

Quantifying the Economic Impact of Psoriasis

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List of Abbreviations

CEA: Cost-effectiveness analysis

CRD: Centre for Reviews and Dissemination

DCE: Discrete Choice Experiment

DLQI: Dermatology Life Quality Index

EIA: Economic Impact Analysis

EQ5D: European Quality of Life 5 dimension

FCA: Friction Cost Approach

GPA: Global Psoriasis Atlas

HCA: Human Capital Approach

HRQoL: Health-Related Quality of Life

NHS: National Health Service

NICE: National Institute for Health and Care Excellence

OOP: Out of pocket

PEST: Psoriasis Epidemiological Screening Tool

PsA: Psoriatic Arthritis

QALY: Quality Adjusted Life Years

QoL: Quality of Life

SG: Standard Gamble

SIGN: Scottish Intercollegiate Guidelines Network

UK: United Kingdom

US: United States

WTP: Willingness to Pay

Glossary

Absenteeism: Being away from work due to an illness typically identified and measured as time absent from work and valued as a cost using wage rates.

Burden-of-disease: Non-financial consequences of a disease on a population. These consequences could be identified, measured and valued in line with the welfarism or extra-welfarism approach and could include, for example, limitations on individual productivity, long-term or permanent disability, impaired quality of life, impaired capability, or premature death.

Cost-Effectiveness Analysis (CEA): A method of comparing the opportunity costs of various alternative courses of action measured using a common unit of output relevant to clinical effectiveness. It is referred to as Cost-Utility Analysis (CUA) when a generic measure of outcome such as Quality-adjusted life-years (QALY) is used.

Contingent valuation: Survey-based experimental method of eliciting valuations of goods or services by which individuals are asked to state their maximum willingness to pay or minimum willingness to accept going without, contingent on a specific hypothetical scenario (e.g., making a purchase) and a description of options available.

Cost-of-illness: Financial consequences of a disease in a population. The magnitude of the economic impact of the disease is calculated by identifying, measuring and valuing all relevant direct and indirect costs for the relevant study perspective and time horizon.

Direct Costs: Defined based on the study perspective and time horizon, they can be divided into direct medical and direct non-medical costs. Direct medical costs are those related to the resource use incurred in delivering formal health and social care. Direct non-medical costs are those incurred by the patient (out-of-pocket), other sectors (such as education), and informal care received from family and friends.

Disability-Adjusted-Life-Year (DALY): It is a summary measure which combines the time lost through premature death and time lived with a disability. It is calculated as

the value of the future years of disability-free life that are lost as the result of premature deaths or cases of disability occurring in a particular year.

Economic Evaluation: Comparison of two or more interventions in terms of both their costs and consequences.

Economic Impact: Magnitude of economic losses of an individual, firm and/or society in terms of costs and consequences.

Friction Cost Approach: An approach to estimating productivity loss incurred during the duration of a vacancy following ill health of the pre-current occupant of the position, including training for a newly recruited individual that fills up the vacancy.

Health-related Quality-of-Life (HRQoL): How health is empirically estimated to affect the quality of life encompassing the different attributes of health.

Human Capital Approach: An approach to estimating the loss of productivity in terms of the present value of the potential future earnings of a working-age population under the assumption that an individual will remain in employment and cannot be replaced

Indirect Costs: Costs suffered because of ill health in terms of productivity or income loss.

Informal care: Care offered to an individual by family and friends outside of the healthcare system.

Macroeconomics: The study of aggregate entities in the economy, like money supply, income, exports or unemployment, and the links between them.

Microeconomics: The study of individual units in a society like persons, households and firms.

Presenteeism: Presenteeism refers to the value of impaired work productivity due to ill health where a sick individual shows up for work even though physically or psychological impaired.

Quality-Adjusted-Life-Year (QALY): Preference-based measure incorporating both the length (capturing mortality) and quality (capturing morbidity) of life

Utility: The level of happiness or satisfaction an individual derives from his or her circumstances.

Willingness to Pay (WTP): Technique used to elicit how much value an individual attaches to a given outcome by asking how much in monetary terms they would pay for it.

Willingness to Accept (WTA): Technique used to elicit how much value an individual attaches to a given outcome by asking how much in monetary terms they would accept to be compensated for it.

Years of full capability equivalent (YFC): Preference-based measure that incorporates the length and capability of life.

Abstract

Psoriasis affects around 3% of the UK population. Evidence of the economic impact of psoriasis in the UK remains limited. Understanding the economic impact of psoriasis can provide useful information for decision-makers to identify the economic losses and how they are spread across the different components of cost-of-illness and burden-of-disease.

The overall aim of this thesis was to quantify the economic impact of psoriasis in the UK by addressing four main objectives: i) Identify, and if necessary develop, a descriptive framework defining a nomenclature system for the relevant components and methods when identifying and quantifying the economic impact of disease; ii) Identify and critically appraise published studies estimating cost-of-illness and burden-of-disease for people living with psoriasis; iii) Estimate health care costs attributable to psoriasis and identifying key drivers of NHS resources use in England; iv) Quantify the burden-of-disease due to psoriasis in the UK.

A mixed-methods approach was used to address the set objectives. The traditional-pearl growing-based review and thematic framework analysis were used to develop and validate a descriptive framework defining a nomenclature system for cost-of-illness and burden-of-disease. Two systematic reviews were used to critically appraise published psoriasis cost-of-illness and burden-of-disease studies. A retrospective observational matched cohort study with regression-based analyses was used to estimate costs attributable to psoriasis. A survey-based study was used to quantify the burden-of-disease in a sample of the UK population.

No pre-existing framework to appraise economic impact of disease studies was identified. A framework to appraise studies reporting the cost-of-illness and burden-of-disease of psoriasis was developed. A limited evidence base relevant to the UK setting reporting the economic impact of psoriasis was identified. The cohort study identified that the costs attributable to psoriasis were found to be substantial. Comorbidities and obesity were observed to be key drivers of health care resource use and costs. The burden-of-disease due to psoriasis was noted to significantly impact both health and beyond health aspects. These findings will contribute to influencing policy recommendations on the need to tackle obesity and comorbidity in people living with psoriasis in the UK to reduce health care resource use.

Declaration

I declare that no portion of the work referred to in the thesis has been submitted in support of an application for another degree or qualification of this or any other university or other institute of learning.

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Dedication

To my parents, Clementina and late Feston “Watch” Ng’ambi.

About the author

In 2018, Peslie Ng'ambi began his PhD in Health Economics at the University of Manchester, in the Division of Population Health, Health Services Research & Primary Care, and School of Health Sciences. He graduated with a Master of Science in International Pharmacoeconomics and Health Economics offered by Cardiff University (United Kingdom) and delivered at the Fresenius University of Applied Science, Germany in 2016. In his second year of study in 2015, he was awarded the German Academic Exchange Service (DAAD) STIBET scholarship in recognition of his outstanding performance in his studies at a Germany University. He also graduated with a Bachelor of Pharmacy degree from the University of Zambia in 2011.

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List of publications

Ng'ambi, P., Jones, C., Ashcroft, D., Griffiths, C. and Payne, K., 2019. PNS14 TOWARDS CONSISTENCY AND COHERENCE IN UNDERSTANDING THE ECONOMIC IMPACT OF DISEASE. *Value in Health*, 22, p.S765. DOI: <https://doi.org/10.1016/j.jval.2019.09.1916>

1 Introduction

Chapter summary

The overarching aim of this thesis was to generate an evidence base to understand the economic impact of psoriasis in the UK. The thesis is presented using the 'traditional' format and is presented in seven chapters. Chapter 1 introduces the key concepts of this thesis, gives an overview of psoriasis, and economic impact analysis and explains the motivation for the thesis. Chapter 1 also includes a summary of the structure for this thesis. Chapter 2 presents a framework for describing economic impact. Chapters 3 and 4 present systematic literature reviews of the cost-of-illness and burden-of-disease for people living with psoriasis, respectively. Chapters 5 and 6 present empirical studies estimating the cost-of-illness and the burden-of-disease of psoriasis in the United Kingdom (UK), respectively. The discussion and conclusion of the thesis are presented in chapter 7.

Chapter 1 is presented in seven sections. Section 1.1 describes and explains psoriasis including the different types. The epidemiology of psoriasis; incidence and prevalence in the UK and globally, is presented in section 1.2. Section 1.3 describes the impact of psoriasis on people living with the condition. Management of psoriasis in the UK is presented in section 1.4. An overview of Economic impact of disease and the definition of cost-of-illness and burden-of-disease presented in section 1.5 and 1.6 respectively. Section 1.7 presents the policy relevance of understanding economic impact. The chapter concludes by stating the aim and objectives of the PhD and outlining the structure of the thesis in section 1.8.

1.1 Psoriasis

Psoriasis is a chronic non-communicable inflammatory skin disease that is mainly characterised by a relapsing-remitting presentation and can occur at any age (WHO, 2016; Griffiths *et al.*, 2021). Relapsing-remitting means the disease will be punctuated with periods of symptoms, followed by periods of recovery. There is a consensus that psoriasis is an autoimmune disease, although there is continued interest in the

aetiology and pathogenesis of psoriasis amongst dermatologists, pathologists and biologists (Nickoloff *et al.*, 2000; Boehncke and Schön, 2015).

Psoriasis is marked by sustained inflammation leading to the uncontrolled multiplication of keratinocytes (Rendon and Schäkel, 2019). Keratinocytes are the primary type of cells found in the outer layer of the skin called the epidermis (Rendon and Schäkel, 2019). The uncontrolled multiplication of keratinocytes results in a histological thickened appearance of the epidermis and is referred to as acanthosis (Boehncke and Schön, 2015; Griffiths *et al.*, 2021). There is also a presence of a large number of inflammatory cells in all skin layers; granulocytes, Langerhans cells and lymphocytes (Carr, 2007). The development and sustained inflammation have been attributed to the disturbance in the innate and adaptive cutaneous immune response due to the presence of lymphocytes and Langerhans cells (Carr, 2007). These cells release cytokines which in turn recruit more inflammatory cells leading to stimulation of epidermal turnover (Carr, 2007).

It has been suggested that the emergence of psoriasis is bimodal with two peak ages (WHO, 2016). For women, the first peak age (early onset) and second (late-onset) have been reported to be between 18-29 years and 50-59 years respectively (Parisi *et al.*, 2020). Whereas, for men, the first peak has been reported as 30-39 years and the late-onset as 60-69 years or 70-79 years (Parisi *et al.*, 2020).

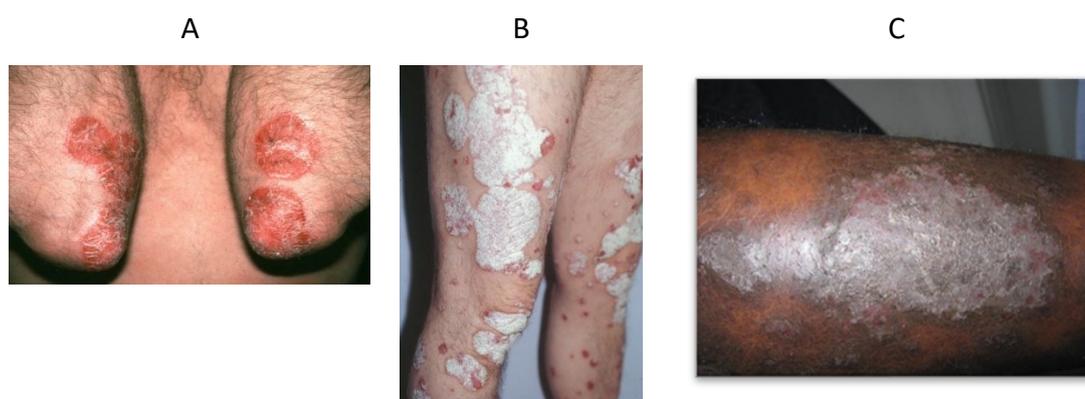
The signs and symptoms of psoriasis are influenced by the type of psoriasis and differ across individuals, as presented in section 1.3. The most common signs and symptoms of psoriasis are plaques, itching, thickened red skin, and thickened nails (Globe, Bayliss and Harrison, 2009; Böhm *et al.*, 2013). Psoriasis mainly affects the extensor aspects of the knees and elbows, lumbosacral regions, scalp and genital regions (Sarac, Koca and Baglan, 2016; Griffiths *et al.*, 2021). Nail involvement is characterised by nail pitting, onycholysis, and subungual hyperkeratosis of the nails, see Figure 1.3.

1.1.1 Types of psoriasis

To have a clear focus on the disease, it is important to understand the different clinical phenotypes of psoriasis. Epidemiological reports show that there is a disproportionate distribution of these types among affected individuals. The six types of psoriasis are:-

Plaque psoriasis (psoriasis vulgaris): Plaque psoriasis, shown in Figure 1.1 A to C, is the most common type accounting for up to 90% of all psoriasis cases globally (Sarac, Koca and Baglan, 2016; Griffiths *et al.*, 2021). Although it can occur on any part of the body, it mainly affects the extensor surfaces of the knees and elbows (Griffiths *et al.*, 2021). The essential clinical feature of plaque psoriasis is well-demarcated lesions with or without silvery-white scales (Abo-Tabik *et al.*, 2021). In white skin, it is characterised by raised salmon-pink to red (erythematous) skin lesions with sharp boundaries known as plaque (Sarac, Koca and Baglan, 2016; Abo-Tabik *et al.*, 2021; Griffiths *et al.*, 2021). These plaques are usually covered with silvery-white scales on white skin and grey on black skin resulting from dead skin (Watkins, 2008; Bagel *et al.*, 2012; Griffiths *et al.*, 2021). The lesions vary in size within and across patients and are symmetrically distributed. The number of plaques can vary from a few to many with possible occurrence on any body part (Langley, Krueger and Griffiths, 2005). Itching or pain is a common presentation in people with plaque psoriasis, especially those with joint involvement (Canadian Psoriasis Guidelines Committee, 2009; Hsu *et al.*, 2012). Being the most common form of psoriasis, the use of the term psoriasis by healthcare professionals, people living with the condition and the National Institute for Health and Care Excellence (NICE) has become synonymous with plaque psoriasis (NICE, 2017b).

Figure 1.1: Chronic plaque psoriasis in white and black skin



Note: Images A and B; Well demarcated and symmetry of plaques is characteristic on white skin. C; The plaques are grey on black skin.

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Guttate psoriasis: This is one of the less common forms of psoriasis that affects young adults and children and is characterised by small droplet-like lesions that mainly appear on the torso, arms, legs and scalp, see Figure 1.2 (Raychaudhuri, Maverakis and Raychaudhuri, 2014; Sarac, Koca and Baglan, 2016; Griffiths *et al.*, 2021). Lesions in guttate psoriasis tend to resolve after several weeks to months, although up to 40% of cases progress to chronic plaque psoriasis (Griffiths and Barker, 2007; Griffiths *et al.*, 2021). Streptococcal infections have been implicated in triggering the onset of the condition, hence showing a link to upper respiratory infections such as pharyngitis (Naldi *et al.*, 2001; Sarac, Koca and Baglan, 2016; Griffiths *et al.*, 2021).

Figure 1.2: Guttate psoriasis



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Erythrodermic psoriasis (Erythroderma): This is the least common form of psoriasis, however, it is mostly severe and life-threatening (Griffiths *et al.*, 2021). It also tends to have the most extensive lesions that cover up to 80 to 100% of the body surface area (Mumoli *et al.*, 2014). The lesions are mainly erythematous, while typical papules and plaques lose their distinct features and tend to itch or burn (Camisa, 2004; Sarac, Koca and Baglan, 2016).

Nail psoriasis: Almost half of the people with plaque psoriasis are affected by nail psoriasis. Nail involvement may ensue in which the nails may start pitting, detach from

the nail bed (onycholysis), thickening of the underside of the nail itself (subungual hyperkeratosis) due to the build of skin under the nail growing abnormally and orange-yellow discolouration of the nail bed (Haneke, 2017; Griffiths *et al.*, 2021). Crumbling (dystrophy) of the nail plates is also a common feature (Haneke, 2017; Griffiths *et al.*, 2021). People presenting with onycholysis carry twice the risk of psoriatic arthritis (Love *et al.*, 2012). Figure 1.3 shows nail psoriasis with prominent onycholysis.

Figure 1.3: Nail psoriasis



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Psoriasis pustulosa: This includes generalised pustular psoriasis, and localised pustular psoriasis (palmoplantar pustular psoriasis and acrodermatitis continua). It is marked by pus-filled blisters that follow after the appearance of red and tender skin (Sarac, Koca and Baglan, 2016). Palmoplantar pustular psoriasis, shown in Figure 1.4 A, has a classical presentation of yellow sterile pustules affecting the palms of the hand and soles of the feet, resolving over several weeks into red or brown macules (Griffiths *et al.*, 2021). Palmoplantar pustular is mainly seen in women and individuals that have a family history of palmoplantar pustulosis and smoking (Sarac, Koca and Baglan, 2016). Generalised pustular psoriasis (GPP), von Zumbusch disease, is a rare form that is characterised by widespread patches of pustules, fever and general malaise and is commonly seen in young individuals, see Figure 1.4 B (Brehmer-Andersson, 2006; Sarac, Koca and Baglan, 2016; Griffiths *et al.*, 2021). Recent research has identified GPP as having the hallmarks of an autoimmune disease associated with periodic flares (Griffiths *et al.*, 2021). Impetigo herpetiformis also called generalised pustular psoriasis

of pregnancy due to its occurrence in the last trimester of pregnancy or puerperal period (Camisa, 2004; Sarac, Koca and Baglan, 2016), has a typical presentation of the generalised pustular psoriasis.

Figure 1.4: Psoriasis pustulosa



Notes: A is Palmoplantar pustulosis and B is Generalised pustular psoriasis

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Inverse psoriasis: This is one of the rare forms restricted to skinfold areas of the body which include armpits, groin region, under the breasts and around genitals. It accounts for 3 to 7% of psoriasis patients, see Figure 1.5 (Syed and Khachemoune, 2011; Sarac, Koca and Baglan, 2016; Griffiths *et al.*, 2021). Fungal infections have been reported to trigger the disease. Bright red and inflamed skin without scaling is the main feature of the presentation. These features are known to get worse with sweating and friction in skinfold areas (Camisa, 2004; Syed and Khachemoune, 2011; Sarac, Koca and Baglan, 2016).

Figure 1.5: Flexural or inverse psoriasis



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Understanding the different types of psoriasis is important from a clinical perspective as this informs the choice of treatment needed. It is important to note that these types of psoriasis are not mutually exclusive, for instance, 50% of people with plaque psoriasis have nail involvement (Ibrahim, Waxman and Helliwell, 2009a; NICE, 2017b). This PhD thesis will focus on plaque psoriasis given its common occurrence and impact on the quality of life. Hereafter, unless indicated otherwise, the term psoriasis will be used to represent plaque psoriasis.

1.1.2 Measures of severity

Understanding the severity of psoriasis is important as it guides the choice of treatment and acts as a baseline measure for evaluation of the subsequent effectiveness of the management (NICE, 2013b). This section presents the common measures of psoriasis severity.

Disease severity in psoriasis has widely been measured using tools such as the Psoriasis Area and Severity Index (PASI) (Fredriksson and Pettersson, 1978; Feldman and Krueger, 2005). The PASI is an index that combines the psoriasis lesions characteristics of erythema (redness), induration (thickness) and desquamation (scales) with how

extensive (area) it covers four regions of the body: head (h), upper extremities (u), trunk (t), and lower extremities (l); each accounting for 10%, 20%, 30% and 40% of the total Body Surface Area (BSA) respectively (Fredriksson and Pettersson, 1978; Feldman and Krueger, 2005). The erythema, induration and scaling for each of the body areas are rated on a scale of zero to four (0 = no involvement; 1 = slight; 2 = moderate; 3 = severe; 4 = very severe (Fredriksson and Pettersson, 1978; Ashcroft *et al.*, 1999). The extent of area involved is rated from zero to six (0 = 0 (clear); 1 = <10%; 2 = 10<30%; 3 = 30<50%; 4 = 50<70%; 5 = 70<90%; 6 = 90 to 100%). The PASI score ranges from 0 to 72 and is generated from the formula shown in Equation 1.1.

$$\text{PASI} = 0.1 (E_h + I_h + S_h) A_h + 0.2 (E_u + I_u + S_u) A_u + 0.3 (E_t + I_t + S_t) A_t + 0.4 (E_l + I_l + S_l) A_l$$

Equation 1.1

Where E=Erythema; I=Induration; S=Desquamation; A=Area; subscripts h=head; u=upper extremities; t=trunk; l=lower extremities.

The limitations of the PASI include: not accounting for psychological severity; and poor sensitivity to changes in cases of small areas of involvement (Ashcroft *et al.*, 1999; Feldman and Krueger, 2005). Since erythema, induration and desquamation are scored with equal weight, a reduction in scaling with a corresponding increase in skin erythema could still have the same PASI score (Ashcroft *et al.*, 1999). Another limitation comprises the translation of PASI score changes into clinical relevance. Whereas a PASI score decrease from 38 to 32 may be statistically significant, its clinical significance may not be obvious (Ashcroft *et al.*, 1999). Potential equality concerns with using PASI score have been raised NICE. The PASI score has been reported to potentially underestimate disease severity in people with darker skin (NICE, 2021d). To account for some of the identified limitations of the PASI, other measures such as the simplified psoriasis index have been developed.

The simplified psoriasis index (SPI) is a measure of psoriasis severity which was modelled on the Salford Psoriasis Index (Kirby *et al.*, 2000; Chularojanamontri, Griffiths and Chalmers, 2013). The SPI is available in two complementary versions; the health professionals (proSPI), and the patient self-assessed (saSPI) completed by patients (Chularojanamontri, Griffiths and Chalmers, 2013). These two differ in the language used, which is simplified for the self-assessed SPI.

The SPI is made up of three components that include measuring severity (SPI-s), psychosocial impact (SPI-p) and passed history interventions (SPI-i). The advantage of the SPI-s over the PASI is its ease of completion by the patient as it does not require one to make body surface area estimates and it removes the need to assess erythema (redness), the extent of scales, and induration (plaque thickness) (Chularojanamontri, Griffiths and Chalmers, 2013). The SPI was the measure of psoriasis used in the empirical study presented in chapter 6. Details of how the severity score measured by the SPI is generated were reported in section 6.2.3.3.

The Physician Global Assessment (PGA) is another useful tool used in measuring the severity of extensive and localised plaques (Feldman and Krueger, 2005; NICE, 2017b). The two types of PGA forms are static and dynamic. The static form measures the physician's impression of the disease at a given point in time whereas the dynamic form measures the improvement from baseline (Feldman and Krueger, 2005). The results of the static form can be classified as clear, nearly clear, mild, moderate, severe or very severe (NICE, 2017b).

To capture the quality of life aspects in dermatology in general and psoriasis in particular, tools such as the Dermatology Life Quality Index (DLQI) and the Skindex are used (Finlay and Khan, 1994; Feldman and Krueger, 2005). The DLQI is a validated tool that measures how much the skin disease impacts an individual concerning the symptoms, feelings, daily activity, leisure activities, work or school, personal relationships and treatment (Finlay and Khan, 1994). Skindex was developed for use in studying the effects of a wide variety of skin conditions on affected individuals (Chren, 2012). There are two versions of Skindex; Skindex-29 and Skindex-16 of which choice of the instrument is driven by the research objective (Chren, 2012). Skindex-29 is the oldest, most widely used, and more comprehensive making it suitable for studies investigating and attempting to understand the effects of a skin condition on quality of life. Skindex-16 is the shorter version consisting of items that had the best performance characteristics in the Skindex-29 as well as additional items (Chren, 2012). The main impact measured by Skindex-16 is bother as compared to the frequency of experience. More generic measures of health and capability such as the EQ-5D and the ICECAP have also been used in estimating the impact on quality of life

and beyond health. The EQ-5D and ICECAP were used in this thesis. Details about the EQ-5D and ICECAP are presented in Chapters 2 and 6.

1.1.3 Obesity and psoriasis

Obesity has been linked to higher incidence and severity of psoriasis symptoms (Kumar *et al.*, 2013; Jensen and Skov, 2017; Kunz, Simon and Saalbach, 2019; Xu *et al.*, 2021). The Body Mass Index (BMI) is a common measure of obesity calculated as a person's body weight in kilograms divided by the square of their height in meters. According to the NICE BMI thresholds for adults, there are five categories which include underweight (below 18.5kg/m²), healthy weight (18.5 to 24.9 kg/m²), overweight (25 to 29.9 kg/m²), obese (30 to 40 kg/m²) and severely obese (at least 40 kg/m²) (NICE, 2020a).

Although it is difficult to identify and quantify the causal pathways between psoriasis and obesity, some authors have claimed that people living with psoriasis have: a higher risk of social isolation; and consume significantly more foods high in saturated fats and alcohol than people without psoriasis (Jensen and Skov, 2017). Some published reviews have reported that obesity predisposes patients to psoriasis and amplifies psoriatic inflammation which in turn exacerbates psoriasis severity (Kunz, Simon and Saalbach, 2019).

Difficulties have been reported when treating psoriasis in obese patients. Some evidence has shown that obesity is associated with a decrease in response to systemic and biologic treatment (Jensen and Skov, 2017). Considering the implications of obesity on the severity and treatment of psoriasis, it is therefore important to account for its influences on healthcare resource use and costs. In estimating costs attributable to psoriasis, reported in chapter 5, obesity was controlled for to observe how it drives costs.

1.1.4 Comorbidities in psoriasis

Psoriasis is a multisystem disease that has been linked to multiple conditions that co-occur (comorbidities). Psoriatic arthritis (PsA) is one of the most notable ones. PsA presents with swelling and pain of any joint typical of arthritis (Sarac, Koca and Baglan, 2016). It is asymmetrical in most cases and mainly affects the distal interphalangeal

joints. PsA causes progressive damage to joints which is irreparable, resulting in disability (Lee, Mendelsohn and Sarnes, 2010; Griffiths *et al.*, 2021). The severity of PsA symptoms can vary from mild to severe. About 0.02 to 0.1% of the general population are affected by PsA and 5.4 to 7% of patients with severe skin involvement (Sarac, Koca and Baglan, 2016). A study by Ibrahim and others reported a 13.8% prevalence of PsA in people with plaque psoriasis (Ibrahim, Waxman and Helliwell, 2009b). Another study reported the prevalence of PsA to range from 6 to 39% in patients with plaque psoriasis (Lee, Mendelsohn and Sarnes, 2010). The existence of PsA as a specific clinical entity remains questionable but there is a clear distinction from rheumatoid arthritis in terms of radiographic appearance, clinical presentation, and genetic predisposition (Camisa, 2004).

Figure 1.6: Psoriatic arthritis



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Other long-term conditions that have been linked to psoriasis include cardiovascular disease (CVD), metabolic syndrome, and depression (Popova *et al.*, 2017). Although people living with psoriasis have been reported to have an increased prevalence of CVD risk factors and other associated CVD conditions, there was no link to the short-to-medium-term risk of CV events such as myocardial infarction, stroke, or unstable angina (Parisi *et al.*, 2015). Conditions such as pulmonary disease, asthma, chronic

kidney disease, hepatobiliary cancer and inflammatory bowel disease have been reported to occur more frequently in people living with psoriasis as compared to the general population (Griffiths *et al.*, 2021). However, the causal direction of this association between psoriasis and other long-term conditions remains unclear (Griffiths *et al.*, 2021).

Noting that living with multiple long-term conditions may impact health care resource utilisation and patient outcomes, it is important that patients with psoriasis are assessed for the presence of co-occurring conditions and managed accordingly (NICE, 2017b; Popova *et al.*, 2017). In the empirical study presented in chapter 6, the presence of co-occurring conditions was recorded as a secondary parameter. Similar to obesity, the occurrence of comorbidities was controlled for in the empirical study estimating the cost attributable to psoriasis in chapter 5.

1.2 Epidemiology of psoriasis: Incidence and Prevalence in the UK and globally

The first step in understanding the economic impact of a disease is to identify the relevant population and understand the occurrence of the disease in that population. Epidemiology is concerned with the occurrence and variation of the disease in the population with regard to factors that determine the variation (Thelle and Laake, 2015). Incidence and prevalence are key concepts in understanding the emergence and population burden-of-disease.

1.2.1 Prevalence of psoriasis

Prevalence refers to the proportion of the population with the disease at a given time as shown in Equation 1.2 (Le, 2003).

$$Prevalence = \frac{\text{number of diseased persons at a selected time of investigation}}{\text{total number of persons examined}}$$

Equation 1.2

The measurement and reporting of prevalence depend on the timeframe of the estimate. Point prevalence is measured at a specific time point; period prevalence is measured under a set period such as 12 months; and lifetime prevalence considers the proportion who had the disease at some point during their lifetime (Parisi *et al.*, 2013).

The prevalence reported for any given condition is, therefore (partly), determined by the chosen measuring method. Therefore, it is important to consider the method of measure when reporting and interpreting the prevalence. For example, studies looking at the prevalence of psoriasis have reported different prevalence within and across countries which to some degree has been attributed to the method of measuring prevalence (Parisi *et al.*, 2013). In general, methods used to estimate the prevalence have the greatest impact on the subsequent results affecting the comparison between studies (Parisi *et al.*, 2013). Some of these methodological differences include diagnostic methods, for example, self-reported psoriasis patients or dermatologist-diagnosed patients, the timing of the data collection, e.g. point, monthly, annually, period, or lifetime prevalence (Parisi *et al.*, 2013). For instance, a systematic review on the epidemiology of psoriasis attributed some of the differences in the reported prevalence to variations in the case definition of psoriasis, prevalence and research methodology (Parisi *et al.*, 2013, 2020).

Although there are limited data with regards to the epidemiology of psoriasis among non-Caucasian groups, the prevalence has been established to vary across geographical locations and ethnicities (Alexis and Blackcloud, 2014). It has also been established that knowledge of the global incidence and prevalence of psoriasis remains poor and most studies have been conducted in Europe and the United States (US) (Parisi *et al.*, 2013). Even fewer studies have been conducted on children (<18 years) (Parisi *et al.*, 2013). The WHO Global report on psoriasis indicated that studies on the epidemiology of psoriasis were mainly from 20 countries, with most of the studies conducted in Australia, China, Germany, Norway, the UK, and the US (WHO, 2016). Other countries in which studies were done but less evidence was gathered were Egypt, Italy, Sweden, Brazil, Croatia, Denmark, France, Spain, Portugal, Sri Lanka, Poland, Japan, Tanzania, and Tunisia (WHO, 2016). A more recent study found that up to 67% of psoriasis prevalence studies were conducted in high-income countries (Parisi *et al.*, 2020). This exposes the knowledge gap concerning geographical regions (WHO, 2016; Parisi *et al.*, 2020).

The global prevalence of psoriasis is estimated at 60 million people (Parisi *et al.*, 2020). A recent study reported the regional prevalence of psoriasis to be 0.14% in east Asia to

1.99% in Australasia, 1.92% in western Europe and 1.83% in central Europe (Parisi *et al.*, 2020). In North America, it was reported to be 1.50%, and 1.1% in high-income Latin America (Parisi *et al.*, 2020). Country-specific prevalence has been reported to vary such as 1.88% in Australia, 1.86% in Norway, 1.81% in Israel, and 1.79% in Denmark.

A study using the Clinical Practice Research Datalink (CPRD) reported the prevalence of psoriasis in the UK to be 2.8% (Springate *et al.*, 2016). This prevalence was noted to be slowly increasing with improvements in life expectancy experienced over the last 20 years (Springate *et al.*, 2016). This slow increase has important implications for resource planning and allocation (Springate *et al.*, 2016). Another study from the US found a prevalence of 2.5% among Caucasians compared to only 1.3% among African Americans (Gelfand *et al.*, 2005). One review estimated that psoriasis affected 7.4 million people in the US alone in 2013 (Vanderpuye-Orgle *et al.*, 2015). A similar result of a 3.0% prevalence of psoriasis in the US, about 7.55 million people, has been reported in a more recent study (Armstrong *et al.*, 2021).

1.2.2 Incidence of psoriasis

Incidence is a measure of the number of new cases of a disease that develop in a population in a specified period as shown in Equation 1.3 (Le, 2003).

$$\text{Incidence} = \frac{\text{No. of persons who developed the disease over a defined period}}{\text{No. of persons initially without the disease who were followed for the defined period}} \quad \text{Equation 1.3}$$

The number of studies focusing on trends in incidence over time remains low (Springate *et al.*, 2016). Using the CPRD database in the UK, the incidence of psoriasis had declined slightly from 159 cases per 100 000 person-years in 1999 to 129 per 100 000 person-years (95% CI 126-133) in 2013 (Springate *et al.*, 2016). The review by Parisi *et al.* (2013) found seven studies conducted in four countries (US, UK, Netherlands, and Italy) that investigated the incidence of psoriasis (Parisi *et al.*, 2013). Studies under this review reported incidences of 59.9 per 100,000 person-years (95% CI: 49.5 -70.3) in the US in 1991, 120 to 130 and 140 per 100,000 person-years in the Netherlands and

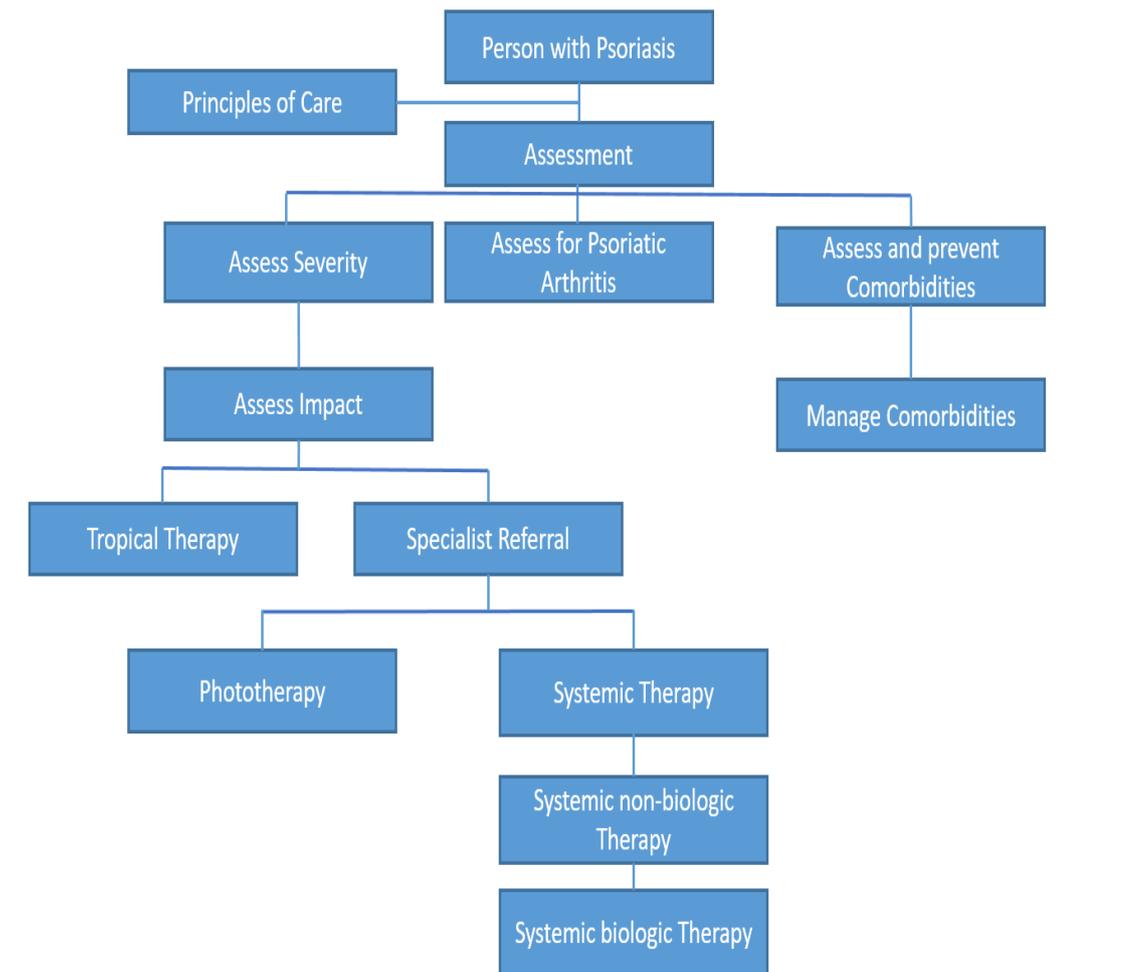
UK respectively (Parisi et al., 2013). This further confirms the wide knowledge gaps existing in psoriasis epidemiology globally.

1.3 Management of psoriasis

Regardless of current advances in the treatment of psoriasis, the problem of delayed diagnosis and under-diagnosis has persisted (Kim, Jerome and Yeung, 2017). Psoriasis remains an incurable disease even with an enhanced understanding of the multifactorial causes and diagnosis (WHO, 2016). Several guidelines for the management of psoriasis have been developed. Among these guidelines are the National Institute for Health and Care Excellence (NICE) guidelines in England and Wales (NICE, 2017b) and the Scottish Intercollegiate Guidelines Network (SIGN) in Scotland (SIGN, 2010). The European S3-guideline for the systemic treatment of psoriasis is a more specific guideline on the management of plaque psoriasis (Nast *et al.*, 2017).

These guidelines share common principles which include the assessment of the severity of the disease, presence of psoriatic arthritis and other comorbidities (SIGN, 2010; NICE, 2017b). The principles of care in psoriasis aim to offer information to patients to help them understand the condition (psoriasis), the lifestyle risk factors that can trigger symptoms, provide available treatment options, safe and effective use of prescribed treatments, and how to deal with physical, psychological and social well-being (NICE, 2017b). Lifestyle change advice offered includes encouraging smoking cessation for smokers, weight loss in overweight and obese patients, reducing alcohol consumption, having a controlled diet and avoiding other identified trigger factors (SIGN, 2010; NICE, 2017b). These principles promote tailoring care to each patient based on understanding the individual's disease impact and needs. The NICE clinical guideline (CG153), for National Health Service (NHS) England, on the assessment and management of psoriasis offers recommendations on the principles of care, assessment and referral, topical therapy, phototherapy and systemic therapy as shown in Figure 1.7 (NICE, 2017b).

Figure 1.7: Diagnosis and management of psoriasis in the United Kingdom



Source: adapted and reproduced from the NICE clinical guideline (CG153) (NICE, 2017b).

1.3.1 Treatment of psoriasis

Improvements in terms of treatments for psoriasis have been achieved, from the historical coal tar topical creams to systemic biologics. Treatment can be highly influenced by the type of psoriasis, severity of the condition and availability of the medication (Azizam *et al.*, 2015). The current treatment options are categorised as topical, systemic and phototherapy. The systemic treatment category is further split into non-biologic and biologic treatments.

1.3.1.1 Topical treatments

Topical therapies such as corticosteroids, vitamin D analogues (e.g. calcipotriol, calcitriol and tacalcitol), dithranol and coal tar, remain the first line of treatment, especially in mild cases (Canadian Psoriasis Guidelines Addendum Committee, 2016;

NICE, 2017b). These treatments are commonly used in combination e.g. calcipotriol and betamethasone as Dovebet® or Estillar® (Joint Formulary Committee, 2021). The face, flexures, genitalia, scalp, palms, and soles of the feet make up what is referred to as the 'difficult-to-treat sites' due to the high impact and possible functional impairment that it causes (NICE, 2017b). Prescribing topical treatment for 'difficult-to-treat sites' requires careful consideration (NICE, 2017b).

1.3.1.1.1 Emollients

Emollients are useful for very mild cases of psoriasis and adjuncts to other more specific treatments. These have an effect on relieving symptoms of dryness, scaling and cracking by soothing, smoothing and hydrating the skin (Joint Formulary Committee, 2021). The choice of an emollient is driven by the severity of the condition, patient preference, and affected body site (Joint Formulary Committee, 2021). A caution about the risk of severe and fatal burns with emollients has been raised by the Medicines and Health Products Regulatory Agency (MHRA). This risk has been attributed to build-up residue on clothing and bedding and patients are advised to avoid smoking or going near naked flames (Joint Formulary Committee, 2021).

1.3.1.1.2 Corticosteroids

Corticosteroids include betamethasone which is the most common and probably overused psoriasis treatment (Carr, 2007; Joint Formulary Committee, 2021). These treatments are most useful in acutely inflamed psoriasis. Specific sites, such as the face, flexures, scalp, palms, and soles are suitable for topical corticosteroid treatment. However, topical corticosteroids are less suitable as the only treatment of extensive chronic psoriasis. Their limitations in extensive chronic psoriasis are because of unsustainable early improvement and the risk of the condition deteriorating (Joint Formulary Committee, 2021).

1.3.1.2 Phototherapy

Phototherapies such as broad or narrowband ultraviolet B light (UVB) and photochemotherapy combining psoralen plus UVA light (PUVA) are used as second-line treatment in moderate to severe psoriasis (Canadian Psoriasis Guidelines Addendum Committee, 2016; NICE, 2017b). Psoriasis patients with plaques that are resistant to UVB or show poor response can be offered topical adjunctive therapy (Joint Formulary

Committee, 2021). The role of psoralene in PUVA is to enhance the effects of UVA and can be administered orally or topically (Joint Formulary Committee, 2021). These treatments are administered in specialist centres by appropriately trained healthcare professionals (Joint Formulary Committee, 2021).

1.3.1.3 Non-biologic systemic treatment

Systemic traditional agents that include apremilast, acitretin, ciclosporin, and methotrexate are used as second-line treatment in moderate to severe psoriasis (Canadian Psoriasis Guidelines Addendum Committee, 2016; NICE, 2017b).

Methotrexate is the first choice systemic treatment and remains the most widely used other than systemic steroids (Morrone *et al.*, 2020). Ciclosporin has been considered a first-line treatment in some patients such as those who need rapid, short-term treatment, or considering conception (Joint Formulary Committee, 2021). Acitretin is only considered in cases where methotrexate and ciclosporin are contraindicated or failed (Joint Formulary Committee, 2021). Similarly, apremilast has been licenced in moderate to severe plaque psoriasis in patients with a contraindication or failed response to ciclosporin, methotrexate or PUVA (Joint Formulary Committee, 2021).

Another class of systemic non-biologic systemic treatment are fumarates, e.g. dimethyl fumarate (NICE, 2017a). Dimethyl fumarate is recommended for use in severe psoriasis when other systemic treatments are contraindicated or not tolerated (NICE, 2017a). Although dimethyl fumarate has been reported to be less effective than biologic therapies and apremilast, there is some evidence it is cost-saving under the English NHS (NICE, 2017a).

1.3.1.4 Biologic and biosimilar systemic treatment

The introduction of biologics has made it possible to achieve disease control with an acceptable safety profile (Cohen *et al.*, 2017). The introduction of biologics saw a major clinical improvement in the management of psoriasis. The use of biologics in psoriasis typically constitutes the third-line treatment (Canadian Psoriasis Guidelines Addendum Committee, 2016; NICE, 2017b). Biologics are categorised into three main groups based on their mechanism of action; tumour necrosis factor (TNF)- α inhibitors, interleukin (IL)-23 inhibitors, and IL-17 inhibitors as shown in Table 1-1 (Kamata and

Tada, 2020). TNF- α inhibitors include adalimumab, certolizumab-pegol, etanercept, golimumab and infliximab (Kamata and Tada, 2020). The interleukin (IL)-23 inhibitors group is made up of ustekinumab an anti-IL-12/23p40 antibody, and guselkumab, risankizumab, and tildrakizumab the anti-IL-23p19 antibodies. In addition, the IL-17 inhibitors are secukinumab, and ixekizumab which are anti-IL-17A antibodies, brodalumab an anti-IL-17RA antibody, and bimekizumab an anti-IL-17A/F antibody which blocks both IL-17A and IL-17F. The use of biologics and biosimilars should be left to specialist settings only such as dermatology or rheumatology clinics (Garg *et al.*, 2017; NICE, 2017b).

Table 1-1: Biologics used in psoriasis

<i>Class (Target) of biologic</i>	<i>Drug</i>
<i>TNF-α inhibitors</i>	Adalimumab
	Certolizumab-pegol
	Etanercept
	Infliximab
<i>IL-12/23 inhibitor</i>	Ustekinumab
<i>IL-23 inhibitors</i>	Guselkumab
	Risankizumab
	Tildrakizumab
<i>IL – 17 Inhibitors</i>	Bimekizumab
	Brodalumab
	Ixekizumab
	Secukinumab

Between 2006 and 2021, NICE has produced up to 16 technology appraisal (TA) guidance on biologic treatments for psoriasis. Two of these appraisals are specific to the use of secukinumab, adalimumab, etanercept, and ustekinumab in treating plaque psoriasis in children (NICE, 2021b). NICE's TA guidance (TA734) recommends the use of secukinumab as an option for treating psoriasis in 6- to 17-year-olds. The recommendations were based on some of the committee considerations which included that the total costs for secukinumab were similar to or lower than those for ustekinumab, etanercept and adalimumab (NICE, 2021d). The clinical benefits of secukinumab were also reported to be similar or greater than ustekinumab, etanercept and adalimumab (NICE, 2021d). According to NICE's TA350, secukinumab is recommended as an option in treating adults with severe psoriasis and failed response to systemic non-biologic treatments (NICE, 2015). The most recent NICE TA guidance (TA723) concluded that evidence from clinical trials showed bimekizumab was more effective than adalimumab, secukinumab and ustekinumab in treating moderate to severe psoriasis in adults (NICE, 2021a). It has also been suggested that indirect comparisons show bimekizumab to be similar to or more effective than other biological treatments available in the UK (NICE, 2021a). Total costs associated with using bimekizumab have been reported to be similar to or lower than those of brodalumab, risankizumab and ixekizumab (NICE, 2021a).

Despite the significant clinical benefits of biologics, access is still limited in many settings due to prohibitive treatment costs (Carrascosa *et al.*, 2018; Cohen *et al.*, 2020). Following the expiration of patents on several biologics, biosimilar agents have been developed and introduced to the market (Cohen *et al.*, 2020). Biosimilar refers to a biological product that is highly similar to the originator biologic medicine in terms of mechanism of action with no clinically meaningful differences on safety and efficacy (Carrascosa *et al.*, 2018; Cohen *et al.*, 2020). Countries such as the UK have been reported to have a high penetration of biosimilars (Cohen *et al.*, 2020). The use of biosimilars has been hailed as one way for healthcare systems to maximise value for money in patients that would otherwise be treated with biologics (Cohen *et al.*, 2020).

1.4 Economic impact of disease

The World Health Organisation (WHO) has defined the economic impact of disease as the 'magnitude of economic losses of an individual, firm and/or society in terms of costs and consequences' (WHO, 2009). Studies designed to provide estimates of economic impact have been described as those that provide a descriptive cost and consequence estimate of the magnitude of economic losses due to disease (Roux and Donaldson, 2004; Tarricone, 2006; Jo, 2014). Capturing the net economic impact of disease accounts for the fact that some expenses such as treatment costs, especially for chronic non-preventable diseases, will always be incurred (WHO, 2009). These descriptions of economic impact are a simplification of a complex concept involving various methods to identify, measure, and value economic impact. Terms such as economic impact, economic consequences and economic burden are used interchangeably by different authors (WHO, 2009; Chisholm *et al.*, 2010). Chapter 2 in this thesis presents a study that produces a nomenclature for economic impact in terms of burden-of-disease and cost-of-illness.

Humans attach value not only to the consumption of goods and services but to other aspects of health such as quality of life, capability, and functionality. Therefore, to capture the full economic impact of a disease on an individual it is important to value both the costs-of-illness and the consequences (burden-of-disease). The information generated from studies designed to quantify economic impact is useful in guiding decision-makers to identify the economic losses and how they are distributed by highlighting the cost and consequences ensuing under each component.

Understanding the distribution of economic loss helps in identifying pivotal points for policy implementation and provides useful information that can be used to cast a spotlight on a disease which is useful for advocacy (Onukwugha *et al.*, 2016). In addition, this information is also useful for periodic evaluation of the performance of health care systems (Roux and Donaldson, 2004).

Broadly, the two subfields of economics are macroeconomics, which looks at the economy-wide phenomena (societal level), and microeconomics which looks at how households (individuals) make decisions and interact with firms or health care systems (Mankiw, 2004). Therefore, the economic impact of disease can be analysed from a

macroeconomic or microeconomic view. Macroeconomics and microeconomics are interlinked but remain standalone disciplines (WHO, 2009; Chisholm *et al.*, 2010). Considering the relevant decision-maker and the focus on the NHS healthcare budget, this PhD will focus on the microeconomic impact of psoriasis (see section 1.4.2).

1.4.1 **Macroeconomic impact**

The macroeconomic impact is concerned with aggregated effects (supply and demand) on the economy as a whole and includes parameters such as the country's gross domestic product as well as future growth prospects (Sloman, 2006; WHO, 2009). A macroeconomic understanding of the economic impact of diseases entails aggregating its impact across different economic agents in three areas related to economic welfare; non-health consumption, leisure time and health status (WHO, 2009). At this level, the impact of disease may, for instance, be assessed based on its effect on the gross domestic product (GDP) through increased health expenditure, reduced labour supply and productivity losses, and reduced investment in human and physical capital formation (WHO, 2009). GDP refers to the country's total value of goods and services produced within a year and encompasses all industries including health (Mankiw, 2004). Ill health has also been linked to lower saving rates, lower return on capital, and lower levels of domestic and foreign investment; factors which are linked to affecting economic growth (WHO, 2009).

Some publications suggest cost-of-illness studies provide only a partial macroeconomic assessment as it solely considers health sector spending and productivity loss without accounting for depleted capital accumulation, investment in human capital and demographic change to diminished economic growth (WHO, 2009). Based on its mere consideration of the health sector and productivity loss, cost-of-illness is a classic case of microeconomics.

1.4.2 **Microeconomic impact**

The microeconomic perspective of the impact of illness is looked at in terms of the players involved which are individuals, firms, or government (WHO, 2009; Zweifel, Breyer and Kifmann, 2009). This looks at how individuals make decisions in pursuit of health, how governments or other players provide health care, how firms such as

pharmaceutical companies get the medicines to the market, management of hospitals and ultimately how all these interact (Zweifel, Breyer and Kifmann, 2009). In addition, individuals and firms interact in a market where households supply labour to firms and receive income, and firms produce goods and services which they sell to households generating profits, (Leibowitz, 2004; WHO, 2009; Zweifel, Breyer and Kifmann, 2009). Individuals need good health to fully participate in economic activities by supplying labour (Leibowitz, 2004; WHO, 2009; Zweifel, Breyer and Kifmann, 2009).

This PhD takes a microeconomic view of the economic impact of psoriasis. The microeconomic view is relevant to decision-making under a constrained health care budget. This view informs decision-makers on the extent and pattern of health care resource use and costs by people living with psoriasis. The microeconomic view also informs decision-makers on how living with psoriasis impacts the individual's health-related quality of life and capability. Overall, taking the microeconomic view provides an understanding of the cost-of-illness and burden-of-disease due to psoriasis.

1.5 Cost-of-illness and burden-of-disease

In this thesis, the economic impact is assumed to be made up of two elements: costs and consequences. The types of costs and consequences are dependent on the study perspective and time horizon (see Chapter 2). The cost element represents the resource use incurred in alleviating the disease and productivity loss. Quantifying the costs is referred to as cost-of-illness. The consequences element may account for the health and non-health-related impact the disease exerts on the affected individual (Roux and Donaldson, 2004). Quantifying the consequences is referred to as burden-of-disease. For each of these two elements, there is a need to identify, measure and value the element consistent with the given framework: welfarism or extra-welfarism. Chapter 2 provides a taxonomy for identifying, measuring, and valuing the costs and consequences of disease.

1.6 Importance of understanding economic impact of psoriasis

Knowledge of the economic impact of psoriasis is potentially relevant to addressing policy concerns regarding its consequences to individuals and society (WHO, 2009). Quantifying the economic impact of psoriasis has become necessary in estimating its

impact on individuals and relevant sectors of society. Critics of economic impact studies argue that information from these studies is not sufficient in setting priorities for resource allocation because they do not evaluate alternative methods of managing the disease, as is the case with an economic evaluation which compares two or more interventions in terms of both their costs and consequences (Roux and Donaldson, 2004; O’Sullivan, Thompson and Drummond, 2005; Kymes, 2014). Nonetheless, producing evidence of the economic impact of a condition, such as psoriasis, can still have useful policy relevance.

The information from economic impact studies can be useful in identifying strategies for reducing the cost-of-illness and burden-of-disease. Looking at the holistic approach of economic impact analysis, these studies offer an understanding of the different elements that contribute to the burden-of-disease by offering insights into the health and non-health consequences. This also offers a window of comparison between countries. Different countries have different healthcare system setups which ultimately influence the economic impact of disease.

The 67th World Health Assembly recognised the consequences of psoriasis and encouraged member states to raise awareness of the disease and draw attention to the public health impact of psoriasis (WHO, 2014a). Understanding the economic impact of psoriasis will complement the clinical and epidemiological burden and at the same time help address some policy questions (WHO, 2009).

1.7 Current psoriasis cost-of-illness and burden-of-disease estimates

Published systematic reviews have frequently reported the considerable economic impact that psoriasis exerts on patients and healthcare systems (Feldman *et al.*, 2014; Azizam *et al.*, 2015; Brezinski, Dhillon and Armstrong, 2015; Kawalec and Malinowski, 2015; Vanderpuye-Orgle *et al.*, 2015; Burgos-Pol *et al.*, 2016). The economic impact of psoriasis has been noted to be similar to or higher than other non-communicable diseases such as pancreatic cancer, melanoma, prostate cancer and asthma (Feldman *et al.*, 2014; Azizam *et al.*, 2015).

People living with psoriasis have reported their condition as having a significant impact on their quality of life. Reports of discrimination and stigma are common in people living with psoriasis, see Chapters 4 and 6 for more details on the burden-of-disease.

According to one systematic review, the 2013 costs due to psoriasis in the US were estimated to range from US\$51.7billion to US\$63.2 billion, US\$23.9 billion to US\$35.4 billion, and US\$36.4 billion annually for direct, indirect and medical comorbidities respectively (Brezinski, Dhillon and Armstrong, 2015). Another systematic review on the economic burden of psoriasis in the US found that economic burden included indirect costs (productivity loss), disability burden, quality of life, mental health effects, social stigma, and caregiver burden, and direct costs which included out of pocket costs and health care utilization (Vanderpuye-Orgle *et al.*, 2015).

The shortcomings of these reviews motivated the need to conduct this PhD. The lack of a clear systematic definition of the economic impact of psoriasis was the motivation for chapter 2. There were also a lack of current burden-of-disease and cost-of-illness estimates for 'clear' reporting. This motivated the conduct of chapters 3 and 4. The need for UK estimates of the cost-of-illness attributable to psoriasis and the burden-of-disease on people living with psoriasis led to empirical studies reported in chapters 5 and 6.

1.8 Aim and Objectives

The aim of this thesis was to generate an evidence base to understand the economic impact of psoriasis in the UK.

This thesis addresses five objectives to:

- Describe a nomenclature for defining the economic impact of disease;
- Identify and critically appraise published studies that have estimated the cost-of-illness of psoriasis;
- Identify and critically appraise published studies that have estimated the burden-of-disease of psoriasis;

- Estimate the healthcare costs attributable to psoriasis in the UK;
- Estimate the burden-of-disease of people living with psoriasis in the UK.

These five objectives are addressed in five chapters. The aim, objectives and overview of the methods used in these five chapters are now described below.

Chapter 2 reports a study to develop a descriptive framework to enable the design and reporting of studies that identify, measure, and value the economic impact of disease. A rapid review using the pearl-growing method was conducted to identify relevant existing frameworks. No relevant framework was found, and a de novo framework was conceptualised and developed to provide a mechanism to define economic impact including cost-of-illness and burden-of-disease. The framework highlighted approaches to identify, measure and value economic impact.

Chapter 3 presents evidence from a systematic literature review of studies reporting the cost-of-illness for people living with psoriasis. Existing published systematic reviews were identified to inform the understanding of the current scale and scope of the assimilated evidence base reporting estimates of the economic impact of psoriasis together with the methods used to generate these estimates. This systematic review was aimed at critically appraising the published studies. The framework developed in chapter 2 was used in conjunction with the Centre for Review and Dissemination (CRD) recommendation to critically appraise the studies. The objectives were to identify all cost-of-illness studies of people living with psoriasis, describe the included studies, and summarise the published estimates for the UK and other countries.

Chapter 4 presents a systematic review that focused on the burden-of-disease in people living with psoriasis. Similar to chapter 3, this chapter was aimed at critically appraising studies reporting on the burden-of-disease in people living with psoriasis. Burden-of-disease components from the developed framework in chapter 2 in combination with the CRD recommendations were used.

Chapter 5 is an empirical study that used routinely collected primary and secondary care data to estimate the cost-of-illness attributable to psoriasis and the driver of these costs. Data sources included Clinical Practice Research Datalink (CPRD GOLD) linked to the Hospital Episodes Statistics (HES) and Office of National Statistics (ONS)

mortality data. The study also explored drivers of healthcare resource use and costs in people living with psoriasis by controlling for variables such as obesity measured by Body Mass Index (BMI) and the presence of comorbidities.

Chapter 6 reports the results from a burden-of-disease survey for people living with psoriasis. This study aimed to quantify the burden-of-disease of a sample of people with psoriasis living in the UK. The main objectives of the study were to quantify the impact of living with psoriasis on health status and wellbeing. Physical disease severity was also quantified and its influence on health and capability impact was also assessed.

Chapter 7 brings together the results from each chapter and discusses implications in terms of the economic impact of psoriasis. The overall research, methods implication, policy implications and future research needs are also presented in this chapter.

2 Towards consistency and coherence in identifying, measuring and valuing the economic impact of disease

Chapter summary

This chapter reports a study to develop a descriptive framework to enable the design and reporting of studies that identify, measure, and value the economic impact of disease. This study was motivated by the need to improve consistency and coherence in understanding and comparing published estimates of cost-of-illness and burden-of-diseases, such as psoriasis.

Section 2.1 presents the background, motivation, aims and objectives for the study. The methods and results section presenting the proposed descriptive framework are reported in sections 2.2 and 2.3 respectively. Finally, the discussion and conclusion are presented in section 2.4 and 2.5 respectively.

2.1 Background

In general terms, quantifying the economic impact has been defined as methods to provide an estimate of the magnitude of economic losses due to a disease (Roux and Donaldson, 2004; Tarricone, 2006; Jo, 2014). This general definition is necessary but not sufficient to design and interpret studies that aim to identify, measure, and value the economic impact of disease. Analyses of the economic impact of disease comprise some of the earliest forms of economic analyses applied to health and health care, and these are primarily cost-of-illness studies (Tarricone, 2006; Jo, 2014; Onukwugha *et al.*, 2016). However, some commentators suggest that studies examining the economic impact of disease should go beyond cost-of-illness to include the measurement of the burden-of-disease (consequences) (WHO, 2009).

Cost-of-illness studies gained recognition around the 1960s as an early method of economic costing applied to health and health care (Jefferson, Demicheli and Mugford, 2000; Onukwugha *et al.*, 2016). Methods to estimate cost-of-illness have improved over the years (Rice, Hodgson and Kopstein, 1985; Löfvendahl, 2016; Onukwugha *et*

al., 2016). However, methodological diversity and conceptual shortcomings in studies identifying, measuring, and valuing cost-of-illness continue to exist even in recent studies (Onukwugha *et al.*, 2016). The diversity and conceptual shortcomings limit the comparability of studies within and across disease areas (Thacker *et al.*, 2006; Löfvendahl, 2016).

Anecdotal evidence suggests that there has not been any commensurate discussion of the shortcomings in studies identifying, measuring, and valuing the burden-of-disease as a component of economic impact. Although there is a consensus that poor health influences economic outcomes, the appropriate specific methods used to quantify the economic impact of the disease remain contentious. Different methods that have been used to quantify the economic impact of disease at a macroeconomic (see glossary for definition) level include econometric approaches; simulation-based calibration; general equilibrium models; full-income models (Trogdon, Finkelstein and Hoerger, 2008; WHO, 2009; Jo, 2014). On a microeconomic (see glossary for definition) level, methods include bottom-up or micro-costing; top-down costing; regression-based econometric methods; human capital approaches; friction cost approach. Methods used to quantify the impact of burden-of-disease include; willingness to pay (WTP) or willingness to accept (WTA) methods such as the contingent valuation method and discrete choice experiments; measures of wellbeing; measures of health status or health-related quality of life.

In many instances, the components of what constitutes economic impact within the same methods also tend to vary. For example, in cost-of-illness methods, some studies only consider direct costs such as healthcare expenditure whereas other studies include indirect costs such as productivity losses. This further contributes to the challenges of comparability (Finkelstein and Corso, 2003; Thacker *et al.*, 2006; WHO, 2009).

2.1.1 Aim and objectives

This study aimed to identify, and if necessary develop, a descriptive framework defining a nomenclature system for the relevant components and methods when identifying and quantifying the economic impact of disease.

This study addresses four objectives to:

1. Describe the analytical framework for the economic impact of disease in terms of welfarism and extra-welfarism;
2. Highlight the importance of specifying study perspective and time horizon in economic impact analysis;
3. Describe the aspects of identifying, measuring, and valuing cost-of-illness;
4. Describe the aspects of identifying, measuring, and valuing burden-of- disease.

2.2 Methods

Developing the framework comprised three stages: i) Identifying existing frameworks; ii) Conceptualisation; iii) Validation. The traditional pearl-growing method was used to identify relevant reviews, guidance, and texts describing methods used to quantify the economic impact of disease (Schlosser *et al.*, 2006). This review was supplemented with a study to collate the views of key opinion leaders in health economics to validate the developed schematic framework, see Appendix 2.1.

Traditional pearl-growing, also known as citation pearl-growing, refers to a process of using characteristics of a known and influential paper to search for other relevant materials (Ramer, 2005; Schlosser *et al.*, 2006). This strategy is iterative and involves six steps, which were followed in this review (Schlosser *et al.*, 2006):

1. Finding the first relevant article (pearl) is the first step in a traditional pearl-growing strategy. The initial influential paper is referred to as the pearl (Ramer, 2005; Schlosser *et al.*, 2006). This study identified two studies that reported the methods of identifying, measuring, and valuing economic impact of disease (Jo, 2014; Onukwugha *et al.*, 2016);
2. Finding the terms under which the article is indexed in a selected database. The initial database selected in this study was Medline via OVID. The articles were found to be indexed under healthcare costs and humans;
3. Finding the other relevant articles in the database-1 by using the index terms in a building block query;
4. Repeat steps two and three in other databases;
5. Repeat steps one to four for other relevant articles;

6. Stop when articles retrieved provide diminishing relevance to the research question.

The traditional pearl-growing method was supplemented with a targeted search of grey literature using keyword-based searches of publicly available literature on the World Health Organization (WHO) website and hand-searching of textbooks relevant to health economics (WHO, 2019). Only literature published from 1999 to 2019 was included. The period restriction was chosen under the assumption that more recent publications in the last two decades would reflect the trends and advancements in methods for identifying, measuring, and valuing the economic impact of disease. After a draft version of the descriptive framework had been produced based on the published literature, a sample of experts in health economics was consulted to provide comments and suggested edits to the framework (see Appendix 2.1 for a description of this process).

2.3 Results

No existing relevant framework was identified. A total of six publications were identified that provided a starting point to conceptualise a descriptive framework to provide a nomenclature system to describe the parts of the economic impact of disease (Jefferson, Demicheli and Mugford, 2000; Tarricone, 2006; Clabaugh and Ward, 2008; WHO, 2009; Larg and Moss, 2011; Jo, 2014). The next six sections describe the descriptive framework used to identify, measure and value the economic impact of disease; the analytic framework for quantifying the economic impact of disease; the relevant study perspective; the relevant study time horizon; identifying, measuring and valuing cost-of-illness; identifying, measuring and valuing burden-of-disease.

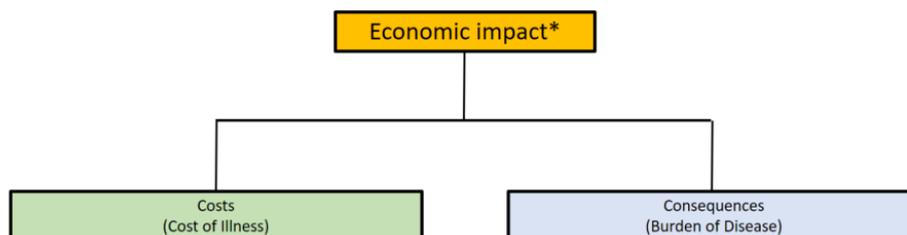
2.3.1 A descriptive framework for quantifying the economic impact of disease

The identified reviews (Jo, 2014; Onukwugha *et al.*, 2016) that aimed to assimilate values of the economic impact of disease acknowledged that there was no clear definition. Neither of these reviews presented a descriptive framework to provide the basis for understanding published estimates of economic impact of disease. The five identified publications which included reviews, a WHO guide, and a book chapter were collectively used to develop a descriptive framework to conceptualise the economic

impact of disease (Jefferson, Demicheli and Mugford, 2000; Akobundu, J.Ju and L.Blatt, 2006; WHO, 2009; Jo, 2014; Onukwugha *et al.*, 2016) (see Figure 2.1-2.3).

The framework that was developed describes a nomenclature system for the relevant components and methods to use when quantifying the economic impact of disease, considering welfarist and extra-welfarist approaches (see section 2.3.2). The initial framework which was used in the expert opinion survey is shown in Figure A2.1 under Appendix 2.1. The final framework, modified after receiving feedback from the sample of experts is shown in Figures 2.1, 2.2 and 2.3. These three figures show the three components representing (i) the economic impact of disease (Figure 2.1); (ii) cost-of-illness (Figure 2.2); (iii) burden-of-disease (Figure 2.3). Figure 2.2 and Figure 2.3 describe the components for identifying, measuring and valuing cost-of- illness and burden-of-disease, respectively.

Figure 2.1: Description of the components of the economic impact of disease



* depends on defined relevant study perspective and time horizon

Figure 2.2: Description of the components of Cost-of-Illness

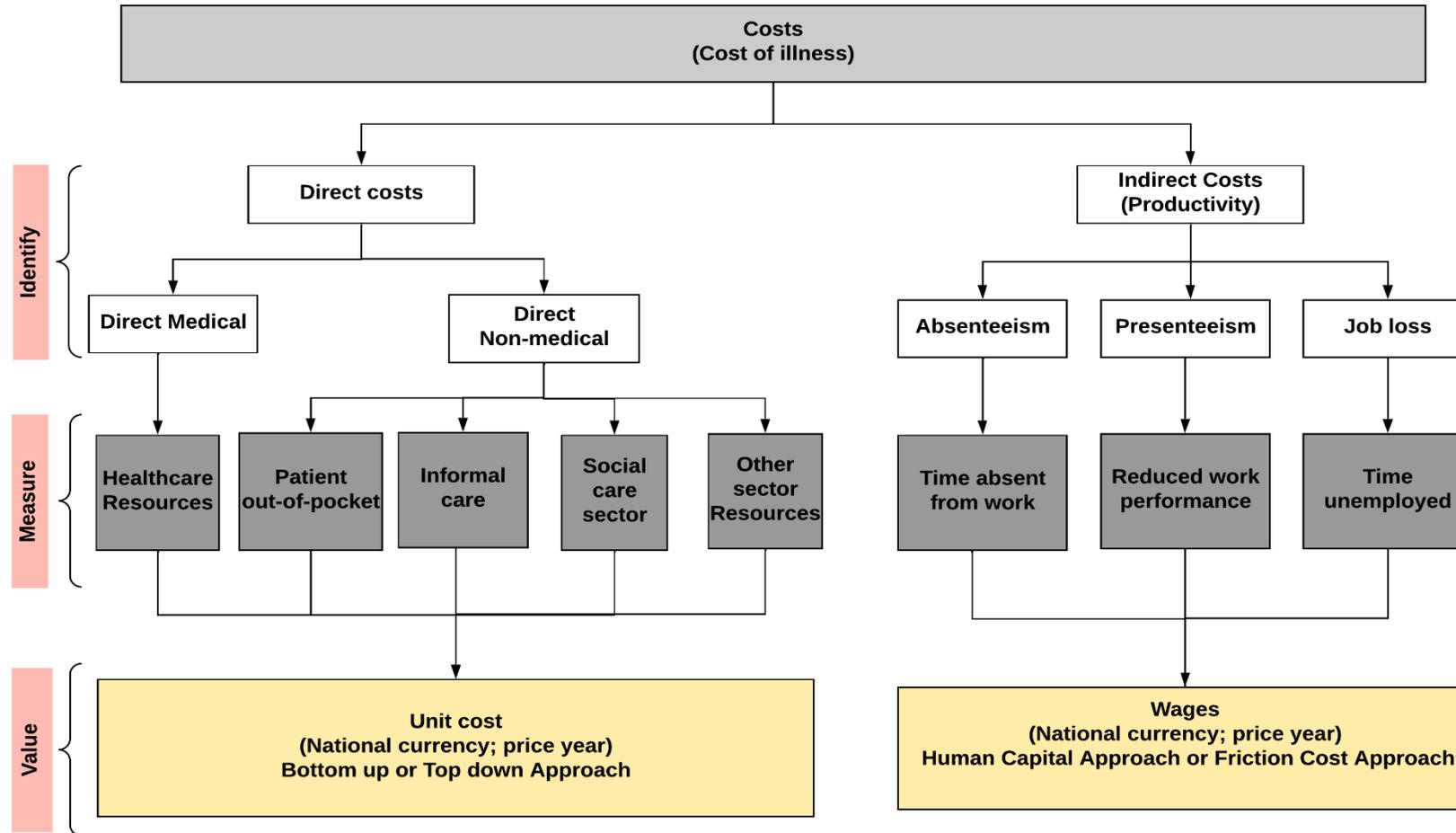
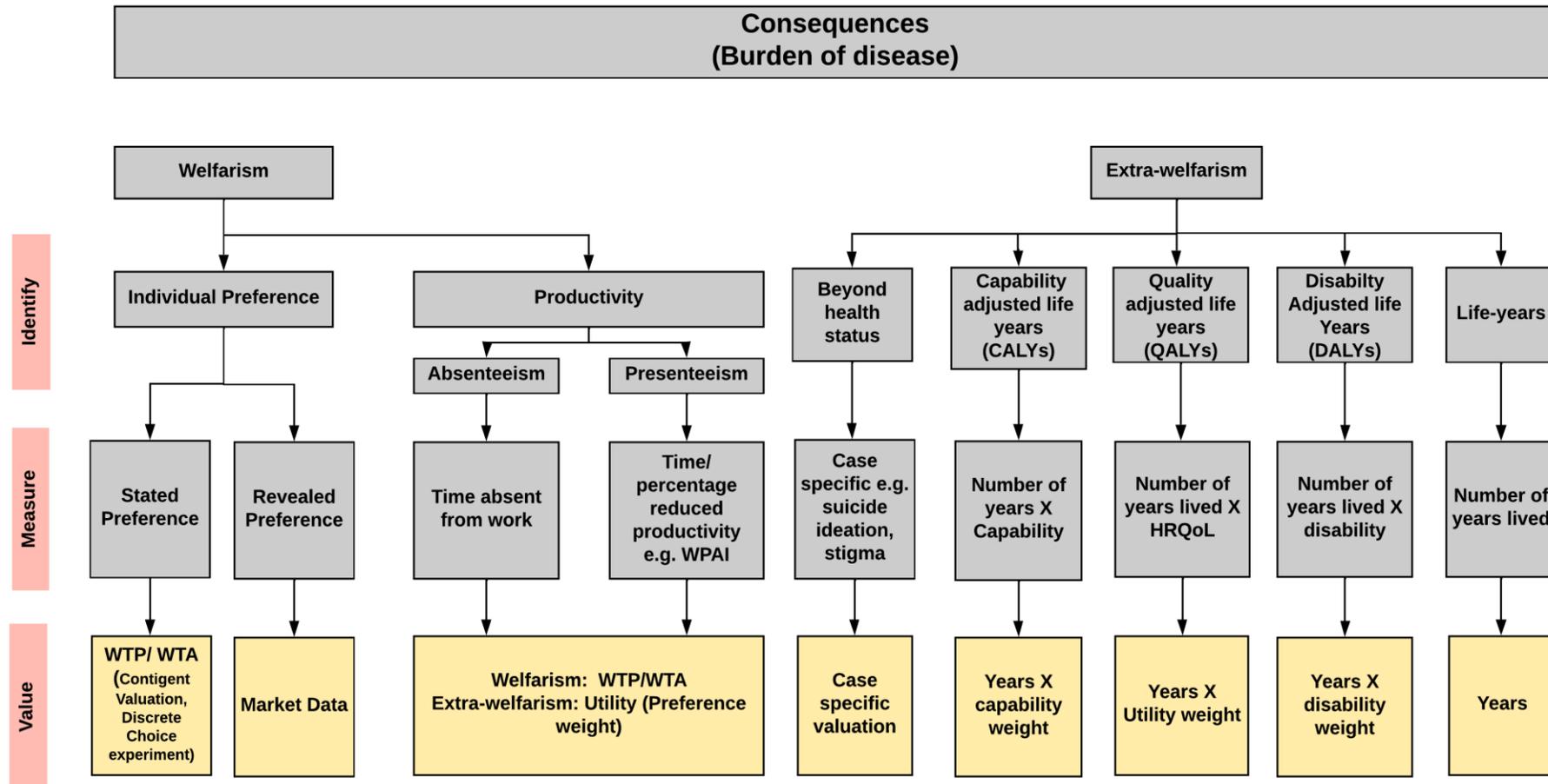


Figure 2.3: Description of the components of the Burden-of-Disease



2.3.2 The analytical framework of economic impact of disease

To quantify the economic impact of disease, it is important to consider the role of positive and normative economics. Positive economics is concerned with how society 'is' based on statistics and is concerned with factors such as prices and quantities (Mankiw, 2004). Positive economics of healthcare is concerned with describing healthcare inputs in terms of the use of resources (cost-of-illness) and outputs in terms of health and non-health consequences (burden-of-disease). Normative economics, in contrast, is concerned with how society 'ought to be' (Morris, Devlin and Parkin, 2007b). Normative economics hinges on the use of value judgements and determines the analytical perspective that ought to be adopted when quantifying cost-of-illness or burden-of-disease. Normative economics addresses issues such as whether it is appropriate to include productivity when estimating the economic impact of disease (Morris, Devlin and Parkin, 2007a). The boundaries of the economic impact analysis are set according to whether a positive or normative stance is taken.

In the analysis of economic impact, as with any form of economic analysis and evaluation, it is important to decide on what costs and consequences should be included (Drummond *et al.*, 2015). Two analytical perspectives which guide the boundaries for inclusion of health and non-health burden-of-disease (consequences) in normative economics are welfarism and extra-welfarism. These are now described (section 2.4.2.1 and section 2.4.2.2) in terms of how they influence approaches to quantify the economic impact of disease (section 2.4.2.3).

2.3.2.1 Welfarist economics and welfarism

The origins of health economics are rooted in the tenets of welfare economics (Arrow, 1963). Welfare economics is concerned with how the allocation of resources affects social welfare (Mankiw, 2004). According to Gyrd-Hansen (2005), "welfarists believe that output of healthcare should be judged according to the extent to which it contributes to overall welfare" in terms of the weighted sum of individual utilities. In this regard, welfare is measured based on individual preferences for health states or health outcomes relative to the consumption of other goods or healthcare processes in the utility function (Gyrd-Hansen, 2005). In increasing welfare, it is assumed that value

judgements are used to achieve a rational and constant ordering of competing strategies that allocate scarce resources (Morris, Devlin and Parkin, 2007b). Welfare economics is anchored on four key principles summarised in Table 2.1 (Brouwer *et al.*, 2008).

Table 2.1: Four principles of the welfare economics

Principle	Meaning
Utility	Individuals make rational decisions to maximise their utility by ranking their options and choosing the preferred option.
Individual sovereignty	Individuals are the best judges of what is good for them.
Consequentialism	Utility is only obtained from the outcome of behaviour and processes. The utility during the processes is not considered.
Welfarism	The goodness of any state of affairs can only be judged based on utility information.

Although welfarism has been used by some authors as a synonym for welfare economics, others have argued that it is not synonymous but is an important element of it (Morris, Devlin and Parkin, 2007a; Brouwer *et al.*, 2008; Zweifel, Breyer and Kifmann, 2009). The welfarist principle states that individuals are the best judges of 'goodness' and that their choices are based on preferences to maximise utility (Morris, Devlin and Parkin, 2007a; Brouwer *et al.*, 2008; Drummond *et al.*, 2015). Based on utilitarianism, one approach within classical welfare economics, the optimum level of social welfare can be obtained from the sum of the maximum individual utilities of the society population (Brouwer *et al.*, 2008). The downside of utilitarianism is that it

ignores “need” and is characterised by being uncaring, calculating, and consequentialist which results in discriminating against the less capable that derive less marginal utility from the same consumption of goods and services as the more capable one (Byford and Raftery, 1998). For example, a person with disabilities would not be allocated resources from which an able-bodied person could achieve a higher marginal utility and ultimately increase aggregate social welfare (Culyer, 2012).

Neoclassical welfare economics considers the Paretian approach and the Bergson-Samuelson social welfare function described as one of constructing a social utility function corresponding to a particular configuration or "profile" of individual preferences (Pollak, 1979). Under the Paretian approach, overall societal judgement is attained by using the Pareto principle, which states that improvement is achieved when utility increases for one individual without any loss to another. Furthermore, Pareto-optimum is achieved when it is not possible to increase the utility of one individual without making another one worse off (Morris, Devlin and Parkin, 2007a; Brouwer *et al.*, 2008; Zweifel, Breyer and Kifmann, 2009). Under the Bergson-Samuelson approach, analysts can select the preferred distributions of welfare on a welfare frontier, given that some clear normative option was made regarding distribution concerns (Brouwer *et al.*, 2008). Welfarism has been criticised for confining the evaluative space to the individual utility, hence leading to the rise of extra-welfarism, detailed in section 2.4.2.2 (Coast, Smith and Lorgelly, 2008).

2.3.2.2 Extra-welfarist economics and extra-welfarism

Distinct from welfare economics which focuses on maximising welfare, the extra-welfarist approach as most generally applied in health economics focuses on maximising health. This approach suppresses any variation across income or social groups in utility derived from health improvement (Culyer, 2001; Gyrd-Hansen, 2005). Extra-welfarism is a framework that incorporates aspects of (health) functioning into the process of comparing social welfare (Morris, Devlin and Parkin, 2007a). Extra-welfarism can also incorporate aspects of capability (Coast, Smith and Lorgelly, 2008). Extra-welfarism provides for the extension of economic impact from an individual level to the population level (Neumann *et al.*, 2016). Sen (1980) put across that sole consideration of individual utility, gained from consumption of goods and services, in

making social decisions is too narrow and calls for a broader perspective. Proponents of extra-welfarism have argued that it has broadened the evaluative space to account for characteristics cardinal to individual wellbeing (Brouwer *et al.*, 2008; Coast, 2009). Unlike non-welfarism which excludes individual utilities from the value judgement of social welfare, extra-welfarism supplements the welfarism framework by adding information such as utility derived from the process (Morris, Devlin and Parkin, 2007a; Brouwer *et al.*, 2008).

Extra-welfarism allows the use of outcomes beyond utility, hence increasing the evaluative space (Brouwer *et al.*, 2008; Neumann *et al.*, 2016). In addition to individual utility, extra-welfarism incorporates other measures and indicators of well-being. Outcomes are chosen on their relevance to the disease, quantity of interest, scope, and perspective of the study (WHO, 2009). While welfarism depends on the affected individual as the source of valuation, extra-welfarism includes experts, elected decision-makers or sample representatives of the public (Brouwer *et al.*, 2008). Social values may differ from individual values, hence they cannot only be derived from individuals (Neumann *et al.*, 2016). This is founded on Arrow's impossibility theorem which states that no rank-order electoral system can be designed that satisfies the "fairness" criteria (Arrow, 2012; Snyder, 2019). Therefore, a deviation from the welfare framework by introducing the extra-welfare framework does not invalidate Arrow's theorem (Neumann *et al.*, 2016). Extra-welfarism takes into consideration the elected decision-maker as a source of valuation. Considering other valuation sources takes into consideration what the individual may not know. This is more relevant in healthcare, where there is a great deal of information asymmetry (Brouwer *et al.*, 2008).

Principles other than preference-based ones are used for weighting diverse outcomes. Although weighting is sometimes allowed under the social welfare function approach in welfarism, it is not clear if such weighting would still be classified as utility information. Nonetheless, extra-welfarism allows and regards weighting as an important way of including equity and other considerations. Weights are influenced by the relevant outcome and based on many ethical considerations. Whereas welfarism allows some theoretical approach to interpersonal comparability, extra-welfarism

explicitly allows interpersonal comparability for outcomes such as capability, health, and handicap.

2.3.2.3 Welfarism, extra-welfarism and quantifying economic impact of disease

Taking into consideration welfarism and extra-welfarism, a comprehensive look at the economic impact of disease entails that a broad view of burden-of-disease is assumed. This assumption justifies the choice of preference-based measures of health and non-health outcomes under the burden-of-disease. This view is taken because the impact of disease on an individual and society goes beyond utility and health. Welfarism provides consideration of non-health outcomes, although it only relies on a measure of utility. Extra-welfarism provides a broader approach as it takes into consideration outcomes beyond utility including health outcomes such as health status, well-being such as capability, and potentially (although no examples exist in practice) non-health status outcomes.

2.3.3 Relevant Study Perspective

Similar to economic evaluation, an economic impact analysis of disease should be designed, conducted and interpreted using the relevant study perspective (Drummond *et al.*, 2015). The relevant study perspective under cost-of-illness should be guided by the decision-maker and target audience. The choice of study perspective influences estimates of who the economic impact affects, what should be counted (identified) and how should they be measured and valued.

Reference case analysis in economic evaluation, which refers to a standard set of methods to serve as a point of comparison across studies, is equally applicable to economic impact analysis (Neumann *et al.*, 2016). Reference case analysis, recommended by the Washington panel, advocates for using the societal perspective due to its comprehensive representation of the public interest instead of any group (Neumann *et al.*, 2016). This is consistent with health economics' foundation in welfare economics which is concerned with society's welfare (Byford and Raftery, 1998; Jönsson, 2009). For tax-financed healthcare systems, it is argued that the societal perspective is the most appropriate one as it expresses the opportunity cost of the whole population (Byford and Raftery, 1998). However, in several studies, the societal

perspective is often poorly specified and not perceived to be the relevant one when informing health care resource allocation decisions (Claxton *et al.*, 2010).

The healthcare sector perspective is another recommended perspective that although narrow, resonates more closely with the decision-maker responsible for the healthcare budget. The healthcare sector perspective considers costs incurred within the formal healthcare sector such as National Health Service (NHS) in England during the provision of care. This perspective includes costs such as diagnostic, treatment, and rehabilitation. Depending on the setup of the healthcare system, other sectors such as social care can be included. Under NHS England, the budget covers health and social care and so in this context social care should be included when taking the healthcare perspective (Brien *et al.*, 2020). Taking the healthcare perspective determines the intervention mix that maximises health outcomes within the boundary of the healthcare budget (Byford and Raftery, 1998). Nonetheless, it is also argued that maximising healthcare may not necessarily maximise social welfare because there may be spillover costs to sectors beyond the health sector (Byford and Raftery, 1998).

Several different narrower perspectives relevant to a specific payer are feasible, for example: the patient; third-party payer (insurance); employer; social care sector. These depend on the research question (Byford and Raftery, 1998). A patient perspective gives the estimates of what impact accrues onto the patient. The organisation of the healthcare system dictates the costs incurred by the patient such as transport, out-of-pocket payments to access treatment, purchase of over-the-counter medicines, and lost income.

Under the burden-of-disease component of economic impact analysis, it is also important to define the perspective from the outset of the study. The possible perspective reflects whose burden is being considered. This could be a patient, caregiver, or a combination of patients and their caregivers.

2.3.4 Relevant time horizon

The time horizon considers how long into the future costs and consequences should be identified, measured, and valued (Drummond *et al.*, 2015; Neumann *et al.*, 2016). The relevant time horizon should be long enough into the future to capture important differences in the costs and consequences attributed to the disease of interest

(O'Mahony, Newall and van Rosmalen, 2015). Similar to economic evaluation, it is important to provide an economic impact analysis based on a relevant time horizon that is driven by data availability and the relevant decision problem.

Most chronic conditions result in increased consumption of healthcare resources as time advances, for example, a patient with psoriasis cited to be at risk of cardiovascular (CVD) events may not be immediately commenced on medication for the CVD until a certain risk threshold is reached. Using a short-term time horizon, such as one year is likely to underestimate the full economic impact. The choice of time horizon should reflect the interest of the decision-maker and target audience.

In simulating the long-term costs and consequences of disease, it is important to be explicit about the length of the simulation (analytical horizon). The effect of time on the costs and consequences should be accounted for as these may vary (O'Mahony, Newall and van Rosmalen, 2015). Therefore, in accounting for the effect of time, it is important that discounting is applied (Drummond *et al.*, 2015). Discounting is an important concept that brings future costs and consequences to their present value (Drummond *et al.*, 2015; O'Mahony, Newall and van Rosmalen, 2015). Keeping in mind that people prefer to enjoy benefits now and incur costs later, a tendency called positive time preference, it is important that all costs and consequences occurring in future are valued in terms of the present (Severens and Milne, 2004; Drummond *et al.*, 2015; O'Mahony, Newall and van Rosmalen, 2015). Unlike budget impact analysis which presents undiscounted costs and consequences, discounting is relevant in economic impact studies as it helps decision-makers to compare results from the same temporal baseline (Basu and Ganiats, 2016; Mauskopf *et al.*, 2017).

Although some literature proposes differential discounting between costs and consequences, the Washington panel argued that this was logically inconsistent (Basu and Ganiats, 2016). Therefore, it is recommended that costs and consequences are discounted at the same rate (Drummond *et al.*, 2015; Basu and Ganiats, 2016). For instance, NICE in the UK recommends a discounting rate of 3.5% (Drummond *et al.*, 2015). Discounting is based on an exponential model (see Equation 2.1) which is derived from the compound interest formula used in calculating the future value of an investment (Basu and Ganiats, 2016).

$$PV = \frac{FV}{(1 + r)^t}$$

Equation 2.1

Where *PV* is the present value, *FV* is the future value, *r* is the discount rate and *t* is the time in years. The first year is considered as time 0 and thus not discounted.

In economic evaluation, the impact of discounting is mainly influenced by the timing of the costs and consequences of the illness and intervention (Severens and Milne, 2004). Acknowledging the influence of timing on the impact of discounting, there should be a clear consideration of the three most important frameworks for time horizon when estimating the costs and outcomes of interventions: intervention duration; implementation duration; and analytic horizon (O'Mahony, Newall and van Rosmalen, 2015). Intervention duration refers to the length of time over which an intervention is applied per person or cohort (O'Mahony, Newall and van Rosmalen, 2015). The implementation period is the period over which an intervention is applied to all simulated cohorts and the analytic horizon is the period over which costs and consequences are assessed (O'Mahony, Newall and van Rosmalen, 2015). The most important 'time horizon' applicable to economic impact analysis is the analytic horizon because the assessment is not limited to a single intervention.

Price inflation is another important concept that helps adjust costs used in an economic analysis coming from different time periods or when projecting costs for different time periods. Price inflation allows for bringing past prices into the current terms, hence allowing for a direct comparison of prices from different years (Neumann *et al.*, 2016). For example, prices from 2007 would be adjusted to 2018 to allow for meaningful comparisons. Choice of an appropriate inflation index is important. Some of the common indices used are Consumer Price Index and Healthcare Inflation Price Index. The consumer price index is useful for adjusting costs such as wages or other products that rise at the general price inflation (Neumann *et al.*, 2016). The Healthcare inflation Price Index is a healthcare-specific index which is appropriate for adjusting healthcare resource use costs.

2.3.5 Identifying, measuring and valuing cost-of-illness

Cost-of-Illness has been referred to as the financial consequences imposed by poor health in terms of healthcare spending and productivity loss (Finkelstein and Corso, 2003; Culyer, 2005). This definition omits to mention the relevance of the study perspective in deciding which resources should be included and quantified. Cost-of-illness is a descriptive method that gives the financial magnitude of the economic impact of disease by identifying, measuring and valuing all relevant direct healthcare costs and indirect costs (productivity loss) resulting from the condition (Rice, 1967; Rice, Hodgson and Kopstein, 1985; Finkelstein and Corso, 2003; Roux and Donaldson, 2004; Tarricone, 2006; Jo, 2014).

The definition of cost-of-illness as applied in empirical studies has been inconsistent and, in some cases, used to be synonymous with economic impact. This lack of consistency means it is potentially useful to provide a structured system to name the different components. Figure 2.2 provides a classification of the type of costs to potentially include in a cost-of-illness study. These types of costs are now described in terms of the approaches to identify and measure them in a cost-of-illness study. Costs will always be valued using the appropriate measure of currency relevant to the study location, such as pounds sterling (£), and the price year for the study.

2.3.5.1 Identifying direct costs

When identifying the relevant direct costs, which are defined based on the study perspective, they can be divided into direct medical and direct non-medical costs (Roux and Donaldson, 2004; Onukwugha *et al.*, 2016). Direct medical costs are those related to the resource use incurred in delivering formal health and social care. These costs encompass healthcare expenditure for the prevention, diagnosis, treatment, and rehabilitation (Rice, 1967). These are broken down to include among other resources, outpatient visits, inpatient stays, emergency department visits, diagnostic tests and imaging, and prescription medication (Drummond *et al.*, 2005; Onukwugha *et al.*, 2016).

Direct non-medical costs become relevant when moving beyond the healthcare sector perspective. They could include resource use incurred by the patient (out-of-pocket)

and other sectors, such as education, and informal care received from family and friends. For the patient, non-medical costs could include spending on non-prescribed medication, informal care costs, transport to access treatment, social care, and other sectors (Onukwugha *et al.*, 2016).

2.3.5.2 Identifying indirect costs

In economic impact studies, similar to economic evaluation, the phrase indirect cost is frequently used to be synonymous with productivity loss (Drummond *et al.*, 2005). Productivity loss is often defined as work and leisure time lost due to illness or premature death (Finkelstein and Corso, 2003). Therefore, productivity loss will be used to mean indirect costs throughout this thesis. The main aspects of productivity loss due to reduced labour supply because of ill health are identified as absenteeism and presenteeism. Absenteeism refers to one being absent from work due to illness whereas presenteeism is an individual's reduced work performance whilst at work due to ill health (Gosselin, Lemyre and Corneil, 2013).

In economics, productivity refers to the ratio of inputs used per unit of output within a firm (Mankiw, 2004; Sloman, 2006). Productivity is influenced by factors of production which include capital, labour, land, and enterprise (Sloman, 2006). Holding everything else constant and taking into consideration labour input, productivity is defined as the number of goods and services produced from each hour of a worker's time (Mankiw, 2004). As highlighted in chapter 1, individual health affects labour supply and therefore factors of production. Any disruption of good health tends to impact across the spectrum of individual utility, including economic activity participation and hence exerts an impact on the affected individual and society (WHO, 2009).

The chosen study perspective informs whether productivity costs are included in an economic impact analysis. At an individual level, productivity losses may equate to income loss, and therefore it is relevant to account for these costs from the patient perspective. Where productivity costs are included they should be reported separately from direct costs to be transparent when reporting the components in an economic impact study (WHO, 2009). It is not necessary to include indirect costs when taking the healthcare study perspective (Neumann *et al.*, 2016).

2.3.5.3 Measuring direct costs

Measuring the quantity of each cost-generating component (resource use) is an important step following identification (Tarricone, 2006). For instance, the measure of direct costs entails quantifying those items of resource use borne by healthcare and include, for example, outpatient visits, inpatient stays, emergency department visits, diagnostic tests, and prescription medication (Drummond *et al.*, 2005; Onukwugha *et al.*, 2016).

Outpatient visits could be measured in absolute numbers of visits and broken down into the average time (minutes) of each visit. Similarly, inpatient stays could be measured in terms of the number of days and are usually reported as the length of stay. Other resources can be quantified in terms of usage or consumption, for instance, the number of diagnostic tests completed or the number of tablets/injections (doses). How these quantities are measured is influenced by how accurate (or precise) cost estimates are required to be, time, and data constraints (Drummond *et al.*, 2015). The hierarchy of precision from least to most precise is: average daily cost; disease-specific daily cost; case-mix-group; and micro-costing (Drummond *et al.*, 2015).

For a cost-of-illness study, this information can be captured from patients by using resource use questionnaires, interviews or diaries. Healthcare resource use can also be measured from a variety of sources such as routine administrative data, registries, patient case reports, and insurance claims data. Tools used in measuring resource use in economic evaluation are also applicable under the cost-of-illness study. Therefore, tools that are publicly available on websites such as the database of instruments for resource use measurement could be modified to fit the cost-of-illness study (DIRUM, 2019).

Measuring the cost-generating components in cost-of-illness studies can be described in terms of the data used such as: i) Epidemiological data used (Incidence versus prevalence) and ii) Temporal relationships (prospective or retrospective) between the initiation of the study and data collection, see Table 2.2. (Tarricone, 2006).

Table 2.2: Methods to measure costs in cost-of-illness studies

Cost-of-illness study		Description
Epidemiological	Prevalence	Estimate disease direct costs and productivity loss attributed to all cases occurring in a given period or point in time.
	Incidence	Estimate the present value of the lifetime costs of the new cases of a condition with onset in a given period.
Temporal relation	Prospective	Based on data to be collected during the study commencement
	Retrospective	Based on data collected before the study commencement

Source: Rossana Tarricone (26)

Prevalence-based approach

The prevalence-based approach tends to estimate the actual cost of the existing cases in a given period, usually a year, relative to a hypothetical alternative case prevalence (Larg and Moss, 2011). The prevalence-based approach accounts for the different disease stages because of the inclusion of a cross-section of cases but does not depend on when the disease first occurred (Finkelstein and Corso, 2003; Larg and Moss, 2011). This approach has also been noted to generate higher cost estimates than the incidence-based approach (Tarricone, 2006). However, this is useful for conditions in which the disease burden is underestimated (Tarricone, 2006). Furthermore, the prevalence approach is useful for cost containment policy planning (Tarricone, 2006).

The use of econometric methods in estimating cost-of-illness is quite common. To ascertain the proportion of costs (or consequences) that can be attributed to a condition or group of conditions, economists have turned to using attributable fractions, a concept borrowed from epidemiology (Trogon, Finkelstein and Hoerger, 2008). Other literature using this concept report it as a counterfactual analysis (Trogon, Finkelstein and Hoerger, 2008). Regression methods using incremental effects have been used to calculate the attributable fraction (Trogon, Finkelstein and Hoerger, 2008). There is a conflicting choice of the counterfactual. According to

theories surrounding counterfactual analysis of event causation, for two independent events, one event (A) is counterfactually dependent on the other event (B) if its occurrence would not happen without the occurrence of event B (Bennett, 1987; Zalta, 2014). For economic impact studies in health, the counterfactual can either be an assumption of no disease existence or no occurrence of new cases (WHO, 2009). For example, what would be the economic situation if no cases of psoriasis existed? The other counterfactual would be an assumption that no new cases of psoriasis occur. The assumption of no occurrence of new cases is relevant for the non-curable disease but where the occurrence of new cases can be halted or controlled. The assumption of no existence of disease is made for curable and preventable diseases. However, as with the noted heterogeneity in cost-of-illness methods, no consistent meaning can be given to the counterfactual that is conventionally adopted (WHO, 2009).

Incidence-based approach

The incidence-based approach estimates the costs that can be potentially averted by preventing new cases. This approach estimates the present value of the lifetime costs of these new cases. Estimating the present value of lifetime costs provides a baseline for assessing new interventions (Finkelstein and Corso, 2003; Roux and Donaldson, 2004; Tarricone, 2006; Larg and Moss, 2011; Jo, 2014). The incidence-based approach accounts for cost variability due to the duration of the disease and its severity (Tarricone, 2006; Larg and Moss, 2011; Jo, 2014). This makes the approach to be useful when considering new case preventive measures or disease stage-specific measures (Tarricone, 2006; Larg and Moss, 2011). The incidence approach is however known to be labour intensive (Roux and Donaldson, 2004).

2.3.5.3.1 Prospective or retrospective study designs

Depending on the time between when the study is commenced and when the event of interest occurred, cost-of-illness can either be prospective or retrospective. Under the prospective approach, data are collected as events of interest unfold. Whereas, under the retrospective approach, data are collected from events that occurred in the past. Retrospective studies have the advantage of costing fewer resources including time (Jo, 2014). However, the retrospective approach is very much dependent on sufficient

observation datasets (Jo, 2014). On the other hand, the prospective approach tends to be costly but offers 'complete' datasets as data collection tools are specifically tailored to capture what is required (Jo, 2014). Estimating costs can be described by the nature of the costing approach which can either be bottom-up or top-down (Tarricone, 2006; Neumann *et al.*, 2016). The main difference is largely based on the level of disaggregation at which individual resources are measured and valued as separate components (Morris, Devlin and Parkin, 2007a).

2.3.5.3.2 The bottom-up approach to measuring costs

The bottom-up approach is an activity-based method where the cost estimation is based on the sum of every single input consumed from a service provision (Mogyorosy and Smith, 2005; Tarricone, 2006). For example, in estimating an outpatient visit resource use, resources such as personnel, medications, and diagnostic tests are identified and measured. The bottom-up approach remains the most preferred method and can be used in both retrospective and prospective studies (Mogyorosy and Smith, 2005). This approach is also often associated with primary data collection within randomised controlled trials (RCTs) or observational studies (Neumann *et al.*, 2016). The main advantages of the bottom-up approach include its use of more comprehensive and more accurate data, ease in places of fee for service settings, much more suitable for non-homogenous services, and billing systems can be used as a source of data (Mogyorosy and Smith, 2005). The bottom-up approach ensures that the sum of estimated costs for the disease can not exceed the healthcare budget. One of the disadvantages of this approach however is that it is data intensive, time-consuming and costly (Mogyorosy and Smith, 2005). It has limited external validity and transferability when the estimation of resource use is based on a specific hospital (Mogyorosy and Smith, 2005; Frick, 2009). This limited external validity is substantial when there is a significant difference in health service needs and delivery between the measured sample and the target population (Raftery, 2000; Mogyorosy and Smith, 2005).

2.3.5.3.3 The top-down approach to measuring costs

The top-down approach is a population-based approach in which resource use is measured based on an episode of care. Under this approach, costs are not broken down into their constituent quantities and prices (Morris, Devlin and Parkin, 2007a). Measurement of resource use under the top-down approach differs from the bottom-up approach in that activities are aggregated. For instance, instead of measuring the quantify of each health input during an outpatient visit such as items used during a clinical examination, the activity is measured as an aggregate service of outpatient visit measured in time spent.

2.3.5.3.4 Cost-of-illness Calculation methods

Measurement of health care resource use is mostly influenced by the method of calculating cost-of-illness. One systematic literature review classified the methods of cost-of-illness estimation into six groups as shown in (Onukwugha et al., 2016). The six methods include all medical costs, disease-specific, other total methods, matched methods, regression, and other incremental techniques. These methods are further categorised into two: total cost methods and marginal cost methods as summarised in Table 2-1.

- (a) Disease-specific costs:** In this approach, only costs directly incurred under the diagnosed disease are included. This approach excludes spill-over resource use resulting from related conditions. For instance, when a person with plaque psoriasis develops diabetes, only costs identified to accrue directly under plaque psoriasis are measured. Similar to budget impact analysis, this is the narrowest approach and should only be pursued where assumptions of related conditions are weak and credible data are not available (Sullivan *et al.*, 2014).
- (b) All condition-related costs.** In this approach, all patients with the condition are identified and resource use resulting from related conditions (comorbidity) is measured. An illness may lead to costs in other related conditions - someone with uncontrolled diabetes may end up experiencing diabetic foot ulcers that would incur treatment costs in their own right. Similarly, people with multiple long-term conditions (also called multi-morbidity) are likely to incur additional

resource use (The Academy of Medical Science, 2018). For example, people with psoriasis may also develop other conditions, such as cardiovascular diseases (CVD). Therefore, when considering the resource use associated with psoriasis in a population of patients, it may be necessary to take into account co-occurring health conditions. The inclusion of related resource use for multiple long-term conditions will be influenced by the availability of credible data. This approach has the potential to overestimate the costs as some of the costs may not be due to the condition. Where these costs are included, it is crucial to report both disease-specific costs and condition-related costs separately to allow users to make a clear distinction.

(c) Econometric analysis using matched cohorts. Under this approach, all patients with a diagnosis are identified and the costs are totalled. To calculate the incremental cost of the treatment for the diseased population (i.e. with the diagnosis), the average cost of the sample or the matched cohort is subtracted (Onukwughu *et al.*, 2016).

(d) Regression method. This is another econometric method in which all patients with the diagnosis are identified and regression analysis is completed to indicate the individual beta value for each diagnosis.

In countries with well-established electronic healthcare records such as England, identification of patients can be done using primary diagnosis codes or both primary and secondary diagnosis codes when using observation data from electronic health records such as the linked Clinical Practice Research Datalink (CPRD) and hospital episode statistics (HES) (CPRD, no date).

Table 2-1: Summary of methods for Calculating Cost-of-illness

	Costing Method	Description
Total Cost Methods	All medical	All patients with a specific disease diagnosis and all costs incurred on each individual are identified and all resource use measured. This includes the costs of all other diseases affecting the person at the time.
	Disease-specific	All patients with a diagnosis of the disease of interest are identified and the sum of all costs associated with the diagnosis is obtained.
	Other Total	All patients with a diagnosis of the disease of interest are identified and either a novel technique or mathematical modelling to sum the costs is employed.
Marginal Cost Methods	Matched	All patients with a diagnosis are identified and all the costs are measured. Subtract out the average cost of the sample to find incremental costs for treatment; alternatively, subtract out the average cost of a matched cohort instead
	Regression	All patients with a diagnosis are identified, a regression analysis is conducted and the individual constants (beta) for each diagnosis are indicated. All patients with a diagnosis are identified, a matched cohort (similar to a clinical trial) is found and regression analysis to quantify the individual constants for each diagnosis is conducted.
	Other incremental	Novel techniques or modelling study that determines the incremental cost associated with the disease of interest

Adapted from Onukwugha et. al. (2016)

2.3.5.4 Measuring productivity loss

Productivity loss can be measured in terms of absenteeism or presenteeism. Absenteeism is measured by counting the number of days or hours an individual is absent from work (Mullen and Rennane RAND, 2017). The measure of absenteeism is included in several validated productivity loss questionnaires. The need for reliable and valid ways to capture presenteeism has led to the development of several self-reported instruments. The Outcome Measures in Rheumatology (OMERACT) study recommends Work Productivity and Activity Impairment (WPAI), Work Productivity Survey (WPS) and Work Ability Index (WAI) to measure presenteeism (Tang *et al.*, 2014). Other tools useful for measuring productivity loss are the Work Limitation Questionnaire (WLQ), Work Productivity Short Inventory (WPSI) the Stanford Presenteeism Scale (SPS-34 and SPS-13), and Work and Health Interview (WHI) (Johns, 2009).

2.3.5.5 Valuing direct costs

Following the identification and measurement of resources used, the final step in cost estimation is valuation by attaching unit costs (assigning a monetary value) to each quantity of resource use (Tarricone, 2006). Unit cost refers to the total expenditure incurred to produce one unit of output. In theory, the unit cost of a resource reflects the opportunity cost (Neumann *et al.*, 2016). Opportunity cost is the value of the benefits given up by choosing to use resources in one way than another. (Mankiw, 2004; Tarricone, 2006; Drummond *et al.*, 2015). For instance, resources used in managing an illness in one way could be used differently. It is assumed that market prices offer a reasonable approximation of opportunity cost (Tarricone, 2006; Drummond *et al.*, 2015). Healthcare markets are prone to imperfections which should be recognised when undertaking a cost-of-illness estimation by analysis of resources used in the production of health (Tarricone, 2006). Market prices are generally available for most resource items and can be in the form of list prices, routine purchase prices for drugs, and agreed salaries for staff inputs. The source of unit costs to attach to resource use should be guided by the study perspective and decision-maker. For instance, reference costs are preferred when using the provider perspective and tariff prices for the payer perspectives (Monitor, 2012).

When valuing health care resources using the top-down approach, unit costs are assigned (national) average figures on a non-patient specific basis using diagnostic related groups (DRGs), or health resource groups (HRGs) derived from national or regional administrative databases (Mogyorosy and Smith, 2005; Neumann *et al.*, 2016). The top-down approach involves the allocation of part of a known total budget to a specific service or an average of the level of expenditure incurred by the service is used to reflect the per-patient cost (Tarricone, 2006; Mason, 2019). This approach is appropriate when costing market technologies such as medicines, medical devices and consumables (Mogyorosy and Smith, 2005). The top-down approach is much cheaper, faster, and feasible when costing complex healthcare services (Mogyorosy and Smith, 2005). One of the weaknesses of the top-down approach is its assumption of negligible practice variation (Mogyorosy and Smith, 2005). This assumption is unlikely to hold considering the variation in health care resource use between patients based on the condition, severity, and heterogeneity. In addition, the accuracy of the top-down approach relies on the availability of good quality secondary data (Mogyorosy and Smith, 2005; Drummond *et al.*, 2015). The top-down approach attributes all costs to the primary diagnosis which creates a problem as patients tend to have multiple diagnoses (Tarricone, 2006).

To deal with some of the weaknesses of the bottom-up and top-down approaches, a mixed-method approach can be employed. This helps deal with such problems as missing data and collecting data that is not routinely collected (Mogyorosy and Smith, 2005). Although the mixed method reduces the variance caused between the national average and local utilisation pattern, it may not eradicate the resource use inclusion/exclusion bias (Mogyorosy and Smith, 2005).

Econometric estimation, an alternative to the bottom-up and top-down approach, is used to predict unit costs (Adam, Evans and Murray, 2003). Under the econometric approach, data collected across other countries or settings are used to predict unit costs in countries that have scanty availability of costing data (Adam, Evans and Murray, 2003). Using this method leads to the inevitable rise in uncertainty due to not knowing the exact value of beta and alpha (Adam, Evans and Murray, 2003). Statistical simulations are used to account for this uncertainty (Adam, Evans and Murray, 2003).

Although this is presented as a separate approach, it is important to note that cost estimates in the countries or settings this is extrapolated from are likely to have used the top-down or bottom-up approach.

2.3.5.6 Valuing productivity loss

The measured productivity loss due to absenteeism, presenteeism and job loss are most frequently valued using two approaches: Human Capital Approach (HCA) and the Friction Cost Approach (FCA) (van den Hout, 2009). The HCA values the loss of productivity in terms of the present value of the potential future earnings of a working-age population under the assumption that an individual would remain in employment and cannot be replaced (Jo, 2014). The HCA values productivity loss by multiplying the time lost not working by the relevant wage (van den Hout, 2009).

Reliance on the HCA to value presenteeism, absenteeism and job losses due to ill-health has been deemed unrealistic in most settings as it does not take into account the existence of a pool of underemployed or unemployed labour (WHO, 2009). Similar to Hout, Shiell and colleagues expressed their concerns regarding cost-of-illness and questioned the use of the HCA as it tends to overestimate the productivity loss by assuming that the worker is not replaced (Shiell, Gerard and Donaldson, 1987; van den Hout, 2009). It is also argued that the HCA assigns higher values to the group in the high social-economic bracket by assigning higher wages which then causes statistical biases and spurious estimates (Jo, 2014).

The FCA takes an employer's perspective and estimates productivity loss incurred during the duration of a vacancy following ill health. FCA can include training costs for a newly recruited individual that fills up the vacancy (Tarricone, 2006; van den Hout, 2009; Löfvendahl, 2016; ONS, 2018). The FCA has been criticised for underestimating costs (van den Hout, 2009). In addition, the FCA is also criticised for considering a single friction period under the assumption that the vacancy is filled by someone previously unemployed (van den Hout, 2009).

These two methods, HCA and FCA, provide different estimates of the indirect costs due to productivity loss (van den Hout, 2009). Proponents of the HCA argue that it gives the full weight to productivity loss and hence the economic impact of a disease (van

den Hout, 2009). It is also argued that using FCA instead of the HCA gives less weight to productivity costs which makes using biologics in a disease like psoriasis prove to be too expensive (van den Hout, 2009).

2.3.6 Identifying, measuring and valuing burden-of-disease

The term burden-of-disease has been so widely used in public and population health literature that one might assume there is clarity, consensus, and uniformity in its definition (Isfeld-Kiely and Balakumar, 2015). Beyond the reference to the global burden-of-disease and the definition of its summary measure, disability-adjusted life years, it is less clear what authors refer to when the term “burden-of-disease” is used (Isfeld-Kiely and Balakumar, 2015).

Ignoring the non-financial aspects of burden-of-disease in an economic impact analysis distorts the overall economic and social costs as it implies the economic value of burden-of-disease is zero (Rice, 1967). Therefore, whenever burden-of-disease is used, it raises questions about which burden and whose burden is being referred to. Burden-of-disease cuts across physical, mental and social health. Physical health burden is concerned with such things as functionality, disability and general health. Mental health burden takes into consideration aspects of mood, self-esteem, depression and anxiety, perceived stigma, and a diverse range of psychological impacts. The social health burden concerns itself with establishing an individual’s social activities and relationships (Isfeld-Kiely and Balakumar, 2015).

Burden-of-disease is sometimes conflated with cost-of-illness. In this PhD, it shall be used to refer to the non-financial consequences of disease in line with the welfarism and extra-welfarism approach. Disease (or ill-health) in itself has been established to inflict various consequences on an individual and society (Ilenloa, 2017). These consequences could be limitations on individual productivity, long-term or permanent disability, impaired quality of life, or premature death (Ilenloa, 2017). Efforts to lend consistency and rigour to these consequences of disease in health economics have led to the establishment of summary measures of both health and beyond health outcomes. Figure 2.3 shows a classification system to name the component elements of burden-of-disease.

The different types of consequences shown in Figure 2.3 are now described in terms of the approaches to identify, measure and value them in a burden-of-disease study to be consistent with the chosen framework (welfarism or extra-welfarism). When identifying the relevant consequences of disease to include in a burden-of-disease study the analysts must be clear about the relevant research question and decision problem being addressed. In addition, one needs to be aware of identifying, measuring and valuing these consequences consistent with the welfarism or extra-welfarism frameworks.

2.3.6.1 Identifying consequences: welfarism

Applying the welfarism approach, economists suggest that the best way to allocate resources in society to improve welfare is by using the Pareto criterion (Sloman, 2006). Under the Pareto criterion, welfare improvement is attained when some individuals can be made better off without making anyone else worse off (Sloman, 2006). This is referred to as the Pareto improvement. Pareto optimal is attained when some people cannot be made better-off without making another worse-off (Sloman, 2006). To ascertain the value of exchange under the Pareto criterion, individual preference is estimated. Therefore, one way of estimating the value that someone places on the disease impact is by identifying their individual preference taking into consideration all other competing factors available. Estimating individual preference is in perfect alignment with welfarism in which the consequences of the disease are best judged by utility (Brouwer *et al.*, 2008).

2.3.6.2 Identifying consequences: extra-welfarism

Applying the extra-welfarism approach, economists suggest the consequences of disease should be identified in terms of how different aspects of an individual's life are affected. The consequences identified may impact the dimensions of health status (health-related), beyond health status (non-health) or both. The health-related aspects include morbidity (health-related quality of life and disability), mortality, or survival (length of life). Quality of life and survival can be combined into quality-adjusted life years (QALYs) and similarly disability can be combined with survival into disability-adjusted life years (DALYs) (Sassi, 2006; WHO, 2014b; Neumann *et al.*, 2016).

The impact of some diseases measured in terms of health might not give the full extent of the burden (P. Lorgelly *et al.*, 2010; Lorgelly, 2015; Goranitis *et al.*, 2017). Taking into consideration the effects that do not neatly fit the traditional health focus, consequences such as capability can be identified (Coast, Smith and Lorgelly, 2008; Goranitis *et al.*, 2017).

The consequences of disease could also be quantified in terms of how much they impair someone's productivity referred to as productivity loss. Productivity loss can be considered both as a cost or a consequence. It is classified as a consequence in cases where it is considered a (dis)benefit of having the condition and not looked at in monetary terms (Jones, 2017). For example, someone living with psoriasis may not be able to work if they experience a flare of their condition. It is important to understand that there is no universally accepted 'gold standard' that can be used to identify productivity loss as a cost or consequence (Jones, 2017).

Impacts beyond health such as stigma and impaired social interaction are identified as a consequence of disease. People living with psoriasis have been reported to experience low self-esteem, embarrassment, frustration, stigma, self-consciousness regarding their appearance, and feelings of shame (Novartis, 2015). Such consequences are less likely to be captured using health-related quality of life measures such as the EQ-5D.

When assessing economic impact, and keeping to extra-welfarism in allowing for cross-comparison between populations in different disease areas, identified consequences should subsequently be measured and valued. Therefore, the availability of tools to measure the consequences and valuation set (tariff) should guide the selection of identified consequences for inclusion in the assessment.

2.3.6.3 Measuring consequences: welfarism

Under welfarism, traditional economic theory is grounded on the premise that functioning markets usually lead to an efficient allocation of resources (Mankiw, 2004). The link between market economies and valuing consequences of disease may not be that obvious. Given that prices in the market reflect the value individuals and societies

place on utility, revealed preferences or stated preferences are the main approaches used in measuring the preferences.

2.3.6.3.1 Revealed preference

Revealed preference is an estimation method for goods and services that can be connected to real choices based on market data. In most cases, revealed preference studies contain wage-risk approaches. The wage-risk approach estimates the relationship between a particular health risk associated with a certain job and the wage rates that a person requires to accept the job are examined (Drummond *et al.*, 2015). The major strength of this approach is that it is based on real consumer choices and therefore in line with underlying welfarist principles. The setup of healthcare markets poses a challenge to the application of revealed preference methods because health care services are under heavy control and not usually traded in 'markets' (Amaya-Amaya, Gerard and Ryan, 2008). When health care services are traded on the market, prices can be unrealistically low owing to government controls (Amaya-Amaya, Gerard and Ryan, 2008). The challenge with revealed preference methods in health and health care has led to the reliance on stated preference.

2.3.6.3.2 Stated preference

Stated preference refers to estimation methods in which value is derived from surveys based on a hypothetical good or service. To establish the stated preference, individual respondents are asked to think about the contingency of an actual market existing for an intervention and reveal their maximum WTP for such an intervention (Drummond *et al.*, 2015). Considering the uniqueness of healthcare markets in which consumers may not pay directly for interventions and do not know the actual market value, they are instead asked to state what they would be willing to pay if the intervention was available on the market (Drummond *et al.*, 2015).

2.3.6.4 Measuring consequences: extra-welfarism

Under extra-welfarism, the two main approaches to measuring health include direct methods (such as standard gamble, time trade-off, discrete choice experiments) or indirect methods using validated multi-attribute measures of health and capability

outcomes (disease-specific or generic) that require elicitation of preference weights to the domains and levels in the measure (Feeny *et al.*, 2016).

Direct valuation methods

Under the Time-Trade-off (TTO), an individual is tasked to choose between different health states for different periods. Initially, the individual is presented with staying longer in a worse state of health. The time is then varied until the person is indifferent between the states relative to time. The Standard Gamble (SG), on the one hand, is a classical method of measuring preference founded on the utility axioms of von Neumann and Morgenstern (Drummond *et al.*, 2015). In this method, an individual is tasked to choose between an alternative one where the best state occurs with a probability p and the worst state with $1-p$ and alternative two which occurs with certainty. The probability is then varied until the respondent is indifferent between the alternatives. Furthermore, Discrete Choice Experiments (DCEs) involve presenting individuals with a sequence of hypothetical scenarios (choice sets) with several alternatives with various attributes including health and non-health outcomes (Amaya-Amaya, Gerard and Ryan, 2008). The main disadvantages of direct methods of measuring preference are that they are very time-consuming, complex and expensive to conduct (Drummond *et al.*, 2015).

Indirect valuation methods

Indirect valuation methods involve two parts – measuring the relevant domains and preference weights. These instruments are classified into non-preference and preference-based measures of health status. The non-preference measures capture the symptoms, disease severity, and progression without attaching the individual value. Results from these tools provide useful descriptive properties and clinical relevance and can be disease and symptom-specific or generic which are much broader.

Disease-specific: These measures focus on the impact on the quality of life of a particular disease owing to its signs and symptoms (Drummond *et al.*, 2015). For example, the dermatology life quality index (DLQI) is specific to dermatology

conditions (Finlay and Khan, 1994). The DLQI is a simple and practical validated measure that is routinely used specifically in dermatology conditions (Finlay and Khan, 1994). Results from such measures are normally limited to comparisons within the disease area in question. To allow for comparison across disease areas, mapping algorithms are needed to produce utility scores (Davison *et al.*, 2018). Other disease-specific measures used in psoriasis include the SPI, PASI, Skindex, and PGA which are reported in section 1.1.2.

Generic measures: These can be applied to any disease or population and have the advantage of cross-population comparisons (Drummond *et al.*, 2015). The health consequences of disease can be measured with established health-related quality of life tools such as the European Quality of Life 5 dimension (EQ-5D), Health Utility Index (HUI), Short Form 6D (SF-6D) (The EuroQol Group, 1990; Finlay and Khan, 1994; Lloyd and Pickard, 2019). Some of the measures that capture wellbeing include, Investigating Choice Experiments for Adults- Capability (ICECAP-A) a measure of capability for the general adult, Quality of Wellbeing (QWB), Adult Social Care Outcomes Toolkit (ASCOT) and OxCAP-MH (Lorgelly, 2015; Feeny *et al.*, 2016; Goranitis *et al.*, 2017).

2.3.6.5 Valuing consequences: welfarism

Similar to the identification and measuring of resources under welfarism, the valuation is also split into those using WTP or WTA under market data (prices) under the revealed preference and stated preference. This is useful in expressing consequences in monetary terms.

2.3.6.5.1 Revealed preference

Valuing revealed preferences uses actual price data obtained from the markets. Although valuation under revealed preference is straightforward in other sectors as it utilises actual price data obtained from the market this is not the case for the health sector. As highlighted in section 2.3.6.3.1, the health care market is heavily controlled, and prices do not reflect the actual 'value' of the goods and services that individuals are willing to pay.

2.3.6.5.2 Stated preference

Valuing stated preferences uses WTP and WTA methods. One way of estimating individual preference and accounting for both health and non-health impacts of disease is by estimating their maximum WTP to attain their preferred health state or get rid of the disease (Neumann *et al.*, 2016). The mean WTP estimated from stated preference surveys of the sampled patient population or public represent the benefits of available or hypothetical interventions (Ratcliffe, 2000). Contingent valuation and discrete choice experiments are the main ways of estimating the WTP under the stated preference (Amaya-Amaya, Gerard and Ryan, 2008).

Contingent valuation is one of the most common methods used in assessing patient preference to estimate the WTP (Pavel, Chakrabarty and Gow, 2015). The contingent valuation method is a survey-based, hypothetical and direct method used to elicit the monetary value of a health intervention or service (Pavel, Chakrabarty and Gow, 2015). Approaches within contingent valuation can be using open-ended, closed-ended, and payment-card techniques. In the closed-ended technique, respondents are asked whether they would pay a specified amount for a given intervention (Ratcliffe, 2000). The specified amount is then varied across respondents to obtain information about whether the respondents' WTP is above or below the provided amount. Under the open-ended technique, the respondents are asked directly about their maximum WTP to receive an intervention. Under the payment-card technique, respondents are given a range of amounts and asked to select the amount which represents the maximum they would be willing to pay for an intervention (Ratcliffe, 2000).

Proponents of contingent valuation have attributed its usefulness to its welfarist foundation, unrestricted range of benefits valued, and addressing of allocative efficiency by allowing cost-benefit analysis (Smith and Sach, 2009). With an increasing interest in the evaluation of complex public health interventions with non-health outcomes and cross-sectoral costs and benefits, the contingent valuation method may prove useful (Smith and Sach, 2009). For conditions like psoriasis which have a range of beyond-health impacts, contingent valuation methods could be useful in estimating these impacts.

Those opposing contingent valuations have argued that its very foundation in welfarist economics is its flaw (Smith and Sach, 2009). This is because welfarism has been rejected in many health systems such as the UK as it does not reflect societal value judgements (Smith and Sach, 2009). The contingent valuation methods have remained too underdeveloped to be of practical use in health beyond their theoretic. Practical arguments against contingent valuation include its bias in favour of interventions that deliver relatively small benefits and those interventions under evaluation because of its over-sensitivity to methodologically irrelevant aspects of the survey (Smith and Sach, 2009). The other weakness of contingent valuation is the vulnerability of responses to psychological biases and heuristics seen in the construction of preferences which renders them too vague for use with any precision in decision making. A lack of guidance and guidelines for contingent valuation in health has contributed to the unfulfilled theoretical promise in the area. The other criticism of the contingent valuation is the strong correlation between income and WTP i.e. individuals in lower-income brackets are likely to provide a low valuation (P. K. Lorgelly *et al.*, 2010; P. Lorgelly *et al.*, 2010).

Discrete choice experiments, which were earlier referred to as conjoint analysis (CA) in healthcare constitute other methods of estimating WTP (Ratcliffe, 2000; Amaya-Amaya, Gerard and Ryan, 2008). The motivation to introduce DCEs in health economics was to go beyond quality-adjusted life years by realising that burden-of-disease and outcomes of interventions can go beyond health measures. In DCEs, costs and WTP are included as attributes. DCEs are attribute-based measures of the benefits and consequences founded on the assumption that interventions can be described in terms of their characteristics, referred to as attributes, and that individual value depends on the level of these attributes (Ryan, 2004). Undertaking a DCE involves five stages (Ryan and Farrar, 2000);

Stage 1: Identifying attributes- This is guided by the research context. For instance, attributes can be predefined if a policy question is being addressed, and different components of the arms of the trial can be used to define attributes if the DCE is alongside an RCT. Other methods include literature reviews, group discussions, and individual reviews.

Stage 2: Assigning levels to the attributes- Following the identification of attributes, plausible and actionable levels should be assigned to each attribute. The assigned levels can be nominal (categorical), ordinal, or cardinal (numerical). Nominal levels have no natural ordering e.g., specialist nurse, general practitioner, or consultant. Ordinal levels entail a natural order e.g., mild, moderate, and severe and cardinal levels such as length of hospital stay, where two days is twice as long as one day.

Stage 3: Choice scenarios- Different scenarios are then drawn to describe all possible interventions or outcomes configuration in line with the attributes and corresponding levels. The number of generated scenarios is reduced with experimental designs.

Stage 4: Establishing preferences- Respondents are asked to choose their preferred choice from a given number of options. The options can be stating a preference between A or B. Alternatively, it can be on a five-point scale with 1 representing definitely prefer A and 5 representing definitely prefer B.

Stage 5: Data analysis- This last stage involves analysing the data using regression methods which are determined by the type of data collected. Discrete choice data is modelled using a benefit function shown in Equation 2.2.

$$\Delta B = \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 \dots \beta_n X_n \quad \text{Equation 2.2}$$

Where ΔB is the change in moving from intervention A to B, X_j ($j = 1, 2, \dots, n$) are the differences in the attribute levels between A and B, and β_j ($j = 1, 2, \dots, n$) are the estimated model coefficients

2.3.6.6 Valuing consequences: extra-welfarism

The last step after identification and measures of consequences is valuation. Similar to cost-effectiveness analysis, the typical value of health outcomes is generic in terms of health-related quality of life and capability. These generic measures are classified as preference-based valuations and are dependent on preference scores (utility weights).

2.3.6.6.1 Preference weights (Utility scores)

A key component of valuing consequences is the aggregation of the different domains of health (health state) into a single one-dimensional score (Feeny *et al.*, 2016). To achieve this, a scoring system and preference weights should be in place when indirect or multi-attribute measures of health are used. The use of multi-attribute measures of health is considered an indirect approach because the source of preference weights is mostly the general public and not the subjects experiencing the health state (Feeny *et al.*, 2016). The use of general population preference is based on the insurance principles, related social contract, elimination of associated bias using patient preferences, and comparability across studies.

The preference weight approach of valuing health status is focused on the value individuals or societies attach to health states. The interval-scale property is one of the most important features for preference weights to be used to estimate the quality of life. Preference weight generation is grounded in expected utility theory. The expected theory of von Neumann and Morgenstern is an extension of the utility theory which assumes that if A is strictly preferred to B, and B is strictly preferred to C, then A is preferred to C (Feeny *et al.*, 2016). The expected utility theory was further extended to accommodate outcomes consisting of more than one attribute. Some multi-attribute-based measures with preference weights include: European Quality of Life 5 dimension (EQ5D), Health Utility Index 2 and 3 (HUI 2 and HUI 3), Quality of Well-being (QWB), Short Form 6D (SF-6D), and the ICEpop CAPability for adults (ICECAP-A).

Several generic and disease-specific measures of health consequences tend to assign equal weight to each dimension or item included. This means they attach equal importance to each health dimension and do not account for people's preferences (Lamu, Gamst-Klaussen and Olsen, 2017).

Non-preference-based disease-specific measures such as the dermatology life quality index (DLQI) can still be valued indirectly using mapping algorithms (Davison *et al.*, 2018). Regression methods have been demonstrated to be useful in predicting EQ-5D-3L utility scores from DLQI (Davison *et al.*, 2018). Mapping algorithms remain useful in generating utility estimates for future economic evaluations of health interventions for people living with psoriasis (Davison *et al.*, 2018).

2.3.6.6.2 Health-related quality of life: Quality Adjusted Life Years (QALY)

A QALY is a preference-based measure incorporating both the length (capturing mortality) and quality (capturing morbidity) of life (Drummond *et al.*, 2015). An index measure, such as the EQ-5D with published preference weights is useful for measuring health-related quality of life as it condenses the outcome into a single overall score, (Drummond *et al.*, 2015). EQ-5D is a preference-based standardised generic instrument used to measure health-related quality of life that can be used across a wide range of health conditions and treatments (The EuroQol Group, 1990). Equation 2.3 shows how the QALY is calculated. Direct measures of quality of life can also be used to estimate the health-related quality of life.

Equation 2.3

$$QALY = \text{Health-related Quality of life} \times \text{Length of life in years}$$

2.3.6.6.3 Capability-adjusted life years (CALYs)

Noting that consequences of disease are likely to go beyond health, restricting the evaluative space to health-related quality of life is likely to underestimate the true impact of the disease on wellbeing and capability. Therefore, consequences in terms of capability and functionality are useful to consider (P. Lorgelly *et al.*, 2010; Lorgelly, 2015). Capability-adjusted life year (CALY) is a summary measure incorporating length of life and capability. Beyond-health-related consequences of disease such as capability and wellbeing can be captured using ICECAP-A (Al-Janabi, Flynn and Coast, 2012). The ICECAP-A is a measure of capability for the general adult (18 years and over) population that has been mainly used in economic evaluation (University of Birmingham n.d, Al-Janabi, Flynn and Coast, 2012). The five attributes of ICECAP- A are:

Stability (being able to feel settled and secure); Attachment (being able to have love, friendship, and support); Autonomy (being able to be independent); Achievement (being able to achieve and progress); Enjoyment (being able to have enjoyment and pleasure). Each of these attributes can take up any of the four levels ranging from full capability (coded as 4) to no capability (coded as 1), see Table 2-2 (Flynn et al. 2013).

The data collected from the ICECAP-A is used to summarise the impact on the patient's perceived capability to function normally. Results from the ICECAP-A questionnaire are converted into an index value using a country-specific tariff. The UK ICECAP-A tariff, for instance, is used to value and consolidate individual responses to the ICECAP-A questionnaire. The tariff value for each individual is then calculated by summing the values across the individual attributes as selected by each respondent. The best and worst state of an individual would be 4,444 and 1,111 respectively.

Table 2-2: UK General population ICECAP-A tariff adapted from Flynn et al. 2013.

Domain	Level	Tariff
1. Feeling settled and secure		
I am able to feel settled and secure in all areas of my life.	Level 4	0.222
I am able to feel settled and secure in many areas of my life.	Level 3	0.191
I am able to feel settled and secure in a few areas of my life.	Level 2	0.101
I am unable to feel settled and secure in any area of my life	Level 1	-0.001
2. Love, friendship and support		
I can have a lot of love, friendship and support	Level 4	0.228
I can have quite a lot of love, friendship and support	Level 3	0.189
I can have a little love, friendship and support	Level 2	0.096
I cannot have any love, friendship and support	Level 1	-0.024
3. Being independent		
I am able to be completely independent	Level 4	0.188
I am able to be independent in many things	Level 3	0.156
I am able to be independent in a few things	Level 2	0.084
I am unable to be at all independent	Level 1	0.006
4. Achievement and progress		
I can achieve and progress in all aspects of my life	Level 4	0.181
I can achieve and progress in many aspects of my life	Level 3	0.159
I can achieve and progress in a few aspects of my life	Level 2	0.091
I cannot achieve and progress in any aspects of my life	Level 1	0.021
5. Enjoyment and pleasure		
I can have a lot of enjoyment and pleasure	Level 4	0.181
I can have quite a lot of enjoyment and pleasure	Level 3	0.154
I can have a little enjoyment and pleasure	Level 2	0.069
I cannot have any enjoyment and pleasure	Level 1	-0.003

*Example: the tariff on an individual with a state of 4221 would be $0.222+0.084+0.091+0.069=$ **0.406**.*

2.3.6.6.4 Disability-adjusted life years

Health-related disability can be captured in terms of Disability-Adjusted Life Years (DALYs). The DALY is a summary measure that combines years lost due to premature death and years spent in less than optimal health, “disability” (WHO, 2017). This was developed by the WHO in 1993 for their global burden-of-disease and injury study (GBD) (WHO, 2017). The DALY for a given case is given by the sum of the Years of Life Lost (YLL) and the Years Lived with a Disability (YLD) as shown in Equation 2.4 and Equation 2.5;

$$\text{DALY} = \text{YLL} + \text{YLD} \quad \text{Equation 2.4}$$

$$\text{YLL} = \text{Number of deaths} \times \text{Loss functions} \quad \text{Equation 2.5}$$

YLD used to be calculated based on the incidence of the case, disability weight, and average length of the case until remission or death. Historically, the DALY employed a 3% discount rate for time and age (WHO, 2017). However, it has now been simplified to using the prevalence of the case and relevant disability weight when calculating the YLD. Discounting of age and time has been dropped. And the loss function in the YLL is based on the standardised life tables (WHO, 2017).

Before 2010, the quality of life under the DALY was assessed by experts through the agreed disability weights whereas in the Quality Adjusted Life Year (QALY) the quality of life is assessed by the individuals (potential or actual patients) (Zweifel, Breyer and Kifmann, 2009). Nevertheless, a major re-estimation of disability weights was undertaken under the 2010 study in which respondents were surveyed from the general population on their judgement about health losses due to given diseases and injuries (WHO, 2017).

2.4 Discussion

With a growing demand for economic impact of disease estimates among policymakers, the need for a clear framework cannot be overemphasised (Chisholm *et al.*, 2010). No explicit framework was identified in the extant literature on economic impact of disease (Jefferson, Demicheli and Mugford, 2000; Akobundu, J.Ju and L.Blatt, 2006; WHO, 2009; Jo, 2014; Onukwugha *et al.*, 2016). This study defined economic impact of disease to reinforce the importance of considering both the cost-of-illness and burden-of-disease. The framework developed in this study aligns with methods used in the costing and valuation of health and non-health outcomes applied in economic evaluation and the underpinning analytical framework as welfarist and extra-welfarist. Expert consultation on the developed framework rendered the face validity to use it in looking at reporting economic impact of disease studies. The developed framework provided a structured approach to critically appraising the available cost-of-illness and burden-of-disease evidence reviewed in chapters 3 and 4 respectively. The framework developed was used to assess the reporting of cost of illness studies and not the appropriateness of the methods of cost of illness studies as there was no existing reference standard. For instance, the framework provided for checking if the study perspective had been reported and the method used to identify, measure and value costs under cost of illness studies. Without the 'reference case' it was not possible to ascertain the appropriateness of the methods used and ultimately comparing the results from different studies.

2.4.1 Limitations

One of the limitations of this study is the potential to miss existing frameworks. This is due to the method used in identifying the existing frameworks. A serious risk of selection bias cannot, therefore, be discounted. Another limitation identified was the method used to obtain expert opinion on the initial framework developed. This would be improved by having structured criteria for validating consensus. However, there was a majority consensus on the main aspects of the framework among the expert participants, excluding one who had expressed concerns regarding the inclusion of the

extra-welfarist perspective arguing that the welfarist perspective was sufficient. The framework developed was based on a traditional pearl-growing method, instead of the formal guidance for developing of health research reporting guideline (Moher *et al.*, 2010). This PhD did not produce a checklist as it was beyond the set aims and objectives. According to Moher et al. (2010), “reporting guidelines need to be differentiated from other efforts that produce a checklist or other guidance not specific to reporting research. The authors proposed a working definition of a reporting guideline: a checklist, flow diagram, or explicit text to guide authors in reporting a specific type of research, developed using explicit methodology.”

2.4.2 Method implications

Findings from this study suggest that this framework provides an easy-to-use tool to standardise the assessment of the design and reporting of economic impact of disease studies. This is useful for other researchers in health economics working on estimating the economic impact of disease.

2.4.3 Policy implication

This study sets out a framework that policymakers can easily use in appraising economic impact of disease evidence to inform their decisions. The framework provides policymakers using economic impact of disease studies with knowledge on how to judge how meaningful and relevant the estimates are to their settings. Due to the noted poor quality of economic impact of disease studies carried out and published, consumers of such evidence must utilise them with caution (Chisholm *et al.*, 2010).

2.4.4 Future research

Advancements in developing methodologies for quantifying the economic impact of disease have been sluggish. Therefore, there is a need to invest in developing methodological approaches that better estimate the economic impact of disease. Going beyond the developed framework, there is also a need to develop recommendations for reporting economic impact studies. Developing recommendations for reporting economic impact studies will require application of formal methods as recommended by Moher et al 2010. This will make it easier for consumers of evidence from such studies to appraise the evidence.

Recognising the heterogeneity and the unresolved methodological issues in cost of illness studies, there is need to develop a standardised approach for the conduct and reporting of cost of illness studies. This will allow for comparing of results from different studies. For examples, the reference case proposed for economic evaluations takes into consideration the good methodological principles of conducting and reporting an economic evaluation(Drummond *et al.*, 2015; Neumann *et al.*, 2016).

2.5 Conclusion

A framework to enhance consistency and coherence in identifying, measuring and valuing economic impact of disease was developed. Undertaking and reporting economic impact studies using a framework grounded in a coherent set of conceptual foundations in health economics will contribute to the accelerated use of results and a healthy policy dialogue (WHO, 2009). This framework was then used in guiding the critical appraisal for the systematic review reported in Chapters 3 and 4. Headings based on the framework were used to assess the clarity on how well studies were reported.

3 A systematic review to identify the cost-of-illness of psoriasis

Chapter summary

This chapter reports the findings from a systematic review to identify published studies reporting the cost-of-illness of psoriasis. The aim was to critically appraise the published estimates of the cost-of-illness of psoriasis and to identify any methodological differences that may limit the comparability of published estimates.

The common result across all studies was that psoriasis had a high cost-of-illness. There were substantial differences in the methods used to estimate the cost-of-illness of psoriasis. The methodological heterogeneity poses a challenge when policy makers try to interpret and compare these costs.

In this chapter, section 3.1 presents the background and motivation for the study and section 3.1.1 describes the aims and objectives. The methods and results are presented in section 4 and 3.3 respectively. The discussion and conclusion are presented in section 3.4 and 3.4.

3.1 Background

Due to the chronic nature of psoriasis and its prevalence, the cost-of-illness has been estimated to be significant (Vanderpuye-Orgle *et al.*, 2015). As detailed in chapter 2, cost-of-illness is one component of the economic impact of disease. This focuses on the financial costs imposed by poor health in terms of spending on healthcare services such as medical costs and productivity loss (Culyer, 2005). Cost-of-illness is a descriptive method that provides a structured approach to estimating the magnitude of the economic impact of disease by identifying, measuring and valuing all relevant costs incurred (Roux and Donaldson, 2004; Tarricone, 2006; Jo, 2014). Due to inconsistencies in the definition of cost-of-illness, different studies covering the same disease tend to report different findings within the same settings. The framework

developed in chapter 2 formed a potential basis for guiding the critical appraisal of the design and reporting of studies that identify, measure and value the cost-of-illness of psoriasis

Five systematic reviews aimed at summarising cost-of-illness studies on psoriasis were published up to 2016 (Feldman *et al.*, 2014; Azizam *et al.*, 2015; Brezinski, Dhillon and Armstrong, 2015; Vanderpuye-Orgle *et al.*, 2015; Burgos-Pol *et al.*, 2016). These reviews collated and reported on the various costs of psoriasis. Some of the reviews covering a similar search period were found to include a different number of studies (Feldman *et al.*, 2014; Azizam *et al.*, 2015; Vanderpuye-Orgle *et al.*, 2015). In addition, the reported cost-of-illness showed a difference even within countries. The potential source of the different estimates could be attributed to definitions of economic impact (cost-of-illness), identification, measuring and valuing of costs, data collection methods, and limited study samples.

A systematic review of 14 studies on the costs associated with managing and treating psoriasis and psoriatic arthritis in five European countries was published in 2016 (Burgos-Pol *et al.*, 2016). Even though Burgos-Pol and colleagues claimed to have analysed the economic burden of psoriasis, it was clear they only considered direct costs of treatment such as acquisition costs of medicines used in the treatment of psoriasis. The cost-of-illness in terms of direct costs per person was reported to range between US\$ 2,007 to US\$ 13,132 and the introduction of biologics led to a 3 to 5 times increase in costs (Burgos-Pol *et al.*, 2016). Another systematic review published in 2015 assessed the annual economic burden of psoriasis in the US (Vanderpuye-Orgle *et al.*, 2015). In the review, economic burden included productivity loss, disability burden, quality of life, mental health effects, social stigma, caregiver burden, and direct costs which included out-of-pocket costs and health care utilization (Vanderpuye-Orgle *et al.*, 2015). Based on the broad definition of economic burden of psoriasis in this review, up to 91 studies were included. This review estimated that psoriasis affected 7.4 million people in the US alone in 2013 (Vanderpuye-Orgle *et al.*, 2015). The incremental direct medical costs were estimated to be US\$ 2,284, whereas the reduction in health-related quality of life (HRQOL) and productivity loss were estimated at \$2203, and \$1935 respectively (Vanderpuye-Orgle *et al.*, 2015). The total

cost of psoriasis to society in the US was estimated at \$35.2 billion broken down into \$12.2 billion in incremental medical costs, \$11.8 billion reduction in HRQOL and \$11.2 due to a loss in productivity (Vanderpuye-Orgle *et al.*, 2015).

In 2015, another review using a search strategy across a similar period compared to the Vanderpuye-Orgle review included fewer studies (Azizam *et al.*, 2015; Vanderpuye-Orgle *et al.*, 2015). The inclusion of fewer studies can be attributed to the difference in the definition of economic burden in the two reviews. Azizam and colleagues only included articles that reported direct and indirect costs of psoriasis whereas Vanderpuye-Orgle and colleagues had additional inclusion of prevalence and incidence studies. The Azizam review noted that the most cited costs due to psoriasis were hospitalisation, high insurance coverage, outpatient services, prescription medication, over-the-counter medicines and productivity loss (Azizam *et al.*, 2015). Productivity loss was noted to account for up to 43% of the total costs (Azizam *et al.*, 2015). The definition or components of productivity loss was not stated in the Azizam and colleagues' review, therefore, it was not clear if both absenteeism and presenteeism were accounted for (Azizam *et al.*, 2015). In addition, hospitalisation has been cited as the highest component of costs associated with psoriasis ranging from 30 to 45% and medication accounts for 20% of total costs (Azizam *et al.*, 2015). Although biologics were only used in 5% of patients, they accounted for 67% of the total medication costs (Azizam *et al.*, 2015). The review reported that the US healthcare system incurred US\$1.4 billion in 2004 in terms of total direct and indirect costs due to psoriasis (Azizam *et al.*, 2015). The annual per patients costs for Sweden, Italy, Germany, Canada and Hungary were reported to be US\$15,108, US\$10,603, US\$3,632 to \$8,494, and US\$7,117 respectively (Azizam *et al.*, 2015).

Another systematic review included 22 studies that reported on the direct, indirect and intangible costs (Brezinski, Dhillon and Armstrong, 2015). Studies reporting on the costs due to comorbidities in adult patients with psoriasis were also included (Brezinski, Dhillon and Armstrong, 2015). The 2013 costs due to psoriasis were estimated to range from US\$51.7billion to US\$63.2 billion, US\$23.9 billion to US\$35.4 billion, and US\$36.4 billion annually for direct, indirect and medical comorbidities respectively.

In a systematic review by Feldman *et al.*, (2014) which included 35 studies from 11 countries, it was reported that the US and Canada incur the highest economic impact of psoriasis followed by countries in Europe (Feldman *et al.*, 2014). Due to the paucity of psoriasis cost-of-illness research in other countries, the information in this review was biased toward the US, Canada and European countries (Feldman *et al.*, 2014). The attention to psoriasis in these countries could also be explained by the high incidence and prevalence of psoriasis in these countries compared to others with a predominantly non-white population and less health economic influence in decision making (Parisi *et al.*, 2013). Feldman and colleagues also put across that most cost-of-illness studies in psoriasis might underestimate the costs of psoriasis as they tend to omit the indirect costs due to the presence of comorbidities and lost productivity of family as a result of informal care (Feldman *et al.*, 2014).

Evidence suggests there is extensive variation in the reported values of the economic impact of psoriasis both within and between countries. Although several studies aimed at quantifying the economic impact of psoriasis have been conducted, there has been variation in the reported results both between and across countries (Feldman *et al.*, 2014; Azizam *et al.*, 2015; Brezinski, Dhillon and Armstrong, 2015; Vanderpuye-Orgle *et al.*, 2015; Burgos-Pol *et al.*, 2016). This variation in the findings might be attributed to methodological heterogeneity. Without any consensus on the methods and reporting criteria for cost-of-illness in psoriasis, these results might potentially be misleading and spurious owing to a lack of a clear framework (WHO, 2009). However, there was the need to provide a critical summary of all published estimates and explore which evidence was relevant to the UK.

3.1.1 Aims and objectives

This study aimed to identify and critically appraise published studies estimating cost-of-illness for people living with psoriasis.

This study addressed four objectives:

1. Find all published studies reporting the cost-of-illness of psoriasis;
2. Describe the included published studies;
3. Summarise published estimates;

4. Critically appraise published studies in terms of the methods and reporting for cost-of-illness.

3.2 Methods

A systematic review was conducted in line with published recommendations from the Centre for Reviews and Dissemination (CRD, 2009). The reporting was consistent with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement, a statement developed to facilitate transparent and complete reporting of systematic reviews, see Appendix 3.1 (Liberati *et al.*, 2009; Moher *et al.*, 2009; Page *et al.*, 2021).

3.2.1 Eligibility

The study inclusion was defined around the stated 'PICOS' (population, intervention, comparator, outcome, study design) see Table 3-1. The review included studies reporting on adults aged at least 18 years old with plaque psoriasis. Studies reporting psoriatic arthritis as comorbidity with psoriasis were also included. However, studies reporting psoriatic arthritis as a primary and only condition were excluded.

Only empirical studies that reported the cost-of-illness of psoriasis were included. These were studies reporting outcomes of psoriasis in monetary terms. Economic evaluation studies were excluded. Studies not published in the English language were excluded.

Table 3-1: Inclusion criteria summary based on PICOS

	Description
Population	Adults (18 years or over) with plaque psoriasis.
Interventions	Not applicable as the focus was not on a single intervention
Comparator	Not applicable
Outcomes	Financial and productivity costs from different perspectives
Study designs	Cost-of-illness studies

3.2.2 Search strategy

Electronic databases were searched for relevant articles published from database inception to June 2020 using the Ovid platform. The literature search was run on 15 June 2020. The databases searched included Medline and Embase. These databases were sufficient considering the performance of the search filter where they have shown a high sensitivity despite the low precision (Glanville, Kaunelis and Mensinkai, 2009). The reference list of four published systematic reviews were also searched (Feldman *et al.*, 2014; Azizam *et al.*, 2015; Brezinski, Dhillon and Armstrong, 2015; Burgos-Pol *et al.*, 2016).

The search strategy was built around two concepts: psoriasis and cost-of-illness. The detailed search strategy is presented in Appendix 3.2. The primary key search terms used were informed by other published systematic reviews of psoriasis economic impact (Feldman *et al.*, 2014; Azizam *et al.*, 2015; Brezinski, Dhillon and Armstrong, 2015; Kawalec and Malinowski, 2015; Burgos-Pol *et al.*, 2016). The **psoriasis-related terms** were psoriasis, plaque psoriasis, psoriasis vulgaris, psoriatic arthritis, arthritis psoriatica, arthropathic psoriasis, psoriatic arthropathy, psoriasis arthropathica, psoriatic arthropathies and arthritic psoriasis. The **cost-related terms** were cost, cost analysis, economics, cost-of-illness, direct services costs, direct costs, treatment failure, drug costs, employer health costs, caregiver burden, family/ parental/sick leave, absenteeism, presenteeism, length of stay, workdays and loss of productivity, health care costs, economic burden, direct cost, indirect costs, productivity costs, human capital and economic burden. In addition, hand searching through references of the studies identified from the electronic database search was used as another method of identifying relevant studies. References and studies included in the published systematic reviews were also included if they met the eligibility criteria for this study (Feldman *et al.*, 2014; Azizam *et al.*, 2015; Brezinski, Dhillon and Armstrong, 2015; Kawalec and Malinowski, 2015; Vanderpuye-Orgle *et al.*, 2015; Burgos-Pol *et al.*, 2016).

3.2.3 Study selection

One main reviewer (PN) conducted the electronic search. Double screening of all identified abstracts was employed during the study selection process. PN and one other reviewer (CJ) reviewed the titles and abstracts based on the inclusion and

exclusion criteria. The third reviewer (KP) helped resolve any disagreements. Full articles were obtained if their titles or abstract was judged to meet the inclusion criteria.

3.2.4 Data collection process and items

A standardised data extraction form was designed by two reviewers (PN and KP). The form was piloted between the same two reviewers and initial data extracted were discussed to arrive at a consensus on what goes under each heading. The final data were extracted by one reviewer (PN). The other reviewers (DA, CG and CJ) were asked to comment on the extracted data. The data extraction was summarised as shown in Appendix 3.3.

The extracted data summarised the included studies. Information was collected to describe each study in terms of:

- Author,
- Country of publication,
- Year of publication,
- Disease of relevance and whether comorbidities were identified.

Information on the study sample included:

- Number of psoriasis patients and if they were self-reported or clinician diagnosed,
- The mean age distribution,
- Gender,
- The sampling frame and,
- Study country.

Finally, the information on the data analysis methods and results was extracted.

3.2.5 Critical appraisal

The framework described in chapter 2 (see section 2.3.1 and Figure 2.2) was used to critically appraise the published studies included in this review to establish if they reported: study perspective; study time horizon; approaches to identify, measure and

value costs. The appraisal assessed the clarity of how well the studies reported cost of illness due to psoriasis. The main components from the framework used to generate heading of what was reported in the studies are summarised in Table 3-2.

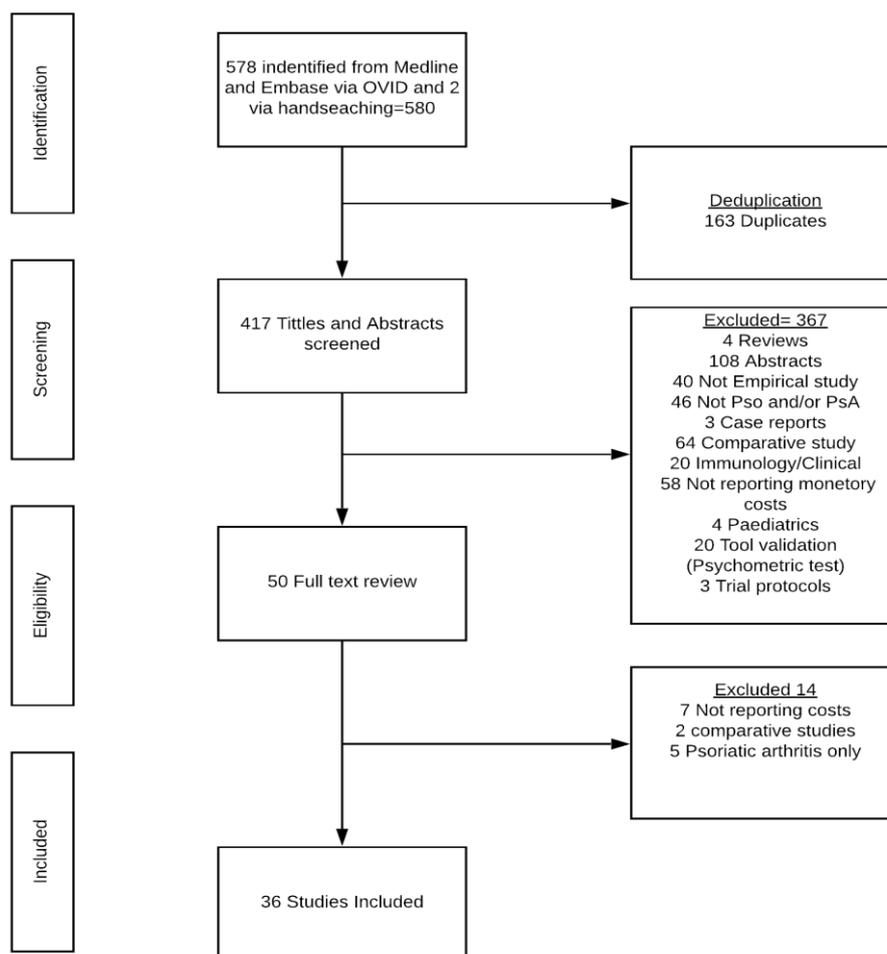
Table 3-2: Summary of headings used in the appraisal on reporting of studies

Item	Reported		
	Yes	No	Not clear
Aim/Objectives			
Study Perspective			
Time Horizon			
Cost identification			
Cost measurement			
Cost valuation			

3.3 Results

A total of 36 cost-of-illness studies were included in this review, see reference list in Appendix 3.4. Overall, 580 citations were identified during the Medline and Embase database and hand searching. Deduplication removed 163 citations, leaving a total of 417 unique citations for the title and abstract screening. The 50 full-text articles were assessed for eligibility, which resulted in 36 studies being included in the review. An overview of the search results is presented in the PRISMA diagram shown in Figure 3.1.

Figure 3.1 PRISMA flow diagram of the cost-of-illness systemic review



Note: Diagram based on PRISMA recommendations (Page et al., 2021)

A description of the distribution of studies in terms of country of origin, year of publication, reporting comorbidities, time horizon, and type of costs reported are presented in the respective sections below. Table 3-3 summarises the included studies. Table 3-3 also reported whether only psoriasis specific costs were included. Psoriasis specific costs were defined as costs related to direct management and productivity loss due to psoriasis. This was in line with cost of illness calculation definition summarised in 2.3.5.3.4. The costs information extracted and reported in Table 3-3 have not be standardised and thus it was futile to provide a range of the estimates as they were not comparable. The detailed data extraction table is included in Appendix 3.3.

Table 3-3: Summary of study description and reported costs

Lead Author (date)	Country	Study perspective	Time horizon	Currency; price year	Only Psoriasis specific costs*	Direct medical costs	Direct non-medical costs	Indirect costs	Total costs
Per patient costs									
Pilon (2019)	US	Not reported	7 years	US dollar; 2017.	No	US \$ 1,590	Not reported	\$335	US \$ 1,925
Jungen (2018)	Germany	Societal	1 year	Euro; 2013	Yes	€ 5, 164	Not reported	€379	€ 5, 543
Feldman (2017)	USA	Third-party payer (Insurer)	2 years	US dollar; 2011	No	US \$25,035.9	Not applicable	Not reported	US \$25,035.9
Ha (2018)	Korea	Healthcare	1 year	US dollar; 2017.	No	US \$ 185.65	Not applicable	Not applicable	US \$ 185.65
Lofvendahl (2016)	Sweden	Societal	3 years	Euro; 2011	No	€10, 500	Not reported	€4,666	€1516.6
Svedbom (2016)	Sweden	Societal	1 year	US dollar; 2010	No	US \$ 1,365	Not reported	US \$ 3,319	US \$ 4,684

Takahashi (2016)	Japan	Not reported	1 year	YEN; not reported	Yes	Cyclosporin YEN 680581 Secukinumab YEN 631 600 Ustekinumab YEN 448 550 Adalimumab YEN 532 850	Not reported	Not reported	Cyclosporin YEN 680581 Secukinumab YEN 631 600 Ustekinumab YEN 448 550 Adalimumab YEN 532 850
Feldman (2015)	USA	Third-party payer (Insurer)	1 year	US dollar; 2012	No	US \$ 22,713	Not applicable	Not applicable	US \$ 22,713
Feldman (2015)	USA	Third-party payer (Insurer)	1 Year	US dollar; 2012	No	US \$ 27, 123	Not applicable	Not applicable	Us \$ 27, 123
Mustonen (2015)	Finland	Societal	1 year	Euro; 2011	Yes	Not applicable	Not applicable	€ 2250	€2250
Schaeffer (2015)	USA	Not reported	6 months	US dollar; 2012	Yes	US \$ 11,291	Not reported	US \$ 2,101	US \$13,392

Balogh (2014)	Hungary	Societal	Not reported	Euro; 2012	Yes	€7,790	€208.00	HCA: €1,255 FCA: €307	HCA: €9,254 FCA: €8,305
Chen (2014)	Taiwan	Payer (insurer)	1 year	Taiwan Dollar; 2009.	No	NT\$ 41,525	NT\$ 13,095	NT\$6203	NT\$60,823
Ekelund (2013)	Sweden	Societal	1 year	Euro; Not reported.	Yes	€2169	Not reported	€1,230.00	€3,399.00
Tang (2013)	Malaysia	Not reported.	1 year	Ringgit, Malaysia	Yes	RM 1327.4	RM 350.39	Not reported	RM 1,677.79
Ghatnekar (2012)	Sweden	Societal	1 month	Euro; 2009	Yes	€758	€75	€161	€994
Gunnarsson (2012)	USA	Third-party payer and patient	10 years	US dollar; 2008)	No	US \$ 5,802	Not applicable	Not applicable	US \$ 5,802
Levy (2012)	Canada	Societal	1 year	CAN dollar;	Yes	CAN \$ 4,471	CAN \$ 86	CAN \$ 3,442	CAN \$ 7,999
Driessen (2010)	Netherlands	Not reported	1 year	Euro; Not reported	Yes	€17,712 ^a	Not applicable	Not applicable	€17,712 ^a

Navarini (2010)	Switzerland	Societal	1 year	Swiss Franc –CHF (2005 price year)	Yes	Mild=CHF 1136.33 Moderate =CHF 2492 Severe=CHF 13574	Mild=CHF 631 Moderate =CHF 1122 Severe=CHF 2442	Not reported	Mild=CHF 1768 Moderate =CHF 3613 Severe=CHF 16017
Fonia (2010)	UK	Health Sector	1 year	GBP; 2008	Yes	£11, 981	Not applicable	Not applicable	£11,981
Chan (2009)	Canada	Patient	1 year	Can Dollar; 2005	Yes	Not applicable	Not applicable	CAN \$2,270.84	CAN \$2,270.84
Yu (2009)	USA	Not reported	1 year	US dollar; 2007	No	US \$5,529	Not included	Not included	US \$5,529
Colombo (2008)	Italy	Societal	3 Months	Euro; 2006	Yes	€5,690.10	Not reported	€2,681.51	€8,371.61
Fowler (2008)	USA	Employer	7 years	US Dollar; 2006	No	US \$ 614	Not applicable	US \$ 229	US \$ 843
Schoffski (2007)	German	Societal	1 year	Euro; not reported	Yes	€4603	€794	€1,310	€6,707

Carrascosa (2006)	Spain	Societal	1 year	Euro; 2003	Yes	€890	Not reported	€ 188.50	€1078.50
Berger (2005)	Germany	Societal	1 year	Euro; 2002	Yes	€ 864.35	€561.68	€1,440.20	€2,866.23
Feldman (2005)	USA	Third-party payer perspective	1 year	US dollar; not reported	Yes	US \$2,067	Not applicable	Not applicable	US \$2,067
Kulkarni (2005)	USA	Not reported	Not reported	US dollar; not reported	Yes	US \$460	Not reported	Not reported	US \$ 460
Crown (2004)	USA	Payer (insurer)	1 year	US Dollar; Not reported	No	US \$ 7,778	Not applicable	Not applicable	US \$ 7,778
Jenner (2002)	Australia	Not reported	2 years	AUS\$; 1998	Yes	AUS \$ 632.62	AUS \$ 189.76	Not applicable	AUS \$ 823.54
Poyner (1999)	UK	Patient and Health	6 months	GBP; 1993	Yes	£55.61	Not reported	Not applicable	£55.61
Feldman (1997)	USA	Patient	1 year	USD; Not stated	Yes	Not applicable	US \$ 800	Not applicable	US \$ 800
Total Population costs									

Schmitt (2006)	USA	Societal	1 month	US dollar; 2002		Not reported	Not reported	Presenteeism: 7.6% US 8,862,415,000 Absenteeism: 6.6% US \$ 7,696,308,000	US \$ 16.558 Million
Javitz (2002)	USA	Societal	3 years	US dollar; 1997	No	US \$ 646.6 Million	Not reported	Not reported	US 649.6 million
<i>* Only direct medical costs associated with managing psoriasis and/or productivity loss due to psoriasis (see also Disease-specific costs in section 2.3.5.3.4)</i>									

Disease of interest

This review considered studies that reported diverse populations of people with psoriasis in terms of severity. In line with the inclusion criteria, only studies reporting on plaque psoriasis were included. Studies that were not explicit on the type of psoriasis, i.e., those that only reported “psoriasis” were assumed to report plaque psoriasis and thus included. Only two-thirds (61.1%; n=22) of the included studies reported identifying patients based on the ICD-10 codes. Over one-third of the studies were explicit on the plaque psoriasis population (33.3%; n=12). One study (2.8%; n=1) reported having included self-reported psoriasis patients. Studies reporting on Psoriatic arthritis only were excluded.

Just over half of the identified studies reported on the prevalence of comorbidities with psoriasis (55.6%; n=20). Psoriatic arthritis was the most common co-existing condition reported alongside psoriasis in almost one-third of the studies (27.8%; n=10). Other comorbidities reported were metabolic disorders (diabetes, hyperlipidaemia, hypothyroidism), malignancies, hypertension, autoimmune conditions, hepatotoxicity, nephrotoxicity, and gastrointestinal disorders, see Appendix 3.5 which shows the comorbidities reported. The method of identifying comorbidities varied from study to study. The most common systematic method of identifying the number of comorbidities reported in these studies was the Charlson Comorbidity Index (16.7%; n=6). A few studies (8.3%; n=3) used standardised questionnaires to establish the presence of comorbidities (Navarini *et al.*, 2010; Schaefer *et al.*, 2015; Jungen *et al.*, 2018). One study that did not indicate the method of quantifying comorbidities only compared the costs based on the presence or absence of comorbidity (Schmitt and Ford, 2006). Other studies (11.1%; n=4) just listed the comorbidity conditions without stating the method of quantifying them (Kulkarni *et al.*, 2005; Ghatnekar *et al.*, 2012; Gunnarsson *et al.*, 2012; Tang *et al.*, 2013). One study from Sweden only considered joint involvement as a comorbidity (Ekelund *et al.*, 2013).

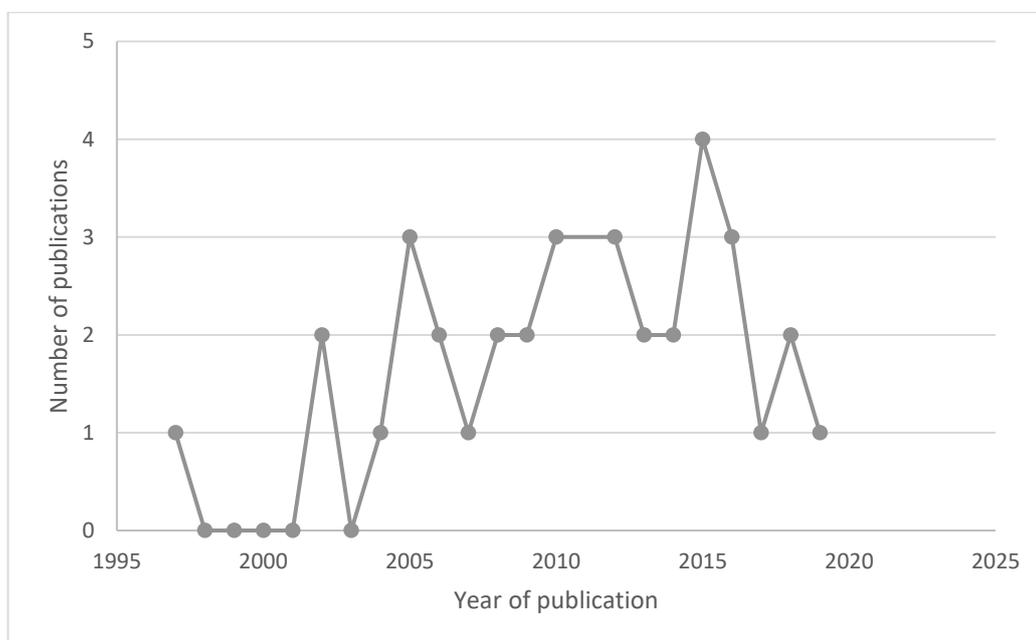
3.3.1 Description of identified papers

This section presents a description of the included studies in terms of the year of publication, country of origin for the study, and the type of study. All the included studies reported an aim and objectives. This sets the decision context into perspective.

3.3.1.1 Year of publication

The most recent cost-of-illness study for psoriasis was published in 2019 and the earliest included in this study was published in 1997 (Feldman *et al.*, 1997; Pilon *et al.*, 2019). The two UK studies included were published in 1999 and 2010 (Poyner *et al.*, 1999; Fonia *et al.*, 2010). Figure 3.2 shows the pattern of publication over time.

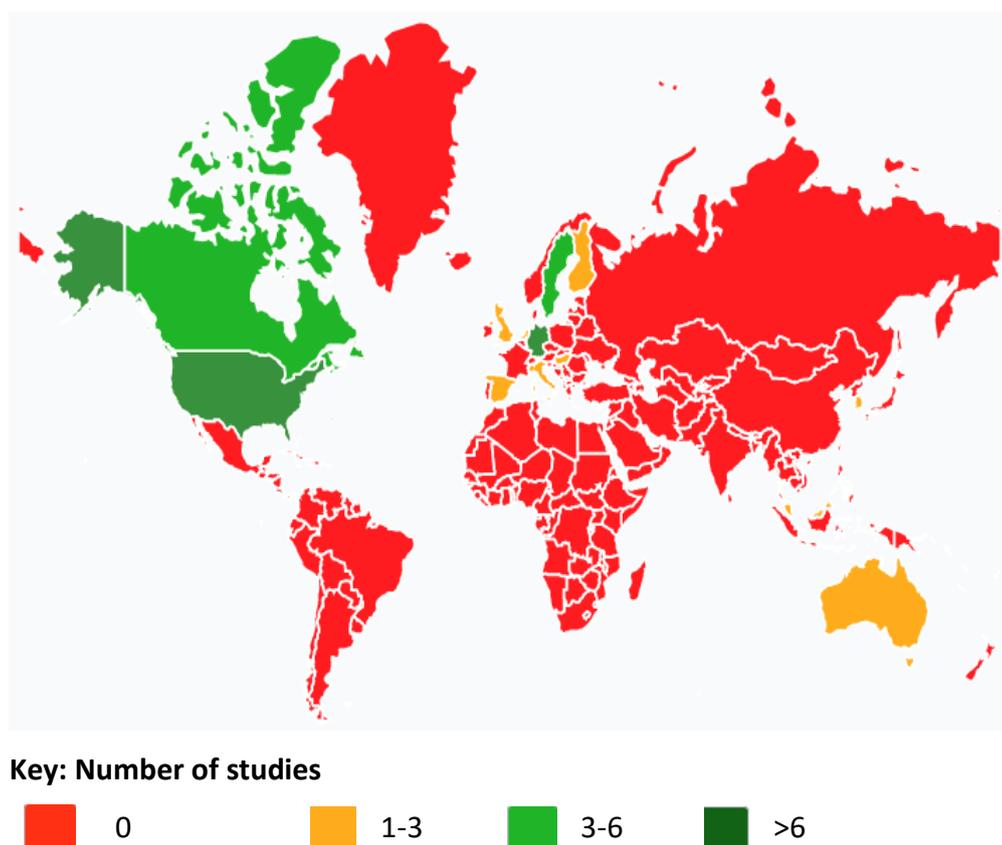
Figure 3.2: Publication pattern over time



3.3.1.2 Publication country of origin

The 36 studies included originated from 16 countries. The majority of the studies included in the review were conducted in the US (36.1%; n=13), followed by Sweden (11.1%; n=4), Germany (8.3%; n=3), Canada (8.3%; n=3) and UK (5.6%; n=2). The rest of the countries had one study each. These countries included Australia, Finland, Hungary, Italy, Japan, South Korea, Malaysia, Netherlands, Spain, Switzerland and Taiwan, see Figure 3.3.

Figure 3.3: Number of studies per country



The majority (69.4%; n=25) of the studies were standalone cost-of-illness. Almost one-third (27.8%; n=10) of the other studies combined Cost-of-illness and Burden-of-disease (Marks *et al.*, 2002; Schöffski *et al.*, 2007; Colombo *et al.*, 2008; Navarini *et al.*, 2010; Ghatnekar *et al.*, 2012; Levy *et al.*, 2012; Ekelund *et al.*, 2013; Tang *et al.*, 2013; Balogh *et al.*, 2014; Jungen *et al.*, 2018). The burden-of-disease measure in studies reporting both cost-of-illness and burden-of-disease was quality of life. The burden-of-disease studies are summarised in Chapter 4 of this thesis.

3.3.1.3 Study design

Information concerning the study design of the included studies was also extracted. Over one third of the studies included were cross-sectional surveys (36.1%; n=13) (Feldman *et al.*, 1997; Kulkarni *et al.*, 2005; Schmitt and Ford, 2006; Schöffski *et al.*, 2007; Chan *et al.*, 2009; Navarini *et al.*, 2010; Ghatnekar *et al.*, 2012; Levy *et al.*, 2012; Tang *et al.*, 2013; Ekelund *et al.*, 2013; Chen *et al.*, 2014; Schaefer *et al.*, 2015; Jungen *et al.*, 2018). Some of the included studies used data that was collected as part of

larger cross-sectional surveys (5.6%; n=2) (Kulkarni *et al.*, 2005; Schmitt and Ford, 2006). One-third of the studies were retrospective (30.6%; n=11) as compared with only 13.9% (n=5) prospective studies. Observational studies made up 38.9% (n=14) of the included studies. Just a quarter (25.0%; n=9) of the included study reported a survey study design.

3.3.1.4 Study perspective

Of the 36 studies, 75.0% (n=27) reported the study perspective. Up to 30.6% (n=11) reported taking the societal perspective, 5.6% (n=2) assumed a combination of the societal, health sector, and patient perspectives, and 2.8% (n=1) assumed both the societal and patient perspective. Up to 22.2% (n=8) of the studies reported having assumed the third-party payer perspective. The most common third-party payer was the insurer, with 16.7% (n=6) and 5.6% (n=2) health sector perspective. Only one study, 2.8%, reported having assumed both the third-party payer and patient perspective. Another study reported having solely assumed a patient perspective. Another 2.8% (n=1) of the publications reported taking the employer perspective. The remaining 25.0% (n=9) of studies did not report a clear perspective.

The studies that took the societal perspective were judged to offer a comprehensive representation of the public interest. Considering the spillover effects of psoriasis beyond the healthcare sector and the use of cost-of-illness studies in advocacy, taking the societal perspective is deemed the most appropriate. However, almost half of the studies reporting the societal perspective were noted to poorly specified as they only included healthcare costs. Furthermore, where the decision is to influence a decision within the healthcare sector, studies choosing the health sector or the third-party payer like insurer was judged to be useful. The one study reporting the patient perspective is less relevant to the English NHS setting which is tax financed and free at the point of use. Nonetheless, considering the potential over-the counter spending due to psoriasis, such a perspective would be useful in estimating the financial impact on the individual living with psoriasis. However, a firm conclusion on the appropriate study perspective cannot be made without a 'reference case'.

3.3.1.5 Time horizon

The majority of the included studies (94.4%) reported the study time horizon. The most common study period or follow-up was 1 year (61.1%; n=22). Only 13.9% (n=5) of the studies reported less than 1 year of study or follow-up period. The remaining studies reporting more than 1 year of study or follow-up period included 2 years (5.6%; n=2), 7 years (5.6%; n=2) and 10 years (2.8%; n=2).

As noted in section 2.3.4, the relevant time horizon should be long enough to capture important cost attributed to psoriasis. Studies using a shorter time horizon such as 1 year were more likely to underestimate the full cost implication of psoriasis. With most studies reporting a 1-year follow-up period, it can be implied that costs due to psoriasis have been underestimated. However, the chosen time horizon is influenced by the decision maker and target audience. Like the choice of study perspective, it is not possible to ascertain the appropriate time horizon without having a reference case.

3.3.2 Identification of costs

The majority of the studies included in this review reported direct costs that mainly comprised medication costs (n=32; 88.9%). One fifth of the studies (n=7; %) reported on out-of-pocket (OOP) spending and 3% (n=1) reported informal care costs. Costs in other sectors were loosely defined and reported. Up to 5.6% (n=2) of the studies that reported costs in other sectors included public transfers, sick leave benefits, and lost leisure time. Costs due to psoriasis productivity loss in terms of absenteeism, presenteeism, and job loss were reported in 58.3% (n=21), 16.7% (n=6) and 25% (n=9) of the included studies respectively. All the studies reporting the study perspective reported relevant identified costs consistent with the study perspective. Nonetheless, of the 14 studies taking the societal perspective, just over half reported direct medical and indirect costs (i.e., 57.1%; n=8), almost one-third reported all the three components-direct medical, direct non-medical and indirect costs (28.6%; n=4), and about a quarter reported indirect costs only (14.3%; n=2).

3.3.3 Measurement of costs

The majority of studies (94.4%; n=34) considered costs per patient per year, see Table 3-3. The included studies used different measurements of resource use and productivity loss. As highlighted above, half of the studies included measured productivity loss in terms of absenteeism (58.3%; n=21).

The minority of studies used validated measures of absenteeism and presenteeism which included the work limitation questionnaire (2.8%; n=1) and the work productivity activity impairment questionnaire (8.3%; n=3) (Schmitt and Ford, 2006; Chan *et al.*, 2009; Balogh *et al.*, 2014; Schaefer *et al.*, 2015). A few more studies used sick leave benefits, hospital visits, and inpatient days from claims data to measure absenteeism (Fowler *et al.*, 2008; Löfvendahl *et al.*, 2016; Svedbom *et al.*, 2016; Feldman *et al.*, 2017; Pilon *et al.*, 2019). Only one study (2.8%) used a patient diary to measure absenteeism and presenteeism (Carrascosa *et al.*, 2006). The majority of studies (33.3%; n=12) used study-specific standardised patient questionnaires to measure absenteeism (Berger *et al.*, 2005b; Schöffski *et al.*, 2007; Colombo *et al.*, 2008; Navarini *et al.*, 2010; Ghatnekar *et al.*, 2012; Levy *et al.*, 2012; Tang *et al.*, 2013; Ekelund *et al.*, 2013; Chen *et al.*, 2014; Mustonen *et al.*, 2015; Jungen *et al.*, 2018). A small proportion of studies (5.6%; n=2) used study-specific patient questionnaires to measure presenteeism (Colombo *et al.*, 2008; Mustonen *et al.*, 2015)

3.3.4 Valuation of costs

In the majority (92%; n=33), the source of unit costs for the valuation of direct costs was clearly stated. The most common source of unit costs for direct costs in one-third of the studies (33%; n=13) was the insurance reimbursement from the claims database. Other sources included official price lists and tariffs, diagnostic related group (DRG) rates, benefits rates, government average per diem rates, schedule fees, national average wages, and published literature. No publication attempted to value intangible costs. One study that measured hospital utilisation did not include monetary valuation (Sato *et al.*, 2011).

Close to half the studies (n=15; 43%) reported the sources for the indirect costs (Berger *et al.*, 2005a; Carrascosa *et al.*, 2006; Schmitt and Ford, 2006; Colombo *et al.*, 2008;

Fowler *et al.*, 2008; Chan *et al.*, 2009; Levy *et al.*, 2012; Ghatnekar *et al.*, 2012; Ekelund *et al.*, 2013; Chen *et al.*, 2014; Schaefer *et al.*, 2015; Svedbom *et al.*, 2016; Feldman *et al.*, 2017; Jungen *et al.*, 2018; Pilon *et al.*, 2019). The human capital approach was reported in 17% (n=6) of the studies (Berger *et al.*, 2005a; Colombo *et al.*, 2008; Ekelund *et al.*, 2013; Balogh *et al.*, 2014; Mustonen *et al.*, 2015; Löfvendahl, 2016; Feldman *et al.*, 2017; Jungen *et al.*, 2018). Only 3% (n=1) of the studies reported using the Friction cost approach in valuing productivity loss (Balogh *et al.*, 2014). A few other studies used the GDP per capita to value indirect costs (Schöffski *et al.*, 2007; Colombo *et al.*, 2008). Most studies (56%; n=22) had clearly stated the price year and currency, see Appendix 3.3.

3.3.5 Types of analyses used

Over half of the studies (n=21; 54%) reported descriptive statistics (Berger *et al.*, 2005b; Feldman, Evans and Russell, 2005; Carrascosa *et al.*, 2006; Schöffski *et al.*, 2007; Colombo *et al.*, 2008; Andrew P. Yu *et al.*, 2009; Navarini *et al.*, 2010; Driessen *et al.*, 2010; Balogh *et al.*, 2014; Chen *et al.*, 2014; Steven R Feldman *et al.*, 2015; Svedbom *et al.*, 2016; Feldman *et al.*, 2017; Kristensen *et al.*, 2017; Jungen *et al.*, 2018; Ha *et al.*, 2018; Pilon *et al.*, 2019). Analysis of variance, Chi-square and Student's t-test were among the most common statistical tests reported. Only one study (3%) explicitly reported conducting a sensitivity analysis (Gunnarsson *et al.*, 2012). One-fifth of the studies conducted a regression-based analysis to estimate drivers of costs (Crown *et al.*, 2004; Kulkarni *et al.*, 2005; Schmitt and Ford, 2006; Fowler *et al.*, 2008; Andrew P Yu *et al.*, 2009a; Chen *et al.*, 2014; Mustonen *et al.*, 2015; Feldman *et al.*, 2017).

3.4 Discussion

This study adds to the existing systematic reviews on the cost-of-illness component of the economic impact of psoriasis (Feldman *et al.*, 2014; Azizam *et al.*, 2015; Brezinski, Dhillon and Armstrong, 2015; Kawalec and Malinowski, 2015; Vanderpuye-Orgle *et al.*, 2015; Burgos-Pol *et al.*, 2016).

In this study, it was found that out of the 36 published studies included in the systematic review only two were in the UK (Poyner *et al.*, 1999; Fonia *et al.*, 2010). The

two UK studies identified were judged to be outdated and did not reflect current treatment options for psoriasis (Poyner *et al.*, 1999; Fonia *et al.*, 2010). One study only provided a comparison of two non-biologic systemic treatments (Poyner *et al.*, 1999). Another only looked at the impact of biologics on medical resource use and costs in moderate to severe (Fonia *et al.*, 2010). The coming of biosimilars on the market is likely to drive total health care costs down. However, the previous studies have not accounted for this as they were published before more biosimilars were introduced on the market.

This systematic review disaggregates cost-of-illness estimates into direct medical, direct non-medical and indirect costs. Another important finding was that the cost-of-illness of psoriasis estimates reported from within and across countries differed significantly. This posed a challenge in translating the reported estimates to the UK settings. The observed differences in estimates of cost-of-illness of psoriasis were attributed to differences in the study designs.

Some studies that reported on comorbidities did attempt to ascertain the impact on costs. Similar to other reviews, one thing that was clear from this study was that psoriasis poses a significant cost-of-illness to health systems and individuals (Burgos-Pol *et al.*, 2016). However, it is difficult to generalise findings within and across different countries due to study heterogeneity.

3.4.1 Strengths

This study collated evidence on the diversity of cost-of-illness estimates for psoriasis which were attributed to methods heterogeneity. One of the strengths of this study was the critical appraisal of the published studies using the framework developed in chapter 2. The studies were critically appraised in terms of the reporting of methods used to identify, measure and value costs in psoriasis in line with the reported study perspective and time horizon. This allowed for disaggregation of reported estimates by taking into consideration the study perspective, time horizon, identification, measurement and valuation of costs.

In addition, this study did not have a limited scope based on psoriasis severity. This study considered all publications from the inception of the searched databases which

provided an opportunity to include studies before and after the introduction of biologics.

Another strength of this study was to separate cost-of-illness from burden-of-illness. This provided for an in-depth consideration of cost-of-illness without conflating estimates.

3.4.2 Limitations

Excluding non-English publications might have resulted in missing studies from predominantly non-English speaking regions. For instance, no study was identified for the whole South American region which is predominantly Spanish and Portuguese speaking.

This study did not standardise the reported costs from the different studies included into a single currency and price year. This limits the comparison of the results across studies. The decision to avoid the standardisation of the reported costs was informed by the identified heterogeneity in the methods of cost-of-illness applied in the different studies. Although another systematic review went on to standardise the reported costs from the studies it included, the authors acknowledged that a direct comparison between the results could not be made due to heterogeneity in the methods (Feldman *et al.*, 2014). Another review also reported the challenge in comparing estimates from several studies due to variability in methodology in the different studies (Burgos-Pol *et al.*, 2016). The use of different costing years and currencies added to the challenge of comparing estimates from the different studies (Burgos-Pol *et al.*, 2016). Another notable difference in cost-of-illness studies in psoriasis was the choice of study perspective. Even though the same study perspective was chosen, the costs identified and methods of measuring and valuing costs differed. For instance, two studies taking the 'societal perspective' had one reporting all the three components (direct medical, direct non-medical and indirect costs) while another one only reported indirect costs.

Economic evaluation studies were not included in this study as it was beyond the scope of the review. This resulted in limited conclusions on costs attributable to specific treatments. This limitation was similar to other published systematic reviews

(Feldman *et al.*, 2014). The exclusion of conference abstracts resulted in the removal of studies that were considered in another systematic review (Feldman *et al.*, 2014). This review had more studies as compared to another review that focused on the US alone (Brezinski, Dhillon and Armstrong, 2015). This review also differed in the approach of appraisal by using the framework with a focus on assessing the suitability of the methods of quantifying cost-of-illness. This review summarised costs by category of cost component i.e. direct medical, direct non-medical and indirect costs whereas another went further to categorise based on the type of treatment (Brezinski, Dhillon and Armstrong, 2015). The assessment of the appropriateness of the methods used was not possible due to a lack of guidance on the best methods. In addition, no gold standard or reference case exists for cost of illness studies. The Framework developed in chapter 2, was not adequate to assess the appropriateness of the methods used besides looking at the clarity of how well the studies were reported. However, the review tried to explore how similar the methods used in the studies were by considering the reporting.

Considering the UK health system is publicly funded and free at the point of use, results from most of the studies in this review were not generalisable to the UK. This assumption is similar to what has been reported in disease areas such as estimating the economic burden of cancer survivors (Marti *et al.*, 2016).

3.5 Conclusion

This study explored the different methods applied in cost-of-illness studies looking at people living with psoriasis. The prominent observation was methodological heterogeneity in estimating cost-of-illness due to psoriasis. Heterogeneity in methods for costs-of-illness studies for psoriasis poses a challenge for decision-makers when comparing results within and across countries. However, the consensus among the included studies was that psoriasis poses a significant cost to the health care systems and society. Without standardisation of the reported costs and a comparator, it was difficult to ascertain how significant the costs to the healthcare system were. The included UK studies were outdated and did not reflect the most recent practice. At the time the UK study was published, biosimilars were not yet introduced as most of them

were still under patents. The UK study was also focused on patients with severe psoriasis. This motivated the need to conduct a cost-of-illness study for psoriasis which is reported in chapter 5.

4 A systematic review to identify the burden-of-disease of psoriasis

Chapter summary

This chapter reports findings from a systematic review to identify published studies reporting the burden-of-disease of psoriasis. This study aimed at critically appraising the published estimates of the burden-of-disease of psoriasis and to identify any methodological heterogeneity that may limit the comparability of published estimates.

Section 4.1 of this chapter presents the study background, motivation and the aim and objectives. Section 4.2 and 4.3 present the methods and results of the study respectively. Lastly, sections 4.5 and 4.6 present the discussion and conclusion, respectively.

4.1 Background

The burden-of-disease on people living with the condition has been reported to be significant (Weiss *et al.*, 2002; Dubertret *et al.*, 2006; Löfvendahl, 2016). Burden-of-disease due to psoriasis as defined in chapter 2 refers to both the health and beyond health consequences of living with psoriasis, see section 2.3.6. The potential burden-of-disease of psoriasis on people living with the condition cuts across the physical, psychological and social health (Weiss *et al.*, 2002; Dubertret *et al.*, 2006; Löfvendahl, 2016). The impact of psoriasis on individuals has been reported to be higher than other skin diseases or chronic conditions (Dubertret *et al.*, 2006). Physical health impact on people living with psoriasis has been reported to include pain, red and scaly skin appearance, itching, pain, and disability (Dubertret *et al.*, 2006). Some psychological impact includes aspects of mood, self-esteem, depression, anxiety, perceived stigma, and suicidal ideation (Dubertret *et al.*, 2006). The social impact concerns itself with establishing an individual's social activities and relationships (Isfeld-Kiely and Balakumar, 2015). People living with psoriasis have affected personal relationships and tend to self-isolate due to feelings of embarrassment (Tang *et al.*, 2013).

No systematic review aiming to summarise the burden-of-disease in people living with psoriasis was identified at the time of conducting this study. Therefore, this review was motivated to close the gap for the missing systematic reviews. The framework developed in chapter 2 provided a structure for the critical appraisal of the design and reporting of studies that identify, measure and value the burden-of-disease of psoriasis in people living with the condition

4.1.1 Aim and objectives

The aim of this study was to critically appraise published estimates of burden-of-disease for psoriasis.

This study addressed four objectives:

1. Find all psoriasis burden-of-disease studies;
2. Describe the included published studies;
3. Summarise the published psoriasis burden-of-disease estimates for the UK and other countries;
4. Critically appraise published studies in terms of the methods and reporting for burden-of-disease.

4.2 Methods

A systematic review was conducted in line with published recommendations by the Centre for Reviews and Dissemination (CRD) and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (CRD, 2009; Page *et al.*, 2021). The PRISMA statement was developed to facilitate transparent and complete reporting of systematic reviews (Liberati *et al.*, 2009; Moher *et al.*, 2009; Page *et al.*, 2021).

4.2.1 Eligibility

The inclusion and exclusion criteria were determined beforehand in accordance with population, Intervention, Comparator, Outcomes and Study type (PICOS), see Table 4-1. Only published studies reporting on the adult (at least 18 years) population with psoriasis were included.

Table 4-1: Inclusion criteria based on PICOS

	Description
Population	Adults (18 years or over) with plaque psoriasis.
Interventions	Not applicable.
Comparator	Not applicable
Outcomes	Health and beyond health burden of psoriasis.
Study designs	Burden-of-disease studies for psoriasis. A variety of designs ranging from cohort studies to case reports. Economic evaluation studies were excluded.

Only burden-of-disease for psoriasis empirical studies were included. Cost-of-illness and economic evaluation studies were excluded. Non-English language publications were also excluded.

4.2.2 Search strategy

Two concepts underpinned the search strategy: Psoriasis and burden-of-disease (consequences), see Appendix 4.1 for a detailed search strategy. Psoriasis-related terms used were the same as those used in chapter 3, see section 3.2.2. The concept of burden-of-disease was in line with the framework developed in chapter 2, see section 2.3.6. Burden-of-disease terms relevant to this review were quality of life, quality-adjusted life years, disability life years, years of full capability, capability, years lost, life years, disability, and dermatology life quality index. The hand searching method through references of the studies identified from the electronic database was also employed to identify relevant studies.

Medline and Embase electronic databases were searched for relevant articles using the Ovid platform. The two databases were considered to be sufficient in capturing burden-of-disease studies that use generic measures and valuation tools relevant to health economics (Arber *et al.*, 2017; Bramer *et al.*, 2017). The search covered articles published from database inception to 15 June 2020 when the search was run.

4.2.3 Study selection

One main reviewer, PN conducted the electronic search. Double screening of all identified abstracts was employed during the study selection process. PN and one other reviewer, CJ reviewed the titles and abstracts based on the inclusion and exclusion criteria. The third reviewer, KP helped resolve any disagreements. Full articles were obtained if their titles or abstract was judged to meet the inclusion criteria.

4.2.4 Data Extraction and critical appraisal

Data were extracted from the included published articles by one reviewer (PN). The information collected was used to describe each study in terms of the lead author, country of publication, year of publication, study aim and study sample characteristics. Some of the information collected concerning the study sample characteristics was disease relevance (psoriasis; psoriatic arthritis; both psoriasis and psoriatic arthritis) and if the condition was a self-reported or clinician-reported diagnosis. Information to ascertain if interventions were considered was also included. Data collection methods in the included studies were also reported. The framework presented in chapter 2 (see section 2.3.6 and Figure 2.3) was used to critically appraise the included studies to identify if they had reported: study aim, sample, severity of psoriasis, study design (data collection method), study time horizon, and approaches to identify, measure and value burden-of-disease. These extracted data were summarised as shown in Appendix 4.2. The Joanna Briggs Institute (JBI) critical appraisal checklist was also used to complement the framework from chapter 2 (Moola *et al.*, 2017).

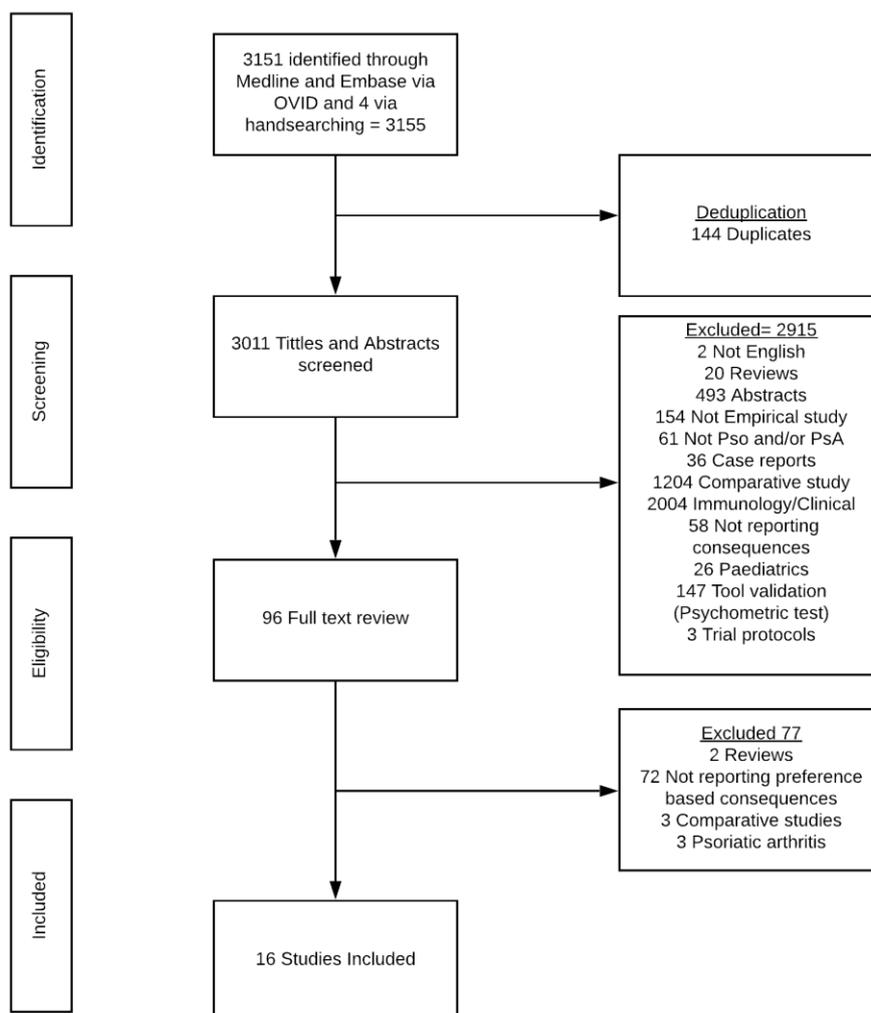
Data were only extracted from studies that included preference-based measures with an established valuation set such as EuroQoL-5 Dimension (EQ-5D)(Gray *et al.*, 2012). Studies that only reported clinical severity using PASI, DLQI and other similar disease-specific measures without a valuation set were listed in the review but data were not extracted.

4.3 Results

This review included a total of 16 burden-of-disease studies for psoriasis, see Appendix 4.3 for a list of included studies. A search of Medline and Embase retrieved 3151 citations and 4 hand-searched records were identified which resulted in a total of 3155 records for screening. Following deduplication, 44 records were removed and the

remaining 3011 were subjected to title and abstract screening. Articles eligible for full-text review were 96 of which 16 were included for review as they met the inclusion criteria, see Figure 4.1.

Figure 4.1: PRISMA flow diagram of systematic review



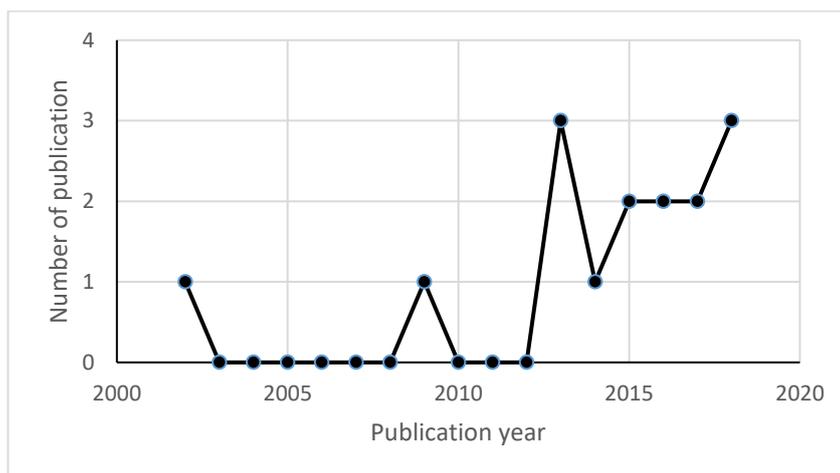
4.3.1 Study characteristics

Just over one-third ($n=7$) of the studies focused on psoriasis only without considering psoriatic arthritis as a comorbidity (Wu, Mills and Bala, 2009; Daudén *et al.*, 2013; Balogh *et al.*, 2014; Masaki *et al.*, 2016; Lesner *et al.*, 2017; Sojević Timotijević *et al.*, 2017; DiBonaventura *et al.*, 2018). Although most studies ($n=9$) considered psoriasis as the primary relevant disease, they also included psoriatic arthritis as a comorbidity (Weiss *et al.*, 2002; Pearce *et al.*, 2006; Mattila *et al.*, 2013; Tang *et al.*, 2013; Moradi *et*

al., 2015; Ng *et al.*, 2015; Korman *et al.*, 2016; Bronckers *et al.*, 2018; Hjalte, Carlsson and Schmitt-Egenolf, 2018).

The year of publication for the identified studies ranged from 2002 to 2019. Most of the studies were published in 2013 (n=3; 19%) and 2018 (n=3; 19%). The year 2015 to 2017 had two publications each while the rest had one each year, see Figure 4.2.

Figure 4.2: Publication pattern over time



Most of the studies published were from the US (n=3; 19%). The rest of the countries which included, Brazil, Finland, Hungary, Iran, Japan, Malaysia, Netherland, Poland, Serbia, Spain, Sweden, Taiwan, and Thailand had one publication each, see Figure 4.3. The majority of studies (n=13; 81%) were cross-sectional studies. Therefore, the JBI critical appraisal checklist for cross-sectional studies was used to appraise the 13 studies.

In the case of using the JBI critical appraisal checklist (Moola *et al.*, 2017) (Moola *et al.*, 2017), see Table 4-2, all the 13 cross-sectional studies had a clearly defined criteria for inclusion in the sample. The clear description of the study sample inclusion criteria allows for comparison of populations of interest. Considering the broad population and outcomes of interest in this review, there was no judgement on which population was appropriate. In this case, some studies included split the psoriasis population by severity and presence of psoriatic arthritis whereas others just reported the psoriasis population as one. Only a few studies (n=3; 23%) did not describe the study subjects and the settings in details. About 92% (n=12) of the studies used the standard criteria to measure the condition, and all the studies used valid and reliable ways of measuring outcomes. However, there is no set gold standard for measuring burden of disease

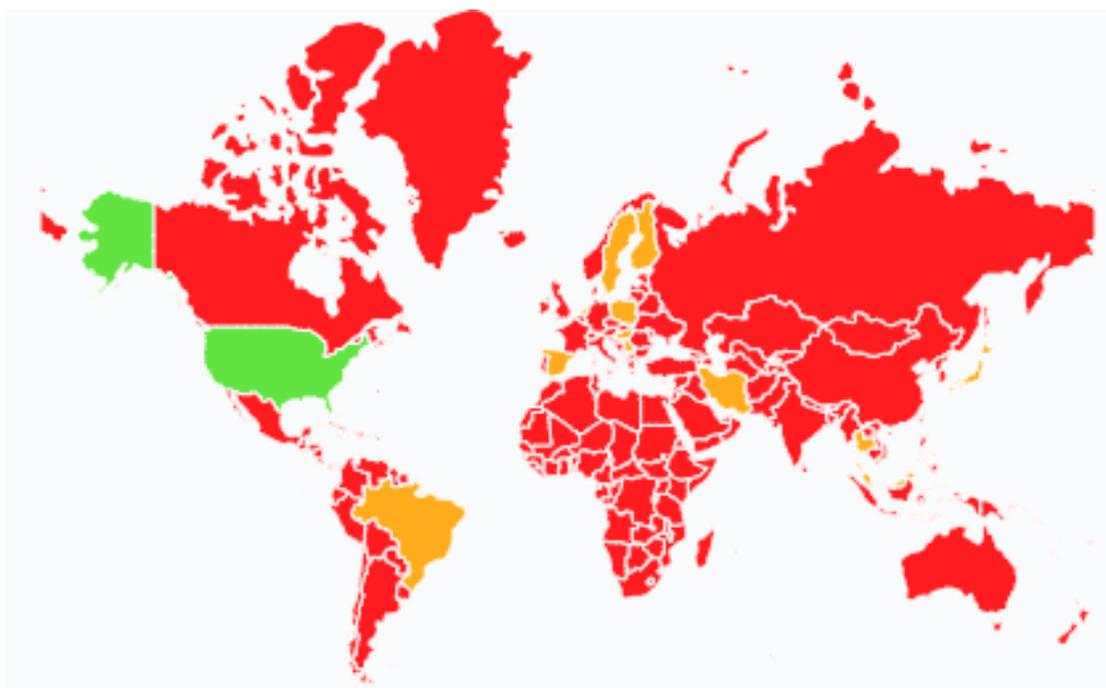
outcomes in psoriasis. Therefore, the methods of measuring outcomes in psoriasis could not be assessed in terms of appropriateness. Up to 38% (n=5) of the studies were not clear on the statistical analysis used. This poses a challenge on the assessment of the appropriateness of the statistical methods used. The statistical analysis methods in the 62% (n=8) of the studies that reported them were judged to be appropriate to the reported aim.

Table 4-2: Results of the critical appraisal using JBI cross-sectional studies checklist (Moola *et al.*, 2017)

Author (Year)	Were the criteria for inclusion in the sample clearly defined?	Were the study subjects and the setting described in detail?	Was the exposure measured in a valid and reliable way?	Were objective, standard criteria used for measurement of the condition?	Were confounding factors identified?	Were strategies to deal with confounding factors stated?	Were the outcomes measured in a valid and reliable way?	Was appropriate statistical analysis used?
Balogh, O. <i>et al.</i> (2014)	Yes	Yes	Yes	Yes	Not clear	Not clear	Yes	Yes
Bronckers, I. M. G. J. <i>et al.</i> (2018)	Yes	Yes	Yes	Yes	No	No	Yes	Yes
DiBonaventura, M. <i>et al.</i> (2018)	Yes	No	Not clear	Yes	Yes	Yes	Yes	Yes
Korman, N. J. <i>et al.</i> (2016)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Lesner, K. <i>et al.</i> (2017)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Masaki, S. <i>et al.</i> (2016)	Yes	No	Yes	Yes	Not clear	Not applicable	Yes	Yes
Mattila, K. <i>et al.</i> (2013)	Yes	Yes	Yes	Yes	Not clear	Not applicable	Yes	Not clear
Moradi, M. <i>et al.</i> (2015)	Yes	Yes	Yes	Yes	No	Not applicable	Yes	Not clear

Ng, C. Y. <i>et al.</i> (2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Pearce, D. J. <i>et al.</i> (2006)	Yes	Yes	Yes	Yes	No	Not applicable	Yes	Not clear
Tang, M. M. <i>et al.</i> (2013)	Yes	Yes	Yes	Yes	Not clear	Not clear	Yes	Not clear
Weiss, S. C. <i>et al.</i> (2002)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Wu, Y., Mills, D. and Bala, M. (2009)	Yes	No	No	No	Not clear	Not clear	Yes	Not clear
Daudén, E. <i>et al.</i> (2013)	-	-	-	-	-	-	-	-
Hjalte, F., Carlsson, K. S. and Schmitt-Egenolf, M. (2018)	-	-	-	-	-	-	-	-
Sojević Timotijević, Z. <i>et al.</i> (2017)	-	-	-	-	-	-	-	-

Figure 4.3: Number of studies per country



Key: Number of studies



4.3.2 Reported treatments

About one-third of the identified studies reported treatments the population were receiving (n=5; 31.3%). Two studies reported topical, phototherapy, systemic non-biologic and biologic treatment (Korman *et al.*, 2016; Bronckers *et al.*, 2018). Similarly, two studies compared pre and post-biologic therapy in the study population (Moradi *et al.*, 2015; Hjalte, Carlsson and Schmitt-Egenolf, 2018). In another study, all patients received psoralen plus ultraviolet A (PUVA) phototherapy (Sojević Timotijević *et al.*, 2017). The rest of the studies did not report any intervention (n=11; 68.8%).

4.3.3 Identification, measurement and valuation of burden

The framework developed in chapter 2 was used to summarise and critique the articles in this review. The identified outcomes were health-related quality of life, disease severity and productivity loss as a beyond health measure. These outcomes were broadly classed into the welfarism or extra-welfarism analytical framework, see section 2.4.2

Identification of consequences

The majority of studies (n=13; 81.3%) estimated the health-related quality of life (HRQoL). Two identified studies reported on anxiety and depression. Very few studies explicitly reported disability as a consequence (n=3; 18.8%). Physical disease severity was reported in up to half of the identified studies (n=8; 50%).

One study identified individual preference as a consequence. Another one identified the impact on capability (wellbeing) as a consequence of psoriasis. Almost one-third of the studies reported productivity loss and impaired activity (n=5; 31.3%).

Studies using generic preference-based measures with valuation sets

Almost half of the studies reporting on HRQoL used the EQ-5D-3L (n=8; 47.3%) and the others (n=2; 12.5%) did not specify if it was the 3L or 5L. A quarter of the identified studies used the EQ-Visual Analogue Scale (EQ-VAS) (n=4; 25). The other generic, non-disease-specific, measures of health-related quality of life were SF-6, SF-12 and the SF-36. The SF-12 was used in 1 study (6.3%) and SF-36 was used in 4 studies (21.1%) (Weiss *et al.*, 2002; Daudén *et al.*, 2013; Ng *et al.*, 2015; Bronckers *et al.*, 2018; DiBonaventura *et al.*, 2018). The two studies reporting on anxiety and depression utilised the Hospital Anxiety and Depression Scale (HADS) questionnaire to measure the impact. No study reported the use of other generic measures such as the health utility index (HUI) and the ICECAP-A. Up to half of the identified studies reported the use of the disability life quality index (DLQI) to estimate the quality of life alongside generic-preference-based measures.

The Psoriasis Area Severity Index (PASI) was the most common tool used in measuring disease severity (n=11; 68.8%). Almost one-third of the studies used the Psoriasis Global Assessment (PGA) tool to measure disease severity (n=3; 31.3%).

Beyond health-Productivity loss

Seven studies had reported beyond health status outcomes (n=7; 43.8%). The most common consequence was productivity loss. A third of the studies identified reporting on productivity loss and activity impairment used the work productivity and activity impairment questionnaire for measurement (Pearce *et al.*, 2006; Wu, Mills and Bala, 2009; Korman *et al.*, 2016; Bronckers *et al.*, 2018; DiBonaventura *et al.*, 2018). One of the included studies that quantified the impact on wellbeing used the Satisfaction With

Life Scale (SWLS), a short 5-item instrument designed to measure global satisfaction with life (Arrindell, Heesink and Feij, 1999; Weiss *et al.*, 2002; Kobau *et al.*, 2010).

Valuation of consequences.

Valuation of consequences was dependent on the tool used to measure the consequences. For instance, a quarter of the identified studies using the EQ-5D used the UK tariff to value HRQoL consequences (n=4; 25%). One study reported using the Dutch EQ-5D tariff. A small number of studies using the EQ-5D did not attach any preference weights to the reported descriptive outcome (n=3; 18.8%) and one-eighth of the identified studies did not specify the EQ-5D tariff used (n=2; 12.5%) (Daudén *et al.*, 2009; Korman *et al.*, 2016; Masaki *et al.*, 2016; Lesner *et al.*, 2017; Sojević Timotijević *et al.*, 2017). The studies using the EQ-VAS used the patient's self-reported score that ranges from 0 to 100, where 0 is the worst and 100 is the best health status. The study reporting on individual preference used the WTP method to value the consequences of psoriasis (Masaki *et al.*, 2016).

4.3.4 Summary of estimated results

The quality of life in people living with psoriasis was reported to range from 0.62 in a study from Hungary to 1 (full-health) in a study from the Netherlands (Balogh *et al.*, 2014; Bronckers *et al.*, 2018). In the US, a survey reported a correlation between increased severity and a decrease in quality of life as shown by the mean EQ-5D scores of 0.93, 0.88 and 0.47 in mild, moderate, and severe cases respectively (Korman *et al.*, 2016).

Treatment was noted to be driven by disease severity. For instance, one study reported an overall EQ-5D score of 0.69 and EQ-VAS 64 in all psoriasis patients regardless of the type of treatment (Balogh *et al.*, 2014). When patients were stratified by treatment, those not taking any systemic treatment had the highest QoL (EQ-5D=0.75), those on non-biologic systemic treatment had the lowest QoL (EQ-5D=0.62), and those on biologics had an EQ-5D score of 0.65. These results were similar to those reported in a study from Malaysia (EQ-5D=0.64; EQ Vas=60.46) (Tang *et al.*, 2013). Biologics were reported to have a significant positive impact on EQ-5D scores. A Swedish study reported the mean EQ-5D score of 0.74 in biologics naïve patients and 0.82 after starting biologics treatment (Hjalte, Carlsson and Schmitt-Egenolf, 2018).

A Finnish study focusing on the impact of psoriasis on work found that 17% of the respondents considered their retirement was motivated by psoriasis. Those still in employment reported an average of 4.5 and 8.3 hours of lost productivity in terms of absenteeism and presenteeism respectively during the last four weeks (Mattila *et al.*, 2013). Another study from the US reported an odds ratio of 1.37 missed hours of work in the last week due to ill health for those with psoriasis as compared with the matched controls (Wu, Mills and Bala, 2009). Furthermore, presenteeism was reported with an odds ratio of 1.66 in psoriasis patients compared to matched controls (Wu, Mills and Bala, 2009).

4.4 Discussion

This study provides the first review focusing on the burden-of-disease in people living with psoriasis as a component of the economic impact of psoriasis. The review concentrated on the different methods of quantifying burden-of-disease considering the health and non-health consequences. Due to the heterogeneity of the study designs, outcome measures and lack of a gold standard, it was challenging to conduct an objective critical appraisal of the studies included in the review beyond description of the reported components.

Broadly, the identified burden-of-disease methods were based on the framework developed in chapter 2. The results in this review suggested that the number of burden-of-disease studies in people living with psoriasis using extra-welfarist approach components remains very small. Furthermore, no relevant UK study was identified in this review.

This review found that only a few studies used generic measures of health and non-health impact. The EQ-5D was the most common type of generic measure of health used which has validated preference weights to value the measured health description. The observed wide use of the EQ-5D is consistent across several disease areas (Devlin, 2016).

One study reported people living with psoriasis to be in perfect health based on EQ-5D scores of the surveyed groups (Bronckers *et al.*, 2018). This could be attributed to selection bias in the study having predominantly had mild cases as noted from the

DLQI score (Bronckers *et al.*, 2018). The majority of study participants' DLQI score was interpreted as 'no or small effect on the QoL'. When higher BMI was taken into consideration, young adults were reported to have a worse health state (Bronckers *et al.*, 2018). Although one of the studies included had used the EQ-5D to estimate HRQoL, it did not value the responses by attaching preference weights (Sojević Timotijević *et al.*, 2017). This makes it hard to compare findings across other studies using the EQ-5D.

One study reported a higher QoL in patients receiving biologics treatment (Hjalte, Carlsson and Schmitt-Egenolf, 2018). On the contrary, another study reported a lower QoL in patients receiving biologics treatment (Balogh *et al.*, 2014). The contradicting QoL reported in these studies could be attributed to different psoriasis severity in the sample sizes and duration of treatment (Balogh *et al.*, 2014; Hjalte, Carlsson and Schmitt-Egenolf, 2018). Considering biologic treatment is given as third-line the different QoL reported could be attributed to the severity of psoriasis in those receiving biologics and a survey conducted before the effects of the treatment takes effect.

This review showed that burden-of-disease studies in psoriasis have heavily relied on estimating the physical severity of the condition and disease-specific measures. Studies attempting to estimate burden-of-disease in psoriasis using generic measures have been biased towards estimating HRQoL using the EQ-5D. This has resulted in neglected measures of capability and wellbeing even though it has been established in most studies that psoriasis impact goes beyond physical appearance and health-related quality of life, the use of wellbeing tools has remained underutilised (Finlay and Khan, 1994; Novartis, 2015; Armstrong A *et al.*, 2021). Productivity loss in terms of absenteeism or presenteeism as a burden-of-disease estimate has also continued to be underutilised as can be seen from a very low number of studies estimating and reporting it. This could be attributed to a lack of clear guidelines on incorporating productivity loss in burden-of-disease estimates in many health care systems. Similar to reviews on other diseases, the hesitance to include presenteeism in burden-of-disease studies has been attributed to a lack of consensus on the definition (Jones, 2017).

A study across 13 different European countries found a significant variation in HRQoL among the different countries (Lesner *et al.*, 2017). The observed differences were speculated to be due to differences in culture, healthcare system organisations, access to treatment, and climate (Lesner *et al.*, 2017).

4.4.1 Strengths

This review collated all the evidence for the inclusion of generic health and non-health consequences of psoriasis. This review provided the first critical appraisal of the methods used to identify, measure and value the health and non-health consequences of psoriasis. The review summarised the literature by comparing the different measures of burden-of-disease in psoriasis. The review focused on the non-financial burden of psoriasis which included aspects beyond disease severity. This review was focused on the health and non-health burden-of-disease in people living with psoriasis. The use of the framework developed in chapter 2 to appraise studies in this review was noted to be one of the strengths.

Another strength of this review was the use of the CRD which guided the stages of conducting the review such as parallel independent assessment to minimise the risk of errors, third reviewer was further engaged to resolve conflicts, and piloting of the data extraction.

4.4.2 Limitations

The first limitation of this review was that only English publications were included. This potentially led to the omission of important information from non-English publications. Although the selected databases, Medline and Embase, were deemed enough, this did not eliminate publication bias as this approach made it unlikely to identify studies not published in peer-reviewed journals (CRD, 2009). Nonetheless, scanning reference lists of relevant studies was done to minimise the publication risk bias. This review was also limited by the scope of existing literature on burden-of-disease in people living with psoriasis. This limitation was compounded more by the exclusion of economic evaluation studies as they were beyond the scope of this study. Another limitation in this study was the exclusion of studies that did not include any generic measure of health, wellbeing or both. Exclusion of studies that did not use generic measures of health or wellbeing resulted in missing information describing such aspects as physical severity, signs and symptoms.

4.5 Conclusion

This review identified the lack of UK burden-of-disease studies in people living with psoriasis. This motivated the need to conduct a burden-of-disease study on people living with psoriasis in the UK, see chapter 6. The limited utilisation of beyond health measures of burden-of-disease was also identified. Taking into consideration the differences in HRQoL scores attributed to cultural differences across countries it was justified that a UK-specific study is conducted. The framework developed in chapter 2 and the identified gaps in this review guided the design for a burden-of-disease in people living with psoriasis in the UK presented in chapter 6.

5 Estimating health care costs attributable to psoriasis and the determinants of these costs

Chapter summary

This chapter reports a cost-of-illness study for people with psoriasis using longitudinal, linked CPRD-HES data covering the period 2007 to 2017. This study estimated the health care costs of patients living with psoriasis in England and factors influencing these costs. The association of obesity and comorbidities on health care resource use by people with psoriasis compared with matched controls without psoriasis was explored.

Section 5.1 of this chapter gives the background and motivation for the study.

Section 5.2 describes the study design which gives details of the study sample, the data sources and analysis procedures. This is followed by the presentation of results in section 5.3. Finally, section 5.4 presents the discussion and conclusion.

5.1 Background

Chapter 3 found that cost-of-illness studies conducted outside of the United Kingdom (UK) showed that psoriasis patients incur significant health care costs. Increasing health and care costs resulting from ageing populations more generally remains one of the major concerns of all countries (Carrascosa *et al.*, 2006). An accurate estimate of costs and their determinants for people with psoriasis is key in informing strategies to minimise costs and improve outcomes.

In recent decades, obesity has been globally recognised as an increasing public health concern (Roux and Donaldson, 2004). Although an association has been reported between psoriasis and metabolic disorders such as obesity, it is not clear how much this association drives health care costs (Colombo *et al.*, 2008). Additionally, obesity has not only been identified as one of the common comorbidities of psoriasis but has also been shown to influence both the occurrence of psoriasis and the severity of

symptoms (Colombo *et al.*, 2008; Paroutoglou *et al.*, 2020). Obesity is associated with higher incidence, prevalence and severity of psoriasis (Paroutoglou *et al.*, 2020).

Some studies have reported that people with inflammatory skin disease, including psoriasis, are relatively more likely to have other long-term conditions (Narla and Silverberg, 2020). Some of the most common comorbidities reported in psoriasis patients include psoriatic arthritis, hyperlipidaemia, hypertension and diabetes (Colombo *et al.*, 2008; Steven R Feldman *et al.*, 2015). For instance, psoriatic arthritis was one of the most common comorbidities affecting up to 10 to 15% of people living with psoriasis (Colombo *et al.*, 2008). These conditions have also been linked to a higher incidence and prevalence in obesity (Carrascosa *et al.*, 2006; Colombo *et al.*, 2008). The presence of comorbidities in psoriasis has a significant impact on health care resource use (Steven R Feldman *et al.*, 2015; Feldman *et al.*, 2017). Failing to account for comorbidities in cost-of-illness studies may lead to a substantial upward bias in the estimated expenditure impact of the condition of interest (Gunnarsson *et al.*, 2012).

At present, there are only two outdated cost-of-illness studies that have quantified the impact of drivers of health care costs in psoriasis patients in the UK (Poyner *et al.*, 1999; Fonia *et al.*, 2010). Since 2010, NICE has recommended 12 biologics for managing psoriasis in the NHS and obesity and morbidity due to chronic disease have increased in the UK population (Public Health England, 2018; NICE, 2021c). Other changes since 2010 include the organisation of the health system, population ageing, and the move towards integration of care and chronic disease management in the community setting. This is likely to impact NHS resource use and associated costs. Therefore, in this study, the influence of obesity and the presence of comorbidities on the use of NHS resources and associated costs for people living with psoriasis in the UK was explored using retrospective routinely collected electronic health record data.

5.1.1 Aim and objectives

This study aimed to estimate health care costs attributable to psoriasis and identify key drivers of NHS resource use in England using retrospective routinely collected electronic health record data.

The two objectives of this study were to:

1. Estimate the attributable cost of psoriasis on health care.
2. Understand the key drivers of healthcare costs in people with and without psoriasis by controlling for covariates (age, sex, Index of Multiple Deprivation (IMD), obesity and comorbidities).

5.2 Study design

This was a retrospective observational cohort study using a matched cohort design, in which control patients were matched with psoriatic equivalents based on gender, age and GP practice. Section 5.2.1 describes the data sources, data cleaning and structuring procedure. Section 5.2.2 describes the methods including healthcare resource use identification and the approach taken to generate an estimate of total healthcare costs. All analyses were estimated using Stata 16.0 (StataCorp LLC, College Station, TX).

5.2.1 Data

Data from the Clinical Practice Research Datalink (CPRD GOLD) linked to the Hospital Episodes Statistics (HES) and Office of National Statistics (ONS) mortality data were used in this study. These data covered the period from 01 April 2007 to 31 December 2017.

5.2.1.1 CPRD data structure

The CPRD GOLD dataset comes from a primary care database comprising anonymised electronic medical records from the general practices (GP) in the United Kingdom (UK) (Bhaskaran *et al.*, 2013; Herrett *et al.*, 2015; Gkountouras, 2020). Henceforth, the shorthand 'CPRD' shall be used to be synonymous with CPRD GOLD in this thesis unless where specified.

In the UK, up to 98% of the UK population is registered with a GP (Herrett *et al.*, 2015). As of 2015, nearly 8% (11.3 million) of the UK population from about 674 practices were included in CPRD (Herrett *et al.*, 2015).

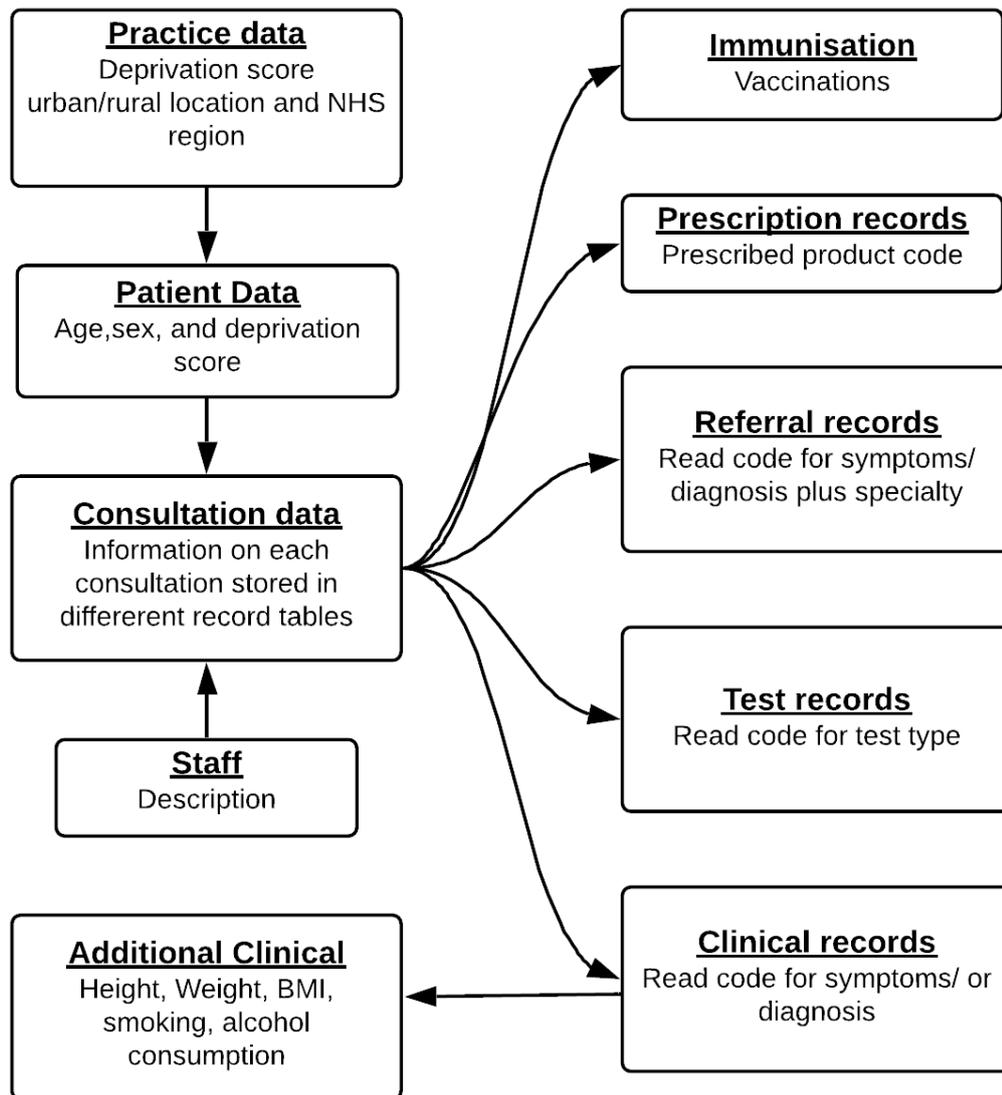
The UK runs a tax-financed, 'universal' health system in which most health care services are free at the point of use. The GP acts as the gatekeeper to the UK health system (Bhaskaran *et al.*, 2013; Herrett *et al.*, 2015). Therefore, GPs are the first point of contact for non-emergency consultations (Herrett *et al.*, 2015). These non-

emergency patients can be managed within primary care or referred to secondary care or both when deemed necessary (Herrett *et al.*, 2015). The gatekeeping setup allows for a general overview of the population's health as primary health records form the key to all other records.

Data from primary care service use are routinely recorded and subjected to quality checks. The auditing team in the Medicines and Health Products Regulatory Agency (MHRA) carry out the validity and quality control of the data received from GPs. The MHRA is an executive agency sponsored by the Department of Health and Social Care, that regulates medicines, medical devices and blood components for transfusion in the UK (MHRA, no date). Based on the audit, GP practices are designated as 'up to standard' (UTS) if they meet specified data entry criteria (Bhaskaran *et al.*, 2013).

CPRD has a total of ten files with the main ones being the patient, practice and consultation files. The other six files are the test, therapy, clinical, additional clinical, staff, and referral, see Table A5.1 in Appendix 5.1 for a description of the file contents. The database structure overview is depicted in Figure 5.1 (Gkountouras, 2020). Most of the information in the CPRD is stored in form of 'Read codes'. These codes support detailed encoding of multiple patient phenomes such as clinical signs and symptoms, diagnoses, laboratory tests and results as well as patient characteristics such as ethnicity, religion, occupation and social circumstances.

Figure 5.1: CPRD database structure overview



5.2.1.2 Cleaning and structuring CPRD data

In the first instance, irrelevant variables in the extracted CPRD files were dropped. Key measures of dates and time were constructed from the raw data: the period of primary care consultation was generated based on the index date and the event date. Each patient's index date was defined as the date on the first appearance of the psoriasis Read code (first recorded diagnosis) after the date at which the practice data were deemed to be of research quality, the date at which the patient's current period of registration with the practice began and within the study window. The follow-up period ended: when the patient either died (ONS death date), transferred out of the practice, last data collection (lcd), or the study period ends (31/12/17). The period of

primary consultation was calculated as the difference between the event date and the index date divided by the total number of days in a year (365.25 days). This resulted in a period of consultation ranging between years 0 and 10. The follow-up duration was also calculated as a difference between index date and follow-up end date, hence ranging from 0 to 10 years. The resulting primary care resource use file from CPRD data was merged with the secondary care utilisation file from HES using the unique patient ID.

5.2.1.3 Hospital Episodes Statistics (HES) data

To estimate secondary care resource use, this study used data from the 'admitted patient care' (APC), 'accident and emergency care' (A&E), and 'outpatient care' (OPC) from the Hospital Episodes Statistics (HES). HES are structured episode-level data of hospital care in England. These data cover hospital care records for all NHS Clinical Commission Groups (CCGs) in England including privately paid patients treated in NHS hospitals, non-English residents and care delivered by non-NHS providers but funded by the NHS (NHS Digital, 2021).

HES data are packaged into four main files; admitted patient care (APC), Accident and Emergency (A & E) attendance, outpatient visits and critical care in England (Boyd *et al.*, 2018; NHS Digital, 2021), see Table 5-1 for a summary of the information available from these files. The respective files contain records of hospital admissions, diagnoses and procedures, patient demographics, administrative information (such as admission and discharge date) and geographical information for the patient and the hospital location, see Table 5-1. Admissions data are captured under the admitted patient care (APC) data. This study used the admitted patient care, outpatient and A& E data files. A summary of the key fields in the different files of HES is given in Table 5-1.

Episode-level data in HES make up what is known as a spell. Spells refer to periods of continuous care under one hospital and are made up of episodes. A spell could be a single episode or multiple episodes and covers the period from admission to discharge.

An episode refers to periods of continuous care from a single specified consultant (Boyd *et al.*, 2018; NHS Digital, 2021). For example, a visit to the dermatologist and the cardiologist on the same day at the same institution will constitute two episodes that

combine into one spell. Therefore, each row in any one of the four HES files (for example, the APC), gives the number of 'finished' consultant episodes (FCE). The FCE refers to the time spent in the care of one consultant (Leal, Manetti and Buchanan, 2018). An indication of a finished episode was based on the financial year in which it ends. Episodes starting in one financial year and finishing in another were considered 'unfinished' in the year they began and 'finished' in the year they ended. Costs were thus attributed to the year in which the episode was deemed finished.

For this study, the diagnosis of psoriasis and existence of comorbidities was based on the CPRD data using Read codes. The estimated secondary care costs were based on the total secondary care resource use during the study period.

Table 5-1: Key HES field for each of the four domains

HES domain (File)	Identifier	Clinical Information	Demographic information	Administrative
Admitted patient care (APC)	HES ID* Episode ID Date of admission A&E link ID Provider details (e.g., hospital code). Registered GP practice	Diagnoses and procedures (up to 20 primary and secondary) Operation Dates Consultant Speciality Augmented care location	Age (years) at admission and discharge. Gender. Index of Multiple Deprivation (IMD). Health, Electoral and census geographies. Ethnic group.	Method of admission (e.g., elective or emergency, birth, transfer) Episode start and end date Discharge method (e.g., self- discharge, died, transferred) Discharge destination (e.g., home, other destination Time waited
Out-Patient (OP)	HES ID Appointment Date Registered GP practice.	Diagnosis (up to 12 primary and secondary diagnoses) Operative procedure(s) Consultant Speciality (E.g., Dermatologist, Cardiologist)	Age (years) at appointment Gender IMD	Attendance details Waiting time

			Health, electoral and census geographies Ethnicity	Appointment type (e.g., Face-to-face, telephone)
Accident and Emergency records (A&E) A&E	HES ID Appointment ID Arrival date and time Registered GP practice	Incident location Patient group (e.g., RTA, sports injury) Diagnosis (Up to 12 codes) Anatomical area and side A&E investigation (e.g., x-ray, toxicology)	Age (years) at appointment Gender IMD Health, electoral and census geographies. Ethnicity	Arrival mode (Ambulance or other) Attendance category (first or follow-up) Disposal (e.g., admitted, died, referred) Source for referral (e.g., self, GP, Police) Visit duration
Adult critical care	HES ID Provider code Start date and time Registered GP	Treatment function (e.g., transplantation surgery, burns, care) Critical care level and duration of care at the level	Age (years) at appointment Gender IMD	Admission source (e.g., same hospital, transfer) ACC Unit function (e.g., renal, neuroscience)

		<p>Variables indication duration of care in specific areas (e.g., renal support)</p> <p>Maximum number of organs being supported.</p>	<p>Health, electoral and census geographies</p> <p>Ethnicity</p>	<p>Discharge location (e.g., ward details home)</p>
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5.2.1.4 Cleaning HES data

The first step in cleaning HES data involved sorting the data by patient identifier, case, and event start and end date. In the first instance, HES were restructured from episodes to spells. A spell identifier was generated as a sequence variable to help identify episodes belonging to the same spell for each patient.

After grouping data into spells, appropriate data entry error checks were conducted such as not having an admission date after the follow-up end date. All admission dates were checked to ensure they occur after discharge within a given spell.

5.2.1.5 Study Sample

This study included patients with records classified as acceptable for research purposes, up to standard (UTS), in CPRD. The study population covered adults (≥ 18 years of age) people living with psoriasis in the CPRD with Index of Multiple Deprivation (IMD), HES and Office for National Statistics (ONS) mortality records linkage eligibility. The IMD is a measure of relative deprivation for small areas in England. This metric is made up of a combination of measures of deprivation based on a total of 37 separate indicators that have been grouped into seven domains. The seven domains include income, employment, education, health, crime, barriers to housing and services, and living environment (Ministries of Housing, 2019). These patients were identified using psoriasis Read codes in CPRD during the study period between 01 April 2007 and 31 December 2017, see Table A5.1 under Appendix 5.2 for psoriasis Read codes.

Each patient's index date was defined as the date on the first appearance of the psoriasis Read code (first recorded diagnosis) after the date at which the practice data were deemed to be of research quality, the date at which the patient's current period of registration with the practice began and within the study window. The follow-up period ended: when the patient either died (ONS death date), transferred out of the practice, last data collection (lcd), or the study period ends (31/12/17). The sample for

the control cohort was determined using matching methods outlined fully in section 5.2.1.7.2.

5.2.1.6 Identifying, measuring and valuing health care costs

5.2.1.6.1 Study perspective

The study perspective guides the identification, measuring and valuing of cost in a cost-of-illness study, see section 2.3.3. In the estimation of the cost-of-illness due to psoriasis, the NHS study perspective was taken in this study. The choice of the NHS study perspective informed the inclusion of resources incurred in the health care sector.

Health care resources were identified, measured and valued as detailed in the relevant sections below. The identifying was generally split into those resources incurred in primary care and those in secondary care. In the final analysis, the total cost was made up of primary and secondary care costs. A bottom-up approach was used in valuing primary and secondary costs.

5.2.1.6.2 Identifying primary and secondary care costs

Only direct medical costs incurred in the primary and secondary care sector were identified. Direct medical costs are those related to the resource use incurred in delivering formal health and social care, see section 2.3.5.1.

Resources identified under primary care were general practice consultations and prescription costs. Merging staff files with the consultation files allowed the identification of the role of the attending staff. Each consultation was assigned based on the staff role, and consultation type which could be surgery consultation, night visit, face-to-face, telephone consultation, and emergency consultation. Data from the merged staff and consultation file contained the role of the attending staff, type of activity and the duration of the activity for each consultation.

Prescription data from primary care consultations were obtained from the therapy file of the CPRD. Identified medicines prescribed in primary care were not limited to

psoriasis specific treatment. In the therapy file, the prescribed therapies are recorded using unique product codes. The quantities and number of days the treatment lasted are also indicated. The total quantity of medicine prescribed was obtained as a product of the prescribed daily quantities and the number of days of the treatment. Secondary care prescription costs were not included due to failure to identify the relevant information from the available CPRD and HES datasets.

The linked HES data were used to identify secondary care resource use. Secondary care resource use was identified in terms of the sector's service which included accident and emergency care (A&E), outpatient hospital visits and inpatient care. Outpatient attendances were identified in terms of the first appointment or follow-up appointments. Inpatient care was further identified in terms of the type of admission which could be elective, non-elective, or day-case.

5.2.1.6.3 Measuring primary and secondary care costs

Each of the identified resources was measured in terms of the quantity used. Under primary care, the resource use was measured in terms of the number of consultations and the duration of the consultation. The duration of the activity was rounded to the nearest minute. In the CPRD, activities lasting less than a minute were rounded to zero and those lasting more than what could be considered as a 'normal' duration of interaction had durations lasting more than an hour. The assumptions used during the analysis were that those activities having a zero-minute record were considered to last half a minute and those recorded as lasting more than one hour were cut off to be 60 minutes. These assumptions were similar to other studies using CPRD data (Gkountouras, 2020).

Secondary care resources identified were measured in terms of the number of appointments for out-patients, number of admissions for inpatient care and number of A&E visits. For inpatient care, the length of hospital stay was also measured. A threshold of three appointments from the same speciality per patient per day was set. This was assumed as the realistic number of attendances per patient per day. Therefore, observations that had more than three appointments per day were dropped. The number of patients with fewer than three appointments per day was

99.5 per cent. Before counting the number of appointments, only those appointments recorded (attendance type [atentype]) as attended the first appointment, attended subsequent appointment, and attended but unknown type were included.

5.2.1.6.4 Secondary care costs

The length of stay was another factor taken into account when attaching the relevant cost for inpatient care. The Health Resources Group (HRG) tariff was used to identify the unit costs relevant to the inpatient admission. The HRG tariff was based on the type of admission. This tariff is a lump sum paid for each activity given the type of admission and influenced by the length of stay. In cases where the length of stay was beyond a set threshold called the trim point, an additional amount was considered to be paid to the provider. The addition amount is calculated as a product of the HRG-specific per diem rate the difference between the length of stay and the trim point.

For the rest of the identified secondary care resources, the quantity used was, e.g., the number of outpatient visits, and the number of A&E visits was the measure of the quantity of the resource used.

Total costs across all health care activities were aggregated to a year-total for each patient. Years in which a patient had no health care activity were assigned a cost of zero. Data outside the observation period were excluded by dropping all observations before 1st April 2007 and after 31st December 2017. The annual total costs for each patient were estimated.

5.2.1.6.5 Unit costs and valuing primary and secondary care costs

Unit costs refer to the total expenditure incurred to produce one unit of output (PSSRU, 2021). In health and social care, this could be the cost of one dose of a biologic used in treating psoriasis, one hour of GP time, one dermatologist outpatient consultation, or one hospital admission. The source for unit costs was dictated by the cost category. Three main sources for unit costs were utilised to value primary care and secondary care resources identified and measured. The unit costs were all expressed in the 2018 prices using the Healthcare inflation price index (Curtis and

Burns, 2016). Unit costs are useful for providers and payers to estimate the most efficient use of the available resources.

Two sources of unit costs were used in valuing primary care resources. One of the sources for unit costs was used in valuing general practice consultation and another was used to value the primary care prescriptions. The unit costs used in valuing general practice consultation were obtained from the Personal Social Services Research Unit (PSSRU) (Curtis and Burns, 2016). The PSSRU unit costs of health and social care are compiled and published annually since 1992 (Curtis and Burns, 2016). The cost estimation approach used under the PSSRU is based on economic theory and is both transparent and flexible (PSSRU, 2021). To ensure reliability, transparency and flexibility, the cost estimation approach ensures that financial implications for all services are included, unit costs reflect the long-run marginal opportunity costs for that service, a bottom-up approach is taken, sources are fully referenced, account for several responsibilities of care staff and regional weightings are provided where possible (PSSRU, 2021). The PSSRU gathers information needed to estimate unit costs by performing literature searches of new studies, drawing information from secondary data sources, collaborating with relevant organisations, and occasional commissioning primary research.

The CPRD AURUM was used as a source for unit costs used in valuing medicines for primary care prescriptions. Data from the therapy file in CPRD GOLD and the drug issue file containing the product codes and corresponding prices in the CPRD AURUM were used in costing medicines. Lookup tools were used to identify product codes from CPRD GOLD and AURUM which were matched using product descriptions.

The Health Resources Group (HRG) tariff was used as a source for the unit costs relevant to the secondary care resource which included A&E, inpatient, and outpatient care. The HRG tariff is a currency, unit of healthcare for which a payment is made, of the national tariff payment system (NTPS) (NHS England, 2021). The NTPS refers to the payment system used by the commissioner and providers of secondary healthcare in England by setting the rules and prices used by commissioners to pay providers for NHS services (NHS England, 2021). Two other potential sources of unit costs for costing hospital care are FCE-level reference costs and spell-level reference costs (Leal, Manetti and Buchanan, 2018). The reference costs represent the cost of providing one

unit of care in a given financial year and reflect direct medical and overhead costs incurred by the NHS provider (Leal, Manetti and Buchanan, 2018). Only the tariff unit costs were used in this study.

All forms of NHS secondary care services, with a few exceptions, are covered by the tariff (NHS England, 2021). Some prices excluded from the HRG tariff price are specific medicines that are typically only prescribed by specialists such as biologics and offered by a selected and relatively small number of centres (NHS England, 2021).

For inpatient care, the HRG tariff was based on the type of admission which could be elective or non-elective (NHS England, 2021). Elective care refers to scheduled care in contrast to unplanned admission in emergency cases (NHS England, 2021). This tariff is a lump sum paid for each activity given the type of admission and influenced by the length of stay. In cases where the length of stay was beyond a set threshold called the trim point, an additional per-day amount was considered to be paid to the provider. The addition amount is calculated as a product of the HRG-specific per diem rate the difference between the length of stay and the trim point.

In the cost valuation, each identified and measured resource was multiplied by the relevant unit cost. For outpatient visits, the unit cost used was dictated by the type of visit i.e., first, follow-up, consultant-led, or non-consultant led.

5.2.1.6.6 Identifying comorbidities

The number of people with multiple long-term conditions (comorbidities occurring with psoriasis) seen by GPs and specialists has continued to be significant and put pressure on healthcare systems (Payne *et al.*, 2020). Several methods have been employed to estimate the impact of living with multiple long-term conditions on healthcare systems (Payne *et al.*, 2020). Some of the methods used to quantify comorbidities include simple counts of the conditions and weighted approaches (Payne *et al.*, 2020). Although simple counts of conditions show an association between the number of conditions and outcomes such as health care utilisation, they do not give allow for differences in the strength of association between specific conditions and the given outcome like weighted approaches do. One of the most common weighted approaches that have been used since the 1980s is the Charlson

Comorbidity Index (Payne *et al.*, 2020). The advancement in clinical practice since the development of the Charlson Comorbidity Index and the basing of the weightings on outcomes such as death has cast doubts on its effectiveness in estimating outcomes such as health care utilisation (Zavascki and Fuchs, 2007; Payne *et al.*, 2020). The highlighted issues with the Charlson Comorbidity Index led to the development of the Cambridge Multimorbidity Score. The Cambridge Multimorbidity Score is a simple measure of comorbidities developed using data from 148 GP practices in the UK contributing data to CPRD records and weighted on different clinical outcomes making it useful in studies using health care resource use as an outcome (Payne *et al.*, 2020).

The calculation of the Cambridge Multimorbidity Score in this thesis was based on 20 common comorbidities (Payne *et al.*, 2020). The disease status, of the 20 Cambridge Multimorbidity Score diseases, was based on the information from the medical code (medcodes), product code (prodcodes) and entity type (enttype) which was merged with the patient list. For anxiety or other neurotic disorders, the condition was identified based on the Read code in the last 12 months or at least 4 anxiolytic/hypnotic prescriptions in the last 12 months. This was also the same for depression, irritable bowel syndrome, and eczema. Asthma and epilepsy were identified based on the existence of a Read code or prescription in the last 12 months. Migraine and other painful conditions were identified based on at least 4 prescriptions in the last 12 months. Kidney disease was identified based on the enttype. The rest of the conditions were based on the Read code ever recorded. Logic rules were then applied to the Read codes, product codes and test codes. A detailed presentation of the method to calculate the CMS in the study has been given in Appendix 5.3.

5.2.1.6.7 Identifying BMI data

Weight, height and body mass index (BMI), data were recovered from the “additional file” of CPRD under entity type. BMI, weight and height records were identified based on the entity type (enttype) code (CPRD, 2021). The enttype is an identifier representing the structured data area in CPRD which entails the data entered. The enttype code 13 indicated the presence of weight record in kilograms (kgs) under the data1 column and BMI under data3. The enttype code 14 indicated the availability of

height in meters (m) recorded in data1. There was a need to clean the data, considering that some records for weight, height or BMI tend to be implausible. Besides having some implausible values, some measurements for BMI, weight or height were missing. Due to the missing BMI data, there was a need to impute BMI values, see appendix 5.4. The method of BMI data imputation was based on the `mibmi` command in Stata (Kontopantelis *et al.*, 2017).

Data cleaning of the variables BMI, weight and height were performed according to a published procedure (Bhaskaran *et al.*, 2013). The minimum age at height, weight and BMI fitting within the lookback period was 18 years. It was assumed that BMI is only a good predictor of per cent body fat in adults hence a good measure of obesity and fluctuations in over 18-year-olds are not drastic (Vanderwall *et al.*, 2017).

The BMI cleaning was considered on those with a record at the index date (baseline BMI). In addition, those with the event date close to the index date and have weight and height records separately were included. Available weight records were married with the nearest height record (within 5 years provided the record was taken at least at age 18 years). The maximum look-back period was three years prior to the index date for weight and BMI and the minimum age at the time of the event was 18 years. For an individual that did not have their BMI recorded but had both weight and height records, the BMI was calculated using the formula in Equation 5.1. Observation with no record of BMI, height and weight or neither height nor weight were excluded.

$$BMI = \frac{w}{h^2} \quad \text{Equation 5.1}$$

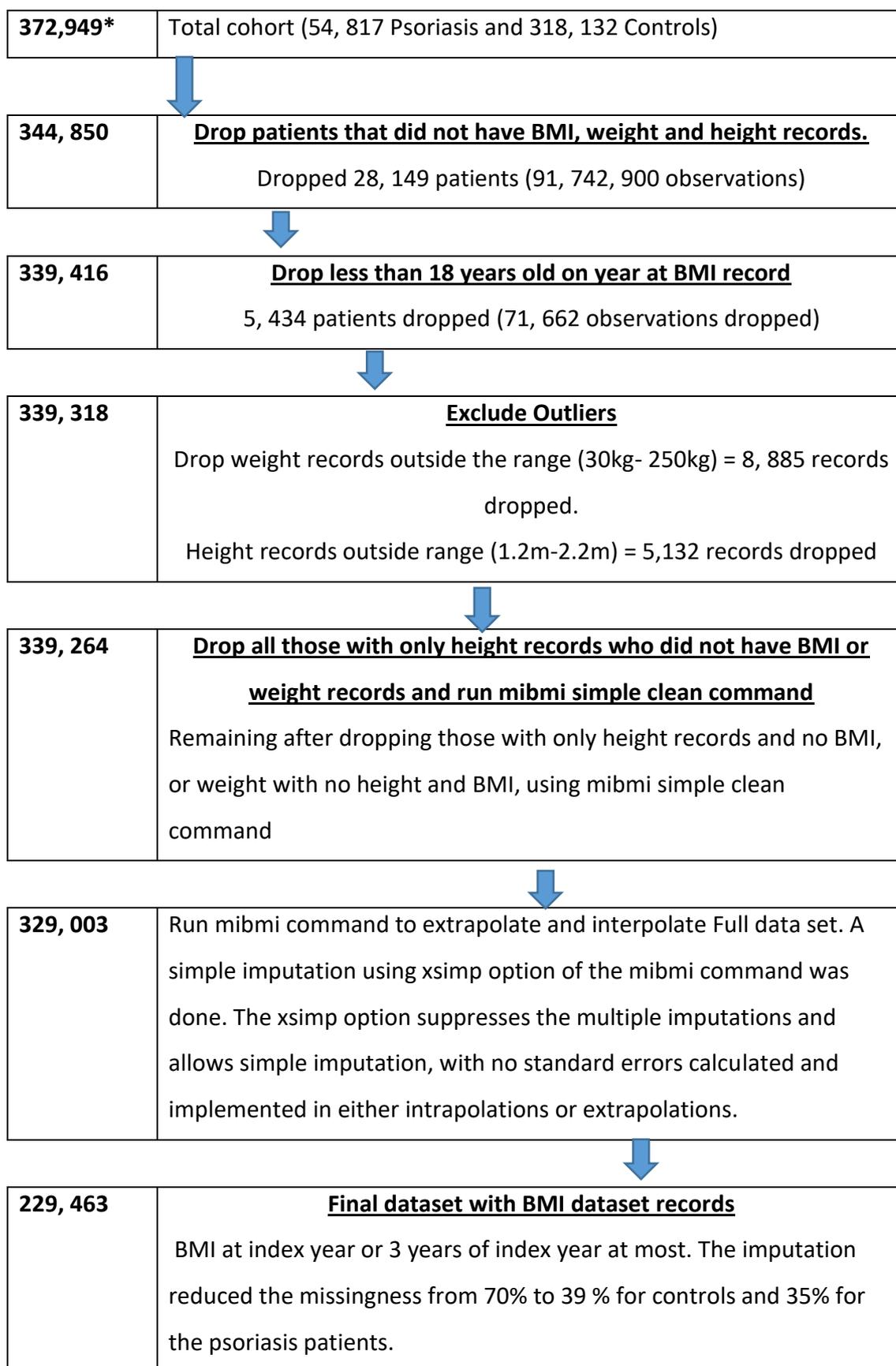
Where w represents weight in kgs, and h represents height in meters.

After calculating BMI, all those observations with an age at BMI record of less than 18 years were dropped. This process was then followed by the exclusion of observations with outliers. The outliers excluded were those with a height below 1.2 metres or higher than 2.2 metres. Those with weight below 30kgs or above 250kgs were also excluded. The time-window frame was generated from the difference between the index date and event date on either side of the index date i.e., before and after the

index date. Only those observations with event date occurring at the index date or closest to the index date were considered. The minimum date for weight and height were considered separately because if there was no information on height on the same date weight was recorded, information on height closer to that record was considered. The data was later explored for the existence of doubles. Preference was given to records with both weight and BMI as compared to those with weight only because using BMI and weight, one could calculate the height. Also, doubles for weight or height resulting from the difference between index date and event date being equal before and after the index date were dropped.

The relevant BMI ranges were defined according to the categories recommended by NICE. Further data cleaning and imputation were carried out using the `mibmi` command for BMI see appendix 5.4.

Figure 5.2: BMI data cleaning and imputation process.



**=51 patients with index date beyond 31st December 2017 were excluded.*

5.2.1.7 Analytical methods

Descriptive statistics methods and regression analysis were used to analyse the data.

5.2.1.7.1 Descriptive analysis

Descriptive analyses of patient characteristics were performed using standard descriptive statistics for continuous and categorical variables. The factors considered were case, age, gender, smoking status, alcohol consumption, body mass index (BMI), and the index of multiple deprivation (IMD).

For continuous variables, relevant descriptive statistics included the number of observations, minimum and maximum, means, standard deviations, and median. Frequency tables and proportions for categorical variables were reported. Unadjusted values were compared between the matched psoriasis patients and the controls using formal tests for statistical significance.

5.2.1.7.2 Matching

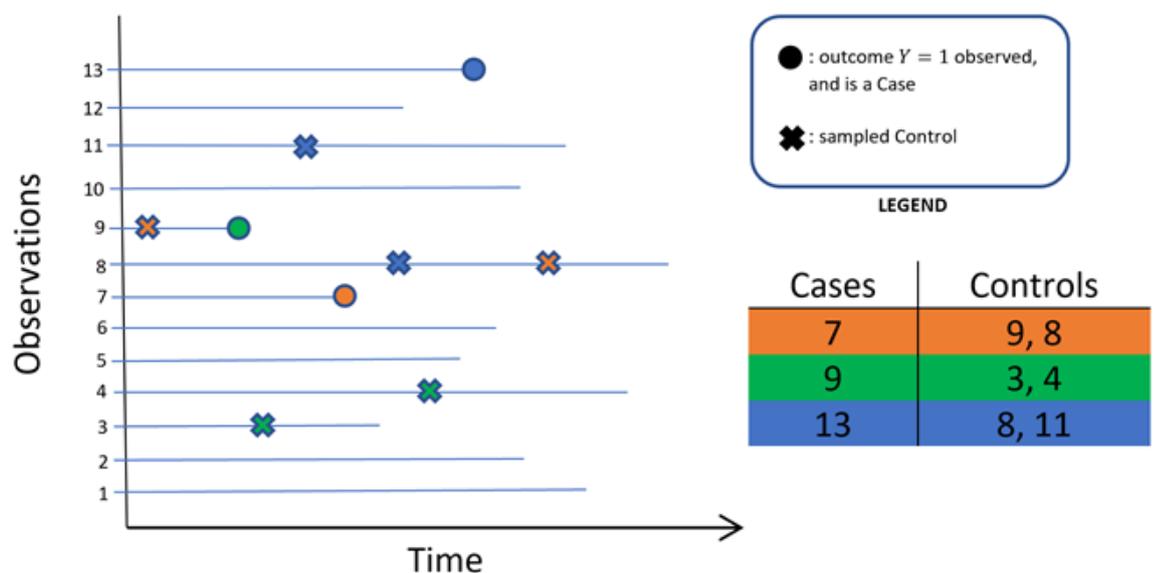
Individuals with a psoriasis diagnosis were identified by a diagnostic Read code in the primary care record (CPRD) within the study window as detailed above in section 5.2.1.5. To allow for comparability across the cases and controls and to minimise selection bias matching was applied to construct the study population in which selected variables (index date, age, sex, and GP practice) have the same distribution (Jones, 2007; Angrist and Pischke, 2014; Hernán and Robins, 2020). Estimating attributable costs using regression relies on the assumption that selection bias is minimised when key observed variables have been made as similar as possible across the case and control groups (Jones, 2007; Angrist and Pischke, 2014).

Incidence density sampling was used to select control patients for the matching. The incidence density sampling method was chosen because it is the recommended unbiased method for sampling controls. Under incidence density sampling, controls are selected from the at-risk source population at the same time as cases occur with a weighted random sampling based on the length of person-time (Alexander *et al.*, 2015; Rothman, 2020). The incidence density sampling method allows for controls to become cases over the course of the study (Alexander *et al.*, 2015). Secondly, observations were sampled with replacement, which meant that one control could be

matched with several cases (Rothman, 2020). Figure 5.3 illustrates the incidence density sampling method, (Rothman, 2020).

Each eligible psoriasis patient was matched with six non-psoriasis controls (1:6 matching ratio) on the index date of psoriasis, year of birth (as age marker), sex, and general practice. The reason for matching on 1:6 is because psoriasis is relatively rare and the higher ratio gives more statistical power (Hennessy *et al.*, 1999; Stuart and Rubin, 2008; Parisi *et al.*, 2019; Trafford, 2021). The matching ensured an accurate estimate of the differences in costs that can be attributable to psoriasis.

Figure 5.3: Illustration of incidence density sampling



Republished with permission of Andrew Rothman (2020)

This figure illustrates incidence density sampling. Coloured Xs represent corresponding sampled controls.

Observation (individual) 9 was sampled as a control match for 7 but later became a case. Observation 8 was sampled twice as a control i.e., for 7 and 13. Observation 8, with longer person-time, has a higher probability of being sampled as a control than observation 12.

5.2.1.7.3 Regression analyses.

To examine how health care costs compare in psoriasis and non-psoriasis controls, the primary dependent variable for this study 'total annual health care costs (per patient)'

was constructed. Other secondary dependant variables were mean annual primary care costs and secondary care costs. The primary care costs were further split into GP consultation and prescription costs. Secondary care costs were split into outpatient, inpatient and A&E costs. The secondary dependant variables were necessary to establish which component of costs was mainly influenced by psoriasis, obesity and multimorbidity. The main explanatory variable of interest was a binary indicator for whether the patient has psoriasis or not.

Regression analyses were used to examine the relationship between total annual costs per patient and psoriasis. A number of covariates were included (age, sex, IMD, obesity and CMS) which are likely to affect health care costs. The most important step in regression analyses is the choice of the estimation method and this choice was guided by several assumptions.

One of the estimation methods for linear regression modelling is Ordinary Least Squares (OLS). OLS represents the simplest and most commonly used linear econometric estimator (Gujarati, 2004; Wooldridge, 2010; Devlin, Parkin and Janssen, 2020). OLS is based on the process of minimising the squared difference between the observed values of a random variable and the predicted values by the model (Wooldridge, 2002; Angrist and Pischke, 2014). Although OLS is recommended in most instances, it is bound by the assumptions of;

- Linear models (in parameters)
- Zero conditional means. The error terms are assumed to be random with a zero mean.
- Absence of serial correlation across observations.
- All observations are randomly sampled from the population.
- Homoskedastic error term. This means variances of the error terms exist and are all equal.

The dependent variables in this study, mean annual health care costs, mimic the properties of underlying health care resource use. Measures of health care resource use exhibit marked skewness, due to a small number of very high resource use

patients comprising a disproportionate share of population costs, nonnegative measurements, and a nontrivial fraction of zero outcomes (Jones, 2007). These highlighted properties of health care costs violate OLS assumptions. Also, this study used a panel data structure which violates the assumption of independent observations hence rendering OLS inappropriate (Rice and Jones, 1997). This led to a search for alternative econometric estimation methods for non-linear models.

Count data regression techniques, such as Poisson and negative binomial regression, have been shown to be appropriate for health care resource use data. This study considered non-linear alternatives to standard linear regression approaches based on whether the outcome exhibited marked skewness. The choice of count model depended on whether the assumption of mean-variance equivalence was met (in the case of Poisson regression), or whether the variance exceeded the mean (in the case of negative binomial regression).

In addition to these covariates (age, sex, IMD, obesity and multimorbidity score), a patient-specific random effect was included in the regression analyses to minimise bias in estimating costs for patients with different levels of severity. Standard errors were clustered on patient ID, and (where appropriate) effects were reported as incidence rate ratios to aid interpretation (compared with exponentiated coefficients). Marginal effects were also estimated, which gave a predicted value for each regression run. The rationale to estimate marginal effects was to show the actual difference in monetary terms rather than IRR. Keeping to the assumption of holding other variables constant, the marginal effects were estimated at the reference category across all models: males from the fifth IMD decile aged between 48 and 57. The reference category variable was selected to reflect the mean age of the study population, healthy BMI (18.5 to 25) and the middle index of multiple deprivation.

Table 5-2 gives an outline of the model build and specifications to help meet the set objectives. The initial model (model 0) started with regression estimates of the psoriasis impact on mean annual health care costs controlling for age, sex, sex-age interaction and duration with psoriasis. Model 1 was then built by adding more controls to model 0, i.e., comorbidity and obesity category, to estimate the influence of comorbidities and obesity on costs. Model 2 was based on adding psoriasis and

comorbidity interaction, model 3 was an addition of psoriasis-obesity interaction to model 2 and model 4 was an addition of the triple interaction of psoriasis, obesity and comorbidity.

Table 5-2: Model Specifications

Explanatory variables	Model ID
Psoriasis, sex, age category, sex*age category, duration with psoriasis	0
Model 0 + Cambridge Multimorbidity Score (CMS), obesity category.	1
Model 1 + psoriasis*CMS interaction terms	2
Model 2 + psoriasis*obesity	3
Model 3 + psoriasis*Obesity category*CMS	4

5.2.1.7.4 Time horizon

The primary analysis in this study was a 6-year follow-up duration model. The 6-year cut-off was chosen because it was the mean follow-up duration for the study population. Furthermore, a secondary analysis was conducted using the full 10-year study period for the total healthcare costs and a 6-year follow-up duration for primary care costs and secondary care costs. The unit costs were all expressed in the 2018 price year and British Pound (£) using the Healthcare inflation price index (Curtis and Burns, 2016).

5.3 Results

5.3.1 Descriptive statistics

Table 5.3 summarises the study sample characteristics. The final study sample comprised 372,949 individuals (N=2,098,699 observations) for the period 2007 to 2017. The psoriasis group was made up of 54,817 individuals (N=282,300 observations) and the control group had 318,132 individuals (N=1,816,399 observations). A total of 2,667 individuals that were initially sampled as controls became cases (incident) during the observational period from 2007 to 2017.

The mean age at baseline was similar in both groups at 50.1 years for controls and 50.4 for psoriasis patients. The frequency of the age categories has been provided in Table

5.3. The proportion of males and females was similar in both psoriasis and the control group. There were slightly more females, representing 52.2% in both study groups. The distribution of patients in psoriasis and control groups by age and IMD were similar, see Table 5-3.

A slightly higher proportion of obese (30 to 39.9 kg/m²) and severely obese (at least 40kg/m²) people were observed in the psoriasis group than in the control group. The number of smokers and those who quit smoking was higher in the psoriasis group (n= 7,647; 29.4%) than in the control group (n=30,181; 22.7%). A similar proportion of the psoriasis group consumed alcohol (n= 8,467; 78.0%) as compared to the control group (n= 44,576; 78.5%).

The mean number of comorbidities was found to be higher in the psoriasis group (mean=1.8) compared to the control group (mean=1.3), see Table 5.3. Consequently, the Cambridge multi-morbidity score was also higher in the psoriasis group (mean= 0.5) compared to the control group (mean=0.4).

Table 5-3: Study sample baseline characteristics

	Control group n=318,132	Psoriasis n=54,817	Total n=372,949
-Sample demographic-			
Gender			
Male	152,013 (47.8%)	26,204 (47.8%)	178,217 (47.8%)
Female	166,119 (52.2%)	28,613 (52.2%)	194,732 (52.2%)
Age at index date (years)			
Mean (SD)	50.1 [17.1]	50.4 [16.9]	50.1 [17.0]
Range	18 to 103	18 to 103	18 to 103
18 to 27 years	32,893 (11.4%)	5,600 (11.2%)	38,493 (11.4%)
28 to 37 years	44,374 (15.3%)	7,578 (15.2%)	51,952 (15.3%)
38 to 47 years	54,921 (19.0%)	9,388 (18.8%)	64,309 (19.0%)
48 to 57 years	53,169 (18.4%)	9,098 (18.3%)	62,267 (18.4%)
58 to 67 years	51,035 (17.7%)	8,783 (17.6%)	59,818 (17.6%)
68 to 77 years	34,036 (11.8%)	5,904 (11.8%)	39,940 (11.8%)
Over 77 years	18,686 (6.5%)	3,482 (7.0%)	22,168 (6.5%)
BMI ranges			
Underweight (<18.5)	3,192 (1.6%)	517 (1.4%)	3,709 (1.6%)
normal weight (18.5-25)	65,163 (32.4%)	10,276 (28.6%)	75,439 (32.3%)
Overweight (26-29)	75,586 (37.6%)	12,751 (35.5%)	85,337 (36.5%)
Obese (30-39)	49,865 (24.8%)	10,692 (29.7%)	60,557 (25.9%)
Severely obese (>40)	7,044 (3.5%)	1,720 (4.8%)	8,764 (3.7%)
MISSING	120,282 (37.8%)	18,861 (34.4%)	13,9143 (37.3%)
Smoking status			
Yes	30,181 (22.7%)	7,647 (29.4%)	3,7828 (10.1%)
No	62,757 (47.2%)	9,133 (35.1%)	71,890 (5.2%)
Ex	39,925 (30.0%)	92,63 (35.6%)	49,188 (31.0%)
MISSING	185,269 (58.2%)	28,774 (52.5%)	21,4043 (57.3%)
Alcohol consumption			
Yes	44,576 (78.5%)	8,467 (78.0%)	53,043 (78.4%)
No	10,112 (17.8%)	1,864 (17.2%)	11,976 (17.7%)
Ex	2,127 (3.7%)	530 (4.9%)	2,657 (3.9%)
MISSING	261,317 (82.1%)	43,956 (80.2%)	30,5273 (81.9%)
Comorbidity			
No. of comorbidities, mean			
[range; SD]	1.3 [0 to 17; 1.8]	1.8 [0 to 17; 2.1]	1.3 [0 to 17; 1.8]
With 0 conditions, %	49.8	38.7	48.2
With 1 condition, %	21.5	22.5	21.7

	Control group n=318,132	Psoriasis n=54,817	Total n=372,949
-Sample demographic-			
With 2 conditions, %	9.8	11.9	10.1
With >= 3 conditions, %	18.9	26.9	20.0
Cambridge Multimorbidity Score,			
mean [SD]	0.41 [0.6]	0.56 [0.9]	0.4 [0.6]
IMD deciles			
IMD 1, Most deprived	40,320 (12.7%)	6,947 (12.7%)	47,267 (12.7%)
IMD 2	37,102 (11.7%)	6,516 (11.9%)	43,618 (11.7%)
IMD 3	36,244 (11.4%)	6,267 (11.4%)	42,511 (11.4%)
IMD 4	34,832 (11.0%)	5,909 (10.8%)	40,741 (10.9%)
IMD 5	31,519 (9.9%)	5,388 (9.8%)	36,907 (9.9%)
IMD 6	30,712 (9.7%)	5,286 (9.6%)	35,998 (9.7%)
IMD 7	30,035 (9.4%)	5,140 (9.4%)	35,175 (9.4%)
IMD 8	29,587 (9.3%)	5,068 (9.3%)	34,655 (9.3%)
IMD 9	25,405 (8.0%)	4,403 (8.0%)	29,808 (8.0%)
IMD 10, least deprived	22,041 (6.9%)	3,840 (7.0%)	25,881 (6.9%)
MISSING	335 (0.1%)	53 (0.1%)	388 (0.1%)

IMD= Index of Multiple Deprivation, SD = standard deviation. Proportions are presented in parenthesis and standard deviations in brackets.

A comparison of health care resource use and costs for the study period is outlined in Table 5-4. The mean annual health care resource use and costs per person were higher in the psoriasis group compared to the controls. The annual primary care costs were 47.48% higher per patient for psoriasis patients compared with corresponding controls (£428.31 vs £290.41). A similar pattern was observed in annual secondary care costs which were 49.94% higher per patient for the psoriasis patients compared with corresponding controls (£ 563.04 vs £ 375.50). Overall, the mean annual total healthcare costs per person were 48.87% higher in the psoriasis groups compared to controls (£ 991.35 vs £ 665.90).

The psoriasis group had 41.2% more admissions compared to the control groups per person per year (0.24 vs 0.17). In addition, the length of stay was 70% longer in the psoriasis group compared to the control group (0.51 vs 0.30). This resulted in 46.6%

higher inpatient costs in the psoriasis group compared to the control group (£359.55 vs 245.23).

Table 5-4: Health care resource use and costs per patient summary statistics for the period 2007 to 2017

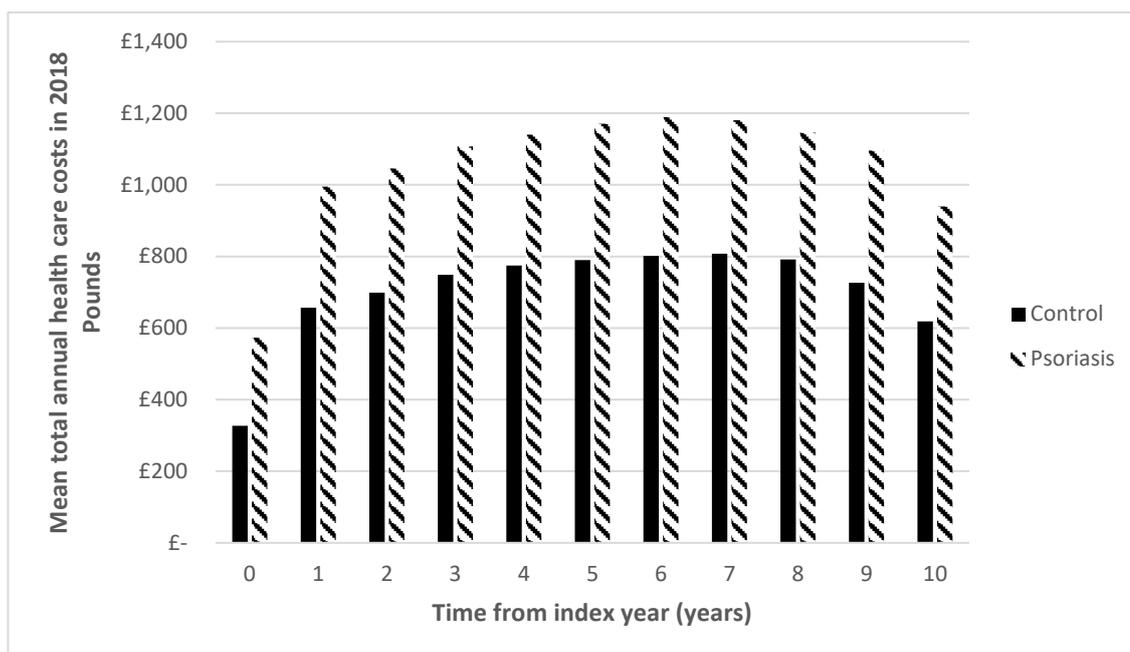
	Means [SD]	
	Psoriasis (1)	Control (2)
GP visits	10.91 [12.87]	7.95 [10.64]
GP costs	£ 191.40 [253.2]	£135.69 [208.80]
Prescription costs	£ 236.87 [541.90]	£ 154.70 [440.55]
Total primary costs	£ 428.31 [681.30]	£ 290.41 [552.87]
Outpatient visits	2.00 [5.03]	1.06 [2.91]
Outpatient costs	£ 176.91 [422.71]	£ 110.33 [301.29]
Hospital admissions	0.24 [1.20]	0.17 [1.20]
Hospital LOS	0.51 [4.4]	0.30 [3.25]
Inpatient costs	£ 359.55 [1,627.72]	£ 245.23 [1,246.53]
A&E visits	0.26 [0.91]	0.20 [0.66]
A&E costs	£ 26.58 [91.30]	£ 19.95 [68.54]
Total secondary costs	£ 563.04 [1,837.99]	£ 375.50 [1,410.10]
Total health care costs	£ 991.35 [2,153.50]	£ 665.90 [1,662.84]

Notes: This table reports means for health care resource use and costs. Column (1) and (2) shows the mean of psoriasis and non-psoriasis control group respectively. Standard deviations (SD) are reported in brackets

Figures 5.4, 5.5 and 5.6 show the trends over time for the mean total health care, annual primary care and secondary care costs for psoriasis versus controls during the 2007 to 2017 study period, respectively. The figures are based on the time elapsed from index year. In all the three figures, the mean cost under the psoriasis group was higher than that under the control group. The mean annual primary care costs were observed to be increasing with each passing year (

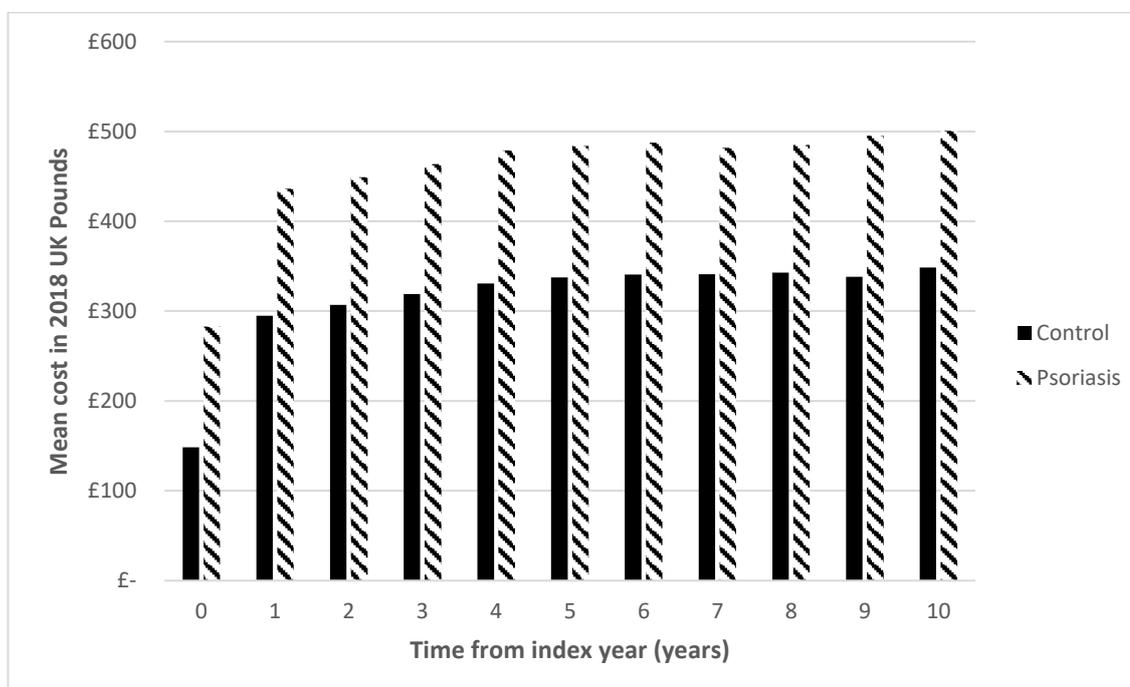
Figure 5.5). For instance, the primary care cost for the psoriasis group was just slightly under £ 300.00 per patient in the index year and almost £500.00 in year 10 in the psoriasis group.

Figure 5.4: Mean total annual health care costs per patient by psoriasis status



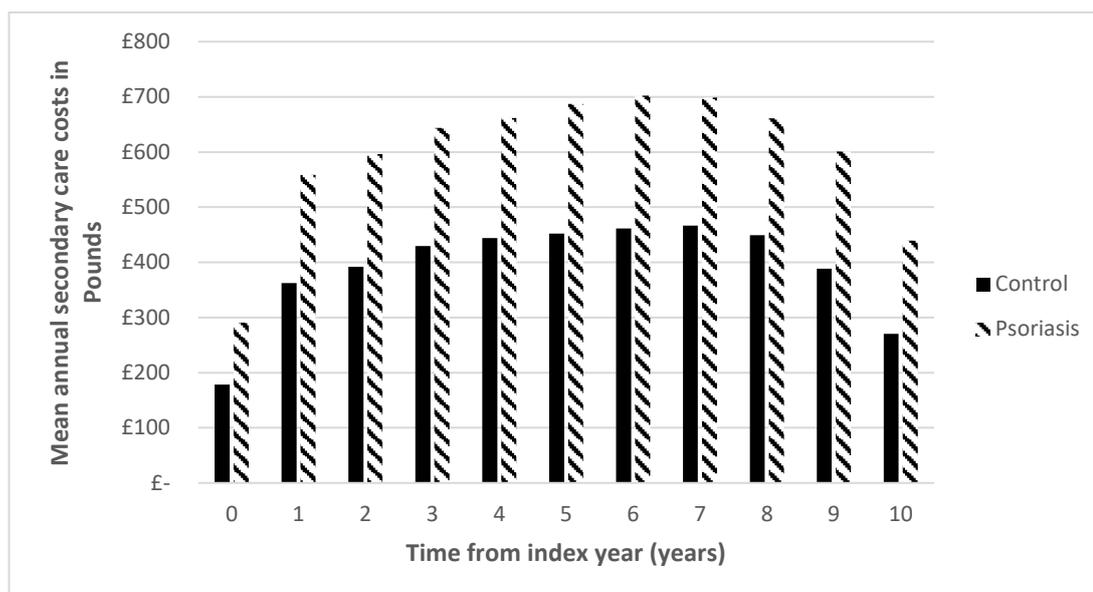
Note: The figure shows the mean annual total health care costs of psoriasis versus non-psoriasis control using patient-level data on activity from linked CPRD-HES for the year 2007 to 2017. This was a sum of primary care and secondary care costs for the 2018 price year.

Figure 5.5: Mean annual primary care cost per patient by psoriasis status



Note: The figure shows the mean annual primary care costs of psoriasis versus non-psoriasis control using patient-level data on activity from CPRD for the year 2007 to 2017. Unit costs were PSSRU for GP consultation and drug prices from CPRD-AURUM for the 2018 price year.

Figure 5.6: Mean annual secondary health care costs per patient by psoriasis status



Note: The figure shows the mean annual secondary care costs of psoriasis versus non-psoriasis control using patient-level data on activity from HES for the year 2007 to 2017. Unit costs were from the national reference costs schedule for the 2018 price year.

5.3.2 Regression analysis

This section presents the results from the regression analyses, in which negative binomial regression was used to estimate the primary and secondary analyses based on the significance of the dispersion parameter. The reference category was: males from the fifth IMD decile aged between 48 and 57 years with healthy BMI (18.5 to 25kg/m²).

5.3.2.1 Costs attributable to psoriasis

Results from the negative binomial regression estimating the costs attributable to psoriasis in the first 6 years of the study period are shown in Table 5.5. Models were estimated for mean total health care costs, primary care costs and secondary care costs with results for each of these presented in sections 5.3.2.1.1, 5.3.2.1.2 and 5.3.2.1.3.

5.3.2.1.1 Health care costs

The mean annual health care costs for individuals with psoriasis were 1.4 times higher than individuals in the control group [IRR=1.40; 95% CI 1.34-1.46]. Mean annual health care costs were similar between males and females, [IRR=1.0; 95% CI 0.96 to 1.04].

The estimates on the age effects showed a consistent trend of costs rising with an increase in the age group. Compared with the reference group (aged between 48 and 57 years), the costs for the younger age groups were relatively lower. The mean annual health care costs for the youngest group (18 to 27 years) were lower at 0.79 times those of the reference group [IRR=0.79; 95% CI 0.73 to 0.86]. These costs had a slight drop to 0.77 times for the 28 to 37 age group before rising to 0.81 times for the age 38 to 47 age group when compared with the reference group. Also, these costs rise steadily and remain higher in the groups older than the reference group. The costs for the over 77 years were 1.79 times higher than the reference group, [IRR=1.79; 95% CI 1.71 to 1.87].

The age-sex combined effect showed that younger females had higher costs than the reference group (males aged 47 to 58). For instance, costs for females aged between 18 and 27 were 1.25 times higher costs than the reference group [IRR=1.25, 95% CI 1.13-1.37]. On the other hand, females older than the reference groups showed higher mean annual health care costs than the reference groups.

The duration with psoriasis showed a consistent trend with costs rising with each passing year of living with psoriasis. Compared to the index year (year 0), costs were 1.93 times higher a year after the index and peaked at 2.15 times in year 4 before decreasing to a rate considerably lower than the index year [IRR=1.62; 95% CI 1.57 to 1.67].

Using BMI to estimate the influence of obesity status showed a higher cost association for both underweight and obese individuals when compared to the healthy BMI category (18.5 to 25). The underweight group, with less than 18.5kg/m² BMI, were associated with 1.42 times costs higher than the healthy BMI category [IRR=1.42; 95% CI 1.32 to 1.54]. An increase in the BMI category was associated with a steady increase in costs. The overweight BMI category showed 1.06 times costs higher than the

healthy BMI category. These costs jumped to 1.40 in the severely obese category when compared to the healthy BMI category [IRR=1.42; 95% CI 1.32 to 1.48]

The impact of comorbidity, estimated using the Cambridge Multimorbidity Score, was associated with higher costs. The combined obesity and comorbidity effect was noted to be similar across BMI categories. The estimates on the combined impact of psoriasis and comorbidity showed that an increase in comorbidities in psoriasis patients is only associated with an increase in total healthcare costs. The estimate on the psoriasis-obesity combined effect showed that the difference was not statistically significant between psoriasis and non-psoriasis patients with similar BMI.

The IMD was noted to have no impact on mean annual healthcare costs as there was no statistically significant result. The IMD was found to have no impact on mean annual costs. See Table 5.5, for a summary of results that includes the 95% confidence interval.

Table 5-5: Regression results for health care costs attributable to psoriasis

Variable	Total costs (1)		Primary care costs (2)		Secondary Care costs (3)	
	Incidence Rate Ratio	[95% CI]	Incidence Rate Ratio	[95% CI]	Incidence Rate Ratio	[95% CI]
Psoriasis	1.40	[1.34 to 1.46]	1.47	[1.43 to 1.52]	1.36	[1.28 to 1.44]
Female	1.00	[0.94 to 1.04]	1.03	[1.00 to 1.06]	0.98	[0.93 to 1.03]
18 to 27 years	0.79	[0.73 to 0.86]	0.77	[0.72 to 0.83]	0.81	[0.71 to 0.91]
28 to 37 years	0.77	[1.34 to 1.46]	0.81	[0.75 to 0.86]	0.75	[0.68 to 0.83]
38 to 47 years	0.81	[0.78 to 0.84]	0.74	[0.72 to 0.77]	0.85	[0.81 to 0.91]
58 to 67 years	1.33	[1.30 to 1.38]	1.32	[1.29 to 1.36]	1.34	[1.27 to 1.41]
68 to 77 years	1.59	[1.53 to 1.65]	1.47	[1.42 to 1.51]	1.69	[1.60 to 1.78]
Over 77 years	1.79	[1.71 to 1.87]	1.48	[1.43 to 1.54]	2.02	[1.90 to 2.15]
Female * 18 to 27 years	1.25	[1.13 to 1.37]	1.06	[0.98 to 1.15]	1.38	[1.21 to 1.58]
Female * 28 to 37 years	1.33	[1.23 to 1.44]	1.08	[1.00 to 1.16]	1.54	[1.37 to 1.72]
Female * 38 to 47 years	1.097	[1.05 to 1.15]	1.10	[1.06 to 1.15]	1.10	[1.03 to 1.17]
Female * 58 to 67 years	0.88	[0.84 to 0.94]	0.89	[0.85 to 0.93]	0.87	[0.81 to 0.94]
Female * 68 to 77 years	0.916	[0.87 to 0.96]	0.93	[0.89 to 0.96]	0.91	[0.85 to 0.98]
Female * over 77 years	0.885	[0.84 to 0.94]	0.95	[0.90 to 0.99]	0.85	[0.79 to 0.92]
1 year post index	1.926	[1.90 to 1.96]	1.86	[1.85 to 1.88]	1.97	[1.93 to 2.02]
2 years post index	2.019	[1.99 to 2.05]	1.91	[1.89 to 1.92]	2.10	[2.05 to 2.06]
3 years post index	2.124	[2.09 to 2.16]	1.96	[1.89 to 1.92]	2.25	[2.18 to 2.31]
4 years post index	2.151	[2.11 to 2.19]	2.00	[1.98 to 2.03]	2.26	[2.20 to 2.33]
5 years post index	2.079	[2.11 to 2.19]	1.94	[1.91 to 1.97]	2.19	[2.11 to 2.26]

Variable	Total costs (1)		Primary care costs (2)		Secondary Care costs (3)	
	Incidence Rate Ratio	[95% CI]	Incidence Rate Ratio	[95% CI]	Incidence Rate Ratio	[95% CI]
6 years post index	1.618	[1.57 to 1.67]	1.55	[1.52 to 1.59]	1.67	[1.59 to 1.75]
<18.5 kg/m ²	1.424	[1.32 to 1.54]	1.31	[1.23 to 1.39]	1.50	[1.36 to 1.66]
26 to 29.9 kg/m²	1.061	[1.32 to 1.54]	1.06	[1.04 to 1.09]	1.06	[1.02 to 1.09]
30 to 40 kg/m²	1.214	[1.04 to 1.09]	1.25	[1.22 to 1.28]	1.19	[1.14 to 1.23]
>=40 kg/m ²	1.396	[1.32 to 1.48]	1.53	[1.45 to 1.61]	1.32	[1.22 to 1.42]
Cambridge Multimorbidity Score	1.808	[1.77 to 1.84]	1.89	[1.85 to 1.93]	1.76	[1.72 to 1.80]
IMD 1, Most deprived	0.983	[0.95 to 1.02]	0.98	[0.95 to 1.01]	0.99	[0.94 to 1.03]
IMD 2	1.001	[0.97 to 1.03]	0.99	[0.96 to 1.02]	1.01	[0.96 to 1.05]
IMD 3	1.003	[0.97 to 1.04]	0.98	[0.95 to 1.01]	1.02	[0.97 to 1.06]
IMD 4	1.008	[0.98 to 1.04]	0.98	[0.95 to 1.00]	1.03	[0.98 to 1.07]
IMD 6	1.02	[0.98 to 1.06]	0.97	[0.94 to 1.00]	1.05	[1.00 to 1.11]
IMD 7	1.018	[0.98 to 1.05]	1.00	[0.97 to 1.03]	1.03	[0.98 to 1.07]
IMD 8	1.004	[0.97 to 1.04]	0.95	[0.92 to 0.98]	1.04	[0.99 to 1.09]
IMD 9	1.018	[0.98 to 1.06]	0.98	[0.95 to 1.01]	1.04	[0.99 to 1.09]
IMD 10, Least deprived	1.013	[0.98 to 1.05]	0.98	[0.95 to 1.01]	1.03	[[0.98 to 1.08]
Psoriasis*comorbidity	0.931	[0.90 to 0.97]	0.85	[0.82 to 0.88]	0.98	[0.94 to 1.03]
Psoriasis*Underweight	1.213	[0.96 to 1.53]	1.03	[0.91 to 1.16]	1.33	[0.97 to 1.81]
Psoriasis*Overweight	0.983	[0.93 to 1.04]	0.99	[0.95 to 1.03]	0.98	[0.90 to 1.07]
Psoriasis*Obese	0.977	[0.92 to 1.04]	0.99	[0.95 to 1.03]	0.97	[0.87 to 1.06]
Psoriasis*Severely obese	1.076	[0.97 to 1.20]	1.03	[0.95 to 1.12]	1.10	[0.95 to 1.28]

Variable	Total costs (1)		Primary care costs (2)		Secondary Care costs (3)	
	Incidence Rate Ratio	[95% CI]	Incidence Rate Ratio	[95% CI]	Incidence Rate Ratio	[95% CI]
Underweight*Comorbidity	0.88	[0.83 to 0.93]	0.87	[0.82 to 0.87]	0.88	[0.80 to 0.95]
Overweight *Comorbidity	0.95	[0.92 to 0.97]	0.98	[0.96 to 1.01]	0.92	[0.90 to 0.95]
Obese * Comorbidity	0.91	[0.89 to 0.93]	0.96	[0.93 to 0.98]	0.88	[0.85 to 0.80]
Severely obese*Comorbidity	0.94	[0.90 to 0.98]	0.97	[0.93 to 1.02]	0.91	[0.86 to 0.97]
Psoriasis*Underweight*Comorbidity	0.94	[0.82 to 1.07]	0.96	[0.88 to 1.06]	0.92	[0.78 to 1.08]
Psoriasis*Overweight*Comorbidity	1	[0.95 to 1.05]	1.00	[0.96 to 1.04]	1.00	[0.94 to 1.07]
Psoriasis*Obese*Comorbidity	1	[0.95 to 1.05]	1.01	[0.96 to 1.05]	1.01	[0.94 to 1.07]
Psoriasis*Sev obese*Comorbidity	0.917	[0.85 to 0.99]	0.97	[0.90 to 1.04]	0.89	[0.80 to 0.99]
Constant	263.81	[252.53 to 275.60]	113.65	[109.79 to 117.65]	150.24	[140.96 to 160.12]
Inalpha	0.83	[0.82 to 0.83]	0.50	[0.49 to 0.50]	2.60	[2.59 to 2.60]
Number of obs	688,250					
Akaike crit. (AIC)	10116682		9141649.2		5928739.1	
Bayesian crit. (BIC)	10117243		9142210		5929300	

Note: All models were estimated using negative binomial regression including patient random effects and clustered on patient ID. Constant gives baseline costs in reference group males from the fifth IMD decile aged between 48 and 57 years with healthy BMI (18.5 to 25). Columns (1), (2) and (3) present results for the Incidence rate ratio (IRR) for mean annual total health care, primary care, and secondary care costs respectively. PSO=Psoriasis; bmi=Body Mass index; IMD=Index of Multiple Deprivation; Sev obese= severely obese

Table 5-6 shows the predicted value of mean annual health care costs for the first 6 years from the index date. Holding all the variables constant, at the means, the predicted cost in psoriasis patients was higher at [ME=£964.97; 95% CI £947.99 to £981.95] than for control patients [ME=£722.98; 95% CI £628.94 to £639.24].

Table 5-6: Marginal effects for mean annual health care costs in psoriasis vs control

	<u>Marginal Effects [95% CI]</u>	
	Psoriasis	Controls
Total health care costs	£ 964.97 [947.99 to 981.95]	722.98 [716.52 to 729.44]
Primary care costs	£ 391.64 [386.68 to 396.58]	£ 292.54 [290.14 to 294.54]
Secondary care costs	£ 570.00 [555.71 to 585.22]	£ 428.21 [422.93 to 433.49]

Notes: This table shows the marginal effects on mean annual health care, primary and secondary care costs for psoriasis versus controls holding all the other variables constant.

5.3.2.1.2 Primary care costs

Models were also estimated for the mean annual primary care costs, see Table 5.7. A similar pattern and scale of results like that of the mean annual total health care costs were observed with primary care costs. In addition, models were estimated for each cost component of the mean primary care costs, i.e., the GP consultation costs and prescription costs, see Table 5.7.

The mean annual primary care costs for individuals with psoriasis were 1.47 times higher than individuals in the control group [IRR=1.47; 95% CI 1.43 to 1.52]. Females had 1.03 times higher costs than males, [IRR=1.03; 95% CI 1.00 to 1.06].

The estimates on the age effects showed a consistent trend of costs rising with an increase in the age group. Compared to the reference group (aged between 48 and 57 years), the mean annual primary care costs for the youngest group (18 to 27 years) were lower at 0.77 times those of the reference group [IRR=0.77; 95% CI 0.72 to 0.83]. These costs had a slight drop to 0.74 times for the age 38 to 47 age group when compared to the reference group [IRR=0.74; 95% CI 0.72 to 0.77]. These mean annual primary care costs rise steadily and remain higher in the groups older than the reference group. The age group just above the reference age group start at 1.32 times

the rate of the reference group [IRR=1.32; 95% CI 1.29 to 1.36]. The mean annual primary care costs for those over 77 years were 1.48 times higher than the reference group [IRR=1.48; 95% CI 1.43 to 1.54].

The age-sex combined effect showed no statistically significant difference in mean annual primary care costs between younger females (18 to 27 years) and the reference group (47 to 58 years). Overall, other female age groups below the reference group showed higher costs with respect to the reference group, [IRR=1.08; 95% CI [1.00 to 1.16] and [IRR=1.1; 95% CI 1.06 to 1.15] for the 28 to 37 and 38 to 47 years groups respectively. The opposite trend was observed for female age groups above the reference group, see Table 5.7. These age groups above the reference group showed 0.89, 0.93 and 0.95 times as much costs as the reference groups for 58 to 67, 68 to 77 and more than 77 years age groups respectively.

The duration with psoriasis showed a consistent trend with costs rising with each passing year of living with psoriasis. This reflected what was observed for the mean annual health care costs. Using BMI to estimate the influence of obesity status showed a higher cost association for both underweight and obese individuals when compared to the healthy BMI category with BMI ranging from 18.5 to 25. The underweight group, with less than 18.5 BMI, were associated with 1.31 times costs higher than the healthy BMI category [IRR=1.31; 95% CI 1.23 to 1.39]. An increase in the BMI category was associated with a higher cost rate than the healthy BMI category. The overweight BMI category showed a 1.06 times costs higher than the healthy BMI category [IRR=1.06; 95% CI 1.04 to 1.09]. These costs jumped to 1.53 in the severely obese category when compared to the healthy BMI category [IRR=1.45; 95% CI 1.45 to 1.61].

The presence of multiple long-term conditions estimated using the Cambridge Multimorbidity Score was associated with higher costs. The estimates on the psoriasis and comorbidity interaction showed that an increase in the Cambridge Multimorbidity Score in psoriasis patients was associated with an increase in primary care costs. The combined obesity-multimorbidity effect was only statistically significant in those in the underweight and obese groups when compared to the healthy BMI category. The estimate on the psoriasis-obesity combined effect showed that the difference was not statistically significant between psoriasis and non-psoriasis patients when BMI categories were compared to the healthy BMI category. The IMD was noted to have no

impact on mean annual primary care costs as there was no statistically significant result except for IMD 4, 6 and 8. See Table 5.7, for a summary of results that includes the 95% confidence interval.

Table 5-7 Regression results for the mean annual costs for primary care components

Variable	Total Primary care costs		GP consultation costs		Prescription costs	
	(1)		(2)		(3)	
	Incidence Rate Ratio	[95% CI]	Incidence Rate Ratio	[95% CI]	Incidence Rate Ratio	[95% CI]
Psoriasis	1.47	[1.43 to 1.52]	1.36	[1.33 to 1.4]	1.7	[1.62 to 1.80]
Female	1.03	[1.00 to 1.06]	1.2	[1.18 to 1.23]	0.86	[0.81 to 0.90]
18 to 27 years	0.77	[0.72 to 0.83]	0.86	[0.81 to 0.92]	0.68	[0.59 to 0.77]
28 to 37 years	0.81	[0.75 to 0.86]	0.88	[0.85 to 0.91]	0.72	[0.64 to 0.82]
38 to 47 years	0.74	[0.72 to 0.77]	0.77	[0.76 to 0.79]	0.72	[0.68 to 0.75]
58 to 67 years	1.32	[1.29 to 1.36]	1.19	[1.16 to 1.21]	1.46	[1.40 to 1.53]
68 to 77 years	1.47	[1.42 to 1.51]	1.34	[1.31 to 1.37]	1.61	[1.54 to 1.69]
Over 77 years	1.48	[1.43 to 1.54]	1.49	[1.45 to 1.54]	1.51	[1.42 to 1.60]
Female * 18 to 27 years	1.06	[0.98 to 1.15]	1.14	[1.07 to 1.22]	0.83	[0.72 to 0.96]
Female * 28 to 37 years	1.08	[1.00 to 1.16]	1.14	[1.09 to 1.19]	0.92	[0.80 to 1.05]
Female * 38 to 47 years	1.10	[1.06 to 1.15]	1.12	[1.09 to 1.15]	1.05	[0.99 to 1.12]
Female * 58 to 67 years	0.89	[0.85 to 0.93]	0.88	[0.86 to 0.91]	0.93	[0.86 to 0.99]
Female * 68 to 77 years	0.93	[0.89 to 0.96]	0.9	[0.87 to 0.93]	1	[0.93 to 1.06]
Female * over 77 years	0.95	[0.90 to 0.99]	0.87	[0.83 to 0.9]	1.07	[0.99 to 1.16]
1 year post index	1.86	[1.85 to 1.88]	1.84	[1.83 to 1.86]	1.88	[1.86 to 1.90]
2 years post index	1.91	[1.89 to 1.92]	1.86	[1.85 to 1.88]	1.97	[1.94 to 2.00]
3 years post index	1.96	[1.89 to 1.92]	1.88	[1.87 to 1.9]	2.08	[2.04 to 2.11]
4 years post index	2.00	[1.98 to 2.03]	1.89	[1.87 to 1.91]	2.18	[2.13 to 2.22]

Variable	Total Primary care costs		GP consultation costs		Prescription costs	
	(1)		(2)		(3)	
	Incidence Rate Ratio	[95% CI]	Incidence Rate Ratio	[95% CI]	Incidence Rate Ratio	[95% CI]
5 years post index	1.94	[1.91 to 1.97]	1.79	[1.77 to 1.82]	2.16	[2.11 to 2.22]
6 years post index	1.55	[1.52 to 1.59]	1.39	[1.37 to 1.42]	1.79	[1.72 to 1.86]
<18.5 kg/m ²	1.31	[1.23 to 1.39]	1.27	[1.21 to 1.34]	1.33	[1.20 to 1.48]
26 to 29.9 kg/m ²	1.06	[1.04 to 1.09]	1.05	[1.03 to 1.06]	1.11	[1.06 to 1.15]
30 to 40 kg/m ²	1.25	[1.22 to 1.28]	1.18	[1.16 to 1.2]	1.39	[1.33 to 1.46]
>=40 kg/m ²	1.53	[1.45 to 1.61]	1.37	[1.32 to 1.42]	1.83	[1.66 to 2.01]
Cambridge Multimorbidity index	1.89	[1.85 to 1.93]	1.51	[1.49 to 1.53]	2.46	[2.35 to 2.56]
IMD 1, Most deprived	0.98	[0.95 to 1.01]	1.01	[0.99 to 1.03]	0.93	[0.89 to 0.98]
IMD 2	0.99	[0.96 to 1.02]	1	[0.98 to 1.02]	0.98	[0.93 to 1.03]
IMD 3	0.98	[0.95 to 1.01]	1	[0.98 to 1.02]	0.95	[0.91 to 1.00]
IMD 4	0.98	[0.95 to 1.00]	0.99	[0.97 to 1.01]	0.95	[0.90 to 0.99]
IMD 6	0.97	[0.94 to 1.00]	1	[0.97 to 1.02]	0.95	[0.89 to 1.00]
IMD 7	1.00	[0.97 to 1.03]	1	[0.98 to 1.03]	0.99	[0.93 to 1.05]
IMD 8	0.95	[0.92 to 0.98]	0.97	[0.95 to 0.99]	0.93	[0.88 to 0.98]
IMD 9	0.98	[0.95 to 1.01]	0.97	[0.95 to 0.99]	0.98	[0.93 to 1.03]
IMD 10, Least deprived	0.98	[0.95 to 1.01]	0.94	[0.92 to 0.96]	1.01	[0.95 to 1.06]
Psoriasis*comorbidity	0.85	[0.82 to 0.88]	0.93	[0.91 to 0.95]	0.75	[0.71 to 0.79]
Psoriasis*Underweight	1.03	[0.91 to 1.16]	1.03	[0.92 to 1.17]	1.02	[0.84 to 1.23]
Psoriasis*Overweight	0.99	[0.95 to 1.03]	0.99	[0.95 to 1.02]	0.98	[0.91 to 1.05]

Variable	Total Primary care costs		GP consultation costs		Prescription costs	
	(1)		(2)		(3)	
	Incidence Rate Ratio	[95% CI]	Incidence Rate Ratio	[95% CI]	Incidence Rate Ratio	[95% CI]
Psoriasis*Obese	0.99	[0.95 to 1.03]	1	[0.97 to 1.04]	0.94	[0.88 to 1.02]
Psoriasis*Severely obese	1.03	[0.95 to 1.12]	1.06	[0.99 to 1.14]	0.96	[0.84 to 1.11]
Underweight*Comorbidity	0.87	[0.82 to 0.87]	0.88	[0.85 to 0.92]	0.86	[0.78 to 0.94]
Overweight *Comorbidity	0.98	[0.96 to 1.01]	0.97	[0.96 to 0.99]	0.97	[0.92 to 1.02]
Obese * Comorbidity	0.96	[0.93 to 0.98]	0.95	[0.93 to 0.97]	0.92	[0.87 to 0.97]
Severely obese*Comorbidity	0.97	[0.93 to 1.02]	0.95	[0.92 to 0.97]	0.94	[0.87 to 1.02]
Psoriasis*Underweight*Comorbidity	0.96	[0.88 to 1.06]	1	[0.93 to 1.08]	0.94	[0.80 to 1.10]
Psoriasis*Overweight*Comorbidity	1.00	[0.96 to 1.04]	1.01	[0.98 to 1.04]	1	[0.93 to 1.08]
Psoriasis*Obese*Comorbidity	1.01	[0.96 to 1.05]	1	[0.97 to 1.03]	1.04	[0.96 to 1.12]
Psoriasis*Severely obese*Comorbidity	0.97	[0.90 to 1.04]	0.96	[0.91 to 1.01]	1.01	[0.90 to 1.14]
Constant	113.65	[109.79 to 117.65]	63.27	[61.69 to 64.9]	47.44	[44.53 to 50.53]
Inalpha	0.50	[0.49 to 0.50]	0.49	[0.49 to 0.5]	1.06	[1.06 to 1.07]
Number of obs	688,250					
Akaike crit. (AIC)	10116682		9141649.2		5928739.1	
Bayesian crit. (BIC)	10117243		9142210		5929300	

Note: All models were estimated using negative binomial regression including patient random effects and clustered on patient ID. Constant gives baseline costs in reference group males from the fifth IMD decile aged between 48 and 57 years with healthy BMI (18.5 to 25).

Table 5-8: Marginal effects for mean annual primary care costs in psoriasis vs control

	<u>Marginal Effects [95% CI]</u>	
	Psoriasis	Controls
Total costs	£ 391.64 [386.68 to 396.58]	£ 292.54 [290.14 to 294.54]
GP consultation cost	£ 195.26 [193.18 to 197.34]	£ 149.46 [148.62 to 150.31]
Prescription costs	£190.75 [186.93 to 194.57]	£ 134.12 [132.14 to 136.10]

Notes: This table shows the marginal effects on primary care costs for psoriasis versus controls holding all the other variables constant. The 95% Confidence intervals are reported in parenthesis

5.3.2.1.3 Secondary care costs

Models were also estimated for the mean annual secondary care costs, see Table 5.5. A similar pattern and scale of results similar to that of the mean annual health care costs were observed with secondary care costs.

The mean annual secondary care costs for individuals with psoriasis were 1.36 times higher than individuals in the control group [IRR=1.36; 95% CI 1.28 to 1.44]. There was no difference in costs between male and female individuals [IRR=0.98; 95% CI 0.93 to 1.03].

The estimates on the age effects showed a consistent trend of costs being lower for lower age groups and higher with age groups bigger than the reference age group (48 to 57 years). The mean annual secondary care costs for the youngest group (18 to 27 years) were lower at 0.81 times those of the reference group [IRR=0.81; 95% CI 0.71 to 0.91]. These costs had a slight drop to 0.75 times for the age 38 to 47 age group when compared to the reference group [IRR=0.75; 95% CI 0.68 to 0.83]. These costs rise steadily and remain higher in the groups older than the reference group. The secondary care costs for age groups above the reference age group ranged from 1.34 [95% CI 1.27 to 1.41] to 2.02 [95% CI 1.90 to 2015] times for the 58 to 67 and over 77 years higher compared to the reference age group respectively.

The age-sex combined effect showed reversed the trend observed in the effect of age only. Female age groups below the reference group showed higher costs with respect to males in the reference age group, [IRR=1.38; 95% CI [1.21 to 1.58] and [IRR=1.54;

95% CI 1.37 to 1.72] for the 18 to 27 and 28 to 37 years groups respectively. These costs for females aged 38 to 47 years dropped to 1.1 times that of male individuals.

The estimate of the influence of obesity status showed a higher cost association for both underweight and obese individuals when compared to the healthy BMI category (18.5 – 25). The underweight group, with less than 18.5 BMI, were associated with 1.50 times costs higher than the healthy BMI category [IRR=1.50; 95% CI 1.36 to 1.66]. An increase in the BMI category was associated with a higher cost rate than the healthy BMI category. The overweight BMI category showed 1.06 times costs higher than the healthy BMI category [IRR=1.06; 95% CI 1.02 to 1.09]. The severely obese category had 1.32 times higher costs than the healthy BMI category [IRR=1.31; 95% CI 1.22 to 1.42].

The estimates on psoriasis and multimorbidity joint effect showed a non-statistically significant difference in secondary care costs between psoriasis and non-psoriasis patients. The combined obesity-multimorbidity effect was statistically significant across all BMI categories when compared to the healthy BMI category.

The estimate on the psoriasis-obesity combined effect showed that the difference was not statistically significant between psoriasis and non-psoriasis patients when BMI categories were compared to the healthy BMI category. However, a combined effect of psoriasis-obesity-multimorbidity was only statistically significant in the severely obese group [IRR=0.89; 95% CI 0.80 to 0.99].

The IMD was noted to have no impact on mean annual primary care costs as there was no statistically significant result except for IMD 6. See Table 5.9, for a summary of results that includes the 95% confidence interval.

Table 5-9: Regression results for mean annual costs for secondary care components

Variable	Outpatient costs		Inpatient costs		A&E costs	
	(1)		(2)		(3)	
	Incidence Rate Ratio	[95% CI]	Incidence Rate Ratio	[95% CI]	Incidence Rate Ratio	[95% CI]
Psoriasis	1.49	[1.42 to 1.57]	1.31	[1.21 to 1.43]	1.25	[1.18 to 1.33]
Female	1.16	[1.11 to 1.21]	0.91	[0.85 to 0.97]	0.92	[0.87 to 0.98]
18 to 27 years	0.73	[0.67 to 0.8]	0.74	[0.62 to 0.87]	2.06	[1.85 to 2.30]
28 to 37 years	0.73	[0.68 to 0.78]	0.71	[0.61 to 0.81]	1.38	[1.27 to 1.49]
38 to 47 years	0.8	[0.77 to 0.84]	0.86	[0.80 to 0.91]	1.03	[0.98 to 1.08]
58 to 67 years	1.31	[1.26 to 1.37]	1.39	[1.30 to 1.48]	0.86	[0.81 to 0.91]
68 to 77 years	1.6	[1.53 to 1.68]	1.78	[1.66 to 1.90]	0.94	[0.89 to 0.99]
Over 77 years	1.7	[1.6 to 1.79]	2.2	[2.04 to 2.37]	1.31	[1.23 to 1.40]
Female * 18 to 27 years	1.25	[1.13 to 1.38]	1.6	[1.33 to 1.93]	0.79	[0.70 to 0.89]
Female * 28 to 37 years	1.42	[1.31 to 1.55]	1.7	[1.46 to 1.99]	0.89	[0.80 to 0.98]
Female * 38 to 47 years	1.06	[1.01 to 1.12]	1.13	[1.04 to 1.24]	0.99	[0.92 to 1.05]
Female * 58 to 67 years	0.83	[0.78 to 0.88]	0.9	[0.82 to 0.98]	0.97	[0.90 to 1.05]
Female * 68 to 77 years	0.8	[0.75 to 0.85]	0.97	[0.88 to 1.06]	1.09	[1.01 to 1.18]
Female * over 77 years	0.71	[0.66 to 0.76]	0.92	[0.83 to 1.01]	1.06	[0.97 to 1.17]
1 year post index	1.89	[1.86 to 1.92]	2.02	[1.95 to 2.09]	1.97	[1.92 to 2.02]
2 years post index	1.92	[1.88 to 1.95]	2.2	[2.12 to 2.28]	2.07	[2.02 to 2.12]
3 years post index	2.02	[1.98 to 2.06]	2.36	[2.27 to 2.46]	2.17	[2.11 to 2.23]
4 years post index	2.04	[1.99 to 2.08]	2.38	[2.29 to 2.48]	2.18	[2.12 to 2.24]

Variable	Outpatient costs		Inpatient costs		A&E costs	
	(1)		(2)		(3)	
	Incidence Rate Ratio	[95% CI]	Incidence Rate Ratio	[95% CI]	Incidence Rate Ratio	[95% CI]
5 years post index	1.99	[1.94 to 2.04]	2.28	[2.17 to 2.39]	2.24	[2.16 to 2.31]
6 years post index	1.56	[1.51 to 1.61]	1.7	[1.60 to 1.82]	1.92	[1.83 to 2.01]
Below 18.5 kg/m ²	1.21	[1.12 to 1.3]	1.64	[1.44 to 1.85]	1.51	[1.37 to 1.67]
26 to 29.9 kg/m ²	1.02	[0.99 to 1.05]	1.08	[1.04 to 1.13]	0.97	[0.94 to 1.00]
30 to 39.9 kg/m ²	1.1	[1.06 to 1.13]	1.24	[1.18 to 1.30]	1.12	[1.08 to 1.16]
Above 40 kg/m ²	1.27	[1.19 to 1.36]	1.35	[1.23 to 1.48]	1.29	[1.19 to 1.39]
Cambridge Multimorbidity index	1.56	[1.52 to 1.59]	1.85	[1.80 to 1.91]	1.58	[1.55 to 1.62]
Index of Multiple Deprivation 1	1.01	[0.97 to 1.05]	0.98	[0.93 to 1.04]	0.93	[0.88 to 0.98]
Index of Multiple Deprivation 2	1.02	[0.98 to 1.06]	1.01	[0.95 to 1.07]	0.94	[0.89 to 0.99]
Index of Multiple Deprivation 3	1.02	[0.98 to 1.06]	1.02	[0.96 to 1.08]	0.92	[0.87 to 0.97]
Index of Multiple Deprivation 4	1.01	[0.97 to 1.04]	1.04	[0.98 to 1.10]	0.96	[0.91 to 1.01]
Index of Multiple Deprivation 6	1.01	[0.97 to 1.05]	1.08	[1.01 to 1.14]	1.01	[0.96 to 1.06]
Index of Multiple Deprivation 7	1.03	[0.99 to 1.07]	1.03	[0.97 to 1.09]	1.05	[1.00 to 1.11]
Index of Multiple Deprivation 8	1	[0.96 to 1.04]	1.05	[0.99 to 1.12]	1.06	[1.01 to 1.12]
Index of Multiple Deprivation 9	1.03	[0.99 to 1.07]	1.04	[0.97 to 1.11]	1.13	[1.07 to 1.19]
Index of Multiple Deprivation 10	1.01	[0.97 to 1.06]	1.03	[0.97 to 1.10]	1.09	[1.03 to 1.15]
Psoriasis*comorbidity	0.91	[0.87 to 0.95]	1.01	[0.95 to 1.07]	1.01	[0.96 to 1.07]
Psoriasis*Underweight	1.22	[1 to 1.49]	1.42	[0.93 to 2.16]	1.06	[0.82 to 1.37]
Psoriasis*Overweight	1.05	[0.98 to 1.12]	0.95	[0.84 to 1.07]	1	[0.92 to 1.08]

Variable	Outpatient costs		Inpatient costs		A&E costs	
	(1)		(2)		(3)	
	Incidence Rate Ratio	[95% CI]	Incidence Rate Ratio	[95% CI]	Incidence Rate Ratio	[95% CI]
Psoriasis*Obese	1.08	[1.01 to 1.16]	0.91	[0.81 to 1.03]	0.97	[0.89 to 1.05]
Psoriasis*Severely obese	1.23	[1.08 to 1.4]	1.04	[0.84 to 1.28]	1.05	[0.90 to 1.23]
Underweight*Comorbidity	0.82	[0.78 to 0.88]	0.88	[0.80 to 0.97]	0.95	[0.86 to 1.03]
Overweight *Comorbidity	0.98	[0.95 to 1]	0.9	[0.87 to 0.94]	0.95	[0.92 to 0.98]
Obese * Comorbidity	0.94	[0.92 to 0.97]	0.85	[0.82 to 0.88]	0.88	[0.86 to 0.91]
Severely obese*Comorbidity	0.96	[0.9 to 1.01]	0.89	[0.83 to 0.96]	0.95	[0.88 to 1.03]
Psoriasis*Underweight*Comorbidity	0.99	[0.87 to 1.13]	0.88	[0.71 to 1.09]	0.94	[0.80 to 1.10]
Psoriasis*Overweight*Comorbidity	0.98	[0.93 to 1.03]	1.02	[0.94 to 1.12]	0.98	[0.92 to 1.05]
Psoriasis*Obese*Comorbidity	1	[0.94 to 1.05]	1.02	[0.94 to 1.11]	0.99	[0.92 to 1.06]
Psoriasis*Severely obese*Comorbidity	0.91	[0.82 to 1]	0.9	[0.79 to 1.03]	0.82	[0.73 to 0.93]
Constant	47.12	[44.74 to 49.62]	94.52	[87.15 to 102.52]	8.77	[8.15 to 9.45]
Inalpha	2.68	[2.67 to 2.69]	4.09	[4.08 to 4.1]	3.61	[3.60 to 3.62]
Number of obs	688,250					
Akaike crit. (AIC)	10116682		9141649.2		5928739.1	
Bayesian crit. (BIC)	10117243		9142210		5929300	

Note: All models were estimated using negative binomial regression including patient random effects and clustered on patient ID. Constant gives baseline costs in reference group males from the fifth IMD decile aged between 48 and 57 years with healthy BMI (18.5 to 25). A&E=Accident and Emergency; IMD=Index of Multiple Deprivation

Table 5-10: Marginal effects for mean annual secondary care costs in psoriasis vs control

	Marginal Effects [95% CI]	
	Psoriasis	Controls
Total costs	£ 570 [555.71 to 585.22]	£ 428.21 [422.93 to 433.49]
Outpatient costs	£ 171.12 [167.76 to 174.47]	£ 116.13 [114.93 to 117.33]
Inpatient costs	£ 367.80 [354.69 to 380.91]	£ 288.58 [284.04 to 293.12]

Notes: This table shows the marginal effects on mean annual secondary care costs, outpatient and inpatient for psoriasis versus controls holding all the other variables constant.

5.4 Discussion

This study estimated the health care costs attributable to psoriasis. In addition, factors that influence these costs were explored using linked primary and secondary care data. The primary analyses focused on estimating the mean annual total health care costs. To disaggregate variations in total health care costs, secondary analyses were performed separately for primary and secondary care.

The results showed that costs were differentially higher in primary care, (1.47 times) as compared to secondary care (1.36 times) for patients with psoriasis. This was consistent with the prior expectation that chronic conditions are increasingly being managed in primary care (Williams and Law, 2018). This was also noted that multimorbidity had a relatively higher influence on primary than secondary care costs.

An increase in the Cambridge multimorbidity score in people with psoriasis had a relatively lower influence on mean health care costs compared to its influence in people without psoriasis. This is because, in primary care, a single patient with two comorbidities may cost less to manage than two separate patients with a single condition. Therefore, as the number of comorbidities increases in an individual, the rate of change in cost decreases (Chaplin *et al.*, 2016). This phenomenon was true for primary care costs and not statistically significant in secondary care costs. This is consistent with the hypothesis that, compared to people without psoriasis, multimorbidity in people with psoriasis is more likely to have a relatively lower impact on primary care costs as GPs could bring in a patient and deal with multiple conditions at the same time in a planned manner. In secondary care, an individual with multimorbid conditions is more likely to be managed by a separate specialist for each

condition, for example, a psoriasis patient with cardiovascular conditions and arthritis is more likely to be seen by a dermatologist, cardiologist and rheumatologist.

There was an observed association between deviation from the normal BMI (those below and above normal BMI) and health care costs. Underweight individuals were observed to have differentially higher secondary care costs, 1.50 times as much as healthy BMI, compared to primary care costs, 1.31 times as much as healthy BMI individuals. The estimates attributed to underweight individuals raise the need to also consider these groups seriously besides a sole focus on obesity.

However, compared to individuals with a healthy BMI, there was a similar increase in health care costs regardless of psoriasis status. This suggests that the effect of psoriasis on costs is not moderated by BMI. Due to the high proportion of missing BMI information in the dataset, it is required that such conclusions are taken with caution. The high proportion of missing data reduced the sample used in the analyses and potentially resulted in biased estimates (Hughes *et al.*, 2019).

Even though the IMD variable improved model fit it did not have much of an influence on health care costs. The gender differential was only statistically significant in primary care costs.

5.4.1 Strengths

One of the strengths of this study was the longitudinal study design using CPRD-HES data and a ten-year study period. This is the largest psoriasis cost of illness study conducted in the UK using CPRD-HES data. Other known psoriasis cost-of-illness studies conducted in the UK utilised survey methods and had very small populations (Poyner *et al.*, 1999; Fonia *et al.*, 2010). Using data from CPRD-HES to estimate health care resource use eliminated the high risk of recall bias which is prominent when using patient surveys (Löfvendahl, 2016; Mason, 2019). This study also used the spell-level tariff unit costs which provide a more accurate method of calculating payments and accounts for episode inflation (Aylin *et al.*, 2004). Another strength of using a large sample is that it allows for greater precision when estimating effects. Furthermore, using administrative data provides for better capturing of people with different stages of disease severity. In most cases, people with more severe conditions are likely to be missed by surveys and other primary methods as they are often the most vulnerable

and not included or reached by research. In addition, people with more severe conditions are less likely to respond to surveys.

Using observational and population-based studies makes results generalisable because they reflect clinical practice. The data used in this study considered both primary and secondary care activities, which reflect the majority of health care activities in the UK. Details of the different health care services reflect the patterns of health care consumption making the results generalisable to the general population.

The attributable cost method with matching was another important strength of this study. Other methods used in cost-of-illness studies tend to be accounting exercises and therefore do little to mitigate potentially biased estimates resulting from confounding. The rich set of controls minimised the potential confounding of the effects of psoriasis on costs. By using a rich set of controls, the study attempted to minimise selection bias and ensure a *ceteris paribus* (all things being equal) (Angrist and Pischke, 2014). Under *ceteris paribus* conditions, results can have a causal interpretation (Angrist and Pischke, 2014). The use of a matching study design to include controls allowed for a better way of estimating costs attributable to psoriasis, i.e. net economic consequences (Chisholm *et al.*, 2010). Only a few studies estimating the cost-of-illness due to psoriasis have implicitly used the attributable cost method (Crown *et al.*, 2004; Fowler *et al.*, 2008; Andrew P Yu *et al.*, 2009a; Gunnarsson *et al.*, 2012; Steven R Feldman *et al.*, 2015; Feldman *et al.*, 2017; Pilon *et al.*, 2019).

Disaggregation of costs into different domains of health care allowed for a better understanding of where the costs are currently incident. This is useful in informing health policy concerning planning for future care pathways. To my knowledge, this was the first study that presented disaggregated costs based on the health care setting.

5.4.2 Limitations

Despite the strengths of the dataset and methods used in this chapter, some limitations were noted. One of the limitations with the CPRD-HES linked dataset was the lack of provider codes for secondary care, which limited the possibility to control for provider fixed effects. This could lead to biased estimates if psoriasis patients were disproportionately from more costly providers. Nonetheless, this limitation was

minimised by matching individuals at GP practice level. It was reasonably assumed that people from certain GPs are likely to use similar hospital services geographically closer to them.

Another limitation was not using HES data to identify more occurrences of multiple long-term conditions using the ICD-10 codes. This was because some of the conditions of the Cambridge multimorbidity scores have no validated ICD-10 codes. Furthermore, limiting estimation of multimorbidity to conditions under the Cambridge multimorbidity score resulted in the omission of psoriasis relevant chronic conditions such as hyperlipidaemia. This potentially underestimated the prevalence of multimorbidity in psoriasis and ultimately costs. As highlighted earlier, attributable cost estimation assumes elimination of selection bias. Matching and regression were aimed at minimising the bias. However, there is still potential for selection bias resulting from failure to include the relevant variable during matching. Similarly, regression estimates attempt to make all things equal by controlling for observed variables. There is often a possibility of not observing something that might be correlated with psoriasis that, due to its omission, could be biasing the estimated attributable cost of psoriasis. This type of bias is referred to as omitted variable bias (Angrist and Pischke, 2008, 2014). For instance, this study did not control for differences in smoking and alcohol consumption which seemed to show an important difference under the descriptive statistics. The omission of the smoking and alcohol controls in the regression was due to the high missing data. One of the main reasons for the high proportion of missing data on smoking and alcohol consumption is as a result of it being self-reported information. Self-reported prevalence of smoking has been reported to be significantly lower than when objective measures such as cotinine biomarker, a predominant metabolite nicotine, measurements (Williams *et al.*, 2020). Cotinine is a biomarker used to measure exposure to tobacco smoke.

This study did not break down costs based on the class of treatment. This was not possible due to limited information from the dataset. Fonia *et al.* (2010) reported treatment costs which were estimated at £ 10,707 (£13843; 2018 price year) overall treatment costs, £10,423.3 (13843; 2018 price year) for biologics and £278.2 (£369; 2018 price year)

This study did not explore the impact of the choice of unit costs to value secondary care resource use. Similar to economic evaluation, the choice of costing method and source of unit costs is likely to have an impact on the cost estimates (Leal, Manetti and Buchanan, 2018). The three main diagnosis-related group (DRG)-based national unit costs that are possible in valuing hospital resource use in England are spell-level tariffs, Finished Consultant Episode (FCE) and spell-level reference costs estimates (Leal, Manetti and Buchanan, 2018). Where reference costs are used, a specific HRG Grouper software is used. Using the Grouper software, patient-level data is read at the FCE level to produce one HRG at the FCE level and another at the spell level (Leal, Manetti and Buchanan, 2018). The FCE and spell level HRG produced by HRG grouper may differ (Leal, Manetti and Buchanan, 2018). The derived HRGs are then matched to the corresponding unit costs to convert hospital resource use to the relevant costing year e.g., 2017 to 2018.

One CPRD data limitation is the high proportion of missing BMI data and the findings in this study were consistent with other studies (Bhaskaran *et al.*, 2013). During multiple imputation for missing BMI, the data was assumed to be missing at random which might have led to biased imputed figures for BMI. This study did not include informal care and productivity costs due to limitations of the dataset used which does not link to any dataset that would allow for estimation of productivity costs. However, this was inevitable considering the UK health care system.

Another key limitation was the lack of data on biologic treatments. Using HRG-tariffs does not account for high-cost treatments such as biologics (NHS England, 2021). This could have resulted in underestimating the cost-of-illness due to psoriasis. Since biologics are prescribed in secondary care by dermatologists, the lack of information on these medicines affects secondary care cost estimates and not primary care costs. One way to address the lack of data on systemics and biologics in future research is to pursue improved linkage of health records between primary and secondary care specialists within the NHS.

5.5 Conclusion

This study identified that the cost-of-illness for psoriasis was higher than a matched control group in the UK setting. Obesity was noted to be one of the key drivers of health care costs. Lower than normal BMI was also noted to be a key driver of health care costs. These two drivers can be manipulated by tackling the causes of obesity.

The main 3 main take home points from this chapter are: -

- People with psoriasis are more likely to use health care services as compared to those with without psoriasis. The difference in health care service use is even higher in primary care as compared to secondary care. However, it is also clear that secondary care costs might be underestimated because cost for biologics were not captured in the dataset used.
- Although obesity and being underweight were associated with increased health care costs, this observation needs to be taken with caution as there was a high proportion of missing BMI information in the dataset.
- The lack of information on the prescribed biologics potentially underestimates the costs attributable to psoriasis. Biologics used in psoriasis, prescribed by dermatologists in secondary care, are normally not captured in CPRD. Therefore, to account for this information there is need to improve linkage of health care records within the NHS to allow for comprehensive cost estimates.

6 Understanding the impact of living with psoriasis

Chapter summary

This chapter reports the results of an on-line survey designed to understand the impact of living with psoriasis from a sample of people living in the UK.

In this chapter, Section 6.1 will give the background and motivation for the study and section 6.1.1 will give the aims and objectives of the study. Section 6.2 is the methods section which will describe the study sample, data collection tools, prior plan of handling missing data and the data analysis plan. Section 6.3 presents the results from the analyses and section 6.4 presents the discussion.

The conclusion is presented in section 6.5.

6.1 Background

Understanding the impact of living with psoriasis refers to estimating and quantifying the burden-of-disease from the perspective of the individuals with the condition. Such an approach is useful in developing disease management strategies that account for both health and non-health consequences of the condition to improve patient outcomes.

Chapter 2 of this thesis reported a potential framework to differentiate between burden-of-disease and cost-of-illness. It highlighted the existing methods to quantify the burden-of-disease. This chapter focused on applying concepts developed in chapter 2, to understand the impact of living with psoriasis from the perspective of the individual with the condition. In this study, the burden-of-disease referred to health and non-health consequences of psoriasis accruing to an individual.

Chapter 4 summarised the current evidence base reporting the burden-of-disease due to psoriasis. It also summarised the existing methods that have been applied in quantifying the impact of living with psoriasis. Current evidence suggested psoriasis has a significant impact on an individual's physical, psychological and social health

(Weiss *et al.*, 2002; Dubertret *et al.*, 2006; Löfvendahl, 2016). According to Dubertret *et al.* (2006), the impact posed by psoriasis on individuals has been noted to be higher than other skin diseases or other chronic conditions.

A systematic review, completed as part of this thesis (Chapter 4), identified that no such studies have been conducted in the UK. Therefore, this study was motivated by the identified gap in estimating the burden of living with psoriasis in the UK. The primary objective was to estimate both the objective outcomes such as HRQoL and wellbeing as well as subjective patients' perspectives on the impact of psoriasis on lifestyle and satisfaction with the available treatments.

Although several studies have been conducted to estimate the burden of psoriasis, they have mainly concentrated on healthcare service users with severe disease (Dubertret *et al.*, 2006). This has resulted in fewer studies estimating the burden of psoriasis from the patients' assessment (Dubertret *et al.*, 2006). Furthermore, most studies have focused on evaluating a given set of treatments without taking a holistic approach to other aspects such as treatment satisfaction, the impact of the disease on lifestyle, and capability.

In light of the above, this study was set up to gather evidence relevant to the UK, collect data directly from people with psoriasis and measure health status and capability alongside disease severity.

6.1.1 Aim and Objectives

This study aimed to quantify the burden of psoriasis in the UK, which describes the impact on people living with psoriasis.

The four objectives were to:

1. Quantify the impact of living with psoriasis on health status
2. Quantify the impact of living with psoriasis on capability
3. Quantify physical disease severity of psoriasis
4. Understand whether the impact of living with psoriasis on health and capability was associated with patient characteristics, severity of psoriasis and/or type of treatment reported.

6.2 Methods

This study designed a cross-sectional survey that included standardised and validated tools to collect data from a specified sample of UK residents living with psoriasis. Data were analysed using descriptive statistics and regression methods to estimate the association between patient and disease-related characteristics and health status and capability. Ethics approval was granted by The University of Manchester research ethics committee (Ref: 2020-10508-17097 26/11/2020).

6.2.1 Survey design

A bespoke online survey was created for data collection, see Appendix 6.1 for the final survey. An online survey method was chosen because of its convenience to reach a large number of respondents. The design of this survey was informed by findings from chapter 2 and the systematic review presented in chapter 4 of this thesis. These two chapters guided on the concept of burden-of-disease and the relevant instruments used in quantifying the burden of psoriasis.

The majority of the survey contained questions aimed at eliciting quantitative information. To get a deeper understanding of the burden of psoriasis based on lived personal experiences, open-ended questions were also included in the questionnaire. The survey gave a brief introduction about the study, who was eligible to complete it, general instructions on how to answer the questions, and an estimated time needed to complete the survey.

A brief patient information sheet was also included in the survey. This gave a brief study background, the research purpose, selection of participants, confidentiality, publication of research findings, and contact details of the researcher. A link to the full patient information was embedded in the survey, see Appendix 6.2.

The survey prompted respondents to read through the patient information sheet and thereafter consent to take part in the study. The survey had nine parts which captured among other aspects eligibility, patient demographics (age, sex, education, smoking

status, and alcohol consumption), health status, capability wellbeing, disease severity, and treatment satisfaction. Living with other long-term conditions was also captured during this study. Parts two to eight were the main data collections part of the survey while parts one and nine provided for participant eligibility screening and survey design feedback respectively. The nine parts of the survey were:-

- Part 1: Screening questions
- Part 2: Measuring health status using EQ-5D-5L
- Part 3: Measuring capability using ICECAP-A
- Part 4: Measuring psoriasis severity
- Part 5: Psoriasis medication
- Part 6: Living with other long-term conditions
- Part 7: Psoriasis impact on work.
- Part 8: Patient demographics
- Part 9: General feedback

Part 1 of the survey contained two screening questions on eligibility to complete the survey. The questions were meant to establish if the respondent had psoriasis and was not below the age of 18 years. Furthermore, respondents were asked if the psoriasis was diagnosed by the clinician or self-diagnosed.

Parts 2 and 3 contained the EQ-5D-5L (see section 6.2.3.1) and icecap-a (see section 6.2.3.2), respectively. The EQ-5D-5L collected data on the health status and the ICECAP-A collected data on capability. Part 4 focused on the respondent's experience with regards to the duration of living with psoriasis, frequency of flare-ups, disease status and severity. This section included a combination of the saSPI questionnaire (see section 6.2.3.3) and a set of bespoke questions focused on estimating how long the respondent lived with psoriasis, if they were experiencing a flare-up, and a free-text question about their personal experience and impact of living with psoriasis.

Part 5 of the survey asked respondents about their current treatment and the self-reported treatment effectiveness.

Part 6 of the survey asked respondents whether they had other long-term conditions other than psoriasis. The provided list of conditions was based on the Cambridge multimorbidity score list (Payne *et al.*, 2020). The conditions included in the Cambridge multimorbidity score are good predictors of primary care use, unplanned hospital visits and death (Payne *et al.*, 2020). The Cambridge multimorbidity Score has been reported to outperform the Charlson Comorbidity Index (Payne *et al.*, 2020). In addition, the option to report any long-term conditions not provided on the list was included as a free text.

Part 7 collected data on the impact of psoriasis on work activities. These data included reporting the extent of the impact on work taking into account the nature of the job. Data were also collected to establish if having psoriasis had impacted one's ability to get a job. Information on the employment status, number of hours worked, nature of work activities, and psoriasis impact on the ability to work was gathered under this section.

Part 8 collected data on study sample demographics including sex, age (estimated from the year of birth), ethnicity, level of education, smoking status, and alcohol consumption. Patient identifiable information such as name and address were not collected. The need to collect the listed characteristics was motivated by an evolving body of evidence showing that lifestyle and patient behaviour such as smoking status, and alcohol consumption increase the risk of flare-ups in psoriasis (Zhou *et al.*, 2020). Part 9 asked respondents for feedback on the survey. This also provided the respondents with an opportunity to give any information on the impact of living with psoriasis in general that they may have forgotten to include in the other parts.

6.2.2 Rationale for including open-ended questions

The survey also included open-ended 'free-text' questions to elicit more information on patients' lived experiences. Keeping in mind that lived experiences might vary from one person to another. Free text questions must be used in capturing the individual burden of psoriasis (Cleland, 2017). For example, what might be seen as an effective topical treatment may be considered an inconvenience that needs constant application. Open-ended questions help in answering the "how" and "why" research

questions which allow for a deeper understanding of experiences, phenomena, and context (Cleland, 2017), beyond those captured using the EQ-5D and the ICECAP-A.

6.2.3 Selection of measures of health status, capability and psoriasis severity

The measure of health in terms of survival, mortality and life expectancy have only offered a limited one-dimensional view of health. Therefore, measures have been developed to provide a multi-attribute dimension of health status (e.g., EQ-5D) and capability (e.g., ICECAP-A). Similarly, tools to measure disease severity for specific diseases, such as the simplified psoriasis index have been developed. Although disease and condition-specific measures are sensitive to changes in HRQoL, they mostly do not have valuation sets. Preference weights have been established to provide a population-level tariff to capture changes in health (EQ5D-5L) and capability (ICECAP-A).

In this study, three measures were chosen to quantify the impact of psoriasis on health status (EQ-5D-5L), capability (ICECAP-A) and psoriasis severity (SPI).

6.2.3.1 Measure of health status: The EQ-5D-5L

The EQ-5D is a preference-based standardized instrument used to measure health status (EuroQol, no date). It is a generic instrument that has widespread use in health economics (EuroQol, no date). The EQ-5D has also been used in a wide range of health conditions (EuroQoL 2017). The EQ-5D was selected for this study because it is a measure of choice by the NICE in economic evaluations which forms part of the appraisal and guideline programmes (NICE, 2013a). The EQ-5D is useful in population health surveys (Devlin *et al.*, 2017).

The EQ-5D questionnaire is made up of two parts. The first part is the descriptive section which needs respondents to rate their health based on five dimensions. The five dimensions are mobility, self-care, usual activities, pain/discomfort and anxiety/depression. This produces a description of the health status based on the five dimensions.

The other part of the EQ5D uses a self-rated assessment of health status using a visual analogue scale (VAS) (EuroQol, no date). The vertical visual analogue scale has one of

the endpoints labelled “the best health you can imagine” marked at 100 and the other endpoint labelled “the worse health you can imagine” marked at 0.

The most recent EQ-5D-5L has five levels of severity for each of the five dimensions, thereby giving 3,125 possible unique health states as opposed to the three-level (EQ-5D-3L) which gives 325 possible health states (The EuroQol Group, 1990; Van Reenen and Janssen, 2015; Devlin *et al.*, 2017). Under the 5L, The five levels of severity are “no problems”, “slight problems”, “moderate problems”, “severe problems”, and “extreme problems” (Lloyd and Pickard, 2019). On the other hand, the three levels of severity under the EQ-5D-3L are “No problem”, “Some problem”, and, “extreme problems” (EuroQol Group, 2017). Development of the EQ-5D-5L by the EuroQoL Group task force in 2015 culminated from a need to improve sensitivity and reduce the ceiling effects identified from the EQ-5D-3L (Herdman *et al.*, 2011). Even though NICE supports EQ-5D-5L for use in prospective research, it currently does not recommend using the 5L value set for England that was published by Devlin *et al.* (2018) (NICE, 2019). Instead, it prescribes using the 3L as the reference case and the ‘Hernandez’ mapping function from 5L onto 3L developed (Hernández Alava, Pudney and Wailoo, 2020; NICE, 2020b).

The descriptive health status from the EQ-5D-5L was aggregated into a single index report of the utility weight using the UK tariff. The tariff depicts the population preference weighted health index, where one represents perfect health, zero represents death and negative figures such as -0.59 in the UK represent conditions worse than death (EuroQoL 2017). These preference weights reflect the relative importance people attach to different health problems. Since the 5L value set is not yet available, the Hernandez and Hout *et al.* crosswalk from 5L to 3L were used in generating the single index (Van Hout *et al.*, 2012; Hernández-Alava and Pudney, 2018). Since the Hernandez crosswalk requires age for each respondent, values for those respondents that did not report their year of birth could not be generated. Therefore, the results from the Hout *et al.* (2012) crosswalk were used in the regression analysis.

6.2.3.2 The ICECAP-A

The ICECAP-A is a measure of capability for the general adult (18 years and over) population which has seen increased use in health economics (University of Birmingham n.d). This tool focuses on an individual's wellbeing and capability which is captured under five attributes. The five attributes of ICECAP-A are 1) Stability 2) Attachment 3) Autonomy (being able to be independent), 4) Achievement 5) Enjoyment. Each of these attributes can take up any of the four levels ranging from full capability coded as 4 to no capability coded as 1 (Flynn *et al.*, 2015). The data collected from the ICECAP-A were used to summarise the impact on the patient's perceived capability to function normally.

The UK ICECAP-A tariff, see Table 2.1 in chapter two, was used to value and consolidate study participant responses to the ICECAP-A questionnaire (Flynn *et al.*, 2015). The best and worst state of an individual would be 4444 and 1111 respectively. The value for each individual was calculated by summing the values across the individual attributes as selected by each respondent. Compared to the EQ-5D, the ICECAP has not been as extensively used in dermatology. The ICECAP-A was only recently validated as a capability wellbeing measure in patients with dermatological conditions (Rencz *et al.*, 2021).

6.2.3.3 Disease severity and the Simplified Psoriasis Index

The simplified Psoriasis Index (SPI) was used in this study as psoriasis specific measure of severity. The SPI was developed around 2006 and modelled on the Salford Psoriasis Index (Kirby *et al.*, 2000; Chularojanamontri, Griffiths and Chalmers, 2013). The Salford Psoriasis Index was developed in the late 1990s to offer a concise but holistic summary of psoriasis severity (Kirby *et al.*, 2000; Chularojanamontri, Griffiths and Chalmers, 2013).

The SPI is available in two complementary versions; the health professionals (proSPI), and the self-assessment SPI completed by patients (Chularojanamontri, Griffiths and Chalmers, 2013). These two differ in the language used, which is simplified for the self-assessed SPI. This study used the self-assessed SPI. Henceforth, the term SPI shall be used to mean self-assessed SPI in this thesis.

The SPI is made up of three components that include measuring severity (SPI-s), psychosocial impact (SPI-p) and passed history interventions (SPI-i). This study only utilised the severity component, which was developed from the Psoriasis Area Severity (PASI) and has been shown to highly correlate with PASI (Chularojanamontri, Griffiths and Chalmers, 2013). The advantage of the SPI-s over the PASI is its ease of completion by the patient as it does not require one to make body surface area estimates and removes the need to assess erythema (redness), the extent of scales, and induration (plaque thickness) (Chularojanamontri, Griffiths and Chalmers, 2013).

The aggregated single SPI severity score is calculated from scores generated from two parts of the assessment. The first part generates the extent score ranging between 0 and 10 points. The extent score is a sum of scores from the 10 body part demarcations, with each part having three possible score options of “clear or so minor that it does not bother me (0)”, “Obvious but still leaving plenty of normal skin (0.5)” and “Widespread and involving much of the affected area (1). The second part of the assessment is the six-point average plaque severity score ranging from 0 to 5 (Chularojanamontri, Griffiths and Chalmers, 2013), see part of the questionnaire in. The single aggregate score of severity is a product of the extent score and average plaque score. For example, the most severe case would be a score of 50, resulting from an extent score of 10 and plaque score of 5 ($10 \times 5 = 50$), and the least severe would be $0 \times 0 = 0$. Therefore, the psoriasis severity score measured by the SPI ranges between 0 and 50.

6.2.4 Study population, sampling frame, and sample selection

The relevant study population were adults, aged 18 years and above, living with psoriasis and resident in the UK. For this study, people with psoriasis included individuals who had been diagnosed by a clinician or self-diagnosed. People with self-diagnosed psoriasis were defined as those that identify to have psoriasis but not diagnosed by a clinician and were members of the Psoriasis Association. Anecdotal evidence shows that some people might “self-diagnose” a condition based on a combination of several factors such as signs, symptoms and family history.

The study sample in this survey was drawn from the members of the Psoriasis Association UK. The Psoriasis Association UK is the leading national charity and membership organisation for people affected by psoriasis in the UK (Psoriasis Association, no date). Although the Psoriasis Association UK is headquartered in England, it works throughout the UK (Psoriasis Association, no date). Patients were recruited via contacts of the Psoriasis Association UK. As of December 2021, the traditional membership of the Psoriasis Association UK stood at 1500 with 996 having an email address on the record.

Participants in this study were selected using convenience sampling which is a non-probability-based sampling criteria (Etikan, 2016). The pre-defined inclusion criteria were a minimum age of 18 years, living with psoriasis in the UK and implied informed consent.

This study relied on obtaining the largest possible sample size given the available sample frame. Due to the non-probability nature of the sampling method, the sample size could not be calculated because it was impossible to calculate the sampling error which is a cardinal parameter needed to calculate the sample size. Besides, the different measures being used in this survey such as health, wellbeing and psoriasis severity as well as the different weightings of these measures, limit the calculation of the sample size. Therefore, this study aimed to obtain a sample as big as possible using convenience sampling (Etikan, 2016).

6.2.5 Piloting

The survey was piloted on 10 people living with psoriasis to establish the functionality and technical issues of the online system, the flow and skip logic of the questions, and estimate the maximum time it took to complete the survey. Respondents were recruited through purposive sampling of psoriasis patients contacted through friends and relatives. The piloting sought respondent feedback on the preliminary questionnaire. The feedback from the piloting exercise informed the modification which included putting title pages at the beginning of each section e.g. "This section will ask you about your general health today with regards to psoriasis". The survey was later fully fielded in February 2021.

6.2.6 Data collection

An online version of the survey was created using Sawtooth Lighthouse Studio 9.3.1 software (Sawtooth Software, 2017). The online survey was housed on a server held at The University of Manchester.

The Psoriasis Association UK sent out an email invitation to potential respondents from their membership pool, see Appendix 6.3. The invitation contained a brief description of the topic and a URL link to the survey. One reminder email was sent four weeks after the initial email.

All data collected were stored in an anonymised format at a secure location on a university-owned desktop computer in a locked office.

6.2.7 Data Analysis

The two main methods of data analysis for the quantitative data were descriptive statistics (see section 6.2.7.1), to summarise the data, and ordinary least squares regression analysis, to explore the impact of some of the patient characteristics on health and wellbeing. Other regression estimation methods explored were the Tobit and Censored Least Absolute Deviation (CLAD) (see section 6.2.7.3). All statistical analyses were performed using STATA version 16 (StataCorp LLC, no date).

Framework analysis was used to analyse the free-text responses on impact of psoriasis, see section 6.2.7.2. RQDA, a computer-assisted qualitative data analysis software (CAQDAS) was used to analyse the free-text responses. RQDA is an R package for qualitative data analysis (HUANG, 2009).

6.2.7.1 Descriptive analysis

In the first instance, a summary of the study sample was provided in terms of descriptive statistics, see section 6.2.7. Standard descriptive statistics for continuous variables and categorical variables were presented. For continuous variables, relevant descriptive statistics were the number of observations, minimum and maximum, mean, median and standard deviations. Proportions were reported for categorical variables. The extent of missing data was reported as it informs the limitations of generalisability. The reported information regarding missing data in the descriptive statistics was the number of missing values. The study sample characteristics reported

in the descriptive statistics section included age, gender, alcohol consumption, smoking status, presence of comorbidities, types of psoriasis treatment, ethnicity, and education level.

Descriptive analysis summarised the data for health status (EQ5D-5L), capability (ICECAP-A) and disease severity (SPI) responses. To examine the response spread across the different dimensions of the EQ-5D and ICECAP-A, a histogram was plotted. This provided information on which aspects of health and capability were mostly affected due to the condition. The frequency of these profile data was reported to reveal the distribution of the observations in the sample of respondents.

Considering that the data are collected in the form of health and wellbeing descriptions (profiles), the first step in the data analysis is to aggregate these individual responses into a single utility and wellbeing index score using preference weights. The published UK EQ-5D and ICECAP value sets were used to generate the single index score of health and wellbeing respectively. Two versions of algorithms were used to generate the single score for the EQ-5D and one version for the ICECAP-A (see sections 6.2.3.1 and 6.2.3.2 respectively).

For the health status domain, mean and median utility scores for EQ-5D with a kernel density plot were reported to show the distribution of these scores. A similar summary of the plot for the wellbeing using ICECAP data was also reported. All continuous variables were described by the mean, median, standard deviation, minimum and maximum.

The final SPI-s score was a multiplication of scores from the two-part assessment. This carries a minimum and maximum score of 0 and 50 respectively. This results from the multiplication of the extent score and average plaque score (Chularojanamontri, Griffiths and Chalmers, 2013). For instance, the maximum score of 50 was based on the product of a 10-extent score and 5 average plaque score.

6.2.7.2 Framework analysis

The framework analysis method provides a clear record of how themes and final outcomes are derived from participants' words. This was used to analyse free-text responses (Gale *et al.*, 2013). This approach involves identifying what is common and different in the qualitative responses, after which it focuses on relationships between these responses to draw descriptive and/or explanatory conclusion clusters around themes (Gale *et al.*, 2013).

The five steps followed in the analysis were similar to those used in analysing expert opinions in chapter 2. Themes in the data were identified by two researchers PN and KP. PN conducted the first round of coding and KP carried out the second round. KP also checked for consistency and accuracy by identifying themes that might have been missed. These themes were later discussed by the two researchers. The data was then fully coded and analysed by PN. To illustrate aspects of the data analysis, examples of direct quotations have been included in the results sections. Only anonymous participant IDs were included alongside the quotations.

6.2.7.3 Regression analysis

Regression analysis was used to estimate the influence of patient age, sex, psoriasis duration, type of treatment, and frequency of flare-ups on health status and capability. Regression refers to using a statistical model to study the relation between two or more variables. Simple regression is when only two variables, i.e. a dependent and an independent variable, are involved and a multiple regression involves more than one independent variable. (Wooldridge, 2002).

Multivariable regression methods, to estimate the influence of the patient characteristics on HRQoL and wellbeing, were used in this analysis (Devlin, Parkin and Janssen, 2020). Candidate regression methods were: Ordinary Least squares (OLS); Tobit; censored least absolute deviation (CLAD) (Devlin, Parkin and Janssen, 2020).

The two dependent variables considered in this study were the health status score and the capability score. Independent variables included in the global model were SPI score, age, sex, duration of psoriasis, smoking status, alcohol consumption, type of treatment, treatment effectiveness, and the number of flare-ups in the last 12 months.

These variables were selected based on background knowledge (Heinze, Wallisch and Dunkler, 2018). A variable selection algorithm, stepwise selection, was used to select the final variables.

Ordinary Least Squares (OLS)

Ordinary Least Squares (OLS), Equation 6.1, represents the simplest and most commonly used linear econometric estimator (Gujarati, 2004; Wooldridge, 2010; Devlin, Parkin and Janssen, 2020). OLS has been recommended for use when dealing with utility data from preference-based measures (Pullenayegum *et al.*, 2010). Furthermore, OLS is in some instances recommended as its simplicity provides a link to other techniques in econometrics (Wooldridge, 2010). Where the data is unimodal, and normally distributed, OLS has been seen to suffice. However, OLS is limited by the assumptions of homoskedasticity and normally distributed residuals (Pullenayegum *et al.*, 2010; Wooldridge, 2010). A violation of these assumptions results in OLS giving biased estimates (Pullenayegum *et al.*, 2010). SPI score, age, sex, duration of psoriasis, smoking status, alcohol consumption, and type of treatment.

$$y = \beta_0 + \beta_1 x_1 + \dots + \beta_k x_k + u \quad \text{Equation 6.1}$$

Where y is the dependent variable, β_0 is the intercept, β_1 is the regression coefficient associated with the independent variable x_1 , β_k is the regression coefficient of the k^{th} independent variable x_k , and u being the error term.

Tobit Models

Tobit models, Equation 6.2, are useful in handling health status data that are characterised by clustering and censoring (Pullenayegum *et al.*, 2010; Devlin, Parkin and Janssen, 2020).

These models are used in describing the relationship between a dependent variable (y_i) that is bound (censored) within any given range and a row vector of independent variables (x_i) including the constant term. When using a Tobit model, it can be censored from below (left-censored) see Equation 6.3, from above (right censored) see Equation 6.4, or from both ends. Left censored data (lower limit) occurs when the

values are unobserved if the true value is below a cut-off point L . For instance, using health status (eq5d) data for the UK population, the lower limit is -0.59 and the upper limit is 1.

Tobit models rely on the assumption of homoscedasticity because they give biased results in the presence of heteroscedasticity (Pullenayegum *et al.*, 2010).

$$y_i^* = x_i^T \beta + u_i \quad \text{Equation 6.2}$$

Where y_i^* , is the latent unobserved dependent variable, x_i^T the vector of independent variables, β is the vector of coefficients associated with the corresponding independent variable and u_i the error term.

Left regression censored model

$$y = \begin{cases} y_i^* & \text{if } y_i^* > c \\ c & \text{if } y_i^* \leq c \end{cases} \quad \text{Equation 6.3}$$

Right regression censored model

$$y = \begin{cases} y_i^* & \text{if } y_i^* < c \\ c & \text{if } y_i^* \geq c \end{cases} \quad \text{Equation 6.4}$$

Where, y_i^* , is the latent unobserved variable, c is the constant limit threshold.

Censored Least Absolute Deviation (CLAD)

Censored Least Absolute Deviation (CLAD) refers to a model estimator which is a generalisation of the Least Absolute Deviation (LAD). The LAD is a standard estimator for the conditional median, see Equation 6.5, Equation 6.6 and Equation 6.7 (Wooldridge, 2002, 2010). Unlike the OLS which minimises the sum of squares, LAD minimises the absolute residuals as shown in Equation 6.7 (Wooldridge, 2002, 2010). LAD estimates the effects of the independent variables on the conditional median (see Equation 6.5), instead of the mean, of the dependent variable (Wooldridge, 2010). Where the median function is known, the sample analogue to the conditional median is defined by choosing so that the function is minimized, see Equation 6.6. LAD

assumes the error term (u_i) is continuously distributed with a median zero, see Equation 6.5. This can then be verified as shown in Equation 6.6.

Using the conditional median results in the reduction of outlier influence on the estimate. In addition, CLAD gives robust results even in the presence of heteroscedasticity (Powell, 1984; Wilhelm, 2008).

Conditional Median Assumption

$$Med(u|x) = 0 \quad \text{Equation 6.5}$$

$$\begin{aligned} Med[y|x] &= \max(0, Med [y^* |x]) = \max(0, x\beta + Med[u|x]) \\ &= \max (0, x\beta) \end{aligned} \quad \text{Equation 6.6}$$

LAD estimator

$$\check{\beta} = \min_{\beta} \sum_{i=1}^n |y_i - x_i' \beta| \quad \text{Equation 6.7}$$

Where $\check{\beta}$ is an estimate that is an arbitrarily selected vector of the same dimensionality as β , $x_i' \check{\beta}$ refers to the transpose matrix such that $x_i' \check{\beta}$ is a scalar that results from the product of x_i and $\check{\beta}$. The CLAD estimator (see Equation 6.8) is a generalisation of the LAD estimator which also allows for censoring (see Equation 6.9), similar to the Tobit model (Powell, 1984).

$$y_i^* = x_i' \check{\beta} + u_i \quad \text{Equation 6.8}$$

Where y_i^* is the observed dependent variable, $x_i' \check{\beta}$ is the transpose matrix of the LAD estimator.

$$y_i = \begin{cases} y_i^* & \text{if } y_i^* > 0 \\ 0 & \text{if } y_i^* \leq 0 \end{cases} \quad \text{Equation 6.9}$$

Where y_i is the bounded dependent variable and y_i^* is the observed dependent variable.

Selection of the regression model

The choice of regression was guided by several assumptions which relate to the nature of the data. The characteristics of the EQ-5D data, which are well documented, influenced the choice of regression methods. The well-established characteristics of EQ-5D include censored data, right bound at one (perfect health) and left bound at the worst imaginable health depicted by a negative value e.g. -0.59 for UK using the EQ-5D-3L (Devlin, Parkin and Janssen, 2020). EQ-5D data is also characterised by gaps between values resulting in bimodal or trimodal distributions due to clustering (Hernández Alava, Wailoo and Ara, 2012; Alava and Wailoo, 2015).

Statistical tests are available to inform the selection of the regression model. Akaike's and Bayes Information Criteria (AIC and BIC) were included to inform the selection of the preferred model between regression approaches (Sauerbrei *et al.*, 2020). A backward stepwise model selection approach was used to select initial variables. However, using background knowledge, some variables were excluded based on being bad controls (Angrist and Pischke, 2008).

6.3 Results

6.3.1 Descriptive statistics for the study sample.

The Psoriasis Association UK emailed the survey link to 996 of its members. The 996 were members with an email address on their record held by the association. The survey link was active from 26th February to 30th April in 2021. From this potential sample, 494 respondents opened the survey but some respondents: did not proceed with the survey (n=81); did not give consent (n=8); did not meet the eligibility criteria (n= 1 individual was under 18 years old two individuals did not have psoriasis). A total of 402 respondents started the survey but of these 28 respondents did not complete the questions on outcomes (health status, wellbeing and psoriasis severity) and were excluded from the analyses. A further 8 respondents who did not report their demographic information were excluded resulting in the final sample of 366.

The final study sample (see Figure 6.1) comprised respondents who completed the survey (n=366). This represents a response rate of 37% (366/996). Only 1 of the 366 (0.3%) respondents reported to think they had psoriasis without a diagnosis by a clinician. Of the 366 that completed the survey, 302 (82.5%) respondents reported that they found it extremely easy to complete and 52 (14.2%) reported that they found it moderately easy. A further 8 (2.2%) respondents had no opinion.

Figure 6.1: The process of identifying the study sample

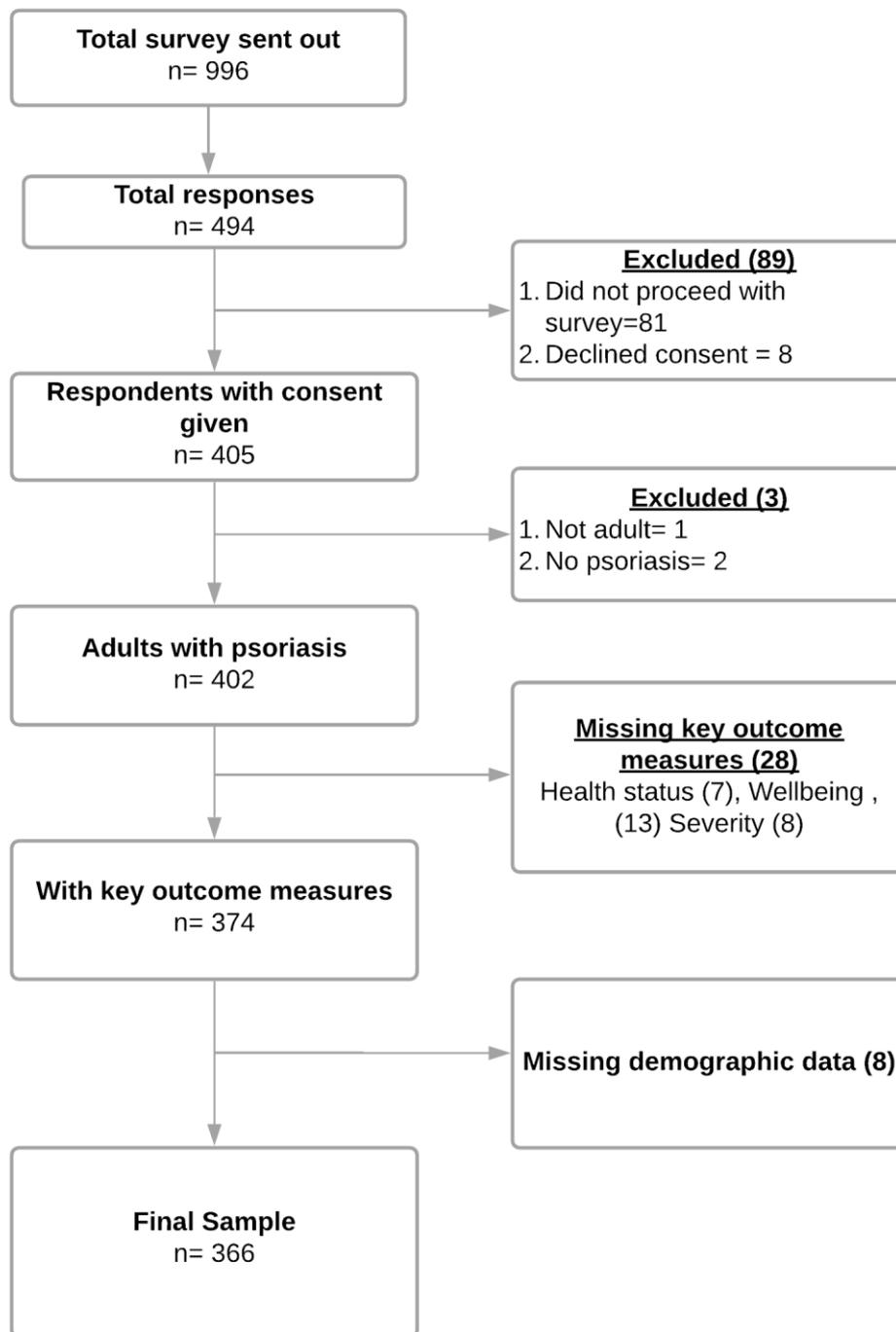


Table 6-1 reports the characteristics of the final study sample. The mean age of the respondents was 55.2 years (range: 20 to 90 years; standard deviation 17.0 years). The majority of the respondents were female, representing 62% (n=227) of the study sample.

The study sample mainly comprised white individuals accounting for 95% (n=347) of the respondents (see Table 6-1). The study sample did have some, albeit modest representation of respondents from different ethnic backgrounds: 3% (n=11) were Asian (1.6% Indian, Bangladeshi or Pakistan, and 1.4 other Asian ethnicities), 0.8% (n=3) mixed black and white. Arab and other ethnicities accounted for 1.4% (n=4).

The majority of the study sample reported they were currently non-smokers (n=337; 92.1%). Within the study sample, 36.4% (n=134) respondents reported that they had been smokers in the past and 7.9% (n=29) respondents were current smokers. Just under one-third of the study sample (n=105; 28.7%) reported that they did not consume any alcohol. A proportion of respondents (n=32; 8.7%) reported that they consumed alcohol daily. Just under one-third of respondents reported that they consumed alcohol more than once a week (n=116; 31.7%) or once a week (n=113; 30.9%).

Over half of the respondents (n=197; 53.8%) reported that they were living with another long-term condition (Table 6-1). Arthritis was the most common co-existing condition reported by nearly one-third of the respondents (n=106; 29.0%). Mental health conditions such as anxiety or depression (n=60; 16.4%) and high blood pressure (n=57; 15.6%) were also commonly reported long-term conditions.

Table 6-1: Study sample characteristics

Characteristics	Number of respondents (n=366)	Percentage of the sample
Sex		
Male	139	38.0%
Female	227	62.0%
Age Mean [SD], years	55.2 [17.0]	-
Ethnicity		
White UK	334	91.2%
White other	13	3.6%
Mixed black-white	3	0.8%
Asian- IBP*	6	1.6%
Asian other	5	1.4%
Arab	1	0.3%
Other ethnic	4	1.1%
Smoking status-Current		
Yes, daily	25	6.8%
Yes, less than daily	4	1.1%
Not at all	337	92.1%
Smoking status-Past		
Yes, daily	92	27.0%
Yes, less than daily	32	9.4%
Not at all	215	63.0%
Prefer not to say	2	0.6%
Alcohol consumption		
Never	105	28.7%
Once a week	113	30.9%
More than once a week	116	31.7%
Daily	32	8.7%
Co-occurrence of long-term conditions		
No	155	42.3%

Yes	197	53.8%
I do not know	9	2.5%
Prefer not to say	5	1.4%
Other long-term conditions **		
Arthritis	106	29.0%
Blindness/partial sight	4	1.1%
Breathing condition	27	7.4%
Cancer	7	1.9%
Deafness or hearing loss	21	5.7%
Diabetes	22	6.0%
Heart condition	20	5.5%
High blood pressure	57	15.6%
Kidney/liver disease	8	2.27%
Mental health^b	60	16.4%
Neurological condition^c	13	3.6%
Schizophrenia or bipolar	1	0.3%
Stroke	1	0.3%
Ulcer or stomach disease	4	1.1%
Other not listed	60	16.4%
Prefer not to say	3	0.8%

** IBP= India, Bangladeshi, Pakistan. ** Occurrence of multiple long-term conditions and not mutually exclusive, b= Mental health conditions such as anxiety or depression. c= conditions such as epilepsy or migraine*

Table 6-2 provides a description of the self-reported level of education attained, employment status, weekly hours of work, the nature of work activity, and if psoriasis had impacted their ability to find a job. The study sample comprised a high proportion of respondents (n=225; 68.5%) with a university education. About one-third of the respondents (n=127; 34.7%) reported being in some form of employment. Most of the respondents (n=106; 29%) that were employed reported that they worked in a job that required sitting. Some respondents (n=28; 7.7%) reported that living with psoriasis did affect their ability to find a job.

Table 6-2: Self-reported education and employment status in the study sample

Characteristics	Number of respondents (n=366)	Percentage of the sample
Qualifications^a		
University	225	68.5%
A level or vocational level 3	66	18.0%
Below level 1	2	0.6%
Other qualifications	6	1.6%
No qualifications	8	2.2%
Employment status		
Full-time	127	34.7%
Part-time	29	7.9%
Self-employed	19	5.19%
Retired	142	38.8%
Unemployed	8	2.2%
Long term sick	5	1.4%
Homemaker	13	3.6%
Student	14	3.8%
Other	9	2.5%
Weekly working hours		
Less than 10 hours	4	1.1%
10 to 15 hours	6	1.6%
16 to 20 hours	16	4.4%
21 to 25 hours	13	3.6%
26 to 30 hours	12	3.3%
31 to 35 hours	16	4.4%
36 to 40 hours	66	18.0%
41 hours or more	50	13.7%
Prefer not to say	1	0.3%
Work activity		
Sitting	106	29.0%

Stand or walk	53	14.5%
Lift light loads	19	5.2%
Carry heavy loads	6	1.6%
Impact of psoriasis on finding a Job		
Yes	28	7.7%
No	298	81.4%
Do not know	36	9.8%
Prefer not to say	3	0.8%
^aprefer not to say 3 (0.8%); ^bNot applicable=182 (49.7%); ^cMissing=1 (0.3%)		

Most of the respondents in the study sample (n=304; 83.0%) were receiving prescribed treatment (see Table 6-3). This sample comprised respondents that were using prescribed treatment from a doctor (n=223; 60.9%) and respondents using a combination of prescribed and non-prescribed treatment (n=81; 22.1%). In addition, 36 (9.8%) respondents reported that they were only using the non-prescribed treatment and 26 respondents (7.1%) were not using any treatment. Topical creams and ointments were the predominantly prescribed (n=275; 75.1%) treatment. Just over half of respondents (n=212; 57.9%) stated that they felt the prescribed treatments were effective. Of the 127 respondents (34.7%) that reported using non-prescribed treatments, 90 (24.6%) of these respondents stated they felt these treatments were effective.

Table 6-3 describes the self-reported duration of living with psoriasis, frequency of flare-ups, and types and effectiveness of treatments. The majority of respondents, (n=308; 84.1%), had lived with psoriasis for more than 10 years. About half of the respondents (n= 186; 50.8%) reported that they were currently experiencing a flare-up. Nearly one-third of respondents reported that they (n=106; 29.0%) had one-flare-up in the last 12 months before the survey. A further 47 respondents (12.8%) reported that they experience varying frequencies of flare-ups. Nearly two-fifths of respondents (n=140; 38.3%) reported that they experienced constant symptoms. One-fifth of respondents (n=73; 19.9%) did not experience any flare-ups in the last 12 months before the survey.

Table 6-3: Summary of the psoriasis duration, flare-up frequency and treatment.

Characteristics	Number of respondents (n=366)	Percentage of the sample
Years of psoriasis^a		
Less than 2 years	11	3.0%
3 to 5 years	16	4.4%
6 to 10 years	30	8.2%
> 10 years	308	84.1%
Currently flaring-up		
Yes	186	50.8%
No	180	49.2%
Flare-up in last 12 months		
No flare-up	73	19.9%
One flare-up	106	29.0%
Constant symptoms	140	38.3%
Other	47	12.8%
Currently on Prescribed treatment		
Yes, only prescribed	223	60.9%
Yes, prescribed and other	81	22.1%
No, only other	36	9.8%
Not using any	26	7.1%
Prescribed treatment		
Topical	275	75.1%
Oral	61	16.7%
Injectable	55	15.0%
Light	4	1.1%
Is prescribed treatment effective?^b		
Yes	212	57.9%
No	54	14.8%
Not sure	38	10.4%

On other non-prescribed treatment		
No	239	65.3%
Yes	127	34.7%
Other treatment		
Special diet	22	6.5%
Alternative treatment	28	8.2%
Homoeopathy	6	1.8%
Non-medical UV	7	2.1%
Sun	17	5.0%
Snail gel	3	0.9%
Other not listed	78	22.9%
Is other treatment effective?^c		
Yes	90	24.6%
No	14	3.8%
Not sure	23	6.8%

^a Cannot remember = 1 (0.3%); ^b Not applicable = 62 (16.9%); ^c Not applicable = 239 (65.0%)

Disease severity

Figure 6.2 describes the self-reported severity of psoriasis using the three levels of the extent of psoriasis as measured by the SPI. The total number of respondents that completed the self-assessed SPI was 366. The top five affected body areas reported to have widespread psoriasis were: the scalp and hairline (n=66; 18.0%); knees, lower legs and ankles (n=65; 17.8%); buttocks and thighs (n=54; 14.2%); arms and armpits (n=46; 12.6%); chest and abdomen (n=45; 12.3%). In addition, respondents reported obvious signs of psoriasis but with a large extent of normal skin in the following body areas: arms and armpits (n=169; 46.2%); knees (n=134; 36.6%); lower legs and ankles (n=134; %); chest and abdomen (n=130; 35.5%); scalp and hairline (n=127; 34.7%); buttocks and thighs (126=x; 34.4%). A small proportion (n=13; 3.6%) of respondents reported they had widespread psoriasis on the face and a further 107 respondents (29.2%)

reported that they had obvious psoriasis on the face but there was plenty of normal skin.

The mean overall severity calculated from the combination of the extent of the body area and overall state of the self-assessed SPI in this study sample (see Figure 6.3) was 6.3 (range: 0 to 50). Figure 6.4, showed that a small number of respondents (n=34; 9.3%) reported that the overall state of their psoriasis was clear or showed slight signs of redness. One-third of respondents (n=121; 33.1%) reported mild redness or scaling or reported definite redness (n=122; 33.3%). In addition, a proportion of respondents reported that they had moderately severe (n=54; 14.8%) or very red and inflamed psoriasis (n=32; 8.7%). Less than one per cent of the respondents reported intensely inflamed psoriasis, (n=3; 0.8%).

Figure 6.2: Description of the extent of psoriasis per given body area

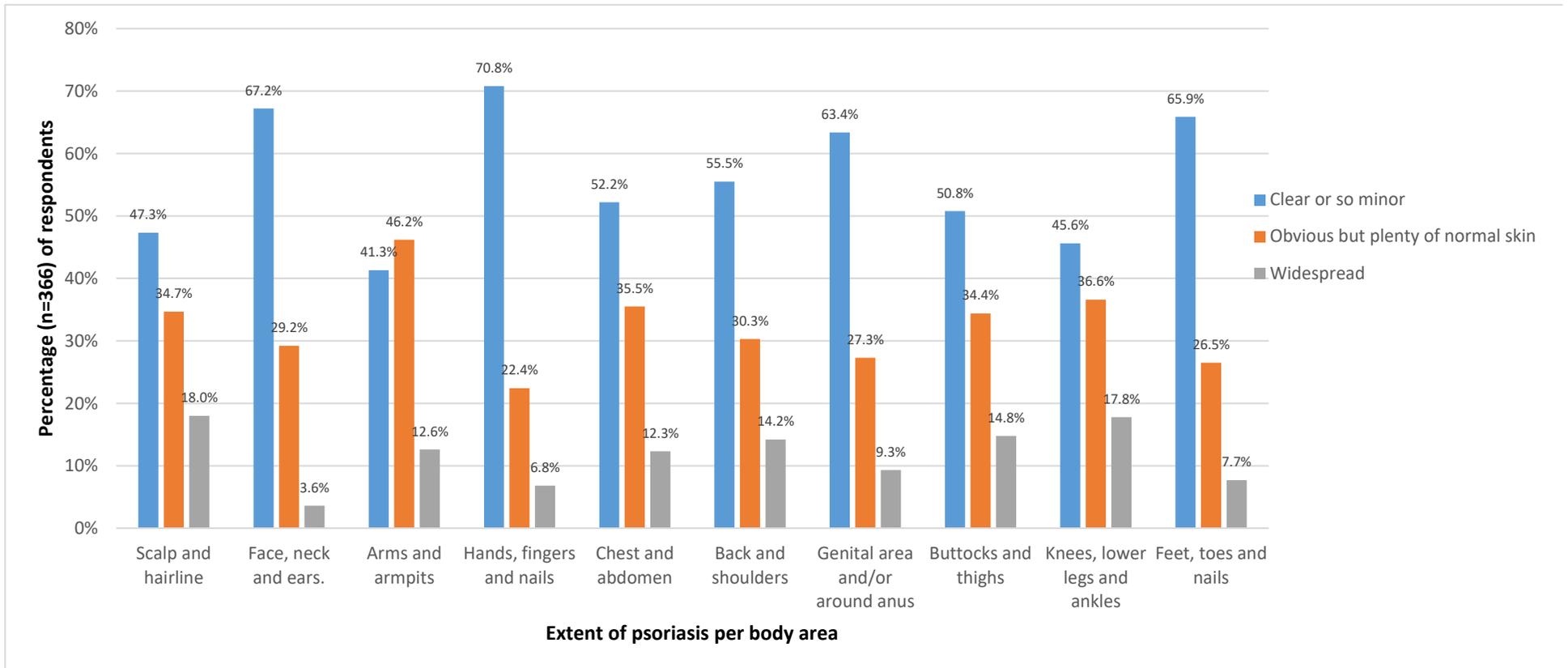


Figure 6.3: Distribution of the self-reported psoriasis severity score measured using the self-assessed Simplified Psoriasis Index.

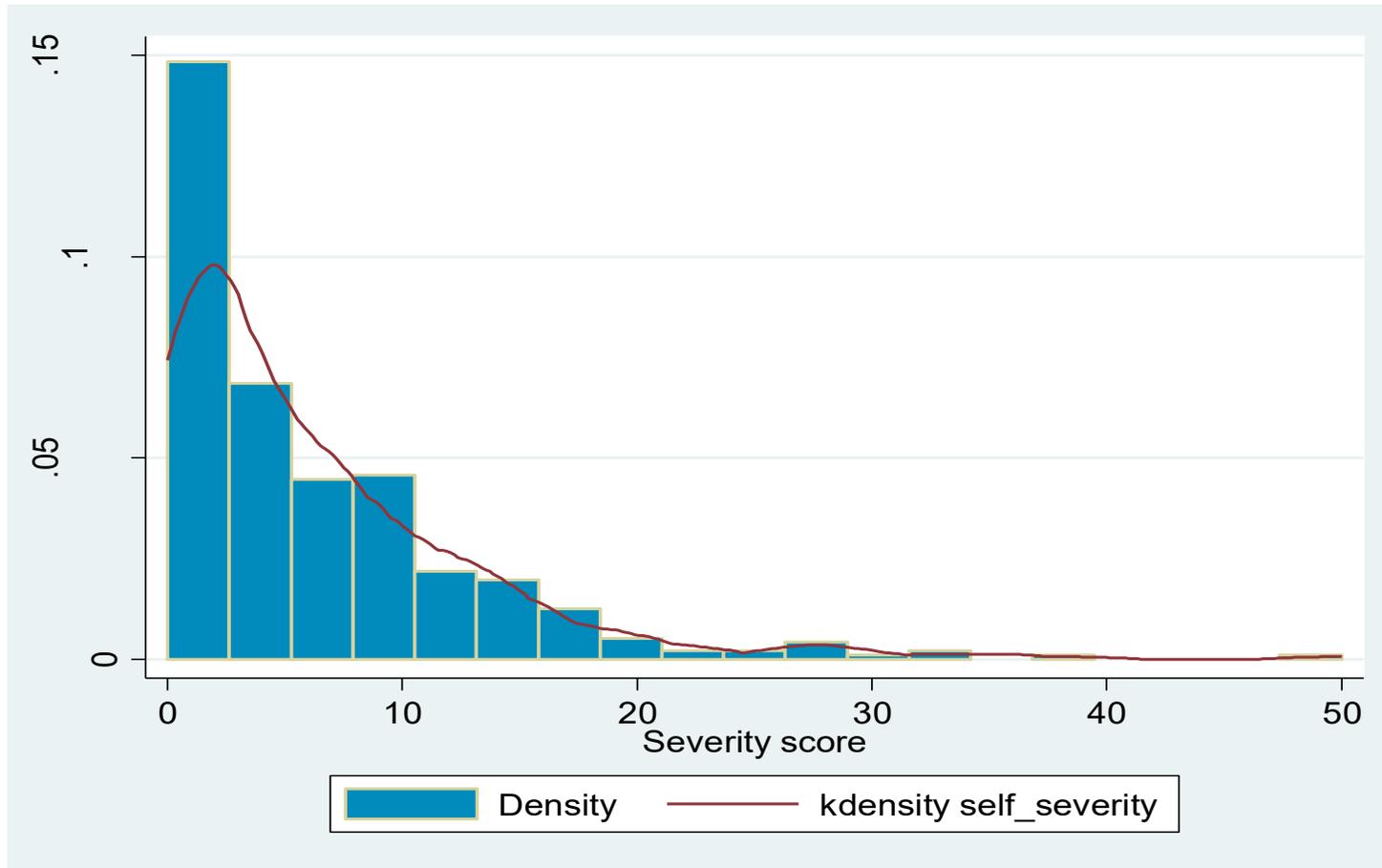
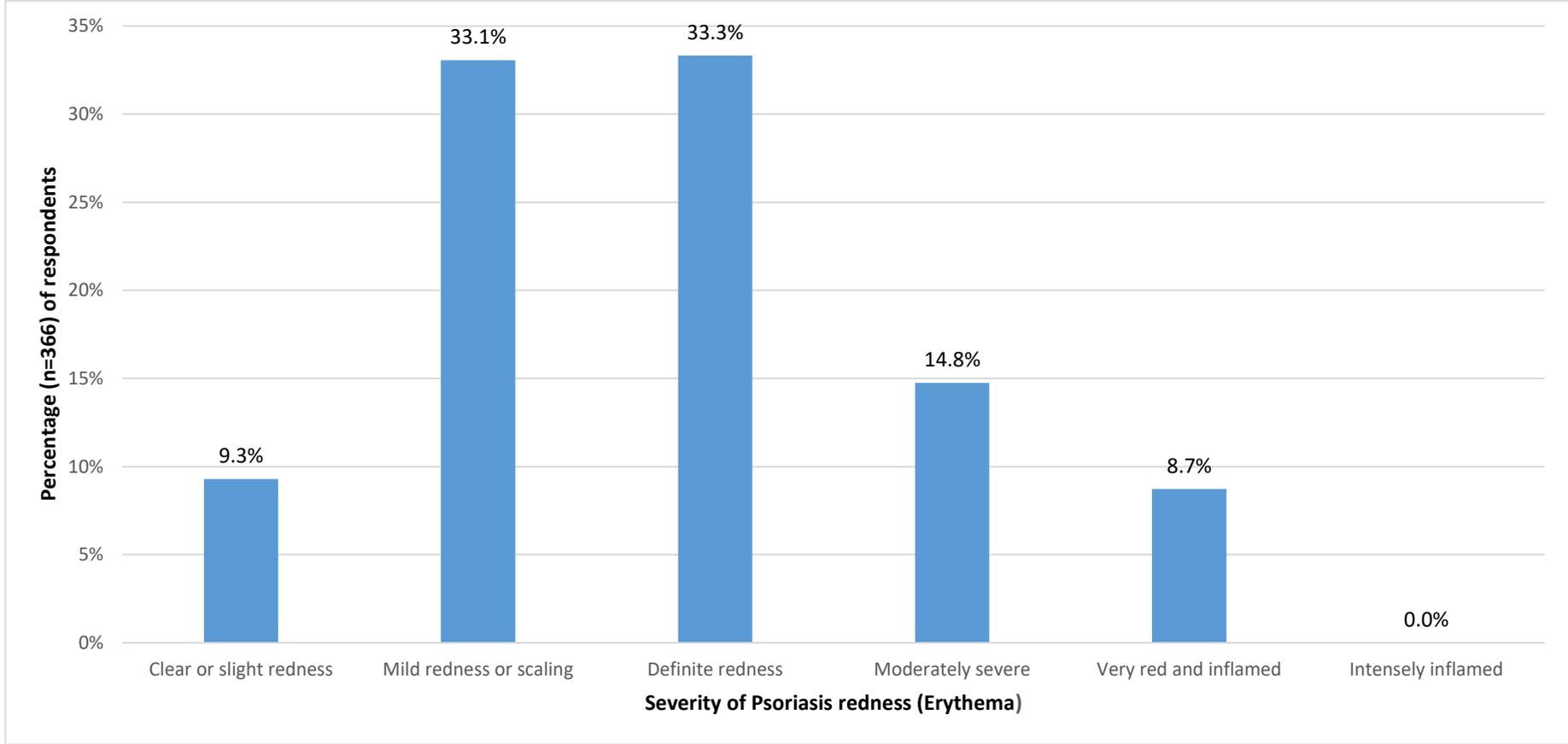


Figure 6.4: Psoriasis severity (erythema) measured with self-assessed Simplified Psoriasis Index.



6.3.1.1 Health status

Figure 6.5 shows the reported level of health status using the EQ5D-5L in this study sample. Nearly two-fifths of the sample (n=70; 19.1%) reported 'perfect' health at the time they completed this survey. A few respondents (n=7; 1.9%) reported the most severe level (extreme problems) under the anxiety and/or depression domain. Almost two-thirds (n=253; 69.1%) of respondents reported some level of problem with pain/discomfort. It was interesting to note that usual activity (n=133; 36.3%) and mobility (n=102; 27.9%) were also affected by psoriasis. About 0.6% (n=2) reported extreme problems under the usual activity domain and 0.3% (n=1) reported extreme problems under both safe care and pain/discomfort domain. No respondent reported extreme problems with mobility.

Figure 6.5: Distribution of EQ-5D-5L responses by level

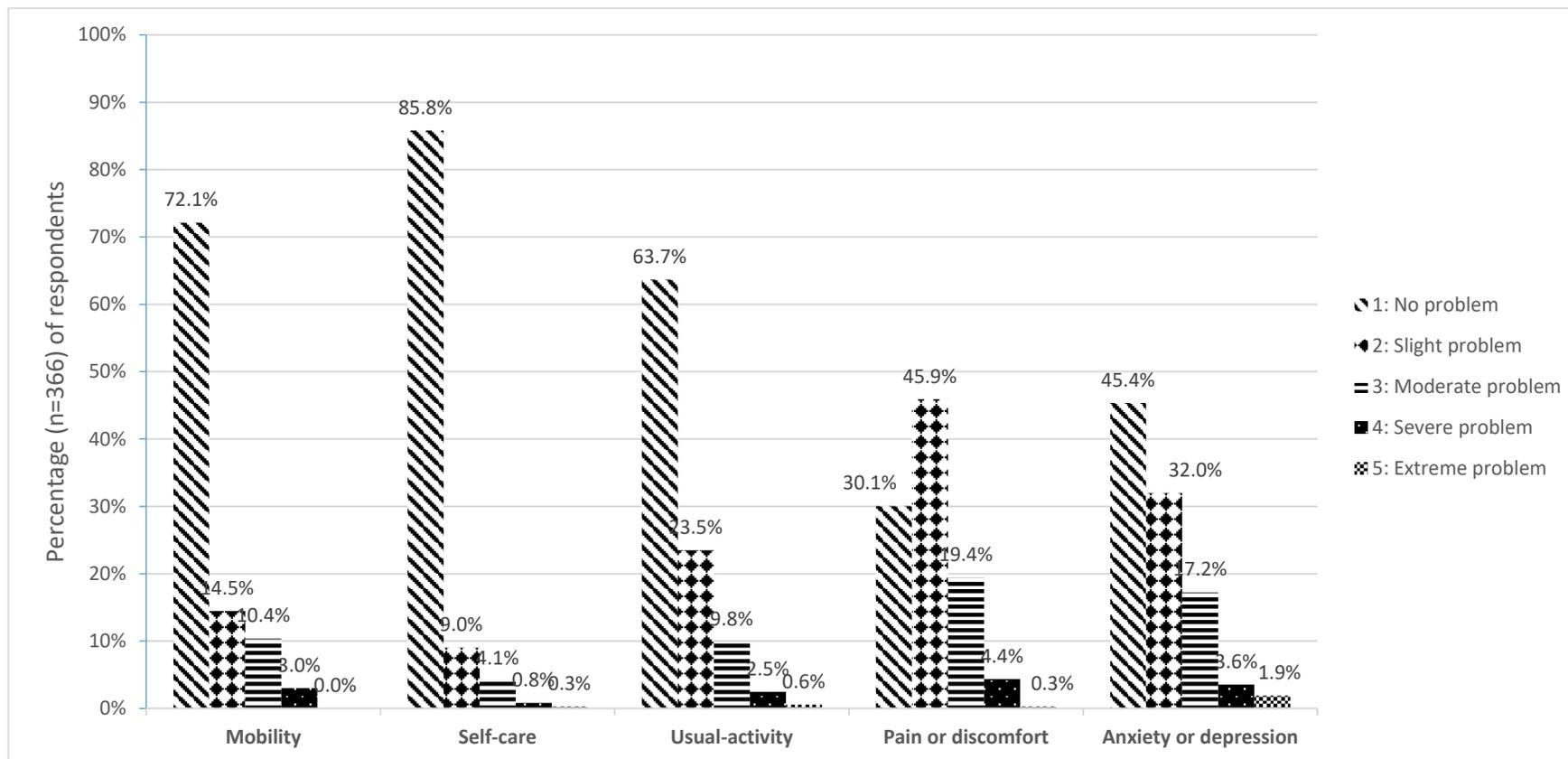


Table 6-4 shows the utility scores generated by using two different approaches to calculate preference weights for the EQ5D-5L.

Table 6-4: Summary of measures of health status, wellbeing and psoriasis severity

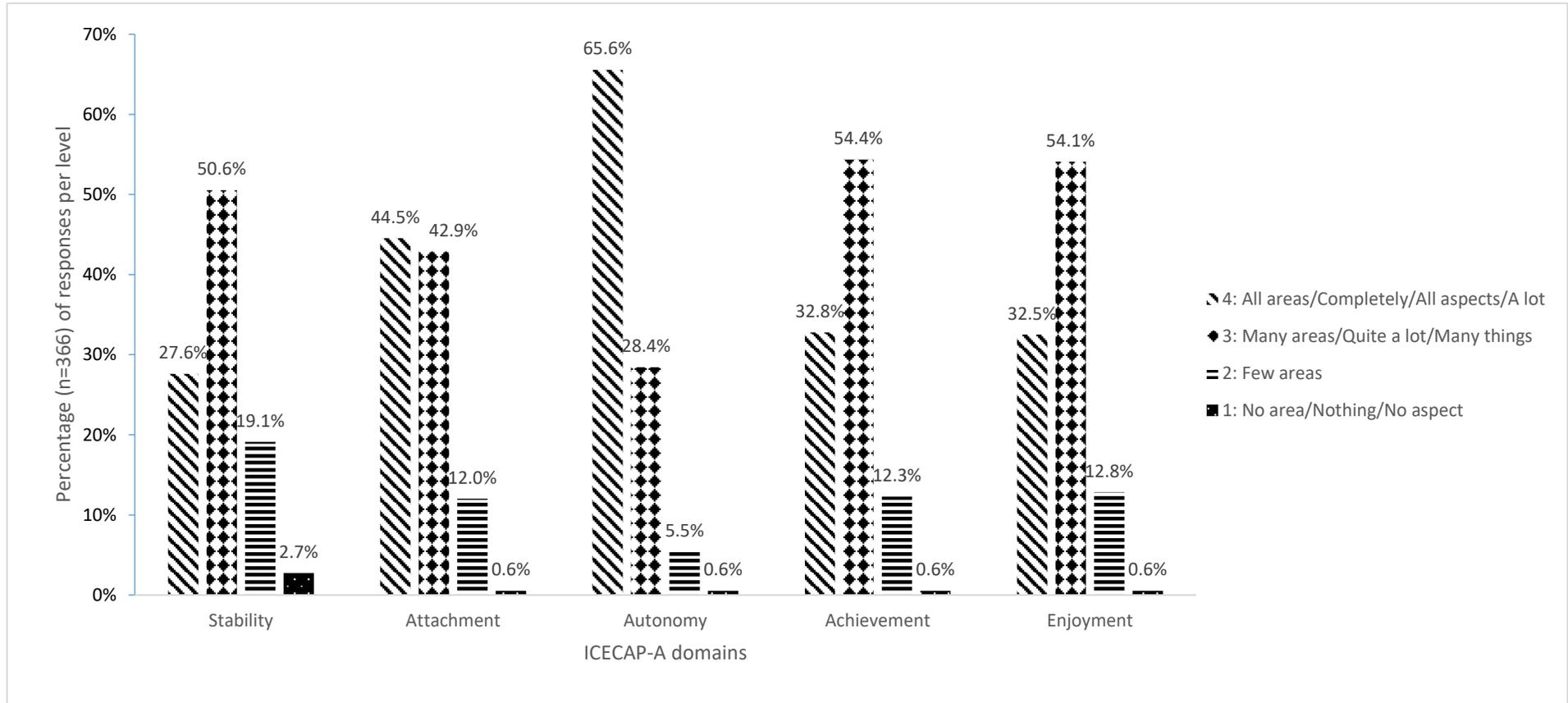
Summary statistic	Outcome measure score				
	Health status			Capability	Disease Severity
	'Hernandez' EQ5D-5L utility score ^a (n=346)	'Van Hout' EQ5D-5L utility score ^b	EQ5D-5L Visual analogue scale score	ICECAP-A ^c	Self-assessed Simplified Psoriasis Index score (SPI)
Mean value [Standard Deviation]	0.75 [0.19]	0.76 [0.20]	74.26 [17.13]	0.85 [0.15]	6.3 [6.9]
Median value	0.77	0.77	80.0	0.89	4.25
25 th percentile value	0.67	0.68	65.0	0.80	1.50
75 th percentile value	0.85	0.85	90.0	0.95	9
Minimum value	-0.25	-0.25	5.0	0.15	0.0
Maximum value	0.99	1.0	100	1.0	50.0

^avalued using Hernández-Alava and Pudney, (2018) approach; ^bvalued using Van Hout et al., (2012) approach; ^cvalued using the UK index values (Flynn et al., 2015);

6.3.1.2 Capability

Figure 6.6 shows the reported impact on well-being measured using the ICECAP-A. The most affected commonly domains were stability, enjoyment, achievement and attachment. The mean capability score generated using the ICECAP-A weight was 0.32 (range: 0 to 0.95) (see Table 6-4) (Flynn *et al.*, 2015). The capability weights are calculated on a constant scale in which a score of zero represents 'no capability' and a score of one represents 'full capability' (Flynn *et al.*, 2015).

Figure 6.6: Summary of reported levels for each domain of ICECAP-A



6.3.2 The broader impact of living with psoriasis

Over three quarters (n=280; 76.5%) of survey participants provided responses to the open-ended question. Following a framework approach to thematic analysis of the open-ended question responses to understand the broader impact of living with psoriasis, ten recurrent themes were identified, see Appendix 6.6). A thematic framework of these ten recurrent themes, under which the responses were sifted and sorted, was set up. Prior to the data analysis, two themes considered were health-related quality of life (HRQoL) and wellbeing. These two themes were later split into physical and mental impact. Six other themes that could not fit under these four themes emerged. The different spheres of the impact of psoriasis were identified to include HRQoL (physical and mental), wellbeing (physical and mental), the impact of severe disease on the individual as well as their lifestyle, the impact of treatment, impact of external factors, the unclassified impact of the disease and the impact of the presence of other long-term conditions. The ten themes are presented below with example comments from respondents.

Theme 1: Physical impact on HRQoL

Several respondents reported a variety of physical impacts on HRQoL that were caused by living with psoriasis such as bleeding/split skin, burning sensation, dry skin, flare-ups, itching, pain, and scaling/thickening of the skin. One respondent reported:

“Thickening and splitting of soles of feet causes much pain and discomfort when trying to walk”. [ID 12]

Theme 2: Mental Impact on HRQoL

Living with psoriasis also had an impact on the mental aspects of HRQoL. One of the respondents reported being anxious because of their appearance:

“My anxiety levels are through the roof and the thought of baring any skin throughout the summer cripples my mind” [ID 256]

Theme 3: Physical Impact on wellbeing

Physical impacts on wellbeing included appearance, occupation, sexual intimacy, and sleep. Several respondents highlighted how appearance influenced their daily lives. For example:

“Although my skin is clearer now than it has ever been, I still have remaining body image issues and appearance anxiety... I think I have been so conditioned into worrying about the way my skin looks, that worry has never gone away - even though my skin has cleared!”, [ID 13]

A few participants noted the occupational challenges resulting from the appearance of psoriasis:

“I work in the NHS so I have to be bare below the elbow - I find exposing my arms embarrassing and understandably people do stare (yes even in the NHS!)”. [ID 238]

Others struggling with the appearance of psoriasis are those in customer-facing roles:

“With it being on my face it is difficult to treat while maintaining a full time, customer-facing role”. [ID 340]

Sexual intimacy was also said to be impacted. In cases where the genital areas are affected, it proved to be a barrier to sexual intimacy:

“I also get psoriasis in my private areas” and “Being intimate with my husband is also difficult”. [ID 224]

Theme 4: Mental Impact on wellbeing

Mental aspects of the impact of living with psoriasis included feelings of distress/upset:

“Living with psoriasis is such a battle and when I get a flare-up it really upsets me” [ID 235],

Some respondents also reported feeling drained:

“Mentally psoriasis is very draining and very little is said about it” [ID 266].

Feelings of embarrassment were reported by several respondents:

“...the total embarrassment of leaving skin behind when you move”. [ID 112]

Low confidence/self-esteem was also a common impact that several reported:

“I really struggled in school and my confidence has always been very low” [ID 13]

Those with low confidence/self-esteem tended to struggle with socialising:

“When not under control, affects confidence and socialising”. [ID 173]

In addition, several respondents highlighted being self-conscious:

“When it is flaring up, I am more self-conscious and aware of other people’s looks and stares and adjust my day to day regime to compensate” [ID 1]

Of great concern, one respondent reported being suicidal:

“want to kill myself”. [ID 276]

Theme 5: Impact of severe disease on the Individual

Severity of the disease was reported to influence the impact of psoriasis on an individual. Individuals that lived with psoriasis for a long time tend to adapt and found it easier to cope with the mild condition than the severe one:

“I have become used to living with mild outbreaks, but this one is the worst” [ID114].

Theme 6: Lifestyle Impact of psoriasis

Several respondents reported a variety of lifestyle choices impacted by living with psoriasis, such as diet, hygiene routines, hobbies, exercising, clothing choice, socialising, dating, and constant vacuuming of their surroundings. One respondent reported:

“It has such an impact that I have to decide which clothes to wear so it is not obvious or the applications do not affect the look when at work...“There are times when flexural psoriasis in the genital area is so bad I cannot do my fitness” [ID1].

Theme 7: Impact of psoriasis treatment

People living with psoriasis have not been spared from the burden of treatment that comes with most chronic diseases. Several respondents highlighted the impact of the treatment they were receiving for psoriasis. For example:

“So far not reacting well to medication from GP nor what "cured" it the previous time” [ID214]

Theme 8: Impact of external factors

Several external factors have been implicated in triggering flare-ups and psoriasis severity, see Appendix 6.6 The external factors reported were Coronavirus Disease (COVID 19), hormones, winter and stress.

The most recent of these external factors was the Coronavirus Disease (COVID 19) pandemic, due to an infectious newly discovered severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) (WHO, 2020). Most of the impact was attributed to the lockdown measures and constant hand sanitising. One respondent reported:

“The palms of my hands and my knuckles started due to the constant handwashing at the beginning of the covid epidemic” [ID314].

Theme 9: Other impacts of Disease

Other impacts of disease established during this study were a lack of support from the public and healthcare professionals, negative comments and lack of psychological support. For example:

“Once in a gym, a lady insisted that the machine I had been using was thoroughly cleaned as she had noted the psoriasis patches on my elbows” [ID231]and

In addition, a lack of support from the healthcare profession was noted in the comments such as:

“Embarrassing Health professionals worst commentators (little or no understanding)” [ID264],

Theme 10: Impact of other long-term conditions

Several respondents reported being impacted by psoriatic arthritis. The major impact reported was how pain limited their activities. For instance:

“I have psoriatic arthritis and that can make me have some pain and I can get tired” [ID121]

6.3.3 Describing the link between health status and psoriasis severity and capability and psoriasis severity

This section presents the results from a correlation and linear regression analysis to describe the association between health and disease severity and capability and disease severity. The correlation gives the strength of the association whereas the regression presents how much the health status and capability change by a unit change in psoriasis severity.

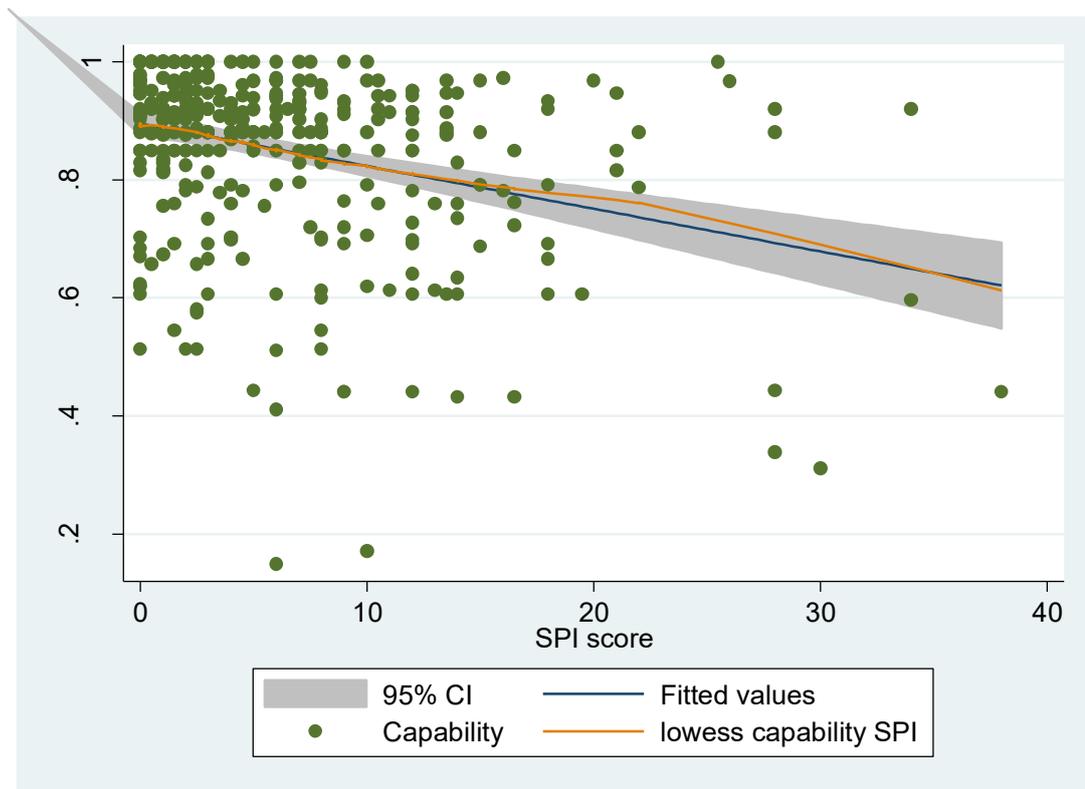
Figure 6.7 shows that there was an observed linear relationship between health status and psoriasis severity. The scatter plot for capability and psoriasis severity showed a similar trend, see Figure 6.8.

Figure 6.7: Scatter plot of EQ5D-5L scores and psoriasis severity (SPI score) with an OLS regression line



EQ5D-5L score calculated using the Van Hout et.al. mapping algorithm based on the UK preference weights (Van Hout et al., 2012).

Figure 6.8: Scatterplot of ICECAP-A scores and psoriasis severity (SPI score) with an OLS regression line



ICECAP-A Scores calculated using the UK preference weights (Flynn et al., 2015).

To quantify the strength of this linear relationship, results from the Spearman rank correlation showed a weak (range 0.20 to 0.39) negative correlation with $r=-0.350$ between health status and severity score. A weak negative correlation was also observed between capability and severity score ($r=-0.282$). This meant that as the SPI score increases, depicting increased severity, the health status or capability, decreased. The severity domains of the SPI were found to be negatively correlated with health status and capability. These domains were “Scalp and hairline”, “face, neck and ears”, “hands, fingers and nails”, “chest and abdomen”, and “genital and anal area”, see Table 6-5.

Table 6-5: Spearman rank correlation between total health status, capability and SPI domains

	Total score SPI score	Scalp and Hairline	Face, Neck, Ears	Arms and Armpits	Hands, Fingers and nails	Chest and Abdomen	Back and Shoulders	Genital and anal area	Buttocks and thighs	Knees, lower legs, and ankles	Feet, toes, and toenails	Overall state of psoriasis
Health status, rho (p-value)	-0.35 (0.00)	-0.25 (0.00)	-0.24 (0.00)	-0.09 (0.09) ^a	-0.16 (0.00)	-0.17 (0.00)	-0.102 (0.05) ^a	-0.189 (0.00)	-0.076 (0.15) ^a	-0.102 (0.05) ^a	-0.182 (0.00)	-0.334 (0.00)
Capability rho (p-value)	-0.28 (0.00)	-0.185 (0.00)	-0.233 (0.00)	-0.080 (0.13) ^a	-0.089 (0.09) ^a	-0.071 (0.17) ^a	-0.120 (0.02)	-0.109 (0.04)	-0.059 (0.26) ^a	-0.056 (0.28) ^a	-0.034 (0.52) ^a	-0.289 (0.00)
<p>Note. Strength of correlation using rho score: very weak (0 to 0.19), weak (0.20 to 0.39), moderate (0.40–0.59), strong (0.60–0.79), and very strong (0.80–1).</p> <p>a= not statistically significant</p>												

Full results from the linear regression using OLS estimation (see Equation 6.10) are presented in Table 6-6 (health status) and Table 6-7 (Capability). The preferred model used was selected based on the information criterion, AIC and BIC.

$$y = \beta_0 + \beta_1 x_{severity} + \beta_2 x_{duration} + \beta_3 x_{sex} + \beta_4 x_{mm} + \beta_5 x_{injection} + u \quad \text{Equation 6.10}$$

Estimating health status, Equation 6.10, using OLS regression showed that as the severity score increased by one unit, health status decreases by -0.01 (95% CI [-0.013 to -0.008]) while controlling for duration of psoriasis, sex, number of comorbidities and receiving injectable treatment.

Factors that were seen to influence health status were duration of psoriasis, sex, and the number of comorbidities. Duration of psoriasis showed the greatest impact on health status followed by the number of comorbidities. In addition, the use of injectable treatment was seen to be linked to severity and health status. Those on injectable treatment were seen to have a lower health status (-0.06, 95% CI [-0.109; -0.012]). Variables that were not statistically significant were omitted from the final regression model.

Table 6-6: Results from OLS estimate regression showing the impact of psoriasis severity on health status

	Coef.	St.Err.	t-value	p-value	[95% Conf Interval]		Sig
Psoriasis severity	-.011	.002	-6.66	0	-.015	-.008	***
Sex (male=1)	.06	.017	3.61	0	.027	.092	***
Psoriasis duration (years)							
1 to 2	.654	.042	15.74	0	.572	.736	***
3 to 5	.551	.058	9.48	0	.437	.665	***
6 to 10	.659	.038	17.19	0	.584	.735	***
More than 10	.642	.024	26.21	0	.593	.69	***
Comorbidities							
1	-.077	.021	-3.61	0	-.119	-.035	***

2	-.102	.024	-4.23	0	-.15	-.055	***
>=3	-.187	.029	-6.44	0	-.244	-.13	***
Injection treatment	-.062	.031	-1.98	.048	-.124	-.001	**
Constant	.241	.029	8.26	0	.184	.299	***
Mean dependent var	0.756		SD dependent var		0.199		
R-squared	0.382		Number of obs		350.000		
Akaike crit. (AIC)	-286.856		Bayesian crit. (BIC)		-248.277		

*** $p < .01$, ** $p < .05$, * $p < .1$ Reference group: Female, in the first year of psoriasis, with no comorbidity.

As shown in Table 6-7, capability reduced by 0.007 units (95% CI [-0.01; -0.004]) for every unit increase in psoriasis severity. Duration of psoriasis and being male had a positive impact on capability. Receiving injectable treatment had a negative impact on capability, alas it was not statistically significant.

Table 6-7: OLS regression estimates of the effect of psoriasis severity on capability

	Coef.	St.Err.	t-value	p-value	[95% Conf Interval]		Sig
Psoriasis severity	-.007	.002	-4.36	0	-.01	-.004	***
Sex (male=1)	.034	.014	2.39	.017	.006	.061	**
Psoriasis duration (years)							
1 to 2	.132	.047	2.81	.005	.04	.224	***
3 to 5	.15	.044	3.38	.001	.063	.238	***
6 to 10	.141	.029	4.91	0	.085	.198	***
More than 10	.149	.02	7.60	0	.111	.188	***
Comorbidities							
1	-.022	.018	-1.19	.234	-.058	.014	
2	-.045	.018	-2.47	.014	-.08	-.009	**
>=3	-.096	.026	-3.62	0	-.148	-.044	***
Injection treatment	-.034	.023	-1.52	.129	-.079	.01	

Constant	.767	.024	31.64	0	.72	.815	***
Mean dependent var	0.852		SD dependent var		0.146		
R-squared	0.194		Number of obs		350.000		
Akaike crit. (AIC)	-412.138		Bayesian crit. (BIC)		-373.559		

*** $p < .01$, ** $p < .05$, * $p < .1$ Reference group: Female, in the first year of psoriasis, with no comorbidity.

6.4 Discussion

The study aimed to quantify the burden-of-disease in people living with psoriasis by eliciting patient-reported impacts and establishing a link between measures of HRQoL, Capability and disease severity. This study showed the wide range and substantial impact of psoriasis that encompasses different spheres of life for individuals living with psoriasis. Findings from this study provide a comprehensive assessment of the burden of psoriasis by providing evidence of its impact on health status and wellbeing. Results from the open-ended questions showed that the impact of psoriasis goes beyond health status and wellbeing measures. Similar to the study by Dubertret *et al.* (2006), this study covered conventional indicators of psoriasis, like psoriasis severity, and physical, emotional and social wellbeing.

Both the EQ-5D and ICECAP-A were able to capture psoriasis severity. This was shown by inverse relationship i.e., as the SPI score increased, the health status and capability score decreased. Similarly, those self-reporting mild to moderate disease severity also reported minimal to no impact on their health status and capability.

Being a wellbeing tool, the ICECAP was expected to be more sensitive to changes in severity than the EQ-5D owing to the various non-health-related impact of psoriasis. The EQ-5D in practice proved to be more responsive than ICECAP-A to changes in psoriasis severity. This could be partly explained by individual adaptation to living with psoriasis. For instance, several respondents had indicated the impact was worse in their younger days than in adulthood. With the average age of around 50 years in the study, it can be assumed that most people had adapted to the condition. Nonetheless, the ICECAP-A was recently validated for use in dermatology conditions (Rencz *et al.*, 2021). This is expected to drive an increase in the use of ICECAP in dermatology

conditions such as psoriasis. Increased use of the tool will serve as a starting point to validate the findings of how psoriasis impacts capability.

The EQ-5D is a measure of health status that is likely to be more sensitive to physical signs of psoriasis such as pain and mobility. Although health status and capability are measured on a different scale, standardised coefficients were used to compare which tool was more responsive to changes in psoriasis severity. Findings from one study, looking at the validity and responsiveness of QoL measures in psoriasis, concluded by supporting the continued use of dermatology-specific measures, Dermatology Life Quality Index (DLQI), and the Short-form (SF)-36 in assessing psoriasis treatment. It further recommended consideration of the EQ-5D as a general measure of patient-reported outcomes. This recommendation can further be extended to the assessment of burden-of-disease in psoriasis. Studies including the ICECAP-A and the DLQI should be conducted to compare the responsiveness.

The health status mean score of 0.77 was lower than the UK population average of 0.856, and the 55 to 64 years old score of 0.804 (Szende, Janssen and Cabasés, 2014). A systematic review comparing the health status in psoriasis patients to those with other chronic conditions found EQ-5D scores to be similar (Møller *et al.*, 2015). The results from this study were also within the range (0.52 to 0.9) identified in the systematic review (Møller *et al.*, 2015).

It is important to note that comparisons of health status across different study populations and conditions are limited by the study design and sample size. Several studies are powered to detect clinical or biological changes and not to detect differences captured by preference-based measures. This approach has continued to bring challenges when calculating the sample size for studies such as this one. There was evidence of a number of comorbidities impacted on the HRQoL and capability (Yang, Brazier and Longworth, 2015). However, the marginal difference in those with or without psoriasis could not be ascertained in this study as it was only based on individuals living with psoriasis.

Several respondents reported the impact of psoriasis as being worse during childhood and adolescent age. In this study, it was assumed that people with psoriasis tend to adapt with increasing age in adulthood. The duration of living with psoriasis was

included as one of the independent variables in the regression analysis. Duration with psoriasis was found to be positively associated with health status and capability.

Identified themes from the framework analysis, showed that the burden of psoriasis goes beyond what is captured by measures of health status (EQ-5D) and capability (ICECAP). There is evidence that the EQ-5D has some limitations in a specific context such as psoriasis (Swinburn *et al.*, 2013). For example, impacts like the choice of clothes, lack of support from healthcare professionals, and external factor impacts such as weather, vacuuming etc. did not seem to fit under the dimensions of the EQ-5D and ICECAP-A. Several respondents reported perfect health and capability, i.e., a score of 1, yet some of them still indicated; self-consciousness, feeling dirty, unattractive, embarrassed, frustration, anger, choosing special clothes, treatment inconveniencing etc. This showed that relying on measures of health status and capability results in undervaluing the impact accruing to the people living with psoriasis. Similar to the findings of Dubertret *et al.* (2006), this study found that psoriasis impacted daily activities such as sleep, sexual relationship, and enjoyment of pastimes. This evidence suggests a need to critically consider bolt-on EQ-5D measures that capture disease-specific aspects of impact (Swinburn *et al.*, 2013).

A significant number of respondents were receiving prescribed treatment and non-prescribed treatment. Overall, up to 93% were receiving some form of treatment. Therefore, the respondent's perspective on treatment effectiveness was also investigated in this survey. Although almost 70% of the respondents in the survey were satisfied with their treatment, others reported that their treatment was either ineffective or they could not categorically state if it was effective or not. This study also found that perception of treatment effectiveness changed with time in some patients. A significant number of respondents reported that in the long run, some treatment that was once effective stopped working. This results in frustration. This information is cardinal in managing and reviewing treatments to ensure patient satisfaction. Some people also felt the need to be started on biologics but felt their access was being hindered by the costs that the NHS might incur.

Several respondents lamented the inconvenience and frustration of using topical treatments. These treatments were also reported to be greasy and messy which impacted the choice of clothes and presumably adherence.

Outliers from SPI scores above 35 exhibited a violation of linearity. These outliers were excluded from the data analysis. By accounting for these outliers, the relation is still assumed to be linear and a linear regression was fit to the data.

The Adjusted Limited dependent variable mixture model (LDVMM) was another potential option for modelling EQ-5D data. Considering the known characteristics of EQ-5D data distribution adjusted limited dependent variable mixture models are better performing than other traditional models (Hernández Alava, Wailoo and Ara, 2012; Alava and Wailoo, 2015).

Other traditional models have the potential of generating implausible values. The adjusted limited dependent variable mixture model is a mixture of adjusted Tobit-like models (Hernández Alava, Wailoo and Ara, 2012; Alava and Wailoo, 2015). Being a mixture of Tobit-like models allows for the benefits from the strength of Tobit models while taking care of its weaknesses. Tobit models give biased results in the presence of heteroscedasticity and thus rely on the assumption of homoscedasticity (Pullenayegum *et al.*, 2010). Although other models such as the Censored Least Absolute Deviation (CLAD) have been recommended, adjusted dependent variable mixture models perform better when the data is not unimodal, has a gap and is heteroscedastic (Pullenayegum *et al.*, 2010; Hernández Alava, Wailoo and Ara, 2012). Data that is unimodal with a gap between the highest score (perfect health) and the second-best can be modelled using an adjusted limited dependent variable model (Devlin, Parkin and Janssen, 2020).

Nevertheless, ALDVMM could not be fit in this study due to the range of the health status scores obtained from the mapping algorithm. The ALDVMM has values bound between -0.59 to 0.83 and 1. Outcomes from the mapping algorithms had scores between 0.83 and 1.

6.4.1 Strengths

The main strength of this study was that it was answered by residents in the UK living with psoriasis. This was in with the identified lack of UK burden-of-disease studies in people living with psoriasis, see chapter 4. This captured the burden of living with psoriasis on HRQoL, wellbeing, and patient-reported impact.

This study used validated tools which included the EQ-5D, ICECAP and SPI to estimate HRQoL, capability, and disease physical severity respectively. Results from generic measures of health and capability allow for comparison across other disease areas. Therefore, this made it possible to compare the burden-of-disease of psoriasis to other diseases. Estimating HRQoL and capability for treatment naïve respondents was also useful as it provides baseline values for economic evaluation.

The study included open-ended questions that allowed respondents to explain the importance of psoriasis in terms of its impact on elements not fully captured by the EQ-5D and ICECAP-A. Using open-ended questions to capture patient-reported impact provided an opportunity in capturing burden-of-disease of psoriasis that would otherwise not be captured by generic measures of health and capability. Impacts such as time spent on skincare and limitations in performing daily activities such as gardening were only elicited from the open-ended questions.

The patient reported impact from the survey provides a basis for following up with interviews or focus groups. A significant number of patients with psoriasis have been identified to have alexithymia, a condition where people often have difficulty recognising and expressing emotions (Sampogna *et al.*, 2017; Tang *et al.*, 2022). The failure to acknowledge and express emotions may leave emotions unresolved, which can impact on the patient's health (Sampogna *et al.*, 2017; Tang *et al.*, 2022). A meta-analysis of 16 studies involving 3752 found that more than a quarter (28%) of people with psoriasis have alexithymia. Another study reported alexithymia in about 25% of the respondents (Sampogna *et al.*, 2017; Tang *et al.*, 2022). The prevalence of alexithymia in psoriasis is higher than that in the general population (Tang *et al.*, 2022).

6.4.2 Limitations

The survey was completed by a relatively small sample size compared with the number of people living with psoriasis in the UK. There are around 2.8% (2815 per 100,000) of the UK population living with psoriasis. Some studies have surveyed about 18,000 respondents covering five countries but these did not include the UK (Dubertret *et al.*, 2006). Nonetheless, the results generated in this study are similar to those from the large European study (Dubertret *et al.*, 2006).

The sampling frame was another limitation of this study as the study sample from the Psoriasis Association UK was not representative of the UK psoriasis population. The strategy of recruiting from the Psoriasis Association UK membership pool was prone to cause bias. This was because not everyone with psoriasis might be interested in networking and seeking information from the association. Anecdotal evidence and the sex distribution of respondents in this survey shows that the membership of the Psoriasis Association UK is prominently Caucasian women. This shows a bias in the study sample which gives an over representation of Caucasian women contrary to the expected prevalence distribution by age and sex. Other studies have reported more or less equal prevalence of psoriasis in both males and females. For instance, results from chapter 5 showed that up to 52.2% of those with psoriasis between 2007 to 2017 were female. This was also similar to results from a UK study (Springate *et al.*, 2016). Generalisation of findings in this chapter to the psoriasis population in the UK should be carried out with caution as this study sample did not reflect the country demographic of people living with psoriasis. Recruiting through GPs and dermatology clinics would have helped eliminate this potential bias and increase the sample size.

To recruit study participants via the NHS, the fundamental steps are identifying collaborators and participants. Understanding the target collaborators or participants is important in helping to tailor the message that addresses their needs and explore their interest in the topic. In the case of psoriasis, potential collaborators would be dermatologists and GPs. During the proposal draft stages, it would be helpful to approach potential collaborators who could also give helpful input into the final study proposal. NHS REC review for sites in England would be needed to recruit patients in the NHS. This is because the study would involve potential research participants identified in the context of, or in connection with, their past or present use of services

(NHS and adult social care), including participants recruited through these services as healthy controls. Considering the low-risk nature of the study, NHS RECs proportionate review process would be appropriate in this instance. The benefit of using the proportionate review process is that it is quicker and does not require attending meetings. However, where study ethical issues are noted, full REC would be required. An application for NHS REC is prepared using the Integrated Research Application System (IRAS). The IRAS is a single system for applying for the permissions and approvals for health and social care / community care research in the UK (University of Manchester, 2021). Some of the mandatory requirements for NHS REC application are evidence of qualification in relevant matters relating to research and governance, honorary contract with the relevant Trust or research passport if more than one Trust is involved, sponsor green light, site approval, reporting amendments, incident reporting and progress and final report (IRAS, 2021).

In addition, this sampling strategy could have resulted in the under-representation of some groups. Although psoriasis prevalence is higher in the Caucasian group, the ethnic sample distribution in this study could have underestimated the prevalence in other ethnic groups. Similarly, the higher proportion of individuals with higher education could be explained by sampling strategy, as more educated individuals are more likely to engage with support from charities and groups as compared to the lower educated ones. This observation was similar to that observed in a study quantifying presenteeism in people with rheumatoid arthritis (Jones, 2017).

Given the prominence of co-morbidities and obesity in psoriasis reported in previous chapters, another limitation of this study was the omission of details on obesity in the survey. The logic to omit obesity related details in the survey related was to encourage respondents to complete the survey by reducing the burden of asking them for information that might not be handy and keeping the survey relatively shorter. In addition, subjective methods of estimating BMI using weight and height have been reported to be prone to systematic errors in reporting by different body size and social demographic characteristics, response bias and potential recall bias can be high. Another study concluded that standard subjective measures of obesity do not often provide reliable measurements for people with severe obesity, especially those with mobility difficulties (Williamson, Blane and Lean, 2022). Therefore, an inclusion of

questions on obesity would potentially be prone to selection bias. People with mobility issues would also find it difficult to have their height and weight measured. To address these challenges, recruiting participants from a clinical setting and obtaining objective measures of weight and height would provide a more accurate measure of BMI.

The other limitation could be attributed to the cross-sectional study design. Because cross-sectional studies have no time dimension and only give a snapshot of findings, they can limit the inference on risk or disease or causal relationships. For instance, the results showed that people with a higher consumption of alcohol had a higher quality of life and capability. It was unreasonable to assume drinking more increases quality of life, instead, the findings reflect that those with the less severe condition and consequently higher quality of life were more likely to socialise and drink more. The results also reflected attempts to cut down on alcohol consumption and smoking for those individuals experiencing an increasing severity of the condition.

6.5 Conclusion

Psoriasis has been identified to affect health status and beyond health outcomes such as capability. Findings from this study provide an opportunity for a holistic approach in managing psoriasis taking into consideration all stakeholders. For instance, it calls for healthcare practitioners to be sensitive to the needs of the patient.

The three main findings in the chapter were:-

- Existence of other long-term conditions were common in people living with psoriasis. This reiterates the need for continued research focused on interventions tackling multimorbidity in people living with psoriasis.
- Significant reduction in both health and wellbeing in people living with psoriasis. The broader impact of psoriasis was identified to transcend the impact health and wellbeing to include other aspects such as lifestyle, and treatment disutility.
- The longer people live with psoriasis the more they endure it and less likely describe the full impact that can be captured by standardised health related quality of life measures such as the EQ-5D and wellbeing measures such as the

ICECAP. This justifies the need to include open ended questions in survey and utilise study designs that allow for people to fully express themselves, for example in in focus groups.

7 Discussion

Chapter summary

The overall aim of this thesis was to quantify the economic impact of psoriasis in the UK. This thesis used four main methods to address five objectives presented in five chapters.

This chapter will present the discussion of the main findings from the empirical chapters comprising this PhD. Section 7.1 and 7.2 will present the summary of the findings and reflections across the thesis respectively. Strengths and weaknesses, policy implications, methodological implications and future research will be presented in sections 7.3, 7.4, 7.5, and 7.6 respectively.

7.1 Main findings

This section presents the discussion of the main findings from the reviews and empirical studies presented in chapters that fulfil each of the main thesis objectives presented in section 1.8.

Chapter 2 set out with the aim of identifying, and if necessary developing, a descriptive framework defining a nomenclature system for the relevant components and methods when identifying and quantifying the economic impact of disease. No pre-existing framework to enable the consistent and coherent reporting and appraisal of studies that identify, measure and value economic impact of disease was identified. The lack of a pre-existing framework posed a challenge in establishing the scope of reviewing cost-of-illness and burden-of-disease in people living with psoriasis. To address this challenge, chapter 2 conceptualised and produced a de-novo framework defining economic impact of disease by taking a microeconomic view. The framework clearly outlined the distinction between cost-of-illness and burden-of-disease, see section 2.3.1. Based on expert opinion, the framework had face validity to look at methods for economic impact of disease studies. This provided a structured approach to critically

appraising the available cost-of-illness and burden-of-disease evidence reviewed in chapters 3 and 4 respectively.

A focus on both cost-of-illness and burden-of-disease was motivated by the direct value for policy-makers and stakeholders working within economic impact analysis and trying to understand the financial, health and beyond health implications of living with psoriasis.

Items that must be considered during critical appraisal of economic impact of disease were identified and outlined in chapter 2. The framework allowed for the evaluation of the completeness of reporting of economic impact of disease studies by taking into consideration the study perspective, time horizon and research objectives or research question. Using the framework in the critical appraisal of cost-of-illness and burden-of-disease of psoriasis allowed for the evaluation of the quality and relevance of each reported item by taking into account the identification, measurement and valuation of the selected outcome.

Economic impact of psoriasis studies should attempt to provide information on both the cost-of-illness and burden-of-disease. Utilising the developed framework in designing studies in psoriasis provides for a 'fuller' estimation of the total economic impact of disease which is meaningful to economists. Information from the cost-of-illness allows for estimation of the financial impact of the disease on the payer in terms of direct and indirect costs (productivity loss). Information from burden-of-disease in people living with psoriasis should be concerned with estimating health and beyond-health consequences on the affected individual. Guidance concerning a clear framework for appraising economic impact of disease evidence is useful to decision-makers who seek to fully understand the costs and consequences posed by the condition. Having a set framework helps decision-makers have a consistent and coherent way of evaluating evidence and reporting the economic impact estimates in order to make informed decisions for the benefit of the population.

Chapter 3 of this thesis critically appraised cost-of-illness studies for psoriasis using the framework developed in chapter 2. No up-to-date UK relevant studies were identified. Studies from the UK were judged to be outdated in terms of reflecting current

practice. The lack of reliable UK published studies motivated the need to conduct a cost-of-illness study, as reported in chapter 5.

The majority of studies included in the cost-of-illness of psoriasis systematic review were conducted in five countries, with most of the studies conducted in the US. This highlighted the unequal distribution of cost-of-illness studies for psoriasis in terms of country of origin. The high number of cost-of-illness studies in the US can be attributed to the intense competition between patient advocacy groups, medical associations, research institutions and governmental agencies to obtain funding to support-disease specific research programmes (Kymes, 2014). Secondly, the open hostility and outright prohibition of the use of economic evaluation by government payers in the US could be linked to the high output of economic impact studies aimed at driving advocacy agendas (Kymes, 2014).

A summary of the evidence showed a difference in estimates and a lack of clarity. It became apparent that economic impact of disease was not a 'single' outcome. The varying evidence of cost-of-illness within and across countries highlighted the significant variation in the methods used to identify, measure and value cost-of-illness of psoriasis, type of data and level of aggregation. A number of studies in the economic impact of disease space have been noted to be conceptually flawed and offer little economic meaning (Chisholm *et al.*, 2010). The varying evidence poses a challenge for decision-makers to compare evidence across studies and inform their decisions.

The second contribution reported in chapter 3, a systematic review of cost-of-illness of psoriasis, was identifying a gap in the cost-of-illness of psoriasis evidence relevant to the UK. No up-to-date cost-of-illness evidence from the UK was identified. The evidence from the UK was deemed outdated considering the evolution of the management of psoriasis. Up-to-date evidence is important for organisations such as the global psoriasis atlas (GPA) that 'seek to drive continuous improvement in the understanding of psoriasis and to uncover how it affects both the individual and society at large' (GPA, 2021). Realising this gap is useful for the GPA because one of the four areas of evidence they seek is an understanding and characterisation of the economic impact of psoriasis. Understanding this knowledge gap is helpful for the GPA to identify relevant research areas and commission research aimed at plugging this gap. Similarly, noting that most of cost-of-illness due to psoriasis is mainly generated

by five developed countries provides the GPA with a chance to advocate for research on people living with psoriasis in other countries in order to provide accurate global estimates.

Findings from the systemic review of published burden-of-disease studies were presented in chapter 4. Similar to chapter 3 findings, the unequal distribution of research on burden-of-disease for people living with psoriasis, in terms of countries of origin, was also noted in chapter 4. The majority of studies were conducted in the US. The majority of studies reported on the HRQoL and no study reported on capability. The EQ-5D was the most common generic measure of HRQoL. Although there is an established link between disease severity, HRQoL and capability, only half of the studies reported disease severity alongside HRQoL.

Chapter 5 of this thesis explored the impact of psoriasis on health care resource use and ultimately estimated costs attributable to psoriasis in the UK taking a health sector perspective. The main focus was to understand factors driving health care costs attributable to psoriasis by using a matched cohort study design to analyse linked CPRD-HES data with national coverage for England from 2007 to 2017. The study found that the presence of psoriasis increased health care costs as compared to the control patients without psoriasis. This result was consistent across the primary and secondary care sector. The impact of obesity and multimorbidity conditions on health care costs was also explored in this study. The underweight population had a similar increased health care cost impact as the severely obese population (42%) when compared to the population with a normal BMI. An increase in the multimorbidity score was associated with up to 81% increased health care costs. Similarly, a combined increase in multimorbidity score and obesity was associated with an increase in health care costs. However, the rate of change in health care costs was lower for psoriasis patients with increasing multimorbidity index and obesity as compared to non-psoriasis. This can be attributed to economies of scale in managing chronic health conditions, especially with increased management of chronic conditions in primary care.

This study did not explore alternate costing approaches, top-down and bottom-up, to establish the effect on cost-of-illness estimates. Cost-of-illness estimates have been known to be influenced by the costing approach (Mason, 2019).

Another weakness of using administrative datasets is the lack of stratifying costs by disease severity. This is because there is a lack of information on psoriasis severity from CPRD-HES. It is well established in health economics that disease severity is likely to impact health care resource use and costs. This observation was consistent with that of other scholars (Löfvendahl, 2016; Thompson, 2019).

Similar to not accounting for disease severity, this thesis did not account for the type of treatment. For instance, biologics are well known to be high priced and therefore likely to impact overall health care costs.

Chapter 6 reported results from an empirical study estimating the burden-of-disease in people living with psoriasis in the UK. The burden-of-disease study was focused on estimating the physical disease severity, HRQoL and capability which were measured using the SPI, EQ-5D and ICECAP respectively. Lived experiences of people living with psoriasis were also gathered during the survey. Most studies estimating the burden-of-disease in people living with psoriasis have mainly focused on physical severity and disease-specific psychological impact. The study reported in chapter 6 opted to include validated generic measures of health status and capability that have valuation sets hence rendering the results to be comparable across disease areas. The study found a negative relationship between increasing psoriasis severity and HRQoL. A similar relationship was also observed between increasing psoriasis severity and capability. HRQoL was found to be more sensitive to changes in physical disease severity than capability. Framework analysis of data from open-ended questions showed that some burden-of-disease effects in people living with psoriasis could not be fully captured using the EQ-5D and the ICECAP.

7.2 Overall thesis

This thesis contributes to the understanding of the economic impact of psoriasis in the UK through evidence generated from the observational cost-of-illness study and the burden-of-disease survey. Psoriasis poses a substantial economic impact on society including the monetary costs to the NHS, reduced individual health, and beyond health consequences. These contributions are relevant to researchers and decision-makers in the health and care sectors.

The framework developed in chapter 2 was the first contribution to the body of knowledge. This closes the gap on the need for a clear framework to assess studies reporting the economic impact of disease in general and psoriasis, in particular, to enable decision-makers to interpret the reported evidence and evaluate the relevance of such findings to their jurisdictions. The design and reporting of the cost-of-illness study was based on the framework developed in chapter 2. Taking the health care (NHS) perspective influenced the sole inclusion of direct health care costs. The nature of the CPRD-HES data posed limitations on the inclusion of direct non-medical costs and indirect costs.

The burden-of-disease study design and reporting were also guided by the framework. The evidence generated from the burden-of-disease study was in line with the proposed methods of identification, measurement and valuing burden-of-disease in people living with psoriasis. Using validated tools to capture disease severity, health, and capability allows for replication of the study in other jurisdictions and ultimately direct comparison of results.

Evidence from this thesis suggested that a substantial part of total healthcare costs was attributable to psoriasis. No similar studies have reported UK estimates. However, a similar trend has been reported in other countries. It should be noted that these studies from other countries cannot be compared to cost-of-illness estimates in this thesis. The difference in healthcare systems, clinical practice and source health care resource use and data limits the generalisation and comparisons of findings from other studies to those from this thesis.

Psoriasis cost-of-illness studies from other countries have also reported substantial costs attributable to psoriasis. For instance, a study from Sweden using observational population-based methods reported a mean annual cost of €10,500 in the psoriasis/psoriatic arthritis group compared to €6,700 (Löfvendahl *et al.*, 2016). Another Swedish study published in the same year reported substantially high annual biologics cost estimates of US\$ 23,293 (Svedbom *et al.*, 2016). The substantially higher estimates in the Svedbom *et al.* (2016) study were due to focusing on psoriasis patients receiving biologic treatment. Another study that had a similar study design as the cost-of-illness study in this thesis also reported higher costs in the psoriasis group with a mean cost difference of \$ 1,590 (Pilon *et al.*, 2019). Three population-based studies

using the insurance databases reported substantially higher cost-of-illness estimates in the psoriasis group compared to non-psoriasis controls (Andrew P Yu *et al.*, 2009b; Steven R Feldman *et al.*, 2015; Steven R. Feldman *et al.*, 2015). These higher estimates could be explained by the heavy private insurance payer health care system in the US.

It was also noted that obesity was linked to higher healthcare costs in both psoriasis and non-psoriasis controls. This suggests that lifestyle interventions aimed at managing weight in people living with psoriasis would have a substantial decrease in healthcare resource use.

Evidence on the burden-of-disease in people living with psoriasis shows that psoriasis exerts health and beyond health costs on individuals. It was clear that the impact of psoriasis is beyond being a mere skin condition. Health state utility values reported in this thesis for people living with psoriasis were lower than those reported in other conditions within the UK such as asymptomatic/mild prostate cancer (0.83), autoimmune hepatitis (0.89), and dementia (0.78) (Zhou *et al.*, 2021). HRQoL and capability estimates reported in chapter 6 could be useful for baseline estimates in economic evaluation, especially for treatment naïve people living with psoriasis

The updated information on cost-of-illness of psoriasis generated from the observation study and burden-of-disease in people living with psoriasis is relevant to the UK and useful for the GPA and health policymakers who aim to reduce the economic impact of psoriasis and improve health and care outcomes by increasing access to cost-effective treatments.

7.3 Strengths and Limitations

7.3.1 Strengths

The overall strength of this thesis was the breadth of the work covered and the various methods utilised. This thesis developed a framework for assessing economic impact of disease studies, appraised economic impact of psoriasis studies, and estimated the cost-of-illness and burden-of-disease in people living with psoriasis. The thesis utilised pearl review methods, systematic review, statistical, and survey methods to meet the research objectives.

One of the strengths of this thesis was developing the economic impact framework (Chapter 2) which was informed by the theoretical foundations of health economics accounting for both welfarist and extra-welfarist analytical frameworks. The framework was informed by peer-reviewed published literature and validated by academic health economists from within and outside the UK (Jefferson, Demicheli and Mugford, 2000; Akobundu, J.Ju and L.Blatt, 2006; WHO, 2009; Jo, 2014; Onukwugha *et al.*, 2016). The developed framework had face validity and formed the basis for the design of the cost-of-illness and burden-of-disease empirical chapters of this thesis.

Another key strength of this thesis was the use of a large administrative dataset, linked CPRD-HES, to estimate costs attributable to psoriasis. This also allowed for a detailed analysis of the impact of multimorbidity and obesity on health care resource use in people living with psoriasis. Previous cost-of-illness studies for psoriasis in the UK have relied on small sample sizes from a single centre or survey (Poyner *et al.*, 1999; Fonia *et al.*, 2010).

In addition, using the CPRD-HES data allowed for a longitudinal study design. This provided for a longer follow-up period which allowed for the identification of common time trends in health care resource use and costs (Mason, 2019). This allowed for consideration of whether outcomes were sensitive to how long one has lived with psoriasis. Most studies reviewed in chapter 3 have mainly reported a one-year follow-up. Longer follow-up periods and larger datasets result in generation of robust estimates (Löfvendahl, 2016). Using CPRD Read codes also provided for a robust case ascertainment method for psoriasis cases because most people living with psoriasis are much more likely to consult and be managed in primary care. This assertion was backed by the cost impact in primary care as compared to secondary care costs. Using the CPRD-HES linked dataset minimised the risk of excluding psoriasis cases by relying on secondary care consultations only (Löfvendahl, 2016).

The use of econometric methods in chapter 5 allowed for a causal interpretation of results which helped in estimating costs attributable to psoriasis. Using econometric methods made it possible to address the questions: How does having psoriasis impact health care costs? Do obesity and multimorbidity influence healthcare costs in psoriasis patients?

The inclusion of both the cost-of-illness in chapter 5 and burden-of-disease in chapter 6 in estimating the economic impact of psoriasis attests to the broad cover taken under this thesis. The cost-of-illness study took the health care study perspective, which is relevant for the UK. With an understanding of the potential consequences of living with psoriasis, this thesis took a more pragmatic view of the burden-of-disease of psoriasis to include severity, health status and capability estimates. Estimates of burden-of-disease of psoriasis especially for treatment naïve patients will be useful in informing economic evaluation of alternative technologies and practices in psoriasis management. Most economic impact of disease studies within and outside psoriasis have mostly reported cost-of-illness only (Poyner *et al.*, 1999; Fonia *et al.*, 2010). Even with several tools to measure and value health and beyond health consequences, most economic impact studies have assumed “intangible” costs to be unquantified (WHO, 2009).

7.3.2 Limitations

The main limitations in this thesis were influenced by each of the empirical chapters set out to address the objectives. One of the limitations was due to the sole inclusion of English language studies in the cost-of-illness and burden-of-disease systematic reviews. That might have potentially led to missing out on studies from non-English speaking countries.

Secondly, this thesis did not estimate costs beyond direct medical costs. In addition, only some direct medical costs were included in the cost-of-illness study. Due to a lack of information on biologics, these costs were not included. Costs such as out-of-pocket spending on non-prescription treatments have been reported to be substantial in other countries. Similarly, informal care costs in people living with psoriasis remain under-reported. It is conceivable that excess costs of psoriasis would significantly be greater had costs for biologics, direct non-medical and productivity costs been included. However, anecdotal evidence shows that psoriasis is not disabling in most people and is hence assumed to have a low impact on informal care costs. This thesis took a healthcare perspective on economic impact of disease. This was judged to be appropriate for the publicly funded UK healthcare system which is free at the point of use. According to the chosen NHS perspective, it was reasonable to forgo estimation

of direct non-medical costs. Also, productivity loss in terms of presenteeism, absenteeism, and job loss was not estimated in this thesis. However, a general picture of the impact of living with psoriasis on finding jobs and the overall time in work duration was estimated. Most individuals reported working the 'UK' workweek hours, 36-40 hours per week. The reported 'normal' hours of work were influenced by the disease severity of most respondents. Most respondents in the burden-of-disease survey reported mild psoriasis. Thirdly, the cost-of-illness study did not include a lifetime horizon. Although time since diagnosis (index date) was adjusted for, there was potential for the persistence of time-dependent bias in cost estimates. Being a chronic condition and potential risk factor for developing other chronic conditions, the longer one has psoriasis, the greater the risk of developing other conditions. The more other conditions develop over the course of a lifetime, the higher the health care costs.

The fourth main limitation was due to using a single time point in a purposive sample of the burden-of-disease survey. This limited the understanding of the impact of the condition on health and beyond health outcomes in individuals at different time points.

7.4 Implications for health policy

Research findings presented in this thesis have several health policy implications. Economic impact studies play a role in addressing a number of policy questions (Chisholm *et al.*, 2010). Some of the policy-relevant implications include: societal recognition of the importance of addressing the economic impact of psoriasis; a case for using biologic treatment; the need to find better ways of managing psoriasis; how psoriasis is viewed in society; and how to address the impact of comorbidities on cost-of-illness and burden-of-disease in people living with psoriasis.

The substantial cost-of-illness and burden-of-disease of psoriasis on the individual and society in the UK suggest the need for continued advocacy for society to recognise the importance of understanding the economic impact of psoriasis. Evidence from this thesis is also relevant for patient organisations such as the Psoriasis AssociationUK who have an important role in driving the advocacy agenda on behalf of people living with

psoriasis. This reiterates the calls by the WHO for policymakers to raise awareness of how psoriasis impacts peoples' lives (WHO, 2016). The need to find better ways of managing psoriasis suggests the need to continue the research and development agenda. Considering the substantial impact of psoriasis on the wellbeing of individuals, interventions tailored to improve wellbeing are more likely to offset the critical unmet need.

This thesis helped identify patient characteristics that influence costs in people living with psoriasis. Although there was a high proportion of missing BMI data in the CPRD-HES dataset, the results showed an association between BMI health care costs. Health care costs were higher in individuals with the BMI category outside the 'healthy' category. This finding is consistent with other published studies (le Roux *et al.*, 2018). Similarly, increased multimorbidity was associated with increased costs in both psoriasis and non-psoriasis patients. This suggests the need to continue research on policies aimed at encouraging healthy lifestyles to reduce obesity and minimise the incidence of chronic non-communicable diseases. This in turn will minimise health care resource use while improving population health. However, the causal direction between psoriasis and obesity remains uncertain.

A drive towards use of real-world evidence (RWE) in the UK requires that policymakers at both national and local levels should explore ways of including generic measures of health-related quality of life and capability within datasets such as CPRD and HES. One of the anticipated challenges of such an approach would be feasibility of measuring such outcomes in the current settings. Successful implementation of including patient-reported outcome measures of health and capability will be a key source of data for methodological work, means for quantifying the economic impact of the disease and subsequent interventions on population or patient health (Thompson, 2019).

The findings from the burden-of-disease for psoriasis highlight that consequences for certain conditions cannot be fully captured by HRQoL such as QALYs. This raises the need for policymakers developing guidelines for organisations such as NICE to enhance the pursuit to increase the evaluative space beyond health maximisation (NICE, 2014; Goranitis *et al.*, 2017). Even though the NHS has evolved over the years, the principal objective has remained to maximise the aggregate health status of the community (Culyer, 2012). The reduction in capability and reported impacts of psoriasis on

wellbeing suggests the need to explore possibilities of increasing the evaluative space for economic evaluation of health and care interventions. Currently, economic evaluation of medicines by NICE is still bound by the principle of health maximisation. The continued rise of chronic illness that impact on individual wellbeing re-emphasise the need to increase the evaluative space. Increasing the evaluative space is also more likely to influence decisions on the cost effectiveness of biologics which would otherwise be deemed expensive.

In summary, the health policy implications of findings from this thesis include: -

- Need to enhance advocacy and increase society awareness of the conditions. Not only would this increase committing resources to improve management of the psoriasis, but it would also help in addressing some of the impact on the wellbeing of people living with psoriasis which result from the lack of support from other people.
- The need to include measures of health-related quality of life and wellbeing in routinely collected health data and surveys. This will provide an easy assessment of linking cost-of-illness and burden of disease.
- Improve linking of health records within the NHS to allow for access to a full picture of health care resource by an individual. For instance, there is need to link data on systemic and biologic prescriptions from dermatologists to primary care records.
- More research and investment in curbing long-term conditions that worsen the reduction of health-related quality of life and wellbeing.

7.5 **Methodological implications**

The outcomes of this thesis provide a useful resource for researchers working in the economic impact of disease analysis space such as health economists, health service researchers, and statisticians. The presented framework in chapter 2 was also intended to promote consistency and transparency in the appraisal and reporting of economic impact of disease studies. This framework backed by the theoretical foundations of health economics is useful for health economists working on estimating economic impact of disease.

The developed framework for the appraisal of economic impact of disease studies in this thesis provides a useful and pragmatic approach that serves both the producers and consumers of economic impact of disease studies. The framework is not prescriptive and acknowledges the varied contexts for decision-makers and recommends flexibility though keeping to the objective of enhanced comparability. To enhance comparability across studies, specific items relevant to the decision-maker and the healthcare setting should always be included. Critical aspects that should be explicitly reported for cost-of-illness are study perspective and time horizon. The choice of study perspective is driven by the research question and study objectives because these aspects guide the research. A clear set choice of study perspective and time horizon will ultimately dictate the identification, measurement and valuation of costs.

Similarly, the choice of items to report in the burden-of-disease section should be influenced by the study objective. For instance, in the pursuit to estimate the impact on health-related quality of life, QALYs should be reported. The QALY is a preferred generic measure of health as it incorporates both the quantity and quality of life. Of course, the QALY is plainly fraught with value judgement (Culyer, 2012). The choice of outcome measures such as the EQ-5D, HUI, and SF 6 should be informed by what is the most preferred within the healthcare jurisdiction. For instance, the choice of the EQ-5D was motivated by preference by NICE, hence relevant to the UK setting. For conditions such as psoriasis, the inclusion of non-health such as capability and beyond health consequences of living with the condition should be included and reported.

Given the need to increase the evaluative space beyond health maximisation, estimating capability should be considered. Researchers involved in estimating wellbeing and capability impact of living with psoriasis can utilise the ICECAP. Findings from this study are in line with a recent study which validated the use of ICECAP in dermatological conditions such as psoriasis (Rencz *et al.*, 2021). Just like the EQ-5D is the preferred measure of HRQoL by NICE, there is a need to establish a generally acceptable and validated generic measure of capability and wellbeing.

Although the use of linked CPRD-HES data was able to provide answers around the cost-of-illness of psoriasis estimates, some issues were noted with the dataset. The lack of secondary care provider IDs posed a challenge in controlling for provider

effects. Multi-level modelling methods are available to address clustering, but this is limited to what the data can offer. Considering the reliance on Read codes for case ascertainment which are prone to misclassification of disease, it is important to establish the validity of psoriasis conditions in the CPRD. The CPRD-HES data does not provide for the estimation of costs borne by the patients regardless of the chosen perspective. Therefore, direct non-medical costs such as out-of-pocket spending for alternative treatments and transport. Studies from other countries have reported significant OOP costs for people living with psoriasis. Even though the framework noted the significance of productivity loss in estimating the cost-of-illness and burden-of-disease in people living with psoriasis, CPRD-HES data does not allow for the inclusion of such estimates.

The survey to estimate the burden-of-disease of psoriasis provided a snapshot of the extent of the problem at a single time point. Prospective study surveys would be useful in estimating the change of burden-of-disease in people living with psoriasis over time.

7.6 Future research

Development of methodological approaches that ensure consistent and better ways of estimating the economic impact of chronic diseases such as psoriasis have not been progressing as fast as other areas of health economics such as economic evaluation. Considering the need to improve comparability of estimates of economic impact of disease across studies, key research should focus on validating methods and developing reporting criteria and checklists.

As noted in chapter 3, most cost-of-illness have mostly focused on direct medical costs. Future research could take the societal perspective in order to understand the impact of direct non-medical costs (out of pocket, informal care) and indirect costs (productivity loss).

This thesis took a microeconomic view of the economic impact of psoriasis. Including the macroeconomic perspective in future research will be useful, especially for countries that can link health records to fiscal contributions like taxation. One of the benefits of considering both micro and macroeconomic views is that it provides a more pragmatic quantification of the impact and helps to make a case for reimbursement of

treatments that would otherwise be deemed 'expensive' (Kotsopoulos and Connolly, 2014). The macroeconomic approach also helps in the advocacy for public health interventions such as obesity reduction campaigns.

The inclusion of a capability measure in estimating burden-of-disease in chapter 6 provides an insight there is need for future research to utilise such tools in chronic inflammatory dermatology conditions like psoriasis (Rencz *et al.*, 2021). Following the validation of ICECAP in dermatology conditions, additional research estimating the burden of psoriasis should consider estimating capability.

7.7 Conclusion

The economic impact of psoriasis estimates from previously published studies were noted to be diverse. Findings from this thesis showed that there was a need for a framework to assess economic impact of disease studies. A framework with face validity was developed and used to assess cost-of-illness and burden-of-disease in psoriasis studies. It was also clear that psoriasis poses are significant cost on the healthcare system and the burden-of-disease on the individuals which extends beyond health. The evidence of the economic impact of psoriasis generated from this thesis will contribute to influencing policy recommendations on the need to tackle obesity and comorbidity in people living with psoriasis in the UK to reduce health care resource use. The three key take home messages highlighting the contribution to new knowledge are: -

- Production of a clear framework used to assess studies reporting economic of disease in general.
- Psoriasis significantly impacts on financial costs to the NHS, reduced health and beyond health.
- Health-related quality of life and capability estimates due to psoriasis reported in chapter 6 are useful as baseline estimates in economic evaluation, especially for treatment naïve patients.

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Appendix 2.1: Validation of the schematic outlining economic of disease

This appendix describes the process involved in validating the framework for economic impact of disease that was presented in chapter 2. After developing the first schematic framework, expert opinion on the framework was sought from prominent health economists. Expert opinion was sought to validate the proposed framework.

Aim and objectives

The main aim of this exercise was to validate the proposed framework for economic impact of disease.

The three objectives addressed were:

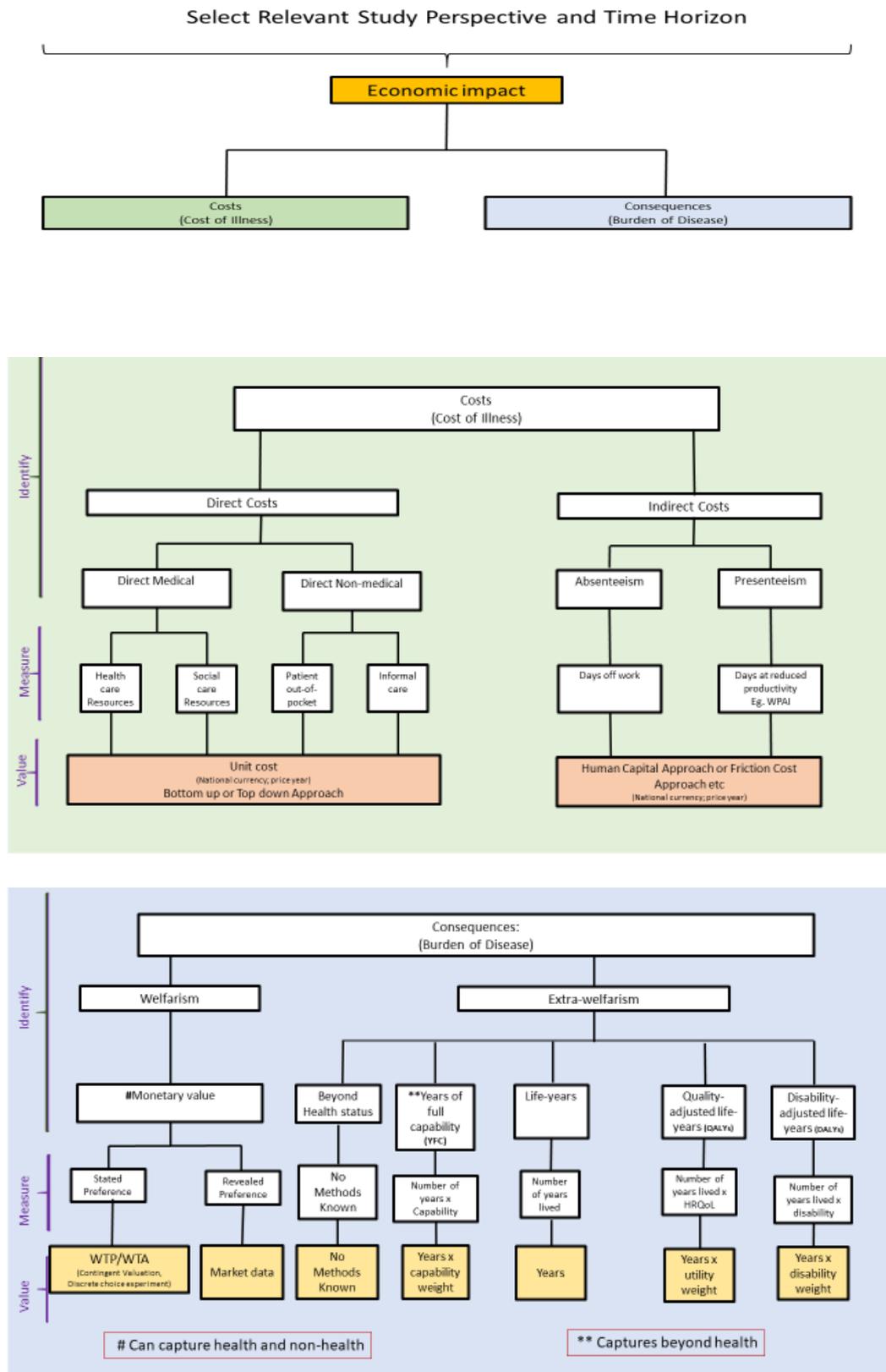
1. To establish whether the schematic captured all the appropriate components of cost-of-illness and burden-of-disease.
2. To get suggestions on how the schematic diagram might be improved, and
3. If need be, modify the proposed schematic diagram.

Methods

A sample of nine prominent health economists known to have published work on economic evaluation and/or use of economics in decision-making was identified and contacted. The respondents were selected based on purposive sampling (Etikan, 2016). Consideration of experts was based on their exhibited knowledge backed by publications and their roles and experience in health. The experts were drawn from the United Kingdom, Canada, Australia, and the US of America.

An e-mail was sent to these experts asking them for comments on a draft of the proposed schematic diagram of the descriptive framework, see Figure A2.1. The responses from these experts were analysed by collating the key themes in the written responses, which were then used as criteria to modify the proposed framework.

Figure A2.1: Originally proposed framework



Framework analysis was used to analyse the responses from the experts. This method is one of the several methods used in thematic or qualitative content analysis (Gale *et al.*, 2013). This method provides a clear record of how themes and outcomes are derived from participants' words (Gale *et al.*, 2013). This approach involves identifying what is common and different in the qualitative responses, after which it focuses on relationships between these responses to draw descriptive and/or explanatory conclusion clusters around themes (Gale *et al.*, 2013). The five steps of framework analysis were followed for this study. These five steps were; 1) Familiarisation with the responses; 2) developing the thematic framework through the identification of key issues in the responses (coding which involves carefully reading the responses line by line to paraphrase or label the description of the response interpretation; 3) Grouping of codes together to form the analytical framework, 4) Exploration and review of the full pattern across cases 5) Data mapping and interpretation. The analysis was done by one researcher (PN) who consulted with a second researcher with qualitative data expertise (ME). To illustrate aspects of the data analysis, direct quotations have been included in the results sections. No participant names have been included for privacy reasons.

Results

Six out of the nine (67%) experts in health economics drawn from four countries responded to the email. Four of the experts responded with detailed comments on what was missing, ambiguous, or not relevant in the proposed framework and associated schematics. These comments were grouped into seven key themes: general schematic structure; the need for precision in terminology; clarity of study perspective; depiction of Extra-welfarism components; depiction of welfarism; valuation of consequences; inclusion of other sectors. These comments (see Table 2.1) were then used as criteria to modify the proposed descriptive framework. The key theme headings and proposed modifications to the proposed descriptive framework are described in the sections below.

Table A2.1: Categories, sub-categories and example comments

Category	Sub-categories	Verbatim expert comment
General schematic structure	Full endorsement	<i>ID6: 'Looks good to me'</i>
	Endorsement with a caveat	<i>ID5: 'This looks okay to me'</i> <i>ID1: 'I think as a schematic for organising literature it is fine. But there are many nuances associated with these categorisations which you may or may not want to capture or reflect in the schematic' [ID1].</i>
	Separate stages of 'measurement' and 'valuation'	<i>ID1: 'Might be helpful to have separate stages of 'measurement' and 'valuation' for both costs and outcomes. At the moment your 'bottom lines' are a mixture of the two'.</i>
	Missing categories	<i>ID4: 'The other thing that I think might be missing is intangible costs – so I was thinking of something like stigma – but where you draw the line between things like that and consequences, I think might be difficult to ascertain!'</i>

Extra Welfarism	<p>Weakness of extra-welfarism depiction.</p> <p>Criticism of extra-welfarism</p> <p>Strength of extra-welfarism to consider beyond health impact</p>	<p>ID1: ‘.....It’s a pretty sad reflection on extra welfarism if they have no way of measuring outcomes beyond health.’</p> <p>ID1: ‘.... There are clearly ways of measuring this. Just one simple example of the extra-welfarist omissions.’</p> <p>ID1: ‘..... To extra welfarists this is of no consequence since it is the great dictators values that count, not the subjects/recipients. but if recipients values aren’t considered then what help is the EW analysis from a positive perspective. People will not adhere to interventions that don’t reflect their values, irrespective of what the great dictators’ values are.’</p> <p>ID4: ‘.... There are extra-welfarist ways of going beyond health using DCEs that don’t include a monetary valuation – there are lots of these types of studies – quite how to use them in practice isn’t that clear I don’t think, but they are definitely there, and aiming to capture aspects for example of process utility – so I think to say there are no known methods isn’t quite correct.’</p> <p>ID2 ‘... Extra-welfarism doesn’t just have to focus on health and could include effects in other sectors.’</p>
Welfarism	Depiction of welfarism	ID2 ‘Monetary valuation isn’t unique to welfarism – it can be used generally.’

Precise terminology	Criticism of cost-of-illness/burden Criticism of indirect costs	ID2... <i>‘Personally, I don’t like the terms ‘cost-of-illness’ and ‘disease burden’ as they mean different things to different people. I would just be as precise as you can about what you are including.’</i> ID2... <i>‘I think the term ‘indirect costs’ is now rather outmoded. The term ‘productivity costs’ is more often used.’</i>
Study perspective	Influence of study perspective	ID3... <i>‘The current schematic seems focused on the healthcare perspective plus indirect costs. There is no justification for including indirect costs unless one is taking a societal perspective, but a societal perspective should consider many other costs as well’.</i> ID3... <i>‘There is no justification for including indirect costs unless one is taking a societal perspective’</i>
Valuation of consequences	Monetary valuation of consequences	ID3... <i>‘The schematic should address the monetization of QALYs and DALYs as either costs or benefits’.</i>
Other sectors	Education Residential care Criminal justice	ID3 <i>‘a societal perspective should consider many other costs as well</i> <i>a) Education sector – Children with disabling conditions may require special education services</i> <i>b) Residential care – Individuals with disabilities as well as children of individuals who are unable to care for children due to mental illness, substance use, disability, etc. may require care by non-family members, e.g. foster care, group homes. I assume you meant to include this under</i>

		<p><i>Social care, but is not appropriate to put that under Direct medical costs.</i></p> <p><i>c) Criminal justice system – Individuals who experience brain damage in utero or early childhood are at elevated risk of being tried and incarcerated, both as juveniles and adults’.</i></p>
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Modification of the original schematic

The original schematic was modified to the final version, see Figures 2.1, 2.2 and 2.3, using comments from the experts. Four experts suggested the need to more clearly express that extra-welfarism covers outcomes beyond health. Based on the comments from the respondents, the schematic was modified. One of the modifications included introducing a link between welfarism and extra-welfarism. Coupled with the response on monetary valuation of burden-of-disease, this led to showing a link between welfarism and extra-welfarism. Therefore, a link between beyond-health and welfarism was drawn. This link showed that extra-welfarism is an extension of welfarism and not a mutually exclusive analytical framework.

Clarity on covering other sectors when considering beyond health measures under extra-welfarism was also included. This involved writing down some explicit examples of other sectors. It is also emphasised that the inclusion of other sectors is influenced by the study perspective and the decision-maker.

The ambiguity in the use of ‘cost-of-illness’ and ‘indirect cost’ was acknowledged in sections 2.4.5 and 2.4.6. The use of the cost-of-illness and burden-of-disease in line with this thesis was also clarified in the same sections. The schematic was modified to include productivity in brackets under indirect costs. The decision to retain the use of ‘indirect costs’ was to maintain the alongside using direct costs.

Considering the first part of the schematic already included the need to be considerate of the study perspective and time horizon, no modification was done in this respect. However, modifications to include other sectors when considering the societal perspective and beyond-health measures were made.

The concern on the valuation of consequences in monetary terms was considered to have been accounted for under the monetary valuation part of welfarism. However, this also led to the modification that included a link between welfarism and extra-welfarism.

Conclusion

The schematic was edited to reflect the suggestions from the expert opinion.

Appendix 3.1: PRISMA checklist of items to include when reporting a systematic review or meta-analysis

Section/Topic	#	Checklist item
TITLE		
Title	1	Identify the report as a systematic review, meta-analysis, or both
ABSTRACT		
Abstract	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.
INTRODUCTION		
Rationale	3	Describe the rationale for review in the context of what is already known
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS)
METHODS		
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.

Section/Topic	#	Checklist item
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis)
Data collection	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).
	14	
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I ²) for each meta-analysis.
Risk of bias in individual studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).
Additional analyses		Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.

RESULTS

Section/Topic	#	Checklist item
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome-level assessment (see Item 12).
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group and (b) effect estimates and confidence intervals, ideally with a forest plot.
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).
Additional Analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).
DISCUSSION		
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., health care providers, users, and policy makers).
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias).
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.
FUNDING		

Section/Topic	#	Checklist item
	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.

Appendix 3.2: Search strategy for cost-of-illness of psoriasis systematic review

#Psoriasis

1. exp psoriasis/ or arthritis, psoriasis

#Cost-of-illness (direct costs

2. Cost-of-illness/
3. (illness cost or illness costs or sickness cost or cost, sickness or costs, sickness or burden of illness or illness burden or illness burdens or burden-of-disease or disease burden or disease burdens or costs of disease or disease cost or cost, disease or costs, disease or disease costs or cost of sickness or sickness costs or cost of disease).ti,ab,kf.
4. "Costs and Cost Analysis"/
5. or/2-4

##Productivity Loss and ##Absenteeism

6. (lost productivity or productivity loss or loss of productivity).mp.
7. absenteeism.mp.
8. Long term absen\$.ti,ab.
9. Long term sick\$.ti,ab.
10. exp sick leave/
11. (sick\$ adj3 leave).ti,ab.
12. (sick adj3 absen\$).ti,ab.
13. (work adj3 absen\$).ti,ab.
14. (return\$ adj3 work\$).ti,ab.
15. work readiness.ti,ab
16. Sick\$ benefit\$.ti,ab.
17. Disability leave.ti,ab.
18. (injur\$ adj3 claim\$).ti,ab.

19. (stay\$ adj3 work\$).ti,ab.
20. (participat\$ adj3 employ\$).ti,ab.
21. (attend\$ adj3 work\$).ti,ab.
22. (attend\$ adj3 employ\$).ti,ab.
23. ((sick\$ or illness\$ or employee\$) adj3 absenteeism).ti,ab.
24. (welfare adj3 work\$).ti,ab.
25. (sicklist\$ or sick list\$).ti,ab.
26. or/6-25

##Presenteeism

27. presenteeism.mp.
28. (reduc\$ adj3 work\$ adj3 perform\$).ti,ab.
29. (work productivity and impairment).ti,ab,kf.
30. wpai.ti,ab,kf.
31. (health and work performance).ti,ab,kf.
32. hpq.ti,ab,kf.
33. (health and work questionnaire).ti,ab,kf.
34. hwq.ti,ab,kf.
35. work ability index.ti,ab,kf.
36. wpi.ti,ab,kf.
37. work limitation questionnaire.ti,ab,kf.
38. wlq.ti,ab,kf.
39. work production short inventory.ti,ab,kf.
40. wpsi.ti,ab,kf.
41. standard presenteeism scale.ti,ab,kf.
42. (sps-34 or sps-13 or sps-6).ti,ab,kf.
43. (work and health interview).ti,ab,kf.
44. whi.ti,ab,kf.
45. (health and labour questionnaire).ti,ab,kf.
46. Hlq.ti,ab,kf.
47. Health Related Productivity Questionnaire Diary.ti,ab,kf.
48. Hrpq-d.ti,ab,kf.

###Combining presenteeism and absenteeism costs

###Combining direct costs and productivity loss results

###Combining Cost results with psoriasis

49. or/27-48

50. 5 or 49

51. 1 and 50

##Exclusions, deduplication and final results

52. letter.pt.

53. editorial.pt.

54. historical article.pt.

55. or/52-54

56. exp animals/ not humans/

57. 55 or 56

58. 51 not 57

59. Remove duplicates from 58

60. Limit 59 to English language

61. Review.pt

62. 60 not 61

Appendix 3.3: Data extraction sheet for Cost-of-illness systematic review

Table A3.1: Cost-of-illness data extraction sheet

First author (year) Country	Aim (as reported by authors)	Study sample	Interventions included	Data collection methods	Reported study perspective	Reported study time horizon	Description of costs included (Analytical perspective reported)	Measurement of costs	Valuation of costs	Statistical analysis methods (sensitivity analysis)
Colombo et al (2008), Italy	To evaluate the direct and indirect costs related to moderate and severe plaque psoriasis in an Italian	N: 150 Age: 48.3 years Gender: Male 66% Sampling Frame: Moderate and severe psoriasis patients attending 6 dermatology	Non interventional Analysis of type of treatment included Topical Systemic Phototherapy	Method: Observational prospective study Date: Nov 2003 to Oct 2004. (Data collection at baseline and 3 months)	Societal, Third-party payer (Insurer) Societal	3 months follow No discounting		Direct, Indirect: Absenteeism, Presenteeism, Job loss and intangible (QoL consequences	Official Italian Price list Price year; 2006 Indirect costs unit: GDP per capita	Descriptive : Mean, median, standard deviation, range, frequencies , and percentages.

	population and to assess the correlation of cost with the different degrees of severity of the disease and to measure the impairment in QoL.	departments in Italy. Italy (Europe)	Non-conventional treatments							Analysis of Variance (ANOVA) Chi-Square test for categorical variables. No sensitivity analysis performed.
Carrascosa (2006), Spain	To estimate the direct and indirect costs	797 Psoriasis patients Age: mean (range) 44.3 (8-87)	Non-interventional Topical Systemic Phototherapy	Method: Observational prospective study	Societal	12 months follow up No discounting	Health care costs Patient costs: Over-the-counter (OTC)	Direct costs: Drugs costs Diagnostic procedure cost Physician visit	Prescription drugs: Spanish pharmaceutical unit cost	Descriptive : Mean, median, standard deviation, range,

	related to psoriasis in Spain.	Gender: 53.1 % Male Sampling Frame: First 10 psoriasis patients visiting 100 clinical investigators from all Spanish autonomic communities in 12 months. Spain (Europe)	Over the counter drugs	Date: Feb 2002 to Dec 2003. (Data collection at baseline and 3 months interval in 12 months)			reduced productivity (Analytical perspective not reported)	Hospital admission. OTC purchased Alternative therapy Indirect costs: Lost production	listings, guideline prices, and tariffs. OTC: Average of the costs of the most representative specialties recorded in the patients' notebooks. Alternative medicine: Published data Productivity loss: Mean income per	frequencies and percentages. No sensitivity analysis performed.
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									working group (Patients were classified according to the Spanish Statistical Bureau (SSB) Currency: Euro (€) Price year: 2003	
Schmitt (2006), Germany	To estimate the cost of work productivity loss in	332 physician diagnosed psoriasis patients Age: mean, [SD] 42.7 years [11.5]	Non-interventional observational cross section study.	Method: observational cross section study.	Societal	Not clearly reported. No discounting	Reduced productivity (Analytical perspective not reported)	Indirect cost: Presenteeism Absenteeism	US Department of labour, bureau of labour statistics:	Chi square test Fisher's exact test

	<p>patients with psoriasis. We were further interested in the association of productivity loss, health-related quality of life (HRQL) and clinical disease severity.</p>	<p>Gender: 38.8 Male</p> <p>Sampling frame: Patients 18 years or older with self-reported psoriasis who accessed the Internet from the USA were eligible.</p> <p>Data were collected from internet users that opted into the study between January and May 2005.</p> <p>Germany (Europe)</p>	<p>Topical, systemic and no treatment.</p>	<p>Date: January to May 2005.</p>					<p>US\$</p>	<p>Spearman Correlation coefficient Univariate and multivariate regression analyses Hosmer-Lemeshow's chi square test.</p> <p>No sensitivity analysis</p>
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Kulkarni (2005), USA	To examine the association between factors related to medication use, health status, and health care costs associated with psoriasis in the United States.	1,100,000 patients Age: Range, 26-49 years. Gender: 43.3% Male Sampling frame: the Medical Expenditure Panel Survey (MEPS) a national survey of noninstitutionalized US civilians. The MEPS dataset quantifies insurance costs and out-of-pocket	Non-interventional study but for the analysis, grouped population in terms of medication received into topical corticosteroids; other medications; combination therapy; systemic medication; and no pharmacologic agents.	Method: Cross-sectional cohort study. Date: Not reported	Not reported	Not clearly reported. No discounting	Healthcare costs (Analytical perspective not reported)	Direct resources: Drug and health care related costs.	MEPS database (insurance and out of pocket costs) Currency: US\$ Price year: Not reported	Bivariate statistics: 1-way ANOVA, Multiple linear regression. No sensitivity analysis
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		<p>spending for all medical services. The MEPS collects self-reported health status data using the EuroQoL (EQ-5D) instrument for all adults aged 18 years or more. The patients for this study were identified using ICD-9 code 696 for psoriasis vulgaris and similar conditions.</p> <p>USA (North America)</p>								
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Jenner (2002), Australia	(i) To record morbidity and cost related to people suffering with psoriasis in Australia; (ii) to undertake a longitudinal study recording these effects over time, rather than	83 physician diagnosed psoriasis patients Age*: Mean, (range) 41 years (13-73years) *Majority (90.4%) 20-59 years. Gender: 47% Male Sampling frame: Patients were recruited in urban and rural areas of Victoria from the following sources: general practitioners' private practice,	Non-intervention study.	Method: Prospective cohort study. Date: 1997 to 1999	Not reported	24 months No discounting reported	Health care costs: (Analytical perspective not reported)	Direct medical costs: Medication costs, Medical consultation Out of pocket (OOP) and government costs	Medical consultation; Medicare benefit schedule rate. Patient diaries. Currency (price year) AU\$\$ (1998)	Statistical analysis methods not reported. No sensitivity analysis.
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	<p>relying on retrospective recall data; and (iii) to relate the cost and morbidity to the severity of the disease using a number of severity measures</p>	<p>dermatologists' private practice, the Dermatology Outpatient Department at St. Vincent's Hospital Melbourne, the photochemotherapy clinic at Alfred Hospital Melbourne, the Psoriasis Association of Victoria, the phototherapy clinic at the Skin and Cancer Foundation, Victoria, and from the staff of St. Vincent's Hospital Melbourne.</p>								
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		Australia								
Poyner (1999), UK	To quantify the effect of treatment with either calcipotriol ointment or short-contact dithranol on personal expenditure by patients and the economic	232 psoriasis patients (122 on calcipotriol and 110 dithranol). Age: Not reported Gender: Not reported. Sampling frame: Chronic plaque psoriasis patients attending their GP for treatment.	Calcipotriol and Dithranol	Method: Randomised prospective study. Date: Not reported	Health sector	Not reported	Healthcare (Analytical perspective not reported)	Direct: healthcare resource use, out of pocket spending by patients	Drug price as listed in MIMS. Published unit costs for the GP visit and hospital consultation i.e., Government expenditure plans and the HFMA/ CIPFA health database.	Descriptive statistics. Wilcoxon rank sum test and Wilcoxon signed ranks. Non-parametric analysis.

	burden to the NHS of treating mild/moderate plaque psoriasis.	United Kingdom (Europe)								
Pilon (2019), US	To evaluate the impact of comorbidities on healthcare resource use (HRU), and direct and indirect work-loss-related costs in	9,078 psoriasis patients. Age: mean, 44 years. Gender: 49% Male Sampling frame: Patients registered in the Optum Health registry reporting and insights	Non intervention	Retrospective cohort study Date; January 1, 2010, to March 31, 2017.	Not reported	12 months No discounting	Healthcare costs Productivity	Direct cost: Health resource utilisation (outpatient visit, inpatient admission, Emergency department, other visits) Indirect costs: Disability days and absenteeism	Employees daily wages Currency (Price year) US doll (2017)	Descriptive statistics: mean, standard deviation, and medians. T-tests for continuous variables and chi-square tests for

	psoriasis patients.	employer claims database. Patients with ICD-9 code 696.1 or ICD-10 code L40.0-L40.4, L40.8, L40.9) or no psoriasis were included. USA (North America)					(Analytical perspective not reported)			categorical variables.
Javitz (2002), USA	To estimate the direct cost of medical care for	2,337,000 psoriasis patients 1,437,000 Clinically	Non-interventional	Not stated	Societal perspective	Time horizon not reported.	Healthcare	Direct: hospitalizations, outpatient and physician office visits, prescription	Published literature, reimbursement rates and wholesale drug costs.	Statistical analysis methods not reported.

	<p>psoriasis (including psoriatic arthritis) from a societal perspective among adults in the United States.</p>	<p>significant psoriasis.</p> <p>Age</p> <p>Gender: varied based on database and psoriasis category.</p> <p>Sampling frame: National medical care utilization surveys and a managed care database. ICD-9 696.0 and 696.1</p> <p>USA (North America)</p>					<p>(Analytical perspective not reported)</p>	<p>and over-the-counter (OTC) medications.</p>	<p>US dollar (1997price year)</p>	
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Ha (2018), South Korea.	To analyse the difference in healthcare utilization and financial burdens between patients with and without psoriasis and compare these patterns according to the	8034 (4016 with psoriasis and 4026 without). Age: 20 years and over. No means reported. Gender: 56.4% Male Sampling frame: The National health insurance database (2012 and 2013) was used. This database all insurance enrollees and	Non-interventional Topical agents, phototherapy, systemic immunosuppressant agents, and biologics.	Descriptive cross-sectional study. Date: 1 st January 2012 to 31 st December 2012.	Not reported	1 year No discounting reported	Healthcare (Analytical perspective not reported)	Direct costs: Healthcare utilization and medical and prescription costs	National Health insurance database US dollar (2017 price year)	Descriptive as counts with proportions, means and standard deviations. McNemar test, Bowker test of symmetry, Wilcoxon matched-pair signed-rank test. Median and

	disease severity.	medical aid beneficiaries in Korea and includes electronic bills for medical treatments, as well as details on the medical treatment, disease, and prescriptions. Study subjects were patients who had a diagnosis of psoriasis in at least one claim from the outpatient, inpatient, and								interquartile range.
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		emergency departments of hospitals and clinics between January 1, 2012 and December 31, 2012. Diagnose was based on ICD-10 code (ICD-10: L00-L99)								
Jungen (2018), Germany	To evaluate the annual costs of psoriasis in Germany from the	1158 psoriasis patients 132 physicians Age: mean [SD] 51.9 [14.3]	Non interventional Topical treatment, systemic therapy (including	Cross sectional study. Date: January 2013 to March 2014.	Societal perspective	Not reported No discounting	Healthcare (Social health insurance) Patient costs	Direct costs: Social health insurance- Topical treatment, systemic therapy, biologics, UV	Lauer Taxes (reliable pharmaceutical information for all drugs and contracts	Descriptive statistics: Mean, median, standard deviations, range.

	societal perspective.	Gender: 57% Male Sampling frame: 18 years or older patients with clear diagnosis of psoriasis vulgaris visiting targeted institutions and their physicians. Germany (Europe)	biologics), other therapy					therapy, inpatient stays and physician fees. Out of pocket- Skin care without active drug agents, systemic treatment, biologics, UV therapy, inpatient stays and physician fees. Indirect costs: Absenteeism	registered in Germany), Drug store chains, online pharmacies and drug stores. Web-based Diagnostic related groups (DRG) Taxi prices Social health insurance cost for cure, rehabilitation, semi-residential care based on	Gaussian distribution by Kolmogorov-Smirnov test. Mann-Whitney U-test Kruskal-Wallis test.
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									data from three clinics National Association of SHI physicians. Human capital approach using disability days and the wages.	
Takahashi (2017) Japan	To evaluate the total costs as well as cost versus efficacy of	N: 148 Age: 18 to 72 years Gender:	Non-Interventional Topical Systemic Biologic	Method: Retrospective observational cohort study	Not reported	No follow up No discounting	Healthcare costs (Drug costs) (Analytical perspective not reported)	Direct resources: Drug costs only	Insurance and pharmacy records Price year: 2016	

	topical and systemic treatments of psoriatic patients under the Japanese health insurance system	Sampling Frame: Psoriasis patients without PsA at clinic in Hokaido Prefecture Japan (Asia)		Date: April 2015 to March 2016						
Fonia (2010)	To describe the impact of biologic therapy introduction on the use of medical resources,	76 psoriasis patients 132 physicians Age: mean [range] 47.3 years [23-74]	Biologics treatment	Method: Retrospective observational study	Health sector	12 months follow up No discounting	Healthcare costs (Drug costs) (Analytical perspective not reported)	Direct resources: Drug costs Home care delivery,	NHS reference costs and British National Formulary.	Paired t-tests, Wilcoxon paired signed tests, McNemar

	<p>costs and where available, outcomes in patients with moderate to severe psoriasis</p>	<p>Gender: 71% Male</p> <p>Sampling frame: Sequential patient cohort with psoriasis attending a tertiary referral severe psoriasis service and initiated on biologics (adalimumab, efalizumab, etanercept or infliximab) for treatment of their psoriasis</p> <p>UK (Europe)</p>								
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		(SHCR). Total population register (TPR) and Swedish prescribed drug register (SPDR) was also used. MikroData för Analys av Socialförsäkringen (MiDAS) Sweden (Europe)								
Feldman (2015), USA	To compare the prevalence of comorbidities, health care resource	5,492 moderate-to-severe Psoriasis patients and 5,492 controls. Age: 47.62 [1.65]	Non interventional . Those included were on at least systemic	Retrospective observational study. Date: January 2007 to March 2012	Payer Perspective (insurance)	Time horizon not reported No discounting reported	Healthcare	Direct resources: medication use, health care utilization	Insurance reimbursement US dollar (2012 price year)	Descriptive statistics; mean, standard deviation, frequencies and percentages.

	<p>utilization, and costs between moderate-to-severe PsO patients and demographically matched controls.</p>	<p>Gender: 55.5% Male</p> <p>Sampling frame: Patients were selected from the OptumHealth Reporting and Insights claims database which represents 15.5 million privately insured individuals. Patients were identified based on ICD-9-CM code 696.1 and the Current Procedural Terminology (CPT) codes.</p>	<p>or biologic treatment</p>							<p>Wilcoxon signed-rank tests</p> <p>McNemar's test</p>
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		Moderate to severe patients where those receiving at least 1 non-topical systemic therapy.								
		USA (North America)								
Schaefer (2015)	To evaluate current health care resource use, productivity, and costs among patients	200 moderate to severe plaque psoriasis. Age: mean 51.4 years Gender: 50% Male Sampling frame: Eligible patients	Non-interventional Topical Phototherapy Systemic therapies Biologic agents	Cross-sectional observational survey. Date: January to May 2012.	Perspective not reported	Horizon not reported No discounting reported	Health care Out of pocket Productivity loss.	Direct resources: Medicines, Hospital outpatient visits, Out of pocket spending. Indirect: Absenteeism	Medicare physician fee schedule, Hospital Outpatient Prospective Payment System, and Hospital Inpatient Prospective	Summary statistics. One-way analysis of variance. Kruskal-Wallis Chi-square test

	with MSPP in routine practice.	were plaque psoriasis with Body surface area (BSA) of 10 or higher on systemic and/or phototherapy.					(Analytical perspective not reported)	and presenteeism	Payment System. Average sales prices Average wholesale prices US dollar (2012 price year)	Fisher exact test.
Mustonen (2015), Finland	To estimate the proportion of productivity losses due to psoriasis	262 psoriasis and psoriatic arthritis patients. Age: mean 49 years Gender: 55% Male	Non-interventional	Questionnaire based survey Date: 1 October 2009 to 30 September 2010	Societal perspective	Time horizon not reported. No discounting reported.	Productivity loss (Analytical perspective not reported)	Indirect costs: Absenteeism and presenteeism	Human capital Approach using average monthly income.	Student's t-test, Chi-square test, linear and logistic regression models

	and due to other medical problems among employed psoriasis patients.	Sampling frame: 498 Dermatology patients visiting the department of dermatology in Turku University hospital (TUH) with a diagnosis of psoriasis of psoriatic arthritis. Finland (Europe)							Euro (Price year not reported)	
Chen (2014), Taiwan	To estimate the economic burden of psoriasis in Taiwan.	9063 moderate to severe patients 36,252 controls 42,737 mild patients 1,707,948 mild controls Age: 47.5+-16.4 moderate to	Non-interventional	Observational and survey Date: August 2009 to May 2010.	Payer perspective	Not reported	Health care: Out of pocket.	Direct resources: Medicines, Hospital outpatient visits. Out of pocket spending on healthcare	Reimbursement fees. Co-payments	Pearson's Chi-square test. Descriptive statistics. Logistic regression

		<p>severe, 46.2+-19.1 Mild.</p> <p>Gender: 69.1% Male in moderate to severe</p> <p>60% Male in mild patients.</p> <p>Sampling frame: National health insurance research database (NHIRD) in Taiwan. Used inpatient and outpatient expenditure records.</p> <p>Taiwan (Asia)</p>					<p>Productivity loss</p> <p>Analytical perspective not reported.</p>	<p>accessibility not reimbursed.</p> <p>Absenteeism</p> <p>Income loss or caregiver visit/per admission.</p> <p>New Taiwan Dollar (2009)</p>	<p>Generalised linear model</p> <p>t-tests</p>
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Balogh (2014), Hungary	To assess the cost-of-illness and quality of life of patients with moderate to severe psoriasis in Hungary	200 psoriasis patients Age: mean [SD] 51 [13] Gender: 68% M Sampling frame: Patients with diagnosis of psoriasis, aged ≥18 visiting two university dermatology clinics in Hungary.	Non interventional	Non-interventional Cross-sectional survey. Date: September 2012 to May 2013.	Societal perspective	Time horizon not reported. No discounting reported.	Healthcare Out of pocket Informal care. Productivity loss	Direct: health care resource use Patient transport costs to the hospital Hours of care Indirect: Absenteeism	Outpatient number of visits, drug costs (national pharmaceutical prices), Hospitalisation (DRGs reimbursement list) Average hourly net wage in Hungary up to 40hrs Human capital approach and the Friction	Descriptive statistics, mean, standard deviation
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	the cost-of-illness.	hospitals between December 2007 and August 2008. Malaysia (Asia)								
Levy (2012), Canada	To estimate the economic burden and impact on quality of life of moderate to severe plaque psoriasis in Canada in 2008.	90 psoriasis patients Age: mean [SD] 50.5 years [14.1] Gender: 70% Male Sampling frame: 18 years and older physician diagnosed patients assessed before January 1, 2007 in British	Non-interventional	Cross-sectional observational study. Date: January 1 to December 31, 2008.	Societal	No time horizon reported. Discounting not reported.	Healthcare	Direct costs: healthcare provider visits, prescription and over-the-counter pharmacotherapy, phototherapy sessions, laboratory tests and/or procedures, hospitalizations, and non-conventional	Provincial schedule fees and private clinic fees.	

		Colombia, Quebec, and Ontario. Data collected from clinical charts and patient survey.					Productivity loss.	treatment and management.		
		Canada (North America)					(Analytical perspective not reported)	Absenteeism and lost leisure time.		
Ghatnekar (2012), Sweden	To estimate the cost of care, psoriasis area and severity index (PASI), and quality of life in a defined patient	164 psoriasis patients (74% plaque psoriasis). Age: range, 19-86 years. Gender: 50 % Male Sampling frame: Adults patients visiting	Non-interventional. Groups considered were Topical treatment, topical treatment plus ultraviolet light therapy	Method: Cross-sectional study. Date: September 2009.	Societal perspective.	No time horizon reported. No discounting reported	Healthcare	Direct medical: Outpatient visits, hospitalisations, pharmaceutical, phototherapy visits, intravenous administration, and naturopathic preparation.	Published literature and Swedish official sources.	Non-parametric Mann-Whitney U-test. Kolmogorov-Smirnov test.

	population in Sweden.	dermatology clinics at Malmo University hospital and Kristianstad Hospital in the south of Sweden.	(LT), traditional systemic treatment (TST) and biologic systemic treatment (BST).					Direct non-medical: Transport to psoriasis related care. Absenteeism and presenteeism.	National average wages. Euro (2009 price year).	
Gunnarsson	To quantify individual	161, 940	Non-interventional	Retrospective study	Not reported	Not reported	Health care (Analytical perspective not reported)	Direct costs: Medical expenditure	Expenditure data from MEPS	Sensitivity analysis conducted.

(2010), USA	and US national estimates of the healthcare insurer expenditures and patient OOP expenditures associated with psoriasis	Age: mean 48 years Gender 42% Male Sampling frame: Medical expenditure panel survey (MEPS), nationally-representative database developed by the Agency for Healthcare Research and Quality (AHRQ) that reports healthcare utilization and expenditures,		Date: 1996 to 2006		No discounting reported	(Analytical perspective not reported)	Out of pocket	Dollar (2008 price year)	
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		health status, health insurance coverage, and sociodemographic and socioeconomic characteristics for the civilian, non-institutionalized population in the US. USA (North America)								
Sato (2010), USA	To evaluate the relationship between QoL, HCRU and employe	897 psoriasis patients Age: mean [SD] 46.27 [14.97] years	Non-intervention	Cross-sectional Observational study Date; 2006	Not reported	Not reported No discounting reported.	Healthcare (Analytical perspective not reported)	Direct costs: Healthcare utilization	Number of visits and hospitalisation days. Not monetary evaluation	Descriptive summary statistics, Fisher exact test.

	nt in European patients with plaque psoriasis	Gender: 58% Male Sampling frame: Patients with plaque psoriasis visiting any of the 300 recruited dermatologists in UK, Germany, France, Italy and Spain.								Pearson correlation coefficient.
Navarini (2010), Switzerland	To obtain data on out-of-pocket expenses, costs of outpatient /office-based care	383 patients Age: mean 55 years Gender: 59% Male Sampling frame: 1200 members of	No interventional study	Observation study (cross sectional). Survey Date: 2005	Societal and individual perspective.	No follow up No discount reported	Healthcare Patient costs	Direct cost: Ambulatory care costs Out of pocket on drugs, skin care products, privately paid	Swiss tariff list (TARMED) Patient reported unit costs	Descriptive statistics

	and inpatient care for psoriasis, and to extrapolate the total costs, by state of severity, to the entire Swiss population .	the Swiss Psoriasis and Vitiligo Society in November 2005 received questionnaires. In addition, 400 dermatologists were contacted for patient documentation. Switzerland (Europe)					Productivity loss (Analytical perspective not reported)	hospitals, inpatient costs. Indirect: Absenteeism	Swiss Franc – CHF (2005 price year)	
Chan (2009), Canada	To determine the lost productivity of Canadian patients	81 patients Age: range 18 to 89 years. Gender: 72 % male	Non-interventional study	Method: Cross-sectional Survey	Patient perspective	No follow up No discount reported	Productivity loss. (Analytical perspective not reported)	Indirect: Absenteeism	Average national wages Canadian Dollar (2005 price year)	-

	with moderate to severe psoriasis.	Sampling frame: Patients with moderate to severe psoriasis treated with psoriasis treated by dermatologists Vancouver, Quebec, Toronto, Markham.								
Yu (2009), USA	To evaluate health care utilization and costs for patients with psoriasis	56,528 Psoriasis Patients Age: mean [SD] 46.0 [11.3] Gender: 48% Male	Non-interventional	Method: Retrospective matched cohort design. Date: 1 st January to 31 st	Not reported	Not reported. No discounting reported	Healthcare	Direct resources: resource Utilisation (hospitalisation, emergency department, outpatient, professional visits)	Reimbursement unit costs	Descriptive statistics. Paired student's t-test McNemar test.

	vs. the general population and by psoriasis severity.	Sampling frame: Patients registered on the Thompson Medstat MarketScan Research database, high-quality resource with the combined claims of approximately 40 employers and several health plans, representing about 18 million covered lives. Adult patients with psoriasis during 2003 were identified and		December, 2003.				Drug utilisation	US dollar (2007 price year)	Wilcoxon test. Chi-square test. Logistic regression. Multivariate two-part regression. Generalised linear model (GLM).
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		matched in a 2:1 ratio with controls that had no psoriasis.								
		USA (North America)								
Fowler (2008), USA	To quantify the incremental direct medical and indirect work loss costs associated with psoriasis	12, 280 psoriasis patients Age: mean [SD] 44.7 [14.0] Gender: 50.6% Male Sampling frame: Administrative claims covering 5.1 million employees, their spouses and	Non-interventional	Method: Retrospective matched cohort design. Date: first psoriasis claim and continuing until the earlier of the health plan termination	Employer's perspective	Time horizon not reported.	Healthcare Productivity loss. (Analytical perspective not reported)	Direct: Inpatient, outpatient, pharmacy prescription. Indirect: Employer disability payments and sick leave	Actual costs paid by employer Employee's wages	student's t-test Logistic regression. Multivariate two-part regression.

		dependents from 31 large private insured Fortune 500 companies. Each psoriasis patient was matched with 3 controls on year of birth and sex). USA (North America)		date or the defined study end date (January 31, 2005).						
Schoffski (2007), Germany	To examine cost-of illness, severity of skin involvement (PASI, BSA) and	184 psoriasis patients. Age; mean 51.7 Gender: 66.3% Male Sampling frame: Multicentre non-	Non-interventional	Multi-centre non-interventional study Date: October 2003 to	Economy (societal), the perspective of the German statutory health insurance (GKV) and the	12 months No Discounting	Healthcare	Direct: consultation, medications, hospitalisation, rehabilitation and out-of-pocket expenses.	German tariff list (EBM), Clinic-specific average daily rate reimbursed. Quarterly flat rates.	Not recorded in methods (Descriptive statistics reported in results)

	quality of life (SF-36, DLQI) in three groups of patients with moderate to severe psoriasis in Germany:	interventional study. Nine outpatient clinic departments and eight office-based dermatologist were the selected study centre. Suitable patients were identified on the basis of their charts and addressed at their next routine visit. Germany (Europe)		February, 2004.	German pension funds (GRV).		Productivity loss. (Analytical perspective not reported)	Indirect: Absenteeism, job loss, early retirement (Analytical perspective not reported)	German pharmaceutical index and for compounded prescriptions using the pharmacists' price index	
Berger (2005), Germany	To assess average annual	192 Psoriasis patients.	Non interventional	Cross-sectional retrospective	Patient, third party payer	12 months	Healthcare	Direct: health resource utilisation,	Respective service charge.	Descriptive statistics.

<p>cost and cost per flare of outpatient and office-based care for patients with moderate to severe chronic psoriasis vulgaris from several perspectives.</p>	<p>Age: mean 47.2 Gender: 55.2% Male Sampling frame: Adults patient (18 to 75 years) with moderate to severe chronic plaque type psoriasis visiting dermatology hospital and office-based dermatologists. Germany (Europe)</p>		<p>e and prospective study. Date: April to October 2002.</p>	<p>and societal perspective.</p>	<p>No discounting</p>		<p>Productivity loss. (Analytical perspective not reported)</p>	<p>Over the counter (OTC), skin care products and nutritional supplements and non-reimbursable therapies. Absenteeism (Analytical perspective not reported)</p>	<p>German tariff list (EBM) by current average value (2002) per point for dermatologists (0.037) Reimbursable prices in the German pharmaceutical index. Wages (human capital approach)</p>	<p>Chi-square test. Mann-Whitney U test.</p>
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Feldman (2005), USA	To estimate failure rates associated with the use of traditional systemic agents and phototherapy in patients with psoriasis, as well as annual direct medical costs of psoriasis treatment	2068 psoriasis patients. Age: Gender: range of means (44.2 to 48.8) Gender: 59% Male Sampling frame: Claims records for adult patients with psoriasis under a managed care insurer in north-	Non-interventional	Retrospective study.	Third party payer perspective	12 Months No discounting	Healthcare. (Analytical perspective not reported)	Direct: Drug treatment costs, health utilisation and professional services (Analytical perspective not reported)	Reimbursement costs US dollar (Price year not reported)	Proportions, means, 99 th Percentile.
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	among patients receiving these therapies									
Crown (2004), USA	To examine the direct costs in psoriasis patients treated with systemic therapy or phototherapy	2489 psoriasis patients. Age: mean [SD], 50.4 [14.5] Gender: 51.1% Male Sampling frame: MarketScan commercial claims and Encounters Database and the Medicare Supplemental	Non-interventional	Retrospective cohort study. Date: 1996 to 2000	Not reported	Not reported	Healthcare. (Analytical perspective not reported)	Direct: Health utilisation, drug costs.	Reimbursement unit costs	Descriptive statistics: Means and standard deviations. Chi-square tests. t-tests. Logistic regression.

		<p>and Coordination of Benefits (COB) Database from 1996 to 2000. Persons with a medical claim for psoriasis (ICD-9-CM 696.1) between 1 April 1996 and 31 December 1999 treated with systemic therapy and/or phototherapy were included.</p> <p>USA (North America).</p>								
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Feldman (2015), USA	To compare the prevalence of comorbidities, health care utilization, and costs between moderate-to-severe psoriasis (PsO) patients with comorbid psoriatic arthritis (PsA) and	1,230 moderate-to-severe Psoriasis patients and 1,230 controls. Age: 48.46 [10.75] Gender: 52.1% Male Sampling frame: Patients were selected from the OptumHealth Reporting and Insights claims database which represents 15.5 million privately insured	Non-interventional. Those included were on at least systemic or biologic treatment	Retrospective observational study. Date: January 2007 to March 2012	Not reported	Time horizon not reported No discounting reported	Healthcare (Analytical perspective not reported)	Direct resources: medication use, health care utilization	Insurance reimbursement US dollar (2012 price year)	Descriptive statistics; mean, standard deviation, frequencies and percentages. Wilcoxon signed-rank tests McNemar's test
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	matched controls.	<p>individuals. Patients were identified based on ICD-9-CM code 696.0 and the Current Procedural Terminology (CPT) codes. Moderate to severe patients where those receiving at least 1 non-topical systemic therapy.</p> <p>USA (North America)</p>								
Lofvendahl (2016)	To estimate increment	15, 283 patients (12,562 PsO and 2721 PsA).	Non interventional	Retrospective cohort	Societal perspective	Not reported.	Healthcare	Direct: Drug treatment	Pharmacy wholesale prices as	Arithmetic mean and

<p>al costs for patients with psoriasis/psoriatic arthritis (PsO/PsA) compared to population-based referents free from PsO/PsA and estimate costs attributable specifically to PsO/PsA</p>	<p>Age: mean [SD] 52 [21] years for PsO and 54 [16] years for PsA</p> <p>Sampling frame: Patients were selected from the Skåne Healthcare Register which covers healthcare use for the population of the Skåne region of Sweden. Patients were classified as having PsO alone (hereby PsO) if they had at least 1 of the ICD-10 codes L40.0,</p>		<p>observational study.</p> <p>Date: 2008 to 2011</p>				<p>Productivity loss</p> <p>(Analytical perspective not reported)</p>	<p>costs, health utilisation</p> <p>Sick leave days.</p>	<p>collected from the Swedish Prescribed Drug Register.</p> <p>Human capital approach</p>	<p>Standard deviation. Nonparametric statistics.</p> <p>2-sample t tests.</p>
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		<p>L40.1, L40.2, L40.4, and L40.8, but not L40.5.</p> <p>Patients with ICD-10 diagnostic code L40.5 alone or at least 1 code for PsO in combination with any of codes M07.1, M07.2, M07.3, or M09.0 were classified as having PsA.</p> <p>Sweden (Europe)</p>								
Ekelund (2013), Sweden	To examine the relationship between measures	<p>443 psoriasis patients.</p> <p>Age: mean, [SD] 51.5 [14.2].</p>	Non-interventional	Method: multicentre, observational, retrospective study.	Societal perspective.	<p>1 year.</p> <p>No discounting</p>	Healthcare	Healthcare resource utilization.	<p>Pharmacy retail prices</p> <p>Standard schedule of fees.</p>	

	of disease severity and costs from a societal perspective in patients with plaque psoriasis	Gender: 68.2% male. Sampling frame: Adult patients (18 years plus) diagnosed with plaque psoriasis in the previous year and visiting dermatology units at 10 hospitals in Sweden and members of the Swedish Psoriasis Association.		Date: June 2008 – January 2010.			Productivity loss (Analytical perspective not reported)			
Feldman (2017) USA	To assess the incremental burden	56,406 Psoriasis patients and controls.	No interventional	Retrospective observational study.	Third party Payer Perspective (insurance)	Time horizon not reported	Healthcare	Direct resources: Outpatient, emergency,	Insurance reimbursement	Descriptive statistics; mean, standard

of comorbidities on healthcare resource utilization, direct costs and indirect costs associated with short-term disabilities among patients with psoriasis in the US	Age: mean [SD] 51.6 [14.6] years Gender: 49.99 % female Sampling frame: MarketScan® Commercial and Medicare Supplemental and Coordination of Benefits databases between January 01, 2010, and December 31, 2011, and from the MarketScan Health and Productivity Management		Date: 1 January 2010 to 31 Dec 2011.			No discounting reported	Indirect costs	inpatient and pharmacy claims. medication use, health care utilization Indirect resources: Human Capital Approach. Those associated with short term disability	US dollar (2011 price year)	deviation, frequencies and percentages. Poisson regression, two-part model (logistic regression and gamma regression) Adjusted costs difference for
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		<p>(HPM) database between January 1, 2011, and December 31, 2011. adult patients (aged ≥18 years) with at least two diagnoses of Psoriasis (International Classification of Diseases, 9th Revision, Clinical Modification [ICD-9-CM]: 696.1, 696.8) on different dates between January 01, 2010, and December 31, 2011, with at</p>								incremental costs.
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		least one psoriasis diagnosis in the year 2010 to ensure patients has psoriasis in year 2010.								
Driessen (2010) Netherland	To investigate the economic impact of psoriasis, including direct costs, before and after the introduction of biologics, with	67 psoriasis patients Age: 47.9 Gender: 34% Female. Sampling frame: all patients with psoriasis treated with biologics at the Radboud University Nijmegen Medical		Retrospective cohort study Date: February 2005 to February 2009					Published Dutch Health Insurance board prices. €0.19per kilometre for transport Standard monthly prices	Descriptive statistics; mean, frequencies and range.

	special focus on hospitalize d patients, treatment effectiven ess and patient satisfactio n with medicatio n. Patients	Centre Department of Dermatology between February 2005 and February 2009							Euro (No price year)	
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Appendix 3.4: Reference of studies included in the cost-of-illness systematic review

Chan, B. *et al.* (2009) 'Work-related lost productivity and its economic impact on Canadian patients with moderate to severe psoriasis', *Journal of Cutaneous Medicine and Surgery*, 13(4), pp. 192–197. doi: 10.2310/7750.2009.08068.

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Driessen, R. J. B. *et al.* (2010) 'The economic impact of high-need psoriasis in daily clinical practice before and after the introduction of biologics', *British Journal of Dermatology*, 162(6), pp. 1324–1329. doi: 10.1111/j.1365-2133.2010.09693.x.

Ekelund, M. *et al.* (2013) 'A Higher Score on the Dermatology Life Quality Index, Being on Systemic Treatment and Having a Diagnosis of Psoriatic Arthritis is Associated with Increased Costs in Patients with Plaque Psoriasis'. doi: 10.2340/00015555-1591.

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Appendix 3.5: Reported comorbidities in the included studies

Chen	Metabolic syndrome Autoimmune Infection Autoimmune Malignancies Other
Crown	GI disorders Hepatotoxicity Hypertension Nephrotoxicity Anaemia Carcinoma Depression Diabetes
Ekelund	Joint Involvement
Feldman (2015)	Lung disease Liver disease Peptic ulcers Dementia Rheumatic disease Rheumatoid arthritis Systemic lupus erythematosus Systemic sclerosis Sjogren's syndrome Hemiplegia AIDS Hyperlipidaemia Hypertension Diabetes Mellitus Obesity

	<p>Coronary heart disease</p> <p>Acute Myocardial infarction</p> <p>Stroke</p>
Feldman (2017)	<p>Hypertension</p> <p>Hyperlipidaemia</p> <p>CVD</p> <p>Diabetes</p> <p>PsA</p> <p>Depression.</p> <p>Anxiety</p> <p>Obesity</p> <p>Cerebrovascular disease</p> <p>Peripheral Vascular disease</p>
Fonia	<p>Hypertension</p> <p>PsA</p> <p>Dyslipidaemia</p> <p>Depression</p> <p>Liver disease.</p> <p>Diabetes</p> <p>Skin cancer</p>
Fowler	<p>Hypertension</p> <p>Hyperlipidaemia</p> <p>Diabetes</p> <p>CVD</p> <p>Malignant neoplasm</p> <p>Disorders of the immune mechanism</p>
Ghatneker	<p>Joint problem</p> <p>PsA</p> <p>Diabetes</p> <p>CVD</p>

	Hyperlipidaemia
Gunnarson	Malignant neoplasm Disease of the digestive system
Jungen	CVD Metabolic disease Depression

Appendix 4.1: Search Strategy for Psoriasis burden-of-disease

#Psoriasis

1. exp psoriasis/ or arthritis, psoriasis

#Quality of Life (Health Utility)

2. Quality-Adjusted Life Years/
3. (quality adjusted or adjusted life year\$).ti,ab,kf.
4. (qaly\$ or qald\$ or qale\$ or qtime\$).ti,ab,kf.
5. (illness state\$1 or health state\$1).ti,ab,kf.
6. (hui or hui1 or hui2 or hui3).ti,ab,kf.
7. (multiattribute\$ or multi attribute\$).ti,ab,kf.
8. (utility adj3 (score\$1 or valu\$ or health\$ or cost\$ or measur\$ or disease\$ or mean or gain or gains or index\$)).ti,ab,kf.
9. utilities.ti,ab,kf.
10. (eq-5d or eq5d or eq-5 or eq5 or euro qual or euroqual or euro qual5d or euroqual5d or euro QoL or euroQoL or euro QoL5d or euroQoL5d or euro quol or euroquol or euro quol5d or euroquol5d or eur QoL or eurQoL or eur QoL5d or eur QoL5d or eur?qul or eur?qul5d or euro\$ quality of life or european QoL).ti,ab,kf.
11. (euro\$ adj3 (5 d or 5d or 5 dimension\$ or 5dimension\$ or 5 domain\$ or 5domain\$)).ti,ab,kf.
12. (sf36\$ or sf 36\$ or sf thirtysix or sf thirty six).ti,ab,kf.
13. (time trade off\$1 or time tradeoff\$1 or tto or timetradeoff\$1).ti,ab,kf.
14. quality of life/ and ((quality of life or QoL) adj (score\$1 or measure\$1)).ti,ab,kf.
15. quality of life/ and ec.fs.
16. quality of life/ and (health adj3 status).ti,ab,kf.
17. (quality of life or QoL).ti,ab,kf. and Cost-Benefit Analysis/
18. ((QoL or hrQoL or quality of life).ti,kf. or *quality of life/) and ((QoL or hrQoL\$ or quality of life) adj2 (increas\$ or decrease\$ or improv\$ or declin\$ or reduc\$

or high\$ or low\$ or effect or effects or worse or score or scores or change\$1
or impact\$1 or impacted or deteriorat\$)).ab.

19. Cost-Benefit Analysis/ and (cost-effectiveness ratio\$ and (perspective\$ or life expectanc\$)).ti,ab,kf.
20. *quality of life/ and (quality of life or QoL).ti.
21. quality of life/ and ((quality of life or QoL) adj3 (improv\$ or chang\$)).ti,ab,kf.
22. quality of life/ and health-related quality of life.ti,ab,kf.
23. models,economic/
24. or/2-23

#Other measure of HRQoL and capability

25. icecap.mp.
26. Year\$ of full capability.mp.
27. Ocap\$.ti,ab,kf.
28. Ascot.ti,ab,kf.
29. capability.ti,ab,kf.
30. or/25-29
31. dermatology life quality index.mp.
32. dlqi.ti,ab,kf.
33. 31 or 32
34. psoriasis area severity index.mp.
35. pasi.ti,ab,kf.
36. ((psoriasis area severity index or pasi) adj (score\$1 or measure\$1)).ti,ab,kf.
37. or/34-36
38. Disability-Adjusted Life Year\$.mp.
39. (disability adjusted or disability-adjusted life year\$).ti,ab,kf.
40. daly\$.ti,ab,kf.
41. disability weight\$.ti,ab,kf.
42. [*disability/.ti,ab,kf.]
43. or/38-42
44. 24 or 30 or 33 or 37 or 43

45. 1 and 44 ##To combine with psoriasis

##Exclusions, deduplication and final results

46. letter.pt.

47. editorial.pt.

48. historical article.pt.

49. or/46-48

50. exp animals/ not humans/

51. 49 or 50

52. 45 not 51

53. Remove duplicates from 52

54. Limit 53 to English language

55. Review.pt

56. 54 not 55

Appendix 4.2: Data extraction sheet for burden of disease

Table A4- 1: Burden-of-disease systematic review study characteristics and methods extracted data

First author (year), Country of origin	Aim (as reported by authors)	Study sample	Severity	Interventions included	Data collection methods	Reported study time horizon	Description of consequences (analytical perspective reported)	Measurement of consequences	Valuation of consequences	Statistical analysis methods (sensitivity analysis)
Lesner et.al (2017), Poland	To identify differences among psoriatic patients from various countries, especially regarding determinants of psychosocial health deterioration, including	682 Clinician diagnosed psoriasis Age: 47.0±15.6 years Gender: 54.2%M Comorbidities: Not included	Reported. (Mild, Moderate, Severe)	Non-interventional	Method: Cross-sectional multicentre Date: Nov 2011 to Feb 2013	No follow up Discounting: N/A	Clinical: Itch Health status: HRQoL Anxiety and Depression.	Generic HRQoL: EQ5D EQ-VAS HADS, DLQI,	EQ5D (tariff not stated) EQ-VAS (0 to 100)	Descriptive statistics. Frequencies (percentage) Mean and standard deviation. Chi-square test, ANOVA, Multiple regression

	HRQoL, anxiety and depression	Sampling frame: Dermatology patients visiting the dermatology centre in 13 European countries								and Pearson's correlation test
Moradi (2015), Iran	To evaluate HRQoL of adult patients with psoriasis in Iran and explore the relationship between general and disease-specific outcome measure in psoriasis.	N: 62 patients Age (SD): 40.4 (17.5) years Gender: 76% Male Comorbidities: Sampling frame: All psoriasis	Reported (PASI scores)	Topical Non-biological therapy Topical plus non-biological therapy	Cross-sectional survey May to Aug 2013.	Study period (4months) Discount: N/A	General Health status:	EQ5D EQ5D-VAS PASI, DLQI, PGA VAS	EQ5D- UK tariff EQ-VAS (0-100)	Descriptive statistics Non-parametric Mann-Whitney U-Test, Kruskal-Wallis test

		outpatients for one physician at Moradi Skin Laser Clinic in Shiraz, Iran. (Middle East)								Spearman's correlation
DiBonaventura (2018), Brazil	Offering a comprehensive assessment of the humanistic and economic burden in Brazil.	N: 210 patient reported psoriasis Age: 40.80 ± 12.65 G: 49.5% M Sampling frame: National Health and Wellness Survey	Reported (Mild, Moderate, Severe)	Non-Interventional	Retrospective analysis of Cross-sectional Survey 2012	No follow up	Health status: HRQoL Beyond health: Productivity	SF-12v2, SF6D Work productivity and impairment (WPAI)		Chi-square test One-way ANOVA Regression

		Brazil (S. America)								
Korman N.J (2016), USA	To examine how QoL, work productivity and clinical symptoms vary between patients with mild, moderate and severe psoriasis.	N: 694 physician diagnosed Age: 44 ± 15.6 years Gender: 55%M Severity: Mild 48%, Moderate 46%, Severe 6%. USA (N. America)	Reported (Mild, Moderate, Severe)	Topical 20.2% Phototherapy 18.7% Systemic 21.5% Biologic 37.8% None 1.9%	Retrospective analysis of Cross-sectional Survey 2011 to 2013	No follow up	Health status: QoL Beyond health: Productivity	EQ5D-3L	Not specified	Mann-Whitney U-test and Kruskal-Wallis Test Chi-square Ordered logistic Regression
Bronckers (2018), Netherlands	To assess QoL, life course, and work productivity in	75 patients Gender: 29% M	Reported	Topical 16%	Cross section, prospective, non-	No follow up	Health status: HRQoL	EQ-5D SF-36	EQ5D Dutch tariff.	Descriptive statistics

	young adults with psoriasis and identify characteristics influencing these patient-reported outcomes (PRO).	Sampling frame: all patients with psoriasis who were seen at the outpatient clinic of the Department of Dermatology, Radboud University Medical Centre. Netherlands (Europe)	(Mild, Moderate, Severe)	UVB phototherapy 28% Conventional systemic 38.7% Biologics 17.3%	interventional study May 2014 and March 2015		Work productivity Beyond health: Life course	Work productivity and impairment questionnaire (WPAI): psoriasis. PROductivity and DISease Questionnaire (PRODISQ) Course of life questionnaire (COLQ)	SF-36 domain score (0 to 100) Index (0 to 30) Percentage of impairment (0 to 100)	Median, Interquartile ranges [IQR] Manna-Whitney U test and Kruskal-Wallis H test Spearman's rank correlation Multivariable general linear modelling (GLM)
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Hjalte (2018), Sweden	To analyse the long-term real-world outcome data of patients who are biologically naïve with moderate-to-severe psoriasis after switching to biological treatment.	583 Psoriasis Patients Age: 47 (14.1) Sampling frame: Biologically naïve patients with moderate to severe psoriasis after switching to biological treatment in PsoReg, a Swedish registry for psoriasis treatment.	Reported (Moderate to Severe)	Biologics	Observational study	10 years follow up	Clinical: Severity Health status: HRQoL DLQI PASI	Generic HRQoL: EQ5D-3L	UK EQ5D tariff	Sensitivity analysis Descriptive statistics Mean, standard deviation. Wilcoxon signed-rank test
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		Sweden (Europe)								
Weiss (2002), USA	To evaluate the health effects of skin disease by comparing psoriasis to other primary medical disorders using 3 different scales of health-related quality of life	35 psoriasis patients Age: Median, 49 years Gender: 60% Male Sampling frame: Patients visiting the dermatology branch of the National cancer institute.	Reported (Moderate to Severe)	Non-intervention	Cross-section survey		HRQoL Beyond Health: Wellbeing Clinical Severity	EQ5D EQ-VAS SF-36	UK EQ5D tariff EQ-VAS (0 to 100) rating scale. SF-36 domain score (0 to 100)	Descriptive statistics Mean or median Step wise multiple linear regression Two tailed Fisher's exact test. Mehta's exact test Spearman's rank

										<p>correlation coefficient</p> <p>Jonkheere Terpstra test.</p> <p>T test</p> <p>Signed rank test,</p> <p>Sing test (median)</p>
Timotijevic (2017), Serbia	To assess the impact of changes in PASI by body region on QoL in	100 psoriasis patients Age: mean (SD): 46.7 (13.4)	Reported (PASI score)	psoralen plus ultra-violet A (PUVA) photochemotherapy	Prospective study	Four weeks follow up	HRQoL	EQ5D	Not reported (wrong interpretation of EQ5D scores)	<p>Descriptive Statistics</p> <p>Mean, standard deviation.</p>

	patients with psoriasis.	Gender: 38% Male Sampling frame: Adult patients with plaque psoriasis treated at the Department of Dermatology, Clinical Centre Zvezdara, Belgrade between January and December 2011						EQ-VAS (PASI, DLQI)	EQ-VAS (0 to 100) rating scale.	Mann-Whitney U-test Spearman's rho correlation
Masaki (2016), Japan	To determine the cost-effectiveness of	133 Clinician diagnosed	Reported (PASI score)	No specific treatment	Cross-sectional study	No follow up	Health status: HRQoL	EQ5D	Not reported	Pearson's correlation

	psoriasis treatment in Japan	psoriasis patients Age: median (IQR) 56 (Q1=46, Q2=68.5) Gender: 79% M Sampling frame: Patients with a clinical diagnosis of psoriasis visiting four university hospitals in Fukuoka Prefecture, Japan					Willingness to pay	Willingness to pay		
							Severity	PASI		

Yee Ng (2015), Taiwan	The purpose of our study is to identify the factors that impact the HRQoL of psoriasis vulgaris patients in Taiwan using the SF-36	496 dermatologist or rheumatologist diagnosed psoriasis patients Age: mean [SD] 45.2 [15.2] Gender: 68.1% M Sampling Frame: Patients treated for psoriasis in the outpatient clinics and inpatients of the	Reported (Mild, Moderate, Severe)	No specific treatment	Cross-sectional observational study. Date: January 2008 to December 2011.	Not reported	Health status: HRQoL Severity	SF-36 PASI	No valuation	Descriptive Chi square test Fisher's test Student t-test ANOVA Linear regression
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		dermatology departments Taiwan (Asia)								
Balogh (2014), Hungary	To assess the cost-of-illness and quality of life of patients with moderate to severe psoriasis in Hungary	200 psoriasis patients Age: mean [SD] 51 [13] Gender: 68% M Sampling frame: Patients with diagnosis of psoriasis, aged ≥18 visiting two university dermatology clinics in Hungary.	Reported (Moderate to Severe)	Non interventional	Non-interventional Cross-sectional survey. Date: September 2012 to May 2013.	12 months	Health status: HRQoL Disability	EQ-5D-3L EQ-VAS	EQ-5D-UK tariff. Disability pay	Descriptive Mean Standard deviation. Non-parametric tests

Tang (2013), Malaysia	To describe the extent to which psoriasis affects the QoL of patients treated in government-run dermatology clinics in Malaysia and to estimate the cost-of-illness.	250 psoriasis patients Age: mean (range) 42.5 (18-83) Gender: 54% M Sampling frame: patients with chronic plaque Psoriasis treated at dermatology centres at eight government run hospitals between December 2007	Reported (Mild, Moderate, Severe)	Non-interventional	Non-interventional cross-sectional survey.	Not reported	Health status: HRQoL	SF-12	No valuation	Descriptive : Mean, standard deviation Fisher's exact test Mann-Whitney U test Independent sample t-tests
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		and August 2008.								
Dauden (2013), Spain	To describe the demographic and clinical characteristics of patients with moderate-to-severe psoriasis and to assess the impact of psoriasis and its treatment on patients' quality of life.	1217 psoriasis patients. Age: mean [SD] 45.11 [13.92] Gender: 60.8% Male Sampling frame: Adults (18 years plus) with moderate-to-severe psoriasis but without psoriatic arthritis visiting one of the 123	Reported (Moderate to Severe)	Non-interventional	Prospective observational study. Date: 9 August to 21 December 2007.	Not reported	Health status: HRQoL	EQ-5D-3L VAS	No valuation set reported.	Descriptive statistics. t-tests. Mann-Whitney U test. Chi-Square test. Fisher exact test

		centres in Spain. Spain (Europe)								
Mattila (2013), Finland.	To evaluate the disadvantages at work caused by psoriasis.	262 psoriasis patients. Age: mean [SD], 58 years [13.8]. Gender: 55% Male Sampling frame: patients with moderate to severe psoriasis or psoriatic arthritis visiting the	Reported (Moderate to Severe)	Non interventional	Cross sectional study. Date: 1 October 2009 to 30 th September 2010.	Not reported.	Productivity loss:	Survey specific questionnaire.	No Valuation	Chi-square test for proportion and student's t-tests for means. Pearson's coefficient of correlation .

		dermatology outpatient clinic in Turku University Hospital.								
Wu (2009), USA	To determine the impact of psoriasis on work and productivity using data from the National Health and Wellness Survey (NHWS).	1127 psoriasis patients. Age: 53.1 [15.1]. Gender: 46.3% Men Sampling frame: 40 730 adults in the US who completed the NHWS Internet survey between 1 May and 30 June	Reported (Mild, Moderate, Severe)	Non- interventional	Method: A matched case- control study. Date: 1 May to 30 June 2004.	Not reported	Productivity loss	WPAI	No valuation	Logistic regression comparing Odds ratios.

		<p>2004 were evaluated.</p> <p>A cohort of respondents without psoriasis was randomly chosen and matched according to age (within 4 years), sex, region, and race. This matched cohort was used to assess whether psoriasis has a negative impact on work</p>								
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		and productivity as measured by the WPAI questionnaire. USA (North America)								
Pearce (2006), USA	To better quantify the impact that psoriasis has on work productivity and social functioning, and investigate what factors may contribute to this impairment	90 psoriasis patients. Age: mean, [SD] 50.5 [13.7] Gender: 50% Male Sampling: Psoriasis patients aged 18 and over	Reported (Mild, Moderate, Severe)	Non interventional	Method: Cross-sectional survey Date: December 2003 to April 2004.	Not reported	Productivity loss	WPAI	No valuation	Not indicated

		with plaque-type psoriasis.								
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Table A4-2: Burden-of-disease systematic review impact of psoriasis results

First author (year) Country	Study sample description	Results
Balogh (2014), Hungary	Disease: Psoriasis Only Mean [SD] for all patients BMI 29.85 [5] PASI index 8 [10] DLQI 6[7] Self-assessed disease activity 35 [33] Physician’s global assessment VAS 23 [22]	<u>Mean EQ-5D [SD]; EQ-VAS [SD]</u> All patients: 0.69 [0.3]; 64 [21] On Biologics: 0.65 [0.3]; 55[20] On Non-biologics: 0.62 [0.3]; 59 [17] No systemic treatment: 0.75 [0.3]; 70 [22]
Bronckers (2018), Netherlands	Disease: Psoriasis as main, Psoriatic arthritis as comorbidity.	SF-36: median [IQR] PCS 53.8 [7.9], MCS 52.3 [9.8] EQ5D: Median [IQR], Overall 1 [0.2], EQ-5D VAS 80 [20] WPAI-PSO number, (%) impaired work productivity 19 [42.2], impaired activity 42 (42.2), Median [IQR] percentage impairment, Impaired caused due to disease related absenteeism 50 [56]

		<p>Impairment while working due to presenteeism 20 [60], total activity impairment 10 [30]</p> <p>COLQ: Median [IQR], Autonomy development (range 6 to 12) 9 [2], Social development (12-24) 22 [3], Psychosexual development (4 – 8) 8 [3]</p>
Dauden (2013), Spain	<p>To describe the demographic and clinical characteristics of patients with moderate-to-severe psoriasis and to assess the impact of psoriasis and its treatment on patients' quality of life.</p> <p>Disease: Psoriasis only.</p>	<p>Mean EQ-5D dimension score [SD]: First visit; Second visit</p> <p>Mobility: 1.21 [0.42]; 1.15 [0.36]</p> <p>Self-care: 1.11 [0.33]; 1.07 [0.26]</p> <p>Usual activity: 1.29 [0.47]; 1.20 [0.43]</p> <p>Pain/ Discomfort: 1.57 [0.58]; 1.42 [0.56]</p> <p>Anxiety/Depression: 1.48 [0.60]; 1.35 [0.55]</p> <p>EQ-VAS 64.41 [18.00]; 72.44 [17.88]</p>
Hjalte (2018), Sweden	Disease: Both Psoriasis and Psoriatic arthritis	<p>EQ5D: Median, mean, (SD) before switching 0.73, 0.74 (0.22), 3-5 months after switching 0.80, 0.82 (0.19), 6-11 months after switching 0.85, 0.82 (0.21), 1-5 years after switch 0.83, 0.79 (0.21), 6-9 years after switch 0.81, 0.75 (0.30)</p>

Korman N.J (2016), USA***	Disease: Psoriasis as main, PSA as comorbidity.	<p>EQ5D: Moderate -0.04(-0.06 to 0.02)</p> <p>EQ5D: Severe -0.18 (-0.23 to -0.13)</p> <p>Absenteeism%; Moderate 3.3 (-0.5 to 7.1) Severe: 6.1 (-1.2 to 13.4)</p> <p>Presenteeism% Moderate 10.1 (6.4-13) Severe: 15.1 (6.6-23.6)</p> <p>Activity impairment: Moderate 10.5 (7.3-13.7) Severe 21.1(12.3-29.8)</p>
Lesner (2017), Poland	<p>Comorbidities:</p> <p>Socio-economic level: Low 7.9, [0.9, 7.5-8.2], middle 7.1, [1.7, 6.9-7.2], high 6.6, [1.4, 6.2-7.0]</p> <p>Education level Low 7.1, [1.8, 6.9-7.4], higher 7.3, [1.9, 7.1-7.6], University 7.0,[1.6, 6.8-7.3]</p>	EQ5D mean, [SD,95% CI]: Male 6.9, [1.7, 6.7-7.1], female 7.4, [1.8, 7.2-7.7],
Mahshid Moradi (2015), Hungary		EQ-5D: 0.62 (0.37)

	Disease: Both (PSO and PSA)	EQ VAS: 60.18± 27.26 VAS: 53.60±26.72
Marco DiBonaventura (2018), Brazil	Disease: Psoriasis only.	SF-12 Mental: 42.92 ± 10.97 SF-12Physical: 51.41 ± 7.52 HS score: 0.654 ± 0.107 Absenteeism%: 8.24 ± 19.27 Presenteeism%: 25.03 ± 27.01 Overall work impairment: 28.80 ± 29.82 Activity impairment: 28.95 ± 29.23
Masaki (2016), Japan	Disease: Psoriasis only.	EQ5D mean [SD]: 0.827 [0.10] WTP mentioned in methods but not reported.

<p>Mattila (2013), Finland</p>	<p>262 psoriasis patients.</p> <p>Age: mean [SD], 58 years [13.8].</p> <p>Gender: 55% Male</p> <p>Sampling frame: patients with moderate to severe psoriasis or psoriatic arthritis visiting</p> <p>Disease: Both Psoriasis and Psoriatic arthritis.</p>	<p><u>Skin Irritation in work (no irritation)</u></p> <p>Absenteeism Mean hours lost Due to psoriasis 9.0 (2.0) due to other conditions 11.5 (14.7)</p> <p>Presenteeism mean hours lost Due to psoriasis 14.1 (5.6) Due to other conditions 13.0 (13.7)</p> <p><u>Type of work</u> White collar Blue Collar All Patients</p> <p>Absenteeism Mean hours lost Due to psoriasis 2.1 7.5 4.5 due to other conditions 13.6 13.2 12.3</p> <p>Presenteeism mean hours lost Due to psoriasis 6.6 11.9 8.3 Due to other conditions 14.3 12.6 12.9</p>
<p>Pearce (2006), USA</p>	<p>90 psoriasis patients.</p>	<p><u>Overall Work productivity activity impairment (WPAI)%</u></p>

	<p>Age: mean, [SD] 50.5 [13.7]</p> <p>Gender: 50% Male</p> <p>Sampling: Psoriasis patients aged 18 and over with plaque-type psoriasis.</p> <p>Disease: Psoriasis as main, Psoriatic arthritis as comorbidity.</p>	<p>All Subjects Mild Moderate Severe 15.5 9.2 25 12.1</p> <p><u>WPAI% while in work</u></p> <p>All Subjects Mild Moderate Severe 15.5 7.9 23.9 15</p> <p><u>Mean SF-8</u></p> <p>Physical component</p> <p>All Subjects Mild Moderate Severe 55.01 56.70 55.07 53.24</p> <p>Mental component</p> <p>All Subjects Mild Moderate Severe 54.90 54.46 56.27 54.07</p>
Tang (2013), Malaysia	Disease: Both	<p><u>Mean SF-12 Score [SD]</u></p> <p>Physical health 43.68 [9.23]</p> <p>Mental Health 42.25 [10.7]</p>

Timotijevic (2017), Serbia	Disease: Psoriasis only	EQ-5D	Baseline	After	%
			Mean±	treatment	Change
			SD	mean	
		Mobility	1.3±0.5	1.1 ±0.3	- 16.9
		Self-care	1.2±0.4	1.0±0.1	- 15.0
		Usual activities	1.7±0.7	1.1±0.3	- 36.8
		Pain/Discomfort	2.0±0.5	1.3±0.5	- 36.3
		Anxiety/Depression	2.1±0.6	1.5±0.5	- 29.9
		EQ VAS	40.2±24.5	79.5±16.6	97.6
Weiss (2002), USA	35 psoriasis patients		No Chronic	Psoriasis	
	Age: Median, 49 years		condition		
	Gender: 60% Male	Metric	Mean	Mean	Median
	Sampling frame:	EQ-5D	0.91	0.724	0.796
	Patients visiting the dermatology branch of the National cancer institute.	EQ5D VAS	82.5	75.1	80.0
	Disease: Psoriasis as main, Psoriatic arthritis as comorbidity.	SF-36 General Health	72.6	63.0	62.0
		SF-36 Physical Functioning	86.0	75.7	85.0
		SF-36 Role-Physical	87.2	76.4	100.0
		SF-36 Mental Health	77.6	67.9	72.0
		SF-36 Body Pain	74.2	65.3	72.0
		SF-36 Social Functioning	92.3	71.8	75.0

		SF-36 Vitality	52.9	55.0
		SF-36 Role-Emotion	67.6	100.0
Wu (2009), USA	<p>1127 psoriasis patients.</p> <p>Age: 53.1 [15.1].</p> <p>Gender: 46.3% Men</p> <p>Sampling frame: 40 730 adults in the US who completed the NHWS Internet survey between 1 May and 30 June 2004 were evaluated.</p> <p>A cohort of respondents without psoriasis was randomly chosen and matched according to age (within 4 years), sex, region, and race. This matched cohort was used to assess whether psoriasis has a negative impact on work and productivity as measured by the WPAI questionnaire.</p> <p>USA (North America).</p> <p>Diseases: Psoriasis only</p>	<p>Odds Ratio</p> <p>95% CI</p> <p>Missed hours of work in the last week due to health</p> <p>Productivity impairment at the work due to ill health</p> <p>Overall work impairment due to ill health</p> <p>Impairment for activity other than work</p>	<p>1.37</p> <p>1.66</p> <p>1.62</p> <p>1.59</p>	<p>1.00, 1.89</p> <p>1.28, 2.18</p> <p>1.25, 2.11</p> <p>1.25, 2.03</p>
Yee Ng (2015), Taiwan	496 dermatologist or rheumatologist diagnosed psoriasis patients	All	PASI <7	PASI: 7-15
				PASI: >15

	<p>Age: mean[SD] 45.2 [15.2]</p> <p>Gender: 68.1% M</p> <p>Sampling Frame: Patients treated for psoriasis in the outpatient clinics and inpatients of the dermatology departments.</p> <p>Disease: Both Psoriasis and Psoriatic arthritis. (Psoriasis was primary focus)</p>	<table border="0"> <tr> <td>SF-36:</td> <td>90.9</td> <td>94.3 (16.0)</td> <td>91.1</td> <td>84.9 (20.9)</td> </tr> <tr> <td>mean (SD)</td> <td>(18.5)</td> <td></td> <td>(18.5)</td> <td></td> </tr> <tr> <td>Physical</td> <td>46.4</td> <td>48.4 (10.5)</td> <td>46.2</td> <td>43.0 (12.9)</td> </tr> <tr> <td></td> <td>(11.7)</td> <td></td> <td>(11.6)</td> <td></td> </tr> <tr> <td>Mental</td> <td>44.5</td> <td>45.9 (13.7)</td> <td>44.8</td> <td>41.9 (14.7)</td> </tr> <tr> <td></td> <td>(14.0)</td> <td></td> <td>(13.4)</td> <td></td> </tr> </table>	SF-36:	90.9	94.3 (16.0)	91.1	84.9 (20.9)	mean (SD)	(18.5)		(18.5)		Physical	46.4	48.4 (10.5)	46.2	43.0 (12.9)		(11.7)		(11.6)		Mental	44.5	45.9 (13.7)	44.8	41.9 (14.7)		(14.0)		(13.4)	
SF-36:	90.9	94.3 (16.0)	91.1	84.9 (20.9)																												
mean (SD)	(18.5)		(18.5)																													
Physical	46.4	48.4 (10.5)	46.2	43.0 (12.9)																												
	(11.7)		(11.6)																													
Mental	44.5	45.9 (13.7)	44.8	41.9 (14.7)																												
	(14.0)		(13.4)																													

Appendix 4.3: Reference of studies included in the burden-of-disease systematic review

Balogh, O. *et al.* (2014) 'COI in patients with moderate to severe psoriasis: A cross-sectional survey in Hungarian dermatological centres', *European Journal of Health Economics*. Springer Verlag, 15(SUPPL. 1), pp. 101–109. doi: 10.1007/s10198-014-0599-z.

Bronckers, I. M. G. J. *et al.* (2018) 'Journal of Dermatological Treatment A cross-sectional study in young adults with psoriasis: potential determining factors in quality of life, life course and work productivity A cross-sectional study in young adults with psoriasis: potential determining f'. doi: 10.1080/09546634.2018.1506077.

Daudén, E. *et al.* (2013) 'Demographic characteristics and health-related quality of life of patients with moderate-to-severe psoriasis: The VACAP study', *Actas Dermo-Sifiliográficas (English Edition)*, 104(9), pp. 807–814. doi: 10.1016/j.adengl.2013.03.008.

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Hjalte, F., Carlsson, K. S. and Schmitt-Egenolf, M. (2018) 'Sustained Psoriasis Area and Severity Index, Dermatology Life Quality Index and EuroQoL-5D response of biological treatment in psoriasis: 10 years of real-world data in the Swedish National Psoriasis Register', *British Journal of Dermatology*, 178(1), pp. 245–252. doi: 10.1111/bjd.15757.

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10.1111/CED.12841.

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Masaki, S. *et al.* (2016) 'Treatment satisfaction, willingness to pay and quality of life in Japanese patients with psoriasis'. doi: 10.1111/1346-8138.13541.

Mattila, K. *et al.* (2013) 'Influence of psoriasis on work', *European Journal of Dermatology*, 23(2), pp. 208–211. doi: 10.1684/ejd.2013.1969.

Moradi, M. *et al.* (2015) 'Health Status and Quality of Life in Patients with Psoriasis: An Iranian Cross-Sectional Survey', *Archives of Iranian Medicine*, 18(3), pp. 153–159.

Ng, C. Y. *et al.* (2015) 'SF-36 healthy survey on psoriasis quality-of-life: A study of 414 Taiwanese patients', *The Journal of Dermatology*. John Wiley & Sons, Ltd, 42(2), pp. 159–165. doi: 10.1111/1346-8138.12748.

Pearce, D. J. *et al.* (2006) 'The negative impact of psoriasis on the workplace', *Journal of Dermatological Treatment*. Taylor & Francis, 17(1), pp. 24–28. doi: 10.1080/09546630500482886.

Tang, M. M. *et al.* (2013) 'Quality of life and cost-of-illness in patients with psoriasis in Malaysia: A multicenter study', *International Journal of Dermatology*, 52(3), pp. 314–322. doi: 10.1111/j.1365-4632.2011.05340.x.

Sojević Timotijević, Z. *et al.* (no date) *ACTA DERMATOVENEROLOGICA CROATICA The Impact of Changes in Psoriasis Area and Severity Index by Body Region on Quality of Life in Patients with Psoriasis*.

Weiss, S. C. *et al.* (2002) 'Quantifying the harmful effect of psoriasis on health-related quality of life', *Journal of the American Academy of Dermatology*, 47(4), pp.

512–518. doi: 10.1067/mjd.2002.122755.

Wu, Y., Mills, D. and Bala, M. (2009) 'Impact of Psoriasis on Patients' Work and Productivity', *American Journal of Clinical Dermatology* 2009 10:6. Springer, 10(6), pp. 407–410. doi: 10.2165/11310440-000000000-00000.

Appendix 5.1: Table showing the description of CPRD data files

Table A5.1: Description of the CPRD data files

File name	Description
Practice	The practice file contains one row of data for each participating GP practice and provides all the details such as practice identifier, region of the GP, date of last data collection and the up to standard date of the data.
Patient file	This provides details of the patient such as their gender, year of birth, marital status, and index of
Staff	This contains practice staff details e.g. GP, practice nurse, administrator etc.
Consultation	Contains one row of data per consultation further leads to details of an event per patient. Details available in the consultation file include the event date, consultation type, staff ID and the duration of the consultation. Also, the date on which data was entered in the GP electronic system is captured as the system date. Events occurring as part of the consultation are linked via the consultation identifier (consid).
Clinical	This file contains medical history events in terms of the diagnosis, signs and symptoms. The data is coded using Read codes. This allows linkage with the pre-determined medical terms.
Additional clinical details file	Contains information entered in the structured data areas in the GP's software. Patients may have more than one row of data. Data in this file is linked to events in the clinical file through the additional details identifier (adid).
Therapy file	The therapy file which is a part of the events section record the type of drugs and therapies that are prescribed. The prescribed therapies are recorded using unique product codes. The quantities and number of days the treatment lasted are also indicated.
Referral	Contains referral details recorded on the GP system. These files contain information involving patient referrals to external care centres (normally

	to secondary care locations such as hospitals for inpatient or outpatient care), and include speciality and referral type.
Test	<p>Contains records of test data on the GP system. The data is coded using a Read code, chosen by the GP, which will generally identify the type of test used. The test name is identified via the entity type, a numerical code, which is determined by the test result item chosen by the GP at source.</p> <p>There are three types of test records, involving 4, 7 or 8 data fields (data1 - data8). The data must be managed according to which sort of test record it is. Data can denote either qualitative entries (for example 'Normal' or Abnormal') or quantitative entries involving a numeric value.</p>
Immunisation	Contains details of immunisation records on the GP system.

Appendix 5.2: Psoriasis CPRD Read codes

Table A5.2: Psoriasis Read codes

Med code	Read code	Read term
162	M161000	Psoriasis unspecified
172	M161z00	Psoriasis NOS
2945	M161B00	Psoriasis plantaris
3193	M161600	Guttate psoriasis
3437	14F2.00	H/O: psoriasis
3733	M16..00	Psoriasis and similar disorders
8014	M161A00	Psoriasis palmaris
11761	M16y000	Scalp psoriasis
17094	M161H00	Erythrodermic psoriasis
18755	M161400	Psoriasis discoidea
20222	M161E00	Psoriasis universalis
21104	M161100	Psoriasis annularis
21633	M161500	Psoriasis geographica
22501	M161.00	Other psoriasis
24136	M161C00	Psoriasis punctata
30210	M161F00	Psoriasis vulgaris
30272	M161200	Psoriasis circinata
30975	M16z.00	Psoriasis and similar disorders NOS
41149	M16y.00	Other psoriasis and similar disorders
42008	M161300	Psoriasis diffusa
48257	M161800	Psoriasis inveterata
60169	M161900	Psoriasis ostracea
65839	M161700	Psoriasis gyrata
66711	Myu3000	[X]Other psoriasis
93511	M161F11	Chronic large plaque psoriasis

Appendix 5.3: Description of the approach to calculate the Cambridge Multimorbidity Score

Aim: To calculate the Cambridge Multimorbidity Score using data from CPRD.

Method

The approach used to calculate the Cambridge Multimorbidity Score (CMS) was based on the methods developed by Payne et al (2020). The method was developed in a retrospective study involving modelling an association between 37 comorbidities and 3 key outcomes (primary care consultations, emergency hospital admissions and death) at 1 and 5 years while controlling for sex and age (Payne *et al.*, 2020). The models were developed using a sample of 300,000 and validated on 150,000 adults aged at least 20 years old (Payne *et al.*, 2020). Payne et al. (2020) used data from 148 GP practices in the UK that contributed data to the CPRD linked to HES and ONS registered on 1 January 2012. Comorbidities were defined based on relevant Read codes or prescriptions before the index date of the relevant chronic condition. National statistics data and HES were used to determine mortality and emergency hospital admissions (Payne *et al.*, 2020). One separate statistical model was built for each outcome resulting in three outcome-specific models (Zero-inflated negative binomial for GP consultations, and Cox regression for Mortality and emergency hospitalisation). Average standardised weights for the three models were then used to construct a general-outcome multimorbidity score (Payne *et al.*, 2020). The general-outcome score model showed a similar performance to the outcome-specific models. The predictors in the model were reduced from 37 to 20. The 20-condition model was developed to generate simplified primary scores based on the most important 20 conditions. The performance of the model with 20 conditions was compared to the 37 conditions one and found to have a similar predictor performance (Payne *et al.*, 2020). Full details of the development and validation of the CMS are published elsewhere (Payne *et al.*, 2020).

The CPRD dataset was used in this thesis to estimate the Cambridge multimorbidity score based on the 20 comorbidities identified by Payne et al., (2020), see Table A5.3

(Payne *et al.*, 2020). The data covered the period from 01 April 2007 to 31 December 2017. The CMS approach involved three steps:-

- Define comorbidities based on medical codes (Medcodes), product codes (prodcode), or entity type (enttype) from CPRD according to a list of 20 comorbidities.
- Identify the defined chronic conditions.
- Calculate the CMS at patient level using the 20 conditions by attaching weights.

Defining Disease status and identifying chronic conditions

In the first instance, the disease status was defined based on information from medical codes (medcodes), product codes (prodcodes) and entity type (enttype).

To implement the disease criteria using prodcodes, the therapy file was first merged with the patient list. This ensured that all patients were included. The codelist containing the 20 conditions, see Table A5.3 was then merged with the merged therapy-patient file. Only product codes which were part of the codelist were retained in the final dataset. The product codes were associated with the conditions by merging with files containing each of the codes. The conditions based on product codes were anxiety and other neurotic, stress-related and somatic disorders. For anxiety or other neurotic disorders, the condition was identified based on the read code in the last 12 months or at least 4 anxiolytic/hypnotic prescriptions in the last 12 months. This was also similar for depression, irritable bowel syndrome, and eczema. Asthma and epilepsy were identified based on the existence of a Read code or prescription in the last 12 months. In addition, migraine and other painful conditions were identified based on at least 4 prescriptions of either analgesics or anti-epileptics in the last 12 months. Kidney disease was identified based on the enttype. The rest of the conditions were based on the Read code ever recorded during the study period. Finally, a multimorbidity matrix was created in the first instance.

Calculate the CMS using established weights

The multimorbidity matrix generated in the previous step contained all the multiple-long term conditions identified from the Read codes, medical codes and product codes in CPRD. Different weights are available for the consultations, A&E, mortality and

general CMS, see Table A5.3. The CMS was calculated for each of the sections.

However, only the general CMS was used in the regression in chapter 5.

Table A5.3: Prevalence and weights for the 20 conditions in the Cambridge Multimorbidity score

	Prevalence	Weight for consultations	Weight for mortality	Weight for emergency admissions	General-outcome weight
Hypertension	19.24	0.66	-2.09	10.76	0.08
Anxiety/Depression	12.85	2.12	7.04	46.61	0.50
Painful condition	11.63	3.43	16.46	84.93	0.92
Hearing loss	11.27	1.04	-3.94	8.93	0.09
Irritable bowel syndrome	7.61	1.82	-1.33	8.55	0.21
Asthma	7.20	1.32	-2.73	22.78	0.19
Diabetes	6.58	3.77	10.23	55.33	0.75
Coronary heart disease	4.79	1.49	4.22	70.87	0.49
Chronic kidney disease	4.50	0.98	16.61	52.13	0.53
Atrial fibrillation	2.72	5.94	22.14	105.21	1.34
Constipation	2.67	3.42	35.42	72.73	1.12
Stroke & TIA	2.55	1.54	20.63	90.84	0.80
COPD	2.46	3.43	42.50	134.51	1.46
Connective tissue disorder	2.33	3.10	-0.39	28.87	0.43
Cancer	2.15	2.58	62.00	104.80	1.53
Alcohol problems	1.60	0.97	12.72	93.59	0.65
Heart failure	1.04	2.90	43.47	73.20	1.18
Dementia	1.02	1.81	124.42	156.90	2.50
Psychosis/bipolar disorder	0.98	2.24	7.20	77.28	0.64
Epilepsy	0.97	2.13	18.26	113.42	0.92

Results

The mean CMS scaled per 1000 person-years was found to be higher in the psoriasis group compared to controls. The mean CMS for GP consultation in the psoriasis group was 2.21 compared to 1.61 in the control group. This means people with psoriasis had on average about 3 consultations per person year associated with their co-occurring conditions. Similarly, people with psoriasis had about 50 emergency admissions and 9 deaths per 1000 person-years as compared to controls with 37 and 6 respectively. The general CMS was 0.5 in the psoriasis group and 0.4 in the control group.

Appendix 5.4: Description of the approach to impute missing BMI data from CPRD

Aim: To impute missing BMI data from CPRD.

Methods

The imputation method of missing BMI data was based on the `mibmi` stata command, a multiple imputation and data cleaning command (Kontopantelis *et al.*, 2017). The `mibmi` command is useful for imputation of BMI in longitudinal data sets (Kontopantelis *et al.*, 2017). The command can also be used for other longitudinal data that has very individual-level variability. Two data cleaning options, standard and regression-based, are also included in the `mibmi` command.

The missingness in both the control and psoriasis cases was estimated at 70%. In this study, only the standard cleaning option was used as a supplement to the manual option. The standard cleaning approach limits values to a logical range (Kontopantelis *et al.*, 2017). The `mibmi` command was then used to impute the missing BMI. The command requires that at least two observations for an individual are available to be able to impute the missing values. Multiple imputation of missing data between observations, referred to as interpolation, is the main feature of the command (Kontopantelis *et al.*, 2017). For instance, where individual observations are available for the year 2007 and 2014, interpolation imputes observation for all the years in between. The available observations are first used to quantify the error in prediction using the `ipolate` command (Kontopantelis *et al.*, 2017). An assumption of missing observations was made for each possible distance between time points. The extrapolation was then done to impute missing values beyond the available observations within the study period. Within the `mibmi` command, the `ipolate` or `regress` commands are used to extrapolate missing values for an individuals. For example, individuals with observations in the first three years will have data for the remaining 7 years extrapolated.

Results

Following the multiple imputation, the missing was reduced to 39% in the control group and 35% in the psoriasis cases group. The proportion of BMI categories for the psoriasis and control groups are summarised in Table A5. 4. The mean BMI in the

psoriasis group was found to be slightly higher than the control group (28.6 vs 27.8). In addition, the proportion of obese and severely obese individuals was found to be higher in the psoriasis group than in the control group, see Table A5. 4.

Table A5. 4: BMI characteristics for the study cohort

	Control group	Psoriasis	Total
BMI ranges	n=318,132	n=54,817	n=372,949
Underweight (<18.5)	3,192 (1.6%)	517 (1.4%)	3,709 (1.6%)
normal weight (18.5-25)	65,163 (32.4%)	10,276 (28.6%)	75,439 (32.3%)
Overweight (26-29)	75,586 (37.6%)	12,751 (35.5%)	85,337 (36.5%)
Obese (30-39)	49,865 (24.8%)	10,692 (29.7%)	60,557 (25.9%)
Severely obese (>40)	7,044 (3.5%)	1,720 (4.8%)	8,764 (3.7%)
MISSING	120,282 (37.8%)	18,861 (34.4%)	13,9143 (37.3%)

Appendix 5.5: Regression outputs

Table A5.5: Total Cost model building regression results

Total	IRR	IRR	IRR	IRR
Psoriasis	1.632***	1.396***	1.42***	1.401***
Female	1.239***	0.998	0.997	0.999
18-27	1.029	0.789***	0.789***	0.79***
28-37	1.108***	0.773***	0.773***	0.773***
38-47	0.652***	0.809***	0.808***	0.808***
58-67	2.413***	1.33***	1.33***	1.333***
68-77	3.403***	1.589***	1.589***	1.59***
Over 77	4.521***	1.801***	1.8***	1.787***
Female x 18-27	0.992	1.243***	1.244***	1.245***
Female x 28-37	1.033	1.33***	1.33***	1.33***
Female x 38-47	1.207***	1.096***	1.097***	1.097***
Female x 58-57	0.733***	0.881***	0.881***	0.88***
Female x 68-77	0.753***	0.917***	0.917***	0.916***
Female x 77 plus	0.718***	0.884***	0.885***	0.885***
1 yr post index	1.949***	1.926***	1.926***	1.926***
2 yr post index	2.138***	2.019***	2.019***	2.019***
3 yr post index	2.349***	2.125***	2.124***	2.124***
4 yr post index	2.5***	2.152***	2.152***	2.151***
5 yr post index	2.555***	2.08***	2.08***	2.079***
6 yr post index	1.995***	1.618***	1.619***	1.618***
<18.5		1.349***	1.323***	1.424***
26-29.9		1.031***	1.034***	1.061***
30-40		1.149***	1.156***	1.214***
40+		1.355***	1.356***	1.396***
Multi_morb		1.714***	1.714***	1.808***

IMD 1		0.983	0.983	0.983
IMD 2		1.001	1.001	1.001
IMD 3		1.003	1.002	1.003
IMD 4		1.009	1.009	1.008
IMD 6		1.021	1.021	1.02
IMD 7		1.019	1.019	1.018
IMD 8		1.005	1.005	1.004
IMD 9		1.019	1.019	1.018
IMD 10		1.013	1.013	1.013
Psoriasis*MM		0.921***	0.922***	0.931***
Psoriasis*BMI			1.126	1.213
1				
Psoriasis*BMI			0.976	0.983
3				
Psoriasis*BMI			0.965	0.977
4				
Psoriasis*BMI			0.992	1.076
5				
BMI 1 * MM				0.875***
BMI 3 * MM				0.946***
BMI 4 * MM				0.91***
BMI 5 * MM				0.94***
Psoriasis*BMI				0.937
2 *MM				
Psoriasis*BMI				1
3 *MM				
Psoriasis*BMI				1
4 *MM				
Psoriasis*BMI				0.917**
5 *MM				
Constant	231.46***	270.815***	270.201***	263.814***
Inalpha	1.203	0.828	0.828	0.828
Number of obs	1108821	688250	688250	688250
Akaike crit. (AIC)	14765048.84	10116969.89	10116956.77	10116682.17
Bayesian crit. (BIC)	14765311.06	10117393.24	10117425.89	10117242.82

A comparison of health care resource use and costs for the first 6 years of the study period was shown. The mean health care resource use and costs were observed to be higher in the psoriasis group compared to the control. For instance, the psoriasis group had higher primary care costs £408.20 [SD=633.70] than the control group £276.30 [SD=559.30] giving a mean difference of £131.90 (SE=1.52). A similar pattern was observed in secondary care costs which were higher in the psoriasis group, £551.00 [SD=1,896], compared to the control group, £351.40 [SD=1,385.70].

Although the number of hospital admissions in the first 6 years of study were almost similar between the psoriasis group, 0.22 [1.20], and the control group, 0.16 [1.30], the duration of admissions were longer in the psoriasis group, 0.53 [4.6], compared to the control group 0.29 [3.5]. This resulted in higher inpatient costs in the psoriasis group, £356.00 [1,687.80] compared to the control group, £227.20 [1,225.90].

Table A5. 6: Health care resource use summary statistics for the first 6 years of study

	Means [SD]		Mean difference (SE)
	Psoriasis	Control	Psoriasis-Controls
	(1)	(2)	(3)
GP visits	10.6 [13.0]	7.6 [10.7]	3 (0.30)
GP costs	£ 186.2 [253.4]	£129.20 [206.70]	£ 57.1 (0.57)
Prescription costs	£ 221.9 [485.90]	£ 147.20 [449.30]	£ 74.70 (1.21)
Total primary costs	£ 408.20 [633.70]	£ 276.30 [559.30]	£ 131.90 (1.52)
Outpatient visits	1.9 [5]	1 [2.9]	0.9 (0.09)
Outpatient costs	£ 167.90 [426.50]	£ 104.60 [293.70]	£ 63.3 (0.85)
Hospital admissions	0.22 [1.20]	0.16 [1.30]	0.06 (0.004)
Hospital LOS	0.53 [4.6]	0.29 [3.5]	0.24 (0.01)
Inpatient costs	£ 356.0 [1687.80]	£ 227.20 [1,225.90]	£ 128.8 (3.48)
A&E visits	0.29 [1.0]	0.20 [0.7]	0.07 (0.002)
A&E costs	£ 27.10 [97.70]	£ 19.60 [69.60]	£ 7.50 (0.2)
Total secondary costs	£ 551.00 [1,896.60]	£ 351.40 [1,385.70]	£ 199.60 (3.94)
Total health care costs	£ 959.20 [2,190.4]	627.80 [1,643.20]	£331.40 (4.62)

Notes: This table reports means for health care resource use and costs. Column (1) and (2) shows the mean of the psoriasis and non-psoriasis control group. Column (3) compares means by reporting the mean difference between the two groups. Standard deviations (SD) are reported in brackets and standard errors (SE) in parenthesis.

Table A5.7: Health care resource use and costs summary statistics for the first 6 years of study

	Control					Psoriasis				
	Mean	Median	Min	Max	SD	Mean	Median	Min	Max	SD
Primary care costs										
Total GP visits	7.6	4	0	838	10.7	10.6	6	0	403	13
GP consultation cost	£ 129.20	£ 54.40	£0	£ 7,709.80	£ 206.70	£ 186.20	£ 100.30	£0	£ 7,229.50	£ 253.40
Prescription Cost	£ 147.20	£ 14.40	£0	£ 59,239.60	£ 449.30	£ 221.90	£ 64.60	£0	£ 18,485.00	£ 485.90
Total primary care costs	276.3	94.7	0	59722.7	559.3	408.2	199.4	0	19379.1	633.7
Secondary care costs										
Outpatient visits year	1	0	0	568	2.9	1.9	0	0	570	5
Outpatient costs total	£ 104.60	£0	£0	£ 46,043.20	£ 293.70	£ 167.90	£0	£0	£ 46,082.30	£ 426.50
Admissions	0.2	0	0	206	1.3	0.2	0	0	119	1.2
LOS	0.3	0	0	919	3.5	0.5	0	0	286	4.6

Admission cost	£ 227.20	£0	£0	£ 113,798.00	£ 1,225.90	£ 356.00	£0	£	£ 140,975.50	£ 1,687.80
Number of A&E visits	0.2	0	0	174	0.7	0.3	0	0	174	1
A&E costs	£ 19.60	£0	£0	£ 15,278.50	£ 69.60	£ 27.10	£0	£0	£ 15,264.90	£ 97.70
Total secondary costs	£ 351.40	£0	£0	£ 123,309.00	£ 1,385.70	£ 551.00	£0	£0	£ 141,319.00	£ 1,896.60
Total costs	£ 627.80	£ 146.00	£	£ 123,834.00	£ 1,643.20	£ 959.20	£ 305.00	£	£ 143,788.00	£ 2,190.40
			-					-		

Table A5.8: Health care resource use and costs summary statistics for the last 6 years of study

	Control					Psoriasis				
	Mean	Median	Min	Max	SD	Mean	Median	Min	Max	SD
Total GP visits	8.3	5	0	471	10.6	11.4	8	0	300	12.7
GP consultation cost	£ 142.70	£ 69.00	£ -	£ 11,095.60	£ 210.70	£ 198.80	£ 115.70	£ -	£ 7,277.90	£ 252.70
Prescription Cost	£ 162.90	£ 19.90	£ -	£ 25,538.10	£ 430.80	£ 258.10	£ 77.40	£ -	£ 37,268.90	£ 612.20
Total primary care costs	£ 305.60	£ 119.80	£ -	£ 25,898.20	£ 545.40	£ 457.00	£ 237.70	£ -	£ 37,620.20	£ 742.90
Outpatient visits year	1.1	0	0	476	3	2.2	0	0	110	5.1
Outpatient costs total	£ 116.50	£ 0	£ 0	£ 53,926.90	£ 309.10	£ 189.70	£ 0	£ 0	£ 15,072.80	£ 416.90
Admissions	0.2	0	0	160	1.1	0.3	0	0	161	1.4
LOS	0.3	0	0	596	3	0.5	0	0	224	4
Admission cost	£ 264.70	£ 0	£ 0	£ 192,619.90	£ 1,268.20	£ 364.60	£ 0	£ 0	£ 53,522.00	£ 1,538.30
Number of A&E visits	0.2	0	0	76	0.6	0.3	0	0	60	0.8
A&E costs	£ 20.30	£ 0	£ 0	£ 6,422.40	£ 67.40	£ 25.90	£ 0	£ 0	£ 4,825.10	£ 81.30

Total secondary costs	£ 401.50	£ 0	£ 0	£ 192,620.00	£ 1,435.60	£ 580.20	£ 0	£ 0	£ 55,659.00	£ 1,751.10
Total costs	£ 707.10	£ 189.00	£ 0	£ 192,771.00	£ 1,682.80	£ 1,037.10	£ 377.00	£ 0	£ 57,198.00	£ 2,099.00

Table A5.9: Health care resource use and costs for the full study period 2007-2017

	Control					Psoriasis				
	Mean	Median	Min	Max	SD	Mean	Median	Min	Max	SD
Total GP visits	7.9	4	0	838	10.6	10.9	7	0	403	12.9
GP consultation cost	£ 135.70	£ 61.30	£ 0	£ 11,095.60	£ 208.80	£ 191.40	£ 106.50	£ 0	£ 7,277.90	£ 253.20
Prescription Cost	£ 154.70	£ 17.00	£ 0	£ 59,239.60	£ 440.60	£ 236.90	£ 71.30	£ 0	£ 37,268.90	£ 541.90
Total primary care costs	£ 290.40	£ 106.30	£ 0	£ 59,722.70	£ 552.90	£ 428.30	£ 214.90	£ 0	£ 37,620.20	£ 681.30
Outpatient visits year	1.1	0	0	568	2.9	2	0	0	570	5
Outpatient costs total	£ 110.30	£ 0	£ 0	£ 53,926.90	£ 301.30	£ 176.90	£ 0	£ 0	£ 46,082.30	£ 422.70
Admissions	0.2	0	0	206	1.2	0.2	0	0	161	1.3
LOS	0.3	0	0	919	3.2	0.5	0	0	286	4.4
Admission cost	£ 245.20	£ 0	£ 0	£ 192,619.90	£ 1,246.50	£ 359.50	£ 0	£ 0	£ 140,975.50	£ 1,627.70
Number of A&E visits	0.2	0	0	174	0.7	0.3	0	0	174	0.9
A&E costs	20	0	0	15278.5	68.5	26.6	0	0	15264.9	91.3
Total secondary costs	£ 375.50	£ 0	£ 0	£ 192,620.00	£ 1,410.10	£ 563.00	£ 0	£ 0	£ 141,319.00	£ 1,838.00

Total costs	£ 665.90	£ 166.00	£ 0	£ 192,771.00	£ 1,662.80	£ 991.40	£ 333.00	£ 0	£ 143,788.00	£ 2,153.50
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Appendix 6.1: Burden-of-disease survey questionnaire


Start

Understanding the impact of living with psoriasis

A survey about how psoriasis affects your health and wellbeing.
Please click next below to continue to the survey.

Next


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Q58

Understanding the impact of living with psoriasis

This survey aims to understand how living with psoriasis may affect your health and wellbeing. In this survey, you will be asked questions relating to your psoriasis.

Any adult living with psoriasis in the UK can take part in this survey.

Please answer all the questions to the best of your knowledge based on your personal experience of living with psoriasis. Most questions can be answered by clicking on the relevant answer. Sometimes you have to write a number in a box or tell us your views. There are no right or wrong answers; we are just interested in hearing about your views.

This survey will take you about 15 minutes to complete.

- Part 1: Should I complete this survey?**
- Part 2: Measuring health**
- Part 3: Measuring wellbeing**
- Part 4: About your psoriasis**
- Part 5: About your psoriasis medication**
- Part 6: Living with other conditions**
- Part 7: Your psoriasis and work**
- Part 8: About you**
- Part 9: Feedback**

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Q3

What to do before you start the survey

Before starting the survey you need to understand what is being asked and decide whether you are happy to take part in.

You are being invited to take part in a research study that aims to understand how living with psoriasis impacts on an individual's quality of life and wellbeing. It is important for you to understand why the research is being conducted and what it will involve.

Please click [here](#) for the full information sheet for this study.

**I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving a reason by exiting the survey.
I confirm that I have read the information sheet.**

Q3=1 Yes, I would like to participate in this study.

Q3=2 No, I do not want to participate.

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Q1

Part 1: Should I complete this survey?

Please confirm that you are aged 18 years or above.

Are you 18 years or over? *Please select one option only*

Q1=1 Yes

Q1=2 No

Q2

Has a doctor diagnosed you as having psoriasis? *Please select one option only*

Q2=1 Yes,

Q2=2 No, but I think I might have psoriasis

Q2=3 No, I do not have psoriasis.

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Next

0%  100%



Q59

Part 2: Your Health

This section will ask you about your general health today with regards to psoriasis.

Click next to continue

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Next

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Q4

Part 2: Your Health

Please select the ONE option that best describes your health TODAY

Mobility

Q4=1 I have **no** problems walking about

Q4=2 I have **slight** problems in walking about

Q4=3 I have **moderate** problems in walking about

Q4=4 I have **severe** problems in walking about

Q4=5 I am **unable** to walk about

Back Next



Q5

Part 2: Your Health

Please select the ONE option that best describes your health TODAY

Self-Care

- Q5=1 I have **no** problems with washing or dressing myself
- Q5=2 I have **slight** problems with washing or dressing myself
- Q5=3 I have **moderate** problems with washing or dressing myself
- Q5=4 I have **severe** problems with washing or dressing myself
- Q5=5 I am **unable** to wash or dress myself

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Q6

Part 2: Your Health

Please select the ONE option that best describes your health TODAY

Usual Activities (e.g. work, study, housework, family or leisure activities)

- Q6=1 I have **no** problems doing my usual activities
- Q6=2 I have **slight** problems doing my usual activities
- Q6=3 I have **moderate** problems doing my usual activities
- Q6=4 I have **severe** problems doing my usual activities
- Q6=5 I am **unable** to do my usual activities

Back

Next

0%  100%



Q7

Part 2: Your Health

Please select the ONE option that best describes your health TODAY

Pain and/or Discomfort

- Q7=1 I have **no** pain or discomfort
- Q7=2 I have **slight** pain and discomfort
- Q7=3 I have **moderate** pain and discomfort
- Q7=4 I have **severe** pain or discomfort
- Q7=5 I have **extreme** pain or discomfort

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Next

0%  100%



Q8

Part 2: Your Health

Please select the ONE option that best describes your health TODAY

Anxiety and/or Depression

Q8=1 I am **not** anxious or depressed

Q8=2 I am **slightly** anxious or depressed

Q8=3 I am **moderately** anxious or depressed

Q8=4 I am **severely** anxious or depressed

Q8=5 I am **extremely** anxious or depressed

Back

Next

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Q9

Part 2: Your health

We would like to know how good or bad your health is TODAY

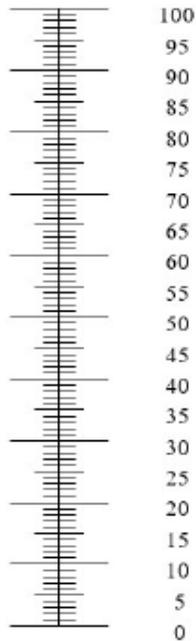
You will see a scale numbered from 0 to 100.

100 means the best health you can imagine

0 means the worst health you can imagine

State a number from 0 to 100 that indicates how your health is TODAY in the box below

The best health you
can imagine



The worst health
you can imagine

Your health TODAY

Back

Next



Q60

Part 3: Your Wellbeing

This section will ask you about your wellbeing today with regards to psoriasis.

Click next to continue

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Next

0%  100%



Q10

Part 3: Your wellbeing

Please indicate which statement best describes your overall quality of life at the moment by selecting ONE option.

Feeling settled and secure

- Q10=1 I am able to feel settled and secure in **all** areas of my life
- Q10=2 I am able to feel settled and secure in **many** areas of my life
- Q10=3 I am able to feel settled and secure in **a few** areas of my life
- Q10=4 I am unable to feel settled and secure in **any** areas of my life

Back

Next

0%  100%



Q11

Part 3: Your wellbeing

Please indicate which statement best describes your overall quality of life at the moment by selecting ONE option.

Love, friendship and support

Q11=1 I can have **a lot** of love, friendship and support

Q11=2 I can have **quite a lot** of love, friendship and support

Q11=3 I can have **a little** love, friendship and support

Q11=4 I **cannot** have **any** love, friendship and support

Back

Next

0%  100%



Q12

Part 3: Your wellbeing

Please indicate which statement best describes your overall quality of life at the moment by selecting ONE option.

Being Independent

Q12=1 I am able to be **completely** independent

Q12=2 I am able to be independent in **many** things

Q12=3 I am able to be independent in a **few** things

Q12=4 I am **unable** to be at all independent

Back

Next

0%  100%



Q13

Part 3: Your wellbeing

Please indicate which statement best describes your overall quality of life at the moment by selecting ONE option.

Achievement and progress

Q13=1 I can achieve and progress in **all** aspects of my life

Q13=2 I can achieve and progress in **many** aspects of my life

Q13=3 I can achieve and progress in **a few** aspects of my life

Q13=4 I **cannot** achieve and progress in **any** aspects of my life

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0%  100%



Q14

Part 3: Your wellbeing

Please indicate which statement best describes your overall quality of life at the moment by selecting ONE option.

Enjoyment and pleasure

Q14=1 I can have a lot of enjoyment and pleasure

Q14=2 I can have quite a lot of enjoyment and pleasure

Q14=3 I can have a little enjoyment and pleasure

Q14=4 I cannot have any enjoyment and pleasure

Back

Next

0%  100%



Q61

Part 4: Your Psoriasis

This section will ask about your experience of psoriasis right now.

Click next to continue

Back

Next

0%  100%



Q15

Part 4: About your psoriasis

How long have you had psoriasis?

Q15=1 Less than 1 year

Q15=2 1 to 2 years

Q15=3 3 to 5 years

Q15=4 6 to 10 years

Q15=5 More than 10 years.

Q15=6 I cannot remember.

Back

Next

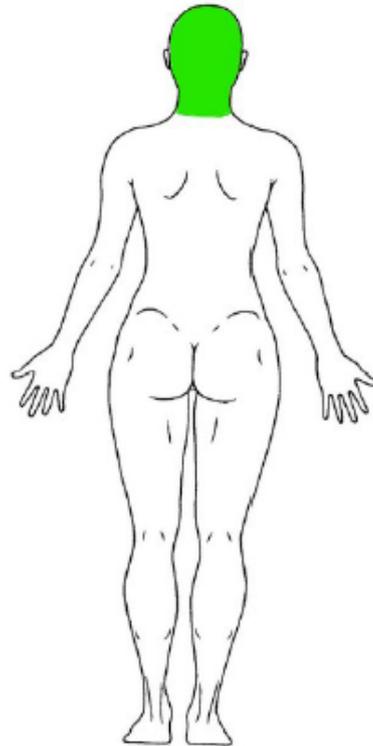
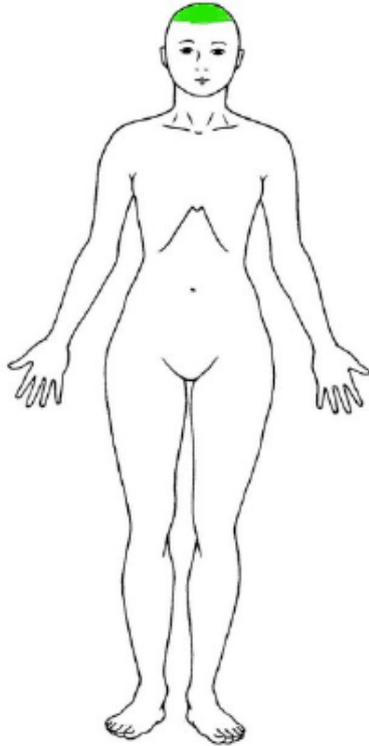


Q16

Part 4: About your psoriasis

For each part of the body indicated on the diagram, please select one choice below that best describes your psoriasis TODAY.

Scalp and hairline [green area marked]



Q16=1 Clear or so minor that it does not bother me

Q16=2 Obvious but still leaving plenty of normal skin

Q16=3 Widespread and involving much of the affected area

Back

Next

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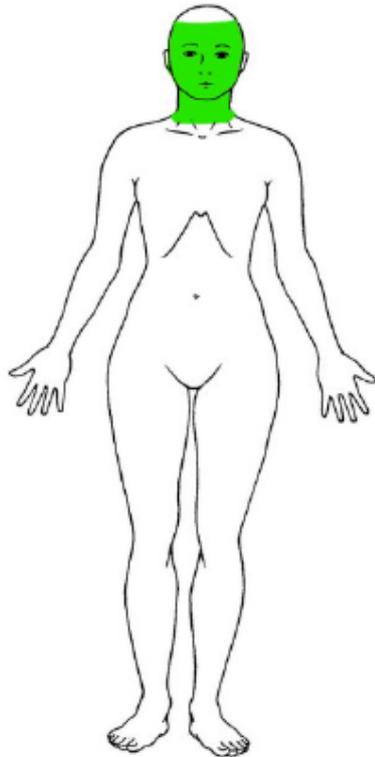


Q17

Part 4: About your psoriasis

For each part of the body indicated on the diagram, please select one choice that best describes your psoriasis TODAY.

Face, neck and ears [green area marked]



Q17=1 Clear or so minor that it does not bother me

Q17=2 Obvious but still leaving plenty of normal skin

Q17=3 Widespread and involving much of the affected area

Back

Next

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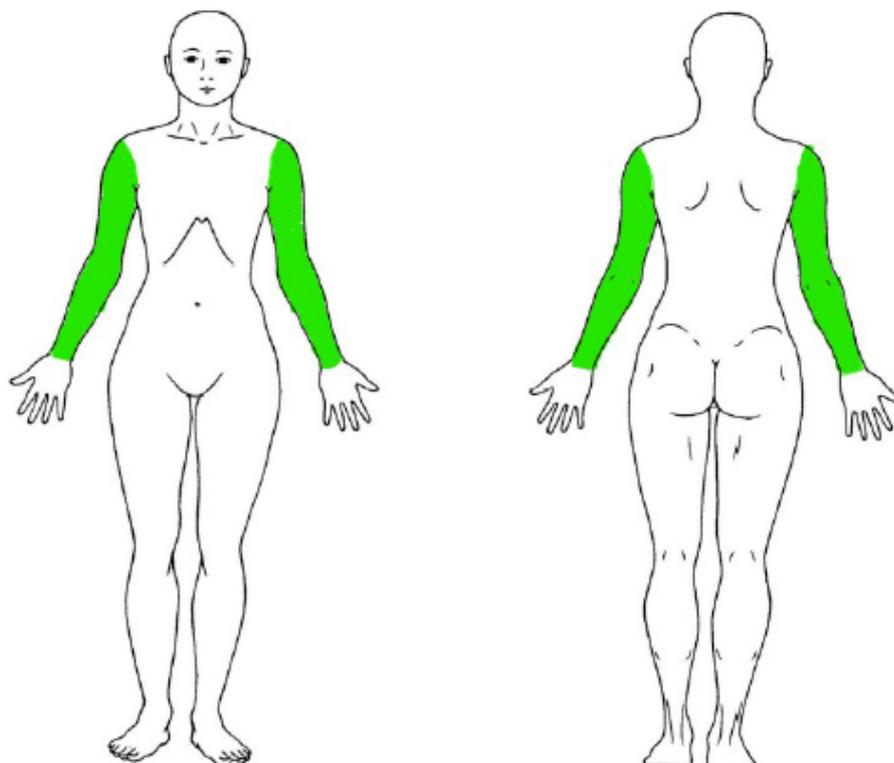


Q18

Part 4: About your psoriasis

For each part of the body indicated on the diagram, please select one choice that best describes your psoriasis TODAY.

Arms and armpits [green area marked]



Q18=1 Clear or so minor that it does not bother me

Q18=2 Obvious but still leaving plenty of normal skin

Q18=3 Widespread and involving much of the affected area

Back

Next

0%  100%



Global Psoriasis Atlas

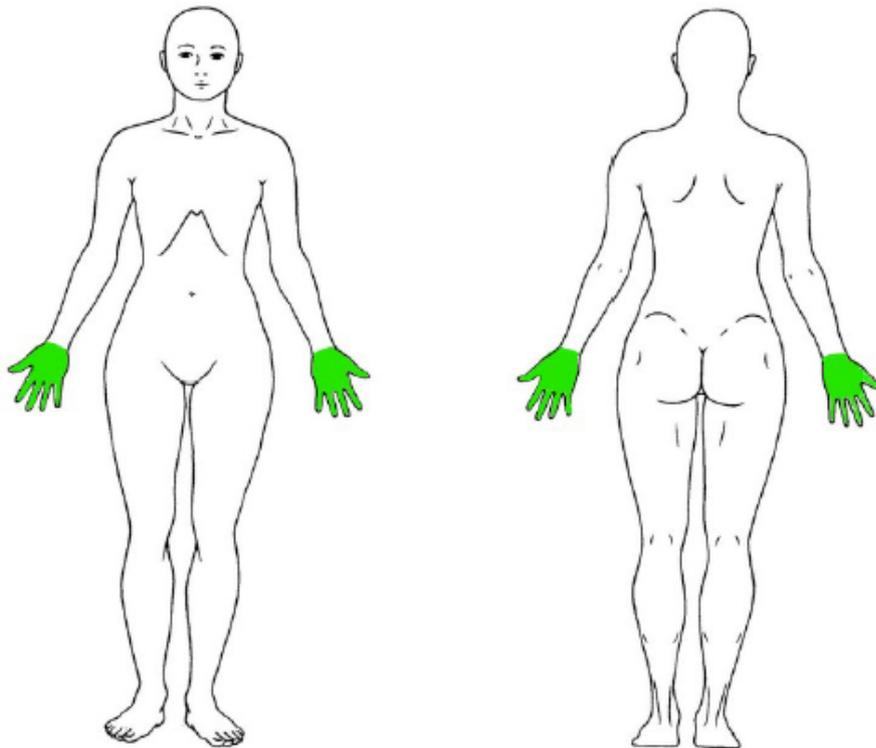
Q19

Part 4: About your psoriasis

For each part of the body indicated on the diagram, please select one choice that best describes your psoriasis TODAY.

Hands, fingers and finger nails* [green area marked]

***PSORIASIS OF THE NAILS:** even if the skin of the hands is unaffected you can score "Obvious but still leaving plenty of normal skin" for severe psoriasis of at least 2 fingers and "Widespread and involving much of the affected area" for 6 or more fingers.



Q19=1 Clear or so minor that it does not bother me



Q19=2 Obvious but still leaving plenty of normal skin



Q19=3 Widespread and involving much of the affected area



Back

Next

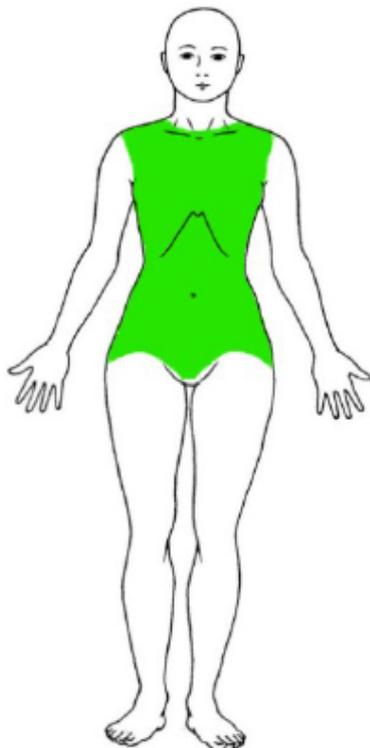
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Q20

Part 4: Your Psoriasis

For each part of the body indicated on the diagram, please select one choice that best describes your psoriasis TODAY.
Chest and abdomen [green area marked]



Q20=1 Clear or so minor that it does not bother me

Q20=2 Obvious but still leaving plenty of normal skin

Q20=3 Widespread and involving much of the affected area

Back

Next

0%  100%

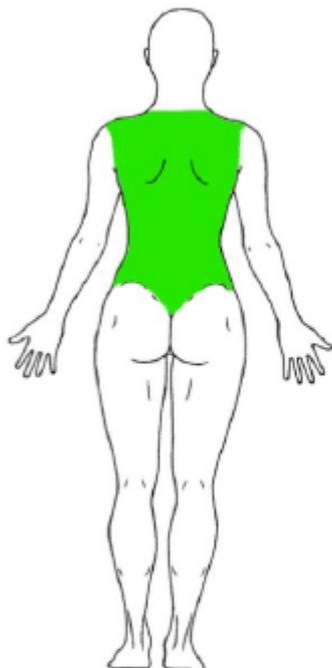


Q21

Part 4: About your Psoriasis

For each part of the body indicated on the diagram, please select one choice that best describes your psoriasis TODAY.

Back and shoulders [green area marked]



Q21=1 Clear or so minor that it does not bother me



Q21=2 Obvious but still leaving plenty of normal skin



Q21=3 Widespread and involving much of the affected area



Back

Next

0%  100%

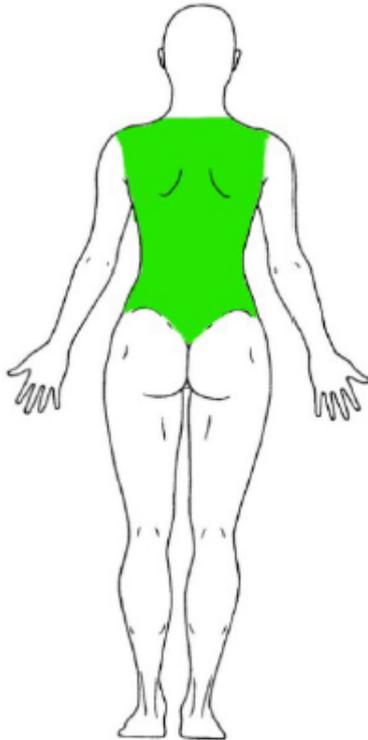


Q21

Part 4: About your Psoriasis

For each part of the body indicated on the diagram, please select one choice that best describes your psoriasis TODAY.

Back and shoulders [green area marked]



Q21=1 Clear or so minor that it does not bother me

Q21=2 Obvious but still leaving plenty of normal skin

Q21=3 Widespread and involving much of the affected area

Back

Next

0%  100%

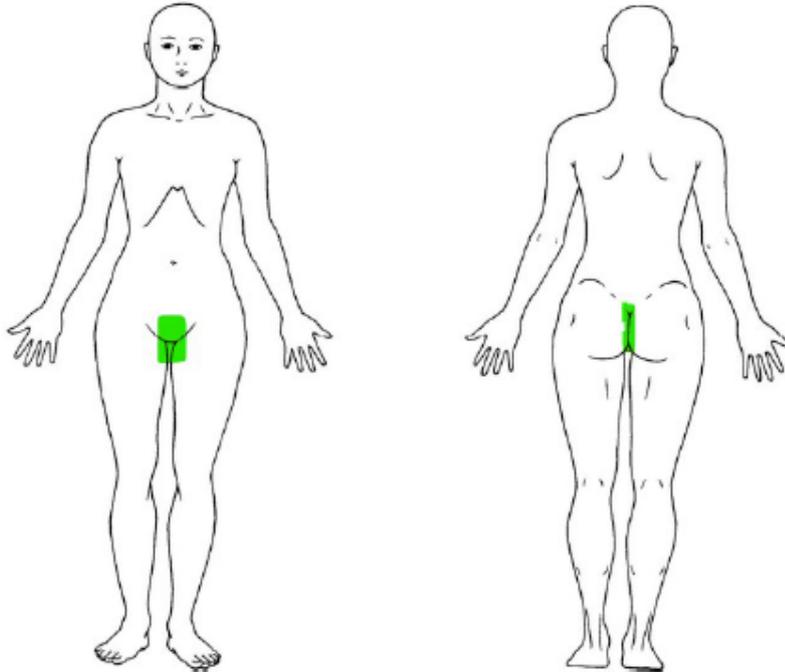


Q22

Part 4: About your psoriasis

For each part of the body indicated on the diagram, please select one choice that best describes your psoriasis TODAY.

Genital area and/or around anus (back passage) [green area marked]



Q22=1

Clear or so minor that it does not bother me

Q22=2

Obvious but still leaving plenty of normal skin

Q22=3

Widespread and involving much of the affected area

Back

Next

0%  100%

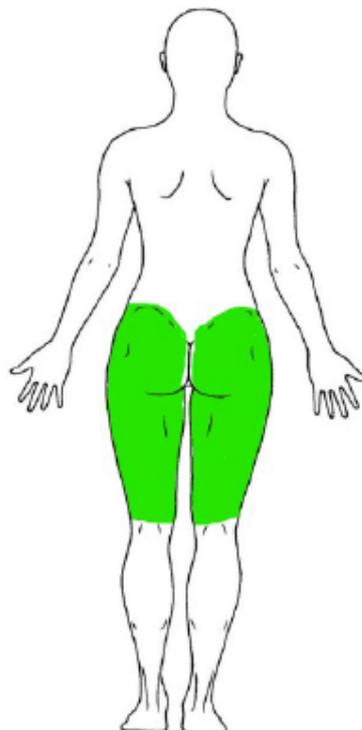
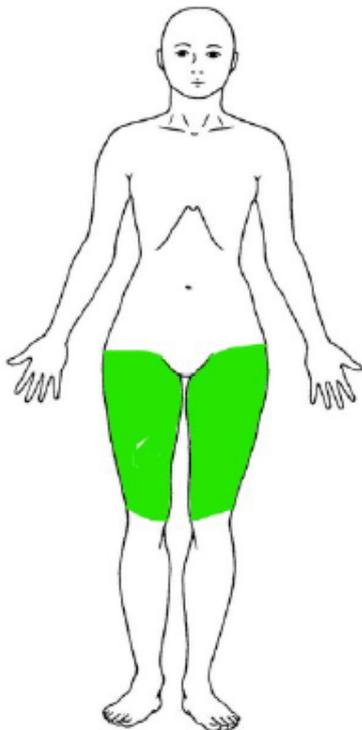


Q23

Part 4: About your psoriasis

For each part of the body indicated on the diagram, please select one choice that best describes your psoriasis TODAY.

Buttocks and thighs [green area marked]



Q23=1 Clear or so minor that it does not bother me

Q23=2 Obvious but still leaving plenty of normal skin

Q23=3 Widespread and involving much of the affected area

Back

Next

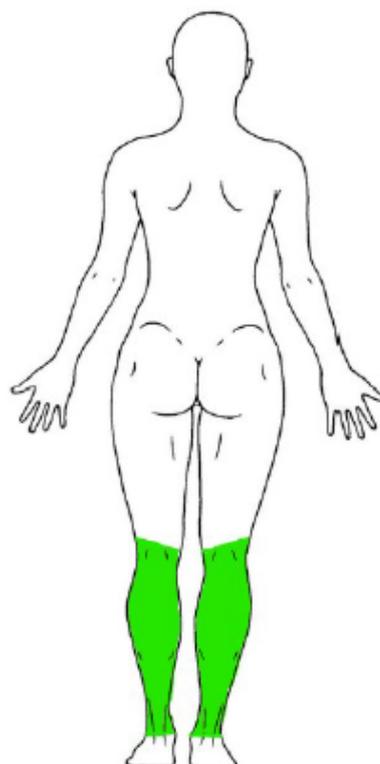
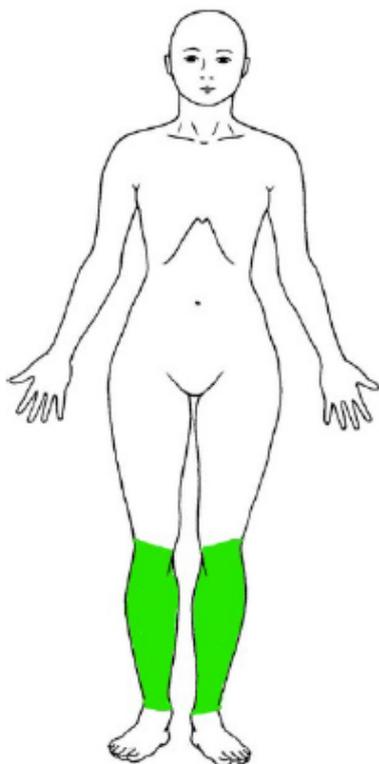


Q24

Part 4: About your psoriasis

For each part of the body indicated on the diagram, please select one choice that best describes your psoriasis TODAY.

Knees, lower legs and ankles [green area marked]



Q24=1

Clear or so minor that it does not bother me

Q24=2

Obvious but still leaving plenty of normal skin

Q24=3

Widespread and involving much of the affected area

Back

Next

0%  100%



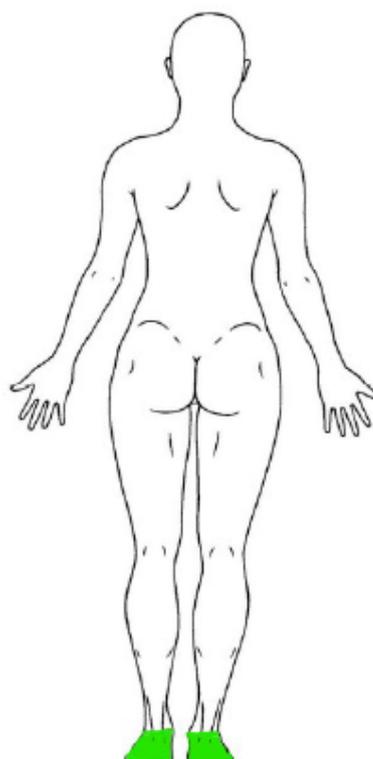
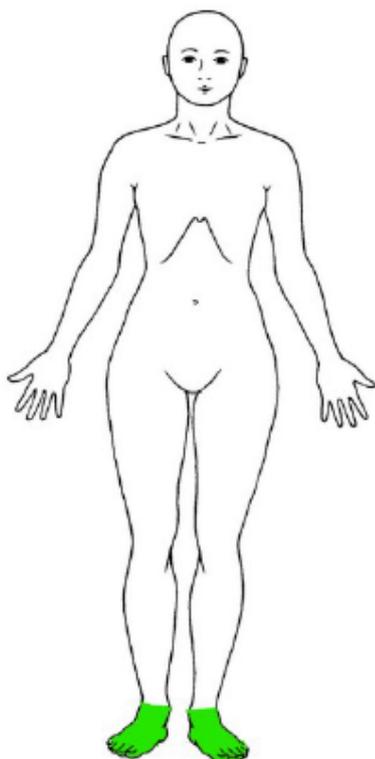
Q25

Part 4: About your psoriasis

For each part of the body indicated on the diagram, please select one choice that best describes your psoriasis TODAY.

Feet, toes, toenails* [green area marked]

**Even if the skin of the feet is unaffected you can score "Obvious but still leaving plenty of normal skin" for severe psoriasis of at least 2 toenails and "Widespread and involving much of the affected area" for 6 or more toenails.*



Q25=1 Clear or so minor that it does not bother me

Q25=2 Obvious but still leaving plenty of normal skin

Q25=3 Widespread and involving much of the affected area

Back

Next

0% 100%



Q26

Part 4: About your psoriasis

Please select whichever of these choices best describes the overall state of your psoriasis TODAY. Your score should reflect the average of all your psoriasis, not just the worst areas. Please select one option only.

- Q26=1 Clear or just slight redness or staining
- Q26=2 Mild redness or scaling with no more than slight thickening
- Q26=3 Definite redness, scaling, or thickening
- Q26=4 Moderately severe with obvious redness, scaling, or thickening
- Q26=5 Very red and inflamed, very scaly, or very thick
- Q26=6 Intensely inflamed skin: with or without pustulation

Back

Next

0%  100%



Q27

Part 4; About Your Psoriasis

How often have you had flare-ups of your psoriasis in the past 12 months? A flare-up means an occasion when your symptoms have worsened. Please select one option only.

Q27=1 I have had no flare-ups in the last 12 months

Q27=2 I have had one flare-up in the last 12 months.

Q27=3 I have had constant symptoms, with no relief in the last 12 months

Q27_4_other Other, please explain

Q27=4

Back

Next

0%  100%



Q28

Part 4: About your psoriasis

Are you currently experiencing a flare-up of your psoriasis?

Q28=1 Yes

Q28=2 No

Back

Next

0%  100%



Q29

Part 4: About your psoriasis

Would you like to tell us anything else about how living with psoriasis affects you?

Back

Next

0%  100%



Q62

Part 5: About your psoriasis medication

This section will ask you about the current treatment you are receiving for psoriasis.

Click next to continue

Back

Next

0%  100%



Q30

Part 5: About your psoriasis medication

Are you **currently** on any medication for your psoriasis prescribed by your doctor? This can include creams, special shampoos, tablets, and injections.

Q30=1 Yes, I am using prescribed treatment.

Q30=2 Yes, I am using both prescribed and other treatments.

Q30=3 No, but I am using other treatments not prescribed by a doctor.

Q30=4 No, I am not using any treatments.

Back

Next

0%  100%



Q31

Part 5: About your psoriasis medication.

What type of treatment has your doctor prescribed for you currently? We are only interested in treatments you are currently using. *Please select all that applies*

Q31_1 Creams, ointments, lotions or shampoos (Topical treatments)

Q31_2 Tablets or capsules (Oral treatments)

Q31_3 Injections

Q31_4 Light treatment (e.g. UV treatment)

Q31_5 Other treatment

Back

Next

0%  100%



Q32

Part 5: About your psoriasis medication

Do you think these prescribed treatment are helping with your psoriasis? *Please select one option only and explain the reason for your answer.*

Q32=1 Q32_1_other: Yes

Q32=2 Q32_2_other: No

Q32=3 Q32_3_other: I am not sure

Back Next

0% 100%



Q33

Part 5: About your psoriasis medication

Are you using other type of treatments for psoriasis not prescribed by a doctor?

Q33=1 Yes

Q33=2 No

Back Next

0% 100%



Q57

Part 5: About your psoriasis medication

Which other treatments are you using? *Select all that apply*

Q57_1 Special diet

Q57_2 Alternative treatment

Q57_3 Homeopathy treatment

Q57_4 UV exposure e.g sunbeds

Q57_5 Sun exposure

Q57_6 Snail gel

Q57_7_other Other, please specify

Q57_7

Back

Next

0%  100%



Q34

Part 5: About your psoriasis medication.

Do you think these treatment not prescribed by a doctor are helping with your psoriasis? *Please select only one option and explain your answer.*

Q34=1

Q34=2

Q34=3

Back

Next

0%  100%



Q63

Part 6: Living with other conditions

This section will ask about living with other long terms conditions other than psoriasis.

Click next to continue

Back

Next

0%  100%



Q35

Part 6: Living with other conditions

Do you have any other physical or mental health conditions or illness lasting or expected to last 12 months or more?

Q35=1 Yes

Q35=2 No

Q35=3 I do not know

Q35=4 I prefer not to say

Back

Next



Q36

Part 6: Living with other conditions

Which, if any, of the following long-term conditions do you have? Please select all applicable options.

- Q36_1 Alzheimer's disease or other cause of dementia
- Q36_2 Arthritis or ongoing problem with back or joints
- Q36_3 Blindness or partial sight
- Q36_4 Breathing condition such as asthma or Chronic obstructive pulmonary disease (COPD)
- Q36_5 Cancer (diagnosis or treatment in the last 5 years)
- Q36_6 Deafness or hearing loss
- Q36_7 Diabetes
- Q36_8 Heart condition, such as angina or atrial fibrillation
- Q36_9 High blood pressure
- Q36_10 Kidney or liver disease
- Q36_11 Mental health condition such as anxiety or depression
- Q36_12 Neurological condition, such as epilepsy or migraine
- Q36_13 Schizophrenia or bipolar disorder
- Q36_14 Stroke (which affects your day-to-day life)
- Q36_15 Ulcer or stomach diseases
- Q36_16 Q36_16_other Other long-term conditions or disability, please specify
- Q36_17 I prefer not to say

Back

Next

Q37

Part 6: Living with other conditions

Do any of these long term conditions listed in the previous question reduce your ability to carry out your day-to-day activities?

Q37-1 Yes, a lot

Q37-2 Yes, a little

Q37-3 No, not at all

Back

Next

0% 100%



Q65

Part 7: Your Psoriasis and Work

This section will ask you about how psoriasis impacts on your work.

Click next to continue

Back

Next

0% 100%



Q38

Part 7: Your Psoriasis and Work

The following questions are about your work. If you have more than one job, please report only on the job that you work the most hours at.

Which of the following best describes your current employment status? *Please select one option only.*

Q38=1 Full-time employee

Q38=2 Part-time employee

Q38=3 Self-employed

Q38=4 Retired

Q38=5 Unemployed

Q38=6 Long term sick

Q38=7 Homemaker

Q38=8 Student

Q38=9 Q38_9_other
 Other, please specify.....

Back

Next

0%  100%



Q39

Part 7: Your Psoriasis and Work

In your main job, how many hours a week (including paid and unpaid overtime) do you usually work?

Q39=1 Less than 10 hours

Q39=2 10 to 15 hours

Q39=3 16 to 20 hours

Q39=4 21 to 25 hours

Q39=5 26 to 30 hours

Q39=6 31 to 35 hours

Q39=7 36 to 40 hours

Q39=8 41 or more.

Q39=9 I do not know

Q39=10 I prefer not to say

Back

Next

0%  100%



Q40

Part 7: Your Psoriasis and Work

Which of the following best describes your work activities? *Please select only one option.*

Q40=1 Usually sit during the day and do not walk around very much

Q40=2 Stand or walk quite a lot during the day but do not often have to carry or lift things

Q40=3 Usually, lift or carry light loads, or often have to climb stairs or hills

Q40=4 Do heavy work or carry very heavy loads

Back

Next

0%  100%



Q41

Part 7: Your Psoriasis and Work

Has your psoriasis affected your ability to get a job? *Please select one option only.*

Q41=1 Yes, please explain

Q41=2 No

Q41=3 I do not know

Q41=4 I prefer not to say

Back

Next

0%  100%



Q64

Part 8: About you

This section will ask general information about you.

Click next to continue

Back

Next

0%  100%



Q42

Part 8: About you

What is your sex? Please select one option only.

Q42=1 Male

Q42=2 Female

Q42=3 Prefer not to say

Q43

Is this the same as your sex registered at birth? Please select one option only.

Q43=1 Yes

Q43=2 No

Q43=3 Prefer not to say

Q44

What is your year of birth? Please select from the drop-down menu. 2002

Q45

What is your ethnicity? Please select one option only.

Q45=1 White British/English/Welsh/Scottish/Northern Irish/Irish

Q45=2 Any other White background

Q45=3 Mixed: White and Black Caribbean/White and African/ White and Asian.

Q45=4 Any other mixed background

Q45=5 Asian: Indian/Pakistani/Bangladeshi

Q45=6 Asian: Chinese

Q45=7 Any other Asian background

Q45=8 Black: African/Caribbean

Q45=9 Any other Black background.



Q45=10 Arab



Q45=11 Any other ethnic group



Q46

What is the highest education qualification you have? Please select one option only.

Q46=1 University Education and Professional/Vocational equivalents



Q46=2 A level, vocational level 3 and equivalents



Q46=3 GCSE/O level A-C, vocational level 2 and equivalents



Q46=4 Qualifications at level 1 and below



Q46=5 Other qualifications: level unknown



Q46=6 No qualification



Q46=7 Prefer not to say.



Q47

What are the first four digits of your postcode? Eg X10 1 or XY10 1

Back

Next

0%  100%



Global Poverty Atlas

Q48

Part 8: About you

Do you currently smoke tobacco (e.g. cigarettes, pipes, cigars etc)? *Please select one option only.*

Q48=1 Yes, Daily.

Q48=2 Yes, Less than daily

Q48=3 No, Not at all

Q48=4 I prefer not to say

Back

Next

0%  100%



Q49

Part 8: About you

In the past, did you smoke tobacco (e.g. cigarettes, pipes, cigars etc)? *Please select one option only.*

Q49=1 Yes, Daily

Q49=2 Yes, Less than daily

Q49=3 No, Not at all

Q49=4 I prefer not to say

Back

Next

0%  100%



Q50

Part 8: About you

How often do you have a drink containing alcohol in a typical week? *Please select one option only.*

Q50=1 Never

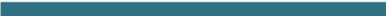
Q50=2 Once a week

Q50=3 More than once a week

Q50=4 Daily

Back

Next

0%  100%



Q66

Part 9: Your feedback

This section will ask about your general feedback on living with psoriasis and the survey.

Click next to continue

Back

Next

0%  100%



Q51

Part 9: Your feedback

The next questions allow you to share with us your thoughts about living with psoriasis and the design of the survey.

How easy was it to answer the questions in this survey? *Please select one option only.*

Q51=1

No opinion



Q51=2

Extremely easy



Q51=3

Moderately easy



Q51=4

Q51_4_other



Difficult, Please explain

Q52

Do you have any general comments you would like to make about this survey? *Please write your comment in the provided space.*

Back

Next

0%  100%



Q55

Thank you for considering to take part in the survey.

0%  100%



Q54

Thank you but you are not eligible to complete this survey.

0%  100%



Q53

Thank you for completing this survey

Should you need information and support on living with psoriasis, please visit the **website** for the Psoriasis Association at www.psoriasis-association.org.uk or contact them on
Tel: 08456 760 076 and
Email: mail@psoriasis-association.org.uk.

0%  100%



Appendix 6.2: Burden-of-disease survey patient information sheet

Understanding the impact of living with psoriasis

Participants Information Sheet

Background to the study

You are being invited to take part in a research study as part of a student PhD project based at The University of Manchester. This study aims to identify aspects of psoriasis that may affect your health and wellbeing. Before you decide whether to take part in this study, it is important for you to understand why the research is being done and what it will involve. Please take your time to read through the following information carefully and discuss with others if you wish. If you have any further questions, please do not hesitate to contact us for further information or clarification via the contact details provided in the last section of this information sheet.

About the research

Who will conduct the research?

The research will be conducted by Peslie G Ngambi, PhD student, who is based in the Manchester Centre for Health Economics at The University of Manchester. His main supervisor is Professor Katherine Payne.

What is the purpose of this research?

The study wants to understand how psoriasis impacts on people's health and wellbeing. The aim is to quantify the extent of the problem in the affected population.

Why have I been chosen?

The study aims to explore the views of people living with psoriasis in the UK. Anyone aged 18 years and over, living with psoriasis in the UK and able to complete this survey can take part.

Will the outcomes of the research be published?

The outcomes of the research will contribute towards the PhD thesis. Findings will be submitted for publication in peer-reviewed journals. Also, we may want to report the findings at national and international conferences. All responses from your participation will remain strictly anonymous.

A summary of results will be shared with the Psoriasis Association, who are at liberty to post them on their website, <https://www.psoriasis-association.org.uk/>. The global psoriasis atlas will also publish a summary on their website, <https://globalpsoriasisatlas.org/>. These websites will also contain details of any publications arising from this research. In addition, presentations will be made to relevant groups such as events organised by the psoriasis association.

Who has reviewed the research project?

Ethical approval for this study has been granted by The University of Manchester Proportionate Research Ethics Committee.

Who is funding this research?

This research is funded by Global Psoriasis Atlas and The University of Manchester.

What would my involvement be?

What would I be asked to do if I took part?

By agreeing to take part, you will be asked to complete an online survey interview designed to gather information on the impact of psoriasis on different dimensions of health and wellbeing. The survey should last around 15 minutes.

Will I be compensated for taking part?

There are no direct benefits to participants for taking part in the survey but we hope to use the information gathered in this study to improve the care received by psoriasis patients in the National Health Service (NHS).

What happens if I do not want to take part or if I change my mind?

If you decide to take part in this study you are free to withdraw yourself from the study at any time and you do not have to provide reasons for your withdrawal.

However, it will not be possible to withdraw your data after it has been made anonymous. If you decide not to take part, then please close the survey or select no when you are asked whether you consent to take part in the survey.

Data Protection and Confidentiality

What information will you collect about me?

In this study, we will not collect any information about you which would enable you to be identified. The information collected about you will relate to your psoriasis condition in terms of health and wellbeing, severity and treatment. We will also collect information on how long you have had the condition, the type of treatment you are taking, alcohol consumption and smoking status, as well as your ethnicity, area of residence, education and work status.

What happens to the data collected?

Your survey responses, along with the responses of others who have also participated in the study, will be aggregated. Your aggregated responses will be made anonymous, after which it will not be possible to remove your responses or your consent for participation in this study. Your responses will then be examined to understand the dimensions of health and wellbeing as well as the impact on your overall health and wellbeing. This data will be stored for 10 years.

Under what legal basis are you collecting this information?

We are collecting and storing this non-identifiable information in accordance with data protection law which protects your rights. These state that we must have a legal basis (specific reason) for collecting your data. For this study, the specific reason is that it is “a public interest task” and “a process necessary for research purposes”.

Will my participation in the study be confidential and my personal identifiable information be protected?

In accordance with data protection law, The University of Manchester is the Data Controller for this project. This means that we are responsible for making sure your personal information is kept secure, confidential and used only in the way you have

been told it will be used. All researchers are trained with this in mind, and your data will be looked after in the following way:

No personal information about you will be collected and none is passed to us by the Psoriasis Association UK. All other information will be collected and stored in accordance with the General Data Protection Regulation (GDPR) and Data Protection Act 2018 which legislate to protect your personal information. The legal basis upon which we are using your personal information is “public interest task” and “for research purposes” if sensitive information is collected. For more information about the way we process your personal information and comply with data protection law please see our [Privacy Notice for Research Participants](#)

Responses to the survey questions will be collected on a secure University server. When we have finished recruiting participants for this study, the information will be downloaded to a secure computer at The University of Manchester. Data will not be shared with any other institution.

Please also note that individuals from The University of Manchester or regulatory authorities may need to look at the data collected for this study to make sure the project is being carried out as planned.

What if I have a complaint?

Contact details for complaints.

If you have a complaint that you wish to direct to members of the research team, please contact:

MR PESLIE GIBSON NGAMBI, PHD STUDENT IN HEALTH ECONOMICS

Email: peslie.ngambi@manchester.ac.uk

Telephone: 0161 306 7970

What if something goes wrong?

If there are any issues regarding this research that you would prefer not to discuss with members of the research team or if you are not satisfied with the response you have gained from the researchers in the first instance then please contact: -

The Research Governance and Integrity Officer, Research Office, Christie Building, The University of Manchester, Oxford Road, Manchester, M13 9PL, by emailing: research.complaints@manchester.ac.uk or by telephoning 0161 275 2674.

If you wish to contact us about your data protection rights, please email dataprotection@manchester.ac.uk or write to **The Information Governance Office, Christie Building, The University of Manchester, Oxford Road, M13 9PL** at the University and we will guide you through the process of exercising your rights.

You also have a right to complain to the [Information Commissioner's Office about complaints relating to your personal identifiable information](#) Tel **0303 123 1113**

Contact Details

If you have any queries about the study then please contact the researcher(s)

Lead Researcher

Mr Peslie Gibson Ngambi

Manchester Centre for Health Economics

Room 4.306, Jean McFarlane Building

The University of Manchester

Oxford Road

M13 9PL

Email: peslie.ngambi@manchester.ac.uk

Supervisor

Professor Katherine Payne

Manchester Centre for Health Economics

Room 4.310, Jean McFarlane Building

The University of Manchester

Oxford Road

M13 9PL

Email: katherine.payne@manchester.ac.uk

Telephone: 07879 177 865

Support Groups and Charities Contact Details

If you are thinking of hurting yourself or someone else, get help right away. In the UK, help is also available through your GP or calling 116 123 to talk to Samaritans. Should

you need information and support on living with psoriasis, please do contact the Psoriasis Association UK on the following detail: -

Support Group / Charity	Contact Details
The Psoriasis Association	Tel: 08456 760 076 Email: mail@psoriasis-association.org.uk Website: www.psoriasis-association.org.uk

Appendix 6.3: Introductory e-mail sent out to the participants

Dear <member's name>

As a Psoriasis Association UK member, you are invited to participate in a short 15-minute survey that is being conducted by a PhD student (Peslie Ng'ambi) from The University of Manchester. This study aims to identify aspects of psoriasis that may affect your health and wellbeing.

You will be asked a few questions at the beginning to confirm that you are eligible to complete this survey.

All responses from your participation will remain strictly anonymous and will be aggregated and analysed together with responses from other members. This invitation will expire once the survey is closed and the number of responses required has been reached.

Click [here](#) to follow the link to the survey or copy this link and paste in your browser <https://ssiweb.humanities.manchester.ac.uk/PsoriasisBurden/login.html>

Thank you for your time.

Best regards,

Psoriasis Association UK.

Appendix 6.4: Other Long-term conditions reported

1. Acid Reflux
2. Acoustic nuvulsa
3. Allergies to certain fruit and vegetables
4. Autism
5. Awaiting more surgery on ankle after nerve has become trapped in metal work following ankle fusion
6. Balance problem walking
7. Bereavement
8. catarrachs
9. Colitis
10. Congenital Hemiplegia
11. crohns
12. diverticulitis
13. DVT
14. Dyslexia
15. familial hyperlipidaemia
16. Fibromyalgia
17. Endometriosis
18. Blespharitus
19. keraticonus
20. Glaucoma
21. Raynauds disease in hands & feet.
22. Gout
23. Had my Aortic valve replaced in 2019 after 10 years of aortic stenosis
24. Heart condition Syncope.
25. High cholesterol
26. Hyperthyroidism
27. IBS; hypertension
28. Lipoedema
29. Lymphoedema
30. Long covid
31. Meniere's

32. Obesity-Morbid
33. Mild Traumatic brain injury (MTBI)
34. Multiple Sclerosis
35. Obesity
36. osteoporosis
37. overactive bladder
38. Parkinson's
39. Polymyalgia Rheumatica (PMR)
40. Polycystic Ovarian Syndrome
41. prostrate
42. Psoriatic Arthritis
43. PTSD
44. sarcoidosis
45. Scoliosis
46. Severe planovalgus deformity to right foot following accident.
47. Sjögren's
48. Skin cancer
49. Spinal injury
50. stress fracture in back
51. Thyroid & autoimmune diseases
52. Tinnitus
53. Ulcerative colitis
54. Under active thyroid
55. Uveitis
56. Vitamin D deficiency
57. Vitiligo

Appendix 6.5: List of treatments

Prescribed

1. Acetretin
2. Biologics (Unspecified)
3. Cyclosporin
4. Methotrexate
5. Steroid (Unspecified)

Non-prescribed

1. Coconut oil,
2. Dead sea salt,
3. krill oil,
4. Multivitamin and food supplements,
5. Oatmeal
6. Shampoos,
7. Variety of moisturisers,
8. Vitamin D cream
9. Vitamin D tablets,

Appendix 6.6: Thematic analysis of the burden-of-disease survey free text response

Table A6- 1: Thematic Analysis of free-text comments

Theme	Number of comments	Free-text comment
<u>Physical impact on HRQoL</u>		
Bleeding/Split skin	9	<p>ID12: Thickening and splitting of soles of feet causes much pain and discomfort when trying to walk.</p> <p>ID174: socks may have a clear discharge in (admittedly, small) patches, or occasional bleeding.</p> <p>ID 224: [I] scratch till I bleed,</p> <p>ID241: Causes skin splitting at the finger tips which can be quite painful</p> <p>ID249: Bleeding without warning</p> <p>ID291: When it is really badly inflamed it often bleeds where it itches so much and it becomes unbearable.</p> <p>ID30: Draws blood when caught.</p> <p>ID314: Thickened skin and splits</p>
Burning	2	<p>ID107: little sleep due to scratching and skin feels like its burning</p> <p>ID282: The intense burn is horrific at the minute.</p>

Dry skin		ID107: In alot of discomfort with skin being so dry hurts to move or catch skin.
Flare-up	4	<p>ID11: I have only a slight flare up on elbows</p> <p>ID166: My dermatologist took me off 25mg of Methotrexate a week and then took 8 weeks to prescribe 300mg of Cosentyx a month. This lead to a flare up of both conditions.</p> <p>ID316: have had 2-4 flare ups a year for 4 years related to a sore throat which without antibiotics causes wide and fast spreading coverage and dehydration and immense pain.</p> <p>ID41: It doesn't at present affect me much, although within the last two years I've had one significant flare up which is tedious, but manageable</p>
Itching	38	<p>ID107: little sleep due to scratching</p> <p>ID110: I suffer mostly from Psoriasis in the genitals, abd find this to be very painful and itchy.</p> <p>ID142: It also causes great discomfort due to itch.</p> <p>ID145: It is the itchiness which is irritating rather than the visual signs.</p> <p>ID151: I'm not bothered so much about the appearence but it's itchy and I hate that.</p>

		<p>ID156: Itchiness in the groin area is aggravating to the extent that I take cetirizine hydrochloride (Piriton) most days</p> <p>ID167: If I am agitated about something it starts itching.</p> <p>ID185: Unattractive, itchy and embarrassed</p> <p>ID 192: Can be itchy</p> <p>ID224: Despite trying very hard not to, I end up scratching to get some relief,</p> <p>ID226: The itch can be almost unbearable.</p> <p>ID232: My psoriasis is limited to small intermittent scaly scabs and itchy areas.</p> <p>ID236: The itch on my scalp is the first thing I notice on waking.</p> <p>ID237: still need to treat and bath with emulsifiers daily if not skin gets very itchy ares that rub still affected slightly im aching quite a lot now (gettig quite old!)</p> <p>ID240: These can become very itchy often at night rising up like small blisters but only one or two places at a time, for instance on one leg, one or two sides of my thigh or the back of my hand.</p> <p>ID246: getting the itches</p>
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		<p>ID249: My itching becomes unbearable.</p> <p>ID267: I'm constantly scratching</p> <p>ID279: Constant itchiness and slight discomfort</p> <p>ID284: Itching, redness</p> <p>ID291: it itches so much and it becomes unbearable.</p> <p>ID302: it's sore & itchy.</p> <p>ID303: Constant itching is frustrating,</p> <p>ID306: I now take an antihistamine at night to help with the itch and moisturize like mad!</p> <p>ID314: For five years i lived with unalleviated pain and itching of the pustular form on the soles of my feet,</p> <p>ID318: the non-stop irritation and itching is a quiet form of torture.</p> <p>ID321: Itchy and painful,</p> <p>ID354: itching and constant flakes of skin.</p> <p>ID355: my back (completely covered down to my buttocks) itches 24-7</p>
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		<p>ID356: constant flakey skins which is itchy all of the time</p> <p>ID357: I'm constantly itching</p> <p>ID358: can be very irritating and itchy</p> <p>ID360: Constantly itching,</p> <p>ID43: Most annoying is pain from continual itch leading to scratching,</p> <p>ID63: When the skin is very itchy, Very hard not to scratch.</p> <p>ID65: I do find it annoyingly itchy which makes me scratch.</p> <p>ID91: always scratching.</p> <p>ID94: tchy scalp for last few months and not sure how best to deal with that.</p>
Pain	25	<p>ID1: the pain and discomfort warrants having to resort to oral medications</p> <p>ID107: very bad back pain and finger pain also leg pain.</p>

		<p>ID110: I suffer mostly from Psoriasis in the genitals, and find this to be very painful</p> <p>ID12: Thickening and splitting of soles of feet causes much pain and discomfort when trying to walk.</p> <p>ID125: It has been hard most of my life living with psoriasis - in the winter being worse, sore and painful.</p> <p>ID150: Occasionally a patch of psoriasis rubs somehow and is sore, but that doesn't happen often.</p> <p>ID166: I have only just got my skin back under control but cannot reduce of the Arthritis pain despite being on 400mg of Tramadol and 150mg of Diclofenac daily.</p> <p>ID174: Walking can be quite painful at times,</p> <p>ID177: DUE TO FOREFOOT PAIN SECONDARY TO Pso/Arth AND BILATERAL HALLUX RIGIDUS WITH RESTRICTION AT THE SUBTALAR JOINT AND MIDTARSAL JOINTS</p> <p>ID189: the onset of psoriatic arthritis over the past 20 years has had more impact - pain management and regular medication being necessary and having to wear special wide-fitting shoe</p>
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		<p>ID195: I have psoriatic arthritis and at time I get quite tired, or aching joints which mildly limits my activities</p> <p>ID220: it is often sore and affects sleep</p> <p>ID224: my legs end up red raw and very painful.</p> <p>ID233: Initially my psoriasis was very extreme, and painful.</p> <p>ID241: Causes skin splitting at finger tips which can be quite painful.</p> <p>ID243: Nails constantly sore and look awful</p> <p>ID249: Very painful.</p> <p>ID284: pain around my head, some days worse than others</p> <p>ID286: I am in constant pain.</p> <p>ID314: For five years i lived with unalleviated pain</p> <p>ID319: I have psoriatic arthritis, so inflammation in joints not necessarily on visible skin</p> <p>ID321: painful, I feel like the pain doesn't get discussed.</p> <p>ID322: Skin feels sore in cold damp weather</p>
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		<p>ID43: Worst problem is pain from psoriatic Arthritis, but held in check by weekly Methotrexate.</p> <p>ID44 Nail psoriasis is so painful.</p>
Scales/Thick skin	8	<p>ID12: Thickening and splitting of soles of feet causes much pain and discomfort when trying to walk.</p> <p>ID67: There is flaky skin around the house</p> <p>ID298: I am constantly aware of leaving skin flakes on seating (in cars, at work desk)</p> <p>ID324: Leave a trail of scales behind me wherever i go.</p> <p>ID325: I feel much more conscious of the 'snow' on my shoulders that it produces.</p> <p>ID351: I just shed everywhere.</p> <p>ID68: See white scales on my clothes.</p> <p>ID91: Dropping skin around the place</p>
Mental impact on HRQoL		
Anxiety	5	<p>ID256: My anxiety levels are through the roof and the thought of baring any skin throughout the summer cripples my mind.</p> <p>ID273: Very anxious about the way I look, has made my confidence decrease massively</p>

		<p>ID335: You constantly anxious especially when people point and say what is that can you not sort it.</p> <p>ID340: It affects my self-esteem and confidence and has given me anxiety.</p> <p>ID67: Anxiety about how other people perceive my psoriasis adds to my social anxiety that is part of my autism.</p>
Depression	18	<p>ID106: It can make me depressed but mostly I just get on with it</p> <p>ID110: I find it depressing</p> <p>ID22: It's depressing to look and stubborn to treat.</p> <p>ID224: Truth [is] I am quite depressed but don't want anyone to know.</p> <p>135 It makes me unhappy</p> <p>ID142: It is a constant worry that it will flare, it takes a mental toll on you.</p> <p>ID191: Living with obvious physical difference takes an enormous amount of effort and takes both a physical and emotional toll.</p> <p>ID200: makes me depressed</p>

		<p>ID217: it can be soul destroying and have a big impact on my life.</p> <p>ID230: After over 50 years of having psoriasis can be depressing at times.</p> <p>ID256: thought of baring any skin throughout the summer cripples my mind.</p> <p>ID271: You put on a thick skin to try to accomplish anything in a day, but the reality is you want to just lie down, don't move and just not exist.</p> <p>ID280: When it's bad a feeling of depression</p> <p>ID333: Making me severely depressed</p> <p>ID356: I the mean time I'm feeling more and more depressed about living with psoriasi</p> <p>ID357: I feel depressed, unhappy and to be honest a freak</p> <p>ID72: It gets me down,</p> <p>ID80: Get depressed</p>
Physical impact on wellbeing		
Appearance	16	ID13: Although my skin is clearer now than it has ever been, I still have remaining body image issues and appearance anxiety... I think I have been so conditioned into worrying about the way my skin

		<p>looks, that worry has never gone away - even though my skin has cleared!</p> <p>ID111: Covering up to hide my body.</p> <p>ID130: I feel my lags are unsightly with psoriasis</p> <p>ID139: Doesn't look very nice which affects my mental health.</p> <p>ID164: deters me from showing my body</p> <p>ID177: I SOMETIMES GET STRANGE LOOKS FROM PEOPLE AS REGARDS THE APPEARANCE OF MY NAILS</p> <p>ID180: Makes me concious of my appearance for future dating.</p> <p>ID185: It makes me feel dirty</p> <p>ID203: It looks unsightly and I have to do my hair in certain ways to mask affected areas.</p> <p>ID252: Mostly it affects me emotionally, because it's obvious</p> <p>ID282: I hate to look at myself in a mirror it terrifies me.</p> <p>ID302: It makes me feel ugly</p> <p>ID312: I don't like my affected areas to be seen</p>
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		<p>ID314: It's so damn ugly</p> <p>ID318: aesthetic impact making me self-conscious</p> <p>ID79: The facial is the most psychologically scaring</p>
Occupational	8	<p>ID14: made worse by being sat down for long periods of time at a desk-based job</p> <p>ID140: Since retiring 20 yrs ago, my symptoms have reduced ,</p> <p>ID153: I have to protect my hands with gloves when working and reduce friction wherever possible.</p> <p>ID238: I work in the NHS so I have to be "bare below the elbow" - I find exposing my arms embarrassing and understandably people do stare (yes even in the NHS!).</p> <p>ID280: Hate that everyone due to the pandemic knows about my psoriasis and methotrexate use as affects job etc.</p> <p>ID299: Career stress Geographical stress relating to jobs away from sun</p> <p>ID340: With it being on my face it is difficult to treat while maintaining a full time, customer facing role.</p>

		ID91: it was hard to live with during my working life.
Sexual intimacy	3	ID14: I also get psoriasis in my private areas ID224: Being intimate with my husband is also difficult, ID254: My relationship, my sex life.
Sleep	4	ID107: little sleep due to scratching ID220: affects sleep ID224: It stops me from sleeping ID254: Psoriasis affects what I wear, what I do, how much sleep I get and the quality.
Mental impact on wellbeing		
Distress/Upset	4	ID211: Even when it's good you are worried about flares, or treatments stopping working ID235: Living with psoriasis is such a battle and when I get a flare-up it really upsets me. ID309: As a young woman I was constantly covering it as I was embarrassed and upset ID96: Annoying but much better that it used to be
Draining/Nuisance	14	ID113: Around the ears, scalp damn nuisance ID187: IT IS A NUISANCE HAVING TO APPLY OINTMENT

		<p>ID237: i think the stellara or my psoriasis causes me to feel somewhat tired at times. this passes if i rest.</p> <p>ID266: Mentally psoriasis is very draining and very little is said about it.</p>
Embarrassed	22	<p>ID 111 Embarrassing</p> <p>ID112: the total embarrassment of leaving skin behind when you move,</p> <p>ID150: In the past I've had psoriasis on my face and neck, which I found embarrassing.</p> <p>ID154: It has on occasions been embarrassing</p> <p>ID185: embarrassed</p> <p>ID19: I am ashamed of bare legs from old scarring and staining from when my psoriasis was very severe.</p> <p>ID192: It's embarrassing.</p> <p>ID20: I feel embarrassed by my skin.</p> <p>ID230: Embarrassing to sunbathe or swim</p> <p>ID235: It becomes embarrassing and I hate the effect it has on close and personal relationships that I develop with people.</p> <p>ID257: Embarrassed.</p>

		<p>ID274: Can be embarrassing</p> <p>ID302: I'm often embarrassed by dry skin on my face, head ears.</p> <p>ID309: I have had psoriasis for 25 years. As a young woman I was constantly covering it as I was embarrassed and upset</p> <p>ID322: Embarrassed wearing short sleeves</p> <p>ID334: Embarrassed to wear shorts/t-shirts</p> <p>ID342: Embarrassing. Looks like I constantly have severe dandruff.</p> <p>ID345: Embarrassing, unable to do some everyday things</p> <p>ID347: The embarrassment when people look at my skin before me.</p> <p>ID351: I get very embarrassed about my scalp psoriasis</p> <p>ID49: It's embarrassing to keep scratching</p> <p>ID93: I was embarrassed and withdrawn.</p>
Frustration	7	ID157: After 50 years and over with this condition terrible

		<p>ID192: Frustrated when skin becomes flaky</p> <p>ID203: I am frustrated as there is very little to no effective treatment,</p> <p>ID243: Fed up of not being able to a simple thing like using someone’s toilet without leaving the floor covered in skin</p> <p>ID351 I’m about to start tablet treatment which I know can have serious side effects but I am so at the end of my tether that I’m willing to try anything.</p> <p>ID354: Also get fed up with soreness</p> <p>ID44: Fed up with asking for help to control my anxiety, as stress makes my skin worse and they just want to treat the symptoms and have no interest in the cause.</p>
<p>Low confidence/Self-esteem</p>	<p>18</p>	<p>ID112: it fades your confidence over the years,</p> <p>ID13: I really struggled in school and my confidence has always been very low.</p> <p>ID173: When not under control, affects confidence and socialising.</p> <p>ID218: very reluctant to show my body even to my wife would like to swim but have not got the confidence</p>

		<p>ID24: Prior to this psoriasis dominated my life choices and left me feeling insecure and worthless.</p> <p>ID256: I hate what it does to my body and my self confidence</p> <p>ID257: Self-confidence.</p> <p>ID262: low self-esteem to name a few things</p> <p>ID265: It affects my self-confidence,</p> <p>ID269: It affects my confidence and self-esteem massively</p> <p>ID299: Body confidence</p> <p>ID328: Affects my self esteem</p> <p>ID334: Lack of confidence</p> <p>ID337: Impacts my confidence regarding my hair</p> <p>ID338: low self esteem</p> <p>ID361: Self-confidence, self-worth</p> <p>ID4: It used to have a huge impact on self esteem</p>
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		ID58: Affects my confidence
Self-conscious	47	<p>ID1: When it is flaring up, I am more self-conscious and aware of other people's looks and stares and adjust my day to day regime to compensate.</p> <p>ID111: self-conscious of it</p> <p>ID116: It makes me very self-conscious about my body</p> <p>ID121: I am very conscious about people seeing it.</p> <p>ID123: I am always aware of it, even when people can't see it.</p> <p>ID13: I still have remaining body image issues and appearance anxiety,</p> <p>ID133: When on holiday or in the gym changing room baring one's body can make one self-conscious as people look at you.</p> <p>ID135: self conscious</p> <p>ID164: It makes me overly self conscious,</p> <p>ID180: Makes me concious of my appearance for future dating.</p>

		<p>ID185: It makes me feel dirty</p> <p>ID188: I am constantly aware that my face and ears are noticeable and creates a shyness in my behaviour</p> <p>ID19: I can't bear to have a hairdresser touch my head, so have to do everything myself.</p> <p>ID203: I am self conscious as I feel others can see the psoriasis and may not know what it is.</p> <p>ID204: It does make you self concious</p> <p>ID219: Self-conscious of it</p> <p>ID234: I feel self-conscious when undressed in front of my spouse - even after 38 years.</p> <p>ID243: Never trying clothes on before buying.</p> <p>ID249: I feel self-conscious.</p> <p>ID251: stops me from being able to wear all deodorant except one which makes me very self conscious.</p> <p>ID253: My scalp psoriasis makes me feel so self conscious,</p> <p>ID257: Uncomfortable</p>
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		<p>ID267: I'm conscious at all times that it can be seen</p> <p>ID267: I'm always thinking about it due to the discomfort on my scalp</p> <p>ID268: makes me feel extremely self conscious.</p> <p>ID274: uncomfortable when my psoriasis is exposed in public</p> <p>ID279: I am very self conscious</p> <p>ID286: I feel very uncomfortable around other people and even myself</p> <p>ID292: It makes me dread events that should be happy times, for example being invited to a wedding means I worry about what I can wear that will cover up most of my psoriasis. I also dread summer for the same reason.</p> <p>ID298: I am constantly aware of leaving skin flakes on seating (in cars, at work desk)</p> <p>ID298: Scalp psoriasis makes me very nervous when standing in queues, people looking at my shoulders and back thinking I have bad dandruff.</p> <p>ID300: It makes me self conscious</p>
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		<p>ID306: I manage my psoriasis, but am conscious of my legs as they are quite bad.</p> <p>ID318: Outside of the aesthetic impact making me self conscious,</p> <p>ID325: I feel much more conscious of the 'snow' on my shoulders that it produces</p> <p>ID339: Being conscious of what to wear, conscious of people looking. Uncomfortable.</p> <p>ID348: make me self conscious and unhappy about wearing shorter skirts or shorts.</p> <p>ID356: Living with psoriasis at the moment makes me very self conscious</p> <p>ID362: Just makes you conscious</p> <p>ID364: Self conscious</p> <p>ID44: It makes me self conscious.</p> <p>ID63: makes me very conscious</p> <p>ID7: People tend to talk looking at your psoriasis</p> <p>ID76: sometimes just looking in the mirror in the morning to see that you look normal to people around you (by which i mean no strange looking thing more so face has happen over night)</p>
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		<p>ID82: Need to cover arms and legs as self conscuous</p> <p>ID87: I am always conscious of my skin (this started when I was on holiday and somebody pointed at me, staring at my poorly legs).</p> <p>ID88: During the summer I am reluctant to wear short when meeting people outside my own garden such as golf, meeting friends or on holiday</p> <p>ID91: People would look at your scales and not your face.</p> <p>ID97: Sometimes self conscious.</p>
Suicidal	1	ID276: want to kill myself.
Impact of severe disease on the Individual		
Adapted	26	<p>ID106: mostly I just get on with it</p> <p>ID112: It has been a part of my life since my early twenties, I am now in my late fifties; hence I have had to adapt so many things, that I sometimes forget how great the impact it has been on my life until I stop and reflect.</p> <p>ID114: I have become used to living with mild outbreaks, but this one is the worst.</p>

		<p>ID13: I am now 25 and I've only just come to terms with my psoriasis, and just about feel comfortable talking about it!</p> <p>ID136: I have had it so long I have learnt to live with it</p> <p>ID140: Since retiring 20 yrs ago, my symptoms have reduced , and I have learned to cope with the symptoms with good support from my doctor and consultants (in past)</p> <p>ID155: Has been much worse in the past but even at it's worst I've coped fine with it.</p> <p>ID177: BUT MY ARTHRITIS IS OF A SEVERE FORM! BUT HAVE LIVED WITH THE CONDITION FOR MANY YEARS AND HAVE NO ISSUES OF NEGATIVITY OR EMBARRASSMENT ABOUT WHAT OTHERS MAY THINK</p> <p>ID187: IT IS A NUISANCE HAVING TO APPLY OINTMENT BUT AFTER 70 YEARS IT BECOMES PART OF DAILY LIFE !!</p> <p>ID189: Having had psoriasis for 65 years I am largely inured to its effects - no longer bothered by appearance as I was in my teens and twenties!</p>
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		<p>ID196: Now I have no problems at all, I play golf with a golf society we have weekends away and weeks abroad sharing rooms I go away with my wife we go on the beach and at the pool side in swimming costumes, I see other people with psoriasis doing exactly the same thing it seems more acceptable now.</p> <p>ID198: I have had PS for so long that I have got used to it</p> <p>ID2: I've had psoriasis for 40 years, so manage well and no longer feel the embarrassment I used to when I was younger.</p> <p>ID205: I have adapted from the very early days and the medication has helped.</p> <p>ID222: For the most part I just live with it and it does not impact my life very much.</p> <p>ID241: I just live with it</p> <p>ID259: I have come to terms with it</p> <p>ID280: Now life long acceptance of immune suppression medication Years of trying different diets and light treatment to varying success</p>
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		<p>ID3: I have lived with psoriasis for more than 30 years and, although it does flare up, I mostly put up with it.</p> <p>ID309: Now I'm older I'm comfortable in my own skin</p> <p>ID31: I have had psoriasis for 61 years so I have become relatively tolerant of it.</p> <p>ID35: You just have to get on with it</p> <p>ID353: Giving that, I realized I should accept</p> <p>ID38: I've lived with it for 40 years now and it does not stop me living my life, but it cannot be ignored.</p> <p>ID41: I have got used to coping over the years so I don't get upset or embarrassed about it, but I know many sufferers do.</p> <p>ID73: It wasn't until I got into my late 20's that I was able to start to ignore the stares and hurtful remarks.</p>
Hair loss	2	<p>ID291: Having it on my scalp has caused hair loss.</p> <p>ID87: i was losing my hair</p>
Hope for a cure	3	<p>ID111: hoping a cure will be found for future generations of sufferers</p>

		<p>ID268: I hope in years to come there are more simpler treatments.</p> <p>ID308: wish there was a permanent cure for it, rather than biologics and topical creams.</p>
Long-term	9	<p>ID111: wishing my daughter doesn't get it</p> <p>ID13: I have had psoriasis since the age of 7, and it completely ruled my childhood.</p> <p>ID151: I have concerns about the long term effects, eg links to cardiovascular disease.</p> <p>ID230: My daughter also has psoriasis presumably from my genes and I hope I do not pass it to my grandchildren.</p> <p>ID262: Fatigue, risk of arthritis,</p> <p>ID266: There are a number of comorbidities that sit alongside a diagnosis (diabetes/heart disease) which need to be looked at more.</p> <p>ID351: I'm about to start tablet treatment which I know can have serious side effects but I am so at the end of my tether that I'm willing to try anything.</p> <p>ID42: Nails are totally shot, so keep them cut as short as possible at all times & slight concerns of</p>

		<p>musculo-skeletal aches and pains possibly foretelling of psoriasis arthritis?</p> <p>ID87: when i became pregnant my fear was that my baby would have psoriasis too</p> <p>ID93: I felt, at an early age, that I should not have children.</p>
Looks/Feels dirty	3	<p>ID203: It looks unsightly and I have to do my hair in certain ways to mask affected areas</p> <p>ID224: My legs used to be one of my best features, they are now my worst as they look disgusting and to make matters worse I now have psoriasis spreading down my arms, to add to the spots on the rest of my body.</p> <p>ID356: feel dirty</p>
No impact or minor	16	<p>ID141: No serious effect. Mild compared with some years ago</p> <p>ID143: I can honestly state that I am totally unaffected by my condition in terms of quality of life.</p> <p>ID146: No effects on my life.</p> <p>ID149: In a sense it doesn't now.</p> <p>ID155: it doesn't affect me at all. It is very minor at the moment.</p>

		<p>ID159: I am lucky and currently it does not affect me in leading a fulfilling life which I hope will resume after Covid.</p> <p>ID168: Having had psoriasis for 70 years I have not been affected too much!</p> <p>ID171: Very little negative impact at present</p> <p>ID196: Now I have no problems at all, I play golf with a golf society we have weekends away and weeks abroad sharing rooms I go away with my wife we go on the beach and at the pool side in swimming costumes, I see other people with psoriasis doing exactly the same thing it seems more acceptable now</p> <p>ID232: Currently I lead a fully normal life.</p> <p>ID28: No</p> <p>ID33: N/a</p> <p>ID34: Psoriasis has little effect on my life</p> <p>ID355: Hardly at all.</p> <p>ID37: n/a</p> <p>ID48: Does not affect me.</p>
Impact of severe disease on lifestyle		

<p>Burden from use of medicine</p>	<p>24</p>	<p>110: I find it depressing as I am constantly using ointments</p> <p>130: Using moisturisers is time consuming.</p> <p>144: Living with psoriasis is just a constant state of applying creams lotions and moisturisers. I am 75 and have known nothing else since I was about 5 years old. At times it has caused much mental distress.</p> <p>15: I have mild psoriasis in certain areas and it takes time, twice a day, to apply lotions and creams etc.</p> <p>158: It is an inconvenience that requires a bit of effort to manage but isn't a major problem.</p> <p>ID210: Having to moisturise dominates a lot of my life</p> <p>ID212: It takes up time caring for skin with various creams etc.</p> <p>ID260: Topical treatments are messy and time consuming.</p> <p>ID169: Dovonex and/or creams once or twice a day is a drag.</p> <p>ID170: Takes time to treat with the ointment and spray every morning.</p>
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		<p>ID170: Taking Methotrexate for last 10 years which has worked really well until the last 12 months so now having to take more tablets. Consultant considering changing me to Ciclosporin which has more side effects.</p> <p>ID176: Takes time to apply topical treatments to difficult to reach areas on lower back.</p> <p>ID181: The time it takes to shower cream and dress.</p> <p>ID187: IT IS A NUISANCE HAVING TO APPLY OINTMENT</p> <p>ID19: It takes me a long time to get ready to go out.</p> <p>ID195: The main issue is using the ointments and creams twice a day. My scalp might really itch.</p> <p>ID21: time it takes to administer creams, how it varies</p> <p>ID357: am continually applying creams and medication ointments, which is soul destroying.</p> <p>ID362: you get fed up with creams</p>
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		<p>ID53: Having to spend anywhere between 30 to 45 mins each morning applying medication</p> <p>ID77: The greatest stress is the time it takes to apply moisturizer and creams. I know I don't do it enough but it's very time consuming especially when spread across a large area.</p> <p>ID88: and needing application of topical treatments and in worse case application of ointments, creams and sprays with steroids.</p> <p>ID89: I have to constantly apply cream to soften the skin.</p> <p>ID99: Requires routine attention.</p>
Diet/Alcohol	5	<p>ID132: I've did [done] a lot of research on which food I should avoid in order to manage my psoriasis symptoms.</p> <p>ID137: It is better since I stopped eating cows milk 10 years ago.</p> <p>ID235: I do most things that I am supposed to do such as eat healthily, exercise and use medications but nothing seems to really ease any symptoms.</p> <p>ID353: understand, and adopt some long-term measures (balanced diet,</p>

		ID4: I have prioritised taking methotrexate over other things in life like alcohol consumption
Hobbies/ Exercise	25	<p>ID1: There are times when the flexural psoriasis in the genital area is so bad I cannot do my fitness and the pain and discomfort warrants having to resort to oral medications</p> <p>ID112: no swimming,</p> <p>ID123: I hate the thought of using a changing room.</p> <p>ID173: When not under control, affects confidence and socialising.</p> <p>ID183: I do not feel comfortable using swimming pools.</p> <p>ID189:also limiting one of my favourite pastimes, rambling.</p> <p>ID195: I've booked for Feb 2022 but am concerned I may find that activity too much!</p> <p>ID20: I haven't been swimming or to the beach in over 20 years.</p> <p>ID207: Stress and/or excessive exercise causes flare up.</p>

		<p>ID218: would like to swim but have not got the confidence</p> <p>ID224: I love playing tennis but cover myself from head to toe no matter what the weather so I don't have to talk about psoriasis when others ask me what is wrong with my skin. Swimming is an even worse issue for the same reason.</p> <p>ID23: Don't feel confident to go swimming.</p> <p>ID230: Embarrassing to sunbathe or swim.</p> <p>ID234: I try and avoid being undressed in public, so swimming pools and the beach present a major challenge.</p> <p>ID243: Unable to take grandchildren swimming.</p> <p>ID287: Before I had psoriasis I used to be a keen walker, walking 10km every day. I can only do this now 1-2 times per week as I have severe psoriasis on the soles of my feet.</p> <p>ID294: and I no longer swim or go to the gym after receiving negative comments about my skin from strangers</p> <p>ID329: avoid going out in public</p> <p>ID353: mild water when taking a shower, cream after shower</p>
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		<p>ID42: That said, still will never go swimming,</p> <p>ID52: Affects relationships and sporting activity both of which i do but then stop when flare ups come.</p> <p>ID57: participating in sport or swimming</p> <p>ID63: or going swimming makes me very conscious</p> <p>ID80: I now can't go swimming because of psoriasis on my pubic areas as the chemicals in the water affects me.</p> <p>ID87: have been afraid to go on a beach, go swimming,</p>
Relationships	11	<p>ID132: I often feel less sociable when someone offers me something to eat I have to refuse because I don't know the ingredients.</p> <p>ID161: I am now 85, As a child and teenager the flare ups were bad, and made it difficult when meeting boys.</p> <p>ID164: deters me from showing my body and therefore mixing with people as freely as i would like.</p> <p>ID180: Makes me concious of my appearance for future dating.</p>

		<p>ID218: very reluctant to show my body even to my wife</p> <p>ID230: Prefer to hide from my wife.</p> <p>ID265: I also feel bad for my partner and friends who have to deal with constant flakes of skin everywhere</p> <p>ID312: I don't like my affected areas to be seen & don't have relationships so no one can see it.</p> <p>ID52: Affects relationships</p> <p>ID87: I never thought i would find someone who would love me and want to marry me, because I had to go to bed with plastic tied over my elbows and knees "to sweat the steroid ointments in".</p> <p>ID93: I know that when I was in my teens and twenties I lost many opportunities to develop relationships</p>
<p>Ruins clothes/beddings</p>	<p>6</p>	<p>ID1: Some cause grease patches so light coloured clothes are not ideal.</p> <p>ID110: I am constantly using ointments which are messy and get everywhere i don't want them to be,</p> <p>ID19: My clothes and furnishings get spoilt by all the greasy emollients I use everyday.</p>

		<p>ID197: ruins clothing also as the creams and ointments are greasy</p> <p>ID84: crea and that requites an elastic tube to prevent ruining the knee of trouses</p> <p>ID91: lesions staining clothing and bedding,</p>
Special clothes	50	<p>ID1: It has such an impact that I have to decide which clothes to wear so it is not obvious or the applications do not affect the look when at work</p> <p>ID112: Clothes I cannot wear,</p> <p>ID121: I try to cover up areas e.g arms/knees when it's flaring up.</p> <p>ID130: I always wear trousers/ leggings etc because I feel my lags are unsightly with psoriasis</p> <p>ID136: Although I do cover up when it is bad.</p> <p>ID148: It is very visible in a bikini.</p> <p>ID150: In recent years, I've been able to cover it up with normal clothes.</p> <p>ID163: Affects what I wear and gets me down on occasions.</p> <p>ID184: Affects what I wear more than anything else. Use clothing to hide areas affected.</p>

		<p>ID188: For many years I have not worn revealing clothes in the summer.</p> <p>ID193: I suffer mainly in the summer months which affects what I can wear.</p> <p>ID197: Affects the clothes I can wear,</p> <p>ID20: It affects my life especially in the way I dress, no short sleeves or shorts,</p> <p>ID213: It affects the clothes I wear</p> <p>ID224: I have a wardrobe full of lovely clothes that I can no longer wear because of my psoriasis and wonder if I ever will again.</p> <p>ID234: It always influences my choice of clothes, to provide coverage and also avoiding synthetics.</p> <p>ID237: cant wear anything with rubber as i have a skin allergy which if rubbed (ie elastis) will welt and turn into psoriasis</p> <p>ID249: Wearing pants or long sleeves. I miss wearing dresses and shorts</p> <p>ID253: I worry about wearing dark clothes in case I have any dry skin fall onto my clothes as I worry that people may perceive me as being unclean.</p>
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		<p>ID26: Cannot wear short sleeve shirts or shorts in public</p> <p>ID265: my ability to wear certain colours of clothing. I often wear hats and cover up if I'm experiencing a flare up.</p> <p>ID27: I can't wear dark clothes on my top half</p> <p>ID270: not being able to wear dark clothes,</p> <p>ID275: Just so I don't have people questioning me about I wear clothes that cover my psoriasis, especially my arms.</p> <p>ID279: clothes I wear and hairstyles I choose are dictated by my skin.</p> <p>ID282: I hate summer because I can wear nice summery clothes as I'm too frightened to get my skin out.</p> <p>ID284: Having to choose to wear lighter colours so as not to show scales</p> <p>ID292: It makes me dread events that should be happy times, for example being invited to a wedding means I worry about what I can wear that will cover up most of my psoriasis.</p> <p>ID294: It affects how I dress,</p>
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		<p>ID298: I cannot wear dark clothes due to obvious flakes.</p> <p>ID308: make sure am covered when going out.</p> <p>ID317: I can't use shorts or skirts because of my skin.</p> <p>ID322: Embarrassed wearing short sleeves</p> <p>ID327: Guttate psoriasis is all over and has an impact on what I wear and what I do</p> <p>ID329: Can't wear short sleeves tops in public</p> <p>ID334: Embarrassed to wear shorts/t-shirts</p> <p>ID335: You want to cover your whole body to stop the questions</p> <p>ID348: I also have psoriasis on my thumb so feel I need to wear gloves when preparing food.</p> <p>ID349: I can't wear clothes I wish</p> <p>ID353: type of clothes,</p> <p>ID354: It affects clothes I wear feel need to cover up arms and legs.</p>
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		<p>ID44: It limits the clothing I can wear - particularly need natural loose fabrics so affects styles and can't buy cheap clothes.</p> <p>ID57: made difference to what clothes i wear</p> <p>ID58: what clothes I wear.</p> <p>ID60: Limits type of textiles which can be worn next to skin.</p> <p>ID63: Wearing shorts</p> <p>ID80: cant wear dark colours as the scales fall from my scalp onto my clothes</p> <p>ID87: I have been afraid to go on a beach, go swimming, wear summer dresses with bare legs and ageing hasn't changed this.</p> <p>ID97: Tend to wear long sleeves & trousers.</p> <p>ID99: I have to wear gloves for all of my gardening activities.</p>
Special Hygiene	4	<p>ID112: the constant study of skin care and makeup products (that is when you can wear makeup without it looking a complete mess of flaky skin all over your face!)</p>

		<p>ID251: stops me from being able to wear all deodorant except one which makes me very self conscious</p> <p>ID270: washing your hair EVERY day</p> <p>ID340: I am caught between wearing makeup to look/feel professional and treating my psoriasis</p>
Vacuuming	6	<p>ID197: Living with someone can be hard as you feel you have to Hoover constantly.</p> <p>ID243: Constant hoovering up dead skin.</p> <p>ID246: Vacuuming bed every day, scales and skin everywhere</p> <p>ID265: it causes extra mess to clean up</p> <p>ID270: from having to change your bed sheets every one to two days, hoovering constantly</p> <p>ID80: Always clearing up scales from the floor.</p>
Other	1	<p>ID14: I am not able to use any sanitary product with a nice fragrance, which is an issue in the Summer when I sweat more.</p>
Impact of treatment		
Bad	16	<p>ID138: My proscribed creams are having little effect.</p> <p>ID194: I will be going back to the clinic after the pandemic because self-management is not working.</p>

		<p>ID203: Topical ointments like coal tar or give little relief and can make symptoms worse.</p> <p>ID214: So far not reacting well to medication from GP nor what "cured" it the previous time.</p> <p>ID22: stubborn to treat.</p> <p>ID235: I find the current medications prescribed for me work only for a short while then become less effective as time goes by</p> <p>ID256: I am currently waiting for biologics as all other medications have failed.</p> <p>ID260: Injections can be sore.</p> <p>ID306: I now take an antihistamine at night to help with the itch and moisturize like mad! It's doesn't go,</p> <p>ID325: I no longer use the steroids prescribed as I feel they suppress it for only a little while and then it comes back with a vengeance.</p> <p>ID343: Relentless no success in any treatments</p> <p>ID346: it sucks, i'm either uncomfortable from the skin or uncomfortable from the treatments.</p>
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		<p>ID356: Have tried a load of different treatments, but had to wait to get a pasi score of 10 before even being considered for biologics, which has now been met but have to wait another 5 months before I see the doctor who gives the final go ahead</p> <p>ID360: no treatment works.</p> <p>ID43: only slightly alleviated by emollient creams and Enstilar.</p> <p>ID65: Nothing works at all other than any soft cream.</p>
Good	40	<p>ID10: If I wasn't using a biological drug (Imraldi) my psoriasis would be body-wide and affect all aspects of life. It is currently controlled.</p> <p>ID104: I had quite a widespread psoriasis for nearly 30 years but it was controlled by Cyclosporin and then Fumaderm/Skilarence.</p> <p>ID108: Before treatment answers would have been very different</p> <p>ID120: Methotrexate has kept it largely under control for me with just the occasional flare-up</p> <p>ID125: I now take Acetretin - for 2 years and am fairly clear - has been a life changer.</p>

		<p>ID126: I feel without access to medication I would much more anxious than I do.I had a flare up early last year but I have been able to settle it down with a combination of medical UVB treatment and Chinese herbs.</p> <p>ID13: I am now taking Biologics to control my psoriasis which have changed my life</p> <p>ID13: I am so thankful now this is all behind me, and my experience of biologics so far has been life changing.</p> <p>ID140: I currently manage my minor symptoms , controlling with them with external moisturising creams and prescinded creams .</p> <p>ID141: Medication greatly helps.</p> <p>ID143: My scalp condition is static and I use Polytar to wash my hair, which is effective.</p> <p>ID149: The treatment I have had for the last few years has all but cleared it therefore most of the effect for me is the treatment itself.</p> <p>ID152: Treatments can be good but most psoriasis is hidden and as such do not use the ointments but moisturise mainly;</p> <p>ID161: I am on steroids for something else and I think that helps.</p>
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		<p>ID170: No scaling because I apply topical treatments every day which is good.</p> <p>ID194 :Right now I use enstillar foam every third day, an exfoliant in the shower and mosturisor everyday day when not using enstillar. The scales are getting a lot better.</p> <p>ID198: However, I am trying a new product and the itching has stopped - almost immediately and I now have to see if it impacts my skin beneficially - that's all I can say for now.</p> <p>ID205: the medication has helped.</p> <p>ID206: well controlled by drugs</p> <p>ID207: Irritation usually relieved with Clobavate 0.05%</p> <p>ID217: A change of biologics has helped immensely.</p> <p>ID221: The psoriasis itself is kept at bay by being on Metojet injections.</p> <p>ID229: as long as I am taking my biologics my psoriasis is under control and doesn't bother me.</p>
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		<p>ID23: I inject with stelara every 12 weeks and this controls it very well but new bits are slowly emerging.</p> <p>ID233: I was eventually prescribed USTERKINEMAB, which is a once every 12 week injection. This treatment has completely cleared my psoriasis.</p> <p>ID24: I now take methotrexate which has dramatically reduced the amount of psoriasis on my body</p> <p>ID268: The only treatment that helped me was Ciclosporin which made me extremely ill.</p> <p>ID283: Am on 20/30g acitretin which doesn't clear it but makes it very tolerable with creams as well. Far better than 4 weeks in hospital with creams.</p> <p>ID300: I'm trying different remedies to keep it manageable</p> <p>ID330: Methotrexate and Alphosyl has really improved my scalp psoriasis.</p> <p>ID353: It seems a never ending battle, but the measures I took definetly improved my life for better.</p>
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		<p>ID4: been taking methotrexate for 13 years and my skin does not affect me at all now it is controlled.</p> <p>ID40: I am now on injections and my skin has never been better I have been on them for 4 weeks and a treatment has never worked like this before.</p> <p>ID42: Much improved by the use of my current medication Enstilar Foam spray, which I now use for maintenance twice weekly too, which helps suppress the severity and frequency of the flares</p> <p>ID42: Happier and more confident however since finding an effective medication that I can use to help myself with.</p> <p>ID50: I have been using steroid medication in the last year to help control the condition. I have not needed it before.</p> <p>ID71: I was more affected by psoriatic arthritis until I started taking Methotrexate.</p> <p>ID72: my quality of life is 100 x better since starting methotrexate in 2013.</p> <p>ID85: I have started taking methotrexate and 10000000% recommend to anyone with psoriasis</p>
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		<p>ID86: I have found self-hypnosis a huge help, I sought professional help for pain and it actually works for both - wonderful.</p> <p>ID92: I am very lucky being able to tolerate Methotrexate with minimal side effects.</p> <p>ID94: On face and body I have creams that usually work.</p>
Harms	4	<p>ID118: Side effects of the acitretin to control my psoriasis leads to higher cholesterol possible cause AF dry hair dry eyes possibly some concentration loss</p> <p>ID13: I've had horrific side effects from every medication, including hair loss, vomiting, diarrhoea, chronic headaches, nail problems and stomach pains.</p> <p>ID80: steroids in the early years has left me with very thin skin problem with my hands and fingers. I now have no proper grip and cannot use fingerprint recognition</p> <p>ID88: This is always a last resort as it causes thinning of the scrim resulting in bleeding under the skin when the skin it lightly banged or pricked BY plants, roses or any DIY activity.</p>
Practicality	5	<p>ID176: Takes time to apply topical treatments to difficult to reach areas on lower back.</p>

		<p>ID220: The psoriasis on my back is always there it has never improved over many years (large patches)</p> <p>ID231: Inability to apply ointments to back and difficult to reach areas of my body. ie daily application of Dovobet.</p> <p>ID238: Also, I live alone so managing the psoriasis on my back is nightmarish!</p> <p>ID94: Putting cream on hands is difficult because of using hands during day, and covering them in bed at night.</p>
Impact of external factors		
COVID 19	9	<p>ID16: Lockdown and lack of sunshine holidays having detrimental effect.</p> <p>ID214: Just as well we are in lockdown, so I don't have to go out much.</p> <p>ID256: Any medical intervention is a fight to get, especially during COVID19.</p> <p>ID268: I'm currently not on any medication due to the impacts of immunosuppressants whilst the Covid pandemic is happening.</p> <p>ID272: I take Methotrexate and so last year I had to shield. Being classed as clinically extremely</p>

		<p>vulnerable affected me mentally in a way I feel has been detrimental to my psoriasis also.</p> <p>ID317: Masks produce me irritation and my psoriasis appears</p> <p>ID341: I am in a mess now due to methotrexate being stopped and no alternative plan in place. Currently caught in the pandemic loop of being unable to get appointments</p> <p>ID4: covid (considered stopping methotrexate to increase immunity)!</p> <p>ID50: Having been in lockdown for most of the last twelve months it is difficult to determine if my deteriorating psoriasis is due to the change from my normal life style or is just getting worse than it was.</p>
Hand washing	2	<p>ID14: The need to sanitise my hands causes me a lot of issues</p> <p>ID314: The palms of my hands and my knuckles started due to the constant handwashing at the beginning of the covid epidemic.</p>
Hormones	1	ID245: Mine seems to be connected to my hormones and is worse when I'm mid-cycle.
Soap/Chemicals	1	ID190: I have to avoid contact with soap
Stress/Exercise	6	ID14: Like many sufferers, stress is also a trigger for me, which is more common at the moment, with uncertainties regarding many aspects of life, including relationships, family, work, etc.

		<p>ID163: I have to be careful psychologically not to feel 'at war' with my own body</p> <p>ID235: I become so stressed and find that I go around in circles such as I become stressed so psoriasis flares up then I stress about that and then the stress never fully goes away so my body never really heals.</p> <p>ID241: Stress related. I just live with it</p>
Sun	9	<p>ID102: It encourages me to attend naturist places, clubs and events where I can take all my clothes off as exposure to sunlight improves my skin</p> <p>ID109: I am looking forward to a sunny Summer - wearing shorts.</p> <p>ID125: In the summer exposing it with lighter clothes but trying to be in the sun as much as possible</p> <p>ID159: In the sunny weather it improves but having had it for so long I endeavour to keep flare ups away by being positive.</p> <p>ID201: but it gets better when exposed to more sun - which is hard to do most summers when I have to dress smartly for work (so cover it up).</p>

		<p>ID224: summer I have to cover myself up which makes me feel very sad as I have medium dark skin and love the sun</p> <p>ID282: I hate summer because I can wear nice summery clothes as I'm too frightened to get my skin out.</p> <p>ID288: My confidence is affected in the spring/summer months as more skin is on show.</p> <p>ID86: Summer I strip off and enjoy the sun I find the plaques fade and vanish as they did last summer.</p>
Winter	5	<p>ID125: It has been hard most of my life living with psoriasis - in the winter being worse, sore and painful.</p> <p>ID201: My psoriasis gets worse the more I cover it up, esp in the winter,</p> <p>ID86: Come winter I get worse with being wrapped up but have never been so bad as I was when younger.</p> <p>ID88: The psoriasis is always worse in the winter due to lack of sunlight</p> <p>ID91: just gets a bit worse in late winter</p>
Other impacts of the disease		

<p>Lack of support- Public</p>	<p>10</p>	<p>ID112: the lack of understanding from others - the affects go on and on.</p> <p>ID13: During particularly bad flares, I would visit the nurse and ask to be collected as I couldn't face my peers.</p> <p>ID154: Once in a gym a lady insisted that the machine I had been using was thoroughly cleaned as she had noted the psoriasis patches on my elbows.</p> <p>ID259: I have come to terms with it but I still get people looking at me and asking if they can catch it. People need to be educated about what psoriasis is.</p> <p>ID275: I get a lot of questions about it if people see it.</p> <p>ID294: I no longer swim or go to the gym after receiving negative comments about my skin from strangers - at first I was resolved to ignore them but I found it was actually too stressful to worry about other people's reactions.</p> <p>ID303: find it uncomfortable when people stare at legs where my psoriasis is worse, seems a lack of understanding of what psoriasis is</p>
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		<p>ID321: Feel like it is something I have to tell people, “hi I am X, I have psoriasis”. When it’s bad, it’s all encompassing.</p> <p>ID340: I think people treat me differently when they can see my facial psoriasis.</p> <p>ID49: Family understand but strangers don’t</p>
Lack of support- Healthcare professionals	7	<p>ID109: I wish my consultant dermatologist didn't discharge me and stop at least a six monthly check ups. I now need to see my GP to get a new referral, and then eventually (with a significant delay) get put back onto the consultant's waiting list!</p> <p>ID264: Embarrassing Health professionals worst commentators (little or no understanding)</p> <p>ID273: Not enough treatment available, have had to seek private UV light therapy which is expensive and often stressful to arrange which doesn’t help with the flare up.</p> <p>ID286: And I find health professionals reluctant to treat the psoriasis with medication that I would like to try.</p> <p>ID316: Often my symptoms are dismissed by GP until it's physically obvious my skin is in great distress and then I get told to go to hospital. I have managed to arrange for a note on my file to try and prevent this but more needs to be done to</p>

		<p>educate healthcare professionals and to help us understand this cruel condition.</p> <p>ID44: Can't get any medical professionals to see me as a whole person, just a set of symptoms.</p> <p>ID73: Medical profession wasn't that helpful either in those days.</p>
Negative comments	6	<p>ID150: It annoys me if a total stranger tells me I have insect bites on my legs, i.e. they haven't recognised the red marks as psoriasis.</p> <p>ID154: Once in a gym a lady insisted that the machine I had been using was thoroughly cleaned as she had noted the psoriasis patches on my elbows.</p> <p>ID294: I no longer swim or go to the gym after receiving negative comments about my skin from strangers - at first I was resolved to ignore them but I found it was actually too stressful to worry about other people's reactions.</p> <p>ID51: Called a leper etc....</p> <p>ID73: other children said I had leprosy!</p> <p>ID80: I have had derogatory remarks about scales on my scalp. My children use to say mother's snow storm.</p>
Support- Other	3	<p>ID13: I have never been offered any psychological support, which is something I think I really would</p>

		<p>have benefitted from as a teenage girl going through comprehensive school.</p> <p>ID197: They also don't understand that it can be very hard to get comfortable and stay in one position for a long time due to pressure on your skin. Watching a film for 90 mins means repositioning constantly</p> <p>ID231: Most of my family understand. However others do not!</p>
Impact of other long term conditions		
Psoriatic arthritis	18	<p>ID121: I have psoriatic arthritis and that can make me have some pain and I can get tired</p> <p>ID124: Also have Psoriatic arthritis in knees and big toe joints. In remission at moment.</p> <p>ID165: am convinced that my arthritis is psoriatic arthritis and this restricts my ability to stand and walk</p> <p>ID166: Its the Psoriatic Arthritis that is giving most discomfort and has done since July 2020.</p> <p>ID172: Having psoriatic arthritis is exhausting and depleting</p> <p>ID177: I HAVE THE MUTILANS FORM OF PSORIATIC ARTHRITIS IN MY HANDS AND FEET ALL OF MY NAILS ARE AFFECTED WITH NAIL PSORIASIS</p>

	<p>ID205: I also think that my skin condition has greatly improved as my psoriatic arthritis has become worse.</p> <p>ID212: I am also on meds for Psoriatic Arthritis</p> <p>ID221: i suffer more with psoriatic arthritis & am affected badly by arthritis in my hands/fingers.</p> <p>ID330: I also have psoriatic arthritis.</p> <p>ID34: It is psoriatic arthritis which is a major factor in my life</p> <p>ID44: The arthritis is especially limiting.</p> <p>ID70: Arthritis</p> <p>ID71: I was more affected by psoriatic arthritis until I started taking Methotrexate.</p> <p>ID75: I gained a lot of weight after guttate psoriasis/ PsA a few years back, which I am still working to lose.</p> <p>ID87: I also have psoriatic arthritis in my feet and hands - and i suspect my knees - as well as psoriasis of the nails.</p> <p>ID92: psoriastic arthritis have been in remission for over ten years.</p>
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		ID98: I suffer also from PsA
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Table A6.2: Impact of other conditions

Impact		Example of comments
Psoriatic arthritis (18)		<p>ID121: I have psoriatic arthritis and that can make me have some pain and I can get tired</p> <p>ID124: Also have Psoriatic arthritis in knees and big toe joints. In remission at moment.</p> <p>ID165: am convinced that my arthritis is psoriatic arthritis and this restricts my ability to stand and walk</p> <p>ID166: Its the Psoriatic Arthritis that is giving most discomfort and has done since July 2020.</p> <p>ID172: Having psoriatic arthritis is exhausting and depleting</p> <p>ID177: I HAVE THE MUTILANS FORM OF PSORIATIC ARTHRITIS IN MY HANDS AND FEET ALL OF MY NAILS ARE AFFECTED WITH NAIL PSORIASIS</p> <p>ID205: I also think that my skin condition has greatly improved as my psoriatic arthritis has become worse.</p> <p>ID212: I am also on meds for Psoriatic Arthritis</p>

		<p>ID221: i suffer more with psoriatic arthritis & am affected badly by arthritis in my hands/fingers.</p> <p>ID330: I also have psoriatic arthritis.</p> <p>ID34: It is psoriatic arthritis which is a major factor in my life</p> <p>ID44: The arthritis is especially limiting.</p> <p>ID70: Arthritis</p> <p>ID71: I was more affected by psoriatic arthritis until I started taking Methotrexate.</p> <p>ID75: I gained a lot of weight after guttate psoriasis/ PsA a few years back, which I am still working to lose.</p> <p>ID87: I also have psoriatic arthritis in my feet and hands - and i suspect my knees - as well as psoriasis of the nails.</p> <p>ID92: psoriastic arthritis have been in remission for over ten years.</p> <p>ID98: I suffer also from PsA</p>
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Appendix 6.7: Kernel density plot for the EQ-5D-5L values

Figure A6. 1: Distribution of health status score from EQ-5D-5L valued using Hernandez crosswalk

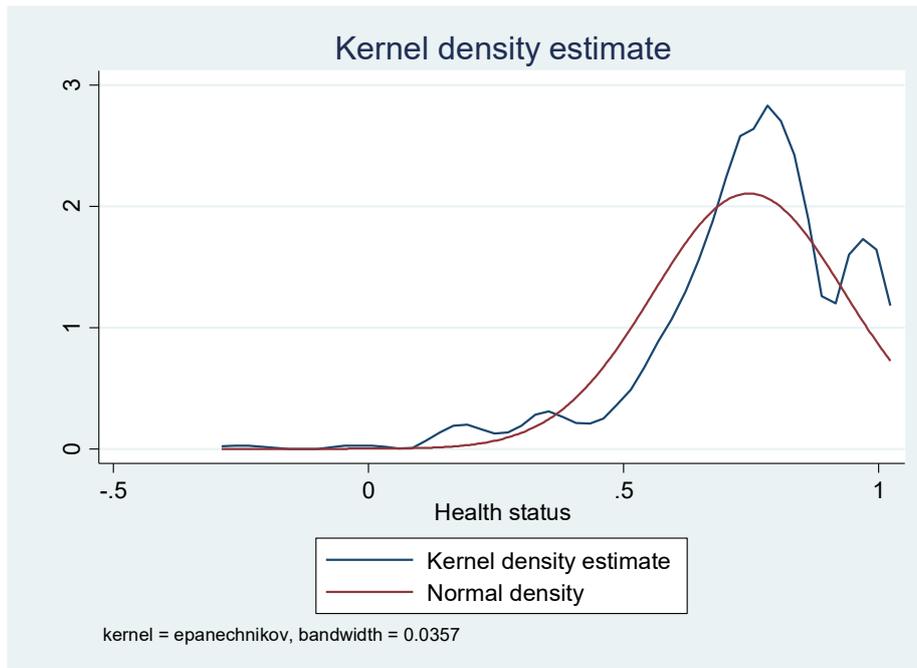


Figure A6. 2: Distribution of health status score from EQ-5D-5L valued using Hout crosswalk.

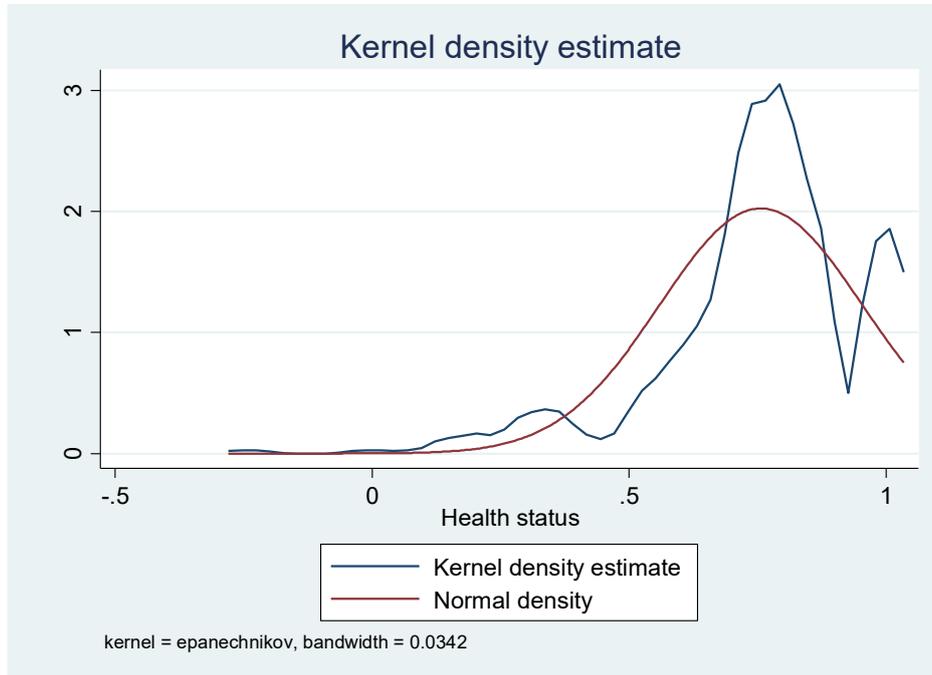
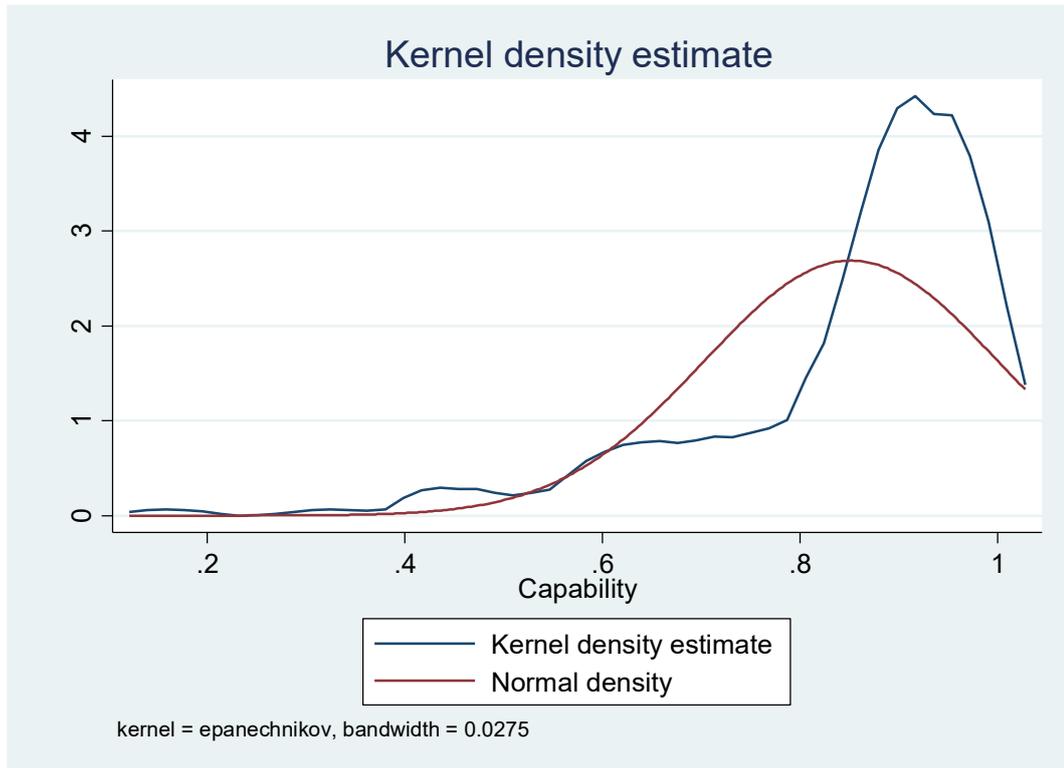


Figure A6. 3: Distribution of the observed scores from the ICECAP-A



Appendix 6.8: Regression Model Build up tables

Table A6. 3: OLS estimation- Health status

	1	2	3	4	5	6	Final Model
Constant	0.83 ***	0.51***	0.48***	0.50** *	0.16***	0.21	0.23
Severity	- 0.01***	- 0.01***	-0.01***	- 0.01** *	-0.01***	- 0.01** *	- 0.01** *
Psoriasis duration							
Less 1 year		0.37**	0.39**	0.37**	0.68***	0.68**	0.66**
1 to 2 years		0.21	0.22	0.19	0.56**	*	*
3 to 5 years		0.31**	0.33**	0.31**	0.69***	0.56**	0.55**
6 to 10 years		0.32**	0.32**	0.30**	0.67***	*	0.66**
Over 10 years						0.69** 0.64** *	0.65** *
Age (Years)			0.00	-0.00	0.001*	0.00	
Age/10			0.04				
(Age/10)^2			-0.00				
Sex (male)				0.06**	0.05**	0.06** *	0.06**
Comorbidity cat							
0					-0.09***	-	-
1					-0.13***	0.08**	0.08**
2					-0.20***	*	*
>=3							

						-	-
						0.12**	0.11**
						*	*
						-0.2***	-
							0.19**
							*
Topical						-0.01	
Oral treatment						-0.01	
Injectable treatment						-0.06**	-0.06**
Light treatment						0.06	
Flare-up in last 12 months						-0.006	
R-squared	0.15	0.18	0.16	0.19	0.35	0.37	
Adjusted R-squared	0.15	0.17	0.15	0.17	0.33	0.34	
No. observations	366	365	346	346	334	334	
RMSE	0.18	0.19	0.19	0.17	0.16	0.17	
MAE	0.13	0.13	0.13	0.13	0.12	0.12	
ME							
AIC	-206.64	-209.98	-194.60	-201.24	-262.40	-	259.40
BIC	-198.83	-186.58	-167.68	-170.47	-224.32	-	202.28

p<0.05; **p<0.01; *p<0.001;*

	1	2	3	4	5	6	Final Model
Constant	0.824 ***	0.51***	0.48***	0.50** *	0.16***	0.21	0.23
Severity	- 0.011***	- 0.01***	-0.01***	- 0.01** *	-0.01***	- 0.01** *	- 0.01** *
Psoriasis duration							
Less 1 year		0.37**	0.39**	0.37**	0.68***	0.68**	0.66**
1 to 2 years		0.21	0.22	0.19	0.56**	*	*
3 to 5 years		0.31**	0.33**	0.31**	0.69***	0.56**	0.55**
6 to 10 years		0.32**	0.32**	0.30**	0.67***	*	0.66**
Over 10 years						0.69** 0.64** *	0.65** *
Age (Years)			0.00	-0.00	0.001*	0.00	
Age/10			0.04				
(Age/10)^2			-0.00				
Sex (male)				0.06**	0.05**	0.06** *	0.06**
Comorbidity cat							
0					-0.09***	-	-
1					-0.13***	0.08**	0.08**
2					-0.20***	*	*
>=3						- 0.12** *	- 0.11** *
						-0.2***	

							- 0.19** *
Topical						-0.01	
Oral treatment						-0.01	
Injectable treatment						-0.06**	-0.06**
Light treatment						0.06	
Flare-up in last 12 months						-0.006	
R-squared	0.15	0.18	0.16	0.19	0.35	0.37	
Adjusted R- squared	0.15	0.17	0.15	0.17	0.33	0.34	
No. observations	334	365	346	346	334	334	
RMSE	0.18	0.19	0.19	0.17	0.16	0.17	
MAE	0.13	0.13	0.13	0.13	0.12	0.12	
ME							
AIC	-206.64	-209.98	-194.60	-201.24	-262.40	-259.40	
BIC	-198.83	-186.58	-167.68	-170.47	-224.32	-202.28	

p<0.05; **p<0.01; *p<0.001;*

Table A6. 3: Tobit Estimation- Health status

	1	2	3	4	5	6
Constant	0.836** *	0.52***	0.48***	0.50***	0.19***	0.24
Severity	- 0.01***	- 0.01***	-0.01***	- 0.01***	-0.01***	-0.01***
Psoriasis duration						
Less 1 year						
1 to 2 years		0.37**	0.39**	0.37**	0.67**	0.67***
3 to 5 years		0.21	0.21	0.19	0.56**	0.54**
6 to 10 years		0.30*	0.32**	0.31**	0.69***	0.66**
Over 10 years		0.32**	0.32**	0.30**	0.62**	0.62**
Age (Years)			0.00	-0.00	0.001**	0.00
Sex (male)				0.06**	0.05**	0.05**
Comorbidity cat						
1					-0.09***	-0.09***
2					-0.13***	-0.12***
>=3					-0.22***	-0.2***
Topical						-0.01
Oral treatment						-0.01
Injectable treatment						-0.05*
Light treatment						0.05
Flare-up in last 12 months						-0.007

R-squared

Adjusted R-squared						
No. observations	366	365	346	334		
RMSE						
MAE						
Log-likelihood	-36.95	-31.62	-26.15	-21.91	12.78	15.07
AIC	79.9	77.25	68.29	61.82	-1.57	3.87
BIC	91.6	104.55	99.06	96.44	44.17	68.66

****p<0.05; **p<0.01; ***p<0.001***

Table A6. 4: Censored latent adjusted dependant (CLAD) variable estimation

	1	2	3	4	5	6
Constant	0.842** *	0.52***	0.48***	0.50***	0.19***	0.24
Severity	- 0.01***	- 0.01***	-0.01***	- 0.01***	-0.01***	-0.01***
Psoriasis duration						
Less 1 year						
1 to 2 years		0.37**	0.39**	0.37**	0.67**	0.67***
3 to 5 years		0.21	0.21	0.19	0.56**	0.54**
6 to 10 years		0.30*	0.32**	0.31**	0.69***	0.66**
Over 10 years		0.32**	0.32**	0.30**	0.62**	0.62**
Age (Years)			0.00	-0.00	0.001**	0.00
Sex (male)				0.06**	0.05**	0.05**
Comorbidity cat						
1					-0.09***	-0.09***
2					-0.13***	-0.12***
>=3					-0.22***	-0.2***
Topical						-0.01
Oral treatment						-0.01
Injectable treatment						-0.05*
Light treatment						0.05
Flare-up in last 12 months						-0.007

R-squared

Adjusted R-squared						
No. observations	366	365	346	334		
RMSE						
MAE						
Log-likelihood	-36.95	-31.62	-26.15	-21.91	12.78	15.07
AIC	79.9	77.25	68.29	61.82	-1.57	3.87
BIC	91.6	104.55	99.06	96.44	44.17	68.66

p<0.05; **p<0.01; *p<0.001*

Table A6. 5: OLS estimation-Capability

	1	2	3	4	5	6
Constant	0.89***	0.87***	0.80***	0.80***	0.80***	0.69**
Severity	- 0.01***	- 0.01***	-0.004***	- 0.004** *	-0.003**	- 0.003* *
Psoriasis duration						
Less 1 year						
1 to 2 years		0.01	0.05	0.04	0.20	0.19
3 to 5 years		0.21	0.00	-0.01	0.15	0.14
6 to 10 years		-0.00	0.01	0.01	0.17	0.17
Over 10 years		0.02	0.03	0.01	0.15	0.14
Age (Years)			0.00**	-0.00**	0.002***	0.001* **
Sex (male)				0.02	0.02	0.01
Comorbidity cat						
1					-0.03	-0.02
2					-0.106**	-0.06**
>=3					-0.12***	-0.1***
Topical						-0.01
Oral treatment						-0.01
Injectable treatment						-0.01
Light treatment						0.04
Flare-up in last 12 months						-0.01
R-squared	0.08	0.08	0.09	0.09	0.20	0.21

Adjusted R-squared	0.08	0.07	0.07	0.07	0.17	0.17
No. observations	366	365	346	346	334	334
RMSE	0.14	0.14	0.14	0.14	0.14	0.17
MAE	0.10	0.10	0.10	0.10	0.10	0.12
ME						
AIC	-385.10	-375.92	-358.40	-358.14	-395.27	-389.35
BIC	-377.29	-352.52	-331.48	-327.37	-357.19	-332.22

****p<0.05; **p<0.01; ***p<0.001***

Table A6. 6: Tobit Estimation capability

	1	2	3	4	5	6
Constant	0.91*** ***	0.92***	0.83***	0.84***	0.64***	0.7***
Severity	- 0.01***	- 0.01***	-0.004***	-0.004***	- 0.004***	-0.002**
Psoriasis duration						
Less 1 year						
1 to 2 years		-0.01	0.02	0.02	0.182	0.171
3 to 5 years		-0.02	-0.03	-0.04	0.139	0.128
6 to 10 years		-0.04	-0.02	-0.03	0.156	0.147
Over 10 years		-0.01	-0.02**	-0.02	0.138	0.128
Age (Years)			0.00	-0.00**	0.001***	0.002***
Sex (male)				0.02	0.020	0.022
Comorbidity cat						
1					-0.027	-0.024
2					-0.059**	-0.059**
>=3					- 0.116***	- 0.112***
Topical						-0.010
Oral treatment						0.012
Injectable treatment						-0.016*
Light treatment						0.051
Flare-up in last 12 months						-0.011

R-squared

Adjusted R-squared						
No. observations	366	365	346	334	334	334
RMSE						
MAE						
Log-likelihood	91.82	91.50	93.17	94.39	119.37	121.73
AIC	-177.63	-169.00	-170.34	-170.78	-214.75	-209.45
BIC	-165.93	-141.70	-139.56	-136.16	-169.01	-144.66

****p<0.05; **p<0.01; ***p<0.001***

Table A6. 7: CLAD estimation- Capability

	1	2	3	4	5	6
Constant [95% CI]	0.93 [0.91 to 0.95]	0.87 [0.64 to 1.00]	0.81 [0.61 to 0.96]	0.83 [0.59 to 0.92]	0.87 [0.70 to 0.95]	0.90***
Severity	-0.01 [-0.01 to -0.00]	-0.01 [- 0.01 to - 0.02]	-0.004 [- 0.01 to - 0.00]	-0.003 [- 0.01 to - 0.00]	-0.003 [- 0.01 to - 0.00]	-0.002 [- 0.01 to - 0.00]
Psoriasis duration						-0.00 [- 0.03 to 0.05]
Less 1 year		0.01 [- 0.02 to 0.06]	0.01 [- 0.02 to 0.05]	0.004 [- 0.02 to 0.05]	0.00 [-0.02 to - 0.5]	
1 to 2 years						
3 to 5 years						
6 to 10 years						
Over 10 years						
Age (Years)			0.001 [0.006 to 0.002]	0.00 [0.00- 0.00]	0.00 [0.00 to 0.00]	0.00 [0.0 to 0.00]
Sex (male)				0.03 [- 0.00 to 0.05]	0.03 [- 0.00 to - 0.07]	0.02 [- 0.00 to - 0.00]
Comorbidity cat						
1					-0.02 [- 0.03 to - 0.01]	-0.02 [- 0.03 to 0.15]
2						
>=3						
Topical						-0.010 [- 0.04 to 0.02]

Oral treatment						0.02 [-0.05 to -0.06]
Injectable treatment						-0.016 [-0.05 to -0.06]
Light treatment						-
Flare-up in last 12 months						-0.01 [-0.3 to 0.01]

R-squared

**Adjusted/
pseudo R-
squared**

No. observations	366	365	346	334	334	334
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RMSE

MAE

Log-likelihood	91.82	91.50	93.17	94.39	119.37	121.73
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AIC	-177.63	-169.00	-170.34	-170.78	-214.75	-209.45
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BIC	-165.93	-141.70	-139.56	-136.16	-169.01	-144.66
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****p<0.05; **p<0.01; ***p<0.001***

Table A6. 8: Model Comparison, full estimates (Factors influencing relation between health status and psoriasis severity)

	OLS	TOBIT	CLAD
Constant	0.21	0.24	0.83***
Severity	- 0.01***	- 0.01***	-0.0***
Psoriasis duration			
Less 1 year			
1 to 2 years	0.68***	0.67***	0.02 ^a
3 to 5 years	0.56***	0.54**	
6 to 10 years	0.69**	0.66**	
Over 10 years	0.64***	0.62**	
Age (Years)	0.00	0.00	0.00
Sex (male)	0.06***	0.05**	0.05**
Comorbidity cat			-0.05 ^a ***
1	-	-	
2	0.08***	0.09***	
>=3	- 0.12*** -0.2***	- 0.12*** -0.2***	
Topical	-0.01	-0.01	-0.02
Oral treatment	-0.01	-0.01	-0.00
Injectable treatment	-0.06**	-0.05*	-0.01
Light treatment	0.06	0.05	
Flare-up in last 12 months	-0.006	-0.007	-0.01

R-squared	0.37		
Adjusted R-squared	0.34		
No. observations	334	334	334
RMSE	0.17		
MAE	0.12		
Log-likelihood		15.07	
AIC	-259.40	3.87	
BIC	-202.28	68.66	