD. This was due to studies reporting significantly poorer QoL in patients with long-term conditions such as arthritis and diabetes (e.g. Malm, 2017; Trikkalinou, Papazafiropoulou, & Melidonis, 2017). A long-term condition in this context was defined in accordance to the NHS definition "a health problem that requires ongoing management over a period of years or decades". Participants were also required to read and understand English in order to complete the questionnaires as these questionnaires were only available in English.

2.5.3 Rationale for method of analysis

The data for this study were analysed using a range of statistical tests including t-tests, ANOVAs, multiple regression and Pearson's correlation analyses. Multiple regression was used in order to assess the contribution of disease severity, mental health variables and socio-demographic characteristics towards the variance in quality of life. Multiple regression has the ability to control for other variables in the model, therefore allowing for the unique prediction of each variable towards the outcome variable. ANOVAs and t-tests explore differences between variables and were used to assess mean differences in QoL and psychological variables between socio-demographic groups and variables surrounding the condition (medication, family history, diagnosis). These tests are the recommended tests to be used to address the research hypotheses for this study (Field, 2013).

2.6 Longitudinal diary study

This section details rationale surrounding study design, sampling, and recruitment methods for the longitudinal diary study.

2.6.1 Study design

Very few longitudinal studies have been conducted with adults with AD, in fact, there has only been one published study exploring AD and stress longitudinally (King & Wilson, 1991). There are a number of reasons for using a prospective diary approach to explore the temporal relationship between psychological stress and AD severity. First, AD exacerbations and severity often change rapidly therefore daily reporting of the condition will reveals even minimal fluctuations. Furthermore, the research of Kalaki and Mizara (2018), Silverberg et al. (2018) and others suggest that psychological stress is related to the onset or severity of skin symptoms in AD Daily diaries detailing levels of psychological stress and state of the skin can provide stronger evidence of this association. Finally, there are a number of conflicting findings regarding the association of skin with emotional distress such as frustration(Patrizi et al., 2011) and anger (Lewis-Jones, 2006). Weekly and daily measurements of these emotional reactions in relation to the fluctuating course of AD will allow for comparisons and the temporal relationship to be examined.

This study was conducted as a feasibility study due to the novelty of the research and thus the researcher needed to explore whether the study would warrant and be appropriate for further testing. Feasibility studies enable an assessment of whether the findings, methodology, and ideas are ideal and can be sustainable. Feasibility studies allow the research to identify what needs to be modified in the research and how these changes may occur. The objectives of this type of study differ from those of a definitive future study and aims to address the issues of uncertainty in preparation for a large-scale study to be conducted in the future. Additionally, feasibility and pilot studies are

not designed to answer or address a research question; this is instead an objective of the future definitive trial (Lancaster, 2015). In 2004, Lancaster, Dodd, & Williamson (2004) proposed a number of recommendations for good practice relative to the design of feasibility and pilot studies.The authors published a number of evidence-based objectives including testing the integrity of the study protocol for the future trial, gaining initial estimates for sample size calculation, testing data collection forms or questionnaires, estimating rates of recruitment and consent, determining the acceptability of the study and selecting the most appropriate primary outcome measures.

2.6.2 Sampling and recruitment methods

For this study, recruitment of all participants was achieved through purposive sampling similar to the qualitative study. Participants were recruited using social media platforms including Facebook and Twitter. It was anticipated that for a longitudinal study, recruitment would be more problematic than for the other studies in this thesis, therefore prior to commencement, the researcher put up a poll on Facebook where AD patients could 'vote' for or against taking part in the three month long study which required daily stress diaries being completed for a month. Thirty-six respondents voted 'for' taking part in the study until the end, and three respondents voted 'against' taking part due to reasons such as tendency to forget and time-consuming, when completing the daily diaries. The suggested adequate sample size for a feasibility study varies greatly, however as rule of thumb, it is suggested that for single-group, the sample size for a feasibility study should be between 15 and 20 for a small to medium effect size (Julious, 2005; Teare et al., 2014).

2.6.3 Rationale for method of analysis

This study aimed to explore the temporal relationship between psychological stress and AD severity. In order to achieve this, the study employed a cross-lagged panel analysis. This is an analysis used to explore and describe reciprocal relationships and directional influences between a number variables over a certain amount of time. Cross-lagged

panel models (CLPM) are also referred to as cross-lagged regression models and cross-lagged path models- this thesis will refer to them as cross-lagged panel models. CLPM are estimated using longitudinal data where each participant or observation is recorded at multiple points in time (Byrne, 2013). The term 'crossed' in CLPM is due to the fact that they estimate relationships from one variable to another, and vice-versa. They are 'lagged' as they estimate relationships between variables at different time points. Put together, these models are able to estimate the directional influence variables have on each other over time (Byrne, 2013). This analysis was used in order to investigate whether psychological stress on day X would predict disease severity on day X + 1, and vice-versa. In CLPM, stability of the constructs is controlled for through the inclusion of autoregressive relationships, therefore often it is thought that the cross-lagged regression parameters acquired in the model are the most suitable measures for examining causality in longitudinal correlational data (e.g., Deary, Allerhand, & Der, 2009; Soenens, Luyckx, Vansteekiste, Duriez, & Goossens, 2008; Wood, Maltby, Gillett, Linley, & Joseph, 2008). Specifically, it is common practice to standardize the cross-lagged regression coefficients and compare their relative strength to determine which variable has a stronger causal influence on the other (Bentler & Speckart, 1981). The analysis was carried out using IBM SPSS AMOS 25 and M Plus software. In addition to CLPM, correlations were sought between mental health variables and disease severity for each week.

Chapter three: Quality of life in adults with atopic dermatitis: systematic review and meta-analysis

This chapter presents a systematic review and meta-analysis of studies exploring QoL in adults with AD. This chapter was written as a journal article and accepted for publication in The International Journal of Dermatology in November 2019 (see appendix 1 for the published paper). A review of the literature identified that no systematic reviews had been conducted on the impact of AD on quality of life in adults. This chapter therefore presents the first systematic review to explore this research question.

3.1 Introduction

Although there have been no previous systematic reviews investigating the impact of AD on HRQoL in adults, a literature review carried out by Lifshitz (2015) on the impact of AD on QoL focussing primarily on infants, children, and their families confirmed that AD has a significant and lasting effect on HRQoL, in particular on psychological wellbeing and social functioning. Patient-assessed severity of AD correlated with HRQoL decrements demonstrating a greater impact on HRQoL as disease severity increased. Additionally, a literature review carried out by Lewis-Jones (2006) on QoL and childhood AD confirmed that QoL in children was severely impaired with issues such as embarrassment and bullying affecting children psycho-socially and physically.

The impairments of QoL caused by childhood AD have also been shown to be greater than other common childhood diseases such as asthma and diabetes, emphasising the importance of AD as a chronic disease (Lifshitz, 2015). If QoL in children with AD is affected to this extent, it is probable that it will have an impact on QoL as children progress to adolescents and adulthood, given the severity and persistent nature of AD in adults (Hoare, Po, & Williams, 2000).

Research conducted on adults with AD suggests that all aspects of HRQoL are affected, and that HRQoL is more compromised in adults with AD when compared to adults with chronic urticaria and psoriasis (Grob, Revuz, Ortonne, Auquier, & Lorette, 2005). Little

is known about how HRQoL of AD patients varies with disease severity; the literature that has investigated this issue has found that greater disease severity is related to poorer HRQoL (e.g. Fivenson, 2001; Haeck et al., 2012; Silverberg, 2018). To draw together what is currently known in this area and identify gaps in knowledge, the present study reports the results of the first systematic review and meta-analysis of the impact of atopic dermatitis on QoL in adult patients.

3.1.1 Aims of this review

This review aimed to synthesise and provide an overview of published empirical literature focussing on quality of life in adults with AD. A clearer understanding of the extent that quality of life is affected can improve awareness and reduce stigma whilst improving outcomes for adults with the condition. In this systematic review and meta-analysis, relevant studies are discussed and critically appraised. A narrative synthesis across the literature is presented alongside a meta-analysis of seven studies. Recommendations for future research have also been considered.

3.2 Methods

3.2.1 Developing the search strategy

Databased searched initially included the Cochrane Database of Systematic Reviews library and Prospero in order to identify any previously published and ongoing reviews exploring quality of life in adults with AD; no such reviews were identified. The researcher conducted initial scoping searches for relevant titles within, Scopus, MEDLINE and Web of Science Core Collection. Databases were searched up to 1st April 2020 with no limit to the start date. Databases were searched using the following terms: Atopic Dermatitis, Atopic Eczema, eczema, AD, atopy, quality of life, QoL, HRQoL, well-being, health status, and their spelling variations. The terms "Atopic Dermatitis" and "quality of life" were searched as keywords, and also searched as a Medical Subject Heading to help target relevant literature.

3.2.2 Inclusion/exclusion strategy and data extraction

To be included in this review studies had to report data from adults. The legal age of adulthood differs according to country. Study search was limited to English-language articles on human populations. Case-reports and conference abstracts were excluded. All study types and designs were included if they reported on a QoL measure. When devising a search strategy, the PICOS framework was used (Richardson, Wilson, Nishikawa, & Hayward, 1995). The PICO tool focuses on the Population, Intervention, Comparison and Outcomes of a (usually quantitative) article.

Table 3.1 PICOS Criteria

	Inclusion	Exclusion
Participants	Adults with Atopic Dermatitis	Infants and children Adults with non-atopic dermatitis
Interventions	-	Comparison of surgical treatment, pain control, palliative medication, or psychological/homeopathic intervention as opposed to the direct impact of AD on QoL regardless of medical interventions.
Comparators	Studies with and without a comparison group will be included	
Outcomes	Primary outcome: Measurement of quality of life	Studies that did not measure the primary outcome
Study design & quality	Any study design Any country Papers written in English Language	No study design will be excluded Papers not written in English language

3.2.3 Population

This review included participants aged 18 and above or 16 and above if defined as an adult in a study. Studies that combined adult and children data into one analysis were excluded. Studies that collected data from both adults and children, but reported data separately for these sub-groups, were retained in the review.

3.2.4 Interventions

Studies that measured QoL as a result of medical or psychological interventions were excluded.

3.2.5 Comparators

Studies measuring QoL on its' own, in relation to disease severity, compared to healthy controls or compared to patients with other conditions were included in the review.

3.2.6 Outcomes

The primary outcome in this review was QoL in adult patients with AD.

3.2.7 Study design

The scoping reviews revealed a range of research designs therefore studies of mixed-method, quantitative and qualitative research designs were considered for inclusion in the review. There was no exclusion based on study quality in this review and quality appraisal was carried out.

3.2.8 Language

Due to a lack of resources to translate papers written in any language apart from English, if non-English papers were identified through study search, they were excluded from the review with language listed as the reason for this.

3.2.9 Study selection

The titles and abstracts of papers retrieved were screened by the researcher for potentially eligible studies based on inclusion and exclusion criteria. The researcher, in an attempt to avoid missing any potentially relevant articles, was inclusive at this initial stage of study searches. Any articles that the researcher was unsure about were discussed with the supervisory team to reach an agreement about the suitability of the study. Following this, full texts were retrieved and screened for inclusion/exclusion criteria by the researcher. Although the Cochrane Handbook for Systematic reviews recommends a second reviewer assessing these studies independently, this was not possible due to resource and time constraint. Instead, if there was any uncertainty regarding eligibility of papers for inclusion, the researcher reviewed these papers with the supervisory team through which an outcome was achieved.

3.2.10 Quality Appraisal

The quality of the included studies was assessed using the Mixed Methods Assessment Tool (MMAT) (Pluye et al., 2011). The MMAT (appendix 2) is a quality appraisal tool for quantitative, qualitative and mixed methods studies included in systematic reviews. For quantitative studies, it addresses methodological issues such as selection bias in recruitment, validity and appropriateness of measures used in a study, whether the most important factors are considered in analyses, and acceptable response rates. For each study, an overall quality score can be calculated; this can be the number of criteria met divided by four (scores varying from 0% no criterion met- to 100% -all four criteria met. All members of the supervisory team reviewed and agreed on the quality ratings for each paper included in the review.

3.2.11 Data synthesis

Where studies reported QoL scores using the same instruments, results were pooled using meta-analysis. In cases where pooling was not considered appropriate, narrative synthesis was carried out. This is an approach which makes the use of text and words to summarise and decipher results of multiple studies (Pope, Mays & Popay, 2006). According to Popay et al (2006), narrative synthesis is suitable for use in reviews which include a range of evidence sources.

3.3 Results

3.3.1 Literature search

Figure 3.1 outlines the search strategy following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards (Liberati et al., 2009). A total of 35 papers met inclusion criteria and were included in this systematic review. No mixed methods or qualitative papers included a measure of QoL, therefore all included papers in this review are quantitative and reviewed using narrative synthesis. Seven papers reported a correlation between the Dermatology Life Quality Index (DLQI) and a validated measure of AD severity (SCORAD). Correlations from these papers were

pooled using random-effects meta-analysis in Comprehensive Meta-Analysis Version 3 (2005, Biostat Inc.).

3.3.2 Study characteristics

Twenty-one studies explored the relationship between disease severity and QoL and twenty of these studies used DLQI as the QoL measure. A total of 16 studies compared QoL in adults with AD to that of healthy controls using both generic and disease-specific QoL measures. Five studies compared QoL in AD patients with other patients groups such as vitiligo and psoriasis. Twenty studies used DLQI to measure QoL, twelve studies used SF-36 either in addition to a disease-specific QoL measure or on its' own. Less frequently used QoL scales included the VQ Dermato and the Skindex-16.Twenty studies were conducted in Europe of which five included participants from the UK, five studies were conducted in the USA, and nine in Asia. Sample sizes for those with AD ranged from 32 to 1467 across the studies. All identified studies were quantitative and cross-sectional. Thirty studies recruited through dermatology clinics/hospitals, three studies recruited through eczema support organisations e.g. National Eczema Society and two studies recruited through universities. AD was defined using the Hanifin & Rajka(1980) AD diagnostic criteria in eighteen studies, the UK Working Party criteria was used in one study, AD criteria set by Adinoff and Clerk (1996) was used in one study, and fifteen studies did not specify which criteria dermatologists used to diagnose the condition in the patient. Table 3.2 reports study characteristics.

Table 3.2 Study Characteristics

Authors	Country	N	Participants	Measures used		Outcomes measured	Outcomes
				Disease severity	Quality of life		
Anderson et al (2019)	France, Germany, UK, USA	1232	1098 with moderate-to-severe AD and 134 with mild AD; 830 females.	PO-SCORAD, POEM	DLQI, EQ-5D	Relationship between disease severity and QoL; Differences between groups for disease severity.	AD severity and EQ-5D scores in patients with moderate-to severe AD showed a negative correlation (Spearman's r = – 0.38; P < 0.001). AD severity was positively correlated (Spearman's r = 0.61; P < 0.001) with DLQI scores. AD severity and the perception of the AD symptoms by the patient (POEM) showed a positive correlation (Spearman's r = 0.51; P < 0.00)

Authors	Country	N	Participants	Measures used		Outcomes measured	Outcomes
				Disease severity	Quality of life		
Arima et al (2018)	Japan	638	Mean age- 38.67 years, 52.37% female. 45.45% rated severity as moderate/severe, 54.54% rated severity as mild. Comparisons with 1268 non-AD controls	Self-rated severity	SF-36	QoL comparisons between patient groups and healthy controls	AD patients reported significantly reduced HRQoL relative to matched non-AD controls (p<0.001) for mental and physical domains of the SF-36.

Baron et al (2006)	UK	63	Mean age – 34 years, Mean duration of AD- 15.2 years, 26 men and 37 women	SCORAD	DLQI	Relationship between disease severity and QoL	The mean DLQI reduced over three visits from 9.5 to 8.8 at T2 to 7 at T3. The DLQI was significantly correlated with SCORAD at T1 (r= 0.389, p <0.01) and at T2 (r=0.321, p < 0.01) but not at T3. Mean SCORAD reduced by 52% from T1 to T2 ($F_{2,62}$ =37.9, <0.001) but there was no significant change in SCORAD from T2 to T3.
Beikert et al (2014)	Germany	384	384 AD patients (mean age 42, range- 18-92, 69.8% female). Patients with AD aged> 18.	Patient-assessed severity	DLQI	Relationship between disease severity and QoL; Comparisons between AD patients and patients with other conditions.	The mean DLQI total score in AD was 8.5, compared to 7.0 in Vitiligo and 6.7 in psoriasis and 4.3 in rosacea. Impairment of QoL measured by DLQI correlated positively with the affected body surface area (r=0.46, p<0.001). Characteristic AD symptoms such as skin dryness, pruritus, and sleep disturbances also correlated significantly with the DLQI total score (r_S=0.34 to 0.53, p<0.001).
Bruin-Weller et al (2019	Canada, France, Germany, Italy, Spain, UK	1467	811 females; 547 with mild AD, 520 had moderate AD, 400 had severe AD.	POEM, SCORAD, EASI	DLQI	Differences between groups for disease severity.	DLQI score among participants with severe AD (16.2 ± 6.9) showed a large effect on quality of life that was higher than those with moderate (10.2 ± 6.3) and mild (5.5 ± 4.9) (both P < 0.001).
Chen et al (2012)	Taiwan	1132	The participants were categorized in to 3 groups:	-	SF-36	QoL comparisons	QoL was significantly lower for patients with AD compared to controls in 5 out of 8 domains

			1) AD (n=90), 2) non-atopic hand eczema (n=205), 3) control group with no aforementioned skin conditions (n=837), average age- 30.5 years, 100% female.			between patient groups and healthy controls; Comparisons between AD patients and patients with other conditions.	including social functioning, bodily pain, vitality, mental health and general health (*ps* <0.05). No significant difference was found between the AD group and the non-atopic eczema group in all domains of QoL investigated.
Chrostowska-Plak et al (2013)	Poland	89	59 females and 30 males. Mean age- 31.6 years. Mean disease duration- 22.8 years.	SCORAD	DLQI	Relationship between disease severity and QoL.	There was a significant correlation between pruritus and HRQoL (r= 0.5, p < 0.001) DLQI also correlated with periods without itching indicating that patients with longer itching-free periods had better HRQoL (r= 0.23, p<0.05) There was a significant correlation between the severity of the disease (using SCORAD) and HRQOL (r=0.65, p < 0.001)
Coghi et al (2007)	Brazil	75	Patients were diagnosed and treated as isolated AD by the attending clinician; 65.33% were females, mean age -26.28 years, average years of duration of AD- 16.74 years.	EASI	DLQI, SF-36	Relationship between disease severity and QoL	QoL and disease control were found to be related but with low scores both in DLQI (r = 0.26) and in SF-36 (r = 0.2) but with greater correlation for SF-36 mental components. Both correlations were significant (p < 0.001).
Eckert et al (2017)	USA	349	Mean age- 46.1 years; 68.3% women; 66.8% White. Matched with 698 non-AD controls.	Self-rated severity	SF-36	QoL comparisons between patient groups and healthy controls; Comparisons between AD patients and patients with other conditions.	AD patients reported significantly reduced HRQoL relative to matched non-AD controls for both mental and physical domains of the SF-36 (P<0.001 & p=0.004 respectively). Compared with psoriasis, AD had a similar impact on HRQoL.

Finlay (1996)	UK	92	43 males and 49 females; average age 33.2 years (range 16-67).	Physician assessed severity	DLQI	Comparisons between AD patients and patients with other conditions.	The mean DLQI index was 18 with subsections relating to 'symptoms and feelings' and 'treatment effects' scoring highest. Disease comparison utility questions demonstrated that patients consider diabetes and hypertension would be better than having eczema whereas bronchitis would be worse than having eczema.
Fivenson et al (2002)	USA	107	298 participants; 107 adults; mean age of whole group- 17.22 years; 62% female.	Rajka & Langeland scoring system, patient-assessed severity	DLQI, SF-36	Relationship between disease severity and QoL; QoL comparisons between patient groups and healthy controls.	46% of adults had mild disease, 11% adults had severe disease. In terms of provider assessed severity, 51% adults had mild disease. The mean DLQI score was 6.6 for adults with a range of 0 to 27. The mean score for DLQI increased with increasing disease severity for all but two questions. For the SF-36, statistically significant differences were detected between the study group and the US population norms for vitality, social functioning, and mental health. Patient-assessed severity had a stronger association with DLQI ($r = 0.57$, $p = 0.0001$) than provider-assessed severity ($r = 0.27$, $p = 0.0036$).
Grob et al (2005)	France	1356	An investigator had to recruit clusters of three patients, one with chronic urticarial (CU), one with psoriasis (PSO) and one with AD, matched by sex and age. Subjective impression of severity was rated by the physicians as minimal/moderate/severe/very severe	Physician assessed severity	VQ-Dermato	Comparisons between AD patients and patients with other conditions.	After adjustment for confounders, HRQoL dimensions were differently affected in the three diseases. The 'physical discomfort' dimension was more degraded in AD and CU than in PSO ($p < 0.001$) and 'leisure activities more in PSO than in CU ($p < 0.001$). No aspect of HRQoL was spared in AD. The mean overall VQ-Dermato index was significantly lower in CU ($M= 36.93$) and in PSO ($M= 38.88$) than in AD ($M= 44.62$, $p < 0.001$).

Haeck et al (2012)	Netherlands	54	Average age of the patients was 37.3. At inclusion, the average objective SCORAD was 43 indicating severe AD, average DLQI was 14.6 indicating a large effect on QoL.	SCORAD,	DLQI	Relationship between disease severity and QoL	At t=0, there was a small non-significant correlation between the DLQI and objective SCORAD, 'rule of nine' or serum TARC level. At t=6 the objective SCORAD, serum TARC and the 'rule of nines' scores showed moderate and significant correlations with the DLQI ($r = 0.34$, $p = 0.02$; $r = 0.31$, $p = 0.03$; $r = 0.49$, $p < 0.001$). An individual's improvement in disease activity (SCORAD, SASSAD and 'rule of nines') with 10 points was associated with an improvement in DLQI.
Higaki et al (2004)	Japan	162	162 patients with AD ranged in age from 17-77 years: the mean age was 29 years; 55% were female. 17 had mild, 107 had moderate and 36 had severe AD.	Rajka & Langeland scoring system (mild, moderate and severe)	Skindex-16	Relationship between disease severity and QoL	Each of the three scale scores (symptoms, emotions and functioning) of the patients with AD were significantly higher than those of patients with isolated lesions. Patients with severe AD showed significantly higher scores in the three scales, as well as the Global Scale than those with moderate dermatitis. There was a significant positive correlation between the severity and each of the three scale scores ($r's = 0.32$ to 0.45, $p < 0.001$).
Holm et al (2004)	Denmark	112	Mean duration of AD of 28.6 years. Females (n=88) and males (n=24); mean age of females- 34.2, males- 39.2.	Patient assessed severity.	DLQI	Relationship between disease severity and QoL, Differences in QoL between men and women with AD	For women, there was a significant positive correlation between disease severity ad DLQI score (KW test, 15.9; $p < 0.001$) and also between DLQI score and visible regions affected by disease (KW test, 14.2; $p = 0.001$); these correlations were not observed in men. No significant differences between men and women were noted for age, disease duration, overall disease severity or QoL as assessed using the DLQI.
Holm et al (2006)	Denmark	101	101 atopic eczema patients, 66 adults with AD, and 23	SCORAD, patient-	DLQI, SF-36	Relationship between	Patients with AE had significantly lower QoL ($p<0.05$) than healthy controls (median DLQI

			adults without AD (control group).	assessed severity		disease severity and QoL, QoL comparisons between patient groups and healthy controls.	score 5 in AD patients vs. 0 in controls) and the general population. DLQI, pruritus and patents and investigator overall assessment of eczema severity were significantly ($p < 0.0001$) and positively correlated with SCORAD, while the generic questionnaire showed only poor correlation.
Holm et al (2016)	Denmark	191	Mean age- 31.32 years, 59.2% females	SCORAD	DLQI	Relationship between disease severity and QoL	Significant relationship between disease severity and HRQoL ($r=0.42$, $P<0.001$), with increase disease severity significantly associated with worsening HRQoL. There was also a significant relationship between DLQI and self-rated health ($r=-0.37$, $p<0.001$).
Kiebert et al (2002)	USA	239	Mean age- 36 years, 79% female; 18.2 years mean duration of disease, 46% mild severity, 41% moderate severity, 11% severe severity.	Patient assessed severity	DLQI, SF-36	Relationship between disease severity and QoL; QoL comparisons between patient groups and healthy controls.	SF-36 scores showed a significant decrease with increasing disease severity. DLQI scores correlated well with patients ratings of disease severity. The SF-36 scores correlated significantly with DLQI scores. The SF-36 scores of patients with AD were significantly lower (indicative of more impairment) than those of the general population. The mental component score of the SF-36 was significantly correlated with patient severity rating ($r=-0.41$, $p<0.001$), the physical component was not.
Kim et al (2012)	Korea	415	Subjects were divided in to three groups; infants, children and adults ((75 males and 72 females). Mean age of adults= 25.8 years.	SCORAD	DLQI	Relationship between disease severity and QoL.	The total mean DLQI score was 10.7. No significant differences in gender and age were observed. Adults with atopic disease including AD with concomitant asthma, allergic rhinitis or allergic conjunctivitis had higher total scores than those with AD alone. Both the Rajka & Langeland eczema severity score ($r=0.261$, $p<0.05$) and SCORAD index correlated

							significantly with all the total QoL scores (r=0.432, p < 0.001).
Kong et al (2016)	Korea	50	22 men and 28 women, mean age 26.4 years.	SCORAD	DLQI	Relationship between disease severity and QoL	Significant relationship between disease severity and HRQoL (r=0.237, P<0.001), with increase disease severity significantly associated with worsening HRQoL. There was also a significant association between sleep disturbance and QoL (r=0.388, p=0.04), with increase sleep disruption associated with worsening QoL.
Kwak et al (2017)	Korea	157	Mean age- 35.2 years; 51.8% Males; 11,756 non-AD controls (mean age- 45.3 years; 49.3% male)	-	EQVAS	QoL comparisons between patient groups and healthy controls	Adults with AD had lower HRQoL (p=0.013) and more stress (p=0.002) than those with AD. Even when controlling for demographic characteristics, HRQoL of adults with AD was lower than adults without AD.
Lee et al (2018)	Korea	677	Mean age 36.1 years; 47.8% females; 36,901 controls- mean age 45.4 years, 50.8% females	-	EQ-5D and EQ-VAS	QoL comparisons between patient groups and healthy controls	EQ-VAS scores were significantly higher in patients with AD than in those without AD (p=0.004). A higher rate of pain/discomfort, and anxiety/depression was found on the EQ-5D in AD patients compared to controls (p=0.003 and p<0.001, respectively).
Linnet & Jemec (1999)	Denmark	54	23 women (mean age=27.5), 9 men (mean age=30.3); average duration of condition=26.1 years. Aged 18-60 years.	SCORAD	DLQI	Relationship between disease severity and QoL; QoL comparisons between patients groups and healthy controls.	AD patients- significantly lower dermatological life quality (Z= 5.1, p<0.001) and higher state (Z= 2.14, p<0.032) and trait (Z= 3.49, p<0.001) anxiety compared to the control group. Significant positive correlation between SCORAD and DLQI (r= 0.54, p<0.002).
Lundberg et al (2000)	Sweden	366	The average duration of AD was 25.83 years and the mean age of AD patients	Patient assessed severity	DLQI, SF-36	Relationship between disease severity	DLQI scores showed poorer HRQoL for patients with AD compared to psoriatic patients but this was not significant when controlling for

			was 34.79 years old; 92% were male. The average duration of psoriasis was 18.39 years and the mean age of psoriasis patients was 49.87 years old; 51% were male.			and QoL; QoL comparisons between patients groups and healthy controls; Comparisons between AD patients and patients with other conditions.	confounding factors. No significant difference on the SF-36 between patients with AD and patients with psoriasis. There was a decreasing DLQI score for patients of higher ages; improved HRQoL. Spearman's correlation coefficients showed that all SF-36 dimensions were significantly correlated with all measures of disease activity (r= 0.182 to 0.526), the DLQI correlations with VAS were also significant (r=0.005 to 0.595).
Maksimovic et al (2012)	Serbia	130	Adults- 56.1% female, mean age 34.18 years, mean age of onset of disease -13.95 years, mean duration of disease- 20.23 years.	EASI	DLQI, SF-36	Relationship between disease severity and QoL, QoL comparisons between patient groups and healthy controls.	The DLQI scores corresponded well with disease severity; increased disease severity was associated with greater impairment in HRQoL (r=0.14 to 0.47 for all domains of the DLQI). In adults, significant differences were only found between DLQI scores for mild and severe AD. The highest correlations were seen between symptoms and feelings and daily activities ($r = 0.75$, $p < 0.01$), symptoms and feelings and work/school ($r = 0.53$, $p < 0.01$) and leisure and work/school ($r = 0.59$, $p < 0.01$). Patients with AD had inferior social functioning and mental health scores compared with the general population.
Mikolajczyk et al (2017)	Poland	59	36 women and 23 men with AD; aged 18 to 46 years; mean age- 26.9 years; mean disease duration- 15.1 years	-	DLQI	Gender differences in QoL; impact of illness duration on QoL	No significant differences between women and men for DLQI scores ($p>0.05$); significant correlations between QoL and health evaluation and body areas satisfaction (r=-0.48), appearance orientation (r=0.31).
Misery et al (2007)	France	266	34.2% patients were males and 65.8% were females. The mean age was 32.7	SCORAD, patient-	DLQI, SF-36	QoL comparisons between patient	The mean DLQI score was 8.8 and the physical and mental composite 12 scores were 50.7 and 39.5 respectively. Analyses according

			years and mean duration was 19.3 years. 1,6% had mild AD, 42.9% had moderate AD, and 55.6% had severe AD.	assessed severity		groups and healthy controls.	to SCORAD showed DLQI scores 6.8 (SD=4.4) and 10.2 (SD=5.6) for moderate and severe AD groups (p<0.0001).
Misery et al (2018)	France	1024	58.3% female; 27.6% mild AD, 40.4% moderate AD, 31.9% severe AD	PO-SCORAD	DLQI; SF-12; EQ-5D	Differences in QoL by visible area involvement	Patients with visible area involvement were found to have lower QoL than those without (p<0.0001), EQ-5D (p<0.05), and the mental score of the SF-12 (p<0.0001). No differences in physical score of SF-12.
Mozaffari et al (2007)	Iran	184	75% AD adults were female, 57.2% control group adults were female. Mean age of AD adults was 38.25 and mean duration of disease was 20.6 years, 9.5% had mild AD, 12% had moderate AD, and 18% had severe AD.	Patient assessed severity	DLQI	Relationship between disease severity and QoL, QoL comparisons between patient groups and healthy controls.	Significant differences between DLQI mean scores in AD group (M=20.5 SD=4.7) and control group (M=1.15, SD=0.85) mean score (p < 0.001). Scores of each question were significantly higher in the AD group than in the control group (p<0.001). Correlation between DLQI and AD severity was significantly positive (r=0.88, p < 0.001).
Noh et al (2013)	Korea	180	27 males (45%), 33 females (55%) with AD, mean age 32.4 years. Mean age of Vitiligo patients was 35.1 (31 males and 29 females), mean age of normal controls was 31.9 (25 males and 35 females).	EASI	DLQI	QoL comparisons between patient groups and healthy controls; Comparisons between AD patients and patients with other conditions.	AD patients- significantly higher scores for all 5 questionnaire items compared with normal controls (p<0.001). In the comparison between the AD and Vitiligo groups, AD patients reported lower QoL (β= 0.752, t=11.522, p < 0.001)
Sanchez-Perez et al (2012)	Spain	323	Adults mean age was 32.3 years and 58.7% were women; over half of adults (55.8%) were aged between	EASI, patient assessed severity	DLQI	Relationship between disease severity and QoL	Significant differences in QoL observed according to investigator assessed severity (mild disease – M=5.5, SD=5.3; Moderate disease- M=7.5, SD=4.8; severe disease-

			18 and 30 years. Concomitant disease was observed in 40% of adults.				M=12, SD=5; p < 0.05). Pruritus caused everyday problems related to sleep and sexual function. The presence and intensity of pruritus was very closely related to HRQoL, with a high correlation coefficient between overall itch severity scale (ISS) score and overall DLQI score (0.72).
Silverberg et al (2018)	USA	602	53.6% female and 71.9% White, with mean age of 52 years. AD severity was measured using self-reported global severity- 53.1% mild, 38.8% moderate, 8.1% severe AD.	POEM, PO-SCORAD	DLQI;SF-12	Relationship between disease severity and QoL; Comparisons between AD patients and patients with other conditions.	SF-12 mental health sub-scores for moderate AD were lower than all other disorders (e.g. diabetes, asthma, anxiety/depression, heart disease) and for severe AD, dramatically lower than all other disorders. Little difference between physical health scores across disorders. Moderate and severe AD (using PO-SCORAD, PEOM and global severity) were significantly associated with DLQI (ps<0.0001).
Torrelo et al (2013)	Spain	282	48.2% were male and mean age of the adults was 33.06 years. 79.4% had moderate AD and 19.9% had severe AD. Mean duration of AD for adults was 19 years.	Patient assessed severity	DLQI	Differences between groups for disease severity.	Statistically significant impact on the daily lives of patients receiving maintenance therapy. However, patients with moderate AD had higher levels of emotional, physical and social well-being compared to those with severe AD (p < 0.05).
Treudler et al (2019)	Germany	372	57% female; median age-52 years; 9109 participants were healthy controls; 51.9% female; median age-58 years	-	SF-36	QoL comparisons between patient groups and healthy controls	Physical Component Score (PCS) and Mental Component Scores (MCS) were significantly lower in subjects with AD compared with controls (mean 46.9 vs. 48.0 and 50.6 vs. 52.5, P < 0.001, respectively). Linear regression showed regression coefficients of -1.7 (PCS; P < 0.001) and -1.5 (MCS; P < 0.001); reduced QoL with regard to physical and mental parameters in subjects with AD compared to healthy controls.

Wittkowski et al (2004)	UK	125	23 males, 102 females; aged 18 to 66 (mean age of 37.2 years). The mean duration of AD was 30.7 years.	Patient assessed severity	DLQI	Relationship between disease severity and QoL	Disease severity was significantly correlated with QoL ($r = 0.49$, $p < 0.01$), perceptions of stigma ($r = -0.28$, $p < 0.01$) and depression ($r = 0.18$, $p < 0.05$). 46.7% of the variance in DLQI scores ($p<0.001$) was explained by depression and disease severity. Disease severity accounted for 23% of the variance in DLQI scores ($p < 0.001$)

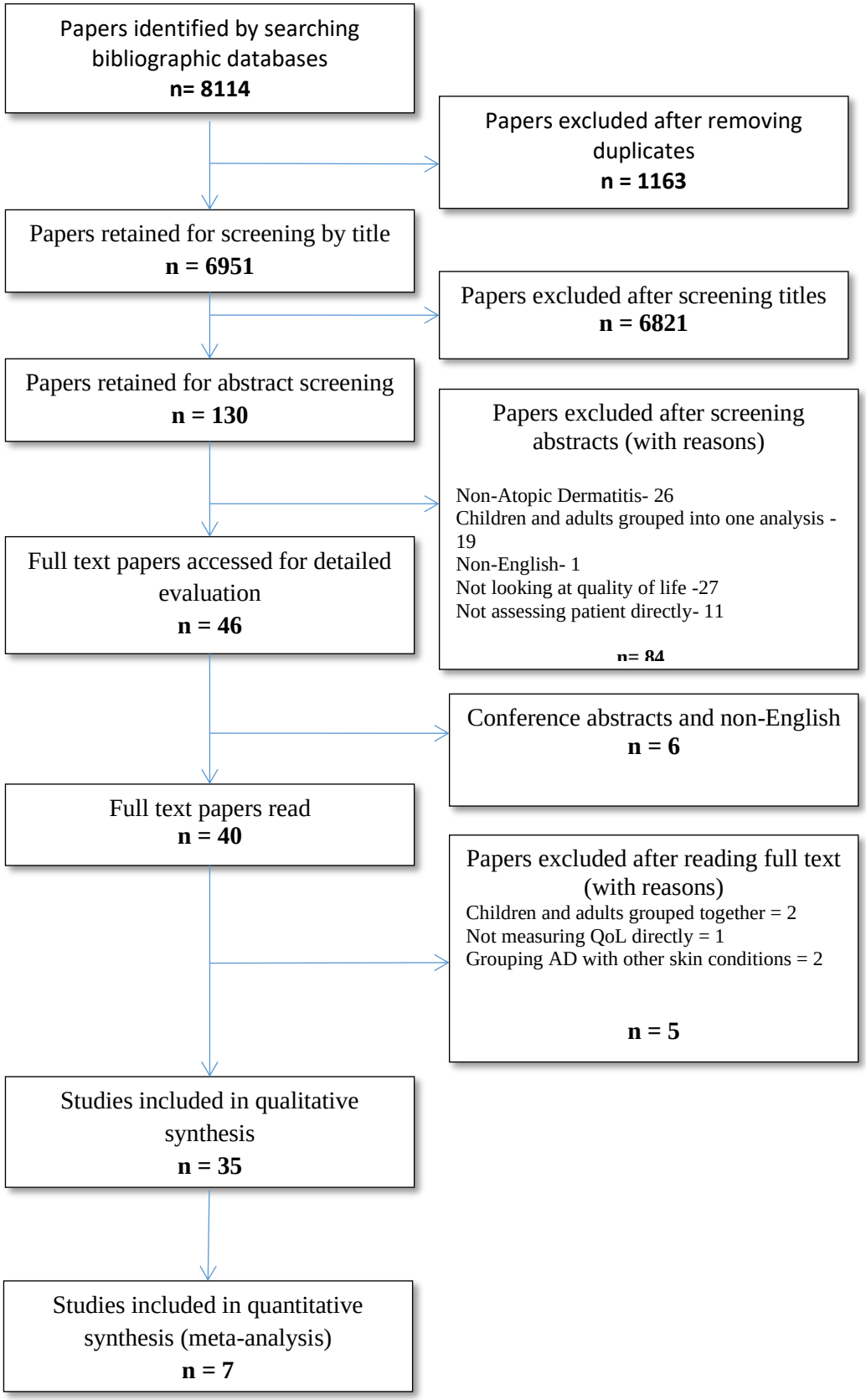

Figure 3.1: Diagram of article flow during literature search and article screening according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards.

3.3.3 Quality of included studies

Methodology of included studies during the data extraction process was appraised using the MMAT version 2011 tool (Pluye et al., 2011). Quality appraisal using the MMAT demonstrated that that 27 of 35 (78%) met 75% of the quality criteria used, symbolic of high-quality studies (table 3.3). The remaining eight studies met 50% or less of the quality criteria. The reasons for the drop in ratings included lack of information about the missing data or the dropout rate of the participants (n=5), invalid tools used to measure QoL in AD participants (n=1) or low response rates (n=2). The majority of the included studies in this review were of high quality, meeting between 75-100% of the criteria detailed in the MMAT.

3.3.4 Quality of Life

The Dermatology Life Quality Index (DLQI) was used to measure QoL in 27 out of 35 studies included in this review. The DLQI was established by Finlay and Khan in 1994 to measure QoL in adults for use in clinical practice. It is a 10-item questionnaire which explores the impact skin disease has on day-to-day activities, social and working life of patients. It is scored from 0 to 3 for each item with a maximum score of 30; a higher score reflects worsening QoL. The DLQI is not a disease-specific instrument but is rather a speciality-specific one and is suitable for use in all skin diseases.

Mean overall DLQI scores ranged across studies from 4.9 (small effect on patient's QoL) to 20.5 (very large effect on patient's QoL). In studies which looked at differences across the dimensions of QoL, the areas that were most affected as measured using the DLQI were symptoms and feelings surrounding AD; patients felt embarrassed or self-conscious due to their AD and symptoms such as itchy, sore, painful and stinging skin had a detrimental impact on their QoL (Finlay, 1996; Holm, Agner, Clausan, & Thomsen, 2016; Holm, Wulf, Stegmann, & Jamec, 2006; Kim et al 2012;; Lundberg, Johannesson, Silverdahl, Hermansson, & Lindberg, 2000;Sánchez-Pérez, Daudén-Tello, Mora, & Surinyac, 2013).

Personal relationships were the least affected dimension of QoL (Finlay, 1996; Holm et al., 2006; Kim et al., 2012; Lundberg et al., 2000). Mozaffari et al (2007) found that patients perceived dressing, undressing and bath-time as being most problematic while the dimension 'family activities' was least affected. Holm et al (2016) also found that dressing was particularly problematic.

Using the EQ-5D as a measure of QoL, daily activity and pain/discomfort parameters were reported to be most affected in patients (Lee et al., 2018). Other less frequently used QoL scales included the VQ Dermato and the Skindex-16. The VQ Dermato is a 28-item questionnaire which was developed from the point of view of patients. It allows computation of seven dimensions; self-perception, daily living activities, mood state, social functioning, leisure activities, treatment-induced restrictions, and physical discomfort. All scales are linearly transformed to a 0-100 scales, with 100 indicating the worst QoL and 0 the most favourable. Skindex is an instrument developed by Chren (1996) assessing quality of life in patients with skin conditions. It is scored on a 7-point scale, with higher scores indicative of a greater effect of skin disease on QoL.

Table 3.3 Quality appraisal using MMAT

Reference	Selection Bias	Appropriate Measurements	Compared Groups	Outcome Data	Overall
Andersen, Nyeland, & Nyberg (2019)	25	25	25	0	**75**
Arima et al (2018)	0	25	25	25	**75**
Baron, Morris, Dye, Fielding, & Goulden (2006)	25	25	0	25	**75**
Beikert et al(2014)	25	0	25	0	**50**
Chen, Wu, Li, Ko, Yu, & Chen et al., (2012)	0	25	0	25	**50**
Chrostowska-Plak, Reich, & Szepietowski (2012)	25	25	25	25	**100**
Coghi, Bortoletto, Sampaio, Junior, & Aoki (2007)	25	25	25	25	**100**
de Bruin-Weller et al (2019)	25	25	25	25	**100**
Eckert, Gupta, Amand, Gadkari., & Mahajan (2016)	0	25	25	25	**75**
Finlay (1996)	25	25	0	25	**75**
Fivenson et al (2002)	25	0	0	0	**25**
Grob, Revuz, Ortonne, Auqueir, & Lorette (2005)	25	25	25	25	**100**
Haeck et al (2011)	0	25	0	25	**50**
Higaki et al (2004)	25	25	0	25	**75**
Holm, Agner, Clausen, & Thomsen, (2016)	25	25	25	0	**75**
Holm, Esmann, & Jemec (2004	25	25	25	0	**75**
Holm, Wolf, Stegmann, & Jemec (2005)	25	25	0	25	**75**
Kiebert et al (2002)	25	0	0	0	**25**
Kim, Li, Seo, Jo, Yim, Kim, et al (2012)	25	25	25	25	**100**
Kong, Han, Lee, & Son (2016)	25	25	0	25	**75**
Kwak & Kim (2017)	0	25	25	25	**75**
Lee et al (2018)	0	0	25	0	**50**
Linnet & Jemec (1999)	0	25	25	25	**75**
Lundberg, Johannesson, Silverdahl, Hermansson & Lindberg (2000)	25	0	25	25	**75**
Maksimovic, Jankovic, Marinkovic, Sekulovic, Zivkivic, & Spiric (2012	25	25	0	25	**75**
Mikołajczyk, Rzepa, Król, & Żaba, (2017).	25	25	25	0	**75**
Misery et al (2007)	25	25	25	25	**100**
Misery et al (2017)	25	25	25	25	**100**
Mozaffari et al (2007)	25	25	0	25	**75**
Noh, Kim, Park, Hann, & Oh (2013)	25	25	0	25	**75**
Sanchez-Perez, Dauden-Tello, Mora, & Surinyac (2012)	25	0	25	25	**75**
Silverberg et al (2018)	0	25	25	25	**75**
Torrelo et al (2013)	25	0	0	25	**50**
Treudler et al (2019)	25	25	25	0	**75**
Wittkowski, Richards, Griffiths, & Main (2003)	0	0	25	25	**50**

Note: 25-criterion met, 0- criterion not met/unable to determine.

3.3.5 Quality of Life and Disease Severity

Twenty-one studies explored the relationship between disease severity and QoL of which twenty studies looked used the DLQI. All of these studies but one reported significant correlation between disease severity and DLQI; the more severe the disease, the lower the QoL. In seven of these studies, QoL using the DLQI was compared with

disease severity measured using the SCORAD (Baron, Morris, Dye, Fielding, & Goulden, 2006; Chrostowska-Plak, Reich, & Szepietowski, 2013; Haeck et al., 2011; Holm et al., 2016; Kim et al., 2012; Kong, Han, Lee, & Son, 2016; Linnet & Jemec, 1999). These studies were pooled together using random effects meta-analysis (See Figure 3.2). The sample-weighted average correlation between HRQoL and disease severity was $r_+ = .44$ (CI 0.27; 0.59), indicating a medium-sized relationship (Cohen, 1992), with greater disease severity relating to poorer QoL. There was significant heterogeneity in the results ($\chi^2 = 13.78$, $p < .05$). This could partly be explained by the small correlation reported by Haeck et al. (2011).

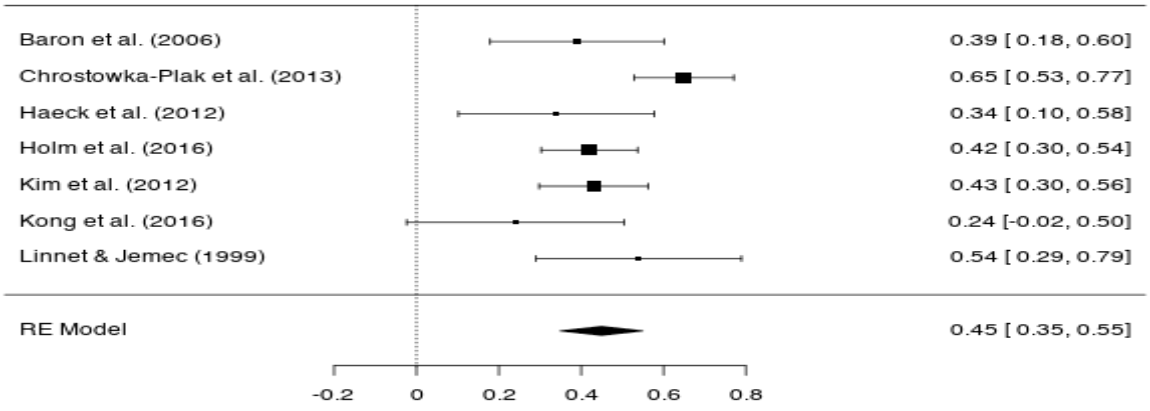

Figure 3.2. Meta-analysis of studies measuring QoL using DLQI in relation to SCORAD

Two studies (Coghi, Bortoletto, Sampaio, Junior, & Aoki, 2007; Maksimovic et al., 2012) used the EASI disease severity measure in relation to DLQI. Both studies found statistically significant relationships between QoL and disease severity (ps < .05); QoL was perceived as being poorer with increasing disease severity, with personal relationships being related to a lesser extent to disease severity than other domains.

Ten studies (Anderson et al., 2020; Beikert et al., 2014; Holm et al., 2006; Kiebert et al., 2002; Lee et al., 2018; Lundberg et al., 2000; Mozaffari et al., 2007; Sanchez-Perez, Dauden-Tello, Mora, & Surinyac, 2013; Silverberg et al., 2018; Wittkowski, Richards, Griffiths, & Main, 2004) explored relationships between patient-assessed disease severity and DLQI scores and reported statistically significant medium to large sized correlations whereby an increase in disease severity was associated with a decrease in QoL. Two studies (Holm, Esman & Jamec, 2004; Mikolajczyk, Rzepa, Król, & Żaba, 2017) also explored gender differences and found a significant positive correlation between patient-assessed disease severity and DLQI score ($p < .001$) and between visible regions and DLQI score ($p = .001$) for women, however neither of these correlations were observed in men.

Two studies (Fivenson et al., 2002; Higaki et al., 2004) assessed severity using the Rajka and Langeland scoring system which measures clinical course, severity, and extent of AD. Both studies found statistically significant correlations between disease severity and QoL. Highest correlations found were between disease severity and symptoms and feelings; higher disease severity was related to worsening symptoms and feelings as a result of AD.

Twelve studies used the SF-36 to measure QoL either alongside the DLQI or on its‘ own. This scale consists of 36 questions and is a multi-purpose tool that is generic as opposed to one that targets AD only (Ware & Sherbourne, 1992). This scale comprises of sub-scales which provide a physical and mental health summary measure as well as an eight scale profile of well-being scores and functional health. The lower the score in the measure the more disability i.e., a score of 100 is corresponds to no disability and a score of 0 is corresponds to the highest disability. The eight subscales of the SF-36 are: social role functioning (SF), and mental health (MH), physical functioning (PF), bodily pain (BP), vitality (VT), general health perceptions (GH), physical role functioning (RF), emotional role functioning (EF),

Ten of the twelve studies using this explored the relationship between SF-36 scores and disease severity (Arima et al., 2018; Coghi, Bortoletto, Sampaio, Junior, & Aoki, 2007; Eckert et al., 2017; Fivenson et al., 2002; Holm et al., 2006; Kiebert et al., 2002; Lundberg et al., 2000; Maksimoc et al., 2012). Nine studies found significant correlations between disease severity and the SF-36, with increased severity associated with poorer QoL. However one study (Maksimoc et al., 2012) found no significant correlation between any SF-36 subscales and clinically measured disease severity (EASI). The correlations between the SF-36 and disease severity across the nine studies ranged from small to large-sized. The mean physical dimension scores appeared to be less impaired in AD patients compared to the mean mental component scores of the scale (Chen et al., 2013; Coghi et al., 2007; Fivenson et al., 2002; Holm et al., 2006; Kiebert et al., 2002; Misery et al., 2007).

3.3.6 Quality of life in patients with AD compared to healthy controls or other patient groups

A total of 16 studies compared QoL in adults with AD to that of healthy controls. Eleven studies used generic QoL scales such as the SF-36 to enable comparison across groups (Arima et al., 2018; Chen et al., 2013; Eckert et al.,2016; Fivenson et al., 2002; Kiebert et al., 2002; Kwac & Kim, 2017; Lee et al., 2018; Lundberg et al., 2000; Maksimoc et al., 2012; Silverberg et al., 2018; Treudler et al., 2020), three studies used dermatology specific QoL scales to make comparisons (Linnet & Jemec, 1999; Mozaffari et al., 2007; Noh, Kim, Park, Hann & Oh, 2013) and three studies (Holm et al., 2004; Misery et al., 2017; Silverberg et al., 2018) used both generic and dermatology specific scales. Overall QoL was significantly poorer in those with AD compared to healthy controls and domains such as mental health and social functioning were affected to a greater extent in AD patients (Holm et al., 2006; Holm et al., 2016; Mozaffari et al., 2007; Silverberg et al., 2018; Treudler et al., 2020) . In a recent study by Misery et. al (2017) scores on the

mental dimension of the SF-12 were lower in AD patients with visible area involvement compared to those without ($p<0.001$).

Two studies compared QoL between vitiligo and AD patients (Beikert et al., 2014; Noh et al., 2013) and found significantly lower QoL in the AD groups compared to the vitiligo groups (*ps*<0.001). Four studies also compared QoL between psoriasis and AD patients (Beikert et al., 2014; Eckert et al., 2016; Grob, Revuz, Ortonne, Auqueir & Lorette, 2005; Lundberg et al., 2000). Two of these studies found that AD patients had significantly lower QoL than patients with psoriasis (Beikert et al., 2014; Grob et al., 2005) whereas Lunderberg et al. (2000) found significant differences in the physical and mental functioning domains; with AD patients scored better than patients with psoriasis. Eckert et al. (2016) found no significant differences in QoL ratings in patients with psoriasis or AD. Grob et al. (2005) also compared AD with chronic urticaria and found that AD patients were more affected by skin discomfort than chronic urticaria patients. They also had lower scores in relation to 'treatment induced restrictions' compared to those with chronic urticaria.

3.3.7 Predictors of Quality of Life

Five studies conducted multiple regression analyses in order explore predictors of QoL (Beikert et al., 2014; Holm et al., 2004; Maksomovic et al., 2012; Noh et al., 2013; Wittkowski et al., 2003). Beikert et al (2014) found that skin dryness, ($p<0.007$), sleep disturbances ($p<0.016$), pruritus ($p<0.001$), facial involvement ($p<0.001$), genital involvement ($p<0.01$), and the affected body surface area ($p<0.001$) were significant predictors of QoL. Noh et al (2013) carried out multivariate regression analyses to determine predictors of QoL, and found that age significantly predicted DLQI scores. Wittkowski et al (2003) found that 46.7% of the variance in DLQI scores was explained by disease severity, and psychological factors such as depressive symptoms ($p<0.001$), however, demographic factors such as age and duration did not significantly contribute to variance in DLQI scores. Holm et al (2004) performed linear regression analyses with

mental and physical components as dependent variables and demographic factors such as age and gender as independent variables. An effect of gender was seen on mental components, where women had lower HRQoL than men (p=0.019). Age was found only to influence the physical components of SF-36; reduced QoL was seen with increasing age. Maksimovic et al (2012) found that age was a significant predictor of the physical functioning and role physical domain of the SF-36, whereas family history of disease was a significant predictor of SF-36 bodily pain domain and DLQI personal relationships domain.

3.4 Discussion

This systematic review examined the impact of AD on QoL in adults. The DLQI and the SF-36 were the most frequently used scales to measure QoL in patients with AD, and studies in this review looked at QoL in relation to disease severity, other chronic skin conditions, or healthy controls. The qualitative synthesis of results and meta-analysis show that there is a consistent relationship between increasing AD severity and poorer QoL in adults, and adult patients with AD have poorer QoL than healthy groups. Findings are more equivocal for comparisons with other chronic skin conditions.

Twenty out of the 21 studies that measured QoL in relation to disease severity found increased disease severity was significantly related to poorer QoL. This finding is consistent with reviews looking at QoL in children with AD (Clarke & Eiser, 2004; Lewis-Jones, 2006). Almost all adult patients had mild to moderate AD in the studies included in this review. Interestingly, in paediatric studies where more patients had moderate to severe AD, QoL correlated less well with disease severity than the adult patients with mild to moderate AD in this review (Hon et al., 2008; O'connell, 2004). The consistent finding that disease severity was related to QoL underscores not only the importance of offering both dermatological and psychological treatment to patients, but also the need to incorporate QoL screening tools in dermatology. Nonetheless, AD is a complex condition and QoL cannot solely be explained by severity of the disease as most studies

reported low to medium correlations between the two variables. One factor that may influence QoL and may explain differences between studies is time of recruitment whereby patients could be experiencing a flare-up during recruitment, thus affecting QoL scores; this is especially the case if participants were recruited during dermatology visits.

All studies that compared QoL in AD patients to healthy controls found significantly lower QoL in AD patients. However, four studies used the DLQI measure to explore this difference; the DLQI is a dermatology specific questionnaire with questions that are not suitable for use in a sample of the general population. In such cases, generic QoL measures such as the SF-36 should be employed. When using the SF-36, better physical QoL was reported by studies in this review compared to mental QoL. This is in line with a systematic review carried out looking at QoL in psoriasis patients (De Korte, Mombers, Bos & Sprangers, 2004). The SF-36 is probably not sensitive enough to measure the physical limitations of AD due to its generic nature; questions relating to walking abilities for example are unlikely to be relevant to this group.

Studies comparing QoL to other chronic skin conditions had mixed results, but for those comparing vitiligo and AD patients, significantly lower QoL was seen for AD. This may be because vitiligo is not accompanied by symptoms such as itching, inflammation, and sleeplessness. Symptoms such as pruritus have more of an impact on QoL than visual aspects; indeed, this review found that the area of QoL most affected was symptoms surrounding AD. Studies reporting better physical and mental functioning scores in patients with AD compared to those with psoriasis and poorer scores in patients with AD regarding skin discomfort compared to urticaria suggests that pruritus is the dominant factor that interferes with everyday life. Further, the contrast between lower scores related to 'treatment induced restrictions' in patients with AD and better scores in patients with chronic urticaria suggest that topical treatments can be highly restrictive to patients. Indeed, alternative/complementary therapies for AD, such as Chinese herbal therapy

have become increasingly popular (Hughes, Ward, Tobin, Keegan, & Kirby, 2007; Tan, Zhang, Chen, Xue,, & Lenon, 2013).

Many of the participants in the included studies were female. Partly this reflects health care utilization, whereby women use more health services and an estimated 67% of women worldwide make all medical choices in society (Legato, 1999); in this case, most of the participants were out-patients in dermatology clinics. Only one study looking primarily at gender differences in QoL and AD and found no significant correlation between disease severity and QoL in males but a significant positive correlation was present in females. Thus, the extent to which the AD severity is correlated with QoL in in relation to females rather than males deserves further research attention. Lesions located in visible areas have been found to affect women more than men (Holm et al., 2004) possibly because women may have a higher ideal of culturally determined physical appearance than men so more attention is given to the skin. Gender differences have been found in other allergic conditions with females presenting more complex allergy-related conditions compared to males (Mandhane, Greene, Cowan, Taylor, & Sears, 2005) and so further research in relation to AD is needed.

3.4.1 Limitations of the studies in this review

The heterogeneity in tools used to measure disease severity made it impossible to pool results across all included studies. The SCORAD and EASI are generally preferred by researchers over patient-assessed severity or visual analogue scales as they are validated measures of disease severity. However, they do not cover all issues affected in AD patients, for example, SCORAD only measures disease severity over the preceding three days, therefore long-term severity effects on QoL cannot be inferred. Nevertheless, studies that included both patient-assessed severity and objective measures found relatively strong correlations between the two, indicating that patients can self-assess their disease severity accurately.

All studies included in this review used cross-sectional methods to assess QoL in relation to disease severity. Results using this methodology should be interpreted with caution

as it's impossible to determine cause and effect. Future studies should utilise prospective designs and collect more longitudinal data to strengthen predictive power of psychological and clinical variables of QoL. AD is generally better during the summer and worse in winter (Baicker, Chandra, & Skinner, 2005). Only one study specified the season.

Although the quality appraisal for the studies showed that the majority had good to excellent ratings, many suffered from methodological weaknesses, such as the use of small sample sizes which can be determined based on an expected prevalence of atopic dermatitis in adults of 10% (Cork, Danby, & Ogg, 2019), a sample size of 250 would provide an adequate estimate with a maximum expected sampling error of ±4.4 percentage points at the 95% confidence level. Other issues included the use of non-validated measures, absence of statistical testing and incomplete presentation of QoL data such as descriptive statistics. In addition, some studies used dermatology specific questionnaires to determine QoL in healthy controls. This review only included intervention studies if they had a baseline measurement of QoL to ensure homogeneity of studies.

3.4.2 Conclusions and directions for future research

This study is the first systematic review and meta-analysis conducted on adults and demonstrates that AD influences all aspects of the lives of adult sufferers. Results support findings from previous research on similar skin conditions (De Korte, et al., 2004; Parsad, Dogra & Kanwar, 2003) and in children (Lifschitz, 2005; Lewis-Jones, 2006; Clarke, & Eiser, 2004). The present review points to several areas for future research. In the present review, overall scores were difficult to interpret because of the variability of scores and the absence of formal reference values or norm scores, or the absence of formal comparisons with population norms. More research with validated psychometric scales is needed to generate a consistent body of knowledge of overall QoL of patients with AD. Furthermore, application of both generic and disease- or dermatology-specific

quality-of-life questionnaire which cover the full range of quality-of-life issues are needed.

Second, data on the relationship between specific AD characteristics and QoL suggest that itch, sleep disturbances, and exacerbations in facial and genital body areas (Beikert et al., 2014) could be relevant predictors of quality of life, as reported by a few studies in this review, (Wittkowski et al., 2004; Beikert et al., 2014; Noh et al., 2013). A deeper insight into these relationships is important because of consequences for disease-severity measurement in quality-of-life research; indeed, a more qualitative approach would help uncover some of these issues.

Researchers in dermatology are encouraged to utilise validated and clinically relevant QoL measures for patients that provide accurate measurement of quality of life and allow for subsequent comparison of results across studies. Factors such as sleep disturbances and pruritus should be included when determining QoL and future studies should also further explore gender differences in QoL in adults with AD; only a few studies in this review considered these factors. Longitudinal study designs are also needed to explore what factors related to AD cause differences in QoL ratings.

Chapter four: A qualitative enquiry into the experiences of living with atopic dermatitis in adults

4.1 Introduction

This chapter presents the findings of a qualitative study which explored participants experiences of living with AD. The findings of this chapter have now been accepted for publication in the European Medical Journal.

As outlined in chapter one**,** AD sufferers report poorer HRQoL and greater psychological distress compared to a healthy population and those with other medical conditions (Kiebert et al., 2002; Lapidus & Kerr, 2001; Linnet & Jemec, 1999; Lundberg et al., 2000). In fact, as many as one-third of adult patients with severe AD being unable to keep their jobs due to flare-ups of the condition (Shum, Williams, Docherty, & Jones, 2000). The systematic review (chapter 3) established that many studies have found a significant correlation between disease severity and QoL- increased severity is found to be related to poorer QoL. Furthermore, all studies in the review that compared QoL in AD patients to healthy people found that QoL was significantly lower in AD patients. Notably, all studies included in the review used cross-sectional methods to assess QoL in relation to disease severity. Results using this methodology should be interpreted with caution as it is impossible to determine cause and effect. Furthermore, data on the relationship between specific AD characteristics and QoL suggested sleep disruption and body surface area affected by AD could be relevant predictors of quality of life. A deeper insight into these relationships is crucial for disease-severity measurement in quality-of-life research; indeed, a more qualitative approach would help uncover some of these issues.

It is important to consider the experiences of living with atopic dermatitis in long-term perspective. ,Existing research does not fully explicate the impact of living with and managing this long-term often life-long condition Indeed experiences of living with different long-term conditions vary greatly from one another; diseases such as cancer may cause severe and

continuing complications, whereas chronicity in skin conditions like AD is one that encompasses distinct influences on daily quality of life, such as the failure to prevent recurrent acute exacerbations and to secure day-to-day control over the condition. Due to the lack of cure for AD, these experiences may be combined with uncertainty regarding the management of and psychosocial reaction to the condition. According to Jobling (2001), the public response to skin conditions does not tend to be one of empathy and compassion, but rather disregard or lack of interest in its' implications on those who have it, in addition to feelings of stigmatisation and prejudice

AD is often associated with negative connotations and moral evaluation such as the association of dirtiness attached to patients with AD, in addition to fears of contagion and infection (Jobling & Naldi, 2006). These responses to the skin condition are deeply rooted in culture and history. These factors amongst others may help explain why QoL is affected in AD and similar skin conditions to similar extents as other long-term and often severe conditions including cancer and diabetes (Silverberg, 2018). Although there are a number of published cross-sectional studies that explore quality of life in relation to AD using clinical and objective measures, subjective experiences of living with the condition may be a more powerful determinant of the to which QoL is affected (Fivenson et al., 2002). Existing quality of life measures do not encompass, summarise and convey the full life experiences of living with AD (Finlay, 2001) as they rely on a limited number of questions with response categories that assess QoL in a particular time-frame e.g. a day or week preceding the assessment.

There is a notable paucity of studies that utilise in-depth qualitative methods to explore the lived experiences of adults with AD As mentioned earlier, all research assessing QoL in adults with AD is quantitative and much is cross-sectional. However, there are few qualitative studies on other similar skin conditions such as psoriasis that explore experiences of living with the disease using in-depth semi-structured interviews and qualitative analysis (Ersser, Surridge, & Wiles, 2001; Jobling, 2005). Consequently, there is lack of knowledge about the experiences of adults living with AD. Interviews with AD patients could help explore and

uncover issues that are not easily addressed in qualitative research, thus allowing for a more in-depth exploration of the extent that AD impacts an individual's daily life. Given the paucity of high quality qualitative research in this area and the need to AD patients' experiences in more depth, an inductive qualitative approach was deemed the most suitable method to collect this data The aim of this study was to understand participants' experiences of living with atopic dermatitis using semi-structured interviews.

4.2 Methods

4.2.1 Study design and setting

This was a qualitative study using semi-structured interviews conducted with adults with AD, face-to-face at Aston University or via telephone. Ethical approval (appendix 3) for the study was obtained from the School of Life and Health Sciences Ethics Committee at Aston University (Ethics application no. 1125).

4.2.2 Sampling strategy

Our aim was to recruit participants of different ethnic backgrounds, perceived severities, and ages in order to allow for contrasts and comparisons. Inclusion criteria for this study were adults aged 18 or above with clinically diagnosed atopic dermatitis. The exclusion criteria for the study were participants living outside the UK, and those under the age of 18.

4.2.3 Participants and recruitment

Participants were identified through advertising the study at Aston University, with the use of posters, and e-mails sent to students and staff. The study was also advertised on Facebook Eczema support groups and Twitter. A total of 19 participants were recruited; four were identified through the University, five were identified through word of mouth and snowballing techniques, and ten were identified through social media.

Participants consisted of one male and eighteen females, with a mean age of 34 years (age range 19- 52). All participants had concomitant atopic conditions. Ten participants were White

British, six were Indian British and three were Pakistani British. Disease duration ranged from seven to fifty years. Fifteen participants were being treated by a dermatologist, and seven participants had a family history of atopic dermatitis. Current medications taken by participants included topical corticosteroids, oral immunosuppressants, antihistamines, and over -the-counter creams and ointments. (Table 4.1).

Table 4.1. Participant characteristics (all names are pseudonyms)

Participant	Age (years)	Ethnicity	AD duration (years)	Concomitant conditions	Patient-assessed severity	Family history (Y/N)
Asha	27	Indian British	27	Food Allergy, hay fever	8/10	Y
Tamar	44	Pakistani British	42	Allergy	8/10	N
Sid	26	Indian British	8	Food allergy	7/10	Y
Amy	32	White British	30	Hay fever	8/10	Y
Pooja	38	Indian British	17	Asthma	6/10	N
Katy	34	White British	34	Hay fever, Food allergy	5/10	N
Karen	47	White British	46	Asthma	7/10	Y
Stephanie	43	White British	43	Food allergy	6/10	N
Leah	31	White British	27	Asthma	7/10	N
Navjot	25	Indian British	25	Food allergy	5/10	N
Emily	37	White British	36	Asthma, Food allergy	8/10	N
Fatema	19	Pakistani British	19	Food allergy	6/10	N
Lorraine	48	White British	42	Asthma, Hay fever	7/10	Y
Tess	52	White British	48	Food allergy	5/10	N
Roslyn	34	White British	32	Hay fever	8/10	Y
Kiran	28	Indian British	25	Food allergy, Hay fever	7/0	N
Needa	28	Pakistani British	28	Hay fever, Asthma	8/10	N
Becky	19	White British	19	Asthma, Food allergy	7/10	N
Manpreet	29	Indian British	27	Hay fever	4/10	Y

Participants read participant information sheets (appendix 4) and completed consent forms (appendix 5) before taking part in the interviews. Those who took part in the interview via

phone calls were sent information sheets and consent forms by post and returned them back to the research team using a pre-paid envelope.

4.2.4 Data collection

An interview schedule (appendix 6) was developed based upon the findings of the systematic review (chapter 3). Issues such as sleep, career and physical activity which are commonly found to be disrupted in AD patients were also explored. Questions were prepared and formatted in a manner which allowed participants to discuss in as much depth about their experiences as possible, as the intention was to allow for an exploration of their experience without drawing upon any pre-existing theories. Participants' experiences of living with AD daily in general, their relationships with significant others, their experiences with treatment and management of the condition as well as physical and psychological implications of living with AD were explored in interview.

Prior to taking part in the interviews, participants completed a demographic questionnaire (appendix 7) which included ethnicity, age, gender, details surrounding their diagnosis (duration, age of diagnosis, diagnosed by whom), family history, and participant assessed disease severity which was rated on a scale of one to ten, with ten representing the most severe.

Questions were framed in an open-ended manner, asking participants to begin by discussing their diagnosis of the condition in order to establish rapport between the researcher and participant. Once this was established, the researcher moved on to more sensitive topics such as exploring the impact of AD on personal relationships. The interviews were audio-recorded, transcribed verbatim. and were conducted at a place and time that was convenient to participants-six by phone and 13 in person at the university and lasted on average 35 minutes (range: 25 to 55 minutes). No participants withdrew from the study. The researcher verbally asked participants for demographic information.

4.2.5 Data Analysis

Data was transcribed verbatim, names replaced by pseudonyms and analysed thematically (Braun & Clarke, 2006) recognising the interaction between the researcher and the data. Thematic analysis has six clearly defined steps: familiarisation with the data, generation of initial codes, searching for themes, reviewing themes, defining and naming themes, and producing the report. The researcher familiarised themselves with the data through a process of reading and re-reading the interview transcripts and then coded the transcripts in detail, using annotations to identify patterns in the participants' use of language to describe or evaluate their experiences. These patterns were explored and discussed with both supervisors, alongside any contradictions within and between the participants' accounts. Through this process the researcher identified preliminary themes and conceptualised a 'theme' as a pattern of meaning which illuminated something distinctive about participants' experience of living with atopic dermatitis and/ or which resolved or conceptualised any conflicting ideas identified within or between the participants' accounts.

4.2.6 Reflexivity

Within the context of the current study, the researcher was involved in telephone or face-to-face contact with participants and therefore reflected upon how prior experiences and assumptions might influence interaction with participants. Although the researcher was invited into participants' lives, it was important to be mindful as the researcher was merely a guest in participants' spaces; respondents were therefore given the lead in 'setting the pace' of the interview. Adopting this approach for the interviews allowed the participants exercise a measure of control over the interview process, as it was imperative that they felt at ease to discuss their experiences and not coerced in any way. By keeping a reflexive diary throughout the process, the researcher was able to learn from the interview process and understand participants' accounts more clearly when analysing interview transcripts.

4.3 Results

Five super-ordinate themes were developed from the analysis of the interviews: Experiencing threats to inner sense of self; Living with the visibility of AD; Coping with threats to physical capacity due to pain and management; Developing confidence in the management and nature of AD; Contrasting reactions and support from others. During the interviews, many of the participants referred to AD as eczema, thus these words have been used inter-changeably through-out the interview transcripts.

4.3.1 Experiencing threats to inner sense of self

This super-ordinate theme encapsulated participants' narratives surrounding the psychological impact of AD, such as issues relating to confidence and self-esteem, clinical depression and anxiety and impact on mood. This theme was reflected in all participants' accounts thus was a very commonly occurring notion. The two aspects to this super-ordinate theme involved the various emotions that participants with AD discuss experiencing because of their condition and issues with self-consciousness.

This theme of recurrent heightened emotional distress captured the notion that although some participants identified feeling 'happy' some of the time, many often experienced periods of intense emotional suffering that they attributed largely to the unpredictability of their condition and loss of control over their flares. Narratives were punctuated with words that powerfully identified their suffering: 'worry', 'fear', 'anger', 'pain', 'sadness', 'depression', 'frustration', 'horrible', and 'embarrassment'. Worry or fear (associated with flares), sadness, dysphoria, or depression, and anger and frustration were connected to and therefore appraised as emanating from the experience of having flares and suffering with the condition for such a long duration. This sense of frustration was closely linked to uncertainty surrounding the allergens and triggers. Pooja describes "drowning" in her own misery when she gets a flare-up:

"…at that point I was just like, I'm not going to do any work, I'm not going to go to college when I'm like this, I'm just going to sit here and just going to drown in my own misery…"(Pooja)

Living with a long-term condition like AD often resulted in an altered view of self. A few participants discussed that their condition had become such a strong part of them that they could not imagine a life with AD, with Becky describing it as a 'constant presence' whereby she could not imagine not being 'itchy everyday'. Participants reported that AD was responsible for unsightly physical appearance and this often resulted in them conveying various emotions especially during times when their AD was more severe and prevalent on areas of the body visible to others. Periods of uncontrolled AD were characterised by low mood for some participants. Some used emotive language to describe how they felt about periods of uncontrolled AD. Participants described their mood using words such as 'snappy' and 'hot-headed' in times of flare-ups. Katy cited her mood being so low that she stayed confined to her room for "days":

"…it affected my mood like when I mentioned how I didn't leave my room for days because my skin was so bad and I was just sort of in there in sort of my own den of skin you know, and sort of not wanting to go out and see anyone or leave the room…" (Katy)

Many participants discussed the degree to which their condition threatened their sense of self. The tone of some of the narratives reflected an underlying desire to be 'normal' and a steadfast belief that if their AD were to be cured, it would confer on them a state of normalcy. It reflected their hope for an idealized 'normal' self. For example, Asha illustrates a low emotional appraisal of her own worth, to the extent that she perceives those without AD as normal:

"…*if I woke up on day and my eczema was gone, I actually think I would pass out. It has taken over my life so badly, everyday is sort of centred around it… what I do… what I think… how I feel…. I just want to be normal like everyone else you know? Its consuming me as I get older…" (Asha)*

There appeared to be differences between those who were diagnosed with AD at an early age and those who were diagnosed at a later age. Many participants who were diagnosed with AD at a young age made references to how self-consciousness in particular was an issue for them

when they were younger. Despite the severity of their condition remaining the same or worsening, as they got older their AD did not bother them as much, as their priorities changed, and they had more to focus on than their appearance. An example of this is demonstrated in the following excerpt, where Karen describes that despite her AD being as severe as ever, she no longer cares about others' perceptions of her:

"…when I was younger would say yeah because It just made you more self-conscious uh, so I would only wear like long sleeve tops or high necks long trousers, now I don't care I'll go out in a tankini it doesn't matter…" (Karen)

A feeling of alienation was also prevalent in participants' accounts with many discussing the desire to live a 'normal' life and not be 'different' from others Many participants talked about a constant awareness of their AD and discussed experiencing low self-esteem and of being extremely self-conscious about their appearance. As Katy explained:

"…I'm more self-conscious of other aspects oy eczema for example rather than the pigmentation…it sounds really horrible but like, I think 'does my skin smell' for example, and then like I get sort of self-conscious because like my colleague said "oh you smell like my boyfriend", I said what do you mean and she said "do you use the same cream as him?" and I said I use diprobase, and diprobase is like an old person cream and I was like well that's not really a compliment is it…" (Katy)

Fatema described that due to her religion, she covered up her skin, but was doubtful of whether she would have the confidence to allow the affected skin to be visible to others as she felt that people within her community would judge due to a lack of understanding. In the following citation, Fatema describes that if covering up was not part of her culture and religion, she would not have the confidence to show her skin :

"…my confidence is really like low because of my skin, like sometimes I just sit there and roll up my sleeves and look at my skin like it's just its such horrible skin it's like a daily thing like, every time I get changed I look at my skin like I don't like it, like it, if I didn't dress like this,

would I ever show parts of my body, I don't think I would have the confidence to be honest which is a shame…" (Fatema)

Similarly, Needa explained that when she visits Pakistan, she feels more judged and less confident than in the United Kingdom, where she believes people are more educated about AD.

Many participants also reported feeling bad-tempered, feeling down, depressed, and being less tolerant when they had flares. In fact, four participants described being diagnosed with clinical depression as a direct result of their AD. Sid had extensive facial scarring due to his AD, which resulted in severe clinical depression, suicidal thoughts, and social withdrawal:

"…I used to be depressed, I had depression. Little things like my skin was so bad on my face that I didn't want to laugh like it hurt to laugh or smile as well, yeah it did affect my mood a lot when my skin was really bad I was always alone I always wanted to be by myself not around people not even family, this was more so when I was in university so like twenty-one years old…" (Sid)

He went on to say that once he received laser surgery to correct his scars, his depression alleviated, and confidence increased. Becky was also diagnosed with clinical depression and anxiety which she described as being a direct result of her AD. She describes feeling withdrawn at times whereby she wants to 'sit very still' in her own 'little bubble'. There were times when these participants felt that they had lost their will to live. The participants used distraction as a way of coping. They described how they chose not to think/ focus on their condition or just tried to forget it when feeling down, which could be adaptive and helpful in such situations. The purpose of this conscious denial was to sustain emotional functioning and therefore be able to live a normal life:

"…it has also had a really bad psychological impact coz when I'm doing things I don't have to think about anything, thinking about it makes it worse in that sense coz you are constantly

looking at it and constantly seeing how it looks and scrutinising it and things like that…". (Fatema)

The appearance and visibility of their AD, the reaction of others and restrictions experienced all adversely affected participants' emotional well-being. Many also worried about the future development of scars/pigmentation and this worry led to feelings of low self-confidence which in turn caused introversion and self-consciousness, social anxiety whereby many participants were fearful of engaging themselves in social situations, feelings of low mood and despair, anger, annoyance and frustration towards their condition and a resulting sense of hopelessness and helplessness.

Thus, this theme captures the extent to which living with AD leads to extensive emotional suffering, and in times also gives rise to severe clinical anxiety and depression. To put in context the mental impact, Amy simply said:

"Eczema more than anything for me is mentally draining more than physically draining, it's affected me more psychologically" (Amy)

4.3.2 Living with the visibility of AD

Atopic dermatitis alongside its characterisation of intense pruritus and inflammation of the skin, also presents itself as cracked, dry, sore and reddened. In time, severe and persistent AD can give rise to complications such as pigmentation of the skin, thinning of the skin, wrinkles and scars. Many participants in the study felt that the visibility of AD contributed to issues with body image whereby many felt stigmatized, judged, and attempted to cover their skin as much as possible. They also found themselves comparing their skin to others- often people they were close to, such as family members and friends. The two sub-themes capturing this are body image and comparison to others.

Body image

Most participants were dissatisfied with the appearance of their AD. They felt that their AD looked unsightly and consequently perceived themselves as abnormal. Their scars, pigmentation and inflammation acted as a constant reminder to the participants and others of their continued suffering. Many felt stigmatized by their condition, particularly when their AD was prevalent on visible areas such as the face, neck and arms. They believed that others would judge them as having other conditions such as scalp AD being mistaken for hair lice, or their condition being contagious. They appeared to care deeply about what others thought of their AD and strived to keep it hidden so as not to raise any questions or thoughts; Stephanie explains in the following excerpt about her fear of what others thought of her condition:

"…I'd be worried about you know whether they were looking at it, I would be looking at them trying to see if they were their eyes were you know sort of drawn to my eczema, I try my very very best not to let my hands wander and start scratching so you know I try to be aware you know a bit more vigilant if I was meeting somebody new…" (Stephanie)

Many participants also felt extremely self-conscious of their condition, to the point that they felt the need to conceal their condition (e.g. wearing long sleeves, covering their legs and feet, wearing corrective foundation on areas with scarring/pigmentation). Amy appeared quite exasperated with the visibility of her AD and stated that because her condition was more prevalent on her face, she considers it as more severe than if it were elsewhere on her body, rating it an 8 out of 10 for severity:

"…because it's on my face I would say it's an eight. Just for the fact that you know, I can't, I can't put on any make up, some days I just want to put a bag over my head, I don't want to come in to work and face people…" (Amy)

Feeling self-conscious in relation to their AD resulted in participants adapting their behaviour in ways to 'hide' their AD such as not liking to see their reflection in the mirror or having their photographs taken. Participants also discussed how their AD made them look 'ugly' or

'horrible' with Stephanie explaining that due to having AD on her hands, she felt compelled to hide her hands when shaking hands with others by flipping down the back of her hand. Tamar also explains in the following extract how AD has affected her body image, and this is primarily due to post-inflammatory pigmentation, which is a common outcome of severe AD. Like Tamar, other participants also felt vulnerable when exposing their condition to the world:

"…I have got pigmentation all over, I have got discoloration, I don't go out without my foundations um… it makes me feel really conscious, especially when you're talking. I would not be able to talk, sit across and, then speak with somebody eye to eye contact…" (Tamar)

Comparison to others

Through participants' accounts of living with atopic dermatitis, many expressed a sense of injustice, describing ways in which atopic dermatitis threatened their personal identity and they made negative comparisons with other people. They reported the unfairness of having to live with the condition and focussed on personal characteristics that they believe had been damaged by living with AD, including not feeling physically and sexually attractive, strong or a good parent.

Many participants felt envious of other people being able to engage in activities or live a life that they wished they could. Fatema for example, stated that she wished she had good skin and every time she looked at her family members she was reminded that she was the only one suffering. Emily, who was part of a mum's club, describes feeling 'envious' of those in the club as they did not have to endure the maintenance regime that comes with AD. She also described feeling left out due to not being able to wear cosmetics and clothes that others were able to:

"…sometimes I just feel a bit left out of the clothes and make up conversation and the, you know they tend to have really busy lives where they can fit lots in and you know they're not having to go home and put their cream on in between and sometimes I feel a bit left out of

those conversations. A little bit envious to be honest because there's the insider that wants to be doing a lot more and then I just can't…" (Emily)

There were however participants who compared themselves to AD patients who were "worse" than them, and '*people who have been sort of bed bound and not being able to go to work or school or whatever' (Katy)* due to their AD, and therefore rated their own severity relative to the cases of AD they had come across. For example, Katy described how in comparison to those she had seen bed-bound, her AD was only a 'good five out ten'. A few participants also compared AD to other conditions, as Becky explained '*there are far worse conditions to have like cancer'*.

Overall, the visibility of the condition appears to have a major impact of participants' daily lives and can result in the condition being perceived as contagious. This is particularly problematic when AD is visible on the face and neck. Many participants take measures to conceal their AD, and often find themselves comparing their condition to others.

4.3.3 Coping with threats to physical capacity due to pain and management

Atopic dermatitis alongside its' mental implications, affected participants physically. A number of participants discussed the anguish surrounding the inability to lead normal lives due to the severe symptoms of the condition such as skin inflammation and pain. These periods of exacerbations appeared to greatly affect engagement in physical activities, social interactions, financial security, sleep and work productivity. Many of these limitations in physical functioning were alleviated by good treatment regimens.

Many participants reported pain and itch. Pain could be severe and was described as 'stinging' or 'sore' and words such as 'raw' and 'wet' were used to described inflamed skin. Others reported symptoms related to inflammation and the altered texture and sensation of their skin, often resulting from years of having the condition.

Limitations in physical functioning due to pain and discomfort from AD were a distressing experience for participants and impacted participants' ability to perform everyday tasks such

as housework, self-care, and leisure activities. The impact of these physical limitations was also expressed as a feeling of being an outsider in a world full of healthy people. Many hoped to live as normally as possible and overcome limitations brought on by their condition. Some participants expressed concerns regarding other aspects of their daily lives, such as having to change bed-sheets more often than they would like due to them being covered in ointment, having to wash clothes more regularly, having to carry pillow cases and duvet for overnight stays away from home:

"…when I go away where am I going to go is there going to be a bath that I can use for my skin to soak, I tend to take my own pillowcase so I know that it's got some bedding that I know has been washed, so it's those things that I would say affects what I do and where I go…" (Karen)

Washing and physical activity were also problematic for many participants due to being unable to face the sensations when cracked or dry skin came into contact with water or sweat. Several participants also discussed impairment to movement being one of the biggest problems faced. AD around joint areas, feet or hands impaired their ability to move and carry out everyday tasks. Movement was often described as painful; Becky, a dance student with AD prevalent on her joints was often unable to attend classes due to the flare-ups in these areas. She discussed how moving her joints hurt and when her AD was exacerbated, she limited her movement to the extent that she 'sits very still' because of the pain. She described feeling 'trapped' both emotionally and physically. She also described leaving her classes 'crying in pain':

"…it always feels and looks like I'm a bit tired and it's stiff and that's really [long pause] weird… and I rely a lot on movement because I'm a dancer and I'm always like stretching, dancing and moving and then when that all hurts, I just kind of sit still, and I know this sounds really bad, but I tend to go really still because I know every movement can like hurt and things and then I feel like trapped and sit still and don't move at all…" (Becky)

Several participants reported being prescribed sedating antihistamines due to lack of sleep caused by AD symptoms. Fatigue meant that participants needed more hours of sleep than usual, although they were not able to get them. Extended naps during the day and earlier bedtimes further reinforced how, physically, these participants were different from people without AD. A few participants reported not being able to concentrate or being less productive at work due to lack of sleep. Stephanie explained how lack of sleep due to AD resulted in fatigue during the day and lack of concentration at work.

"…sleeplessness is the worst and then it's just a horrible cycle because then you're awake and then you're scratching more it's just a vicious cycle just goes on and on you know until you only have three or four hours of sleep in the nights it's just absolutely you know, just zaps you of energy…" (Stephanie)

Participants with good treatment response experienced improvement in their physical condition. However, several participants receiving treatment also described unpleasant side effects such as weight gain after using oral medication and fear of infertility. Many participants described discomfort which resulted from the use of emollients and creams, with some not being able to wear certain materials due to the emollient 'sticking' to their clothes or having to wash bedlinen frequently. In the following excerpt, Tamar explains how she did not receive support from her family, and was in an 'unhappy marriage' which ended mainly due to her AD and its complications:

"…my family hasn't given me the support I needed… I've honestly got to say… because um… as I said when I was sixteen, I got married and I was stuck in a really bad marriage, until about 40 years old…I was on Methotrexate for many years and I think I wasn't able to have children because of that. My husband…he left me because of this. They should have told me about infertility…"(Tamar)

Impact on the family was a commonly recurring theme, especially for women with small children. This was discussed by several women. For example, Emily feels that she is not a

good enough mother to her children as her AD prevents her from being able to give them her full attention as seen in the following excerpt. Similarly, other participants with young children and those with partners felt that they were absent from their social lives their family in times of flares, and had to rely on others to compensate for this absence:

"I do find it much harder to accept having it because I do feel that there are times when I won't be able to do things for the children and I just feel so ill, um, and occasionally my little girl my 4 year old, says she wished that my eczema would go away, go away forever! It is something that they notice and they're aware of…" (Emily)

Many also often felt restricted in clothing due to irritation and pain that certain materials caused, visibility of blood on light fabrics, and flaky skin on dark fabrics:

"…one thing I didn't mention is wearing dark clothes, I get dry skin, it's a nightmare because the dry skin just gets like say it's a vicious cycle and to break it I use betnoscalp I think, it's like an anti-fungal treatment to use in your head. It's just… black is a no-go for me, flaky skin falling on my clothes, so yeah…" (Amy)

Several participants cited that having AD has impacted them financially with many stating that they have had to arrange for Pre-Payment Certificates (PPC) to ease the financial burden. This certificate which is valid for a specified period is ideal for patients with many prescriptions that need to be purchased regularly:

"…so obviously I get the PPC so that's like a 100 pounds a year isn't it? But then on top of that obviously you know you see things and you're like come on I'll try that because that's telling me it's going to fix my skin and you're like I know it's not but I'm going to try it anyway so like, and sometimes those can be quite expensive can't they…" (Manpreet)

Additional to the cost of medication, Stephanie acknowledged that having to purchase clothes of skin-suitable materials and extra bedding has an indirect financial impact on her.

Participants' work life was also impacted in various ways. Many participants had sick leave at some point in their career due to their AD. Needa discussed having to take two weeks off work due to her condition being severe, and at this time she could not move or be around water. Being a hairdresser, it would have affected her ability at work, therefore she just had to 'sit tight' at home. Karen also described having to resign from her job due to complications caused by AD which meant she had surgery and had to be hospitalized:

"…when I first took the job when I was first qualified in 2003, I started the job in July and by the Christmas I was in hospital because my skin was so bad because of the stress of the job. Um so I spent about three weeks in hospital and I think I had about six weeks off all together. Um, It was just everything, an infection, the last time I had a staph infection and it was just the stress of the job…" (Karen)

A few participants described needing to change jobs due to the stress involved exacerbating their condition. Amy felt that she was unable to apply for job promotions due to her AD limiting her ability to perform more challenging tasks, as a result of it leaving her fatigued and lacking energy. Despite the limitations faced by many, the majority expressed that their colleagues at work were understanding of their condition and accommodated it well. Some participants could work from home if their condition got worse. The excerpt below demonstrates the empathy expressed by Amy's colleagues at work towards her condition:

"…luckily my job is not forward facing in the sense that I have to deal with people outside of my office, but I explained that some days it can be horrific and if it is horrendous, they said just work from home, don't bring yourself to come in… so people are understanding in that sense…" (Amy)

Navjot explains how her work colleagues could see her flare-up around her eyes as it was very visible; she describes her face that day was 'gross'. The visibility of the condition on her face ruled out any disbelief from her work colleagues which had been present in the past:

"…my face is gross, look at my eyes and cracked skin, they could see that it was visibly really sore so I think that helped, where as if it was something they couldn't see then they would be like "uhhh you're just saying it"…" (Navjot)

A few participants reported a lack of confidence in the long-term management of their AD. Continuous and impractical treatment regimens with regular follow-up consultations interfered with daily lives. The slow progress of treatments was often frustrating. Participants discussed a 'trial and error' strategy with their treatment and many, despite living with the condition for most of their lives, were unable to treat their condition successfully for a sustained period of time. Roslyn, like many others, explained how she had to plan beforehand for the prospect of a flare up, and took the necessary measures such as carrying medication with her on journeys. Others also appeared to do the same, with Karen having to carry her own bedding with her on overnight stays away from home. Emily engaged in constant washing of her hands in order to avoid any bacterial infections that could arise as a complication of AD:

"…I just can't enjoy stuff as much as other people just because I would have to plan for it, so if I was going somewhere, I mean my handbag is just full of pots and tubes and stuff. If I'm going somewhere I would have to think right, am I going to be comfortable in what I'm wearing, am I going to have enough creams to keep me going through the day, am I going to have a bath, am I going to be back too late to have a bath and it's just…" (Roslyn)

Only a few participants stated that they were able to manage their condition themselves and that their coping strategies had improved with time. For example, Katy cited that she goes to her doctor's appointment knowing exactly what she wants and Amy discussed that she knew best what works for her condition:

"…I just sort of learnt to know what to do what to ask for if I go to a doctor, or sort of how to generally manage it myself…" (Katy)

Many participants also described how their condition has led them to avoid social events and activities, and it was not uncommon for them to describe themselves as being social isolated.

Some felt ashamed of how they look and wanted to isolate themselves from social situations. Social isolation that was not deliberate was also a recurring theme. Some participants described how family, friends and/or the general public sometimes acted towards them in ways that were hurtful. A few mentioned not participating in social events, avoiding eye contact, and having to deal with inappropriate questions about their condition. In the following excerpt, Katy describes confining herself to her room during a period when her AD was severe. Similarly, others also recall missing prominent events such as weddings due to flare-ups:

"…I moved away I lived in a flat with some friends and there were periods then when my skin got so bad that like I remember, quite distinctly that there was a time I didn't really leave my, because you know you have like there en suites um, I really didn't leave my room for like two days and it got to a point where like my flat mates put a note under my door…" (Katy)

Several participants described missing out on social activities due to the fear of an impending flare-up, with Amy describing her fear of a flare-up on her wedding day which was in a few months' time. She stated that she would not be able to dress up how she would like but that the unpredictability of the condition meant that there was no way she could predict a flare-up.

Other participants also provided examples of how their social life was affected by their condition. They made references to the way they were affected when they went out with people from their social circles, such as Sid wanting to hide his face in public and not engaging in activities that would draw attention to him, and Amy wearing clothes that would conceal her AD when with her friends. In fact many contemplated socialising when experiencing a flare-up. A few participants also described their reluctance of staying away from home for long periods of time, such as when going on holiday. Stephanie regularly spends time away from home and carries her pillow and duvet with her each time, due to the fear of unknown materials causing a flare-up:

"…I work in another part of the country um so I have to stay there but I have to take my own bedding with me because the bedding in the hotel I stay at would be too hot too heavy so um,

I take my own bedding with me just so that I can be cooler um, but sometimes I've been so itchy and not able to sleep that I just have to wrap myself in towel…" (Stephanie)

Although numerous participants felt less sociable and generally had a strong desire to be alone and avoid situations where they could be observed: such as shopping, using public transport or participating in social activities, a few participants acknowledged that despite a flare-up of their condition, they did not let this get in the way of their social life, but instead considered measures to overcome barriers to their social life:

"…I was able to go camping last year for the first time ever um, because my consciousness of 'oh I need to be somewhere where I can get to a bath or whatever' and I did four nights in a tent, which I've never done before so to have done that was like wohaaay [that's really good] so that's really good…" (Karen)

Many participants showed hesitance in meeting new people and discussed how they would try and avoid situations where they had to communicate with people who do not know of their condition. For example, Mandy discusses how she feels self-conscious when shaking hands with people who she does not know well:

"…when I have to meet new people at work- because my job involves me having to see new clients all the time- I get really scared that when I shake my hands with them, they will wonder 'oh what's wrong with her hands?' because they are so rough and wrinkly…" (Mandy)

Consequently, in addition to threats to inner sense of self, physical pain and discomfort affected many areas of participants' lives. This paired with the management of the condition resulted in disrupted sleep, social engagement and participation in physical and leisure activities, meant that a large part of participants' daily lives were affected. There was however, a notion of some participants attempting to overcome these limitations with a 'can-do' attitude.

4.3.4 Developing confidence in nature and management of AD

Participants used a variety of coping mechanisms in an attempt to manage and improve their daily lives. , Some discussed the use of active strategies such as avoiding triggers and having strict maintenance regimens, whereas others used distraction in order to cope with their condition such as comfort eating. Many participants reported a sense of control over their situation, and this was more so in those who had been diagnosed with AD at an early age. mechanisms used to cope and manage the condition varied between participants and seemed heavily reliant on past experiences.

Developing mechanisms to help live with AD

In order to cope with their AD, a number of participants discussed the use of distraction and avoidance strategies as a mechanism to maintain daily functioning and improve their quality of life. Methods of escapism included consumption of pharmacological medication such as painkillers and sedating antihistamines comfort eating and focussing on daily stressors (e.g. finances) In the excerpt below Lorraine discusses one of her coping strategies that she acknowledges is not very helpful:

"…my confidence was low, so obviously, what I did was I turned to food a little bit, and when it gets bad, I still do turn to food, and I know which doesn't really help, it's a really vicious cycle which I'm trying to break, comfort eating basically…" (Lorraine)

Other participants engaged in activities that they were aware would exacerbate their AD. They felt that not engaging in these activities would result in them missing out on enjoyable activities. An example of this can be seen in the following excerpt whereby Navjot discussed knowingly engaging in an enjoyable activity even though she knew it had a detrimental impact on her AD. She acknowledges later in her interview that if she limits herself from taking part in certain activities, her QoL would be compromised:

"…I try not to let it affect me um and if, even if I know it's going swimming in the ocean [I: yeah], I know that's going to really affect me, I'm like oh I'm in Vietnam, on a beach, with my

boyfriend like, its once in a lifetime and I'm like forget it I'm going to do it and then deal with the consequences later [laughs] which I think you have to otherwise it will affect your life…" (Navjot)

Many participants also identified instances that demonstrated resilience or defiance. These participants refused to succumb to discrimination as a result of AD and took it upon themselves to find a solution. In one example, Needa described how she assumed responsibility to change her situation by educating her family and relatives about the condition and taking it in her own hands to 'monitor' AD in her relatives who suffer from it:

"…I was obviously none the wiser, I was a child, how to use, what to use, when to use it, when to stop. I don't think education was very good, so now as an adult with nieces or nephews that do have eczema, what I have educated their parents who don't have eczema "this is how to do it, don't use too much of that". So I am making sure it's being monitored…" (Needa)

These participants displayed optimism within their accounts and the importance of a positive attitude in maintaining a good QoL- an 'I cannot let it affect me' attitude. The 'mind-body' connection and the importance of having a positive outlook to guide the future was discussed, whereby thinking positively about their condition would result in an improvement in their AD.

Many participants had managed to integrate AD into their sense of self, even though it had negative effects on various aspects of their lives. This was a process that was helped by duration (as time passed, they learnt to accept their condition), and by acceptance from family and friends. In the following excerpt, Tess explains how one of her mechanisms to improve QoL consists of 'keeping up appearances' ; this makes her feel better on the inside, and helps her maintain a better QoL:

"…I think well actually I am going to put on some make up because it will make me feel a bit nicer about myself, but you know there's things that other people do like you know like oh that would help me, I'll try rubbing that in to my feet for a bit and the there's me thinking well actually that's a bit pointless you know so um, like I said I try not to let it get to me…" (Tess)

Striving for sense of control in the face of unpredictability

Another recurrent theme was the idea that at some point after being diagnosed with AD, participants had made a conscious decision to assume responsibility of their condition, rather than let doctors or family members manage it for them. Several participants appeared to feel in control of their condition, with a few citing that it would not limit them, and they were 'past that stage' where it would control their lives; indeed, many of the participants described the condition having had more of an impact on them when they were younger. A sense of control over their AD appeared to be a means of maintaining a 'normal' QoL, Katy states that the condition 'can affect quality of life' but the aim was not to let it. As the duration of AD increased, participants attempted to prioritise it less within their daily lives. They described accumulating enough knowledge and experience of living with the condition to become relatively desensitized to the effect it was having on them. For example, Stephanie, like Navjot engaged in activities that might exacerbate her AD, such as physical activity, because she was determined not to let it stop her:

"…I try not to let it sort of control anything. I don't think I've ever turned anything down just because I've got eczema but it would probably make me enjoy things less because it's difficult as I might run but at the end of the run I'll be feeling sweaty and itchy and whatever so it might affect the quality of experience but it wouldn't stop me doing anything. I do everything within my control so if I was going somewhere and it would be a long journey, I just take lots of cream with me…" (Stephanie)

Stephanie described doing 'everything possible' to prevent a flare-up, suggesting that certain aspects of her condition were out of her control and there was only so much that she could do to prepare for a potential flare-up. Sid however, described wanting to be control of his environment so staying indoors would be ideal for him, whereby he could control the temperature to obtain the 'perfect conditions' for his AD as can be seen in the excerpt below. Later on, in the interview, Sid discussed losing weight, being mindful of his diet, and cooking his own food which contributed to a reduction in his AD; losing weight consciously, and

controlling his diet was perhaps a way for him to compensate for the things he could not control such as his flares :

"…like I would rather be inside where I know I can, I'm in control of the environment inside so there's perfect conditions for me…I get really warm yeah…I've always felt really hot yeah so I used to bring my ice water to just try and get my temperature down…" (Sid)

Emotions surrounding the unpredictability of flare-ups and loss of control reflected participants' worry about "what if" a flare-up starts, and this concern introduced a great amount of uncertainty in their lives. Due to many participants not knowing what their triggers were, they could only plan to a certain extent. Many participants did not know what to avoid and therefore could only anticipate or predict their allergens without certainty. Kiran explains in the following excerpt how the 'unknown' of AD has resulted in her comfort eating, and the stress of comfort eating further exacerbates her AD:

"…some days depending on the flare up you feel lethargic so I've got this conscious bit, watching what I eat, trying to lose weight, and I have lost weight a little bit but I think because of the, the unknown about the eczema and when it's going to flare up, I don't know when I'm going to have a really bad like food day, you feel worse after comfort eating, it's a vicious cycle…" (Kiran)

Amy also explained that AD 'takes a hold of your body', the unpredictable nature of the condition meant that she had to brace for a potential flare-up at a forthcoming wedding, and her own wedding, where wearing cosmetics would trigger symptoms. She was one of many participants who were not aware of their triggers and described AD symptoms as unpredictable and something a patient should expect at any time without warning:

"…this thing that takes a hold of your body, and you don't know when it's going to take a hold, you know we've got a wedding in October and I think to myself , god I just hope that it doesn't flare upon that day and that's that's myself, when I get married that's the worry ill have, because you know, and I said to my other half, I said 'I'll wear make-up on the day' and he

said well wear it until we have the pictures and then take it off, he says it doesn't make any difference, but its more me…" (Amy)

Some participants discussed how flares were accompanied by apprehension due to lack of certainty of how the flare would be and how long it would last. A few participants also recalled that even when they were better, they were apprehensive of a flare returning and it was always 'at the back of the mind'.

Many participants, through years of living with AD, developed strategies to help them manage their condition better. Some participants made a conscious decision gain control over their condition by taking necessary precautions to avoid flares and avoiding situations that would exacerbate their AD. The unpredictability of the condition however made it more problematic for participants to prepare for potential flares.

4.3.5 Contrasting reactions and support from others

When discussing health care professionals, the majority of participants passionately felt that their GPs and primary care doctors did not understand the psychological impact of AD on them and there was a general idea amongst participants that GPs were not equipped to address and treat mental health issues that arose as a result of AD. Family and friends were a central part of participants' support network and many felt that those who knew them for the longest and those who had AD understood the participants' situations best. Social isolation was also prevalent in many participants, particularly those with AD on areas of the body visible to others. As a result of this social anxiety, many missed out on important events and family functions- they were fearful of what others who were unaware of their condition would think of them.

Dismissed by health care professionals

Upon exploring perceptions of health care from GPs and dermatologists, many participants felt that there was a lack of adequate information on the condition itself, its management and prognosis provided by these health care professionals. One participant also felt that health

care was centred around children and not enough attention or resources were put towards the adult population.

Some participants also reported that their GPs did not ask about the impact of AD on their life. Interestingly, many participants in the study said they were interested in having their GPs explore how their AD may be affecting them. For example, Becky explained that GPs do not understand her condition and she would like to be referred to a mental health professional but does not believe that the NHS has enough funding to implement this as part of her treatment. A few participants also discussed that due to their clinicians not suffering from the condition, the extent of the impact AD had could not be appreciated.

Several participants expressed having to 'push' for further tests or referrals after they were presented to their GPs with worsening symptoms. Complex relationships were evidence between health care professionals and participants in this study, with their perceptions of doctors' expertise regarding AD being variable. Many felt that doctors were often dismissive of the seriousness of their condition and that this attitude reflected either the GPs' lack of experience and interest in the area, or a lack of appreciation of the psychological impact of AD. Becky described never being referred to a mental health professional despite being diagnosed with clinical depression and anxiety and having asked 'twice or three times' to be referred to a 'proper mental health doctor' and not 'just a nurse'. She discusses how it would be ideal to have one person who is specialised in her AD and mental health:

"…I feel that it's not their fault to be honest. If there was more resource and money in the NHS, maybe I could expect to see a psychologist you know, for how severe my eczema is affecting… I think if the dermatologist was combined with the psychologist so I only needed to see one doctor who would understand what m going through, you know it would be nice…" (Becky)

For some participants, GPs' pejorative or unsympathetic attitudes contributed to feelings of guilt or decreased self-esteem. In the following excerpt, Amy discusses the lack of scientific knowledge and understanding of AD which could affect patient care:

"…I just think they don't understand eczema and I don't think there's one trigger for each individual I don't think they've figured out one cause that they can associate which would make it a lot easier like breast cancer for example they know what specific gene, but eczema there's so many different external factors they haven't been pointed one which impacts more than others, so they haven't got a common diagnosis, which I think kind of dilutes what they're trying to sort of say to you..." (Amy)

Unfavourable experiences with health care professionals, particularly GPs were not always seen as a failing on the doctor's part. Many participants acknowledged that although they experienced negative outcomes in consultations, the nature of skin disease management is in itself complex. Many also appreciated various demands placed on GPs such as a ten minute limit for clinical consultations and the acknowledgement that AD is not life-threatening thus it was- at least in some part- understandable why it was trivialised by doctors. Dermatologists were often perceived as knowledgeable in technical expertise. Some experienced positive encounters with dermatologists who showed empathetic approaches. But many felt that dermatologists appeared uninterested in the psychological burden of their condition. Leah discussed the way in which she was treated by her dermatologist:

"… I used to see a dermatologist I used to see him every six weeks or something um they discharged me basically saying there was nothing they can do um, I've just got to deal with it now, it was severe at the time because I used to have to to wrap up in wet towels and stuff that's how bad it got but umm it felt like everybody gave up on me then…" (Leah)

A few participants expressed disbelief that a 'simple condition' like AD does not yet have a cure, and how it is not possible with medical 'technology being so advanced' that there was no known cure for the condition-. A few participants appeared to relate the lack of cure for AD with GPs' lack of knowledge and lack of education of the general public regarding AD. With regard to health care professionals, numerous participants eluded that they were better 'doctors' when it came to their condition than their GPs, and often took it in their own hands to

alleviate flare-ups and educate others of the condition rather than seeking medical help. As Nafisa describes in the following excerpt:

"…I wouldn't say my doctor told my parents about my eczema properly or even gave them any knowledge… I have nieces and nephews with eczema now and I'm always telling them what to do, what to put, what not to put… their doctors don't give them the information they need either…" (Nafisa)

Nafisa also described having had 'insensitive' comments from her health care professional whereby her neck pigmentation was likened to a 'dirty neck'. 'Dirty neck syndrome' is used to describe the post inflammatory hyper-pigmentation many AD patients- predominantly adults- develop on their neck. Even though she acknowledged that this was not a comment towards her, she did not appreciate it being called 'dirty neck syndrome'. Others appeared to disagree with their GPs/dermatologists over their treatment and diagnoses. Corticosteroids due to their potency, are usually prescribed in limited quantities, however, in the following excerpt, Karen discusses this difference in opinion between her and her GP on the amount of corticosteroid prescribed, this in turn results in her perceiving a lack of understanding from her GP:

"my GP, I would say I knows more about eczema than he does and I think that's always been the case so whenever I go to the GP I tend to tell him what I want and he prescribes it, and we always have lots of discussion, even arguments, where he says "here's a 30 gram tube" when I say that that lasts me two days [both laugh] and they say things like "just use a fingertip amount" and I I'm like no what, I use an entire handful…" (Karen)

Relationships with significant others

Participants stated that they did not generally engage in speaking about the impact of their condition to friends and family as they don't want to be perceived in a negative light; many had anxieties that it reflected a sign of weakness. Participants of South Asian background were particularly reticent about talking about their condition to others for this reason. For example, Needa discussed that due to her family being 'conservative', she did not feel that she could

discuss her condition openly with them, similarly Nafisa also perceived a lack of education about AD in her family and relatives and therefore chose not to talk about her condition openly. The majority of participants however described feeling supported by their parents and siblings, especially in circumstances where their family members had a history of AD. While many participants reported strangers viewing their condition as contagious, most felt that this was not the case for friends and family who knew of their AD. Karen, for example explains that those that have known her for a long time are very accommodating of her condition; this is reflected in many participants' accounts whereby an association is made between how well an individual knows the participant and the level of understanding portrayed by them:

"…my friends and family are all great, I mean they know me well enough to know that if I'm having a bad day, will appear in the house in pyjamas and a dress and not go out because I can't get dressed that day because I've been too itchy um, nobody tells me not to scratch, I've asked them not to so they know better um, I've got fabulous support in terms of my skin because there've been times where I've been in hospital with my skin over the years um, and they have just accepted that that's part of me…" (Karen)

Nafisa discussed how she received negative comments from others about her condition, but this was mainly from the 'third world countries' she had visited to meet family. She described how people in these countries are more 'direct' and have 'less etiquette' than those in the UK. Her sense of frustration towards the lack of knowledge of these individuals is evident from the following passage:

"…when I went to Pakistan a few years ago, everyone was looking at my skin and my scars and asking what had happened to my skin- I would never get this here, it's always the third world countries where they don't have the education and they are really direct about things. You kind of get blamed for your illness over there…" (Nafisa)

Many participants discussed how their AD has had a negative impact on their intimate relationships. Some participants felt that engagement in sexual intercourse was inhibited by

flare-ups or the use of topical treatment on their skin. Stephanie describes not sleeping in the same bedroom as her partner due to her scratching keeping him awake at night, and then goes on to describe the 'frustration' he experiences when they have to sleep in one bed, such as when on holiday. She discusses, rather sadly, how their relationship has changed as her AD has become more severe:

"…I think he finds it a bit frustrating in times say when we go on holiday and we do share a bed my scratching keeps him awake and once he starts to sleep it makes him irritable and frustrated and then I think he struggles a bit with understanding it…" (Stephanie)

Other participants discussed how their partners have been understanding of their condition and it had no impact on their intimate relationships as their partners were aware of when the participants was comfortable enough to engage in such activity. This is highly dependent on the severity of their condition. A few participants discussed having to open up to their partners when their relationships were in their early stages and being fearful of what their partners would think of their AD. This was described as a 'hurdle' to overcome. For a few women, physical limitations resulted in changes in roles especially a shift from care giver to care receiver with a few participants being dependent on others as a result. For example, Emily discusses how understanding her partner is with her AD, with him sharing the responsibilities that with AD, such as having medications on time. She likens her partner to a 'carer' although she still has the capacity to undertake these responsibilities herself:

"… I can get a bit irritated by that almost, it feels like he's my carer in that way, not my partner, so I guess some people can't win um, but he's incredibly understanding with me, with my skin…" (Emily)

Some participants found that sometimes their AD was not taken seriously. They reported anger and low mood from being dismissed, trivialised, or disbelieved by members of the public, family or friends. A few participants described not feeling sufficiently supported by their parents and being told to 'just get on with it' or 'just put some cream on'. One participant hesitantly

described how her mother had made a negative comment about her AD, and despite this happening years ago it was something that she could not forget:

"…I remember when I was younger, I didn't really feel I suppose I didn't really feel supported by my… parents like I could have done, like I remember once when my mum said to me, like this was years and years ago so it's one of those thing that just stuck, she was like saying about my legs that my legs look like snake skin, I was like [laughs] is that really what your mum says to you, you know, yeah, and then it's a bit like oh you know yeah it's not really helpful is it?..." (Katy)

Numerous participants also discussed that those without AD would not be able to understand the condition and they did not expect people without AD to even comprehend what they were going through. Becky describes how, even though her mother was her 'carer' for her AD until aged 10, she does not grasp the full extent of how it affects Becky:

"…if the whole of your back's just weeping or something, and like you're so constantly aware of it, I am not sure she can fully understand; you can't really expect a non-eczema patient to understand what you're going through…" (Becky)

Overall, many participants discussed feeling misunderstood by their health care professionals and felt that they could not truly understand the extent of the condition on their lives, in particular, psychological impact. A few participants felt that they needed access to psychological support but were not offered this. Although the majority felt supported by their families and friends, a few, especially of South Asian descent, were less willing to talk about their AD. A few participants had also received negative comments from friends and family.

4.4 Discussion

Summary of results

The findings of this study support previous quantitative studies that have confirmed the profound impact of AD on the quality of life and mental health of adults. In particular it is

highlighted that many participants reported a poor body image and confidence. The visibility of the condition appeared to affect participants greatly as they felt stigmatised. Participants discussed their life experiences of living with AD and offers explanations surrounding their diagnoses of the condition. This study also found a potential lack of public awareness surrounding AD, as well as lack of empathy from family and friends. Many participants discussed hesitation in discussing their condition with others in fear of being perceived in a negative light. The analysis also highlighted cultural and ethnic differences in experiences of living with AD.

Upon exploring participants perceptions of their health care professionals, many discussed the lack of acknowledgement offered by HCPs on the psychological impact of AD. It was also frequently discussed within interviews that HCPs did not offer adequate information on the management of the condition, and although participants placed importance on effective treatment and prompt referrals, they also needed HCPs to empower them by communicating more effectively. Indeed, there was a strong sense that HCPs were not equipped with the knowledge to address the psychological impact that AD had on participants' lives.

Why did participants feel misunderstood by their health care professionals?

The qualitative methodology employed by this study highlighted a number of complexities in relationships between health care professionals and adults with AD, most of which are not apparent in previous studies. Many participants discussed appreciation of time constraints amongst other factors to illuminate apparent failings of health care professionals. The finding that a number of participants perceived their health care professionals having a primary role of treating their skin condition and ignoring psychological implications, is consistent with findings by of a New Zealand study by Bushnell, Mcleod, & Dowell (2005) who found that almost 40% of primary care patients with an impact to mental wellbeing have not disclosed them to their HCP. Reasons cited for this included the perception that a doctor is not a suitable individual to discuss mental health issues with, the stigma of mental illness and health care system issues such as time pressures during a consultation. An area that is largely unexplored

in current literature is how stigma attached to poor mental health may be an issues in skin disease settings, as skin disease itself is related to stigma. This may be further increased by the perceived trivialisation of AD as was found in this study and has been reported by Magin, Adams, Hagin, and Pond (2009). Thus those with AD may be increasingly reluctant to discuss mental health with their HCP; as such this topic deserves further research.

Why do AD patients perceive feelings of stigmatisation due to their condition?

The findings of this study demonstrate the perceived effect of AD on body image, with many participants feeling extremely dissatisfied with the appearance of their condition and feeling compelled to cover areas of scarring and active disease. As a result of feelings of stigmatisation in social interactions, many participants were not willing to disclose their condition to others. AD appeared to be a family secret for some, and there was a sense that not many were willing to reveal this to others. Discussions surrounding the condition with colleagues and friends were accompanied with suggestions for treatment and concerns about participants' wellbeing, which caused feelings of separation from society. Many expressed unwillingness to disclose their condition to others due to the fear of compromising their existing relationships and current social situation.

They were also unwilling to share their problem due to the general population not being equipped with sufficient knowledge of the condition, which could result in rejection by the society; this lack of knowledge was also present within families of a few participants. Participants in this study, such as Sid who had extensive facial scarring as a result of AD, spoke about it stopping him from being part of social events such as weddings. According to Newell (2000), patients with facial disfigurements exhibit similar levels of social and agoraphobia to patients with clinically diagnosed social phobia, in addition to higher levels of social avoidance compared to agoraphobic patients.

Social support and its role in skin disease management has been acknowledged as a buffer of the consequences related to psychological stress (Picardi et al., 2005). The social

withdrawal and avoidance common in skin conditions such as AD can unfortunately result in a smaller support network in those affected (Lapidus & Kerr, 2001). Many participants in our study detached themselves from their families and friends, especially at times when their AD was active. For example Katy described hiding away in her room for days when her AD flared up. Participants testified to feeling at ease with familiar others, who were perceived as able to see the 'real' person underneath and ignore superficial appearances. . Partners and families were the main providers of support, yet they themselves may be trying to deal with their own reactions and distress surrounding the AD. According to the 2012 survey of adults with skin conditions conducted by the British Skin Foundation, 29% of AD patients felt that their skin condition acted as a barrier to finding a partner and 20% also that their skin condition was the primary cause for the breakdown of their most recent relationship. One of the top three areas perceived as most affected by their skin condition were making friends which was ranked third after confidence and impact on their working life.

Why were BME participants less willing to disclose their condition to others?

In this study, BME participants were less willing to talk about their condition, with one South-Asian participant acknowledging that her family in Pakistan was less accommodating of her condition than people in the U.K. BME participants were also less willing to discuss the impact of AD on their personal relationships, however, this impact appeared to be greater in this sub-group in participants who did touch on the subject. For example, Tamar discussed that she was forced to marry when she was 16 years old, and due to her husband and his family not being accepting of her AD, she had to resort to divorce. She blamed the failure of her marriage and inability to conceive purely on AD and the lack of understanding of the condition in her community. Skin diseases have been found to be particularly associated with taboos and belies in different cultures (Tatum, 2010). Within a multi-cultural society such as the UK, it is vital for doctors and other health care professionals to acknowledge that some patients from black and ethnic minority groups may present with different social and psychological needs (Baker, Mead & Campbell, 2002). Beliefs and myths surrounding skin disease has the

potential to profoundly impact the patient and their ability to cope with the condition- false and often derogatory interpretations of the condition were prevalent in some accounts of participants in this study. Thus it is important to gain an understanding of these implications in order to provide effective care to patients. Thompson et al. (2010) reported that British Born South Asian women suffering from vitiligo reported high levels of stigmatisation and this was influences by, and affected, cultural practices.

Another aspect that is often not explored in previous studies is the role of gender in perceptions of living with AD. This is potentially more significant in cultures where a woman's marriage and career prospects may be damaged due to suffering with a skin condition. In some cultures, women may also bear the chief burden for support and treatment of family members with AD. There is also concern surrounding patients who are unable to speak English and whose access to medical care may be compromised by the lack of sympathetic suitably trained interpreters. As such, further research is warranted in this area and on similar skin conditions in an attempt to fully understand the impact of cultural beliefs and how they impacts patients' abilities to cope with their condition, as it is not a widely researched area.

4.4.1 Strengths and limitations

This is the UK first qualitative study exploring quality of life and mental health in adults AD patients known to the researcher at the time of writing. Unlike the vast majority of studies exploring QoL in adults with skin conditions, this study had an ethnically diverse and large sample, which allowed for comparisons between sub-groups as BME participants made up almost half of our study sample. Issues such as the role of AD in intimate relationships and the implications of visibility in AD were among factors that I was able to explore that have not been explored widely in quantitative studies. However, the study lacked male participants, which does not allow for comparison between genders and the findings may not reflect the experiences of men with AD. Additionally, AD diagnosis in the study was self-reported using demographic questionnaires; the questions did however explore details surrounding diagnosis, disease duration, and treatment for AD. Eleven participants were recruited through

an on-line AD support group on Facebook therefore this sub-set of participants do not represent all patients with AD, as they have different characteristics and coping strategies due to being part of a wider platform of AD sufferers. However, the participants were representative of the heterogeneous population of patients with AD in terms of age duration. Subtype and history of disease also varied, adding to a broadening of the findings. There were also no notable differences between participants recruited from support groups and the University for AD severity.

4.5 Conclusion and directions for future research

This study revealed the importance of acknowledging and recognizing AD as a complex long-term condition that causes significant psychosocial implications on patients. Findings of this study emphasize the need for more integrated and accessible psychological support for adults with AD. Quality of life domains should be identified, assessed and addressed in clinical settings and the role of specialist psychologists within Dermatology should be considered. Availability of support material may help adults better manage and prepare for the impact of AD on their daily lives. This study's findings may help raise awareness in health care professionals of the complexity of AD and the need to assess and manage these patients similar to those with other long-term conditions. understanding about AD

Chapter five: An investigation of quality of life and mental health in adults with atopic dermatitis compared to healthy people

5.1 Introduction

This chapter presents a cross-sectional quantitative study that examines the relationship between QoL and mental well-being in adults with AD and compares QoL and mental well-being in this group to a healthy control group. As detailed in the first chapter, in developed countries, the prevalence of AD has increased two to threefold over the last three decades (Grillo, Gassner, Dunn, & Hudson, 2006) and is expected to keep increasing gradually. Relative to children and adolescents with the condition, little research has been conducted on the impact AD has on HRQoL of adults, despite adults representing a more severe and persistent subset of all cases of AD (Hoare, Li, & Williams, 2000).

The systematic review highlighted numerous methodological issues with studies exploring HRQoL in adults. Some of these included the sole use of recruitment through dermatology clinics. This has highlighted the significance of exploring the relationship between psychological and clinical factors in AD. However, Long, Funnell, Collard, & Finlay (1993) emphasised that these relationships also need to be explored in those recruited from the general population as opposed to clinics only. Members of the National Eczema Society (NES) in their study felt dissatisfied with at least their initial clinical consultations. This dissatisfaction may have contributed to motivation in seeking help and support elsewhere, thus possible disability and distress in relation to their AD may be unrecognised in studies recruiting from clinics.

Most current published literature focuses on the reduction of cases, alleviation of symptoms or treatment. There are few studies investigating the relationship between AD and quality of life (QoL), depression or anxiety disorders, and findings are inconsistent (e.g. Ginsburg, Prytowsky, Kornfeld, & Wollland, 1993; Hashiro & Okumura, 1997; Slattery & Essex, 2011) partly due to different measurements used for HRQoL, distress and disease severity.

Moreover, most current research includes small sample sizes of less than 250 (e.g. Linnet & Jemec, 1999; Maksimovic et al., 2012; Mikolajczyk et al., 2017; Noh et al., 2013; Wittkowski et al., 2004) and does not differentiate between clinically diagnosed and self-diagnosed AD.

The relationship between demographic variables such as age and gender, psychological factors, clinical manifestations of AD and quality of life have also been investigated in numerous studies (e.g. Holm, Esmann, & Jemec, 2006; Fivenson, 2002; Mozaffari et al., 2007; Misery et al., 2018) and whilst many studies have found associations between AD severity and quality of life, others have questioned these findings due to methodological problems or weak associations(Witkowski et al., 2003). However, there is a paucity of studies that control for these demographic factors to ascertain predictors of QoL and mental well-being. Additionally, other demographic factors such as ethnicity are seldom taken into consideration despite significant differences between ethnic groups in severity and prevalence of AD (Brunner & Guttman-Yasky, 2018). Moreover, some studies use dermatology specific questionnaires to determine QoL in healthy controls (Birdi, Cooke, & Knibb, 2020).

Studies examining the association between AD and mental health are very limited, and findings are inconsistent (Hashiro & Okumura, 1997; Slattery & Essex, 2011). These inconsistencies could be a result to varying study methodologies and other limitations such as small sample sizes and self-report of conditions without appropriate screening. Other issues include absence of statistical testing and incomplete presentation of QoL data such as descriptive statistics.

There is also lack of research on AD in the United Kingdom, despite the UK having one of the highest prevalence rates of the condition in adults (5%). The majority of previous research on QoL and mental health in AD has been conducted in France, Germany, Spain, Sweden and the USA; prevalence rates in these countries are lower (2-3%) than the UK (Harrop et al., 2007).

5.1.1 Aims

the aims of this study are to overcome some of these issues by using validated quality of life and mental health measures to explore the relationship between these variables and AD in a large UK adult population (>250 AD patients) with clinically diagnosed AD. Mental health and HRQoL in AD patients is also compared with healthy controls using measures appropriate to both populations. Exploring QoL and mental health is of potential value in performing risk-benefit analyses of precarious clinical decisions, for example, in a situation whereby systemic therapy with possible side effects is prescribed.

5.1.2 Hypotheses

This study proposed four main hypotheses:

Hypothesis 1: There are significant relationships between QoL, disease severity and mental health variables

Hypothesis 2: QoL and mental health variables is significantly more impaired in adults with AD compared to healthy people

Hypothesis 3: socio-demographic factors, disease severity and mental health significantly predicts QoL in adults with AD

Hypothesis 4: There are significant differences in adults with AD for socio-demographic and clinical factors

5.2 Methods

5.2.1 Study design

This study was cross-sectional and measured quality of life, disease severity and psychological variables using validated questionnaires in both AD and healthy control groups. NHS/HRA ethical approval (appendix 8) was gained prior to commencing data collection (REC# : 18/NE/0228).

5.2.2 Participants and Procedure

All participants were adults recruited from either a dermatology clinic in Birmingham, where they were provided a web-link by the Principal Investigator during their clinical appointments or responded to an advert on social media platforms such as Facebook & Twitter, an online Qualtrics survey panel, or Aston University. All questionnaires were completed anonymously online on Qualtrics. After reading participant information (appendix 9) and completing an online consent form (appendix 10), participants were presented with a socio-demographic questionnaire followed by validated psychometric measures assessing general quality of life (WHOQOL-BREF), psychological stress (PSS), anxiety, and depression (HADS). Participants with atopic dermatitis also completed a validated measure of disease severity (POEM) and AD related QoL (Skindex-29). All participants were asked whether they had clinically diagnosed AD or were otherwise healthy with no long-term conditions. Those with clinically diagnosed AD were asked questions surrounding their diagnosis, medication, disease duration, family history, as well as socio-demographic information.

5.2.3 Measures

Demographic and Atopic Dermatitis questionnaire

Demographic information was collected, such as age, gender, occupation and ethnic background (appendix 11). For adults with AD, information surrounding diagnosis, medication and family history was also collected.

Skindex-29

The Skindex-29, a questionnaire developed to comprehensively assess the effects of skin disease on health-related quality of life, was created by Chren, Lasek, Quinn, Mostow, & Zyzanski, in 1996.This scale consists of 30 times of which 29 questions are assigned to three scales each scored separately. The scale also provides an overall score for quality of life and covers areas surrounding emotions, functioning, and symptoms. Each question assesses the impact of the skin condition on an individual's quality of life over the previous week, with a

higher score related to a bigger impact of AD on life. The scale has good internal consistency and test-retest reliability (Cronbach's alphas > .70) (Chren, 2012) This scale was completed by people with AD and the internal consistency for this study sample was high (Cronbach's alpha=0.88).

Patient Oriented Eczema Measure (POEM)

The POEM (Charman, Venn, & Williams, 2004) is a measure that is used to subjectively assess disease severity in skin disease and focuses on the illness as experienced by the patient. PEOM is deemed suitable for use in clinical trials, epidemiological studies, outpatient clinic audit and is recommended by clinical guidelines including those issues by the National Institute for Health and Care Excellence (NICE).In order to assist clinicians and patients in understanding their POEM scores, five severity bandings have been established ranging from clear or almost clear to very severe disease; a higher score relates to more severe disease. Internal consistency for this scale is high (Cronbach alpha = 0.88), and test-retest reliability is also good , with 95% of scores falling within 2.6 points on repeat testing (mean score difference, 0.04; SD, 1.32) (Schmitt, Langan, & Williams, 2007). This scale was completed by people with AD and the internal consistency for this sample was high (Cronbach's alpha=0.87).

Perceived Stress Scale (PSS -14)

The PSS-14 measures the extent to which situations in an individual's life are appraised as stressful. . It was developed in 1983 (Cohen, Kamarck, & Mermelstein, 1983). It has been utilised in assessments of stressful situations, effectiveness of stress reducing interventions and exploration of associations between physical disorders and psychological stress. The scale has good reliability (Cronbach's alpha = .78) (Lee, 2012). PSS-14 consists of 14 items that are purported to form a unidimensional scale of global perceived stress and a higher score relates to greater distress. The PSS was completed by both AD and control groups and the internal consistency was high (Cronbach's alpha= 0.79).

Hospital Anxiety and Depression Scale (HADS)

The HADS was originally developed in 1983 by Zigmond and Snaith and is a commonly used measure for determining levels of depression and anxiety that a patient is experiencing. It is a fourteen item questionnaire that yields ordinal data. Seven items relate to depression and seven relate to anxiety. . Each question on the scale is scored from 0-3 with a higher score relating to greater anxiety or depression.. Both subscales (anxiety and depression) have been found to be internally consistent, with values of Cronbach's coefficient (alpha) being 0.80 and 0.76, respectively (Bjelland Dahl, Haug, & Neckelmann, 2002). The HADS internal consistency for this study sample was high for both anxiety and depression subscales (0.82 and 0.75, respectively). This scale was completed by both the AD group and control group.

World Health Organisation QoL Scale- Brief Version (WHOQoL BREF)

The WHOQoL-BREF (Skevington, Lofty, & O' Connell, 2004) is a 26-item QoL scale, using a 1 to 5 Likert scale, which measured four major domains: physical, psychological, social relationships and environment. There are also two one-item questions, which look at overall quality of life and satisfaction with health. The scale has good reliability for physical health, environmental and psychological domains (alphas range from 0.80 to 0.82) but only marginally good for social relationships domain (0.68). The internal consistency for this study sample was high for all sub-scales, ranging from 0.78 to 0.84. This scale was completed by both the AD and healthy control groups. .

5.2.4 Data Analyses

Statistical analyses were conducted using SPSS for Windows (version 22, SPSS, Chicago, IL, USA). Tests were carried out to explore distribution of the data normality indicators included Box-plots, Kurtosis and Shpairo-Wilk test, These indicated 14 outliers in the data which are omitted from analysis; ; the data were normally distributed with no skewness. Post-hoc power calculations with alpha set to 0.05 were computed and showed the study to have 63% power to detect differences with medium effect sizes and 99.9% power to detect differences with

large effect sizes between the AD and healthy controls. ANCOVAs, which controlled for differences in demographics, and t-tests were used to explore differences between groups, whereas Pearson's correlations were used to detect relationships across variables for continuous data and chi-squared tests were used for categorical data. Predictors of quality of life were analysed using multiple regression which adheres by a number of assumptions including: a linear relationship between QoL and the independent variables, multivariate normality, homoscedasticity and no multicollinearity. All tests carried out were two-tailed and significance levels were set at $p<0.05$or $p<0.01$. Bivariate correlations were also conducted between disease severity and QoL in AD groups

5.3 Results

5.3.1 Participant characteristics

There were 301 participants (56.5%) with AD, and 232 healthy controls (43.5%). No healthy controls had any long-term conditions including skin conditions, arthritis or diabetes. All participants with AD reported being clinically diagnosed with the condition. None of the AD participants reported any long-term physical health conditions such as arthritis or diabetes. The participant sample consisted of 390 (73.2%) female and 143 (26.8%) males, 378 (70.9%) were White, 139 (25.9%) were Asian, and 17 (3.2%) were Black. The majority of participants were aged between 25-39 (N=262, 49.2%), 131 (24.6%) participants were aged between 18-24, 124 (23.3%) were aged between 40 and 60, and 14 (2.6%) were aged 61 and above. In the AD group, 43 participants (14.3%) had been recruited via the dermatology clinic, and 258 participants (85.7%) using social media and Qualtrics panel. There were no significant differences in socio-demographic characteristics, QoL, anxiety, depression or stress between these groups. Healthy controls were recruited using social media and Qualtrics panel (table 5.1).

Table 5.1 Participant characteristics [n(%)]

	AD	Control	Total
Total	301 (56.5%)	232 (43.5%)	533 (100%)
Females	221(73.4%)	169 (72.8%)	390 (73.2%)
Males	80(26.6%)	63 (27.2%)	143 (26.8%)
White	178(59.1%)	200 (86.2%)	378 (70.9%)
Asian	115(38.2%)	23 (9.9%)	139 (25.9%)
Black	8 (2.7%)	9 (3.9%)	17 (3.2%)
18-24	78 (25.9%)	53 (22.8%)	131 (24.6%)
25-39	162 (53.8%)	100 (43.1%)	262 (49.2%)
40-60	55 (18.3%)	69 (29.7%)	124 (23.3%)
61+	5 (1.7%)	9 (3.9%)	14 (2.6%)
GP diagnosis	174 (32.6%)		
Dermatologist diagnosis	110 (20.6%)		
Paediatrician diagnosis	17 (3.2%)		
Family History	158 (52.5%)		
Child Diagnosis	132 (44%)		
Adolescent diagnosis	81 (27%)		
Adult diagnosis	87 (29%)		
Allergies	145 (48.2%)		
Asthma	140 (46.5%)		
Topical Corticosteroids	162 (53.8%)		
Emollients	139.00 (46.20%)		
Dupilumab	10.00 (3.30%)		
Calcineurin Inhibitors	34.00 (11.30%)		
Oral Corticosteroids	33.00 (11.00%)		
Antibiotics	20.00 (6.60%)		

When comparing socio-demographic characteristics, there were no significant differences across AD and control groups for occupation and gender. There were also no significant clinical and demographic differences in AD participants recruited from the dermatology clinics compared to the general population. There were however more participants aged 25-39 in the AD group (55%) compared to the control group (43%), $x^2(3) = 13.47$, $p=0.004$. There were also significantly more White participants in the control group (86.2%) compared to the AD group (59.1%), and more Asian/Indian participants in the AD group (38.2%) compared to the control group (9.9%) $x^2(2)=54.65$ $p<0.001$. Therefore, all analyses comparing groups controlled for ethnicity and age.

5.3.2 Differences in Quality of life, Stress, Anxiety and Depression between healthy controls and atopic dermatitis groups

The first set of analyses looked at differences between the healthy control group and atopic dermatitis group (table 5.2). There were statistically significant differences between AD participants and controls for physical QoL (F(1, 533)= 2.27, p<0.001 and $\eta 2p$= 0.05), overall health-related QoL (F(1,533)=26.72, p<0.001, $\eta 2p$=0.04)., and anxiety (F(1,533)=6.51, p=0.01, $\eta 2p$=0.01); those with AD reported lower QoL in these domains and higher anxiety compared to healthy control groups. There were no significant differences between both groups for environmental QoL, psychological QoL, social QoL, overall QoL, depression and stress.

Table 5.2 Quality of life, anxiety, depression and stress means scores (standard deviations) for adults with and without atopic dermatitis

	AD group M(SD)	Control group M(SD)
WHOQOL-BREF		
Overall QoL	3.32 (1.03)	3.37 (1.02)
Overall Health-related QoL	2.83 (1.14)**	3.32 (1.01)**
Physical QoL	12.1 (2.84)**	13.56 (3.19)**
Psychological QoL	11.6 (3.12)	12.14 (3.62)
Social QoL	12.71 (4.08)	13.41 (3.79)
Environmental QoL	13.28 (2.92)	13.22 (3.1)
Perceived Stress Scale	29.84 (7.19)	28.49 (8.11)
HADS anxiety	11.17 (4.09)*	10.29 (4.84)*
HADS depression	8.66 (3.84)	8.66 (4.21)

** p<0.001, *p<0.05

5.3.3 Predictors of QoL in AD patients

In participants with AD, poorer overall QoL, health-related QoL, physical, psychological, social QoL, greater stress, anxiety, depression and disease severity were significantly related with poorer AD-specific QoL . The majority of these correlations were small-medium sized(table 5.3).

Table 5.3. Pearson's correlations between atopic dermatitis specific quality of life, stress and mental health in AD groups

	Skindex	Skindex Emotions	Skindex Psychosocial	Skindex Symptoms
PSS	0.36**	0.39**	0.32**	0.29**
HAD-A	0.34**	0.31**	0.36**	0.25**
HAD-D	0.24**	0.20**	0.32**	0.07
POEM	0.68**	0.65**	0.58**	0.74**
Overall QoL	-0.18**	-0.17*	-0.22**	0.08
HRQoL	-0.33**	-0.33**	-0.26**	-0.34**
Physical	-0.38**	-0.38**	-0.37**	-0.29**
Psychological	-0.32**	-0.35**	-0.28**	-0.21**
Social	-0.16*	-0.19**	-0.16*	-0.08
Environmental	-0.08	-0.09	-0.08	-0.03

* Correlation is significant at the 0.05 (2- tailed), ** correlations significant at the 0.001 level (2-tailed)

Socio-demographic variables, mental health variables and quality of life were entered into a multiple regression model to explore the extent to which they predicted QoL measured using Skindex-29. Demographic characteristics such as age, gender, and ethnicity as well as characteristics related to AD such as concomitant conditions, medication, family history and age of diagnosis were entered first and explained 23.7% ($R^2 = 0.23$, adj $R^2=0.15$) of the variance in QoL ($F(26,248)= 2.96$, $p<0.001$). This model was significant however only the presence of allergies, asthma, and oral cortico-steroid medication significantly predicted QoL. Corticosteroid medication contributed the most towards QoL in this model.

The addition of anxiety, depression, stress, overall QoL, health-related QoL, physical, social, environmental and psychological QoL explained a further 19% ($R^2 =0.42$, adj $R^2=0.34$) variance in QoL ($F(35,296)=11.79$, $p<0.001$). The regression model was significant however only physical QoL, environmental QoL and stress significantly predicted AD-specific QoL. In this model, environmental QoL was the most important predictor of skin-related QoL.

The final model with the addition of AD severity, predicted a further 17.9% ($R^2 = 0.61$, adj $R^2=0.54$) of variance in QoL ($F(25,296)= 0.95$, $p<0.001$) This model was significant, with physical QoL, environmental QoL, stress and AD severity predicting skin-related QoL . In this model, AD severity was the most important predictor of QoL (table 5.4).

Table 5.4 Predictors of atopic dermatitis specific quality of life in adults with AD

	Unstandardized β	Standardised β	95% CI	
			Lower	Upper
Model 1				
Gender	0.12	0.06	-0.11	0.34
Topical corticosteroids	0.06	0.06	-0.07	0.19
Emollients	0.03	0.02	-0.17	0.23
Antihistamines	-0.13	-0.05	-0.49	0.24
Immunosuppressants	-0.20	-0.07	-0.59	0.18
Oral corticosteroids	0.46	0.17*	0.09	0.84
Sedating antihistamines	-0.09	-0.03	-0.66	0.47
Antibiotics	0.33	0.10	-0.18	0.85
Dupilumab	0.14	0.03	-0.46	0.74
Calcineurin inhibitors	0.19	0.07	-0.19	0.57
Diagnosis	0.05	0.03	-0.16	0.26
Allergy	-0.23	-0.14*	-0.44	-0.03
Asthma	0.26	0.15*	0.05	0.46
Food allergy	0.17	0.09	-0.07	0.41
Ethnicity	0.36	0.21	0.10	0.62
Age	0.09	-0.01	-0.26	0.23
Family history	-0.03	-0.02	-0.23	0.17
Model 2				
Gender	0.08	0.04	-0.13	0.28
Topical corticosteroids	0.06	0.06	-0.05	0.17
Emollients	0.05	0.03	-0.13	0.24
Antihistamines	-0.13	-0.05	-0.46	0.20
Immunosuppressants	-0.27	-0.10	-0.63	0.08
Oral corticosteroids	0.36	0.13	0.02	0.71
Sedating antihistamines	0.01	0.00	-0.50	0.52
Antibiotics	0.34	0.10	-0.12	0.81
Dupilumab	0.10	0.02	-0.44	0.63
Calcineurin inhibitors	0.20	0.07	-0.14	0.54
Diagnosis	0.06	0.03	-0.14	0.24
Allergy	-0.17	-0.10	-0.36	0.01
Asthma	0.27	0.16	0.08	0.45
Food allergy	0.06	0.03	-0.15	0.28
Ethnicity	0.12	0.07	-0.14	0.39
Age	0.12	0.07	-0.10	0.35
Family history	-0.01	-0.01	-0.20	0.19
Stress	0.02	0.15*	0.00	0.04
Anxiety	0.03	0.14	0.00	0.06
Depression	0.03	0.12	-0.01	0.07
Physical QoL	-0.07	-0.24**	-0.12	-0.03
Psychological QoL	-0.02	-0.06	-0.07	0.04
Social QoL	-0.01	-0.06	-0.04	0.02
Environmental QoL	0.09	0.30***	0.04	0.14
Overall QoL	0.10	0.11	-0.02	0.21
Health-related QoL	-0.07	-0.09	-0.18	0.05
Model 3				
Gender	0.02	0.01	-0.15	0.19
Topical corticosteroids	0.02	0.02	-0.08	0.11
Emollients	0.07	0.04	-0.08	0.22
Antihistamines	-0.04	-0.02	-0.32	0.23

Immunosuppressants	-0.19	-0.07	-0.49	0.11
Oral corticosteroids	0.20	0.07	-0.09	0.49
Sedating antihistamines	-0.19	-0.05	-0.62	0.23
Antibiotics	0.19	0.06	-0.19	0.58
Dupilumab	0.14	0.03	-0.31	0.59
Calcineurin inhibitors	0.09	0.03	-0.20	0.37
Diagnosis	0.10	0.06	-0.06	0.26
Allergy	-0.19	-0.11	-0.34	-0.03
Asthma	0.06	0.04	-0.10	0.22
Food allergy	0.11	0.06	-0.07	0.29
Ethnicity	0.09	0.05	-0.13	0.31
Age	0.20	0.11	0.01	0.38
Family history	0.06	0.03	-0.10	0.22
Stress	0.02	0.13*	0.00	0.03
Anxiety	0.02	0.09	-0.01	0.04
Depression	0.01	0.03	-0.02	0.04
Physical QoL	-0.06	-0.21**	-0.11	-0.02
Psychological QoL	-0.03	-0.10	-0.07	0.01
Social QoL	-0.01	-0.05	-0.03	0.01
Environmental QoL	0.06	0.20**	0.02	0.10
Overall QoL	0.07	0.09	-0.02	0.17
Health-related QoL	0.04	0.05	-0.06	0.13
Disease severity	0.07	0.53***	0.06	0.08

*p<0.05, **p<0.01, ***p<0.001

Further analyses were conducted with each of the Skindex subscales- psychosocial functioning, emotions, and symptoms- as outcome variables. Disease severity and Physical QoL significantly explained 31% ($R^2 = 0.62$, adj R^2=0.57) % of the variance in AD Symptoms (F(35, 296)= 12.13, p<0.001), as measured by Skindex-29. Depression, disease severity, physical QoL, and environmental QoL significantly explained 33% (($R^{2=}$ 0.54, adj R^2=0.48) of the variance in psychosocial functioning (F(35,296)=8.73, p<0.001). Finally, disease severity, physical QoL, psychological QoL, and environmental QoL explained 34% (($R^2 = 0.57$, adj R^2=0.51) of the variance in the Emotions sub-scale. Disease severity was the most important predictor of QoL scores for both the symptoms and emotions sub-scales (Standardised β= 0.6 and 0.51, respectively).

5.3.4 Differences in socio-demographic and atopic dermatitis characteristics

For the following analyses, in order to address the likelihood of type 1 errors, a stringent significance value of 0.01 was adopted instead of 0.05. Quality of life in this section is

measured using the Skindex instrument. There was a statistically significant difference between severity of AD and skin-related QoL ($F(4,296)= 59.23$, $p<0.001$) with post-hoc tests illustrating that this difference lay between all five categories of the POEM index; clear, mild, moderate, severe, very severe and QoL. Those with clear AD ($M=1.7$, $SD=0.65$) reported significantly better QoL compared to those with mild AD ($M=2.4$, $SD=0.7$), moderate AD ($M=3.0$, $SD=0.64$), severe AD ($M=3.69$, $SD=0.57$) and very severe AD ($M=4.14$, $SD=0.88$).

Socio-demographic and atopic dermatitis specific differences were sought for disease severity, anxiety, depression, stress and QoL; only significant findings have been reported in this section. Those with asthma reported significantly higher AD severity levels than those without asthma ($t(275)=-5.38$, $p<0.001$). They also reported significantly lower QoL than those without asthma ($t(275)=-3.74$, $p<0.001$). Participants who suffered from food allergy alongside their AD also reported poorer QoL compared to those who didn't ($t(299)=-3.75$, $p<0.001$), and higher self-reported AD severity compared to those who reported not suffering from food allergies ($t(299)=-3.58$ $p<0.001$). Table 5.5 reports means and standard deviations for the significant differences detailed in this section.

There was a significant difference between age of diagnosis and disease severity, whereby those diagnosed as children had higher severity of AD than those diagnosed as an adolescent or adult ($f(2,297)=8.91$, $p<0.001$). Post-hoc tests showed that the difference lay between diagnosis as a child and adult ($p<0.001$). There were no significant differences between being diagnosed as child, adolescent or adult and QoL, stress, anxiety or depression.

When exploring the type of medication taken by AD patients, those on topical corticosteroids reported significantly lower QoL ($t(295)= -4.05$, $p(0.001)$ and higher disease severity ($t(295)=-5.89$, $p<0.01$) than those who reported not taking topical corticosteroids. Additionally those who took antihistamines also reported lower QoL ($t(296)=-2.08$, $p=0.009$) and higher AD severity ($t(296)=-2.75$, $p=0.006$) compared to those who did not. Similarly AD participants who were prescribed immunosuppressant medication also reported lower QoL ($t(296)=-2.56$,

p=0.01) and higher disease severity (t(296)=-3.052, p=0.002) compared to those who did not. Participants who were prescribed oral corticosteroids also reported lower QoL (t(296)=-5.401, p<0.001) and higher disease severity (t(296)=-5.72, p<0.001). compared to those who were not.

Those who took medication to help them sleep also reported lower QoL (t(296)=-2.64, p=0.009) and higher disease severity (t(296)=-4.103, p<0.001) compared to those who were not prescribed this medication. Participants on Dupilumab reported lower QoL (t(296)=-2.164, p=0.004) compared to those not prescribed this medication. Finally, those on calcineurin inhibitors reported lower QoL (t(296)=-3.64, p=0.001) and higher severity (t(296)=-3.65, p<0.001) compared to those not on this medication.

There was a significant difference between ethnic groups for severity, depression, and QoL. Asians reported higher disease severity (F(2,298)=5.2, p=0.006), compared to White and Black participants. Asian participants also reported lower QoL(F(2,298)=7.04, =0.001) compared to White and Black participants. White participants reported higher depression levels (F(2,298)=3.52, p=0.001) compared to Asian and Black participants.

When exploring gender differences, female participants reported significantly higher AD severity (t(299)=-2.7, p=0.007), and lower QoL (t(299)=-2.81, p=0.005) compared to males. However males reported higher depression levels compared to females (t(299)=2.16, p=0.002). Participants who were not currently under the supervision of a dermatologist reported significantly better QoL compared to those who were. Finally, there was also a significant negative relationship between stress and age, whereby increasing age was related to lower stress levels (r=-0.14, p=0.012), this was a small-sized correlation.

Table 5.5 Mean scores with standard deviations for differences between socio-demographic groups and AD specific characteristics.

	White [M(SD)]	**Asian [M(SD)]**	**Black [M(SD)]**
AD Severity	15.52 (6.28)	18.67 (8.46)	12.75 (8.32)
QoL	3.21 (0.85)	3.54 (0.84)	2.75 (1.11)
Depression	9.11 (3.65)	7.92 (4.02)	7.80 (4.23)
	Female [M(SD)]	**Male [M(SD)]**	
AD Severity	16.93 (6.82)	14.58 (6.25)	
QoL	3.40 (0.86)	3.01 (0.86)	
Depression	8.35 (4.01)	9.45 (3.23)	
Differences between groups for quality of life			
	Yes [M(SD)]	**No [M(SD)]**	
Antihistamines	3.60 (0.83)	3.20 (0.86)	
Asthma	3.46 (0.81)	3.09 (0.87)	
Calcineurin Inhibitors	3.76 (0.73)	3.26 (0.86)	
Dupilumab	3.91 (0.31)	3.30 (0.87)	
Food Allergy	3.59 (0.82)	3.26 (0.87)	
Immunosuppressants	3.67 (0.84)	3.27 (0.86)	
Oral Corticosteroid	4.06 (0.62)	3.23 (0.85)	
Sedating Antihistamine	3.80 (0.73)	3.28 (0.87)	
Topical Corticosteroids	3.50 (0.90)	3.10 (0.77)	
Differences between groups for disease severity			
	Yes [M(SD)]	**No [M(SD)]**	
Antihistamines	19.11 (6.66)	15.88 (6.66)	
Asthma	18.02 (6.39)	13.91 (6.33)	
Calcineurin Inhibitors	20.17 (5.01)	15.78 (6.77)	
Children Diagnosis	17.90 (6.8)	14.32 (6.26)	
Corticosteroids	13.88 (5.96)	18.88 (6.73)	
Food Allergy	18.32 (6.92)	15.39 (6.47)	
Immunosuppressants	19.60 (6.73)	15.86 (6.63)	
Oral Corticosteroids	22.30 (4.75)	15.53 (6.58)	
Sedating Antihistamine	21.95 (5.54)	15.86 (6.63)	

5.4 Discussion

Measurement of QoL has drawn a lot of attention recently in patients with chronic skin diseases. Both health care professionals and researchers have attempted to evaluate the QoL of patients with AD using various methods, with many studies showing that patients with AD experience severe impairment in their QoL and emotional well-being compared with a healthy general population (Lundberg et al., 2000, Maksomoc et al., 2002; Holm et al., 2006).

It is not surprising that AD has a great impact on HRQoL because of the chronic clinical course of the disease. Since it has no definitive cure, patients with AD suffer not only from the

symptoms caused by the disease itself, but also from a high and life-long psychosocial and economic burden (Hay et al., 2014; Dalgard et al., 2015; Blome et al., 2016).

This study investigated the association of AD with HRQoL and several psychological variables in adults living in UK. Adults with AD reported lower physical and health-related quality of life compared to healthy controls. These findings are in line with the systematic review and meta-analysis reported in chapter 3, that explored QoL in adults with AD and found that all studies included in the review reported lower QoL in AD patients compared to healthy controls (Birdi, Cooke, & Knibb, 2020). Physical QoL may be affected to a greater extent due to the physical discomfort and pain that arises as a result of AD (Mozzafari et al., 2007; Vakharia et al., 2017). However, when using generic QoL measures such as the SF-36, physical QoL is affected to a lesser extent compared to mental QoL (De Korte Mombers, Bos, & Sprangers, 2004). This may be due to generic measures not being sensitive enough to measure the physical limitations of AD e.g. questions relating to walking abilities are unlikely to be relevant to an AD group (chapter 3; Birdi, Cooke, & Knibb, 2020). A number of studies have also used dermatology-specific measures such as the DLQI to compare QoL in AD patients and healthy controls (e.g. Mozzafari et al., 2007; Linnet & Jemec, 1999; Noh et al., 2013; Silverberg et al., 2018). The DLQI is a dermatology specific questionnaire with questions that are not suitable for use in a sample of the general population. In a critical review of dermatology specific and generic HRQOL measures in dermatology, the WHOQOL-bref has been deemed a promising generic measure (Both et al., 2007) above and beyond other measures such as SF-36.

This study also found that AD patients reported higher levels of anxiety compared to healthy controls, but no significant differences were found between the two groups for stress and depression. The incidence of mental health issues among dermatological patients has been found to be approximately between 30% and 40% (Ghosh, Behere, Sharma, & Sreejayan, 2013). Most frequent symptoms reported as a basis for distress and anxiety are disfigurement and itching causing significant insomnia, and sleep deprivation leading to fatigue, mood lability, impaired functioning and suicide in a few cases (Gilchrest , 1982). Furthermore,

frequent bullying and embarrassment due to disfigurement leads to social stigma and social isolation. Disfigurement caused by AD can lower patients' self-esteem, in turn increasing the propensity to suffer from anxiety and depression (Nyugen, Koo, & Cordoro, 2016; Wittkowski, Richards, Griffiths & Main, 2004). However, many studies, like this study, report conflicted findings when exploring anxiety and depression in AD patients (Slattery & Essex, 2011; Thyssen et al., 2018; Whiteley, Emir, Seitzman, & Makinson, 2016;).It is likely that the combination of social isolation, anxiety, depression and disease severity forms a vicious cycle in those with AD (Oh et al., 2010) The inconsistency in findings between AD and depression and anxiety disorders may be due to the various study methodologies including varying anxiety/depression scales and limitations in previous studies including the use of non-validated symptom questionnaire instead of validated measures. Furthermore, many of the studies mentioned above did not adjust for atopic comorbidities and demographic characteristics in their analyses.

Disease severity was associated with stress, anxiety, depression and QoL, such that more severe AD was related to higher stress, anxiety, depression and QoL. Disease severity also significantly predicted QoL even after controlling for demographic characteristics and AD-specific characteristics. This finding is consistent with the systematic review in chapter three which found that higher disease severity was significantly related to poorer QoL in the majority of the studies. The studies in the review were largely based on small sample sizes and recruited through dermatology clinics only. This larger-scale study recruiting from both dermatology clinics and general population using POEM to assess disease severity, the preferred core tool for assessing patient-reported symptoms in AD trials (Chalmers et al., 2016; Spuls et al., 2016), adds further support to this finding. Severe AD can decrease sexual desire, affect interpersonal relationships, reduce work productivity and affect leisure and social activities(as was found and discussed in chapter 3). Those affected by AD are more restless in their sleep, wake more often, spend less time asleep and report daytime fatigue (Jafferany,

2007; Picardi, Mazzotti & Pasquini, 2006). These factors offer potential explanation for the relationship between disease severity and psychological health.

Although psychological variables and disease severity predicted quality of life to a greater degree than socio-demographic variables, the impact of clinical and psychological variables on AD need to be explored in greater detail. Some earlier explorations have ascertained that psychological factors are correlated with clinical manifestations in AD (Badia, Mascaro, & Lozano, 1999; Eun & Finlay, 1990; Linnet & Jemec, 1999) although they suffer from methodological issues including the lack of reliable and valid clinical measures of QoL and AD severity in addition to the use of aggregated scores from AD samples (Badia, Mascaro & Lozano, 1999; Eun & Finlay, 1990). WHOQoL-BREF was included as a QoL measure in the regression model to predict skin-related QoL due to the different aspects of an individual's daily life being explored by both these measures; the generic measure focuses on general daily life activities that are applicable to the majority of a population, whereas the Skindex is primarily focused on the impact of living with skin conditions. This study found that corticosteroid use was a significant predictor of QoL even after controlling for psychological and demographic variables. Although not reported before, it is not surprising as even short-term administration of topical corticosteroid may interfere with collagen production and result in skin atrophy, hypopigmentation or secondary infection, especially with long-term use (Kang et al., 2001). Allergic sensitization also predicted QoL even after controlling for demographic and psychological variables, contrary to previous research that has found no significant influence of allergy on QoL in AD patients (Holm, Agner, Clausen, & Thomsen, 2018).

When exploring demographic and AD-specific characteristics, this study found that those diagnosed as children and adolescents reported higher disease severity than those diagnosed as adults. This may imply that factors earlier on in patients' lives had a long-lasting impact on their disease severity (Ben-Gashir, Seed, & Hay, 2004). Follow-up studies are needed to measure the association over a longer period. Participants in this study prescribed topical/ oral

corticosteroids, antihistamines, immunosuppressants, sedating antihistamines, antibiotics, dupilumab, and/or calcineurin inhibitors to manage their AD reported lower QoL and higher disease severity compared to those who were not on these medications. These is a notable lack of exploration of the impact that standard therapy has on participant QoL in AD. Charman, Chambers, and Williams (2003) conducted a systematic database search and found that quality of life was assessed in only three clinical trials. As there is no remedy available that can cure AD and repeated treatments are necessary to achieve a stable and convenient skin condition, the most important factor to the patient, however, is the question 'which treatment improves the individual's quality of life the best?' (Schiffner et al., 2003). One can assume that the use of different medications should have lowered disease severity in participants in this study, however in this study, medication was related to worse AD severity. Many factors such as side effects, length of time taking the medication ('treatment hopping'), and strength of medication could explain why those taking these medications reported increased disease severity (Hoare, Li, & Williams, 2000; Schiffner et al., 2003).

This study found increased disease severity and lower QoL in Asian participants compared to White and Black participants. This finding has been reflected in previous literature where Asians tend to present more severe skin symptoms such as lichenification (thickening of the skin) compared to Whites (Leung, 2015; Noda et al., 2015) and are at higher risk for developing post-inflammatory dyspigmentation (Alexis, 2007; Alexis, 2014). Hyperpigmentation of the skin is often more visible in black and minority ethnic patients as a result of the contrast with normal skin tone (Child et al., 1999; Ortonne, 2008) Often, the resulting dyspigmentation may be more distressing than the skin findings of AD itself. The use of common disease severity scales such as SCORAD and EASI that rely on the measurement of skin plaques (erythema) dramatically underestimate the severity of AD in darker skin types (Ben-Gashir, 2002; Vachimaron et al., 2012). This study also found that White participants scored higher on the depression scale compared to ethnic minority groups. This is a finding that has not been reflected or explored in the past, but White adults have

been found to be more willing to report suffering from depressive symptoms compared to their minority-ethnic counterparts (Alergria et al., 2008; Sidney et al., 2011; Young et al., 2001).

Females in this study also reported higher disease severity and lower QoL compared to males. This finding is in line with Holm et al (2004) who found that QoL in women are impacted more than men as a result of AD lesions located in visible areas of the body. It can be speculated that women have a higher culturally determined ideal of physical appearances compared to men and as a result pay more attention to their skin, therefore increasing the sensitivity of self-reported skin involvement. Males in this study however, reported higher levels of depression compared to females. This is contrary to a gender-specific association with AD and depression suggested by Timonen et al. (2003) where biological factors may explain higher rates of depression in females than males. The majority of adults with AD in this study were aged between 25-39 and the severity of AD tended to decrease with age.. This is a finding in line with other studies on age-related changes in the severity of AD which appear to decrease with age (Harrop et al., 2007; Kim et al., 2015). Nonetheless, as skin-barrier function often does not recover with age in genetic AD, its' symptoms persist up until adulthood (Cork et al., 2009) reinforcing the fact that adults with AD need regular life-long monitoring.

5.4.1 Strengths and limitations

This study has a number of strengths. Firstly, it is the largest population based study on adults with AD in the UK to date. The use of a culturally diverse sample and adjusting for a number of socio-demographic factors, as well as using a number of recruitment techniques, enabled generalisation of the findings in the UK population, unlike the majority of current studies which recruit primarily using dermatology clinics. A survey conducted in Nottingham found that only 6% of patients with AD were referred for specialist advice in a 12 month period, the exact reasons for referral were not reported (Emerson, Williams, & Allen, 1998). Only cases of severe or difficult AD are often referred to a dermatologist where there is a lack of adequate progress despite use of adequate quantities of emollients/topical steroid preparations according to NICE. More recently, Schofield, Grindlay, and Williams (2009) found that GPs

only refer approximately 6.1 % of the dermatological cases they see to secondary care. Considering the above, it is important to use recruitment strategies above and beyond dermatology clinics and this is one of the very few studies that utilises other means of recruitment to complement dermatology clinics. Future work should aim to include participants recruited through a variety of platforms, such as social media, to ensure that a generalisable group of participants has been studied and adults with wider-ranging AD can take part in such studies. As mentioned above, this study used well-validated assessments of AD severity and controlled for multiple confounding variables in multivariate models. POEM, WHOQoL-BREF, HADS, PSS and Skindex have been found to have excellent overall face validity, construct validity, internal consistency, reliability and/or responsiveness. Additionally POEM is the preferred assessment of AD symptoms for clinical trials by the Harmonising Outcome Measures in Eczema group (Chalmers et al., 2014; Coutanceau & Stalder, 2014; Heinl et al., 2017; Vakharia et al., 2018), and this study used Skindex as opposed to DLQI- the more commonly used QoL instrument- for a number of reasons. Skindex-29 has better sensitivity to clinical severity with minimal floor effect (Fernandez-Penaz et al., 2012, higher rating of skin involvement than using the DLQI (Wervers et al., 2017) and of the dermatology-specific HRQOL tools, it has been deemed the most optimal available instrument (Both et al., 2007).

This study has some also has some limitations, such as the use of surveys, which may be subject to false answers, giving the same answer repeatedly and receiving multiple surveys completed by the same responder (Silverberg, 2018). These however were not thought to be major concerns, given that less than 1% of surveys had the same responses for all the questions, and over 90% of surveys took 10 minutes or longer to complete. Additionally, this study relied on self-reporting of AD diagnosis, and although relevant questions that assessed symptoms, diagnosis and clinical characteristics were asked, there may have been a number of participants in the study who were not clinically diagnosed with the condition. Given the cross-sectional design of the study, it is difficult to ascertain the directionality of the

associations observed, although these relationships may be bidirectional. Future studies are warranted to address these points.

5.5 Conclusion and directions for future research

This study found that the severity of AD is significantly related to poorer QoL and mental health in a large UK sample. More severe AD was associated with worse mental health and QoL. The findings of this study emphasize the importance of the incorporation of mental health symptoms and QoL in clinical practice in order to determine disease burden and identify patients with anxiety and/or depression alongside their AD. Additionally, as some groups appear to be more affected psychologically due to their condition, psychological and pharmacological interventions to target these populations are necessary.

Chapter six: A prospective feasibility analysis of the relationship between psychological stress and atopic dermatitis

6.1 Introduction

This chapter presents findings of a longitudinal feasibility study exploring the relationship between psychological stress and AD severity in adults. As mentioned in the introduction chapter and elsewhere, AD severity and psychological stress appear to form a vicious cycle (Hashizume & Takigawa, 2006). Nonetheless, it remains unclear how stress affects AD. The hypothalamic-pituitary-adrenal (HPA) axis is found to be stimulated by psychological stress, which influences the development and progression of AD, causes epidermal barrier dysfunction, and lowers the itch threshold (Arndt, Smith, & Tausk, 2008).

Numerous studies have found that the severity of AD and psychological stress are related. Early evidence for the this relationship suggested that the emotional stress related to a major life event is associated with the development of AD symptoms (Brown, 1972; Greenhill & Finesinger, 1942; Lammintausta, Kalimo, & Raitala, 1991; Wittkower & Russel, 1953). These studies however used interviews or validated questionnaires to assess psychological stress, which included parental divorce, family problems during childhood or death of a loved one. These findings should be interpreted with caution however due to lack of accuracy of individuals' ability to recall childhood events or the time at which these events occurred may be too unreliable for accurate data to be obtained.

Psychological stress is known to affect the immune and neuroendocrine systems, which are responsible for releasing hormones that regulate numerous systems such as heart rate, digestion, blood pressure and respiration (Ardnt, Smith, & Tausk, 2008). The skin barrier function is also negatively affected by psychological stress, which in turn could give rise to increased loss of moisture from the skin and susceptibility to infection. A compromised skin barrier is prevalent in those with AD as a result to reduced amount of the protein filaggrin, which plays an important role in the formation and structure of skin layers. Psychological stress

in AD patients may further reduce the skin's ability to retain water and keep bacteria out (Arndt, Smith, & Tausk, 2008) Additionally living with a long-term condition such as AD can induce psychological stress and negatively impact QoL. Psychological stress is also one of the most commonly reported mental health issue by AD patients although little is known about how it contributes to the exacerbation of AD.

Several cross-sectional studies illustrate significant relationships between psychological stress and disease severity in AD (Kimyai-Asadi & Usman, 2001; Oh et al., 2010; Picardi & Abeni, 2001; Wright, 2005). Although these studies are cross-sectional, most report that psychological stress exacerbates AD, with patients experiencing a worsening of symptoms following exposure to stress (Buske-Kirschbaum, Geiben, Hölligm, Morschhäuser, & Hellhammer, 2002; Hashizume & Takigawa, 2006; Kimata, 2003). This association has been well established in children and adolescents however there are a lack of population-based studies focusing on adults (Simpson, 2012; Silverberg & Hanifin, 2013).

There is only one known published study (King & Wilson, 1991) that examined the relationship between stress and AD longitudinally. The authors found that interpersonal stress on day X significantly predicted severity of AD on day X+1 using lag-sequential analyses. This relationship was reciprocal as AD severity on day X also indicated stress level on day X+1. A diary technique was used in this fortnight long study of 50 participants. This chapter builds on King and Wilson (1991)'s findings by incorporating daily diary measures which may be too sensitive to detect changes, with weekly validated and robust psychometric measures of mental health and disease severity. Additionally, unlike this study, King and Wilson recruited through dermatology clinics only, which may result in stress and disease severity scores that are not generalizable to the majority of adults with AD living in the UK (Schofield, Grindlay, & Williams, 2009).Additionally, measuring psychological stress for two weeks may not be sufficient to detect changes in disease severity, as opposed to measuring this over a longer period of time as is the case in this study.

Notably, AD patients may suffer from increased stress levels as a result of the chronic condition or due to social skill deficit (Buske-Kirschbaum et al., 2004). The contribution of psychosocial stress in both maintaining and exacerbating AD is also emphasised by the effectiveness of psychotherapeutic interventions that incorporate relaxation techniques or stress management, which have led to significant improvement of AD symptoms (Chida, Steptoe, Hirakawa, Sudo, & Kubo, 2007).

A consistent finding is that psychosocial stress and skin condition in AD appear to be highly related (Buske-Kirschbaum, Geiben & Hellhammer, 2001; Chida, Hamer, & Steptoe, 2008). Stressful situations are often accompanied by exacerbation of AD symptoms; however, worsening of skin condition may also elicit higher levels of psychological stress. Consequently, a vicious circle of emotional stress and skin condition can be initiated (Buske-Kirschbaum, Geiben, & Hellhammer, 2001; Senra & Wollenberg, 2014). Exploring this direction of psychological stress and AD further is needed as most existing research on psychological stress and AD in adults is cross-sectional, thus warranting the need for a longitudinal approach.

Using a prospective design, it may be possible to overcome some of the limitations present in retrospective studies. Indeed, all studies focusing on AD, with the exception of King and Wilson (1991) ask participants to recall stressful events that happened in the past and this can range from a week to a year. Major stressful events may be better recalled, such as an earthquake (Kodama et al., 1999; Losiak, Blaut, Kłosowska, & Losiak-Pilch, 2019), however minor daily stressful events that could contribute to the exacerbation of AD may be forgotten with time when conducting a retrospective study with patients. Stress itself can interfere (Kuhlmann, Piel & Wolf, 2005). Costa, Zonderman, and McRae (1987) and Lida, Shrout, Laurenceau, and Bolger (2012) suggest the use of daily diaries to document AD symptoms in order to reduce retrospective recall bias.

This feasibility study adheres to Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (Elm et al., 2007). The STROBE Statement is a checklist

of 22 items that aids in the reporting of non-randomised pilot and feasibility studies (appendix 12). The checklist compromises of 21 items which include the title, abstract, introduction, methods, results and discussion section. .

The aims of this study were to:

• assess the feasibility of a longitudinal approach using daily diaries

• gauge how many adults with AD will complete diaries and measures for the 3 month duration and how many drop out of the study

• explore the temporal relationship between psychological stress and atopic dermatitis severity measured daily using diaries and weekly using validated psychometric instruments

- explore the temporal relationship between psychological variables (anxiety and depression) measured weekly using validated psychometric instruments and disease severity

6.2 Methods

6.2.1 Study design

This quantitative prospective study used validated measures of psychological variables and AD severity in AD patients completed weekly, in addition to daily stress and symptom diaries. The Life and Health Sciences Research Ethics Committee at Aston University granted the study ethical approval (appendix 13) prior to commencing data collection (application no. 1428). All participants provided informed consent (appendix 14) before taking part.

6.2.2 Participants

Participants clinically diagnosed with atopic dermatitis, and aged 18 and above were all eligible for the study. Participants were recruited from October 2018 to December 2019, and a total of 19 participants with complete data were retained for analysis.

6.2.3 Measures

Demographic and Atopic Dermatitis questionnaire

Socio-demographic information was collected (appendix 15), such as age, gender, occupation and ethnic background including AD-specific information surrounding diagnosis, medication and family history.

Patient Oriented Eczema Measure (POEM)

The POEM (Charman, Venn, & Williams, 2004) is a subjective disease severity measure that is widely used in AD research. It focuses on the illness as experienced by the patient and has five severity bandings, with a higher score related to more severe disease. The POEM was completed by participants at the end of each week for 12 weeks and had high internal consistency for this sample (alpha=0.82)

Perceived Stress Scale (PSS -14)

The PSS-14 is a 14 item validated questionnaire developed in 1983 (Cohen, Kamarck, & Mermelstein, 1983) that measures the degree to which one's situations in life are appraised as stressful.. It is widely used in cross-sectional research and assessed the stressfulness of situations and the effectiveness of stress-alleviating interventions The PSS was completed at the end of each week for 12 weeks and had high internal consistency for this study (alpha=0.85).

Hospital Anxiety and Depression Scale (HADS)

The HADS was originally developed by Zigmond and Snaith (1983) Is a commonly used psychometric measure to assess levels of anxiety and depression in patients. The HADS consists of fourteen items, seven of which relate to anxiety and 7 focus on depression. A higher score relates to greater anxiety or depression. The HADS internal consistency for this

study sample was high for both anxiety and depression subscales (0.82 and 0.75, respectively). This scale was completed once weekly for the 12 week period.

Stress diary

A modified version of King and Wilson (1991)'s diary was used. The diary consisted of a series of questions that assessed interpersonal stress. The diary was modified slightly and included a question on sleep (appendix 16), which has been identified in research as an issue for people with this condition (Kelsay, 2006; Chamlin et al., 2005). For those questions concerned with emotional reactions such as anger, participants rated their responses on a 3-point scale (0- no, 1- a little, 2- a lot). Secondly, participants were asked to state what AD related symptoms they have suffered from and rate the severity of their AD on a three-point scale (0- mild, 1- moderate, 2-severe). Finally, participants were also asked to rate how well they slept the previous night on three-point scale (0- slept well, 1-somewhat, 2- not at all). Participants were asked to complete these diaries for one month, each night prior to retiring for sleep. These participants were instructed to avoid missing days when completing the diary, In order to avoid inaccurate recall at a later stage.

6.2.4 Recruitment and Procedure

Participants were recruited from Facebook through AD support groups. Participant information sheets, consent forms, diaries and questionnaires were posted to participants who responded to the study advert to their home addresses with pre-paid envelopes for participants to send back to the researcher. After reading participant information sheets (appendix 17) and completing written consent, participants completed the demographic questionnaire and validated psychometric measures at baseline. They then completed the daily measures and weekly measures for 12 weeks. Participants were asked to join a study-specific Facebook group where they were sent weekly reminders to complete the measures.

6.2.5 Data Analyses

Statistical analyses were conducted using SPSS for Windows (version 23, SPSS, Chicago, IL, USA). Correlational analyses were conducted between AD severity and psychological variables for each week. Additionally, a cross-lagged panel model (CLPM) analysis was conducted to examine the ability of interpersonal stress to predict skin symptoms on the next day for each participant and vice-versa.

6.3 Results

6.3.1 Participant sample characteristics

Thirty-six participants were initially recruited and sent study packs of which 21 participants returned study packs to the researcher. Nineteen participants out of 21 had no missing data (Figure 6.1). The researcher was unable to perform drop-out analyses as the 15 participants who did not complete the study did not send the study packs back to the researcher. Therefore, data from 19 participants have been analysed. All 19 participants were recruited through social media. All participants reported being clinically diagnosed with the condition and none of the participants reported any long-term physical health conditions such as arthritis or diabetes. The participant sample consisted of all females, 14 (73.7%) were White and 5 (26.3%) were Asian. An equal number of participants were aged between 25-39 (N=8, 42.3%) and 40-46 (N=8, 42.3%), 3 (15.4%) participants were aged between 18-24.. Fifteen participants (N=15, 78.9%) reported being diagnosed with AD by a dermatologist and four participants (N=4, 21.1%) were diagnosed by their GP. Fifteen participants (N=15, 78.9%) reported family history of the condition. All 19 participants reported one or more concomitant atopic condition alongside their AD; 17 (89.5%) had hay fever, 14 (73.7%) reported asthma, and 11 (57.9%) reported suffering from food allergies. Eight (42.1%) reported suffering from all three conditions in addition to AD. There were no significant differences in age distributions, ethnicity, diagnosis or concomitant conditions between participants.

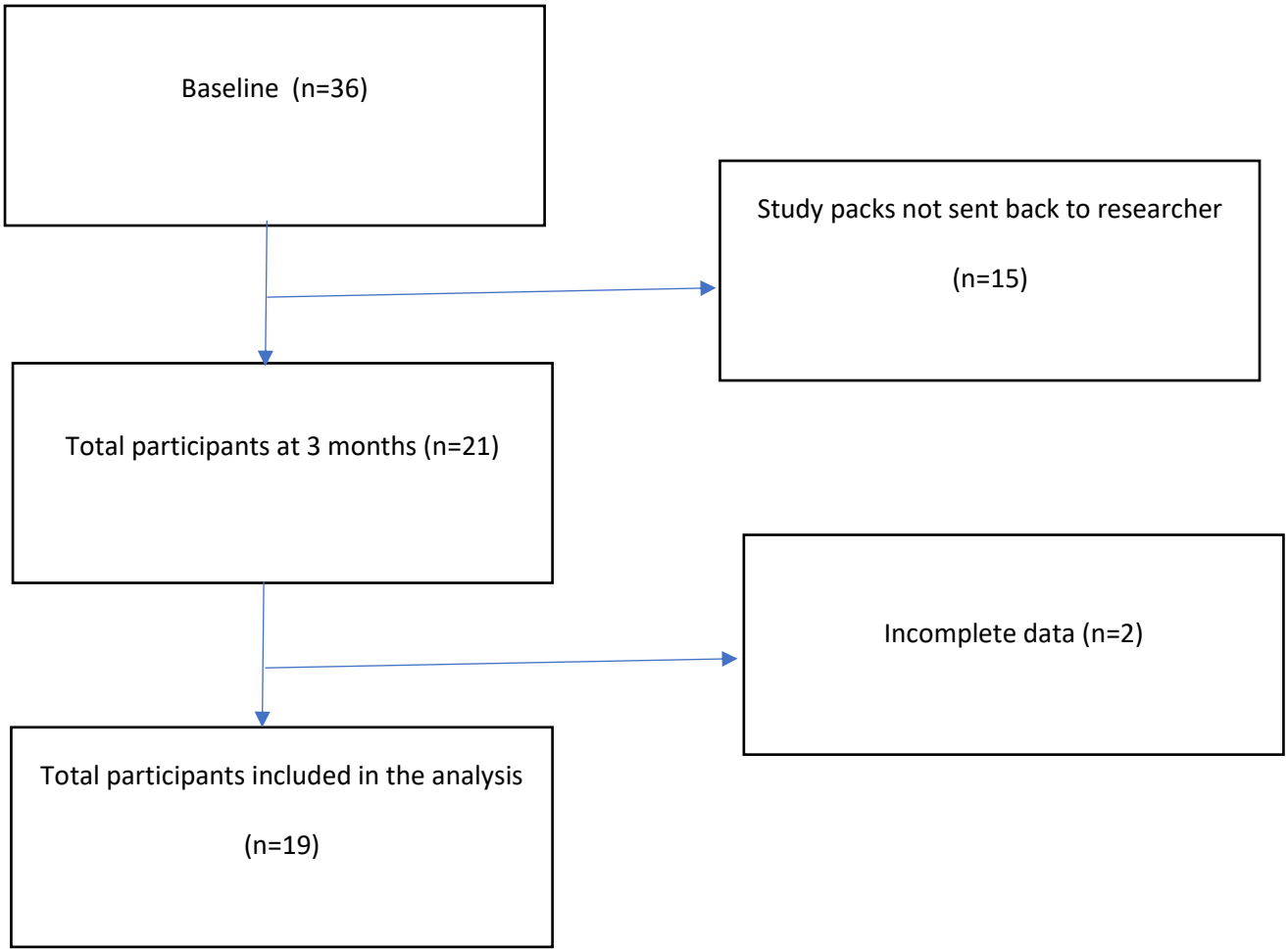

Figure 6.1 Feasibility study recruitment flow chart

6.3.2 Feasibility of the procedure

The nineteen participants completed all measures and there were no missing data for the weekly or daily questionnaires. All but one of the participants completed the questionnaires without needing assistance/clarification. One participant wanted to clarify the time at which weekly questionnaires needed to be completed. Completion of the diaries required approximately five minutes a night, whereas completion of weekly questionnaires required approximately fifteen minutes to complete. Prior to participants being recruited, a study poll on Facebook suggested a high level of interest from members of an AD support group. All participants were recruited within a month through social media and communicated frequently

with the researcher through this platform and via email. The study advertisement was posted on Facebook several times following the study poll.

6.3.3 Weekly correlations and predictions between disease severity and psychological variables

Mean disease severity, depression, stress and anxiety scores for each week were plotted on a line graph (figure 6.2) in addition to an illustration of one participant's scores (figure 6.3). Although the figure does not show a clear pattern between disease severity and psychological variables, there were several significant correlations between the variables.

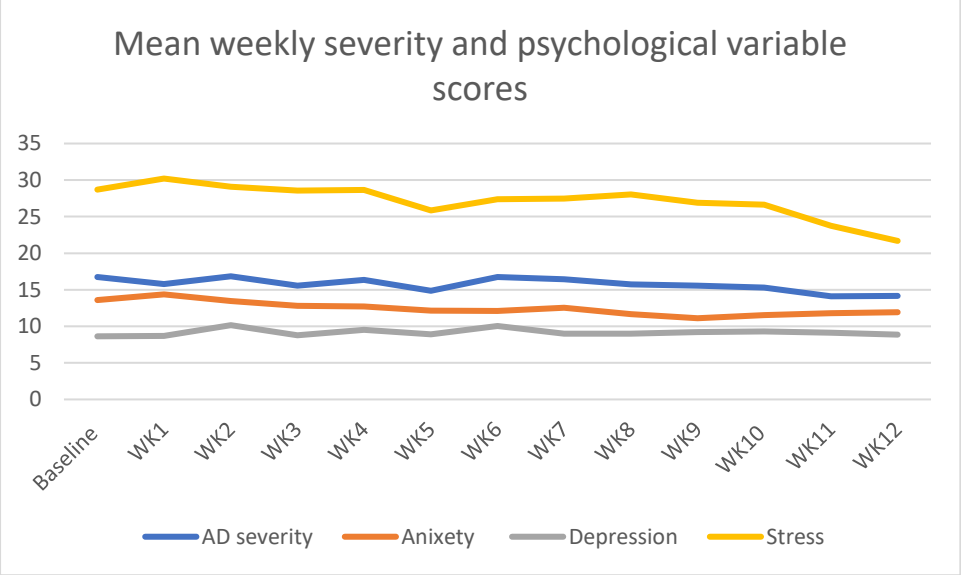

Figure 6.2 Mean weekly disease severity and psychological variable scores

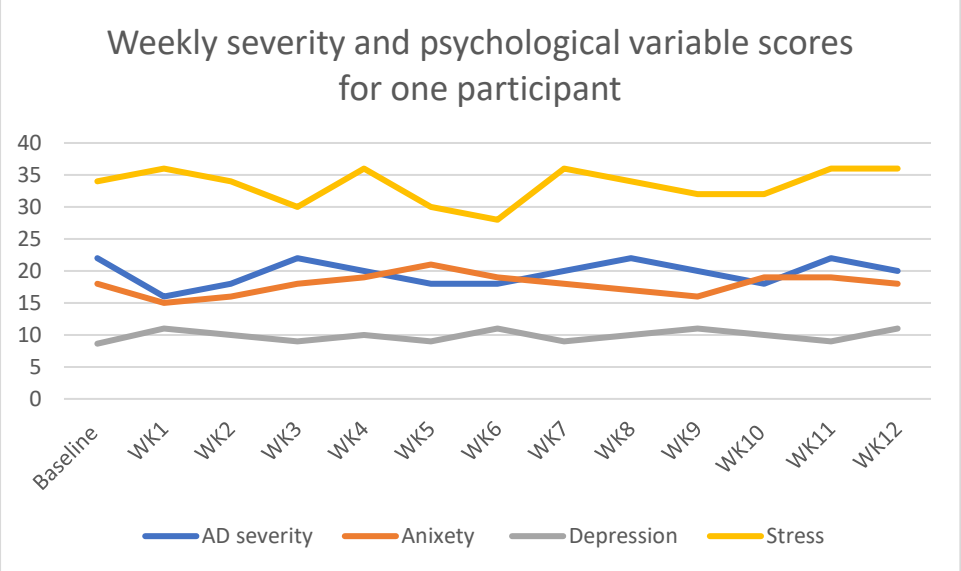

Figure 6.3 Weekly disease severity and psychological variable scores for one participant

Pearson's correlations were conducted for disease severity (POEM scores) and anxiety, depression and stress in the same week (Table 6.1). There were significant positive correlations between disease severity and anxiety (r's= 0.47-0.75), these correlations were medium to large for each week for the 12 weeks. Similarly, disease severity was significantly associated with depression for all 12 weeks apart from week 2; these correlations were also medium to large (rs=0.31-0.69). Psychological stress was also significantly correlated with disease severity for all 12 weeks, these correlations ranged from medium to large (rs=0.55-0.72).

Table 6.1 Pearson's correlations between disease severity and psychological variables

POEM	Anxiety	Depression	Stress
Baseline	.55*	.47*	.63*
Week 1	.65**	.50*	.62**
Week 2	.47*	.31	.52*
Week 3	.51*	.60**	.70***
Week 4	.54*	.69***	.55*
Week 5	.48*	.53*	.55*
Week 6	.55*	.52*	.69**
Week 7	.72***	.59**	.72***
Week 8	.69***	.57*	.67**
Week 9	.59**	.69***	.58**
Week 10	.55*	.51*	.6**
Week 11	.66**	.59**	.66**
Week 12	.75***	.69**	.67**

* p<0.05, **p<0.01 ***p<0.001

Pearson's correlations were also conducted for disease severity on week X, and stress, anxiety, depression on week X + 1 (Table 6.2). Disease severity was significantly positively correlated with anxiety the following week for all weeks apart from two. The correlations were medium to large (rs=0.4-0.69). Similarly, psychological stress was significantly correlated with disease severity in 10 out of the 12 weeks with medium to large correlations (rs=0.44-0.79). Pearson's correlation between depression and disease severity were also significant in 9 out of 12 weeks (rs=0.38-0.69).

Table 6.2 Pearson's correlations between disease severity on week X and psychological variables on week X+1

	Anxiety	Depression	Stress
Baseline & week 1	.57*	.52*	.64**
Week 1 & week 2	.48*	.38	.57*
Week 2 & week 3	.43	.53*	.46
Week 3 & week 4	.48*	.62**	.44
Week 4 & week 5	.40	.48*	.52*
Week 5 & week 6	.54*	.38	.61**
Week 6 & week 7	.48*	.29	.57*
Week 7 & week 8	.69**	.59**	.73***
Week 8 & week 9	.57*	.47*	.58*
Week 9 & week 10	.48*	.48*	.59**
Week 10 & week 11	.62**	.62**	.49*
Week 11 & week 12	.66**	.69***	.79***

*p<0.05, **p<0.01, ***p<0.001

Three cross-lagged panel model analyses (appendix 18) were conducted to explore the temporal relationship between the psychological variables (stress, anxiety and depression) and disease severity. When analysing cross-lagged model fit indices (Byrne, 2013), a non-significant chi-square test is desired, which signifies that that the model approximates the underlying data and therefore should not be rejected (Bollen, 1989). Additionally, the Comparative Fit Index (CFI) is examined with possible values range from 0.00 to 1.00, with higher values signifying a better fitting model (Ullman, 2006; Ullman & Bentler, 2003). Further, the Root Mean Square Error of Approximation (RMSEA)is considered as this accounts for the error of approximation in the population; values less than 0.05 are indicative of good fit and values as high as 0.08 represent several errors of approximation in the population (Browne & Cudeck, 1993). Lastly, the Tucker-Lewis Index (TLI; Tucker & Lewis, 1973) produces values that range from 0 to 1, with higher values indicating a good fit (Hu & Bentler, 1999).

The cross-lagged models indicated poor-average fit for stress and severity ($\chi2(1800) = 1677$, $p<0.001$; CFI = 0.54, TLI = 0.67, RMSEA =0.43, 95% CI [0.42,0.46]), anxiety and AD severity ($\chi2(1654) = 1066.98$, $p<0.001$; CFI = 0.32, TLI = 0.21, RMSEA =0.12, 95% CI [0.09, 0.34]), and depression and AD severity ($\chi2(1435) = 1165.67$, $p<0.001$; CFI = 0.06, TLI = 0.02,

RMSEA =0.61, 95% CI [0.54, 0.67]), due to a number of potential reasons that will be discussed later in this chapter.

When exploring the temporal relationship between psychological variables and disease severity (table 6.3), disease severity on week X significantly predicted stress on week X+1 in eleven out of twelve weeks. Stress on week X also significantly predicted disease severity on week X+1 in eleven weeks. Similarly, bi-directional predictions were found for the majority of the 12 weeks when exploring disease severity, anxiety and depression. Disease severity in week X predicted anxiety on week X+1 in eleven out of twelve weeks, and anxiety on week X also predicted AD severity on week X+1 in ten weeks. Moreover, disease severity in week X predicted depression on week X+1 in ten out of the total twelve weeks and depression in week X predicted disease severity on week X+1 in nine weeks.

Table 6.3 Standardized parameter estimates for random-intercept cross-lagged panel models on psychological variables (stress, anxiety and depression) and AD severity(SEV) (n=19)

Stress					
Cross-lagged	β	SE	Cross-lagged	β	SE
SEV0→STR1	1.41***	0.26	STR0→SEV1	0.45***	0.09
SEV1→STR2	135***	0.25	STR1→SEV2	-0.06	0.10
SEV2→STR3	1.51***	0.30	STR2→SEV3	0.76***	0.09
SEV3→STR4	0.65**	0.20	STR3→SEV4	0.35***	0.09
SEV4→STR5	-0.18	0.18	STR4→SEV5	0.41***	0.11
SEV5→STR6	1.02***	0.22	STR5→SEV6	0.37*	0.15
SEV6→STR7	0.89**	0.28	STR6→SEV7	0.44***	0.10
SEV7→STR8	1.59***	0.15	STR7→SEV8	0.49***	0.07
SEV8→STR9	1.30***	0.26	STR8→SEV9	0.54***	0.08
SEV9→STR10	1.38***	0.18	STR9→SEV10	0.50***	0.10
SEV10→STR11	0.89***	0.22	STR10→SEV11	0.43***	0.08
SEV11→STR12	1.33***	0.15	STR11→SEV12	0.48***	0.08
Anxiety					
Cross-lagged	β	SE	Cross-lagged	β	SE
SEV0→ANX1	0.80***	0.17	ANX0→SEV1	0.79***	0.18
SEV1→ANX2	0.5***	0.14	ANX1→SEV2	0.26	0.17
SEV2→ANX3	0.73**	0.23	ANX2→SEV3	1.03***	0.24
SEV3→ANX4	0.61***	0.11	ANX3→SEV4	0.95***	0.15
SEV4→ANX5	0.35	0.12	ANX4→SEV5	0.62**	0.20
SEV5→ANX6	0.80***	0.15	ANX5→SEV6	0.84***	0.21
SEV6→ANX7	0.41**	0.12	ANX6→SEV7	-0.16	0.11
SEV7→ANX8	0.74***	0.11	ANX7→SEV8	0.85***	0.12
SEV8→ANX9	0.56***	0.11	ANX8→SEV9	0.96***	0.19
SEV9→ANX10	0.64***	0.12	ANX9→SEV10	1.15***	0.18
SEV10→ANX11	0.63***	0.10	ANX10→SEV11	0.76***	0.18
SEV11→ANX12	0.65***	0.10	ANX11→SEV12	1.16***	0.12
Depression					
Cross-lagged	β	SE	Cross-lagged	β	SE
SEV0→DEP1	0.70***	0.14	DEP0→SEV1	0.95***	0.22
SEV1→DEP2	0.53	0.19	DEP1→SEV2	0.30	0.21
SEV2→DEP3	0.74***	0.16	DEP2→SEV3	0.98**	0.30
SEV3→DEP4	0.40***	0.09	DEP3→SEV4	0.95***	0.19
SEV4→DEP5	0.28*	0.11	DEP4→SEV5	0.75*	0.30
SEV5→DEP6	0.21	0.14	DEP5→SEV6	0.66	0.34
SEV6→DEP7	0.43***	0.09	DEP6→SEV7	-0.16	0.21
SEV7→DEP8	0.51***	0.09	DEP7→SEV8	1.01***	0.19
SEV8→DEP9	0.34**	0.11	DEP8→SEV9	1.19***	0.28
SEV9→DEP10	0.41***	0.12	DEP9→SEV10	1.04***	0.28
SEV10→DEP11	0.59***	0.10	DEP10→SEV11	0.89***	0.25
SEV11→DEP12	0.49***	0.07	DEP11→SEV12	1.23***	0.18

*p<0.05, **p<0.01, ***p<0.001

6.3.4 Daily correlations and predictions between disease severity and psychological stress

Mean disease severity, depression and stress scores for each day were plotted on a line graph (figure 6.4) alongside an illustration of scores from one participant (figure 6.5). Although the figure does not show a clear pattern between disease severity and psychological stress, there were several significant correlations between the variables that are reported below.

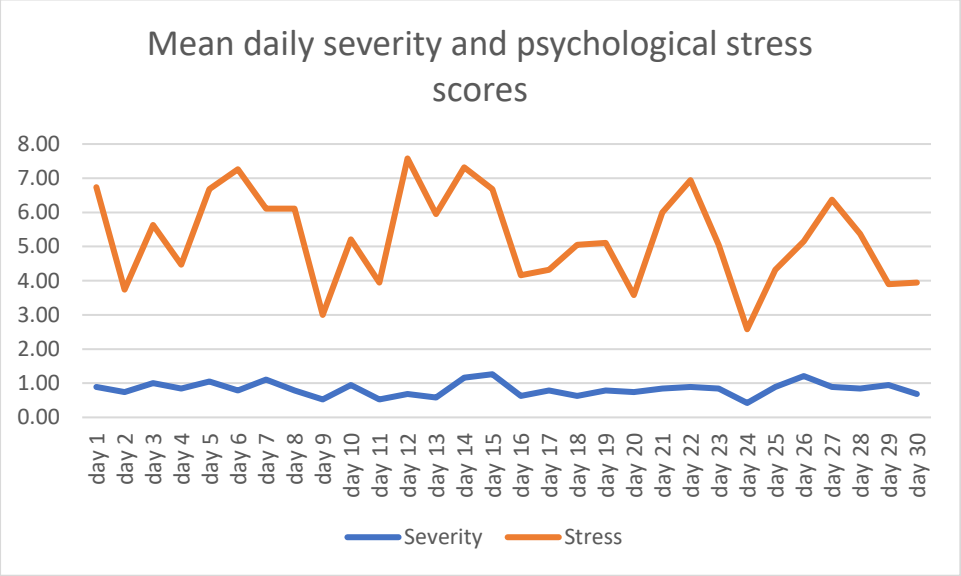

Figure 6.4 Mean daily disease severity and psychological stress scores

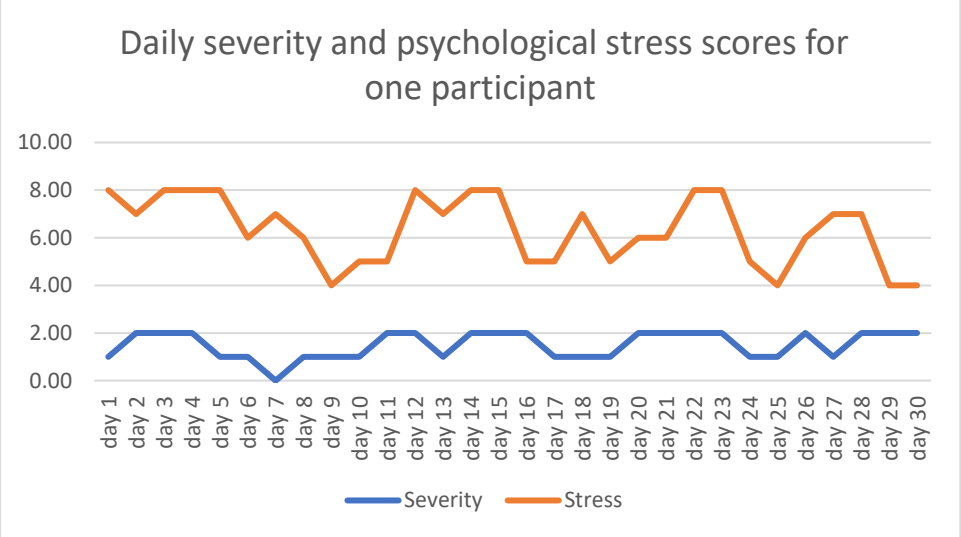

Figure 6.5 Daily disease severity and psychological stress scores for one participant

The cross-lagged model (Figure 6.6) results indicated that the model was a poor-average fit ($\chi2(1769) = 10557.87$, $p<0.001$; CFI = 0.052, TLI = 0.001, RMSEA =0.52, 95% CI [0.51,0.53]).

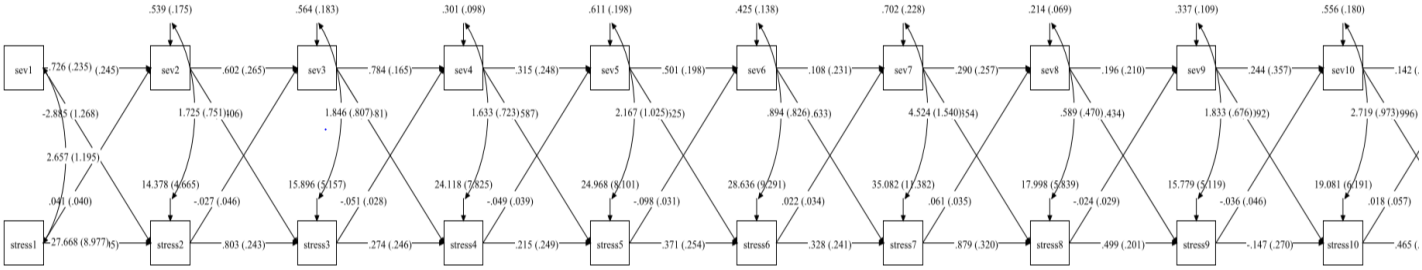

Figure 6.6 Cross lagged analysis snippet for psychological stress and disease severity for 10 days with β coefficients.

Severity on a given day significantly predicted stress the following day in two of the 30 days (day 1: β= -0.54, $p<0.05$, day 22= β=0.83, $p<0.01$). On day one, higher disease severity predicted lower stress levels on the following day, whereas for day 22 higher severity predicted greater stress the following day. Stress on day X predicted AD severity on day X+1 for three out of the 30 days (day 5: β=-0.62, $p<0.001$, day 22: β=0.74, $p<0.001$, day 29: β=-0.41,$p<0.05$).On days five and 29, higher stress predicted less disease severity the next day whereas on day 22, higher stress predicted greater disease severity the next day (table 5.3). The covariances between stress and disease severity showed significant positive relationships for 23 out of 30 days; higher stress was correlated with increased disease severity (table 6.4) and these correlations were medium to large-sized (appendix 19).

Table 6.4 Standardized parameter estimates for random-intercept cross-lagged panel models on stress(STR) and AD severity(SEV) (n=19)

Cross-lagged	β	SE	Cross-lagged	β	SE	Covariance	β	SE
SEV1→STR2	-0.54*	0.22	STR1→SEV2	0.28	0.26	STR1↔SEV1	0.59***	0.15
SEV2→STR3	-0.14	0.21	STR2→SEV3	-0.15	0.24	STR2↔SEV2	0.62***	0.62
SEV3→STR4	0.08	0.24	STR3→SEV4	-0.32	0.18	STR3↔SEV3	0.62***	0.14
SEV4→STR5	-0.35	0.23	STR4→SEV5	-0.31	0.24	STR4↔SEV4	0.61***	0.15
SEV5→STR6	-0.18	0.24	STR5→SEV6	-0.62***	0.17	STR5↔SEV5	0.56***	0.16
SEV6→STR7	-0.15	0.21	STR6→SEV7	0.15	0.22	STR6↔SEV6	0.26	0.21
SEV7→STR8	-0.49	0.36	STR7→SEV8	0.5	0.28	STR7↔SEV7	0.92***	0.04
SEV8→STR9	-0.19	0.24	STR8→SEV9	-0.22	0.27	STR8↔SEV8	0.3	0.21
SEV9→STR10	0.37	0.26	STR9→SEV10	-0.21	0.28	STR9↔SEV9	0.8***	0.08
SEV10→STR11	-0.35	0.37	STR10→SEV11	0.12	0.38	STR10↔SEV10	0.84***	0.07
SEV11→STR12	0.14	0.25	STR11→SEV12	0.29	0.26	STR11↔SEV11	0.64***	0.14
SEV12→STR13	0.05	0.3	STR12→SEV13	0.24	0.37	STR12↔SEV12	0.76***	0.09
SEV13→STR14	-0.15	0.23	STR13→SEV14	-0.17	0.23	STR13↔SEV13	0.47**	0.18
SEV14→STR15	-0.13	0.26	STR14→SEV15	0.1	0.27	STR14↔SEV14	0.63***	0.14
SEV15→STR16	-0.33	0.32	STR15→SEV16	0.39	0.32	STR15↔SEV15	0.76***	0.09
SEV16→STR17	-0.32	0.55	STR16→SEV17	0.57	0.49	STR16↔SEV16	0.93***	0.03
SEV17→STR18	0.07	0.33	STR17→SEV18	-0.47	0.29	STR17↔SEV17	0.7***	0.12
SEV18→STR19	0.14	0.24	STR18→SEV19	-0.06	0.23	STR18↔SEV18	0.31	0.21
SEV19→STR20	0.23	0.3	STR19→SEV20	-0.26	-.29	STR19↔SEV19	0.72***	0.11
SEV20→STR21	0.02	0.34	STR20→SEV21	0.03	0.33	STR20↔SEV20	0.75***	0.1
SEV21→STR22	0.83**	0.29	STR21→SEV22	-0.17	0.38	STR21↔SEV21	0.83***	0.07
SEV22→STR23	0.25	0.26	STR22→SEV23	0.74***	0.22	STR22↔SEV22	0.73***	0.11
SEV23→STR24	-0.07	0.24	STR23→SEV24	0.19	0.25	STR23↔SEV23	0.18	0.22
SEV24→STR25	0.01	0.25	STR24→SEV25	-0.16	0.2	STR24↔SEV24	0.39	0.19
SEV25→STR26	-0.00	0.29	STR25→SEV26	-0.27	0.28	STR25↔SEV25	0.8***	0.08
SEV26→STR27	-0.04	0.3	STR26→SEV27	-0.13	0.28	STR26↔SEV26	0.7***	0.12
SEV27→STR28	-0.16	0.22	STR27→SEV28	-0.33	0.23	STR27↔SEV27	0.54**	0.16
SEV28→STR29	0.13	0.21	STR28→SEV29	0.11	0.2	STR28↔SEV28	0.47	0.18
SEV29→STR30	0.16	0.25	STR29→SE30	-0.41*	0.21	STR29↔SEV29	0.39	0.19

*p<0.05, **p<0.01, ***P<0.001

6.4 Discussion

This study analysed data from 19 participants who completed daily diaries and weekly questionnaires. Twenty-one participants returned study packs to the researcher and 36 study packs were sent to participants who expressed interest in taking part in this study. Thus with the completion rate of 52%, the study provides preliminary support for the feasibility of establishing a longitudinal cohort of adults with AD. Recruitment and retention are challenging factors for researchers conducting longitudinal studies. For example, the more demanding or burdensome the study is, the more challenging the recruitment and retention rates are (Grove, Burns, & Gray, 2012; Panjari et al., 2008). When studies involve numerous data collection points, potential participants may be reluctant to commit or may enrol but underestimate the commitment involved in participating. This study included daily diaries which may have added some burden even though every effort was made to minimize this. Unfortunately, this study was not able to ascertain reasons for declining from all those who expressed initial interest in taking part in the study. Furthermore, only three participants out of the fifteen who did not return the study packs informed the researcher that they could not continue with the study due to various stressful events that prevented them from diligently completing daily diaries.

Where the data were collected on a weekly basis, there was a problem of retrospective recall. Participants were prompted to describe their mood over the past seven days. A truly contemporaneous measure would ask participants to complete measures at the very moment they are prompted. The daily diaries however were short and purposefully designed to be answered on a 3 point Likert scale and should have taken no longer than five minutes to complete daily. Participants were approached to take part in follow-up interviews following the completion of diaries, however none of the 19 participants proceeded with taking part in them. The researcher did however receive feedback from six participants on Facebook; the feedback provided was positive with all six participants agreeing that completing the diaries and questionnaires was not a cumbersome task for them. One participant stated a sense of

‘epiphany’ as she observed patterns between the severity of her AD and stress when completing the diary.

Lag sequential analyses for the relationship between psychological variables and disease severity revealed that both were predictive of the other when measured weekly.. However, when exploring the temporal relationship between stress and disease severity using daily diaries, the study did not find a causation effect of stress and AD severity. The sample fit indices for all cross-lagged analyses were a poor-average fit. One major reason for this is the sample size; according to Kline (2005), an ideal sample size for structural equation modelling should be 100 participants or more. However, as this study was a feasibility study that aimed to, in addition to explore the temporal relationship between stress and AD severity, assess the success of running a longitudinal daily diary study, this issue of sample size could not be overcome. If this study was run with too large a sample size, it may have been unethical as participants would be subjected to burdens and increased risks (Altman, 1980). Additionally, a sample size that is too high could lead to preventable failure to reach the recruitment target (Lancaster, Dodd, & Wiliamsoon, 2004). Meanwhile a sample size that is too small would have an inaccurately estimated variance, impacting the design of a future full-scale study (Julious, 2005).

Psychological stress has been widely researched in the field of atopic dermatitis; a number of studies have found that patients with AD suffer from stress-related exacerbations (Arndt, Smith, & Tausk, 2008; Arck & Paus, 2006; Suárez, Feramisco, Koo, & Steinhoff, 2012). This contributes to an itch-scratch cycle that results in a state of high anxiety and stress (Arck & Paus, 2006). By using daily diaries and weekly measures, the aim of this study was to determine the direction of the relationship between stress and disease severity as much of present research points to a bi-directional relationship ascertained through the use of cross-sectional surveys (Arndt, Smith, & Tausk, 2008; Oh et al., 2010; Suárez, Feramisco, Koo, & Steinhoff, 2012). Considering the findings from the daily compared to the weekly measures, it is possible that the physiological effects of stress, anxiety and depression may need some

lead time before resulting in disease exacerbation AD and therefore, daily measurements of stress and AD severity may not reflect the changes as well as weekly measurements might. The existence of a reciprocal relation between psychological variables and disease severity over a one week lag period suggests that the positive relation between the factors on the same week is the consequence of a complex interaction. Stress, anxiety and depression appear to be both a cause of the AD severity, and caused by the severity of the condition. These findings of the cross-lagged analyses must be interpreted with caution as has been mentioned above, the model fit indices were not ideal due to the small sample size. AD, in addition to other dermatological diseases (e.g. psoriasis, alopecia areata, acne vulgaris) is considered a psychosomatic disease in which psychological factors have an impact on the development of disease and can increase the symptoms. Stressful events and active episodes of the disease are often related to a high level of psychological stress (Benea, Muresian, Manolache, Robu, & Diaconu, 2001). On the other hand, AD as a disfiguring disease is a stressor itself with an influence on the psychosocial state of the patient and on the maintenance of the lesions (Arndt, Smith, & Tausk, 2008).

This study found strong positive relationships between disease severity and psychological variables measured on a weekly basis using validated psychometric questionnaires. These correlations were medium to large sized and significant for the majority of the weeks. This finding is reflected in a number of cross-sectional studies that have found significant relationships between disease severity and psychological variables (e.g. Arndt, Smith, & Tausk, 2008; Kodama et al., 1999; Oh et al., 2010), however unlike the current study, these studies measured these relationships at one time-point, and many do not differentiate between the types of stressors explored. The mechanisms that underlie this relationship between AD severity and psychological stress are insufficiently understood. A probable mechanism that underpins these associations involves the roles of cytokines which help regulate the immune response in an individual (Wilson, Finch, & Cohen, 2002). Alternatively, stress may lead to

AD-relevant immunological changes via pathways such as the HPA axis (Buske-Kirschbaum et al., 2013).

There are a number of potential reasons that may explain the positive relationship between stress and AD severity. Firstly, an increase in severity which is accompanied by itchiness, unsightliness, and soreness of a patient's skin, may result in higher stress levels in interpersonal situations. Furthermore, higher levels of interpersonal stress may result in altered views of AD severity, in patients viewing their condition as more severe than it is. Third, severe AD may result in participants viewing their reactions to interpersonal events more negatively. Finally, this relationship could be a result of other factors such as participant response style.

As discussed in chapters one and three, the vast majority of literature in this area has methodological drawbacks, such as retrospective in design, adjustment for confounder variables. King and Wilson (1991)'s study's clinical implications are limited as the duration of the study was only two weeks. In a further study focussing on adults with acne, Chiu, Chon and Kimball (2003) found significant relationships between acne severity and examination stress in students. This was a small-sized study in which confounding variables may not have been taken into account. The prospective nature of the current study enabled an exploration of changes in AD severity and psychological variables over an extended period and accounted for potential confounding variables in the analyses.

To the researcher's knowledge, this is the first study that uses social networking platforms as the means of recruitment for conducting a longitudinal study on adults with AD. Consequently, there are no published data with which to compare the success of this method. Nevertheless, the ability to recruit participants within 34 days is notable. Of the data returned, 19 out of 21 study packs had no missing data, demonstrating a high degree of motivation among the study population. Many of these participants had completed a 'study poll' on Facebook to state their interest prior to taking part in the study.

Despite the successful use of social media in this type of research, there are a number of potential limitations unique to this method of recruitment. First, the degree of non-response bias could not be ascertained as the researcher was unable to determine a response rate. Additionally, there is potentially a selection bias in favour of young adults with AD, as they are more likely to be Facebook users. Duggan and Brenner (2013) found a statistically significant difference among different age groups who were Facebook users, with 86% of all people aged 18-29 years old using the site compared to 73% of people aged 30-49, 57% of people 50-64 and only 35% of people older than 64 years old. Indeed, the participants in this study were aged 18-49, there were no participants over the age of 50. In addition, the psychological stress responses might also suffer from selection bias as those who suffer from higher stress levels may not be as active on Facebook as those who do not (Brailovskaia, Rohmann, Bierhoff, Schillack, & Margraf, 2019). Another source of bias within the study may result due to the fact that this study's participants were recruited solely from the atopic dermatitis support group where adults may have increased health literacy and knowledge of their disease compared to those who are not part of a support group (Zaid et al., 2014).

In addition to the above limitations this study was not able to recruit any males, although evidence suggests the presence sex differences in the skin-psyche relationship(Picardi et al., 2001; Taieb, Finlay, & Myon, 2004). Measuring AD severity using self-report rather than objective measures is a further limitation. Self-report of skin disease has been used, however, in a number of large cross-sectional community-based studies of psychological and quality of life associations of skin disease (Arnold et al., 2004; Dalgard, Svensson, Holm, & Sundby, 2004; Dalgard, Svensson, Holm, & Sundby, 2005) and there is evidence for the validity of self-reported presence of skin disease (Dalgard, Gieler, Holm, Bjertness, & Hauser, 2008) and of self-reported skin symptoms (Dalgard, Svensson, Holm, & Sundby, 2003; Fivenson, 2001) as measures of objective disease presence.

6.5 Conclusions and directions for future research

This study has a number of clinical implications. The bi-directional prediction of stress and AD severity warrants further longitudinal examination, with the use of more methodologically sound measures such as physical measures of stress and objectively measures disease severity rather than patient oriented. Considering the increasing prevalence of AD and the psychological and psychosocial burden associated with the condition, remedial elements in exacerbation are important. Although psychological interventions and stress reduction techniques are proposed as supplementary treatments for AD, evidence for their efficacy is largely unconvincing (Magin, Sibbitt, & Bailey, 2009). The findings of this study indicate a rationale for these interventions and efficacy trials in addition to further longitudinal analysis. The considerations for a full-scale study are discussed in chapter 7.

Chapter seven: General discussion

7.1 Introduction

This doctoral research sought to examine the quality of life and mental well-being in adults with AD. In order to achieve this, a multi- methods approach was employed to conduct the research. The prevalence of AD in adults has increased significantly in the last few decades (Hoare & Williams, 2000) and the current scenario suggests that it will continue to do so. In recent years there has also been a growing interest in exploring and addressing quality of life in AD patients. However, most published research on AD and quality of life is conducted outside the UK. The UK is unique due to its' National Health System which offers treatment free of charge to its UK residents.

This chapter will summarise the key findings of this PhD research project, compare findings from each of the empirical studies, and discuss how they integrate with each other and relate to existing literature. Methodological considerations will be presented, In addition to implications for practice, policy and future research.

The overall discussion below builds on the previous chapter discussions and synthesises the findings of the thesis as a whole. The chapter will summarise the main findings of this thesis, consider the contribution of the thesis to wider knowledge regarding quality of life and mental health in atopic dermatitis and long-term condition in general. Additionally, this chapter will review the recruitment and data generation methods used and discuss strengths and limitations of the studies in this thesis, make recommendations for clinical practice and discuss future directions. Lastly, reflections of this PhD and an overall conclusion will be discussed.

7.2 Summary of main findings

7.2.1 Systematic review and meta-analysis

The aim of the systematic review and meta-analysis was to explore quality of life in adults with AD. Previous literature has largely investigated quality of life in infants and children with AD or families of those with AD. The systematic review found statistically significant relationships between disease severity and quality of life in adults with AD, as well as poorer QoL compared to healthy controls and those with similar skin conditions. Previous literature has largely investigated quality of life in infants and children with AD or families of those with AD. The systematic review also found methodological weaknesses such as small sample sizes and recruitment of study participants primarily through dermatology clinics. Socio-demographic and clinical factors were not taken into account by most of the studies in the review. Furthermore, a substantial number of studies investigating quality of life have been conducted in the US, therefore not directly applicable to the UK context due to varying health service models. A further gap in the literature was found regarding the use of dermatology-specific questionnaires used to measure QoL in healthy controls as opposed to generic QoL measures. Moreover, all studies in the review were quantitative and cross-sectional thus introducing the issue of causality. The review highlighted areas for future qualitative exploration such as sleep disturbances, personal relationships and impact of AD symptoms. Furthermore, the review highlighted a lack of prospective measurement of QoL and disease severity.

7.2.2 Qualitative study

The aim of the qualitative study was to explore the perceptions and experiences of adults with AD living in the UK. The findings of this study indicated several themes that are important to understand the experiences of living with the condition. The visible aspect of AD was perceived as playing an important role in participants' day-today lives. As AD can give rise to complications such as scarring, pigmentation, wrinkling and thinning of the skin, stigmatization

and judgement by others played an important role in their lives. In this theme, participants also discussed often comparing themselves to others, either positively or negatively. The impact of visible skin lesions on a participant's quality of life and mental well-being is a highly under-researched but important area.

Psychological factors such as low mood, depression, dysphoria, anger and frustration were also prevalent in the vast majority of the participants in this study. Atopic dermatitis alongside its mental implications, affected participants physically, the pain and discomfort associated with the condition were discussed repeatedly. Limitations in physical functioning due to pain and discomfort from AD were a distressful experience for participants and impacted their ability to perform everyday tasks.

This study also shed light on coping and management methods taken by participants in order to improve their daily lives. Some used active mechanisms such as maintaining stringent maintenance regimens and avoiding triggers, whereas others used more negative strategies such as comfort eating in order to cope with their condition. Health care professionals also played a significant role in participants' experiences of living with the condition. The majority of participants perceived a lack of acknowledgement of the mental health implications by health care providers and a notion that GPs were not efficiently equipped to address and treat mental health issues that arose as a result of AD. Again, this a novel finding in adults with AD.

This study also identified some differences in accounts between White and BME participants where BME participants were less willing to talk about their AD to others, and their AD was received more negatively by family and friends compared to White participants. Ethnic and cultural issues in AD are not widely researched and the majority of published literature on QoL and AD does not account for or record ethnic differences.

7.2.3 Cross-sectional survey

The aim of this study was to investigate predictors of QoL in adults with AD and compare QoL and mental health variables in adults with AD and heathy controls. The study recruited a total

of 533 participants- a sample size larger than 80% of the studies in the systematic review, and the largest known sample size of AD participants in the UK. Participants with AD reported significantly lower health related QoL, physical QoL, and higher anxiety compared to the healthy controls. Psychological stress, physical and environmental QoL and AD severity were significant predictors of skin-related QoL even after controlling for clinical and socio-demographic factors in those with AD. Furthermore, patients who were prescribed medication such as topical corticosteroids and immunosuppressants reported lower QoL and higher disease severity compared to those who were not. This study also illustrated socio-demographic differences for QoL and disease severity. The findings of this study support findings from the wider literature of the significant psychological impact AD has on adults in the UK. Medication, concomitant conditions, family history and socio-demographic characteristics play a significant role in the psychological burden of AD.

7.2.4 Prospective longitudinal study

The aim of the final study was to assess the feasibility of conducting a longitudinal diary analysis that explored the temporal relationship between psychological stress and AD severity. As discussed in earlier chapters, psychological stress and disease severity in AD appear to be bi-directionally related. However, most published studies have used cross-sectional designs to explore this. This study recruited 19 participants all of whom reported suffering with clinically diagnosed AD. Participants completed daily stress diaries for a month, as well as validated psychometric questionnaires weekly for a total of 12 weeks. Psychological stress, anxiety and depression were highly correlated with disease severity for the majority of the 12 weeks. A causal relationship between stress and AD severity was not found in this study as measured using daily diaries however there was evidence for a bi-directional causal relationship from the weekly measures; psychological variables and disease severity appeared to be predictive of one another when measured weekly. Considerations for running a full-scale study are discussed below.

7.3 Comparison of findings and relationship to existing literature

This research has attempted to explore, from participants' perspectives, the psychological impact of AD on their QoL and mental well-being. This was achieved through a qualitative study that used semi-structured interviews, a cross-sectional survey using standardised psychometric instruments and finally a prospective analysis also shed light on the temporal relationship between AD and psychological factors in relation to disease severity.

This section focusses on the findings of the studies as a whole and summarise the implications they have on the way quality of life in AD is assessed, the view of health care professionals on management of AD and how those with AD perceive its' impact. It is only through these findings' applicability to the psychological care of AD patients that they are likely to be utilized by health care professionals and researchers and contribute to the patient in real life.

7.3.1 Qualitative study

The systematic review identified several gaps in existing literature including the lack of qualitative exploration of patients' experiences living with AD. The qualitative study demonstrated the multi-faceted nature and complexities involved in living with AD, as although distinct super-ordinate themes were identified in this study, it was almost impossible to separate one from the other.

The five overarching themes were supported with many smaller themes, however lived experiences, as expressed by participants, indicated that these are not necessarily confined within one major category, but are entwined and overlap with one another. . Threats to inner self- which emerged as the first superordinate theme- clearly permeated every aspect of the participants' lives and had a major impact on emotional functioning and self-consciousness surrounding their AD.

A number of studies that have explored the incidence of psychological distress have reported that adults with atopic dermatitis are at an increased risk of experiencing depression (Patel, Immaneni, Singam, Rastogi, & Silverberg, 2019; Silverberg et al., 2019; Yu & Silverberg,

2015). Most recently, a systematic review and meta-analysis of 106 studies (Patel et al., 2019) found that 25% of AD patients presented with depressive symptoms, 17% had clinical depression and 13% had suicidal ideation. . Moreover, there was a higher prevalence of depression in those with compared to those without AD (20.1% vs 14.8%)

The negative emotions experienced by individuals in the qualitative study extended beyond perceptions of grief and low mood. The majority of the participants discussed intermittent periods of anxiety, anger, depression and frustration. The unpredictability and uncontrollability of AD may to some extent promote the emergence of such feelings and support previous findings from studies with AD patients, such as those of Lapidus & Kerr (2001) who found that participants reported feelings of frustration and helplessness in relation to AD severity.

A finding evident in published literature is the increased prevalence of depression in those with AD compared to patients of other chronic conditions and healthy people (Patel et al., 2019). Depression is often thought to result as a consequence of living with AD and its' severity, however this cannot be ascertained due to the array of additional variables that may be involved. Several cross-sectional studies (Hashiro & Okumura, 1997; Slattery & Essex, 2011) have found significant associations between depression and AD severity, however once controlling for other variables such as socio-demographic characteristics, the strength of this significance weakens and even diminishes (Hashiro & Okumura, 1997; Slattery & Essex, 2011). Anxiety and depression appeared to be prominent issues in the current study and many participants discussed that issues such as confidence and self-esteem contributed to hesitation in accessing relevant support from health care providers and social networks. There was a notion that their AD did not warrant GP time and resources and as a result discouraged them from raising concerns about depressive symptoms and emotional distress. These findings reflect others (e.g. Belson, Barker, Griffiths, Cordingley, & Chew-Graham, 2013; Magin, Adams, Heading, Pond, & Smith, 2009), although Pollock (2007) found that psoriasis patients tried to 'maintain face' and conform to the socially sanctioned role of the stoic, good

and uncomplaining patient in order to retain the social esteem and good will of others" (page 175) during clinical consultations and therefore supressed signs of emotional distress.

This study also found the presence of a range of negative feelings at numerous times in participants' daily lives. These feelings, whether fear, frustration or anger, often appeared to be linked to periods of AD exacerbations and the resulting limitations and role changes due to severe pain, discomfort and reduced physical abilities. This has not been reported in similar qualitative literature in the past, however Barlow and Williams (1999) found similar emotional distress from focus groups that explored parenting from the perspectives of parents and grandparents with arthritis, another chronic condition. The participants of their study also reported physical limitations, fatigue and pain which combined to interfere with their roles of parents.

The current study also found that in addition to reduced physical abilities compromising domestic tasks, participants' were concerned about their employment prospects and current jobs. . Twelve participants in the study reported being unable to attend work at some point because of disease exacerbation, whereas two participants had sought employment elsewhere in an attempt to earn a wage but not compromise their health. This finding was later mirrored in the quantitative study where those with AD reported significantly lower physical QoL compared to healthy adults. Participation in paid employment is a role that many adults may aspire to achieve and is central to many peoples' life goals, however, being an AD sufferer may affect employment prospects and ability to retain a job. Individuals with severe skin conditions such as AD and psoriasis report higher levels of employment and missing work more frequently condition (Kwak & Kim, 2017; Linden & Weinstein, 1999; Mansouri et al., 2015).

The participants utilised several strategies in attempts to be able to carry out everyday activities and stay independent. . Some of these involved taking a positive outlook on their condition, find alternatives to their triggers and educating others about AD- these were all positive adaptions and strategies designed to help the participant cope with the condition..

Conversely, in an attempt to deal with their flare-ups, several participants described adapting an unhealthy lifestyle as a way of inducing 'comfort'- clearly a negative coping strategy that may have deleterious implications for their health (Nyugen, Koo, & Cordoro, 2016; Ograczyk, Malec, Miniszewska, & Zalewska-Janowska, 2012).

An unclear finding in this study was the strategy employed with regard to social interaction for an element of contradiction existed. On the one hand, many participants reported feeling lonely and isolated, yet on the other, they reported frequently rejecting offers of help from friends and family, deliberately shunning social contact, reducing communication with friends and avoiding social events - the common reasons being that they felt a burden, or, perceived that other people didn't understand the disease, or people did not offer helpful advice to them**.**

Although contradictory, this is an interesting finding, particularly as social support, either positive or negative has been proposed as an imperative coping source in managing illness and is perceived as a barrier between a patient and the source of demands or stress related to a long-term condition, in addition to providing assistance in meeting needs (Lu, Duller, Van Der Valk, & Evers, 2003; Ohya et al., 2001). In managing illness, one of the more challenging aspects is maintaining social support and preserving interpersonal relationships as coping mechanisms (Silver, Wortman, & Crofton, 1990).

Social support, while not reported in AD literature, has been found to be predictive of pain and long-term functional disability in patients with chronic and long-term conditions, with quantitative aspects of the size of a social network and qualitative aspects of perceived social support playing a part. An older study by Smith and Wallston (1992) found that perceptions of lack of support were associated with higher levels of inability to perform daily activities in those with long-term conditions such as arthritis. Similarly, numerous other findings discuss the increased pain associated with decreased psychological wellbeing (Cohen et al., 2007; Patel, Peterson, & Kimmel, 2005; Waltz, Kriegel, & Bosch, 1998). These findings are reflected in studies exploring social support in similar skin conditions such as psoriasis **(**Cacioppo & Hawkley, 2003; Jankowski et al., 2012; Picardi et al., 2005).

Additionally, social support also contributes to the levels of psychological distress that individuals with skin conditions experience (Evers et al., 2005). Contributors to psychological distress in 248 adults with AD or psoriasis was explored by Evers et al (2005). The authors found that a lack of social support was the strongest predictor of psychological distress in both AD and psoriasis patients. This finding suggests that the notion of perceived or actual social support may be complex as participants in the current study discussed a number of instances where they had intentionally avoided accepting social support.

The interviews in this study gave the participants a voice and facilitated the identification of common themes. In order to explore these themes further, these findings were used to inform the choice of measures implemented in the quantitative study (chapter 5).

7.3.2 Quantitative study

The systematic review (chapter 3) included studies that explored quality of life in AD patients and all studies in this review were cross-sectional quantitative studies. The review highlighted some weaknesses in current literature including the use of small sample sizes, the use of disease-specific quality of life measures in comparing healthy controls and those with AD, lack of UK based studies and lack of consideration of socio-demographic and clinical factors (chapter three; Birdi, Cooke, & Knibb, 2020). Thus, the quantitative study aimed to bridge these gaps by conducting a large-scale cross-sectional study in the UK.

Several findings of this study mirrored findings of studies exploring QoL in adults with AD e.g. in this study, healthy controls reported significantly better health-related QoL compared to AD patients. This was an expected finding and supported the findings of the qualitative study where participants compared their lives to those without AD and reported feeling 'envious' due to the limitations AD had put on them. Moreover, all studies in the systematic review (chapter 3) also found that significantly poorer QoL in AD patients compared to healthy controls.

Similar to findings of previous literature, those with AD reported higher levels of anxiety compared to healthy controls (Oh et al., 2010; Thyssen et al., 2018; Yaghmaie et al., 2013).

The source of this anxiety is largely undetermined and calls for further investigation, particularly considering the variety of psychosocial issues found to impact QoL in those with long-term conditions. Krueger et al. (2001) identified some of these issues being related to workplace difficulties, suicidal ideation, social life and exclusion from public facilities. Numerous participants in this thesis's qualitative study also reported feeling anxious in certain situations such as when required to socialise; some of these participants were prescribed anxiolytics. The quantitative study found no significant difference between healthy controls and AD patients for depression although the qualitative study found that a number of participants reported being diagnosed with depression. The cause for the increase in these psychological concerns in AD patients remains speculative. Although anxiety and depression are related to skin barrier damage, increased itchiness and ultimately increase in disease severity, a more probably explanation is the burden caused by the chronicity of AD; social isolation, disrupted sleep and itch which negatively affects mental wellbeing (Lewis-Jones, 2006; Mathew al, 2016). The social stigma as a result of visible skin lesions may also contribute to an impact on mental wellbeing (Cacioppo et al., 2014; Magin, Sibbritt, & Bailey, 2009).

The quantitative study also found that physical QoL, environmental QoL, stress and AD severity significantly predicted skin-related QoL. These findings are in line with past literature which has ascertained strong relationships between AD severity and QoL (e.g.; Beikert et al., 2014; Chrostowska-Plak et al., 2013; Kim et al., 2012; Silverberg et al., 2018); in fact, the systematic review and meta-analysis (chapter 3) found that all but one studies that explored this relationship found that as AD severity increases, QoL significantly decreases (Birdi, Cooke & Knibb, 2020). Furthermore, the qualitative study also discussed how participants who deemed themselves as 'severe' appeared to be more affected by their condition. This finding is reflected in current literature (e.g. Higaki et al., 2004; Holm et al., 2006; Misery et al., 2007; Silverberg et al., 2018).

In addition to the above, the quantitative study also found that those with asthma and food allergies reported significantly poorer skin-related QoL and increased disease severity compared to those without these conditions. The reason behind this finding of those with concomitant conditions experiencing worse QoL than those with eczema alone is unclear. One possibility for this finding may be due to adults with concomitant disease presenting with more disease complications which consequently impacts their QoL. . Further research is needed to replicate and explain this finding as there is a paucity of literature that explores this despite the fact that many AD patients have accompanying conditions such as asthma (O'Connell, 2004). Those with comorbid atopic diseases experience discomfort as a result of not only intense pruritus, sleep loss, but also coughing and/or wheezing, dyspnoea, concomitant nasal congestion and/or rhinorrhoea (Lee, Ahn, Noh, & Lee, 2011; O'Connell, 2004). Moreover, they may give rise to issues such as concern about personal relationships, adoption of special clothing habits and withdrawal from public places (Spergel & Pellar, 2003).

The study also found that those who were prescribed topical corticosteroids, antihistamines, immunosuppressant medication, sedating medication, calcineurin inhibitors, Dupilumab and oral corticosteroids reported lower QoL and higher disease severity compared to those who did not take this medication at the time of the study. These findings reflect participants' accounts of AD management in the qualitative study. When discussing medication, participants in this study often expressed anguish due to the side effects of taking medication and the impact these effects had on them and their families. At times, these were discussed at length and one participant stated that the side effects of taking immunosuppressants was worse than her condition itself. For many, medication was no longer seen as a means of therapy but rather an obligation that needed to be adhered to, whether or not there were any benefits. This may be due to a lack of knowledge about treatments and their potential side effects in health care professionals; it is perceived as a significant contributing factor towards lack of adherence or anxiety regarding treatment failure and therapeutic regimes (Charman et al., 2003; Lawson et al., 1998). Many, after seeing no change to their AD, may try

complementary or alternative therapy, such as the use of herbal supplements, as a consequences of these anxieties or failure of conventional therapy. .

Johnston, Bilbao, and Gaham-Brown (2003) found a significant relationship between ethnicity and the use of complementary medicine (CM), with more than half of those using this therapy citing lack of efficacy of conventional therapy and 17% having concerns about side effects. . Another reason as to why QoL may have been lower in those taking medication could be due to financial costs incurred by these patients. Although the studies included adults only in the UK which has universal healthcare for its' citizens, there are a number of hidden costs to treating AD over and above health care costs (Fivenson et al., 2002; Herd & Williams, 2000; Su, Kemp, Varigos, & Nolan, 1998; Verboom et al., 2002). These include; cost of medication, loss of financial earnings (from sick leave), special diets, hospital/doctor related costs, extra cleaning and special bedding/clothes (Herd & Williams, 2000). Su et al (1998) reported that such costs relate directly to QoL and disease severity in AD with greater affects than those witnessed in other long-term conditions such as diabetes and asthma (Su et al., 1998).

The quantitative study also found that Asian participants reported significantly higher disease severity and lower QoL compared to their White and Black counterparts. This is a finding that enforces the qualitative findings presented in chapter 4, whereby Asian participants perceived their AD as more detrimental to their daily lives compared to White participants. Some Asian participants in the study discussed issues such as lack of knowledge in their culture, stigmatisation by loved ones, and a lack of willingness to discuss their AD with others. These issues appeared to be more impacted in Asian compared to White participants, with one participant concluding that her divorce to her husband was due to infertility caused by AD medication. The reason for this finding is unclear and warrant further investigation. Studies exploring the role of ethnicity and quality of life in patients and AD and psoriasis have reported similar findings whereby White participants report better QoL compared to BME participants (Boozalis et al., 2018; Kaufman, Guttman-Yassky, & Alexis, 2018; Shah, Stotland, Cheng, Ramos, & Caughey, 2011).

7.3.3 Feasibility study

The final study in this thesis aimed to explore the temporal relationship between psychological stress and disease severity due to the bi-directional relationship assumed by a number of cross-sectional studies. The study employed a longitudinal approach that involved the completion of daily diaries over a period of a month, as well as weekly questionnaires over a period of three months. Although the findings of this study do not point to a causation effect between stress and disease severity for the daily diaries, psychological variables and AD severity were found to be predictive of one another when measured weekly. Being a feasibility study, it was reported in line with STROBE guidelines for reporting of feasibility and pilot studies (Elm et al., 2007). The finding that weekly disease severity was significantly correlated with psychological stress are reflected through the current literature (Arndt, Smith & Tausk, 2008; Oh et al., 2010;Wright, 2005) and chapter 5 also found a significantly positive relationship between the two variables. Therefore although this is not a surprising finding, the significant positive relationship was consistent for majority of the weeks in the 12 week period.

The number of participants were acceptable for a feasibility study (Julious, 2005), however the small sample size may have contributed to many indices violating assumptions for a 'good' model fit in the CLPM analysis. The CLPM should ideally be run with large sample sizes as the model fit statistics are sensitive to sample size (Byrne, 2013). A general rule of thumb for SEM analysis would suggest a minimum of 100-200 subjects; however, these rules can be overly conservative and not generalizable to each study in question (Iacobucci, 2010). Though the sample size was sufficient for the analyses conducted, a larger sample size would allow for better missing data imputation and more comparisons within the SEM model, such as relationships between the individual indicators across latent constructs, and for the addition of other covariates such as medication use and psychological variables.

According to Lancaster et al. (2015), pilot and feasibility studies are not conducted to produce significant results ($p<0.05$) , and it has been suggested that the reporting of these studies

should be primarily descriptive (Lancester, Dodd, & Williamson, 2004; Grimes & Schulz, 2002) as testing a hypothesis requires a powered sample size which is usually not available in feasibility or pilot studies. Pilot studies aim to assess the implementation, retention, feasibility of recruitment, and assessment procedures of the novel study with the aim that each of these factors can be quantified (Leon, Davis, & Kraemer, 2011). Study elements that are considered infeasible or inadequate should be modified in the full-scale trial or removed altogether.

The participants who did not complete measures over the 12 weeks did not send the researcher incomplete study packs, although they were prompted to do so numerous times. Thus, drop-out analyses could not be performed on the remaining seventeen participants who had volunteered to take part. Recruitment took place through atopic dermatitis support groups; advertising through social networking sites yields a greater percentage of valid consents, a greater percentage of individuals meeting eligibility criteria, a greater percentage providing content-specific data, and a greater percentage of participants who complete surveys than other methods of recruitment (Ramo, Hall, & Prochaska, 2010). Therefore, using social media to recruit participants is advantageous, however as discussed above and in earlier chapters, the demographic characteristics of Facebook users do not necessarily reflect the AD population. For this study specifically, it is useful to note that those who use Facebook frequently are also more likely to report higher levels of psychological stress (Labrague, 2014; Nabi, Prestin, & So, 2013; Beyens, Frison, & Eggermont, 2016). Thus, it is likely that participants had higher reports of psychological stress compared to the overall AD population. It would be useful therefore to recruit using a range of methods, including dermatology clinics to complement social media as was the case for chapter 5.

Prior to commencement of the study, a ‘poll’ was initiated on Facebook and many support group users responded favourably stating the importance of such research. Indeed, the majority of the comments on the group are directed towards the lack of appreciation towards the mental health consequences of living with AD. Recruitment methods for this study differ from many previous prospective studies that explore stress and disease severity in skin

conditions (Chiu, Chon, & Kimball, 2003; Evers et al., 2010) where participants have been recruited from Dermatology outpatients clinics.

In addition to issues with the sample size, the lack of a temporal relationship for the daily measures may also be due to the fact that as a whole, the participants were experiencing only low-moderate levels of interpersonal stress that did not change much on a daily basis. Perhaps if all the participants experienced periods of both low and high levels of stress, a stronger relationship may be observed and this might be reflected in the findings from the weekly measures, which were completed over a much longer period of time. In fact, a few participants consistently reported no stress throughout the 30 day period. It may be of benefit to study participants over a period of time when they are likely to be experiencing high levels of stress e.g. starting a new job. It would also be useful to explore the role of social support, coping responses and appraisal in mediating the possible consequences of stressful situations on participants' lives. The qualitative study (chapter 4) revealed that participants deemed social support of great importance when discussing their experiences with AD. Additionally, mental health variables may be only one reason for changes in AD severity. . Climatic and allergic influences have also been implicated (Morren et al., 1994; Kantor & Silverberg, 2017). Therefore, it is possible that exacerbations of participants' AD occurred at times as a result of these additional factors. It is also possible that a certain level of stress must be experienced prior to the physiological effects are observed in AD.

It is important to note that daily stressors were the measure of psychological stress in chapter six. The impact of daily stressors (e.g. getting late for work, misplacing something important) is found to be a significantly better predictor of health outcomes than major stressors (Chamberlain & Zika, 1990; Dekkers, Geenen, & Evers, 2001). Nonetheless, the relationship between various types of stressors, for example disease-related daily stressors or traumatic childhood events (Evers et al., 2010; Evers, Lu, & Duller, 2005) should be explored to determine potential unique relationships with AD severity. Nevertheless, this feasibility study was carried out using daily diaries which enabled sensitive detection of changes in AD severity

and stress compared to using, for example monthly assessments which introduce other issues sauce as recall bias and higher attrition rates (Evers et al., 2010).

This study managed to recruit only female participants similar to chapters four and five in which women accounted for the majority of the sample. There is a possibility that men with AD react in other ways than women to stress-an issue that needs to be investigated further. The daily diary questionnaire seemed to work sufficiently well, as it was rated on a three-point scale and shorter than most validated stress questionnaires. Of course, scales like PSS could be used, but for the purposes of daily recording, it was important that the recording method was as easy as possible to perform. The issue of stress is complicated, and it is often difficult to distinguish between exposure to stressors and the subjective state of stress. Participants were not given a definition of stress, instead, they were asked to use their own definitions of perceived stress.

Relying on self-report is necessary for assessing emotional and other internal states as mentioned elsewhere in this thesis. However, there are potential limitations related to impaired self-awareness and recall bias for more objective problems like disease severity. The ability to provide a self-report of this was required for this study, which meant there was likely a difference in perceptions of what 'severe' meant for participants. A more suitable self-assessed severity tool for future studies would be the POEM or patient-oriented SCORAD which are correlated well with doctor-assessed disease severity (Finlay, 2016). However, those able to provide a self-report are also likely the best candidates for psychological or behavioural intervention, therefore making the study sample still representative of those whose clinical care would likely be informed by these results (Juengst, Myrga, Fann, & Wagner, 2017).

This study shows that like the other studies in this thesis, mental health variables correlate highly with AD severity. Furthermore, stress, anxiety and depression appear to predict disease severity and the disease severity also appears to significantly predict these psychological

variables a week after they are measured. This is a promising result and after addressing the issues discussed above, should be implemented into a full-scale prospective study.

7.4 Recommendations for clinical practice

The findings of thesis have a number implications for clinical practice. Perhaps the most important implication is the importance of awareness that adults with AD are at a higher risk of suffering from anxiety and depression. It is essential for health care professionals to prepare and offer suitable support to these patients. Further, findings reveal that a number of quality of life domains are affects in adults with AD, from physical to environmental. Thus, quality of life assessment needs to be incorporated into clinical assessments of AD where possible.

Findings from the qualitative study (chapter four) revealed the unpredictability of AD which results in difficulty managing the condition over time. Thus, health care practitioners should acknowledge and consider that severity of AD, and associated treatments, will change over a patient's life. Adults with AD should liaise regularly with their health care professionals to ensure that their treatment allows control over their condition, or indeed, change treatment where necessary.

Participants in chapters four, five and six were recruited using online support groups, amongst other recruitment platforms. As many people rely increasingly on the internet, health care providers should provide accurate and up-to-date information regarding AD online. This information should be available from and on a trusted source for example, a hospital or a GP practice website. . Additionally, online communication pathways such as support groups should be regularly moderated by qualified professionals, which could enable AD patients to feel more supported by the health care system and enable more disadvantaged groups being informed. Greene, Choudhry, Kilabu, and Shrank (2010) also emphasise that policymakers should consider that patients may seek social networking websites developed and patrolled by health care professionals to promote accurate and unbiased information exchange.

7.5 Future directions

A number of recommendations have been suggested throughout this thesis. This section will further summarise recommendations detailed in chapters three to seven. Although this research provided insight into lived experiences of those with AD, more in-depth qualitative research which uses interpretative phenomenology is needed to explore these experiences in depth (Chapter 3). Qualitative research has the ability to yield rich explanations and perceptions of an individual's world and how they make sense of living with the condition (Terry, Lyons, & Coryle, 2016). Using different types of qualitative methods such as photovoice which explores daily experiences in more depth would be beneficial.

The vast majority of the participants in this thesis were recruited using social media platforms, yet there is limited information on how patients with long-term conditions use online platforms to keep informed and educated about their illness, as well as how they use support groups on, for example Facebook to support their AD. Using qualitative methodology would also enable adults with AD to discuss their experiences and understanding of using online media and social networking sites to manage their condition and gain information and the use of media for support and relationships with other adults in similar situations.

This thesis also found ethnic differences in experiences with AD and reporting of quality of psychological variables (Chapter four and five). Indeed additional qualitative evaluation would enable a more in depth exploration of these differences. Moreover, further qualitative research could investigate why black and minority ethnic adults appear to be more affected by their AD as well as gender differences in experiences of living with the condition.

Additionally, research is needed to explore the role of health care professionals further, as participants in this thesis (chapter four) strongly perceived a lack of sufficient support from their health care providers. This was not assessed further in subsequent chapters thus it would be beneficial to explore how HCPs communicate with patients regarding the mental impact their AD has on them. Many health care professionals may choose pharmacological

treatments as their first choice to manage anxiety and depression, despite evidence for the effectiveness of psychological interventions in disease management. Astin, Beckner, Soeken, Hochberg, and Berman (2002) conducted a systematic review that explored the effectiveness of psychological interventions such as stress management, biofeedback and cognitive behavioural therapy in patients with long-term conditions. The authors found statistically significant, albeit small, effect sizes for self-efficacy, pain, depression and functional disability following treatment. Their data were based on twenty-five randomised control trials that compared findings from patient groups that received intervention to non-intervention control groups.

Those with AD can also suffer from severe psychological and physical co-morbid conditions in addition to their condition, however this thesis excluded those with co-morbid long-term conditions. Therefore, research exploring the prevalence of co-morbid conditions in those with AD and how these patients manage and experience multiple conditions is warranted.

7.6 Contributions

It is important to recognise that there is not one more suitable method of research, and this thesis infers that it is the combination of input from dermatologists, patients and psychologists that needs to be incorporated together in order to have a positive outcome on prognosis and health status in adults with AD. Using multiple methods, the research in this thesis has firstly using a systematic review identified current literature exploring the impact of AD on quality of life, secondly through a qualitative study, uncovered psychosocial issues that were identified as detrimental to patients' daily lives through their own perspective. Following this, a quantitative study employing validated psychometric measures investigated the impact of psychological variables on adult QoL. Finally, a feasibility prospective study enabled the exploration of the temporal relationship between disease severity and psychological stress over a period of three months. The findings of these studies contribute to the current knowledge that living with AD has an impact on many aspects of a person's life. The systematic review also allowed the researcher to build on what is already known on the topic

and identify areas of weaknesses that need further investigation. Moreover, although acknowledging that findings from qualitative research should not be generalised, the areas of concern highlighted are notable. Cultural and ethnicity differences which have not been explored in the past, were evident in this UK study with BME groups reporting several differences in their experiences of AD compared to White adults. This is a notion that needs exploring in more detail as these differences were also evident in the quantitative study. The quantitative study also comprised one of the largest UK sample of adults with AD at the time of the study. These participants were not just recruited from dermatology clinics (as most AD samples are) but made use of online media platforms to diversify the sample further. Some novel findings were highlighted from this study including the impact of type of medication on quality of life and mental health (chapter 5). This study adds to the existing body of literature by controlling for socio-demographic and clinical variables, using a large sample size, and using a variety of platforms for recruitment of participants. Finally, by implementing the longitudinal prospective study design, the temporal relationship between disease severity and psychological stress was accessible to be assessed consistently by the same observer, which would have been impossible in a cross-sectional survey.

Overall, this thesis has established that quality of life is highly compromised in adults with AD: findings illustrate that QoL in adults with AD reflects social, psychological, physical, environmental and spiritual/personal domains as demonstrated by the WHOQoL Group (2004). The findings of this thesis however suggest that for adults with AD, quality of life concerns fall predominantly within the psychological, physical and social domains (Fayers & Machin, 2007; Testa & Simonson, 1996).The research in this thesis also found that AD-related symptoms such as pigmentation, inflammation and scarring are detrimental to one's quality of life. Although this research has enhanced insight of the impact of AD on quality of life for adults within the UK, there is a need for further research which explored QoL in those with AD and how to improve it.

7.7 Strengths and Limitations

Although each chapter within this thesis identified strengths and limitations of the research, some of these were reflected across the studies in this thesis such as the use of online methods for participant recruitment and data collection. A number of benefits were considered when employing online methods for research; the most apparent was the ability to recruit a large sample of participants from a disease-specific population. Additionally, using online methods for recruitment enabled the researcher to recruit participants living in different regions of the UK as opposed to a specific area. Furthermore, the use of online methods to recruit participants resulted in cost and time savings, for example in the quantitative study, it is highly unlikely that a sample of 560 participants would have been recruited in five weeks if participants were required to complete these measures in a face-to-face scenario as opposed to online. This was also found in Chapter Four where participants who were not able to take part in face-to-face interviews opted instead to take part over the telephone. .

The researcher has severe AD therefore being diagnosed with the condition and sharing this participants may have resulted in participants perceiving the researcher as more relatable and approachable, facilitating recruitment and allowing participants to feel more at ease with sharing, often sensitive and emotion information. The researcher was also a member of the support group from which the majority of participants were recruited. This self-disclosure, defined as 'the act of revealing personal information to others' (Archer & Burleson, 1980, p. 183), potentially aided in building a better rapport with participants.

Meho (2006) and Moon (2000) advise that the researcher when conducting interviews should introduce and provide background information about themselves in order to encourage adults to participate in self-disclosure Similarly, Johnson (2001) found that respondents were more likely to engage in open discussion in internet-based questionnaires when the researchers engaged in self-disclosure. Self-disclosure reciprocity has been identified as the situation where an individual is more willing to engage with self-disclosure if the person conversing with them has also engaged in self-disclosure (Moon, 2000). Likewise, Valerian, Derlaga, and

Berg (2013) propose that if an individual provides information about themselves, the receiver is also more likely to do the same. The authors also suggest that this self-disclosure results in the recipient developing more of a liking for the self-discloser. The vast majority of participants in the studies were females; a study conducted in 1992 by Dindia and Allen concluded, through a large meta-analysis, that women were more likely to self-disclose to other women. Nonetheless, research exploring the impact of researcher gender on consequences of self-disclosure and recruitment using Facebook is warranted. Further exploration exploring the effects of the researcher's gender on recruitment in predominantly female Facebook groups is warranted, as well as the potential outcomes for nature of the data collected and recruitment due to self-disclosure by the researcher.

It is important to note that there are a number of limitations of using Facebook support groups to recruit participants. in addition to recruitment through dermatology clinic (chapter 5) and the university (chapter 4, 5 and 6) exclusion of participants from the studies was based on their self-report . For instance, in Chapter four, prior to participation, participants were required to confirm that they did not suffer from any long-term condition which was not related to their AD. Although, the majority of the participants were open about meeting the criteria, there is a possibility that participants may have suffered from other conditions and not disclosed this, hence taken part in the study.

A strength of this thesis is the multi-method approach utilised (see Chapter Two for more detail). Using this approach enabled the exploration of participants' lived experiences and as a result allowed the quantitative studies to be derived from these experiences detailed in Chapter four. Additionally, research questions to be explored qualitatively were recommended through the findings of the quantitative Chapters. For example, medication played an important role in QoL and disease severity in chapter five, and this identified the need for further qualitative research exploring disease management and medication adherence in adults with AD.

This process is described as sequential, where the researcher uses another method to expand on the findings of one method (Creswell, Clark, & Garrett, 2003), for example, beginning with a qualitative design for exploratory purposes and following up with quantitative approaches to generalise findings to a population. Additionally, employing a mixed-method approach allows for the collection of data sequentially to understand research problems better (Crewell, Clark, & Garrett, 2003). Likewise, Denscombe (2008) advocates that using mixed-methods in research allows for a more comprehensive data production and a better way of building in initial findings and developing further analyses. Future research suggestions derived from quantitative findings in this thesis involve exploring the impact of different types of medication on QoL in those with AD and cultural differences in QoL reporting.

7.8 Reflections through the research journey

In this section, the journey whilst completing this thesis and a number of personal reflections shall be discussed, thus this section will be written in first person. Jasper (2005) states that reflective writing "acknowledges at the outset that what is presented is that relating and purporting to the experiences and perceptions of the author" (p.250). As discussed in Chapter two of this thesis, I have been diagnosed with severe AD. AD affects everyone differently and my experience of the condition is on the severe end of the spectrum, with symptoms that have resulted in severe complications. It was my early diagnosis and experience of AD through adulthood that partly informed my decision to pursue this area of research.

I did not disclose my AD to participants during recruitment, however if asked why I was doing this research, I discussed my diagnosis and experiences of living with AD and how it developed my interest in the field. This discussion with my participants helped build rapport and may have enabled a more in-depth discussion of experiences. I have also been asked numerous times by colleagues, researchers, academics and friends about the reason for choosing this topic and the impact it has on me. I have reflected on these decisions and believe that although my diagnosis of AD enables me to be more empathetic towards participants, my experiences are largely different from many of my participants, therefore my research

analyses were grounded in the data and not my own experiences of AD. Additionally, I frequently had discussions with my supervisory team to ensure that my analyses accurately represented the data, in particular for the qualitative exploration (Chapter Four).

A challenging aspect to my PhD was not my personal experiences, but rather the emotive nature of this research such as participants' discussions of mental health and clinical diagnoses of psychiatric disorders in Chapter four. Nonetheless, although emotive, I regularly discussed them within my supervisory team. As I was a member of the Facebook support group, another emotive factor was when recruiting through this group, I witnessed numerous Facebook posts on my own page due to being part of the group. At times these posts presented stories of patients who were in dire need of pharmacological and psychological interventions; this consequently had a negative impact on my mood. Therefore, after I completed participant recruitment for the feasibility study, I limited the amount of posts I could see from these groups and also removed myself from a number of groups. As such, online data collection and participant recruitment tends to differ from face-to-face scenarios whereby in a face-to-face scenario you play the role of a researcher, being able to collect data from the participant and no longer be part of the participant's life and experiences. However when using social media platforms such as Facebook, participants' lives may become entwined with the researcher's, thus it may be more challenging to remove yourself from the situation. This was overcome in the feasibility study whereby I recruited from the support group but created a designated study page where participants could join and receive study-specific updates and reminders. Overall, these experiences helped shape my role as a researcher and enabled the development of both academic and interpersonal skills in an emotive context such as within this thesis.

7.9 Concluding comments

The findings of this thesis indicate that AD severely impacts the lives of adult patients both physically and psychologically. This research explored the lived experiences of adults with AD and identified issues perceived to be detrimental to their quality of life. A quantitative study

then proceeded to employ standardised psychometric instruments in order to investigate the impact of AD on QoL and psychological variables. Finally, a feasibility study allowed for the exploration of the temporal relationship between psychological stress and AD severity through the use of daily diaries and weekly measures. Whilst the research within this thesis has furthered understanding of the impact of AD on quality of life and mental health for adults living in the UK, there remains the need for research which explores further the quality of life in these adults and how to improve it.

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9 Appendices

9.1 Appendix 1 International Journal of Dermatology paper

TITLE PAGE

Original Article

Title: Impact of atopic dermatitis on quality of life in adults: A systematic review and meta-analysis

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- What is already known about this topic?

Atopic dermatitis (AD) has been found to affect quality of life (QOL) in adults with, studies reporting a greater impact on QoL with increased severity of AD. Adults with AD also report poorer QoL compared to a healthy population and those with other medical skin conditions such as urticaria and psoriasis.

- What does this study add?

This paper provides the first systematic literature review and meta-analysis of the impact of AD on QoL in adults. Across studies, increased disease severity significantly related to poorer QoL. Compared to healthy controls, adults with AD demonstrated significantly lower QoL but findings were mixed in studies that compared QoL in AD to other chronic conditions. Research exploring gender differences in QoL and the use of longitudinal study designs is lacking.

SUMMARY (ABSTRACT)

Background: Atopic dermatitis (AD) can affect quality of life (QoL) of adult patients, in whom the condition can be severe and persistent. There are currently no systematic reviews of the impact of AD on adults.

Objective: This paper provides the first systematic literature review and meta-analysis of the impact of AD on QoL in adults.

Methods: A systematic search was conducted using MEDLINE, Scopus, and Web of Science for articles published until October 2018. Inclusion criteria were a clinical diagnosis of AD, adult patients and QoL as an outcome measure. Interventions were excluded.

Results: A total of 32 studies were included. While QoL was assessed using Dermatology Life Quality Index (DLQI) in 25 studies, there was heterogeneity in the tools used to measure disease severity across studies. Meta-analysis of the seven studies that used the SCORAD to measure disease severity showed severity to be significantly related to poorer QoL. The remaining 18 studies also found increased disease severity significantly related to poorer QoL. When compared to healthy controls, AD patients demonstrated significantly lower QoL but findings were mixed in studies that compared QoL in AD to other skin conditions.

Conclusions: The findings highlight the significant impact that AD has on QoL in adults and the need for validated and relevant QoL measures to be implemented in clinical assessments for AD. Areas that require further research include an exploration of gender differences in QoL and the use of longitudinal study designs to explore factors that may cause differences in QoL ratings.

INTRODUCTION

Atopic dermatitis (AD) is a chronic debilitating inflammatory skin condition which mainly affects children but can also be present in adulthood[1]. AD is a significant health issue globally, with prevalence in children of 15-30% and 2-10% in adults[2]. The prevalence of AD in developed countries has increased two-to threefold over the past thirty years[3]. AD is characterised by symptoms such as itchy, red, dry and inflamed skin. It is a chronic condition in most people, and despite there being no cure for the condition, it can be managed well using emollients, topical corticosteroids and oral treatments such as antihistamines and immunosuppressant tablets. In the UK, 10-20% of all referrals to dermatologists and 30% of dermatology consultations are for AD[4]. A community study conducted in Scotland estimated that 38% of AD cases comprised adults over 16 years old[5]. Thus, although a relatively small percentage patients with AD are adults, studies also indicate a large percentage of adults seek treatment when compared to other age groups with AD.[5,6].

AD has been shown to have an impact on quality of life in children and adults[7-9]. Quality of Life (QoL) is defined by the World Health Organization Quality of Life (WHOQoL) Group[10] as an "individuals' perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" (p. 5). Health related QoL (HRQoL) is considered a valid indicator when monitoring health and service needs of patients[11]. Measuring HRQoL can help inform interventions to alleviate health conditions and is of potential value in performing risk-benefit analyses of clinical decisions for treatment, especially where systemic therapy with possible side effects is prescribed. A review of the literature by Lifshitz[7], which focused on the impact of AD on QoL primarily of infants, children, adolescents, and their families, reported that AD had a significant and lasting effect on HRQoL, in particular on psychological wellbeing and social functioning. A review by Lewis-Jones[8] on QoL and childhood AD confirmed that QoL in children and adolescents was severely impaired with issues such as embarrassment and bullying affecting children psycho-socially and physically.

Relatively little research has been conducted with adults who have AD, but the research that has been conducted suggests that all aspects of HRQoL are affected in adults with AD, and that HRQoL is more compromised in adults with AD when compared to adults with chronic urticaria and psoriasis[9].

In addition, little is known about how HRQoL of AD patients varies with disease severity; the literature that has investigated this issue has found that greater disease severity is related to poorer HRQoL[12,13]. To draw together what is currently known in this area and identify gaps in knowledge, the present study reports the results of a systematic review and meta-analysis of the impact of Atopic Dermatitis on QoL in adult patients.

METHODS

Study searches were conducted using three electronic databases: MEDLINE, Scopus and Web of Science Core Collection. Databases were searched up to 24th October 2018 with no limit to the start date. Search terms can be found in the supplementary information. The initial search was conducted by the lead author; all members of the study team reviewed all full papers retrieved for evaluation.

Inclusion/exclusion strategy and data extraction

To be included in this review studies had to report data from adults. The legal age of adulthood differs according to country. This review included participants aged 18 and above or 16 and above if defined as an adult in a study, adolescents were excluded. Studies that combined adult and children data into one analysis were excluded. Studies that collected data from both adults and children, but reported data separately for these sub-groups, were retained in the review. Studies that measured QoL as a result of medical or psychological interventions were excluded. Study search was limited to English-language articles on human populations. Case-reports and conference abstracts were excluded. All study types were included if they reported on a QoL measure.

Outcomes

The primary outcome in this review was QoL in adult patients with AD. QoL was measured either on its own, in relation to disease severity, compared to healthy controls or compared to patients with other conditions, such as psoriasis.

Quality Appraisal

The quality of the included studies was assessed using the Mixed Methods Assessment Tool (MMAT)[14]. All members of the study team reviewed and agreed on the quality ratings for each paper.

Data synthesis

Where studies reported QoL scores using the same instruments, results were pooled using meta-analysis. In cases where pooling was not considered appropriate, detailed descriptions of study characteristics and results were reported alongside study quality.

RESULTS

Figure 1 outlines the search strategy following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards[15]. A total of 32 papers met inclusion criteria and were included in this systematic review. No mixed methods or qualitative papers included a measure of QoL, therefore all included papers in this review are quantitative and reviewed using narrative synthesis. Seven papers reported a correlation between the Dermatology Life Quality Index (DLQI) and a validated measure of AD severity (SCORAD). Correlations from these papers were pooled using random-effects meta-analysis in Comprehensive Meta-Analysis Version 3 (2005, Biostat Inc.). Table 1 reports study characteristics. Using the MMAT, 24 studies were of higher quality, scoring 75-100% and eight studies were of lower quality, scoring 25-50% (see supplementary Table 1).

Quality of Life

The DLQI was used to measure QoL in 25 out of 32 studies included in this review. Mean overall DLQI scores ranged across studies from 4.9 (small effect on patient's QoL) to 20.5 (very large effect on patient's QoL). In studies which looked at differences across the dimensions of QoL, the areas that were most affected as measured using the DLQI were symptoms and feelings surrounding AD; patients felt embarrassed or self-conscious due to their AD and symptoms such as itchy, sore, painful and stinging skin had a detrimental impact on their QoL[16-21]. Personal relationships were the least affected dimension of QoL[16,17,19,20]. Mozaffari et al[22] found that patients perceived dressing, undressing and bath-time as being most problematic while the dimension 'family activities' was least affected. Holm et al[21] also found that dressing was particularly problematic. Using the EQ-5D as a measure of QoL, daily activity and pain/discomfort parameters were reported to be most affected in patients[23]. Other less frequently used measures included the EQ-VAS, VQ-dermato and Skindex.

Quality of Life and Disease Severity

Twenty studies explored the relationship between disease severity and QoL. Nineteen studies looked at this using DLQI in AD patients (see Table 2). Eighteen of these reported significant correlations between disease severity and DLQI; the more severe the disease, the lower the QoL. In seven of these studies, QoL using the DLQI was compared with disease severity measured using the SCORAD [12,16,26,27,28,29,30]. These studies were pooled together using random effects meta-analysis (See Figure 2). The sample-weighted average correlation between HRQoL and disease severity was $r_+ = .44$ (CI 0.27; 0.59), indicating a medium-sized relationship[31], with greater disease severity relating to poorer QoL. There was significant heterogeneity in the results ($\chi^2 = 13.78$, $p < .05$). This could partly be explained by the small correlation reported by Haeck et al[12].

Two studies[25,32] used the EASI to measure AD severity in relation to QoL. Both studies found statistically significant relationships between QoL and disease severity (ps < .05); QoL was perceived as being poorer with increasing disease severity, with personal relationships being related to a lesser extent to disease severity than other domains. .

Nine studies[13,17,18,19,22,23,24,34,35] explored relationships between patient-assessed disease severity and DLQI scores and reported statistically significant medium to large sized correlations whereby an increase in disease severity was associated with a decrease in QoL.. Two studies[37,38] explored gender differences and found a significant positive correlation between patient-assessed disease severity and DLQI score ($p < .001$) and between visible regions and DLQI score ($p = .001$) for women, however neither of these correlations were observed in men.

Two studies[33,39] assessed severity using the Rajka & Langeland scoring system which measures clinical course, severity, and extent of AD. Both studies found statistically significant correlations between disease severity and QoL. Highest correlations found were between disease severity and symptoms and feelings; higher disease severity was related to worsening symptoms and feelings as a result of AD.

Ten studies used the SF-36 to measure QoL; six of these looked at the relationship between SF-36 scores and disease severity[17,19,24,25,32,33,40,41] . Five studies found significant correlations between disease severity and the SF-36, with increased severity associated with poorer QoL. However one study[25] found no significant correlations between any SF-36 subscales and clinically measured disease severity (EASI). The correlations between the SF-36 and disease severity across the six studies were small to large-sized. The mean physical dimension scores appeared to be less impaired in AD patients compared to the mean mental component scores of the scale[17,24,32,3342,43] .

Quality of life in patients with AD compared to healthy controls or other patient groups

A total of 15 studies compared adults with AD QoL to that of healthy controls. Ten studies used generic QoL scales such as the SF-36 to enable comparison across groups[19,23,24,25,33,35,40,41,43,44] ., three studies used dermatology specific QoL scales to make comparisons[22,26,45] and three studies[35,37,46] used both generic and dermatology specific scales. Overall QoL was significantly poorer in those with AD compared to healthy controls and, domains such as mental health and social functioning were affected to a greater extent in AD patients[17,22,29,35] . In a recent study by Misery et al[46] scores on the mental dimension of the SF-12 were lower in AD patients with visible area involvement compared to those without ($p<0.001$).

Two studies compared QoL between vitiligo and AD patients[34,45] and found significantly lower QoL in the AD groups compared to the vitiligo groups (*ps*<0.001). Four studies compared QoL between psoriasis and AD patients[9,19,34,41]. Two of these studies found that AD patients had significantly lower QoL than patients with psoriasis[9,34] whereas Lunderberg et al.[19] found significant differences in the physical and mental functioning domains; with AD patients scored better than patients with psoriasis. Eckert et al[41] found no significant differences in QoL ratings in patients with psoriasis or AD. Grob et al[9] also compared AD with chronic urticaria and found that AD patients were more affected by skin discomfort than chronic urticaria patients. They also had lower scores in relation to 'treatment induced restrictions' compared to those with chronic urticaria.

DISCUSSION

This systematic review examined the impact of AD on QoL in adults. The DLQI and the SF36 were the most frequently used scales to measure QoL in patients with AD, and studies in this review looked at QoL in relation to disease severity, other chronic skin conditions, or healthy controls. The qualitative synthesis of results and meta-analysis show that there is a consistent relationship between increasing AD severity and poorer QoL in adults, and adult patients with AD have poorer QoL than healthy groups. Findings are more equivocal for comparisons with other chronic skin conditions.

Qol and disease severity

Nineteen of the 20 studies that measured QoL in relation to disease severity found increased disease severity was significantly related to poorer QoL. This finding is consistent with reviews looking at QoL in children with AD[8,47]. Almost all adult patients had mild to moderate AD in the studies included in this review. Interestingly, in paediatric studies where more patients had moderate to severe AD, QoL correlated less well with disease severity than the adult patients with mild to moderate AD in this review[48,49]. The consistent finding that disease severity was related to QoL underscores not only the importance of offering both dermatological and psychological treatment to patients, but also the need to incorporate QoL screening tools in dermatology. Nonetheless, AD is a complex condition and QoL cannot solely be explained by severity of the disease as most studies reported low to medium correlations between the two variables. One factor that may influence QoL and may explain differences between studies is time of recruitment whereby patients could be experiencing a flare-up during recruitment, thus affecting QoL scores; this is especially the case if participants were recruited during dermatology visits.

QOL and patients with AD compared to other healthy controls

All studies that compared QoL in AD patients to healthy controls found significantly lower QoL in AD patients. However, four studies used the DLQI measure to explore this difference; the DLQI is a dermatology specific questionnaire with questions that are not suitable for use in a sample of the general population. In such cases, generic QoL measures such as the SF-36 should be employed. When using the SF-36, better physical QoL was reported by studies in this review compared to mental QoL. This is in line with a systematic review carried out looking at QoL in psoriasis patients[50].

The SF-36 is probably not sensitive enough to measure the physical limitations of AD due to its generic nature; questions relating to walking abilities for example are unlikely to be relevant to this group.

QOL and patients with AD compared to other chronic skin conditions

Studies comparing QoL to other chronic skin conditions had mixed results, but for those comparing vitiligo and AD patients, significantly lower QoL was seen for AD. This may be because vitiligo is not accompanied by symptoms such as itching, inflammation, and sleeplessness. Symptoms such as pruritus have more of an impact on QoL than visual aspects; indeed, this review found that the area of QoL most affected was symptoms surrounding AD. Studies reporting better physical and mental functioning scores in patients with AD compared to those with psoriasis and poorer scores in patients with AD regarding skin discomfort compared to urticaria suggests that pruritus is the dominant factor that interferes with everyday life. Further, the contrast between lower scores related to 'treatment induced restrictions' in patients with AD and better scores in patients with chronic urticaria suggest that topical treatments can be highly restrictive to patients. Indeed, alternative/complementary therapies for AD, such as Chinese herbal therapy have become increasingly popular[51,52,53]

Demographic characteristics of patients

Many of the participants in the included studies were female. Partly this reflects health care utilization, whereby women use more health services and an estimated 67% of women worldwide make all medical choices in society[54]; in this case, most of the participants were out-patients in dermatology clinics. Only one study looking primarily at gender differences in QoL and AD and found no significant correlation between disease severity and QoL in males but a significant positive correlation was present in females. Thus, the extent to which the AD severity is correlated with QoL in in relation to females rather than males deserves further research attention. Lesions located in visible areas have been found to affect women more than men[37] possibly because women may have a higher ideal of culturally determined physical appearance than men so more attention is given to the skin. Gender differences have been found in other allergic conditions with females presenting more complex allergy-related conditions compared to males[55,56] and so further research in relation to AD is needed.

Limitations of the studies in this review

The heterogeneity in tools used to measure disease severity made it impossible to pool results across all included studies. The SCORAD and EASI are generally preferred by researchers over patient-assessed severity or visual analogue scales as they are validated measures of disease severity. However, they do not cover all issues affected in AD patients, for example, SCORAD only measures disease severity over the preceding three days, therefore long-term severity effects on QoL cannot be inferred. Nevertheless, studies that included both patient-assessed severity and objective measures found relatively strong correlations between the two, indicating that patients can self-assess their disease severity accurately.

All studies included in this review used cross-sectional methods to assess QoL in relation to disease severity. Results using this methodology should be interpreted with caution as it's impossible to determine cause and effect. Future studies should utilise prospective designs and collect more longitudinal data to strengthen predictive power of psychological and clinical variables of QoL. AD is generally better during the summer and worse in winter[58]. Only one study specified the season.

Although the quality appraisal for the studies showed that the majority had good to excellent ratings, many suffered from methodological weaknesses, such as the use of small sample sizes, or the use of non-validated measures. Other issues included absence of statistical testing and incomplete presentation of QoL data such as descriptive statistics. In addition, some studies used dermatology specific questionnaires to determine QoL in healthy controls.

Conclusions and directions for future research

This study is the first systematic review and meta-analysis conducted on adults and demonstrates that AD influences all aspects of the lives of adult sufferers. Results support findings from previous research on similar skin conditions[50,60] and in children[7,8,47]. The present review points to several areas for future research. In the present review, overall scores were difficult to interpret because of the variability of scores and the absence of formal reference values or norm scores, or the absence of

formal comparisons with population norms. More research with validated psychometric scales is needed to generate a consistent body of knowledge of overall QoL of patients with AD. Furthermore, application of both generic and disease- or dermatology-specific quality-of-life questionnaire which cover the full range of quality-of-life issues are needed.

Second, data on the relationship between specific AD characteristics and QoL suggest that itch, sleep disturbances, and exacerbations in facial and genital body areas[34] could be relevant predictors of quality of life, as reported by a few studies in this review,[13,34,45]. A deeper insight into these relationships is important because of consequences for disease-severity measurement in quality-of-life research; indeed, a more qualitative approach would help uncover some of these issues.

Researchers in dermatology are encouraged to utilise validated and clinically relevant QoL measures for patients that provide accurate measurement of quality of life and allow for subsequent comparison of results across studies. Factors such as sleep disturbances and pruritus should be included when determining QoL and future studies should also further explore gender differences in QoL in adults with AD; only a few studies in this review considered these factors. Longitudinal study designs are also needed to explore what factors related to AD cause differences in QoL ratings.

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Table 1. Study characteristics

Authors	Country	N	Participants	Measures used		Outcomes measured	Outcomes measured
				Disease severity	Quality of life		
Arima et al (2018)	Japan	638	Mean age- 38.67 years, 52.37% female. 45.45% rated severity as moderate/severe, 54.54% rated severity as mild. Comparisons with 1268 non-AD controls	Self-rated severity	SF-36	QoL comparisons between patient groups and healthy controls	AD patients reported significantly reduced HRQoL relative to matched non-AD controls ($p<0.001$) for mental and physical domains of the SF-36.
Baron et al (2006)	UK	63	Mean age – 34 years, Mean duration of AD- 15.2 years, 26 men and 37 women	SCORAD	DLQI	Relationship between disease severity and QoL	The mean DLQI reduced over all three visits from 9.5 to 8.8 at T2 to 7 at T3. The DLQI was significantly correlated with SCORAD at T1 ($r= 0.389$, $p <0.01$) and at T2 ($r=0.321$, $p < 0.01$) but not at T3. Mean SCORAD reduced by 52% from T1 to T2 ($F_{2,62} =37.9$, <0.001) but there was no significant change in SCORAD from T2 to T3.

Beikert et al (2014)	Germany	384	384 AD patients (mean age 42, range- 18-92, 69.8% female). Patients with AD aged> 18	Patient-assessed severity	DLQI	Relationship between disease severity and QoL; Comparisons between AD patients and patients with other conditions.	The mean DLQI total score in AD was 8.5, compared to 7.0 in Vitiligo and 6.7 in psoriasis and 4.3 in rosacea. Impairment of QoL measured by DLQI correlated positively with the affected body surface area (r=0.46, p<0.001). Characteristic AD symptoms such as skin dryness, pruritus, and sleep disturbances also correlated significantly with the DLQI total score (r_s=0.34 to 0.53, p<0.001).
Chen et al (2012)	Taiwan	1132	The participants were categorized in to 3 groups: 1) AD (n=90), 2) non-atopic hand eczema (n=205), 3) control group with no aforementioned skin conditions (n=837), average age- 30.5 years, 100% female.	-	SF-36	QoL comparisons between patient groups and healthy controls; Comparisons between AD patients and patients with other conditions.	QoL was significantly lower for patients with AD compared to controls in 5 out of 8 domains including social functioning, bodily pain, vitality, mental health and general health (*ps* <0.05). No significant difference was found between the AD group and the non-atopic eczema group in all domains of QoL investigated.
Chrostowska-Plak et al (2013)	Poland	89	59 females and 30 males. Mean age- 31.6 years. Mean disease duration- 22.8 years.	SCORAD	DLQI	Relationship between disease severity and QoL.	There was a significant correlation between pruritus and HRQoL (r= 0.5, p < 0.001) DLQI also correlated with periods without itching indicating that patients with longer itching-free periods had better HRQoL (r= 0.23,

							p<0.05) There was a significant correlation between the severity of the disease (using SCORAD) and HRQOL (r=0.65, p < 0.001)
Coghi et al (2007)	Brazil	75	Patients were diagnosed and treated as isolated AD by the attending clinician; 65.33% were females, mean age -26.28 years, average years of duration of AD-16.74 years.	EASI	DLQI, SF-36	Relationship between disease severity and QoL	QoL and disease control were found to be related but with low scores both in DLQI (r = 0.26) and in SF-36 (r = 0.2) but with greater correlation for SF-36 mental components. Both correlations were significant (p < 0.001).
Eckert et al (2017)	USA	349	Mean age- 46.1 years; 68.3% women; 66.8% White. Matched with 698 non-AD controls.	Self-rated severity	SF-36	QoL comparisons between patient groups and healthy controls; Comparisons between AD patients and patients with other conditions.	AD patients reported lsignificantly reduced HRQoL relative to matched non-AD controls for both mental and physical domains of the SF-36 (P<0.001 & p=0.004 respectively). Compared with psoriasis, AD had a similar impact on HRQoL.
Finlay (1996)	UK	92	43 males and 49 females; average age 33.2 years (range 16-67).	Physician assessed severity	DLQI	Comparisons between AD patients and patients with other conditions.	The mean DLQI index was 18 with subsections relating to ‘symptoms and feelings’ and ‘treatment effects’ scoring highest. Disease comparison utility questions demonstrated that patients consider diabetes and

							hypertension would be better than having eczema whereas bronchitis would be worse than having eczema.
Fivenson et al (2002)	USA	107	Cohort- 298; 107 adults; mean age of whole group- 17.22 years; 62% female.	Rajka & Langeland scoring system, patient-assessed severity	DLQI, SF-36	Relationship between disease severity and QoL, QoL comparisons between patient groups and healthy controls.	46% of adults had mild disease, 11% adults had severe disease. In terms of provider assessed severity, 51% adults had mild disease. The mean DLQI score was 6.6 for adults with a range of 0 to 27. The mean score for DLQI increased with increasing disease severity for all but two questions. For the SF-36, statistically significant differences were detected between the study group and the US population norms for vitality, social functioning, and mental health. Patient-assessed severity had a stronger association with DLQI ($r = 0.57$, $p = 0.0001$) than provider-assessed severity ($r = 0.27$, $p = 0.0036$).
Grob et al (2005)	France	1356	An investigator had to recruit clusters of three patients, one with chronic urticarial (CU), one with psoriasis (PSO) and one with AD, matched by sex and age. Subjective impression of severity	Physician assessed severity	VQ-Dermato	Comparisons between AD patients and patients with other conditions.	After adjustment for confounders, HRQoL dimensions were differently affected in the three diseases. The 'physical discomfort' dimension was more degraded in AD and CU than in PSO ($p < 0.001$) and 'leisure activities more in PSO than in CU ($p < 0.001$). No aspect of HRQoL

			was rated by the physicians as minimal/moderate/severe/very severe				was spared in AD. The mean overall VQ-Dermato index was significantly lower in CU (M= 36.93) and in PSO (M= 38.88) than in AD (M= 44.62, $p < 0.001$).
Haeck et al (2012)	Netherlands	54	Average age of the patients was 37.3. At inclusion, the average objective SCORAD was 43 indicating severe AD, average DLQI was 14.6 indicating a large effect on QoL.	SCORAD,	DLQI	Relationship between disease severity and QoL	At t=0, there was a small non-significant correlation between the DLQI and objective SCORAD, 'rule of nine' or serum TARC level. At t=6 the objective SCORAD, serum TARC and the 'rule of nines' scores showed moderate and significant correlations with the DLQI ($r = 0.34$, $p = 0.02$; $r = 0.31$, $p = 0.03$; $r = 0.49$, $p < 0.001$). An individual's improvement in disease activity (SCORAD, SASSAD and 'rule of nines') with 10 points was associated with an improvement in DLQI.
Higaki et al (2004)	Japan	162	162 patients with AD ranged in age from 17-77 years: the mean age was 29 years; 55% were female. 17 had mild, 107 had moderate and 36 had severe AD.	Rajka & Langeland scoring system (mild,	Skindex-16	Relationship between disease severity and QoL	Each of the three scale scores (symptoms, emotions and functioning) of the patients with AD were significantly higher than those of patients with isolated lesions. Patients with severe AD showed significantly higher scores in the three scales, as well as the Global Scale than those with moderate dermatitis. There was a

				moderate and severe)			significant positive correlation between the severity and each of the three scale scores (r's= 0.32 to 0.45, p < 0.001).
Holm et al (2004)	Denmark	112	Mean duration of AD of 28.6 years. Females (n=88) and males (n=24); mean age of females- 34.2, males- 39.2.	Patient assessed severity.	DLQI	Relationship between disease severity and QoL, Differences in QoL between men and women with AD	For women, there was a significant positive correlation between disease severity ad DLQI score (KW test, 15.9; p < 0.001) and also between DLQI score and visible regions affected by disease (KW test, 14.2; p = 0.001); these correlations were not observed in men. No significant differences between men and women were noted for age, disease duration, overall disease severity or QoL as assesse using the DLQI.
Holm et al (2006)	Denmark	101	101 atopic eczema patients, 66 adults with AD, and 23 adults without AD (control group).	SCORAD, patient-assessed severity	DLQI, SF-36	Relationship between disease severity and QoL, QoL comparisons between patient groups and healthy controls.	Patients with AE had significantly lower QoL (p<0.05) than healthy controls (median DLQI score 5 in AD patients vs. 0 in controls) and the general population. DLQI, pruritus and patents and investigator overall assessment of eczema severity were significantly (p < 0.0001) and positively correlated with SCORAD, while the generic questionnaire showed only poor correlation.

Holm et al (2016)	Denmark	191	Mean age- 31.32 years, 59.2% females	SCORAD	DLQI	Relationship between disease severity and QoL	Significant relationship between disease severity and HRQoL (r=0.42, P<0.001), with increase disease severity significantly associated with worsening HRQoL. There was also a significant relationship between DLQI and self-rated health (r=-0.37, p<0.001).
Kiebert et al (2002)	USA	239	Mean age- 36 years, 79% female; 18.2 years mean duration of disease, 46% mild severity, 41% moderate severity, 11% severe severity.	Patient assessed severity	DLQI, SF-36	Relationship between disease severity and QoL; QoL comparisons between patient groups and healthy controls.	SF-36 scores showed a significant decrease with increasing disease severity. DLQI scores correlated well with patients ratings of disease severity. The SF-36 scores correlated significantly with DLQI scores. The SF-36 scores of patients with AD were significantly lower (indicative of more impairment) than those of the general population. The mental component score of the SF-36 was significantly correlated with patient severity rating (r=-0.41, p<0.001), the physical component was not.
Kim et al (2012)	Korea	415	Subjects were divided in to three groups; infants, children and adults ((75	SCORAD	DLQI	Relationship between disease severity and QoL.	The total mean DLQI score was 10.7. No significant differences in gender and age were observed. Adults with atopic disease including AD with concomitant

			males and 72 females). Mean age of adults= 25.8 years.				asthma, allergic rhinitis or allergic conjunctivitis had higher total scores than those with AD alone. Both the Rajka & Langeland eczema severity score (r=0.261, p<0.05) and SCORAD index correlated significantly with all the total QoL scores (r=0.432, p < 0.001).
Kong et al (2016)	Korea	50	22 men and 28 women, mean age 26.4 years.	SCORAD	DLQI	Relationship between disease severity and QoL	Significant relationship between disease severity and HRQoL (r=0.237, P<0.001), with increase disease severity significantly associated with worsening HRQoL. There was also a significant association between sleep disturbance and QoL (r=0.388, p=0.04), with increase sleep disruption associated with worsening QoL.
Kwak et al (2017)	Korea	157	Mean age- 35.2 years; 51.8% Males; 11,756 non-AD controls (mean age- 45.3 years; 49.3% male)	-	EQVAS	QoL comparisons between patient groups and healthy controls	Adults with AD had lower HRQoL (p=0.013) and more stress (p=0.002) than those with AD. Even when controlling for demographic characteristics, HRQoL of adults with AD was lower than adults without AD.
Lee et al (2018)	Korea	677	Mean age 36.1 years; 47.8% females; 36,901 controls- mean age 45.4 years, 50.8% females	-	EQ-5D and EQ-VAS	QoL comparisons between patient groups and healthy controls	EQ-VAS scores were significantly higher in patients with AD than in those without AD (p=0.004). A higher rate of pain/discomfort, and anxiety/depression was found on

							the EQ-5D in AD patients compared to controls (p=0.003 and p<0.001, respectively).
Linnet & Jemec (1999)	Denmark	54	23 women (mean age=27.5), 9 men (mean age=30.3); average duration of condition=26.1 years. Aged 18-60 years.	SCORAD	DLQI	Relationship between disease severity and QoL; QoL comparisons between patients groups and healthy controls.	AD patients- significantly lower dermatological life quality (Z= 5.1, p<0.001) and higher state (Z= 2.14, p<0.032) and trait (Z= 3.49, p<0.001) anxiety compared to the control group. Significant positive correlation between SCORAD and DLQI (r= 0.54, p<0.002).
Lundberg et al (2000)	Sweden	366	The average duration of AD was 25.83 years and the mean age of AD patients was 34.79 years old; 92% were male. The average duration of psoriasis was 18.39 years and the mean age of psoriasis patients was 49.87 years old; 51% were male.	Patient assessed severity	DLQI, SF-36	Relationship between disease severity and QoL; QoL comparisons between patients groups and healthy controls; Comparisons between AD patients and patients with other conditions.	DLQI scores showed poorer HRQoL for patients with AD compared to psoriatic patients but this was not significant when controlling for confounding factors. No significant difference on the SF-36 between patients with AD and patients with psoriasis. There was a decreasing DLQI score for patients of higher ages; improved HRQoL. Spearman's correlation coefficients showed that all SF-36 dimensions were significantly correlated with all measures of disease activity (r= 0.182 to 0.526), the DLQI correlations with VAS were also significant (r=0.005 to 0.595).

Maksimovic et al (2012)	Serbia	130	Adults- 56.1% female, mean age 34.18 years, mean age of onset of disease - 13.95 years, mean duration of disease- 20.23 years..	EASI	DLQI, SF-36	Relationship between disease severity and QoL, QoL comparisons between patient groups and healthy controls.	The DLQI scores corresponded well with disease severity; increased disease severity was associated with greater impairment in HRQoL (r=0.14 to 0.47 for all domains of the DLQI). In adults, significant differences were only found between DLQI scores for mild and severe AD. The highest correlations were seen between symptoms and feelings and daily activities ($r = 0.75$, $p < 0.01$), symptoms and feelings and work/school ($r = 0.53$, $p < 0.01$) and leisure and work/school ($r = 0.59$, $p < 0.01$). Patients with AD had inferior social functioning and mental health scores compared with the general population.
Mikolajczyk et al (2017)	Poland	59	36 women and 23 men with AD; aged 18 to 46 years; mean age- 26.9 years; mean disease duration- 15.1 years	-	DLQI	Gender differences in QoL; impact of illness duration on QoL	No significant differences between women and men for DLQI scores ($p>0.05$); significant correlations between QoL and health evaluation and body areas satisfaction ($r=-0.48$), appearance orientation ($r=0.31$).

Misery et al (2007)	France	266	34.2% patients were males and 65.8% were females. The mean age was 32.7 years and mean duration was 19.3 years. 1,6% had mild AD, 42.9% had moderate AD, and 55.6% had severe AD.	SCORAD, patient-assessed severity	DLQI, SF-36	QoL comparisons between patient groups and healthy controls.	The mean DLQI score was 8.8 and the physical and mental composite 12 scores were 50.7 and 39.5 respectively. Analyses according to SCORAD showed DLQI scores 6.8 (SD=4.4) and 10.2 (SD=5.6) for moderate and severe AD groups ($p<0.0001$).
Misery et al (2018)	France	1024	58.3% female; 27.6% mild AD, 40.4% moderate AD, 31.9% severe AD	PO-SCORAD	DLQI; SF-12; EQ-5D	Differences in QoL by visible area involvement	Patients with visible area involvement were found to have lower QoL than those without ($p<0.0001$), EQ-5D ($p<0.05$), and the mental score of the SF-12 ($p<0.0001$). No differences in physical score of SF-12.
Mozaffari et al (2007)	Iran	184	75% AD adults were female, 57.2% control group adults were female. Mean age of AD adults was 38.25 and mean duration of disease was 20.6 years, 9.5% had mild AD, 12% had moderate AD, and 18% had severe AD.	Patient assessed severity	DLQI	Relationship between disease severity and QoL, QoL comparisons between patient groups and healthy controls.	Significant differences between DLQI mean scores in AD group (M=20.5 SD=4.7) and control group (M=1.15, SD=0.85) mean score ($p < 0.001$). Scores of each question were significantly higher in the AD group than in the control group ($p<0.001$). Correlation between DLQI and AD severity was significantly positive ($r=0.88$, $p < 0.001$).
Noh et al (2013)	Korea	180	27 males (45%), 33 females (55%) with AD, mean age 32.4 years. Mean age of	EASI	DLQI	QoL comparisons between patient groups	AD patients- significantly higher scores for all 5 questionnaire items compared with normal controls

			Vitiligo patients was 35.1 (31 males and 29 females), mean age of normal controls was 31.9 (25 males and 35 females).			and healthy controls; Comparisons between AD patients and patients with other conditions.	(p<0.001). In the comparison between the AD and Vitiligo groups, AD patients reported lower QoL (β= 0.752, t=11.522, p < 0.001)
Sanchez-Perez et al (2012)	Spain	323	Adults mean age was 32.3 years and 58.7% were women; over half of adults (55.8%) were aged between 18 and 30 years. Concomitant disease was observed in 40% of adults.	EASI, patient assessed severity	DLQI	Relationship between disease severity and QoL	Significant differences in QoL observed according to investigator assessed severity (mild disease – M=5.5, SD=5.3; Moderate disease- M=7.5, SD=4.8; severe disease- M=12, SD=5; p < 0.05). Pruritus caused everyday problems related to sleep and sexual function. The presence and intensity of pruritus was very closely related to HRQoL, with a high correlation coefficient between overall itch severity scale (ISS) score and overall DLQI score (0.72).
Silverberg et al (2018)	USA	602	53.6% female and 71.9% White, with mean age of 52 years. AD severity was measured using self-reported global severity- 53.1% mild, 38.8% moderate, 8.1% severe AD.	POEM, PO-SCORAD	DLQI;SF-12	Relationship between disease severity and QoL; Comparisons between AD patients	SF-12 mental health sub-scores for moderate AD were lower than all other disorders (e.g. diabetes, asthma, anxiety/depression, heart disease) and for severe AD, dramatically lower than all other disorders. Little difference between physical health scores across

						and patients with other conditions.	disorders. Moderate and severe AD (using PO-SCORAD, PEOM and global severity) were significantly associated with DLQI (ps<0.0001).
Torrelo et al (2013)	Spain	282	48.2% were male and mean age of the adults was 33.06 years. 79.4% had moderate AD and 19.9% had severe AD. Mean duration of AD for adults was 19 years.	Patient assessed severity	DLQI	Differences between groups for disease severity.	Statistically significant impact on the daily lives of patients receiving maintenance therapy. However patients with moderate AD had higher levels of emotional, physical and social well-being compared to those with severe AD ($p < 0.05$).
Wittkowski et al (2004)	England	125	23 males, 102 females; aged 18 to 66 (mean age of 37.2 years). The mean duration of AD was 30.7 years.	Patient assessed severity	DLQI	Relationship between disease severity and QoL	Disease severity was significantly correlated with QoL ($r = 0.49$, $p < 0.01$), perceptions of stigma ($r = -0.28$, $p < 0.01$) and depression ($r = 0.18$, $p < 0.05$). 46.7% of the variance in DLQI scores ($p<0.001$) was explained by depression and disease severity. Disease severity accounted for 23% of the variance in DLQI scores ($p < 0.001$)

Table 2 Questionnaires used by studies reporting correlations or mean differences across groups for quality of life.

Study	Correlations between AD and disease severity	Differences between groups		
		AD and control group	AD and other skin conditions	Differences in severity within AD groups
Arima, Gupta, Gadkari, Hiragun, Kono, Katayama, & Eckert(2018)		****		
Baron, Morris, Dye, Fielding, & Goulden (2006)	**			**
Beikert, Langenbruch, Radtke, Kornek, Purwins, & Augustin (2014)	***		***	
Chen, Wu, Li, Ko, Yu, & Chen et al., (2012)		***	***	
Chrostowska-Plak, Reich, & Szepietowski (2012)	**			
Coghi, Bortoletto, Sampaio, Junior, & Aoki (2007)	*			*
Eckert, Gupta, Amand, Gadkari., & Mahajan (2016)		****	****	
Finlay (1996)			***	
Fivenson, Arnold, Kaniecki, Cohen, Frech, & Finlay (2002)	***	***		
Grob, Revuz, Ortonne, Auqueir, & Lorette (2005)			****	
Haeck, Berge, Velsen, Bruin-Weller, Bruijnzeel-Koomen, & Knol (2011)	**			
Higaki, Kawamoto, Kamo, Ueda, Arikawa, & Kawashima (2004)	****			****
Holm, Agner, Clausen, & Thomsen, (2016)	**			
Holm, Esmann, & Jemec (2004)	***			***
Holm, Wulf, Stegmann, & Jemec (2006)	***	**		••
Kiebert, Sorensen, Revicki, Fagan, Doyle, Cohen & Fivenson (2002)	***	***		
Kim, Li, Seo, Jo, Yim, Kim, et al (2012)	**			
Kong, Han, Lee, & Son (2016)	**			
Kwak & Kim (2017)		****		
Lee, Lee, Lee, Lee, Lee, & Park. (2018)		****		
Linnet & Jemec (1999)	**	**		
Lundberg, Johannesson, Silverdahl, Hermansson & Lindberg (2000)	***	***	***	
Maksimovic, Jankovic, Marinkovic, Sekulovic, Zivkivic, & Spiric (2012)	*			*
Mikołajczyk, Rzepa, Król, & Żaba, (2017).				***
Misery, Finlay, Martin, Bousetta, Nguyen, Myon, et al (2007)				**
Misery, Seneschal, Ezzedine, Heas, Merhand, Reguiai, & Taieb, (2017)				**
Mozaffari, Pourpak, Pourseyed, Farhoodi, Aghasmohammadi, & Movahadi et al (2007)	***	***		
Noh, Kim, Park, Hann, & Oh (2013)		*	*	
Sanchez-Perez, Dauden-Tello, Mora, & Surinyac (2012)	***			***

Silverberg, Gelfand, Margolis, Boguniewicz, Fonacier, Grayson, & Fuxench. (2018)	**		**	
Torrelo, Ortiz, Alomar,Ros, Pedrosa, & Cuervo (2013)				***
Wittkowski, Richards, Griffiths, & Main (2003)	***			***

*NOTE: *- studies measuring DLQI in relation to EASI, **studies measuring DLQI in relation to SCORAD, ***Studies measuring DLQI using another measure of severity or no severity measure, ****studies using other QoL measures*.

9.2 Appendix 2 MMAT Tool

Types of mixed methods study components or primary	ia (see tutorial for definitions and examples)		Responses			
			Yes	No	Can't tell	Comments
Screening questions	-	Are there clear qualitative and quantitative research questions (or objectives*), or a clear mixed methods question (or objective*)?				
(for all types)	-	Do the collected data allow address the research question (objective)? E.g., consider whether the follow-up period is long enough for the				
		outcome to occur (for longitudinal studies or study components).				
not feasible or appropriate when the answer is 'No' or 'Can't tell' to one or both screening questions.						
1. Qualitative	1.1. Are the sources of qualitative data (archives, documents, informants, observations) relevant to address the research question					
	(objective)?					
	1.2. Is the process for analyzing qualitative data relevant to address the research question (objective)?					
	1.3. Is appropriate consideration given to how findings relate to the context, e.g., the setting, in which the data were collected?					
	1.4. Is appropriate consideration given to how findings relate to researchers' influence, e.g., through their interactions with participants?					
2. Quantitative	2.1. Is there a clear description of the randomization (or an appropriate sequence generation)?					
randomized controlled	2.2. Is there a clear description of the allocation concealment (or blinding when applicable)?					
(trials)	2.3. Are there complete outcome data (80% or above)?					
	2.4. Is there low withdrawal/drop-out (below 20%)?					
3. Quantitative	3.1. Are participants (organizations) recruited in a way that minimizes selection bias?					
non-randomized	3.2. Are measurements appropriate (clear origin, or validity known, or standard instrument; and absence of contamination between groups					
	when appropriate) regarding the exposure/intervention and outcomes?					
	3.3. In the groups being compared (exposed vs. non-exposed; with intervention vs. without; cases vs. controls), are the participants					
	comparable, or do researchers take into account (control for) the difference between these groups?					
	3.4. Are there complete outcome data (80% or above), and, when applicable, an acceptable response rate (60% or above), or an acceptable					
	follow-up rate for cohort studies (depending on the duration of follow-up)?					
4. Quantitative	4.1. Is the sampling strategy relevant to address the quantitative research question (quantitative aspect of the mixed methods question)?					
descriptive	4.2. Is the sample representative of the population understudy?					
	4.3. Are measurements appropriate (clear origin, or validity known, or standard instrument)?					
	4.4. Is there an acceptable response rate (60% or above)?					
5. Mixed methods	5.1. Is the mixed methods research design relevant to address the qualitative and quantitative research questions (or objectives), or the					
	qualitative and quantitative aspects of the mixed methods question (or objective)?					
	5.2. Is the integration of qualitative and quantitative data (or results*) relevant to address the research question (objective)?					
	5.3. Is appropriate consideration given to the limitations associated with this integration, e.g., the divergence of qualitative and quantitative					
	data (or results*) in a triangulation design?					
to 1.4), and appropriate criteria for the quantitative component (2.1 to 2.4, or 3.1 to 3.4, or 4.1 to 4.4), must be also applied.						

9.3 Appendix 3- Ethical approval form

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Memo

Life and Health Sciences Ethics Committee's Decision Letter

To: Gurkiran Birdi, Dr Rebecca Knibb

Cc: Olivia Knowler

Administrator, Life and Health Sciences Ethics Committee

From: Prof. Ian Stanford

Deputy Chair, Life and Health Sciences Ethics Committee

Date: 3/7/2017

Subject: **Project #:1125 Quality of life in adults with atopic dermatitis**

Thank you for your amendment submission. The amendment for the above study has been considered by the Chair of the LHS Ethics Committee.

Please see below for details of the decision and the approved documents.

Reviewer's recommendation: Favourable opinion

Please see the tabled list below of approved documents:

Documentation	Version/s	Date	Approved
Amendments request document	N/A	19/5/17	✓
Participant information sheet	3	19/5/17	✓
Consent form	2	19/5/17	✓

After starting your research please notify the LHS Research Ethics Committee of any of the following:

Substantial amendments. Any amendment should be sent as a Word document, with the amendment highlighted. The amendment request must be accompanied by all amended documents, e.g. protocols, participant information sheets, consent forms etc. Please include a version number and amended date to the file name of any amended documentation (e.g. "Ethics Application #100 Protocol v2 amended 17/02/12.doc").

New Investigators

The end of the study

9.4 Appendix 4 participant information sheet

Study Title: Quality of Life in Adults with Atopic Dermatitis

INFORMATION SHEET FOR PARTICIPANTS

My name is Gurkiran Birdi and I am a PhD student at Aston University, supervised by Dr Rebecca Knibb, we are running a study looking at how Atopic Dermatitis affects the quality of life of adults. We are inviting you to take part in this study.

Before you decide if you would like to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. If anything is not clear and you would like some more information you can get in touch with me on the above number or email address. Please take your time to decide whether or not you wish to take part.

The purpose of the study:

Atopic Dermatitis seems to be on the increase in adults, yet there is not much research that looks at how it affects peoples' lives. We would like to interview adults who have Atopic Dermatitis to find out how it has affected them. Interviews are being conducted by Gurkiran Kaur Birdi as part of her PhD in Psychology.

Why have I been chosen and what would I need to do?

You have been asked to take part in the study because you have Atopic Dermatitis. If you would like to take part we would like to interview you about how Atopic Dermatitis has affected your life. The interviews can take place at Aston University or another quiet location of your choosing. We can also do interviews over the telephone or by Skype. We will tape the interviews and will ask you if you are happy for us to use your words when we write about the study (with your name removed). In total this will take about 45 minutes to an hour.

Do I have to take part?

No, it is up to you to decide whether or not to take part. If you decide to take part you will be asked to keep this information sheet and to sign a consent form, which says you are happy to take part in an interview. If you change your mind and wish to stop the interview at any point, you may do so and withdraw (stop taking part) from the study without giving a reason.

If after taking part in the interview you wish to withdraw your data from being used, you can do so at any time without giving a reason, but please be aware that your data may have already been anonymised, analysed or published. If you do decide to withdraw your data just contact us and we will destroy all the information you gave us.

What are the benefits of taking part?

We hope that this study will help health care professionals develop ways in which you can be supported to manage your Atopic Dermatitis better and subsequently improve your quality of life and coping mechanisms.

Will I be reimbursed for my time?

In return for your help you will receive £10 in Love to Shop vouchers.

What are the disadvantages of taking part?

There are no disadvantages or risks to taking part but you might feel a little upset talking about your Atopic Dermatitis. If you decide during the interview that you want to stop or take a break, you can do this at any time.

What will I need to do if I decide to take part?

If you would like to take part, please get in touch with Gurkiran Birdi via email on birdigk@aston.ac.uk or by phone on 0121 204 3402**.** We will then get in touch with you to arrange an interview.

INFORMATION ABOUT THE CONDUCT OF THE STUDY

Will the information I give in this study be kept confidential?

Yes, all information collected from you for the study will be kept strictly confidential. That means that no one outside of the research team will see any of the information you give us. Each person taking part in the study will be given a code or study number that we will use when looking at what they have said in the interview. Information will be kept in a locked filing cabinet and on a password protected computer at Aston University for 6 years and then it will be destroyed. The procedures for handling, processing, storage and destruction of the questionnaire data collected during the study are compliant with the Data Protection Act 1998.

If you tell us something which we feel is putting you at risk we may need to talk to you about this or to your doctor, but we will talk to you about that before we talk to anyone else.

What will happen to the results of the study?

We will write a report of the study, which will be published. The information we collect will also be written up as part of a PhD in Psychology being conducted by Gurkiran Birdi. We can send you a copy of the report if you would like. Your name will not be in anything we publish.

What if there is a problem?

If you have any concerns or complaints about anything to do with this study, please speak to the research team and we will do our best to answer your questions. You can ring Dr Rebecca Knibb on 0121 204 3402 or email her on r.knibb@aston.ac.uk. If she cannot help you and you still have any worries about the way in which the study has been conducted, then you should contact the Director of Governance of the University Research Ethics Committee, Mr John Walter, at j.g.walter@aston.ac.uk or telephone 0121 204 4665.

Who has reviewed the study?

This study has been looked by the School of Life and Health Sciences Ethics Committee at Aston University. These are a group of people who check research to make sure that it protects the safety, rights, wellbeing and dignity of anyone who takes part. They have given it a favourable opinion.

Can I get more information?

If you are interested in taking part in this study but would like some more information before you decide, please talk to Dr Rebecca Knibb or email us. If you would like to talk to an independent person about taking part in this study or about research in general in Psychology at Aston University please contact the Director of the Aston Research Centre for Children's and Young People's Health, Professor Helen Pattison, on h.pattison@aston.ac.uk.

Thank you for taking time to read this information sheet.

Yours sincerely

Gurkiran Birdi

Research student

Dr Rebecca Knibb

Chief Investigator and PhD supervisor

Dr Richard Cooke

Associate supervisor

9.5 Appendix 5 Consent form

Ethics Approval Number_____

Study Title: Quality of Life in Adults with Atopic Dermatitis

STATEMENT OF INFORMED CONSENT FOR PARTICIPANTS

Please initial each box to indicate you

I agree to participate in this research study looking at how Atopic Dermatitis has affected my quality of life ☐

I have read the study information (version 1) and know who to contact should I have any questions about my participation in the study. ☐

I understand that my participation in the study is voluntary, and that I am free to withdraw at any time. I do not have to give any reasons or explanations for doing so. I have been provided with details of who I should contact if I wish to withdraw. ☐

I agree for my interview to be recorded and understand that it will be kept confidential and saved using an assigned participant number. ☐

I agree for direct quotes to be used from the interview and understand that any quotes will be anonymised and my name will not be used in any publications from this research. ☐

I understand that all data I provide will be kept confidential and stored securely on a password protected computer. Any hard copies of data will be stored in a locked filing cabinet. ☐

_____ _____ _____

Name of Participant Signature

Date_____ _____ _____

Researcher Signature Date

9.6 Appendix 6 Interview schedule

Question	Rationale for asking the question	Prompts
Could you give me a brief history of your Atopic Dermatitis?	Start with a question that will ease them into the interview Encourage the participant to start talking about their AD Uncover how their diagnosis came about and how long they have suffered with AD.	When were you first diagnosed with AD? How long have you suffered from AD? Are you aware of the triggers of your AD? How severe is your AD?
How has AD impacted your daily life?	Investigate the impact that AD has on a day to day basis Does it affect what they do/where they go/how they behave The activities that they feel they unable to take part in a result of their condition.	How is life different now to how it would ideally be? How does your AD affect your day to day life with regards to money? Do you feel looking after your condition is a burden in financial ways?
How would you describe yourself as a person in relation to your AD?	Understand whether Atopic dermatitis affects the way they identify themselves Do they see their AD as a part of them – is this in a good way or a bad way Does the AD affect their lives in a big way? Investigate their self esteem (mental well-being)	What characteristics would you associate with yourself?
Has AD made a difference to how you view yourself?	Look into emotional well-being – how do they feel towards themselves.	How would you view yourself differently if you did not have the condition compared to having it
How do you think the people around	Understand whether AD affects their social relationships	

you/close to you view your AD?		How did your friends and family react to your AD?
How often do you feel concerned about your AD? Why?	Understand the emotional difficulties they may face towards AD	How often does AD cross your mind? Do you have worries surrounding the condition?
Tell me how you find dealing with AD on a day to day basis?	May uncover information surrounding their physical and environmental QoL Understand whether it takes up a large part of their day How has AD affected their competency in tasks? (productive well-being)	
What do you do to cope with and manage your AD? How do you feel about this?	What are the lengths that they go to to control their AD How much of their day does this take up	Have you made any adjustments to your life as a result of AD?
What are your thoughts about your future?	See whether they believe they can cope with their condition in the future How they plan to do this	What would you like to do in your future? How do you view yourself in 5 or 10 years time? What do you hope to have achieved in 5 or 10 years time?

9.7 Appendix 7 Socio-demographic questionnaire

1. Have you been clinically diagnosed with Atopic Dermatitis/Eczema?

Yes

No

2. Who made this diagnosis? Please tick the box that applies

GP

Nurse practitioner or physician's assistant

Dermatologist

Paediatrician

Other

If you answered 'Other', please state_____

3. At what age were you first diagnosed with Atopic Dermatitis?

_____

4. What medication(s) have you been prescribed for your Atopic Dermatitis?

_____

5. Are you currently being treated by a dermatologist?

Yes

No

6. How often do you have follow-up visits for your Atopic Dermatitis?

More than once a month

More than once every three months

Once every three months

Once every six months

Once a year or less

7. Have you ever had doctor-diagnosed: (choose all that apply)

Asthma

Seasonal Allergies or Hayfever

Food Allergies

None of the above

8. Did your mother, father, siblings or child ever have Atopic Dermatitis?

Yes

No

9. Approximately how often in a month does your Atopic Dermatitis flare up?

_____

9.8 Appendix 8 Ethical approval letter

Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

NHS
Health Research Authority

Dr Rebecca Knibb
School of Life and Health Sciences
Aston University
Birmingham
B4 7ET

Email: hra.approval@nhs.net
Research-permissions@wales.nhs.uk

13 July 2018

Dear Dr Knibb

HRA and Health and Care Research Wales (HCRW) Approval Letter

Study title:	**An investigation of quality of life and mental health in adults with atopic dermatitis compared to healthy people**
IRAS project ID:	**204919**
Protocol number:	**ANA/RCK/1**
REC reference:	**18/NE/0228**
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.

How should I continue to work with participating NHS organisations in England and Wales?
You should now provide a copy of this letter to all participating NHS organisations in England and Wales, as well as any documentation that has been updated as a result of the assessment.

Following the arranging of capacity and capability, participating NHS organisations should **formally confirm** their capacity and capability to undertake the study. How this will be confirmed is detailed in the "*summary of assessment*" section towards the end of this letter.

You should provide, if you have not already done so, detailed instructions to each organisation as to how you will notify them that research activities may commence at site following their confirmation of capacity and capability (e.g. provision by you of a 'green light' email, formal notification following a site initiation visit, activities may commence immediately following confirmation by participating organisation, etc.).

9.9 Appendix 9 Participant information sheet

Study Title: Quality of Life and Mental Health in Adults with Atopic Dermatitis compared to Healthy People

INFORMATION SHEET FOR PARTICIPANTS

My name is Gurkiran Birdi and I am a PhD student at Aston University, supervised by Dr Rebecca Knibb. We are running a study looking at how *clinically diagnosed* atopic dermatitis affects the quality of life and mental health of adults compared to healthy controls. We are inviting you to take part in this study.

You are eligible to take part in this study if you have:

- Clinically diagnosed atopic dermatitis with no other long-term conditions apart from co-morbid conditions such as hay fever, asthma and allergies
- You do not have atopic dermatitis or any other long-term conditions and are otherwise healthy

Before you decide if you would like to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. If anything is not clear and you would like some more information you can get in touch with me on the above number or email address. Please take your time to decide if you wish to take part.

The purpose of the study:

Atopic dermatitis seems to be on the increase in adults, yet there is not much research that looks at how it affects peoples' lives. We are conducting a study exploring how stress, quality of life, depression, and anxiety is linked with atopic dermatitis. We are also comparing quality of life and mental health in adults with atopic dermatitis to adults without atopic dermatitis who are otherwise healthy and do not have any long term/chronic health conditions.

Why have I been chosen and what would I need to do?

You have been asked to take part in the study because you either go to the dermatology clinic at Queen Elizabeth Hospital or have seen an advert for this study.

If you consent to taking part in this study, we will ask you to complete a consent form and some questionnaires that should take no longer than about 30 minutes. The questionnaires ask about your quality of life, levels of stress, anxiety and depression. If you are reading this online, you can find the questionnaires by clicking the bottom of the page. If you have been given this information in clinic or sent this information sheet and questionnaires by post, please fill in the questionnaires and post them back to us. If you want us to send the questionnaires to you by post, just get in touch with us and we can send them to you. You can also complete the questionnaires with the help of Gurkiran Birdi, the PhD researcher.

Do I have to take part?

No - taking part in this study is voluntary and if you decide to take part you can withdraw at any time during completion of the questionnaires without giving a reason.

You do not need to give us your name when taking part in this study, it is completely anonymous.

However, after you have completed your questionnaires and sent the answers to us, we will not be able to withdraw your data from the study.

What are the benefits of taking part?

We hope that this study may help health care professionals develop ways in which patients can be supported to manage their atopic dermatitis better and subsequently improve their quality of life.

What are the disadvantages or risks of taking part?

You may feel upset answering questions about anxiety or depression, or questions about how your condition has affected you if you are a patient. You may stop answering questions at any time you wish and either take a break or decide you do not want to take part anymore.

What will I need to do if I decide to take part?

If you are reading this online, clicking to the next page will take you to a consent form. You will need to fill this in to tell us that you are happy to take part. You then just need to fill in the questionnaires.

If you have been sent this information sheet and questionnaires by post or they have been given to you in clinic, you can find the consent forms with the questionnaires. You will need to fill these in and post them back to us. Or you can find everything online at xxxx.

INFORMATION ABOUT THE CONDUCT OF THE STUDY

Will the information I give in this study be kept confidential?

Yes, all information collected from you for the study will be kept strictly confidential. That means that no one outside of the research team will see any of the information you give us. You do not need to give us your name so we will not know the information has come from you.

After you have completed your questionnaires and sent the answers to us, we will not be able to withdraw your data from the study, as the data collected from you will be anonymous and will not have your contact information on it.

Information collected during this study will be kept in a locked filing cabinet and on a password protected computer at Aston University until the study is complete. The procedures for handling, processing, storage and destruction of the questionnaire data collected during the study are compliant with the General Data Protection Act (2018).

Who is organising this study and acting as data controller for the study?

Aston University is the sponsor for this study based in the United Kingdom. We will be using information from you in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your

information and using it properly. Aston University will keep identifiable information about you for 6 years after the study has finished.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information at www.aston.ac.uk/dataprotection or by contacting our Data Protection Officer at dp_officer@aston.ac.uk.

As a university we use personally-identifiable information to conduct research to improve health, care and services. As a publicly-funded organisation, we have to ensure that it is in the public interest when we use personally-identifiable information from people who have agreed to take part in research. This means that when you agree to take part in a research study, we will use your data in the ways needed to conduct and analyse the research study.

Health and care research should serve the public interest, which means that we have to demonstrate that our research serves the interests of society as a whole. We do this by following the UK Policy Framework for Health and Social Care Research.

If you wish to raise a complaint on how we have handled your personal data, you can contact our Data Protection Officer who will investigate the matter. If you are not satisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO).

Our Data Protection Officer is Victoria Mee and you can contact them at: dp_officer@aston.ac.uk.

University Hospitals Birmingham NHS Foundation Trust will collect information from you and your medical records for this research study in accordance with our instructions.

University Hospitals Birmingham NHS Foundation Trust will use your name, and contact details to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from Aston University and regulatory organisations may look at your medical and research records to check the accuracy of the research study. University Hospitals Birmingham NHS Foundation Trust will pass these details to Aston University along with the information collected from you. The only people in Aston University who will have access to information that identifies you will be people who need to contact you to arrange and undertake research visits or audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name, or contact details.

What will happen to the results of the study?

We will write a report of the study, which will be published. The information we collect will also be written up as part of a PhD in Psychology being conducted by Gurkiran Birdi. We can send you a summary of the results if you would like them. Your name will not be in anything we publish.

What if there is a problem?

If you have any concerns or complaints about anything to do with this study, please speak to the research team (details below) and we will do our best to answer your questions. You can ring Dr Rebecca Knibb on 0121 204 3402 or email her on r.knibb@aston.ac.uk. If she cannot help you and you still have any worries about the way in which the study has been conducted, then you should contact Aston University's Director of Governance, Mr John Walter, at j.g.walter@aston.ac.uk or telephone 0121 204 4665.

Who has reviewed the study?

This study has been looked by xxx NHS research ethics committee. These are a group of people who check research to make sure that it protects the safety, rights, wellbeing and dignity of anyone who takes part. They have given it a favourable opinion.

Can I get more information?

If you are interested in taking part in this study but would like some more information before you decide, please contact one of the research team members (details at the end of this sheet). If you would like to talk to an independent person about taking part in this study or about research in general in Psychology at Aston University please contact the Director of the Applied Health Research Group, Dr Claire Farrow, on c.farrow@aston.ac.uk If you would like independent advice on any aspect of this study, you can also contact the PALS (Patient Advice and Liaison Service) at the Queen Elizabeth Hospital ([redacted], e-mail: PALS@uhb.nhs.uk) . If after taking part in this study you are worried about your health please make an appointment to see your G.P. If you have atopic dermatitis and are worried about that, please see your G.P. or consultant. You can also get further information about atopic dermatitis from www.eczema.org.

Research Team
Gurkiran Birdi
Doctoral Researcher
Email: birdigk@aston.ac.uk
Tel: [redacted]

Dr Ser-Ling Chua
Principal Investigator and Consultant Dermatologist at QEHB
Email: Ser-Ling.Chua@uhb.nhs.uk
Tel: [redacted]

Dr Rebecca Knibb
Chief Investigator and PhD supervisor
Email: r.knibb@aston.ac.uk
Tel: [redacted]

9.10 Appendix 10 Consent form

Aston University
Birmingham

University Hospitals Birmingham NHS Foundation Trust

Ethics Approval Number

_____

Study Title: Quality of Life and Mental Health in Adults with Atopic Dermatitis compared to Healthy People

STATEMENT OF INFORMED CONSENT FOR PARTICIPANTS

PLEASE CLICK EACH STATEMENT TO SHOW THAT YOU HAVE READ AND AGREE WITH IT. YOU MUST CLICK ON EACH STATEMENT BEFORE YOU ARE ABLE TO ACCESS THE QUESTIONNAIRES

I have read the study information (version x dated x) and know who to contact should I have any questions about my participation in the study. ☐

I understand that my participation in the study is voluntary, and that I am free to withdraw at any time during completion of the questionnaires. I do not have to give any reasons or explanations for doing so. I have been provided with details of who I should contact if I wish to withdraw. ☐

I understand that this study will have no impact on my usual medical care. ☐

I understand that all data I provide will be kept confidential and stored securely at Aston University on a password protected database. Any paperwork completed including my consent forms and questionnaire measures will be stored in a locked filing cabinet or on a password protected computer. Only the research team will have access to this. ☐

I understand that these results may be disseminated through conferences and/or published articles. I understand that my data will remain anonymous at all times. ☐

I agree to participate in this research study looking at the impact of atopic dermatitis on quality of life and mental health. ☐

9.11 Appendix 11 Socio-demographic questionnaire

Age _____ Gender _____ Ethnicity _____ Occupation _____

Where did you see the advert for this study? _____

1. Have you been diagnosed with atopic dermatitis/eczema?

☐ Yes

☐ No

2. Do you have any long-term skin condition(s) that is currently active and being treated?

☐ Yes

☐ No

If yes, please state _____

3. Do you currently have any other long term/chronic physical health condition(s) such as diabetes, arthritis, cancer, stroke, coronary heart disease, and heart failure?

☐ Yes

☐ No

If yes, please state _____

If you have answered <u>yes</u> to any of the above, you are not eligible to continue with the study. We appreciate your interest and time.

9.12 Appendix 12 STROBE checklist

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract		
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found		
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported		
Objectives	3	State specific objectives, including any prespecified hypotheses		
Methods				
Study design	4	Present key elements of study design early in the paper		

Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case

Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses
Results		

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure

		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

9.13 Appendix 13 Ethical approval letter

Aston University
Birmingham

Aston Triangle
Birmingham B4 7ET
United Kingdom
Tel +44 (0)121 204 3000

lhs_ethics@aston.ac.uk
www.aston.ac.uk

Memo

To: Dr Rebecca Knibb; Gurkiran Birdi; Dr Michael Larkin

Cc: Kara Hanaphy

Administrator, Life and Health Sciences Ethics Committee

From: Professor Ian Stanford

Deputy Chair, Life and Health Sciences Ethics Committee

Date: 4/2/2019

Subject: **Project #1428: The relationship between psychological stress and disease severity in adults with atopic dermatitis: a feasibility study**

Thank you for your submission. The additional information for the above proposal has been considered by the Chair of the LHS Ethics Committee.

Please see below for details of the decision and the approved documents.

Reviewer's recommendation: Favourable opinion

Please see the tabled list below of approved documents:

Documentation	Version/s	Date	Approved
Response to reviewer's comments	1	01.02.2019	✓
Consent form	2	17.01.2019	✓
Debrief form	1	17.01.2019	✓
Participant Information Sheet	2	17.01.2019	✓
POEM for self-completion	2	17.01.2019	✓
Perceived Stress Scale	2	17.01.2019	✓
Demographic questionnaire	2	17.01.2019	✓
Ethics Application	2	01.02.2019	✓

After starting your research please notify the LHS Research Ethics Committee of any of the following:

Substantial amendments. Any amendment should be sent as a Word document, with the amendment highlighted. The amendment request must be accompanied by all amended documents, e.g. protocols, participant information sheets, consent forms etc. Please include a version number and amended date to the file name of any amended documentation (e.g. "Ethics Application #100 Protocol v2 amended 17/02/12.doc").

9.14 Appendix 14 Consent form

Aston University

The relationship between psychological stress and disease severity in adults with atopic dermatitis: a feasibility study

Consent Form

Name of Chief Investigator: Gurkiran Birdi

Please initial boxes

1.	I confirm that I have read and understand the Participant Information Sheet (V1, 07/11/18) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
2.	I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason and without my legal rights being affected.	
3.	If I decide that I do not want to take part in the study at any point in the 3 month duration, I am happy for my data collected up to that date to be included in analysis.	
4.	I agree to my personal data and data relating to me collected during the study being processed as described in the Participant Information Sheet.	
5.	I agree to my anonymised data being used by research teams for future research.	
6.	I agree to my personal data being processed for the purposes of inviting me to participate in future research projects. I understand that I may opt out of receiving these invitations at any time.	
7.	I am happy for the researcher to send me text message reminders about the study.	
8.	I am happy to be contacted at the end of this study to see if I would like to take part in an interview.	
9.	I agree to take part in this study.	

Name of participant	Date	Signature
Name of Person receiving	Date	Signature

9.15 Appendix 15 Socio-demographic questionnaire

Age _____ Gender _____ Ethnicity _____ Occupation _____

Where did you see the advert for this study? _____

1. Have you been diagnosed with atopic dermatitis/eczema?

☐ Yes

☐ No

[For online surveys, if participants answer “yes”, they will be directed to questions 4 onwards, if they answer “no” to the above, they will be directed to questions 2 and 3).

2. Do you have any long-term skin condition(s) that is currently active and being treated?

☐ Yes

☐ No

If yes, please state _____

3. Do you currently have any other long term/chronic physical health condition(s) such as diabetes, arthritis, cancer, stroke, coronary heart disease, and heart failure?

☐ Yes

☐ No

If yes, please state _____

If you have answered yes to questions 2 or 3, you are not eligible to continue with the study. We appreciate your interest and time.

4. Have you been *clinically* diagnosed with atopic dermatitis/eczema?

☐ Yes

☐ No

If you have answered no to the above question, you are not eligible to continue with the study. We appreciate your interest and time.

5 . Do you currently have any other long term/chronic physical health condition(s) such as diabetes, arthritis, cancer, stroke, coronary heart disease, and heart failure?

Please note that this does **not** include co-morbid conditions such as asthma, hay-fever or food allergies, which commonly occur alongside atopic dermatitis

☐ Yes

☐ No

If yes, please state _____

If you have answered yes to the above question, you are not eligible to continue with this study. We appreciate your interest and time.

6. Who made this diagnosis? Please tick the box that applies

☐ GP

☐ Dermatologist

☐ Paediatrician

☐ Other

7. At what age were you first diagnosed with atopic dermatitis?

_____

8. What medication(s) have you been prescribed for your atopic dermatitis?

_____

____

9. Are you being managed or followed up in clinic by a dermatologist?

☐ Yes

☐ No

If yes, please answer question 6, otherwise please proceed to question 7.

10. How often do you have follow-up visits for your atopic dermatitis?

☐ More than once a month

☐ More than once every three months

☐ Once every three months

☐ Once every six months

☐ Once a year or less

11. Has a doctor ever diagnosed the following? (choose all that apply)

☐ Asthma

☐ Seasonal Allergies or Hay fever

☐ Food Allergies

☐ None of the above

12. Did your mother, father, siblings or children *ever* have Atopic Dermatitis?

☐ Yes ☐ No

9.16 Appendix 16 daily diary

Please complete daily before retiring for sleep

Please spend five minutes telling us how you felt today.

Date _____

Please circle your answer			
Did anyone give you a “hard time” or make life difficult for you today?	0(no)	1 (a little)	2 (a lot)
Did you feel angry or annoyed today?	0 (no)	1 (a little)	2 (a lot)
Did you feel trapped in an uncomfortable situation that you wanted to get out of?	0 (no)	1 (a little)	2 (a lot)
Did you express feelings of anger or annoyance to anyone today?	0 (no)	1 (a little)	2 (a lot)
Did you find yourself in a situation, today, when you had to defend yourself?	0 (no)	1 (a little)	2 (a lot)
Did you experience a feeling of defeat or frustration today?	0 (no)	1 (a little)	2 (a lot)
Did you feel rebuffed or hurt by someone today?	0 (no)	1 (a little)	2 (a lot)
Did you feel tense or anxious today?	0 (no)	1 (a little)	2 (a lot)
Did you feel lonely or isolated?	0 (no)	1 (a little)	2 (a lot)
Did you seek a period of isolation and solitude away from other people?	0 (no)	1 (a little)	2 (a lot)
Has there been anything on your mind today - something you’ve been thinking about a lot?	0 (no)	1 (a little)	2 (a lot)
Did you at any time feel depressed?	0 (no)	1 (a little)	2 (a lot)
Did you feel that other people were intruding into your privacy?	0 (no)	1 (a little)	2 (a lot)
Did you have a feeling you wanted to seek help from someone in solving some of your problems?	0 (no)	1 (a little)	2 (a lot)

Did you have a flare -up that **started** today? Yes_____ No_____

How severe is your atopic dermatitis today? 0 (mild) 1(moderate) 2(severe)

How well did you sleep last night? 0 (slept well) 1 (somewhat) 2 (not at all)

Did you experience a particularly stressful situation today? Yes_____ No_____

If you answered ‘yes’, please provide brief details of the stressful situation:

_____

_____

_____

_____

9.17 Appendix 17 participant information sheet

The relationship between psychological stress and disease severity in adults with atopic dermatitis: a feasibility study

Participant Information Sheet

Invitation

We would like to invite you to take part in a research study.

Before you decide if you would like to participate, take time to read the following information carefully and, if you wish, discuss it with others such as your family, friends or colleagues.

Please ask a member of the research team, whose contact details can be found at the end of this information sheet, if there is anything that is not clear or if you would like more information before you make your decision.

What is the purpose of the study?

Atopic Dermatitis seems to be on the increase in adults, yet there is not much research that looks at how it affects peoples' lives. We would like adults with clinically diagnosed atopic dermatitis to complete daily diaries for one month and weekly questionnaires about psychological stress and atopic dermatitis for 3 months. This study is being conducted by Gurkiran Kaur Birdi as part of her PhD in Psychology.

Why have I been chosen?

You are being invited to take part in this study because:

- You have seen an advert for this study on a support group page on Facebook, social media platforms Facebook/Twitter or an advert at Aston University
- You are an adult with clinically diagnosed atopic dermatitis
- You do not have any diagnosed psychological conditions such as anxiety or depression

What will happen to me if I take part?

You will be sent study materials via post or you will be able to complete diaries via a secure web-link on Qualtrics if you decide to take part in the study. These materials will comprise a diary to complete every night for 4 weeks- this should only take you 5 minutes every night. You will also be asked to complete questionnaires at the start of the study and once a week (ideally towards the end of the week) for the 3 month duration of the study. You will be sent reminders on a study-specific group on Facebook or via text messages if you consent to this. At the end of the study, you will

be asked to post the study pack to Aston University using a pre-paid envelope if the materials were posted to you. After you have participated in the study, we will ask if you would like to take part in an interview to gather your thoughts about taking part in the study. You do not have to take part in this interview if you do not wish to.

Do I have to take part?

No. It is up to you to decide whether or not you wish to take part.

If you do decide to participate, you will be asked to sign and date a consent form. You would still be free to withdraw from the study at any time without giving a reason. If you decide to withdraw from the study during the three month period, you can consent to data already collected forming a part of the study.

Will my taking part in this study be kept confidential?

Yes. A code will be attached to all the data you provide to maintain confidentiality.

Your personal data (name telephone number, contact details and address) will only be used if the researchers need to send you the study pack to your postal address and/or send you text message reminders. Analysis of your data will be undertaken using coded data. Your personal data will be destroyed following completion of recruitment.

The data we collect will be stored in a secure document store (paper records) or electronically on a secure encrypted mobile device, password protected computer server or secure cloud storage device.

To ensure the quality of the research, Aston University may need to access your data to check that the data has been recorded accurately. If this is required, your personal data will be treated as confidential by the individuals accessing your data.

What are the possible benefits of taking part?

While there are no direct benefits to you of taking part in this study, the data gained will help health care professionals develop ways in which patients can be supported to manage their atopic dermatitis better and the mental impact of the condition better.

What are the possible risks and burdens of taking part?

You may feel upset answering questions about anxiety or depression, or questions about how your condition has affected you. You may stop answering questions at any time you wish and either take a break or decide you do not want to take part anymore. As this study has a total duration of three months, time commitment may be a burden, however, we anticipate that it will take no longer than 5 minutes to complete diaries every night, and no longer than 15 minutes to complete questionnaires at the end of each week.

What will happen to the results of the study?

The results of this study may be published in scientific journals and/or presented at conferences. If the results of the study are published, your identity will remain confidential.

A lay summary of the results of the study will be available for participants when the study has been completed and the researchers will ask if you would like to receive a copy.

The results of the study will also be used in Gurkiran Birdi's PhD thesis.

Expenses and payments

You will receive £20 Love to Shop vouchers for your time in the study

Who is funding the research?

The study is being funded by Aston University

Who is organising this study and acting as data controller for the study?

Aston University is organising this study and acting as data controller for the study. You can find out more about how we use your information in Appendix A.

Who has reviewed the study?

This study has been reviewed and received a favourable opinion from the School of Life and Health Sciences Ethics Committee at Aston University.

What if I have a concern about my participation in the study?

If you have any concerns about your participation in this study, please speak to the research team and they will do their best to answer your questions. Contact details can be found at the end of this information sheet.

If the research team are unable to address your concerns or you wish to make a complaint about how the study is being conducted you should contact the Aston University Director of Governance, Mr. John Walter, j.g.walter@aston.ac.uk or telephone 0121 204 4869.

Research Team

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Aston University takes its obligations under data and privacy law seriously and complies with the General Data Protection Regulation ("GDPR") and the Data Protection Act 2018 ("DPA").

Aston University is the sponsor for this study based in the United Kingdom. We will be using information from you in order to undertake this study. Aston University will process your personal data in order to register you as a participant and to manage your participation in the study. It will process your personal data on the grounds that it is necessary for the performance of a task carried out in the public interest (GDPR Article 6(1)(e). Aston University may process special categories of data about you which includes details about your health. Aston University will process this data on the grounds that it is necessary for statistical or research purposes (GDPR Article 9(2)(j)). . Aston University will keep identifiable information about you for 6 years after the study has finished.

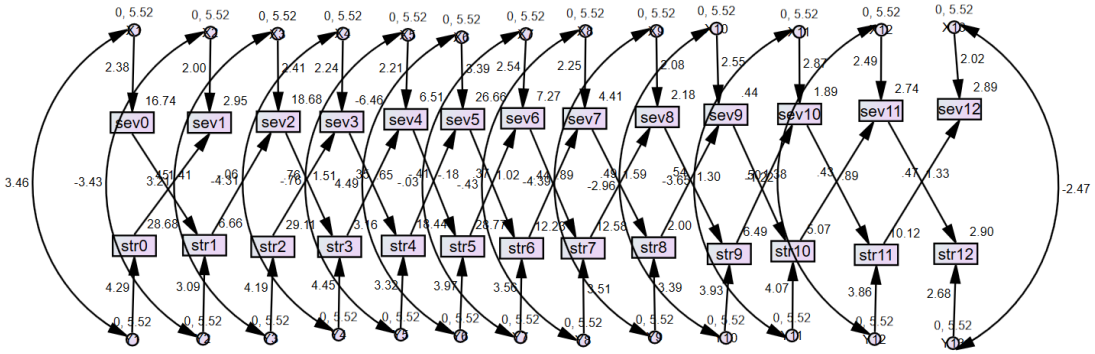
Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally identifiable information possible.

You can find out more about how we use your information at www.aston.ac.uk/dataprotection or by contacting our Data Protection Officer at dp_officer@aston.ac.uk.

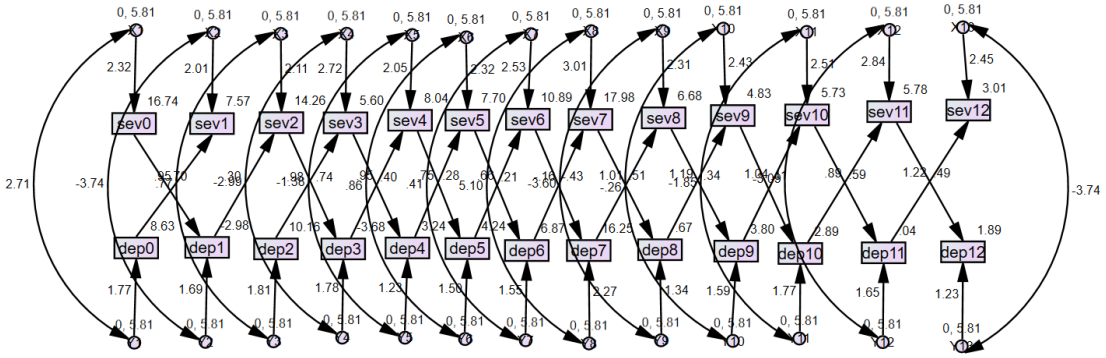
If you wish to raise a complaint on how we have handled your personal data, you can contact our Data Protection Officer who will investigate the matter. If you are not satisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO).

9.18 Appendix 18 Cross-lagged panel models

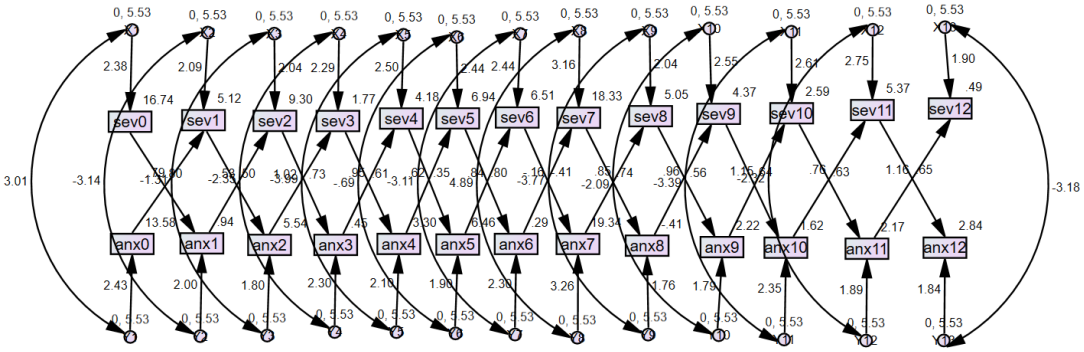
Stress and disease severity



Stress and depression



Stress and anxiety



9.19 Appendix 19 Cross-lagged panel model