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The impact of atopic dermatitis on work life – a systematic review

(running head: Atopic dermatitis, work life and sick leave)

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Abstract

Background: Atopic dermatitis (AD) has considerable multidimensional personal and societal costs. However, the extent to which the patient's work life is affected due to AD is more sparsely described in the literature.

Objective: To examine the impact on work life for patients with AD, with a specific focus on choice of education and occupation, sick leave, social compensations and change of job due to AD.

Methods: A systematic literature search was performed in PubMed, EMBASE and Web of Science up to 7th February 2017 for articles on the impact on work life for patients with atopic dermatitis. Results were summarized taking several measures of study quality into account.

Results: 23 articles were found eligible. 5 studies assessed the influence of AD on educational or job choice, without any consistent conclusion, while 8 out of 9 studies with respect to sick leave and 2 on disability pensions found AD to have a negative impact. Studies of change or loss of job and AD showed more diverse results, as not all studies documented a negative effect of AD on work life.

Conclusions: AD imposes a burden extending beyond personal, emotional and financial costs. This review strongly implies that AD affects sick leave, and though not fully clarified, possible also job choice, change or loss of job and even disability pensions for the more severe cases.

Introduction

Atopic dermatitis (AD) is a chronic, inflammatory skin disease with a 1-year prevalence rate estimated up to 20% among children (1) and 2-10% among adult populations (2, 3).

Predominantly, AD has its onset in infancy with a variable prognosis into adolescents and throughout adulthood (4-6). AD imposes a multidimensional burden on the health care system and has a well-documented negative influence on quality of life (QoL) of the patient and family (7-9). Comorbidities comprise atopy/allergy-related diseases such as allergic asthma, allergic rhinitis, food allergy and eosinophilic esophagitis, as well as other diseases such as cardiovascular and psychiatric disorders (10-14). Furthermore, patients with AD are predisposed to skin- and systemic infections (15). However, the extent to which AD affects education, work life, sick leave and social compensations has been sparsely described, though the socio-economic and individual costs of this may be considerable.

The influence of history of AD prior to deciding education or entering the workforce on the first job has only briefly been studied, and conflicting data has been presented (16-20).

AD is no exception among diseases, which cause increased sick leave or loss of work productivity (16, 19, 21-23). However, knowledge is sparse regarding association between disease severity and sick leave, as well as disability pensions awarded due to AD. A history of AD predicts a lifelong significantly increased risk of hand eczema (HE), especially in wet work occupations (24-28). **Previous reviews have examined patient education and intervention programs as part of the management and treatment of atopic dermatitis, but only few reviews addressing AD in relation to work life problems have been**

presented (29, 30). The aim of this review was to systematically examine the literature regarding impact of AD on work life for the individual patient, with a specific focus on choice of education and occupation, sick leave, change of job and disability pensions due to AD. The hypothesis was that patients with AD, aged older than 15 years, are noticeably affected and limited in their work life, particularly with respect to choice of education and job, increased sick leave, more frequent change of job and more health related pensions compared to the background population.

Methods

Literature search

A literature search was performed in the following databases through February 7, 2017:

PubMed (1946-present), EMBASE (1947-present) and Web of Science (1900-present). The

search strategy approach was wide and included “sick leave”, “change of job”, “change of profession”, work-life, insurance, pension* and additional search terms in relation to AD

(Appendix 1). These search terms were inclusion criteria for the outcome parameters of

interest. Studies published online or in print from all years were considered. Studies in

English, German and Scandinavian languages only were included. All epidemiological and

clinical study designs as well as studies with and without a reference group were included.

No criteria of risk estimate or diagnostics of AD were required. Sick leave was defined as the adult’s own absenteeism from the labor market.

Studies with irrelevant clinical outcomes, as well as reviews were excluded in the full text

reading process. In addition, the full text articles’ reference lists were screened for articles of

relevance not found by the databases searched.

Two reviewers (LBN, TA) independently performed selection of the eligible articles and any differences were resolved by discussion.

Data extraction and quality assessment

The data items collected from the studies were: author; year; objective; study design; population; how AD was diagnosed; severity of AD; and outcome measures as influence on work life for the patients with AD with respect to choice of education or job, sick leave, social compensations awarded and change or loss of job. A quality assessment was performed for each study with basis in a validated list of criteria (31) with adjustments to also fit cross-sectional studies included in this review (Appendix 2). Study design, bias and data analysis were considered of higher emphasis in the overall classification of study quality.

Meta-analysis was not appropriate due to the wide heterogeneity of study populations, objectives, designs and outcome parameters across studies. No RCTs were available.

Results

Literature search

The literature search yielded 1 106 non-duplicate articles. After review of the titles and abstracts, 1 051 articles were excluded; an additional 36 articles were excluded after full-text review. The article reference lists were screened for articles not found in the database searches, and four additional articles were identified and included for the review. In total, 23 studies were included in the review. Some studies included more than one outcome. A total

of five studies assessed the possible influence on educational or occupational choice in patients with AD, nine studies assessed sick leave due to AD and two studies evaluated social compensations. A total of 12 studies focused on other relevant influences of AD on work life, such as change or loss of job, and prognosis of dermatitis, in many of which subgroups of AD-patients were identified in study populations with HE. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flow diagram is presented in Figure 1.

Study characteristics

The studies included showed heterogeneity on objective, design, population and outcome parameters. Study designs were cross-sectional, follow-ups, cohorts or register-based with or without matched control groups, and either retrospective or prospective. Publication year ranged from 1993 to 2016. The 23 studies included a total of 103 343 participants from 12 different countries comprising 7 789 individuals with AD.

Education and job choice

In this category there were two cross-sectional studies, two follow-up studies and one case-control. The two follow-up studies, from Germany and Sweden, respectively, found no evidence of AD influencing the choice of job, with respect to deselecting high-risk jobs regarding hand eczema (16, 17), while three Danish studies did (18-20). An overview is presented in Table 1.

In a prospective follow-up study with focus on choice of the very first job (n=1 027) Wei et al. (17) found that AD-patients with pre-hire-onset of the disease did not notably discard high-risk occupations regarding HE compared to participants without pre-hire-onset AD (OR=1.05, 95% CI 0.59-1.87). Another follow-up study by Nyrén et al. (16) found that the proportions of AD cases (n=378) and controls (n=405) in high-risk jobs regarding HE were similar, as was the job-related exposure to different irritants. Bregnhøj et al. (20) found a significantly lower prevalence of AD among hairdressing school students compared to a matched control group. Based on a questionnaire Holm et al. reported that 38% of the patients from the Danish AD patient Association (n=112) had abstained from a specific education or job due to AD (19). The occupations avoided were high-risk jobs regarding development of HE, such as health care, cleaning etc. Another Danish study found occupational irritant exposure less frequent in individuals who had a diagnosis of AD than in individuals who did not (18).

Sick leave

A total of nine studies contributed with data related to sick leave (Table 2). Eight studies (16, 19, 21-23, 32-34) found increased sick leave due to AD compared with individuals without AD, while one study did not support this finding (35). Two studies assessed sick leave indirectly as work-loss costs (21, 34) and two others by lost work productivity (23, 32). The remaining five studies assessed sick leave as days away from work. Furthermore, four of the studies assessed the association between severity of AD and sick leave, of which three studies reported a correlation (23, 32, 34), while one study did not (22).

In a study on lost work productivity from 2016 by Whiteley et al. (32), an AD-cohort was compared to US adults without AD. The lost work productivity (WPAI(36)) was based on a validated instrument consisting of a questionnaire to measure loss of productivity at work and impairment in daily activities over the past 7 days. The lost work productivity was 30% among AD subjects relative to 16.3% in non-AD individuals ($p<0.0001$). Presenteeism, meaning going to work though not healthy, was significantly more frequent in AD compared to non-AD individuals, and possibly less efficacy during working hours appeared to drive the lost work productivity. A cross-sectional Japanese study including 97 AD individuals (23) also reported lost work productivity positively correlated to disease severity.

Sick leave due to AD, defined as more than 7 days away from work, was assessed in a Swedish follow-up study of people with AD ($n=378$) and a matched group of healthy controls ($n=405$). Sick leave due to AD was markedly higher among cases than controls (9.7% vs. 1.9%, $p<0.05$) (16). Number of days absent from work due to AD was assessed in three uncontrolled studies. A cross-sectional study from the Netherlands (22) including AD individuals ($n=253$) found the prevalence of self-reported sick leave due to AD to be 12% for the last two weeks prior to answering the questionnaire, and 42% for the last year. In a multinational cross-sectional questionnaire study of patients with moderate to severe AD ($n=1098$) 9.6% of the work time was reported to be negatively affected by AD, and absence from work during the last year due to flares was 2.7 days per patient (33). Holm et al. (19) reported loss of 5.8 working days per person within the last 6 months due to AD.

In a retrospective matched cohort study Fowler et al. addressed sick leave and disability as indirect work-loss costs in 1 616 AD-patients, and found the mean sick-leave to be 1.7 times higher as compared to a group of 3 950 non-AD persons (21). An American cohort (n=107) found the average yearly cost due to AD sick leave per patient to be \$274 (34).

A 6-year follow-up cohort study including 1 008 AD-patients and 626 matched controls, did not find significantly increased sick leave among persons with AD. Instead they found, that sick leave due to dermatitis was longer than sick leave due to other causes, and this was significantly correlated to severity (35).

Social compensation

Only two studies, both Danish, regarding social compensations were identified. Ibler et al. (37) investigated the number of permanent disability pensions due to skin diseases rewarded in 2003-2008. In a total of 575 disability pensions awarded due to skin diseases within the time period, AD accounted for 15%, ranking as the fourth most frequent among skin diseases in Denmark next to contact dermatitis (20%), 'other dermatological diseases' (25%) and psoriasis (37%).

A previous study regarding the number of disability pensions in Denmark due to AD reported a steady increase from 4.2 per year in 1970 to 18 per year in 2002 (19) (Table 3).

Influence on work life

With respect to influence of AD on work life 12 studies were included, and in this category, objectives, outcomes and study designs are very heterogeneous (Table 4).

A total of ten studies included patients with occupational skin disease/HE, and subgroups of AD patients, and two studies were matched control designed studies. Outcomes with respect to AD compared to non-AD in the different populations and settings differed, ranging from change of occupation or loss of job, severity of hand eczema and prognosis. Overall, AD was reported to influence change or loss of job significantly in three studies (16, 38, 39), while five other studies (35, 40-43) found no marked association. The remaining studies did not assess this outcome.

Persons with AD were found to have poorer outcomes regarding severity as well as healing of HE (40, 44) (41-43, 45). Work-related aggravation of atopic HE may furthermore lead to sick leave, which was investigated in seven studies with populations of HE patients. Among the patients with HE, AD was significantly associated to increased sick leave in four studies (40, 44, 46, 47), whereas three other studies could not support this association (41-43).

Discussion

The results of this systematic review suggest that patients with AD face an unfavorable impact on work life in many aspects. With respect to sick leave relevant studies almost unanimously reported increased frequency in AD-patients, while results for choice of

education and job, as well as for awarding of disability pensions were less consistent. Patients with occupational HE, and concomitant AD were in many studies markedly negatively influenced in their work life. None of the studies included in the present review found a protective or positive effect of AD with respect to the influence on work life.

Data on whether a diagnosis of AD affects educational or occupational choice is inconsistent. Problematically, two of the studies reporting AD to impact on educational or occupational choice (18, 19) were of the lowest quality ranking, and only included Danish adults, limiting extrapolation of the association to other countries. One explanation could be that Denmark compared to the other countries, might have better implemented pre-employment occupational counseling. A history of AD, which was the case for both studies, might be forgotten prior to entering a high-risk job, potentially uncovering the AD and thereby causing more work-related problems for the individual in contrast to patients with current AD and awareness of the possible problems. The third Danish study (20) documented a healthy worker effect and supported the idea that people with AD avoid certain occupations. Unfavorable for Wei et al. were that the outcome focused on patient's *first* job, which might not be one's real choice of job, and thereby inherently give incorrect results.

With respect to sick leave more consistent results were found. All studies but one reported increased sick leave in AD patients. The study not confirming a significant difference in sick leave is of importance due to the relatively high quality ranking of the study (Table 2); however data were obtained before 1993 and may not be directly comparable to more recent studies. Sick leave is influenced by many factors, such as cultural and personal background, social security system and labor-market fluctuation, and not entirely based on disease

severity. In all studies sick leave was self-reported, inducing a certain risk of recall bias, but ensuring homogeneity between the studies. The recall bias was minimized in the studies where sick leave was counted within the last few weeks (16, 22, 23, 32). Many of the studies, however, may be influenced by selection bias (19, 22, 23, 32, 35), as the study population was collected from patients' organizations or hospital dermatological clinics, where the burden of disease might be higher compared to AD-patients recruited from outside. Severity was self-reported in all studies and in most studies graded as moderate. This implies a possible overestimation of sick leave, and limits the conclusions to patients with moderate and severe disease. On the other hand, a possible aspect of undetected or undocumented presenteeism seems realistic, meaning that people with AD are at work in spite of disease due to the job insecurity related to AD. The countries represented ranged from Europe, including Scandinavia, and America to Japan, demonstrating sick leave among AD individuals as a worldwide problem in developed countries. Interestingly, the costs of sick leave was found to be high (34) and almost doubled (21) in AD individuals. Though no information on AD severity was given in Fowler et al., the study population was large and nationally representative making the cost estimate liable for the average working AD-individual. The calculation of these indirect costs may even be underestimated, since further losses in worker productivity related to adverse effects on QoL were not included.

Sparse information on disability pensions due to AD is eligible in the literature. Two studies available, unfortunately without any reference groups, were included, and no firm conclusions can be drawn on this subject.

A history of AD predicts a lifelong significantly increased risk of HE, since the skin barrier function is compromised in AD patients (48-50). HE is a major occupational skin disease, which can cause chronicity and disability, prolonged sick leave, change of job or social compensations. In populations of HE-patients subgroups with a medical history of AD have been assessed in relation to influence on work life. Although findings are not unanimous, AD in occupational settings overall seems to be a predominantly unfavorable factor. Six studies from low to moderate/high quality found a significantly negative influence on work life, while two studies of moderate study quality did not. No clear tendency was found between newer studies compared to older ones, and no significant differences between countries were detected.

The studies examining change or loss of job reported inconsistent data, as was also the case in patients with occupational HE with respect to the association of AD and sick leave. Possible explanations may be the healthy hire effect, and the healthy survivor effect, where healthy individuals are selected prior to entering a job (20) or individual levels of coping decide whether the job situation is markedly influenced regardless of disease. Neither studies of higher or lower quality were associated to a significant outcome. However, an overweight of studies on job-change did not find a significant association to AD.

International guidelines (51, 52) and textbooks (53-55) support the idea that adolescents with AD should be advised on avoidance strategies and informed about the risk related to entering certain occupations with skin exposure to irritants and physical trauma. Educational programs like eczema schools are highly efficient to improve skin symptoms and recommended by European Dermatology Forum with the highest level of

evidence (52). Patient education/eczema schools, self-help groups and National support groups may benefit the patient in different ways, including reduced sick leave (54), and may help to relieve the burden of the disease.

Strength of this present study was the systematic approach, including a detailed and broad search strategy, resulting in a wide range of studies. Quality assessment was made in order to compensate for the problematic direct comparison of the studies and outcome parameters.

This review has some limitations, as relatively few studies have examined the impact on work life in individuals with AD. The studies were conducted differently with respect to designs, heterogeneity in outcomes, populations and AD diagnosis.

A possible overestimation of impact of AD occurred in studies of patients with more severe dermatitis than the average AD person. Presumably, AD can be a hidden cause of HE, but undetected and thereby underestimating the negative impact of AD on work life.

Future research in this area should focus on prospective cohort studies, including data on disease severity and with diagnosis based on clinical examination rather than self-reporting.

Though the literature up to now describes a higher burden for AD individuals in jobs, future improved patient guiding and new options in medical treatment might lead to other results.

Conclusions

Atopic dermatitis imposes a burden extending beyond personal, emotional and financial costs. This review strongly suggests that AD negatively affects sick leave, and though not fully clarified, in the literature, may also negatively affect job choice and change or loss of job and even disability pensions for the most severe cases.

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Table 1. Studies on the impact on educational or occupational choice for individuals with AD by publication year.

Reference, Author Country, Year (journal)	Study design	Population	AD diagnosis	AD severity	Outcomes	Results	Quality assessment
17 Wei et al., Germany, 2016 (<i>Int Arch Occup Environ Health</i>)	Prospective cohort, followed-up from adolescence until 19-24 years of age Q	N = 1 027; 13% with pre-hire-onset AD. Sampled randomly from schools.	Doctor diagnosed	n.a.	Influence of pre-hire-onset AD on the choice of high-risk exposure of HE in the first job (def. as >8 hours per week)	n.s.: OR 1.05 (95% CI 0.59-1.87)	<i>Moderate/high</i> Strengths: No recall bias Reference group OR adj. for possible confounders Present study Limitations: First job might not be ones real job No info. on AD severity
18 Bandier et al., Denmark, 2013 (<i>Contact dermatitis</i>)	Cross-sectional Q	N = 3 348; 9% AD. Randomly chosen Danish	UK Working Party's diagnostic criteria(49)	n.a.	Occupational irritant exposure in AD vs. non-AD Occupational irritant exposure in adulthood among participants reporting HE before 15 years of age: FLG mutation carriers with AD vs. non-FLG carriers without AD	45.5% vs. 37.8% (p=0.01) OR 0.08 (95% CI 0.01-0.65)	<i>Low</i> Strengths: Large study population Limitations: Recall bias Selection bias (RR low) Misclassification: self-reported HE and AD
20 Bregnhøj et al., Denmark, 2011 (<i>Contact Dermatitis</i>)	Case-control Q	N(hairdressers) = 374, from hairdressing school N(non-hairdressers) = 1 277 age-, gender- and city code matched from the general population	UK Working Party's diagnostic criteria	n.a.	Prevalence of AD among hairdressers (high-risk occupation of HE) vs. controls	21.4% vs. 29.8% (p=0.001)	<i>Moderate/high</i> Strengths: Matched control group High response rate among cases Limitations: Severity not assessed Misclassification: self-reported AD
16 Nyrén et al., Sweden, 2005 (<i>Sc and Work</i>)	Population-based follow-up from childhood until the age of 31-42 years.	N(AD) = 378 N(no-AD) = 405. Recruited from medical records (incl. school	Medical records reviewed by dermatologists	n.a.	Proportion of cases and controls in present high-risk job of HE	n.s.: 16.6 % vs. 17.6 %	<i>Moderate/high</i> Strengths: Population-based and hospital records (no selection bias) Matched control group

<i>Environ Health)</i>	Matched control group. Q	health care). Controls matched for age and gender.					Response rate high (71%) Representative Limitations: No control for confounding Present job might not be ones first choice of job (possible underestimation)
19 Holm et al., Denmark, 2004 (<i>J Eur Acad Dermatol Venereol</i>)	Cross-sectional Q	N(AD) =112; 12 excluded based on insufficient answers to this subject. Patients from the Danish Association of Atopic eczema (AEF)	AEF members	35% mild 50% moderate 15% severe Severity based on Q	Proportion who abstained from a specific educ./job	38 %; not sign. associated to AD severity	Low Strengths: Severity assessed; Compared to responders who did not avoid a specific job Population: high quality of data Limitations: Study design Recall bias Selection bias (AEF members + actively job choice in adult life, not those who subconsciously decided early through advice to avoid certain jobs → possible underestimate) Descriptive values No ref. group Patient-rated severity

Q: questionnaire, n.a.: not assessed, n.s.: not significant, HE: hand eczema

Table 2. Studies on sick leave due to AD by publication year.

Reference, Author Country, Year (journal)	Study design	Population	AD diagnosis	AD severity	Outcome	Results	Quality assessment
32 Whiteley et al., 2016, USA (<i>Curr Med Res Opin.</i>)	Cohort of cases and controls. Q	N(AD) = 428 N(no-AD) = 74 572 From US national survey.	AD during the last 12 months Patient-reported; 84.5% reported diagnosis of AD from a physician	43% mild 33% moderate 8% severe 16% unknown	Lost work productivity (WPAI) among AD vs. non-AD workers regarding in the past 7 days Rate of long-term disability in mild vs. moderate/severe AD	30% vs. 16.3% (p<0.05), increasing with severity of AD 6.5% vs. 13.8% (p<0.05)	<i>Moderate</i> Strengths: Large sample size; generalizability Present study Limitations: Bias: Recall/misclassification, selection No-AD could have had AD earlier (>12m ago), but counted as controls (possible underestimation) General health version of WPAI instrument (possible overestimation) Patient-rated severity
22 Van Os-Medendorp et al., 2015, The Netherlands (<i>J. Clin. Med.</i>)	Cross-sectional Q	N(AD) = 253 recruited from outpatient clinic and patients' organization	Outpatient clinic: dermatologist Patients from AD organization: self-reported	POEM 82% moderate to very severe	Self-reported sick leave due to AD during the past: - two weeks: Mean number of days (sd): - one year: Mean number of days (sd): Sick leave association to severity of dermatitis	12% 0.3 days (0.9) 42% 5.7 days (12.2) n.s.	<i>Low</i> Strengths: Severity assessed Present study Precis def. of sick leave Limitations: Bias: recall and selection bias (study pop. with a higher burden of AD → possible overestimation) Different AD diagnostics Response rate low
23 Yano et al., 2013, Japan (<i>J Dermatol.</i>)	Cross-sectional Q	N(AD) = 97, recruited from the Hospital and included for this analysis	SCORAD(50)	Mean: 35.5±21.9	Total Work Productivity Impairment, TWPI, (number of hours absent from work and influence on productivity due to AD during the past 7 days)	Mean ±SD: 32.8 % ± 23.7 Sign. correlated to severity of AD	<i>Low</i> Strengths: Disease-specific version of TWPI Severity assessed and doctor-diagnosed Recall bias minimal (7 days) Limitations: 7 days: narrow perspective (some might be sick due to AD, but not at the specific time of investigation → underestimation) No ref. group (possible overestimation of impact); however, compares with TWPI in other diseases found in other studies
33	Cross-	N (>17 years) =	The patient's	100% moderate or	Work time affected during flares	9.6 %	<i>Low/moderate</i>

Zuberbier et al., USA, Multinational (<i>J Allergy Clin Immunol.</i>)	sectional, Q (interviewed)	1 098 Recruited by treating physicians, randomly chosen in 8 countries.	treating physician AD flare within the last 6 months	severe	No. of days absent from work due to a flare/year/person	2.7	Strengths: Large sample size Multinational (explorative) and weighted results compared to the prevalence of AD for the countries Geographic spread of participants nationally Limitations: Recall bias Moderate/severe AD (→ possible overestimation of outcome) No control group
21 Fowler et al., 2007, USA (<i>Manag Care Interface.</i>)	Retrospective matched cohort	n(AD)=1 616 n(no-AD)= 3 950 Active employees found via database	ICD-9-CM: ≥2 AD claims	n.a.	Mean indirect work-loss costs (disability + sick leave) in AD vs. no-AD	\$148 vs. \$85 per patient per month (p<0.001)	<i>Moderate</i> Strengths: Sample size: large and nationally representative Matched control-group Diagnosis certain Limitations: Further costs for employers than the disability and sick-leave and losses in worker productivity stemming from adverse effects on QoL (→ possible underestimate) Severity of AD not assessed
16 Nyrén et al., Sweden, 2005 (<i>Sc and Work Environ Health</i>)	Population- based follow- up from childhood until the age of 31- 42 years. Matched control group. Q	N(AD) = 378 N(no-AD) = 405	Medical records reviewed by dermatologists	n.a.	Self-reported sick leave (>7 days) due to AD reported by cases and controls Sick leave in males vs. females among cases:	9.7% vs. 1.9% (p<0.001) 6.3% vs. 12.3% (p<0.05)	<i>Moderate</i> Strengths: Population-based and hospital records (no selection bias) Matched control group RR high (71%): representative Limitations: Recall bias (Q) Imprecise def. of sick leave
19 Holm et al., Denmark, 2004 (<i>J Eur Acad Dermatol Venereol</i>)	Cross-sectional Q	n(AD) = 112 Patients from the Danish Association of Atopic eczema (AEF)	AEF members	35% mild 50% moderate 15% severe Severity based on Q	Mean loss of working days due to AD Sick leave in the AD patients compared to the national average (background pop. in DK, 2001)	5.8 days/6 months 148%, not gender-, age- or occupational matched.	<i>Low</i> Strengths: Compare to background pop. in DK Population: high quality of data Limitations: Recall bias Selection bias (AEF members + actively job choice in adult life, not those who subconsciously decided early through advice to avoid certain jobs → possible underestimate) Ref. group: back ground population, not

							matched (raw data). Descriptive values
34 Fivenson et al., 2002, USA (<i>J Manag Care Pharm.</i>)	Cohort	N(adults with AD) = 107 Recruited from hospital	ICD-9 code of AD defined by a physician, reported by patient	51% mild 29% moderate 3% severe 17% unknown (Provider-assessed)	Cost/year/patient (based on patient's answer and adjusted gross annual income) due to days lost from work due to AD	\$274 Sign. higher for individuals with severe disease	<i>Low/moderate</i> Strengths: Specific cost due to AD sick leave calculated Severity assessed (in two ways; patient and provider) Limitations: Recall bias (in AD severity) Selection bias
35 Lammintausta et al., 1993, Finland (<i>Acta Derm Venereol.</i>)	Cohort, 6-years follow-up. Matched control group	N(AD) = 1 008 recruited from derma. depart. N(no-AD) = 626 Sex- and age matched, no info. how they were recruited	Medical records	63% of AD patients: moderate or severe	Proportion of AD vs. non-AD on sick leave/year	n.s.: 70 % vs. 67 % (n.s.)	<i>Moderate/high</i> Strengths: Study design Diagnosis (no misclassification) Severity assessed (consistent by a dermatologist) Limitations: Recall bias (interviewed at follow-up) Selection bias possible (no info. of controls recruitment) Old study No information on duration of sick leave

Q: questionnaire, n.a.: not assessed, POEM: Patient-oriented eczema measure, SCORAD: Scoring atopic dermatitis

Table 3. Studies on social compensation due to AD by publication year.

Reference, Author Country, Year (journal)	Study design	Population	AD diagnosis	AD severity	Outcome	Results	Quality assessment
37 Ibler et al., 2010, Denmark (<i>Acta Dermatovenerol Croat.</i>)	Register study	Danish adult population	Database: Statistics Denmark, population and disability pension registers, National Social Appeal Board	n.a.	Number of disability pensions rewarded due to AD in 2003-2008 in Denmark	14.2/year	<i>Low</i> Strengths: Registry: bias minimized Ref. to disability pensions rewarded in other skin diseases Limitations: No. ref. to disability pensions in background population or other countries
19 Holm et al., Denmark, 2004 (<i>J Eur Acad Dermatol Venereol</i>)	Register study	Danish adult population	Database: Statistics Denmark, population and disability pension registers, National Social Appeal Board	n.a.	Number of disability pensions rewarded due to AD in Denmark	Year 1970: 4.2/year Year 2002: 18/year (Increase: 450%)	<i>Low</i> Strengths: Registry based: no recall bias, misclassification or selection bias Limitations: No. ref. to disability pensions in background population or other countries

Table 4. Studies on influence on work life due to AD by publication year. Outcome measures: Change of occupation or loss of job, educational level, severity, prognosis and work related aggravation of atopic hand dermatitis leading to sick leave.

Reference, Author Country, Year (journal)	Study design	Population	AD diagnosis	AD severity	Outcome	Results	Quality assessment
38 Landeck et al., 2012, Germany (Br J Dermatol.)	Prospective cohort, 3-year follow-up	N(OICD) = 432; 71.2% with AD. Hospitalized of long-lasting chronic OHE	Dermatologist and Q AD def. ongoing or past flexural eczema and/or >10 points on the Erlangen atopy score(51)	n.a. Severity of HE documented by dermatologist	Sick leave during 1 year in subjects with ICD and AD status vs. 'pure' ICD patients Abandoning one's profession after 3 years: AD in combination with FLG loss-of-function mutation vs. 'pure' ICD patients	n.s.: 6.9% 6.6% OR: 3.1 (95% CI: 1.1-9.1)	<i>Moderate</i> Strengths: Design (prospective, follow-up no recall bias) Limitations: Small subgroups of ICD and atopy and FLG mutation, in spite of large cohort of ICD patients Sick leave at the exact follow-up time (underestimation)
39 Lysdal et al., 2011, Denmark (Contact Dermatitis)	Cohort Q	N = 5 329 All graduates from hairdressing vocational school in DK 1985-2007. 480 (9 %) of ex-hairdressers left the job because of HE	UK Working Party's diagnostic criteria	Amount of flares: Categories based on answers from Q: "only once and for <2w", "only once but for >2w", "several times", "(almost) all the time"	Prevalence of AD history in ex-hairdressers vs. hairdressers OR for AD as explanation among ex-hairdressers who left the job due to HE:	23.7% vs. 21.0% (p = 0.017) OR=1.59 (95% CI: 1.16-2.19)	<i>Low/moderate</i> Strengths: Large sample size High RR (67.9%) Limitations: Recall bias and misclassification: self-reported and not clinically diagnosed Selection bias (high percentage of non-responders among ex-hairdressers)
40 42 Mäлкönen et al., 2010, Finland (Br J Dermatol.)	Follow-up 7-14 years after OHE diagnosis Q	N(OHE) = 605; 15% with AD	Medical records: present or past AD	n.a.	OHE patients with vs. without additionally AD: -Healing rates at follow-up -Continuation of OHE at follow-up Sick leave, change of work tasks or job, change of occupation or loss of job in AD vs. non-AD	31 % vs. 44 % (p=0.004) OR 1.86 (95% CI: 1.08-3-19) n.s.	<i>Moderate</i> Strengths: Large sample size High response rate after a long follow-up Study population: wide range of occupations in the same national referral unit Limitations: Severity of HE nor AD assessed Recall bias Misclassification
44 Agner et al., 2009, Multi-national	Cross-sectional Multi-center (10 European clinics)	N(HE) = 416; 23.5% with AD	Medical history	n.a. (clinical examination of	Multivariate linear regression analysis with AD as independent variable to the dependent variables: - Severity of HE, β		<i>Moderate/high</i> Strengths: International Relatively large sample size

(Contact Dermatitis)				HE: HECSI)	- Frequency of sick leave, β	0.116 (p=0.024) 0.122 (p=0.023)	High RR No selection bias Limitations: AD severity n.a.
46 Lerbaek et al., 2008, Denmark (Contact Dermatitis)	Population-based clinical 8-years follow-up	N = 274; 20.7% AD Subjects with and without HE in a cohort of same- sex twins	UK Working Party's diagnostic criteria. Structured interview	n.a.	AD as independent risk factor for ever having been on sick leave Persistence of HE associated to having AD	OR =2.9 (95%CI 1.0-8.1) OR: 1.0 (0.4-2.5)	<i>Moderate</i> Strengths: Population based Twin study Limitations: Misclas. (and selection bias): HE included from Q ($\rightarrow$ potential overestimate of HE consequences) Recall bias Low participation rate AD diagnose interviewed, however self- reported symptoms if not present at examination.
41 Cvetkovski et al., 2006, Denmark (Arch Dermatol.)	Cohort with 1- year follow-up Q	N(OHE) = 540; 18% AD	Past flexural eczema or AD currently diagnosed by a dermatologist	n.a.	AD vs. non-AD after 1 year: - Persistently severe or aggravated OHE - Prolonged sick leave (>5 weeks) - Loss of job	RR 1.53 (95% CI: 1.1- 2.2) RR 0.58 (95% CI: 0.2- 1.8) RR 1.12 (95% CI: 0.2- 5.3)	<i>Low/moderate</i> Strengths: Design (prospective, control group) Limitations: Selection bias Losses to follow-up (mild cases might be missed $\rightarrow$ overestimation of outcomes) Sample size too small when a reduction of 50% in prolonged sick leave cannot be detected
16 Nyrén et al., Sweden, 2005 (Sc and Work Environ Health)	Population- based follow- up from childhood until the age of 31- 42 years. Matched control group. Q	N(AD) = 378 N(no-AD) = 405	Medical records reviewed by dermatologists	n.a.	Change of job in AD vs. non-AD	8.9% vs. 1.9% (p<0.01)	<i>Moderate</i> Strengths: Population-based and hospital records (no selection bias) Matched control group Response rate high (71%) Limitations: Recall bias (Q) Imprecise def. of sick leave
43 Meding et al., 2005, Sweden (Contact Dermatitis)	12-year follow- up Q	N(OSD) = 517; 26% AD Cases of reported OSD with records of medical investigation on	Mikrofilm records reviewed by dermatologist, incl. info. on previous or on- going AD	n.a.	AD vs. non-AD: - change of job - sick leave - skin symptoms last 12 months	OR 1.0 (95% CI: 0.6-1.6) n.s. (OR not given) OR 2 (95% CI: 1.1-3.5)	<i>Moderate</i> Strengths: Design (prospective, control group) Limitations: Recall bias Selection bias

40 Cvetkovski et al., 2005, Denmark (<i>Br J Dermatol.</i>)	Cross-sectional Q	microfilm N(OHE) = 621; 16.4% AD All new patients with recognized OHE from the Danish National Board of Industrial Injuries	Past flexural eczema or currently diagnosed atop	n.a. Characterized for HE	AD vs. non-AD regarding: - Severity of OHE (ref.: mild OHE): - Prolonged (>5w) sick leave due to OHE (ref.: <5w) - Loss of job	OR 1.22 (95% CI: 1.08- 1.39) OR 1.66 (95% CI: 1.12- 2.46) OR 1.34 (95% CI: 0.93- 1.93)	<i>Moderate</i> Strengths: Reference group Response rate high (82 %) Limitations: Bias: recall and selection (severe cases more likely to participate, mild cases may not be notified as occup.)
45 Dickel et al., 2003, Germany (<i>J Invest Dermatol.</i>)	Cohort	N(OSD) = 3 730; 37% AD. Confirmed OSD between 1990-1999	AD: personal history of flexural involvement or lichenified dermatitis and atopy score ≥ 10	n.a.	Median age of AD cases vs. non- AD Median occupational period of exposure in AD cases vs. non-AD	24y vs. 28y (p<0.0001) 36 vs. 38.5 months (p<0.0001) Conclusion: AD workers developed OSD at a significantly younger age and earlier in working life	<i>Moderate</i> Strengths: Large sample size Population setting (nearly complete reporting of potential cases of OSD) Limitations: OSD possibly underestimated due to underreporting/-diagnosing)
47 Holm et al., 1994, Norway (<i>Acta Derm Venereol Suppl (Stockh.)</i>)	Cross-sectional Q	N = 203; Hairdressers in the county of Oslo without or with current HE	Patient-reported diagnose by own physician	n.a.	Prevalence of AD among hairdressers with current HE vs. hairdressers with earlier HE Sick leave due to eczema in hairdressers with current HE vs. hairdressers with earlier HE	12.7% vs. 3.9% (p = 0.01) 18% vs. 6% (p = 0.05)	<i>Low</i> Limitations: Recall bias Diagnosis of AD (patient-reported, severity n.a.) Sick leave not def. Old study
35 Lammintausta et al., 1993, Finland (<i>Acta Derm Venereol.</i>)	Cohort, 6-years follow-up. Matched control group	N(AD) = 1 008 recruited from derma. depart. N(no-AD) = 626 Sex- and age matched, no info. how they were recruited	Medical records	63% of AD patients: moderate or severe	AD vs. no-AD regarding: - History of ≥ 1 unemployment periods Work changes	69% vs. 30% (p value not given) n.s.	<i>Moderate/high</i> Strengths: Study design Diagnosis (no misclassification) Severity assessed (consistent by a dermatologist) Limitations: Recall bias (interviewed at follow-up) Selection bias possible Old study No information on duration of sick leave

OICD: Occupational irritative contact dermatitis, HE: hand eczema, OHE: occupational hand eczema, HECSI: Hand eczema severity index, OSD: occupational skin disease

1. Williams HC, Burney PG, Hay RJ, Archer CB, Shipley MJ, Hunter JJ, et al. The U.K. Working Party's Diagnostic Criteria for Atopic Dermatitis. I. Derivation of a minimum set of discriminators for atopic dermatitis. *The British journal of dermatology*. 1994;131(3):383-96.
2. Kunz B, Oranje AP, Labreze L, Stalder JF, Ring J, Taieb A. Clinical validation and guidelines for the SCORAD index: consensus report of the European Task Force on Atopic Dermatitis. *Dermatology (Basel, Switzerland)*. 1997;195(1):10-9.
3. Diepgen TL, Sauerbrei W, Fartasch M. Development and validation of diagnostic scores for atopic dermatitis incorporating criteria of data quality and practical usefulness. *Journal of clinical epidemiology*. 1996;49(9):1031-8.

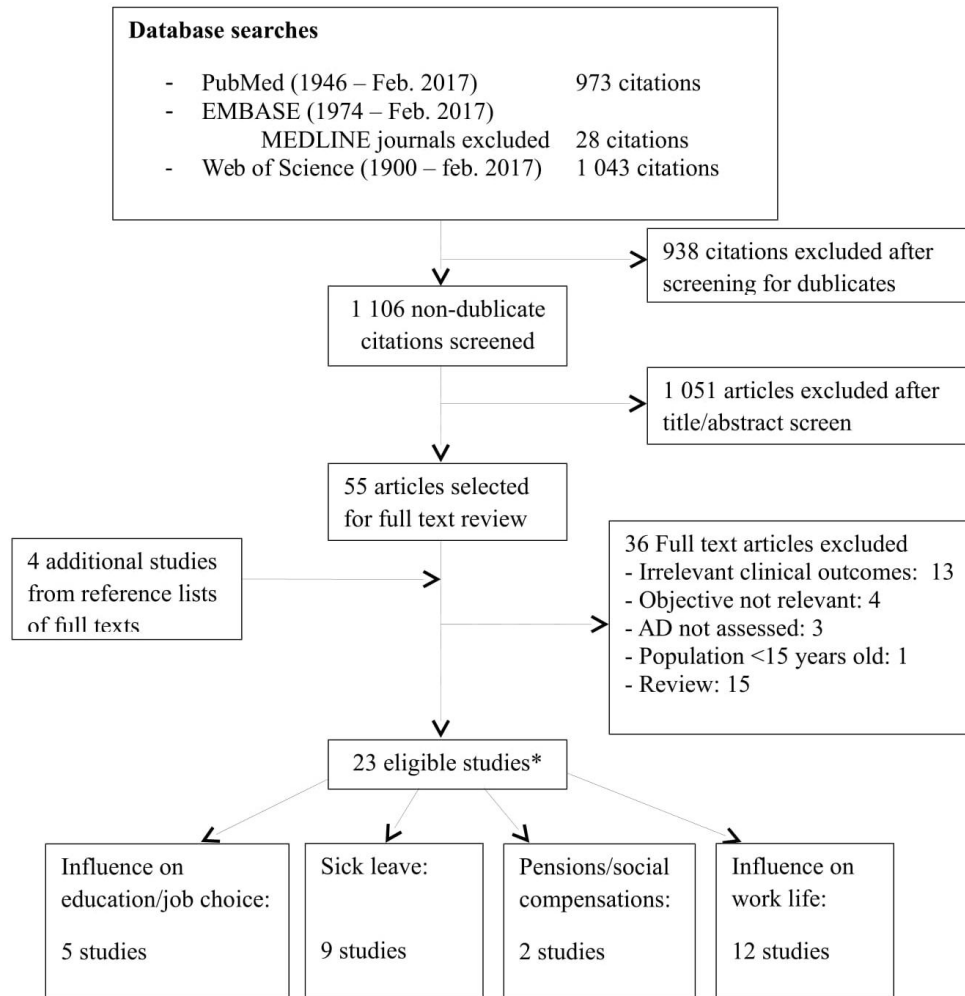
Appendix 1. Literature search scheme for PubMed.

	1) Population: patients with AD (connected with OR)	2) Job situation (connected with OR)	3) Pensions, compensations (connected with OR)
MeSH	Dermatitis, atopic	Socioeconomic factors Including: - Career mobility - Pensions - Social class - Employment - Unemployment - Educational status - Social conditions	Insurance Including: - Disability - Workers compensation - Health insurance
Text word	“atopic dermatitis” “atopic eczema” Atopy	“sick leave” Socio-occupational Unemployment Employment Social impact/factor/problem* “job change” “change of job” “change of profession” work-life	Insurance Pension* “economic compensation”
Search strategy: 1 AND (2 OR 3)			

Appendix 2. Description of quality assessment of studies included in the review

Quality categories	High	Moderate	Low
<i>Study design</i>	Prospective	Retrospective	Retrospective
	Cohort	Case-control Register	Cross-sectional
	Control group	Reference group	None
<i>Response rate</i>	>75%	50-75%	<50%
<i>Sample size</i>	Large (>500 AD patients)	Moderate (100-500)	Small (<100)
<i>Objective measures (specific disease criteria of AD and outcomes given)</i>	Defined by a physician, severity assessed	Partly by physician or the patient	By the patient
<i>Bias (selection, misclassification, recall)</i>	None	One identified	Two or more biases
<i>Control for confounding</i>	Adjustment for at least three factors (or use of randomization) or list of potential confounders	Adjustment for at least one factor	No adjustment for confounding factors
<i>Data analysis</i>	Precise P values or CIs given	Precise P values or CIs given	Not given
<i>Statistical tests</i>	Test statistic specified	Test statistic specified	Not specified
<i>Demographic data</i>	Statistical analysis	Listed	Not mentioned

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) Diagram



* Some studies included more than one of the outcomes reviewed.