# Section 1 Introduction and methods

**Section 1: Introduction and methodology**

**Summary**


- Atopic dermatitis (AD) is an inflammatory skin condition associated with other atopic manifestations such as asthma, rhinitis and food allergy.
- It presents in varying degrees of severity from a mild disease treated with over-the-counter products to severe disease requiring treatment with systemic immunosuppressive agents.
- Common symptoms of AD include itchiness, red to brownish-grey patches on the skin, small, raised bumps, which may leak fluid and crust over when scratched, and/or thickened, cracked, dry, scaly skin.
- Onset of AD occurs most commonly in infants and children, however it can occur at any age with clinical features varying with age of onset.
- Patient Experience, Expectations and Knowledge (PEEK) is a research program developed by the International Centre for Community-Driven Research (CCDR). The aim of PEEK is to conduct patient experience studies across several disease areas using a protocol that will allow for comparisons over time (both quantitative and qualitative components). PEEK studies give us a clear picture and historical record of what it is like to be a patient at a given point in time, and by asking patients about their expectations, PEEK studies give us a way forward to support patients and their families with treatments, information and care.
- In this PEEK study, 100 people diagnosed with AD throughout Australia participated in the study that included a structured interview and quantitative questionnaire. This study in AD is therefore the largest mixed methodology study worldwide conducted in last five years and the only study that focuses on an Australian population. In addition, PEEK is a comprehensive study covering all aspects of disease experience from symptoms, diagnosis, treatment, healthcare communication, information provision, care and support, quality of life, and future treatment and care expectations.

## Introduction

Atopic dermatitis (AD) is an inflammatory skin condition associated with other atopic manifestations such as asthma, rhinitis and food allergy.[1-3] It presents in varying degrees of severity from a mild disease treated with over-the-counter products to severe disease requiring treatment with systemic immunosuppressive agents.[4] AD can be classified into either intrinsic or extrinsic AD with the classification of disease depending on co-existence with allergic features.[5] Common symptoms of AD include itchiness, red to brownish-grey patches on the skin, small, raised bumps, which may leak fluid and crust over when scratched, and/or thickened, cracked, dry, scaly skin.[6] Onset of AD occurs most commonly in infants and children, however it can occur at any age with clinical features varying with age of onset.[7]

Genetic predisposition and environmental factors are known to be related to the development of AD. The biological mechanisms that lead to AD are characterised by epidermal barrier defects and T-helper type 2 mediated inflammation.[8] Barrier defects associated with AD result in what is known as the 'atopic march' which can lead to food allergy, allergic rhinitis and asthma.[9] This march is thought to occur due to epicutaneous sensitization by allergens followed by migration of sensitized immune cells to respiratory epithelia.[10] The mutation of the filaggrin gene, which encodes a protein that is important in maintaining epidermal barrier protection, and is a risk factor for AD.[11] This mutation has been observed to increase susceptibility to asthma and allergic rhinitis in people who also have AD.[11] Abnormalities in other epidermal barrier proteins include loricrin and involucrin.[12]

AD has been linked to multiple non-atopic comorbidities such as learning disorders in children (ADHD), speech disorders, anxiety and depression headaches, anaemia and epilepsy[4]. AD is also associated with injury such as fractures and is likely from low bone mineral density attributable to oral corticosteroid and cutaneous inflammation that leads directly to bone loss.[13,14]

The prevalence of atopic dermatitis in Australia is poorly reported, the most recent publication from the ABS that reports data on eczema was the 2004-5 National Health Survey, and this publication does not report specifically on atopic dermatitis but a more general term of dermatitis and eczema.[15] The prevalence of dermatitis and eczema in Australia in the 2004-5 Australian National Health Survey is estimated at 221, 200, approximately 1.1% of the population.[15] The age group most affected are those aged 0-14, with a prevalence of 99,400, approximately 2.5 % of children aged 0 to 14. Other studies of atopic dermatitis in Australia report the estimate the prevalence rates in children in Australia and New Zealand at 10.7%,[16] in Australian pre-schoolers at 30.8%,[17] and adults in central Victoria at 6.9%.[18]

### *Patient Experience, Expectations and Knowledge (PEEK)*

Patient Experience, Expectations and Knowledge (PEEK) is a research program developed by the International Centre for Community-Driven Research (CCDR). The aim of PEEK is to conduct patient experience studies across several disease areas using a protocol that will allow for comparisons over time (both quantitative and qualitative components). PEEK studies give us a clear picture and historical record of what it is like to be a patient at a given point in time, and by asking patients about their expectations, PEEK studies give us a way forward to support patients and their families with treatments, information and care.

The research protocol used in PEEK studies is independently driven by CCDR. PEEK studies include a quantitative and qualitative component. The quantitative component is based on a series of validated tools. The qualitative component is the result of two years of protocol testing by CCDR to develop a structured interview that solicits patient experience data and provides patients with the opportunity to provide advice on what they would like to see in relation to future treatment, information and care. The structured interview has also been designed so that the outcomes of PEEK studies can inform policy, research, care, information, supportive care services and advocacy efforts.

## Methodology

### *Participants*

To be eligible for the study, participants needed to have been diagnosed with AD, have experienced the healthcare system in Australia, be 18 years of age or older, be able to speak English, and be able to give consent to participate in the study. Recruitment commenced on 7 October 2017 and the study closed for recruitment on 5 December 2017. Participants were recruited via email and social media through CCDR and study partners the Eczema Association of Australasia and Allergy and Anaphylaxis Australia.

### *Ethics*

Ethics approval for this study was granted (as a low or negligible risk research study) by the Centre for Community-Driven Research Ethics Committee (Reference CS_Q4_03).

### *Data collection*

Data for the online questionnaire was collected using Zoho Survey (Zoho Corporation Pvt. Ltd. Pleasanton, California, USA, www.zoho.com/survey). Participants completed the survey between October 2017 and January 2018.

There were seven researchers who conducted telephone interviews and used standardised prompts throughout the interview. The interviews were recorded and transcribed verbatim. Identifying names and locations were not included in the transcript. All transcripts were checked against the original recording for quality assurance.

Interview data was collected from October 2017 and January 2018.

### *Online questionnaire (quantitative)*

The online questionnaire consisted of the 36-Item Short Form Health Survey (SF36) (RAND Health)[1], a modified Cancer Care Coordination Questionnaire for Patients (CCCQ) (Young et al 2011[2]), the Short Fear of Progression Questionnaire (FOP12) (Hinz et al[3]), and the Partners in Health version 2 (PIH) (Petrov 2010)[4]. In addition investigator derived questions about demographics, diagnosis, treatment received and future treatment decisions making were included.

### *Structured Interview (qualitative)*

Interviews were conducted via telephone by a registered nurse, allied health professional or researcher with a background in psychology, who were trained in qualitative research. The first set of interview questions guided the patient through their whole experience from when symptoms were noticed up to the present day.

The next set of questions allowed patients to reflect on what they would like to see in the future in relation to treatment and care, and asked them what their messages to decision-makers would be about the care and treatment patients with their condition receive. The interview also asks patients about the advice they would give to others recently diagnosed with their condition or disease. All interviews were recorded and transcribed verbatim.

### *Questionnaire analysis*

Statistical analysis was conducted using R included in the packages “car”, “dplyr” and “ggplot2” (R 3.4.3 GUI 1.70 El Capitan build (7463). The aim of the statistical analysis of the SF36, CCCQ, FOP12, and PIH responses was to identify variations by respondent type (by disease severity, location and by education), and by co-morbidity or symptom type (co-morbid depression and anxiety). Global scales and sub scales were calculated according to reported instructions.[1,3,4] For comparisons by disease severity, a one-way analysis of variance (ANOVA) analysis was conducted. A Tukey HSD test was used post-hoc to identify the source of any differences identified in the one-way ANOVA test. Where the assumptions for the one-way ANOVA were not met, a Kuskal-Wallis rank sum test on care was conducted with post hoc pairwise comparisons using Wilcoxon rank sum test. When the assumption of

[1] 36-Item Short Form Survey (SF-36) Scoring instructions https://www.rand.org/health/surveys tools/mos/36-item-short-form/scoring.html

[2] Young et al. Measuring cancer care coordination: development and validation of a questionnaire for patients. BMC Cancer. 2011; 11: 298. Published online 2011 Jul 15. doi: 10.1186/1471-2407-11-298

[3] Hinz et al. Fear of progression in patients 6 months after cancer rehabilitation-a- validation study of the fear of progression questionnaire FoPQ-12. Support Care Cancer. 2015 Jun;23(6):1579-87. doi: 10.1007/s00520-014-2516-5. Epub 2014 Nov 21.

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equal variances were not met, a Welch one-way test was used with post-hoc pairwise t-tests with no assumption of equal variances.

For all other comparisons, a two-sample t-test was used when assumptions for normality and variance were met, or when assumptions were not met, a Wilcoxon rank sum test with continuity correction was used.

Questions where participants were asked to rank preferences were analysed using weighted averages. Weights were applied in reverse, the most preferred option was given the largest weight equal to the number of options, the least preferred option was given the lowest weight of 1.

***Structured interviews analysis***

A content analysis was conducted using conventional analysis to identify major themes from structured interviews. Text from the interviews were read line-by-line by the lead researcher and then imported into NVivo 8 (QSR International). Each question within the interview was individually analysed. Initial categories and definitions were identified and registered in NVivo. The minimum coded unit was a sentence however there were also paragraphs and phrases that were coded as a unit.

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A second researcher verified the codes and definitions, and the text was coded until full agreement was reached using the process of consensual validation. In general, a theme needed to occur more than ten times to be discussed within the results.

Data analysis and final reporting was completed on 16 February 2018.

***Position of this study***

A search was conducted in Pubmed to identify AD quality of life or patient experience studies of adults that had been conducted in the past five years in any developed country (Table 1.1).

Thirty-four studies were identified that collected patient self reported data. One study employed mixed methodology that included quantitative data on 110 participants about exercise participation and satisfaction, of this cohort, 11 participants had in depth interviews[19]. The remaining 33 studies including patient reported quantitative data. Fifteen clinical trials were identified of between 15 and 1379 patients (Table 1.1). Three of these studies collected anxiety, Health Related Qulaity of Life (HRQoL) and symptoms[20-23], one collected HRQoL, patient experience and symptoms[24], two HRQoL and symptoms[25,26], one anxiety and symptoms[27], one HRQoL and patient experience[28], three collected symptoms[29-31], two with HRQoL[32,33], and one with anxiety[34].

Three studies focused on HRQoL, two collecting only HRQoL[2,35], and one including HRQoL, patient navigation and patient experience[36]. Tow studies focused on burden of disease with one collecting comorbidities and healthcare utilization[37], and another collecting symptoms[6]. Two studies explored heliotherapy collecting HRQoL and symptoms[38,39]. Two studies extracted data from national health surveys, one collected anxiety, HRQoL and productivity data[40], another collected anxiety[41,42]. The remaining studies include a work productivity study collecting HRQoL, productivity and symptoms[43], two studies that collected anxiety and symptoms, one focused on adherence to treatment[44] and one on symptoms[45]. A willingness to pay study collected anxiety and cost data[46], a patient education study collected anxiety and symptoms data[47], three studies collected symptoms data, one focused on lifestyle[3], one on care models[48] and another on disease markers[49]

In this PEEK study, 100 people diagnosed with AD throughout Australia participated in the study that included a structured interview and quantitative questionnaire. This study in AD is therefore the largest mixed methodology study conducted in the last five years, and the only study focused on an Australian population. In addition, PEEK is a comprehensive study covering all aspects of disease experience from symptoms, diagnosis, treatment, healthcare communication, information provision, care and support, quality of life, and future treatment and care expectations.

## Table 1.1: Comparative studies

| Author, Year Country | Number AD participants | Study Focus | Anxiety | Quality of Life | Care coordination | Patient navigation | Patient experience | Cost | Expectations/priorities for future | Comorbidities | Productivity | Healthcare utilisation | Symptoms | Lifestyle modification | Qualitative |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Lonne-Rahm et al[19], 2014, Sweden | 110 | Lifestyle | | | | | | | | | | | | X | n=11 in depth interview |
| Simpson et aln[21]., 2016, International | 1379 | Clinical Trial | X | X | | | | | | | | | X | | |
| Blauvelt et al[23], 2017, International | 440 | Clinical trial | X | X | | | | | | | | | X | | |
| Simpson et al[20,22], 2016, International | 380 | Clinical Trial | X | X | | | | | | | | | X | | |
| Ständer et al[24], 2016, Germany | 70 | Clinical Trial | | x | | | x | | | | | | x | | |
| Åckerström et al[26], 2015, Sweden | 172 | Clinical Trial | | X | | | | | | | | | X | | |
| Caillaud et al[25], 2014, South Korea | 22 | Clinical trial | | X | | | | | | | | | X | | |
| Lopes et al[27], 2015, Portugal | 78 | Clinical Trial | X | | | | | | | | | | X | | |
| Brandt et al, 2014,[28] USA | 57 | Clinical trial | | X | | | X | | | | | | | | |
| Hoffman and Kircik[50], 2017, USA | 120 | Clinical Trial | | X | | | | | | | | | | | |
| Lynde and Andriessen[29], 2014, Canada | 118 | Clinical Trial | | | | | | | | | | | X | | |
| Jesenak et al[30], 2016, Slovakia | 105 | Clinical Trial | | | | | | | | | | | X | | |
| Kircik [31],2014, USA | 20 | Clinical Trial | | | | | | | | | | | X | | |
| Matsumoto et al[32], 2014, Japan | 44 | Clinical Trial | | X | | | | | | | | | | | |
| Onumah et al[33], 2013, USA | 20 | Clinical trial | | X | | | | | | | | | | | |
| Wyrzykowska et al[34], 2015, Denmark | 15 | Clinical Trial | X | | | | | | | | | | | | |
| Holm et al[35], 2016, Denmark | 191 | HRQoL | | X | | | | | | | | | | | |
| Torrelo et al[36], 2013, Spain | 141 | HRQOL | | X | | X | X | | | | | | | | |
| Heede et al[2], 2017, Denmark | 102 | HRQoL | | X | | | | | | | | | | | |
| Eckert et al[37], 2018, USA | 306 | Burden of AD | | | | | | | | X | | X | | | |
| Vakhariaet al[6], 2017, USA | 305 | Burden of AD | | X | | | | | | | | | X | | |
| Karppinen et al[38], 2017, Finland | 53 | Heliotherapy | | X | | | | | | | | | X | | |
| Karppinen et al[39], 2015, Finland | 13 | Heliotherapy | | X | | | | | | | | | X | | |
| Lee et al[41], 2018, Kwak et al[42], 2017, South Korea | 677 | National health survey | X | | | | | | | | | | | | |
| Eckert et al[51], 2017, USA | 349 | National health survey | X | X | | | | | | | X | | | | |
| Yano et al[43], 2013, Japan | 112 | Work productivity | | X | | | | | | | X | | X | | |
| Ortiz de Frutos et al[44], 2014, Spain | 125 | Adherence to treatement | X | | | | | | | | | X | | | |
| Wei et al[45], 2017, USA | 678 | Symptoms | X | | | | | | | | | X | | | |
| Beikert et al[46], 2014, Germany | 384 | Willingness to pay | X | | | | | X | | | | | | | |
| Heratizadeh et al[47]., 2017, Germany | 315 | Patient education | X | | | | | | | | | | X | | |
| Langenbruchet al[52], 2014, Germany Steinke et al[53], 2014, Germany | 1678 | Therapeutic benefit | | X | | | | | | | | | | | |
| Nosrati et al[3], 2017, USA | 169 | Lifestyle | | | | | | | | | | | X | | |
| Armstrong et al[48], 2015, USA | 156 | Care model | | | | | | | | | | | X | | |
| Mizawa et al[49], 2013, Japan | 30 | Disease marker | | | | | | | | | | | X | | |

## Abbreviations

| | |
|---|---|
| AD | Atopic Dermatitis |
| CCDR | Centre for Community-Driven Research |
| DF | Degrees of Freedom. The number of values in the final calculation of a statistic that are free to vary. |
| IQR | Interquartile range. A measure of statistical dispersion, being equal to the difference between 75th and 25th percentiles, or between upper and lower quartiles. |
| F | F-statistic. An F statistic is a value you get when you run an ANOVA test or a regression analysis to find out if the means between two populations are significantly different. |
| FOP | Fear of Progression. Tool to measure anxiety related to progression. |
| HRQoL | Health Related Quality of Life |
| MS | Mean of Squares. Estimates of variance across groups |
| SD Standard Deviation. | A quantity expressing by how much the members of a group differ from the mean value for the group. |
| SF 36 | Short Form Health Survey 36 |
| SS or $\chi^2$ | Sum of the Squares. The sum of squares is used as a mathematical way to find the function which best fits (varies least) from the data. |
| t | t-Statistic. Size of the difference relative to the variation in your sample data. |
| PEEK | Patient Experience, Expectations and Knowledge |
| PIH | Partners in Health |
| P | Probability value. A small *p*-value (typically ≤ 0.05) indicates strong. A large *p*-value (> 0.05) indicates weak evidence. |
| QoL | Quality of LIfe |
| W | Kendall's W statistic (sometimes called the Coefficient of Concordance) is a non parametric statistic. It's used to assess agreement between different raters, and ranges from 0 to 1. |

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