



The Burden of Atopic Dermatitis: Summary of a Report for the National Eczema Association

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To assess the patient-level and societal burden of atopic dermatitis, we comprehensively reviewed the literature related to quality of life, social, economic, academic, and occupational impacts. Atopic dermatitis has profound impacts on patient and family quality of life. A conservative estimate of the annual costs of atopic dermatitis in the United States is \$5.297 billion (in 2015 USD). People with atopic dermatitis may change their occupation because of their skin disease. Research gaps include quality of life assessments outside of tertiary care centers, impacts on partners and families of adult patients, and updated comprehensive cost estimates.

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INTRODUCTION

Atopic dermatitis (AD), also called eczema, is a chronically relapsing skin disease. It is prevalent in approximately 10.7% and 7.2% of US children and adults, respectively (Shaw et al., 2011; Silverberg et al., 2015). The onset of AD is usually in early childhood, and it can have an impact on the entire family unit. Additionally, AD is increasingly recognized as a disease that often persists into or begins in adulthood (Margolis et al., 2014). Thus, AD can have a detrimental effect on the lives of patients and their families throughout the lifespan. This includes impacts on quality of life (QoL) and social, academic, and occupational impacts. AD places a tremendous financial burden on patients, their families, and society as a whole through direct medical costs and decreased productivity. All of these aspects together—QoL, social, academic, and occupational impacts, along with direct and indirect costs—encompass the burden of disease of AD.

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Abbreviations: AD, atopic dermatitis; CLQI, Children's Life Quality Index; QoL, quality of life; SF-36, Short Form (36) Health Survey

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Recently, the National Eczema Association, a US patient advocacy group, funded a comprehensive review of the literature to document the evidence to date on the burden of AD. This review article summarizes the findings of the report to the National Eczema Association.

RESULTS AND DISCUSSION

QoL

QoL in children with AD. Chamlin et al. (2004) interviewed the parents of 26 children with AD to determine how AD affects QoL for these young patients. That article lists the impacts of AD mentioned by at least 20% of participating families. Impacts on physical health included itching and scratching, sleep, pain, bleeding, and dietary limitations. Emotional impacts included behavioral problems, irritability, crying, and problems with treatments. Physical functioning was impaired via clothing restrictions; interference with activities such as bathing, playing (especially outdoors) and swimming; and having to hold children's hands to prevent scratching. Social functioning was impaired: parents noted that both adults and children avoided interacting with children with AD. Although this qualitative study provides important information on the nature of AD's impacts on children, its generalizability is limited by its conduct in a tertiary care setting. Although AD severity was not measured among children in this study, the population of AD patients was likely skewed toward the more severe end of the AD spectrum.

In other studies, consequences of AD found to most affect QoL in childhood are itching and scratching, impacts on sleep, treatment, sports, and embarrassment related to the condition (Ballardini et al., 2014; Ben-Gashir et al., 2004; Ganemo et al., 2007; Ho et al., 2010; Ricci et al., 2007). Many studies have observed that as AD severity increases, QoL decreases (Alzolibani, 2014; Ben-Gashir et al., 2004; Breninkmeijer et al., 2009; Ho et al., 2010; Hon et al., 2015; Maksimovic et al., 2012; Monti et al., 2011; Torrelo et al., 2013).

A study using the Children's Life Quality Index (CLQI), a generic QoL instrument, compared QoL among children aged 5–16 years with various chronic diseases, including 106 patients with generalized eczema (Beattie and Lewis-Jones, 2006). Generalized eczema had the second-largest impact on QoL, following only cerebral palsy, among all chronic diseases studied. One strength of this study was its use of both generic (CLQI) and skin-specific (Children's Dermatology Life Quality Index) tools for participants with skin disease. Among participants with skin disease, the CLQI and Children's Dermatology Life Quality Index were highly

correlated ($r = 0.72$, $P < 0.001$), indicating that the CLQI was able to capture the impact of skin disease on QoL in general. However, it did not include any other validated generic QoL measures, and so the ability of the CLQI to measure QoL in noncutaneous conditions is unclear.

QoL in adults with AD. Aspects of QoL reported to be most affected by AD in adults are symptoms and emotional impact, with less of an impact on social functioning (Holm et al., 2006b). However, social functioning can be affected as well: in a survey of college students ($n = 336$), 25.5% of participants with self-reported eczema believed that it impaired their social life (Roosta et al., 2010). AD can also limit simple every day activities; in a community-based survey of 559 AD patients, 35% believed that AD affected their choice of clothing, and 32% believed it limited shaving or wearing makeup (Anderson and Rajagopalan, 2001).

Impaired QoL in AD is correlated with disease severity and increased itch and sleep disturbance (Beikert et al., 2014; Chrostowska-Plak et al., 2013; Holm et al., 2006b; Maksimovic et al., 2012; Misery et al., 2007; Sanchez-Perez et al., 2013; Wittkowski et al., 2004). However, the correlation of QoL with objective disease severity is often only moderate (Chrostowska-Plak et al., 2013; Haeck et al., 2012; Maksimovic et al., 2012; Wittkowski et al., 2004), and in one article, which used baseline data from a small ($n = 55$) randomized controlled trial for AD, baseline QoL, measured by the Dermatology Life Quality Index, and disease severity measured by the Objective Scoring Atopic Dermatitis scale were not significantly correlated ($r = 0.17$, $P = 0.23$) (Haeck et al., 2012). Changes in the Objective Scoring Atopic Dermatitis scale and Dermatology Life Quality Index over the course of the 6-week trial were also not correlated ($r = 0.19$, $P = 0.20$). In other studies, involvement of readily visible areas of the body, such as the face, and genital involvement are other predictors of impaired QoL in AD (Beikert et al., 2014; Holm et al., 2004; Misery et al., 2007). These findings suggest that for adults, factors outside of objective AD severity have a significant impact on QoL.

Kiebert et al. (2002) used the Short Form (SF)-36 Health Survey, a generic health status measure, to assess QoL among 107 AD patients and compared their results with previously published SF-36 scores for the general population and other medical conditions (Kiebert et al., 2002). Although physical component scores of the SF-36 were higher (indicating better QoL) for AD compared with patients with depression, type 2 diabetes, and hypertension, mental component scores were lower (indicating worse QoL) for AD patients compared with type 2 diabetes and hypertension. Only clinical depression had worse mental component scores than AD. There were no statistically significant differences between AD and psoriasis in Dermatology Life Quality Index and SF-36 physical component scores, but SF-36 mental component scores were significantly lower (indicating worse QoL) in AD. Although these are important data that help contextualize the impact of AD on QoL, the Kiebert et al. study has limitations. First, as with other studies in this review, recruitment was limited to tertiary care. Further, the study did not take into account basic demographics, such as age and sex, when comparing the SF-36 scores of the participant population (mean age = 36 years, 85% female) with

those of the general population or those of people with other diseases. Comparing SF-36 scores with controls matched by basic demographic characteristics would be more valid.

Based on a large sample ($n = 3,308$) recruited from the general high school population in Oslo, Norway, eczema with itch was associated with suicidal ideation (odds ratio = 3.57, 95% confidence interval = 2.46–5.67) and mental health problems as measured by the Strength and Difficulties Questionnaire (odds ratio = 2.57, 95% confidence interval 1.59–4.15) (Halvorsen et al., 2014). A large US population-based survey found that adults with eczema and fatigue were significantly more likely to rate their overall health as only poor or fair compared with participants without eczema or fatigue (odds ratio = 8.63, 95% confidence interval = 7.15–10.43) (Silverberg et al., 2015). These two studies (Halvorsen et al., 2014; Silverberg et al., 2015) provide important, high-quality evidence about the impacts of itch and sleep, respectively, on the lives of AD patients outside of tertiary care, with large sample sizes and, in the case of Silverberg et al. (2015), a population-based design.

QoL in families of AD patients. The impact of AD on QoL is not limited to patients themselves. The International Study on Life with Atopic Eczema found that 30% of patients and caregivers believe that AD affects other members of their household (Zuberbier et al., 2006). That study's large sample ($n = 2,002$) of patients with moderate to severe AD, multinational design (US, France, Germany, Spain, UK, The Netherlands, Mexico, and Poland), and use of validated outcome measures make it a unique source for data on the burden of AD at the more severe end of the spectrum.

Parents of young children with AD can be particularly burdened by a lack of sleep and by the emotional weight of seeing their children suffer. In a study of 270 AD patients and their parents in Chicago and San Francisco, 61% of parents said that their own sleep was disturbed because of their children's AD (Chamlin et al., 2005). However, that study was limited to tertiary care, did not use a validated measure of sleep disturbance, and did not compare sleep disturbance with a non-AD reference group. A UK study of 26 families with a child with AD and 29 families with a child with asthma aimed to compare the two diseases in terms of their impacts on parental sleep (Moore et al., 2006). Although the small sample size limits the interpretation of this study, the results were striking: mothers spent 78 minutes and fathers spent 90 minutes per night attending to children with AD, compared with no time for parents of children with asthma.

In a German study of parents of children with AD, maternal mental health scores on the SF-12 Health Survey, a generic measure of overall health, were significantly impaired on average compared with normative standards, indicating that AD may have a significant impact on the mental health of parents (Warschburger et al., 2004). This study was conducted in a unique setting (pediatric inpatient AD program), limiting generalizability; there was no association between disease severity and parental SF-12 scores; and reference standards were used as a comparison for SF-12 scores instead of a matched control group.

The time required to care for a child with AD is burdensome for families (Chamlin et al., 2004). One study in a

population of patients with relatively severe AD found that families spent an average of 63 minutes per day managing their children's AD (Holm and Jemec, 2004). Another study by the same group found very different results (mean time spent = 17 minutes/day), despite being conducted in a similar setting (Jemec et al., 2006). Additionally, each study found high variability in time spent on treatment among participants. These disparities with regard to time spent on treatment, both within and between studies, point to wide variability in the amount of time families spend on AD. The small sample sizes (n = 128 combined) and single institution setting of these studies are limitations, and time spent on treatment warrants further study.

Although the impact of AD on the families of children with AD has been relatively well studied, data regarding the impact AD has on the families, and specifically the partners, of adult patients with AD are scant.

Specific social impacts of AD. Social isolation can be seen in children with AD at a very young age. Over half of parents interviewed in the study by Chamlin et al. (2004) stated that adults and other children avoided interacting with their children with AD. Compounding that, parents of children with AD also reported that they themselves limited interactions between their children and family and friends so that they would not have to engage in discussions about the child's skin. The International Study on Life with Atopic Eczema found major impacts of AD on self-esteem: 27% of those surveyed had been teased or bullied because of AD, and 36% said AD affects their self-confidence (Zuberbier et al., 2006).

Economic, academic, and occupational impact

Economic impact. Calculating the totality of the direct and indirect financial costs of AD is difficult. It is a common disease with a broad spectrum of severity. Costs include prescriptions, physician visits, emergency and hospital costs to payers and patients, and over-the-counter pharmacy costs for patients; indirect costs include presenteeism (decreased productivity at work), absenteeism (missing work), and detriment to QoL. Based on data from the 2010 National Health Interview Survey, a high-quality population-based survey, it is estimated that 75% of people with eczema visited a doctor at least once in the last year specifically for their eczema (Silverberg, 2015). In the 2010 and 2012 National Health Interview Surveys, eczema was associated with increased physician visits, emergency department visits, and hospitalizations, but could not directly attribute these visits to AD or its established comorbidities. A study from a US pediatric dermatology inpatient service reported that 86% of their admissions were for AD, suggesting that AD is not just an ambulatory disease in the US (Storan et al., 2013).

Among participants with eczema in the 2010 National Health Interview Survey, 12.2% missed 1–2 days of work because of their eczema, and 2.3% missed 3 or more days (Silverberg, 2015). The population-based design of the National Health Interview Survey is a major advantage, but the 2010 survey is limited by its use of a very nonspecific self-report question to assess eczema history, likely leading to the inclusion of other inflammatory skin diseases such as psoriasis.

Table 1. Annual costs of atopic dermatitis and psoriasis in 2004 from Bickers et al. (2006)

	Atopic Dermatitis	Psoriasis
Direct costs	\$1.009 billion	\$1.244 billion
Indirect costs	\$3.219 billion	\$2.414 billion
Total	\$4.228 billion	\$3.658 billion

The most comprehensive investigation of the economic burden of AD in the US to date came from a joint report of the American Academy of Dermatology and the Society for Investigative Dermatology published in 2006 (Bickers et al., 2006). That study examined the financial impact of skin disease overall in the US using data from multiple sources, including national surveys, databases, and published literature. The researchers were able to estimate the costs of individual diseases in the following areas: direct medical costs (including medical visits and medication use), indirect costs (including lost productivity of patients and caregivers and lost productivity due to early mortality), and indirect costs due to impacts on QoL (using a willingness-to-pay model based on previously published Dermatology Life Quality Index data). The total annual burden of AD in that study was \$4.228 billion (in 2004 USD), compared with \$3.658 billion for psoriasis (Table 1). On the basis of the Consumer Price Index provided by the US Bureau of Labor Statistics (Crawford et al., 2015), that is the equivalent of \$5.297 billion in 2015.¹ Direct costs were \$1.009 billion, lost productivity costs were \$619 million, and costs due to decrements in QoL were \$2.6 billion (Bickers et al., 2006); AD had the fourth-highest overall QoL-related costs among skin diseases. The costs in that study are likely an underestimate of the true costs of AD in the US. The AD prevalence estimate used (15.2 million, roughly 5% of the US population in 2004), is lower than other population-based estimates of the US prevalence of AD in children (10.7% in 2003) (Shaw et al., 2011) and adults (7.2% in 2012) (Silverberg et al., 2015). The estimate does not include the costs of over-the-counter products, and productivity losses in this study include only time away due to medical visits, not presenteeism or missed days not associated with medical visits. Additionally, that study is over 10 years old, and costs may have changed because of trends in disease prevalence and prescribing patterns.

Academic and occupational impact. In the International Study on Life with Atopic Eczema study, 32% of participants believed that AD affected their school or work life, and 14% of participating adults believed that their career progression had been hindered by AD (Zuberbier et al., 2006). AD is a risk factor for occupational skin disease (Dickel et al., 2003), and AD patients have reported avoiding specific jobs as a result. Occupations avoided include those in health care, food preparation, cleaning, hairdressing, and automobile repair (Holm et al., 2006a; Nyren et al., 2005).

¹ September 2004 CPI = 189.9

September 2015 CPI = 237.945

Costs in 2015 = 4.228 billion × (237.945/189.9) = 5.297 billion

Future directions

There are a number of research gaps identified through this review (Drucker et al., 2016). First, many important studies on the burden of AD have involved only participants with moderate to severe disease or recruited solely from tertiary care. Given the wide range of disease severity and that many AD patients are managed in primary care, studies in other populations are necessary to capture the full spectrum of the burden of disease. Knowing that QoL and disease severity are often not strongly correlated, research into the reasons for that disparity are needed. More research is needed on the impact of AD on the partners and families of adult patients. With regard to the economic burden of disease, up-to-date comprehensive estimates are lacking for AD in the US. Given that new, potentially costly, medications are being studied to treat moderate to severe AD, information on the costs of AD stratified by disease severity are required.

MATERIALS AND METHODS

In conjunction with the National Eczema Association, specific topics of interest were identified under the umbrella of QoL and academic and occupational impacts (Table 2). For each topic, literature searches were designed with the help of a medical librarian (ES). All searches were performed between September and December 2015 and included literature published from January 1, 2000 onward. Two reviewers (AMD and ARW) performed title and abstract screening for every search. Inclusion criteria were broad and encompassed original articles relating to the specific topics searched for. Exclusion criteria included studies on other types of eczema (e.g., chronic hand eczema), validation studies of outcome measures, interventional studies, and review articles. Additional articles were found through bibliography reviews or other incidental searches or were brought to the authors' attention through other means, such as staff at the National Eczema Association or members of its Scientific Advisory Board.

Full-text articles were reviewed and pertinent data were extracted by one reviewer (AMD or AW). Some articles were excluded at that

stage if they were not found to be relevant to the topic of burden of disease. Narrative reviews were then compiled on each topic.

Although this process has features of a systematic review, it is not a formal systematic review. Many of the research questions and outcomes studied are expansive and nonspecific, making systematic reporting difficult. No systematic approach was used to judge the quality of papers or assess bias. Some articles and other resources that did not meet predefined inclusion criteria were included if they captured important aspects of the burden of AD. Only studies that are most relevant—studies with impactful, original research of direct relevance to the topic of AD burden of disease—are included.

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CONFLICT OF INTEREST

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Table 2. Specific topics of interest investigated

Impact of Atopic Dermatitis on Quality of Life	Economic, Academic, and Occupational Impact
Impact of AD on quality of life	Costs associated with AD (direct and indirect)
Impact of itch on patients with AD	Health care resource use among patients with AD
Pain in patients with AD	Academic and occupational impact of AD
Impact of AD on sleep and further consequences	Impact of AD on socioeconomic status
Impact of AD on patients' self-esteem	Economic, academic, and occupational impact
Impact of AD on marital status and stability	
Impact of AD on patients' social life	
Impact of AD on the QoL of patients' families or partners	
Impact of AD on patients seeking counseling or mental health care	
Time spent managing AD	
Abbreviations: AD, atopic dermatitis; QoL, quality of life.	

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