Smartphone apps for caregivers of children with atopic dermatitis : user profile, app scope and co-design

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**SMARTPHONE APPS FOR CAREGIVERS
OF CHILDREN WITH ATOPIC
DERMATITIS: USER PROFILE, APP
SCOPE AND CO-DESIGN**

**XU XIAOMENG
LEE KONG CHIAN SCHOOL OF MEDICINE
2019**

**SMARTPHONE APPS FOR CAREGIVERS
OF CHILDREN WITH ATOPIC
DERMATITIS: USER PROFILE, APP
SCOPE AND CO-DESIGN**

XU XIAOMENG

Lee Kong Chian School of Medicine

A thesis submitted to the Nanyang Technological University in
partial fulfilment of the requirement for the degree of
Doctor of Philosophy

2019

Declaration of Originality

I hereby certify that the work embodied in this thesis is the result of original research, is free of plagiarised materials, and has not been submitted for a higher degree to any other University or Institution.

31 October 2019
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Xu Xiaomeng

Supervisor Declaration Statement

I have reviewed the content and presentation style of this thesis and declare it is free of plagiarism and of sufficient grammatical clarity to be examined. To the best of my knowledge, the research and writing are those of the candidate except as acknowledged in the Author Attribution Statement. I confirm that the investigations were conducted in accord with the ethics policies and integrity standards of Nanyang Technological University and that the research data are presented honestly and without prejudice.

31 October 2019

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Date

A handwritten signature in black ink, appearing to read 'Josip Car', written over a horizontal dotted line.

Josip Car

Authorship Attribution Statement

This thesis contains material from five paper(s) published/under review in the following peer-reviewed journal(s) where I was the first and/or corresponding author.

Chapter 4 is published as Xiaomeng Xu, Louise Sandra van Galen, Mark Koh, Ram Bajpai, Steven Thng, Yik Weng Yew, Valerie Ho, Uma Alagappan, Krister Järbrink, Josip Car. Factors influencing quality of life in children with atopic dermatitis and their caregivers: a cross-sectional study. Scientific Report. 2019. Available from: <https://doi.org/10.1038/s41598-019-51129-5>

The contributions of the co-authors are as follows:

- I (XX) conceived the idea, conducted the analysis, wrote and revised the manuscript.
- Dr Louise van Galen (LvG) revised, commented on the manuscript and provided guidance to XX.
- Dr Mark Koh (MK) assisted in data collection, revised and commented on the manuscript.
- Dr Ram Bajpai (RB) provided inputs and supervision on data analysis.
- Assoc Prof. Steven Thng (ST) obtained the funding and commented on the manuscript.
- Dr Yik Weng Yew (YY) obtained the funding, assisted in data collection and commented on the manuscript.
- Dr Valerie Ho (VH) assisted in data collection and commented on the manuscript.
- Dr Alagappan Uma (AU) assisted in data collection and commented on the manuscript.
- Dr Krister Järbrink (KJ) planed the project and commented on the manuscript and provided guidance to XX.
- Assoc Prof. Josip Car (JC) conceptualized the overall study; obtained the funding; supervised the team; provided critical input into all stages of the study; critically reviewed the draft manuscript.

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The contributions of the co-authors are as follows:

- I (XX) conceived the idea, conducted the analysis, wrote and revised the manuscript.
- Dr Louise van Galen (LvG) revised, commented on the manuscript and provided guidance to XX.
- Dr Ram Bajpai (RB) provided inputs and supervision on data analysis.
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- Assoc Prof. Steven Thing (ST) obtained the funding, commented on the manuscript.
- Dr Yik Weng Yew (YY) obtained the funding, assisted in data collection and commented on the manuscript.
- Dr Krister Järbrink (KJ) planned the project and commented on the manuscript and provided guidance to XX.
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The contributions of the co-authors are as follows:

- I (XX) conceived the idea, conducted the analysis, wrote and revised the manuscript.
- Maja Olsson (MO) co-conceived the idea, contributed to manuscript writing and revision.
- Dr Ram Bajpai (RB) provided inputs and supervision on data analysis.
- Dr Louise van Galen (LvG) revised, commented on the manuscript and provided guidance to XX.
- Dr Mark Koh (MK) assisted in data collection, revised and commented on the manuscript.

- Dr Yik Weng Yew (YY) obtained the funding, assisted in data collection and commented on the manuscript.
- Dr Sharon Wong (SW) assisted in data collection and commented on the manuscript.
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- Assoc Prof. Steven Thng (ST) obtained the funding, commented on the manuscript.
- Dr Krister Järbrink (KJ) planned the project and commented on the manuscript and provided guidance to XX.
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- I (XX) conceptualised, developed and refined the study protocol, app assessment criteria, cleaned, analysed and interpreted data; drafted and revised the manuscript.
- Dr Louise van Galen (LvG) provided critical input into the developed app assessment criteria, assessed apps, interpreted data, revised the manuscript.
- Dr Mark Koh (MK) provided critical input to the study and draft manuscript.
- Assoc Prof. Steven Thng (ST) provided critical input to the study and draft manuscript.
- Assoc Prof Josip Car (JC) conceptualized the overall study, obtained the funding; supervised the team; provided critical input into all stages of the study; critically reviewed the draft manuscript.
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- I (XX) conceptualised, developed and refined the study protocol, recruited the participants, conducted the workshops, transcribed data, cleaned, analysed and interpreted data, drafted and revised the manuscript.
- Associate professor Konstadina Griva (KG) facilitated the workshop, contributed to data analysis and data interpretation, provided critical input to the study; edited draft manuscript.
- Dr Mark Koh (MK) provided critical input to the study and commented on the manuscript.
- Dr Elaine Lum (EL) provided critical input to the study and commented on the manuscript.
- Dr Woanshin Tan (WT) facilitated the workshop and commented on the manuscript.
- Assoc Prof. Steven Thng (ST) provided critical input to the study and commented on the manuscript.
- Assoc Prof Josip Car (JC) conceptualized the overall study, obtained the funding, supervised the team, provided critical input into all stages of the study, critically reviewed the draft manuscript.

31 October 2019

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Date

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Xu Xiaomeng

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List of Abbreviations

AAD	American Academy of Dermatology
AD	Atopic dermatitis
APP	Application
CDLQI	Children Dermatology Life Quality Index
CI	Confidence Intervals
CPF	Central Provident Fund
DLQI	Dermatology Life Quality Index
EASI	Eczema Area and Severity Index
ECG	Electrocardiography
FDA	Food and Drug Administration
GP	General Practitioner
HCP	Healthcare Professionals
HDM	House Dust Mite
ICT	Information Communication Technologies
IDQOL	Infants' Dermatitis Quality of Life Index
IGA	Investigator Global Assessment Scale
IHiS	Integrated Health Information Systems Corporation
ILTC	Intermediate and Long-Term Care
IRB	Institutional Review Board
IRR	Incidence Rate Ratios
KKH	KK Women's and Children's Hospital
LAR	Legally Authorized Representative
MOH	Minister of Health
NHGP	The National Healthcare Group Polyclinics
NICE	National Institute for Health and Care Excellence
NSC	National Skin Centre
NTU	Nanyang Technological University
NUS	National University of Singapore
OR	Odds Ratio
PDA	Personal Digital Assistants
POEM	Patient-Oriented Eczema Measure
QoL	Quality of life
RCT	Randomized Controlled Trial
SCORAD	SCORing Atopic Dermatitis
SD	Standard Deviation
SIT	Specific immunotherapy
SGD	Singapore Dollar
TCS	Topical corticosteroids
TCI	Topical calcineurin inhibitors
UN	United Nations

List of Publications

Published papers

Xu X, Posadzki PP, Lee GE, Car J, Smith HE. Digital Education for Health Professions in the Field of Dermatology: A Systematic Review by Digital Health Education Collaboration. *Acta dermato-venereologica*. 2018. Available from: <https://doi.org/10.2340/00015555-3068>.

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[†] Both authors contributed equally to this manuscript

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Summary

Atopic dermatitis, also called eczema, is a chronic inflammatory skin condition that affects up to 20.8% of children in Singapore. The symptoms of atopic dermatitis manifest as intractable itching, skin damage, soreness, and result in sleep loss which can be varying in its severity and it commonly affects quality of life and causes financial burden. Current models of health care delivery do not optimally support self-/caregiver-management of the condition outwit the consultation nor the variability of the disease in-between consultations to support clinical decision making when the patient's management of disease is reviewed by a clinician.

My thesis comprises of several interwoven studies in different overlapping phases. Firstly, cross-sectional studies among paediatric patients, their caregivers, and family as a whole in the Singapore population, examining whether socio-demographic factors (ethnicity, education, occupation, accommodation type) are associated with the quality of life indicators, and how severity of atopic dermatitis impacts patients', caregivers' and families' quality of life. Secondly, concordance between caregiver-reported and physician-rated severity of atopic dermatitis in children with atopic dermatitis was examined and to assess potential explanatory factors. Thirdly, the systematic assessment of existing smartphone apps for atopic dermatitis management identified important gaps in both features and content of the transparency and reliability of health information disseminated via these apps. Fourthly, an app co-design exercise was conducted with carers of children with atopic dermatitis, healthcare professionals and researchers through a series of face-to-face workshops with the eventual development of a wireframe prototype for atopic dermatitis self-/caregiver-management. Above phases can be an early step in developing evidence for digital health interventions to provide digital, tailored support for self-management among children with atopic dermatitis and their caregivers.

My PhD thesis explores the role that apps could play in improving the care for children with atopic dermatitis and management of their disease. The research captures the views of parents, children with atopic dermatitis and their clinicians about functions and features of a smartphone app that could support healthcare

delivery for this target group, co-design of an app, investigation of changes needed to clinical pathways and processes to achieve digital ‘transformation’ by not only moving from paper to a digital platform but ultimately transforming overall processes and experience of care and a range of outcomes.

Chapter 1

Introduction

Chapter 1 presents background information pertinent to the thesis. The aetiology, epidemiology, clinical manifestation, severity measurement, and comorbidity of atopic dermatitis are first introduced in Section 1.1, followed by a description of the social-economic burden of atopic dermatitis in Section 1.2 and Section 1.3. An evidence-based plan for atopic dermatitis treatment is presented in Section 1.4. Digital health in dermatology is subsequently introduced as a potential solution to lever the challenges faced in atopic dermatitis self-management, followed by a discussion of the challenges and gaps of digital health implementation in atopic dermatitis self-management in Section 1.5. Aim and objectives of conducting the research are then presented in Section 1.6. This chapter ends with an outline of the structure of the thesis in Section 1.7.

1.1 Atopic dermatitis in children

Atopic dermatitis is a chronic, pruritic, inflammatory skin disease with specific osmotic tendency caused by a variety of internal and external factors. It is a relapsing disorder which may last several months or years and usually starts in early infancy. The genetic predisposition to make IgE antibody responses to common environmental or food protein antigens has been shown to be strongly associated with atopic dermatitis with an incidence of approximately 80% among infants with atopic dermatitis (1). Clinicians often use “atopic dermatitis” and “eczema” interchangeably as atopic dermatitis is the most common type of eczema. Eczema is a broader term and includes contact dermatitis, dyshidrotic eczema, nummular eczema, seborrheic dermatitis. Although other types of eczema do exist, clinicians won’t call other types of eczema in place of “eczema”. This dissertation will use atopic dermatitis (AD) to avoid any confusion around the term.

1.1.1 Aetiology of atopic dermatitis

The aetiology of AD is not yet clear. Current mainstream views point to explain the aetiology is two main hypothesis - the epidermal barrier hypothesis and immunological hypothesis. The epidermal barrier hypothesis suggests that a primary defect in the epithelial barrier leading to secondary immunologic dysregulation and resulting in inflammation. The discovery of filaggrin gene (FLG) mutations and other decreased gene expression of epidermal differentiation complex genes such as desmoglein-1 (DSG1), corneodesmosin (CDSN) and serine protease inhibitor Kazaltype 5 (SPINK5) have made epidermal barrier theory as the top of the list in understanding the AD and its risk factors (2-4). Filaggrin is an important protein that binds keratinocytes together to maintain epidermal integrity. Defects in filaggrin can lead to abnormal skin barrier function, causing water loss from skin and therefore, irritants, immunogens, and pathogens are easily penetrated when skin is dry, leading to allergic sensitisation (5). The second hypothesis indicates that a primary immune dysfunction resulting in IgE sensitization, allergic inflammation, and a secondary epithelial barrier disturbance. This hypothesis focusing on an imbalance in T-helper cells predominance of Th2 cells over Th1 cells. This results in an increase in immunoglobulin E (IgE) through a pathway involving activation of interleukins (6).”

Figure1.1 Pathogenesis of AD development

1.1.2 Epidemiology of AD

Prevalence of AD varies between different age groups and geographical regions. The prevalence of AD in adults ranges from 2% to 10% across countries while AD in children is estimated to be up to 25% (7-9). AD has increased two to three-fold during the last few decades in industrialized countries (10). In the age group of six to seven-year-olds, the prevalence ranged from 0.9% to 22.5% and data showed prevalence values ranging from 0.2% to 24.6% in the age group of 13–14 years old. The disease usually onsets in their early life stage with 70% to 85% of patients being diagnosed by the age of five (11).

Prevalence of AD varies widely internationally (7, 9). According to a recent systematic review of studies between 1990 to 2010: an increasing trend of AD prevalence has been observed in Asia, western Europe, northern Europe (e.g. UK) and Africa (8, 12-14). In Taiwan, AD occurs among 17.4% of 12-15 years olds (15). In the late 2000s, the prevalence among the same age group in Korea remained stable,

from 15.2% in 2007 to 15.0% in 2010 (16). In China, a lower prevalence of childhood AD (12.94% among Chinese children) has been reported (17). Prevalence trends of AD in southeast Asia are mixed (12). In Malaysia, the occurrence of symptoms of AD is more common among 6-7 years old, and relatively stable among 13–14 years old; while the opposite trend has been observed in Thailand (18, 19). Prevalence of AD in Singapore is described in Chapter 2.

1.1.3 Clinical manifestation of AD

The clinical manifestations of AD are diverse, and the common symptoms are dry skin, redness, and severe itching (20). AD begins in the first 5 years of life in 90% of patients, and usually presents a characteristic age-dependent distribution (21): for infants, the rash usually first occurs on the cheeks, forehead, and scalp, but it can also appear on other areas of the body (22). Most AD cases among older children commence during infancy (22). Symptoms among older children usually occur in the creases of the elbows or knees (22). Other common places for the rash to occur are the neck, wrists, ankles, and/or creases between the buttocks and legs (22). About half (50%) of people experiencing AD during childhood continue to exhibit milder signs and symptoms as an adult, but it is rare for adults to develop AD spontaneously (23). Skin Infection is also common (24), during which the skin appears to bubble up, ooze, weep fluid and develop cracks, and even bleed (particularly when paediatric patients scratch a lot because of the itching) (25). Bacterial infections such as staphylococcus and viral infections may enter the skin barrier through the crack and lead to light-brown crusts, blisters and pain (26). With some patients, these symptoms can flare up periodically and then clear up for a time, and this cycle can last for several years (27).

1.1.4 Disease severity assessment

The severity of AD affects treatment decisions and subsequent successfulness of therapy. AD severity assessment in clinical practice is the lack of a widely accepted quality standard. This poses a problem for doctors, leading to the subjective assessment of AD severity. Apart from this, the diversity of scales also hinders comparisons between different interventions in the research studies. HOME (Harmonising Outcome Measures for Eczema) initiative collaborators realized the seriousness of the problem and is now actively working on developing and promoting a consensus-based core outcome set for AD (28).

i. Objective outcome measures of AD

The three most commonly used objective assessment scales mentioned in a previous systematic review are SCORing AD (SCORAD), Investigator Global Assessment Scale (IGA), and Eczema Area and Severity Index (EASI) (EASI was recommended by HOME) (29). All three scales evaluate the clinical signs of AD such as erythema, lichenification, oedema (induration/papulation), exudation (oozing/crusting/weeping), excoriation, and dryness, while SCORAD also evaluated itchiness and sleep disturbance (28, 30-32). A study in 2017 tested the robustness and reproducibility of the scales by comparing intra- and inter-rater reliability among the three scales evaluated by dermatologists (33). In the study, EASI had the highest intra-rater reliability, whereas SCORAD had the highest inter-rater reliability. The study also underlined that none of the scales showed a distinct advantage over the others, and thus recommended that at least two independent assessments be conducted simultaneously in order to ensure reliability (33).

ii. Patient-reported outcome measures of AD

Patient-reported outcome measures of AD can reflect patients' perspectives and perceptions of their disease/health status. The Patient-oriented Eczema Measure (POEM) is well-validated and is the preferred instrument for measuring patient-reported outcomes of AD (34-37). Other patient-reported outcome measures in

relation to PO-SCORAD, DLQI and the numerical rating scale (NRS)-itch also reflect a modest correlation with self-reported AD severity in adults, but such a correlation with children has yet to be confirmed (14, 38). Previous studies also underscore that current instruments cannot fully capture the full spectrum of disease conditions and, thus, an instrument needs to be selected based on clinical feasibility and suitability (14, 39).

1.1.5 Comorbidity

Patients with AD have been reported to be at risk of having allergic comorbidities. According to the Atopic March theory, AD is considered the first symptom presented followed by a series of subsequent allergic symptoms including asthma, allergic rhinitis, and food allergies (40, 41). In several longitudinal studies, AD in childhood significantly increases the risk of developing asthma and allergic rhinitis later in life compared to children without AD (42-45). Children two to four years old with AD with specific IgE antibodies to common environmental allergens (extrinsic AD) are more likely to progress to allergic rhinitis and asthma subsequently than those with AD without IgE sensitization (intrinsic AD) (46, 47). In addition, evidence shows that IgE-mediated food allergy affects around 35% of children with AD, particularly in early-onset, severe and persistent cases (48).

1.2 Economic burden of childhood AD

Different countries have provided various estimates, but most have indicated that the economic burden of AD is considerable. In 2008, Mancini et al estimated that AD costs the United States healthcare system between USD 364 million to 3.8 billion annually (49). In the UK, the annual cost related to AD treatment and management of children aged one to five years was £47 million, based on population census data, in 1995 – 1996 (50). In Singapore, there is limited evidence on the cost of AD. A study by Bhanegaonkar et al (51) estimated that the annual AD-related healthcare

cost per child was \$957 in 2014 in Singapore, including costs for health care visits and treatments (51). However, other direct costs of AD, such as additional prescriptions, over-the-counter treatments, ambulatory visits, as well as emergency department visits and hospitalizations were not fully accounted for within that study, which point to a significant underestimation of the actual economic burden of AD in Singapore.

1.3 Quality of life burden of childhood AD

AD as a widespread disease poses a significant burden on quality of life (QoL) not only for children themselves but also for their caregivers, and families (52, 53). Previous studies reported that the main affected areas of childhood AD were itching and scratching and sleep disturbance (54). On average, AD patients lose up to two hours of sleep every night (56). Children are also psychosocially affected by AD. The appearance of children with AD causes them to encounter feelings of anger and embarrassment and further impacts their social relationships with others, for instance, the classmates may worry about the contagiousness of the AD condition; consequently hindering social relationship development in school (54-56).

The burden of childhood AD extends to their caregivers and family life as well (57, 58). Caregivers' sleep can be equally affected as parents have to manage their child's AD symptoms during the night which can further influence their performance at home and work (59). In addition, caregivers are often required to perform extra duties, such as prepare special meals for their kids, engage in skincare regimens and clean extensively to minimise outbreaks (57, 59). A child suffering from AD can require approximately two to three hours of care from their caregivers on a daily basis (60). In order to prevent relapses, numerous caregivers deem it necessary to cut down on leisure, defer social activities and events, and even sacrifice their jobs for taking care of their children (61). The stress levels of the caregivers are also reported to be significantly higher which may further affect spousal relationships and parent-child relationships in the family (54, 59, 62).

1.4 Treatment of AD

It is necessary to develop an appropriate treatment strategy for promoting complex AD self-management. This section describes selected recommended practices of AD management with reference to international guidelines, as well as the outcomes of previous AD studies.

1.4.1 Non-pharmaceutical treatment of AD

i. Moisturizers

Moisturizers are a major component among treatment strategies, particularly in combination with other interventions and functions in different AD aetiology pathways (63). Both the NICE and AAD guidelines recommend that moisturizers should be used in the presence of epidermal barrier alteration and reduced epidermal water content; and that they are used to further improve the functions of the skin barrier (63, 64). Previous studies among patients have shown that using moisturizers as part of an active management plan can effectively delay first flare-up, reduce recurrence, produce better clinical outcomes, prolong flare time, and reduce the usage of topical corticosteroids needed to achieve similar improvements in AD severity (65-68). However, more flares were reported by patients using moisturizer alone than among those who combined moisturizers with anti-inflammatory therapies such as fluticasone propionate, indicating that anti-inflammatory therapies can be used to reinforce the moisturizing treatment and thus reduce recurrence (67, 68).

ii. Bathing practices, including additives

The evidence supporting the use of baths in AD management is mixed. In a few studies, bathing with certain additives water was shown to alleviate AD severity as well as permeability barrier function (69, 70). However, there is also evidence suggesting that bathing with use of additives does not lead to a significant improvement in AD-affected skin appearance compared to regular water baths. A systematic review of 4 studies concluded that bath intervention (frequency: single bath to daily bath; duration: 5 mins to 15 mins) did not result in a significant reduction of AD symptoms as the skin hydration caused by bathing disappears quickly (71-73).

‘Soak and seal’ is a strategy that has been recommended by a previous literature review: moisture application after frequent bathing is an effective management strategy that could lead to a reduction in disease severity, irrespective of the frequency of bathing (74). AAD guidelines suggest bathing with warm water, followed by application of moisturizers and also recommend that the frequency of bathing should be up to once per day, and the duration of bathing should be restricted to 5-10 mins using warm water (63).

Water also plays a role in developing/exacerbating AD. Evidence suggests that water hardness could damage the epidermal barrier of the skin, and is therefore associated with increased prevalence of AD. There is evidence showing that children of certain age groups who are exposed to hard water may experience a higher risk of developing AD, and that children living in regions with higher water hardness are more likely to develop AD compared to children living in low water hardness regions (75-77). Even so, solutions such as using water softeners have yielded unsatisfactory results. Softened Water Eczema Trial (SWET) trials conducted in a multicentre with 336 children did not show any significant additional benefits of using ion-exchange water softeners in AD treatment (78, 79).

Evidence as to the benefits of using bath additives in treating AD is inconclusive. AAD guidelines recommend against use of bath additives and acidic spring water, with the exception of bleach (63, 80, 81). Although a few studies with small sample sizes have demonstrated positive outcomes in terms of reduced AD severity, trans-epidermal water loss and stratum corneum hydration, no significant clinical benefits have been observed in studies with larger sample sizes. A multicentred RCT with 483 children aged 1 to 11 years showed no significant improvement in symptoms in the group which used emollient bath additives, compared to the control group (which did not use bath additives) (82).

Similar conclusions were reached in another RCT study of the effects of wearing silk garments on AD symptoms: no statistically significant improvement was found in the sample of children who wore silk garments, compared to the control group (83).

1.4.2 Pharmaceutical treatments of AD

i. Topical corticosteroids

Topical treatments including topical corticosteroid (TCS) and topical calcineurin inhibitors (TCI) have been recommended by official guidelines as the main forms of AD treatment (81). Among both, TCS has considered better treatment due to its more attractive cost-benefit ratio (84). AAD guidelines suggest these be used when non-pharmacologic treatments have failed. The mechanism of TCS treatment is said to involve proinflammatory pathways, whereby the medicine interrupts the antigen processing and therefore inhibits the release of proinflammatory cytokine (85). The potency of topical corticosteroids should be tailored to the severity of the child's AD, which may vary according to body site. According to AAD guidelines, low-potency TCS is recommended as a maintenance treatment, while intermediate and high-potency TCS are recommended for acute control of AD (63).

ii. Topical calcineurin inhibitors

Topical calcineurin inhibitors including tacrolimus and pimecrolimus are also recommended by AAD guidelines. They can be used in second-line treatment of moderate to severe AD in adults and children aged 2 years and older, which has not been controlled by topical corticosteroids (63). International guidelines also encourage patients to use TCI cream twice per day in an effort to relieve inflammation of AD and its pruritus (63, 81). These guidelines also suggest using TCI proactively in treating recurrent sites in order to reduce the relapse of AD (63, 81). The anti-inflammatory mechanisms of TCI include impeding calcineurin-dependent T-cell activation, and thus inhibiting proinflammatory cytokines production (85).

iii. Other topicals

Local anaesthetics are frequently used in combination with topical corticosteroids for the treatment of AD. However, use of topical antihistamines in the treatment of pruritus in patients with AD is not recommended by AAD guidelines as it may increase on the risk of occurrence of photoallergic contact dermatitis (63). AD-affected skin that is infected and oozing requires treatment with an antimicrobial or antiseptic lotion. Topical antimicrobial therapy may be effective in the treatment of localized infected AD. However, the current consensus does not support the use of topical antibiotics to deal with the infection of AD lesions because of concerns related to allergic hypersensitivity and bacterial resistance (63, 81).

iv. Traditional Chinese Medicine (TCM)

Traditional Chinese Medicine (TCM) is prevalent in Singapore. According to a previous study conducted in 2001, 67% of Singaporeans reported that they had taken recourse in TCM (86). Another previous study revealed that Singaporeans tend to prefer traditional Chinese Medicine (TCM) over Western medicine as they think TCM inflicts fewer side effects, especially when they face chronic disease conditions such as AD (87). Since TCM is not mentioned in most of the international guidelines cited, it is necessary to investigate the efficacy of TCM in its treatment of AD. Tan, et al. systematically reviewed 281 studies on TCM and implied that there are clinical benefits of TCM in the treatment of AD (88). Their study concluded that, compared

with placebo, TCM could significantly alleviate symptoms of AD such as erythema, skin appearance, itchiness, and sleep disturbance; and could reduce patients' need for Western treatments. Besides, when comparing TCM to Western treatments, the study revealed that the combination of TCM and Western medicine could lead to a significant reduction in AD disease severity (89-91). On top of that, TCM was also reported as a safer treatment, with fewer adverse events occurring (92, 93). However, it is noted that the quality of the design of these studies was relatively poor, and there remains the need for high-quality randomized controlled trials of TCM and related treatments for AD so that more solid evidence can be provided in future.

1.4.3 Patient education

AD self-management involves the multifaced repeated treatment, which inevitably requires adequate education (94). The American Academy of Dermatology (AAD) and European consensus guidelines for AD management emphasized the importance of patient education for AD patients and/or their caregivers (63, 81). Empowering patients or/and their caregivers with confidence through sufficient education enables them to be more willing to follow the doctor's instructions, and to experience less anxiety and confusion (95).

The need for and benefits of AD self-management have been demonstrated in many studies. A systematic review published positive results in 2016 by critically appraising outcomes of education for AD patients and their caregivers (96). Improvements in terms of disease severity and QoL were observed among children and adolescents with AD who received disease-related education at both the six-week and twelve-week follow-up sessions in two randomised controlled trials (RCTs) (97, 98). Similarly, another RCT with an intensive education program on disease course and treatment led to more significant improvements in terms of disease severity and coping skills among participants who received a structured education program, compared to the controls (95). Even so, it is not easy to integrate the education program into the clinical routine due to personnel and financial constraints. Currently,

patients and their caregivers mainly rely on a larger variety of educational sources outside hospitals such as advice from relatives and friends, online websites and forum but the validity and safety of the information remains unclear.

1.5 Digital health in dermatology

Digital health concerns the use of information communication technologies (ICT) in healthcare, where medical or public health practices are supported by digital devices such as mobile phones, patient monitoring devices, personal digital assistants (PDAs), and other wireless devices (99). Worldwide, the penetration rate of the Internet has reached more than 57.3% of the human population, and the number of smartphone users is around 4.4 billion (100). Recent evidence suggests that digital interventions can improve confidence in self-management, medication usage as well as quality of life among patients with chronic disease conditions such as diabetes, heart diseases and asthma (101-103).

Innovation and advances in digital health are believed to reinforce performance at each and every phase along the patient's clinical journey, from pre-diagnosis to disease follow-up (see Figure 1.2). In clinical practice, digital health can be further unpacked into a number of domains such as education and awareness; helpline, diagnostic and treatment support; diagnostics; communication and training for healthcare workers; disease and epidemic outbreak tracking; remote monitoring; and, remote data collection (104). The development of external devices linked to smartphone apps could also enable patients to detect vital signs, diagnose clinical symptoms, and self-evaluate indicators without the limitations of time and space. Digital health has the potential to promote the emergence of new diagnoses, improve clinical decision-making ability, and become a promising tool that could catalyse the transformation of the traditional care model into a patient-centred care model.

Figure1.2 Digital health reinforces performance along the patient's clinical journey

1.5.1 The role of digital health in supporting disease self-management

Digital health is considered a potentially effective tool, which supports self-management. It can facilitate self-management in various ways:

i. Disease surveillance and tracking

Tracking practices and tracking data via smartphone apps can raise awareness of the patient's condition, empower users with more control over disease management, and develop healthier self-management behaviour in the long run (105). Besides, smart wearable devices (e.g. wearable ECG monitor, portable pancreas system, neurological monitor and wearable physiological monitoring system, etc.) have been demonstrated to be effective and reliable tools for patient self-assessment and monitoring in fields such as cardiopulmonary, vascular, endocrine, neurological function and rehabilitation medicine (106).

ii. Patient education

Smartphone apps aimed at patient education are multiplying rapidly, and patients can now research health-related information without having to schedule appointments with healthcare professionals (HCPs). Knowledge disseminated via smartphone apps can be of a more interactive, understandable formats, such as podcast, video, games, and chatbots. Visualization through technologies such as augmented reality and virtual reality can also be used to help patients and their caregivers understand complex treatment procedures and disease conditions (107, 108).

iii. Medication management and adherence

Digital health can improve medication adherence at the point of care, thereby improving patient-related outcomes as well as treatment satisfaction. Digital health devices such as smartphone apps and smart pillboxes can connect with the electric medical system making it easier for patients to record or view a doctor's prescription, keep track of the medications, and record their progress at any time. Electronic records can also inform the doctors if their patient is complying with the medication regimen.

1.5.2 Benefits and risks of digital health in dermatological care

Of the medical disciplines, dermatology is considered the 'beachhead' for digital health, as a substantial proportion of diagnoses and management is based on visual examination. According to market research in 2017, there are more than 318,000 health apps available in the market for healthcare stakeholders, and more than 200 new health-related apps and 340 new healthcare wearable devices being made available to people every day (109). Among those, dermatology apps only constitute 0.2% of health apps (526 apps) in 2017; however, the number of dermatology apps rose rapidly by 80.8 per cent from 2014 until 2018 (110). The rapid growth can be explained: The skin problems are easier to detect by patients and caregivers. They can simply take a phone and upload images onto the dermatology apps.

The maturity of diagnostic dermatology apps is ascribed to the development of advanced technologies such as artificial intelligence aiming to offer support to professionals who are less familiar with skin cancers. In 2017, a technology article published in *Nature* reporting on a new diagnostic dermatology app demonstrated that its diagnostic performance is equal to or even better than that of board-certified dermatologists (111). Such diagnostic apps also focus on other dermatological diseases, but their accuracy and reliability are still under study.

Non-diagnostic dermatology apps can engage patients and their caregivers better by providing tailored education as well as developing the interventions to facilitate the development of coping skills and diseases management practice. Along with providing tracking data produced via a wearable sensor, non-diagnostic apps can provide broader insights into the spread and impact of dermatological diseases on a daily basis. For example, wound apps now provide highly reliable wound measurements and enable wound patients to monitor the progression of a wound at home (112); however, it has been reported in some studies that many patients harbour doubts about the effectiveness of such monitoring apps (113, 114). Inconsistent results in previous studies have led people to question the usefulness of smartphone apps, and rigorous research in the field is required.

Tele-dermatology is another important category of dermatology apps. With a tele-dermatology app, the patient can make an appointment with a doctor of their own choosing and receive real-time dermatology care services without having to step outside their home. Tele-dermatology has also been demonstrated to improve clinical outcomes, and it has been reported that 80% of patients consider the service a viable alternative to in-person consultations (115). As for patient acceptance, according to Frühauf (2013), there is a high acceptance of tele-dermatology smartphone apps among both patients and tele-dermatologists; and 90% of patients stated, “they are in good hands while benefitting from a more flexible appointment schedule” (116). Meanwhile, concerns about the accuracy of such diagnoses have also been discussed in previous studies. Compared to face-to-face consultations, doctors could be more likely to neglect some important symptoms during a telephone consultation, and

could fail to ask relevant questions, which will lead to poor treatment performance (117). Therefore, any expansion of a tele-dermatology service should be conducted with caution. Tele-dermatology should follow established standards and should fall under the surveillance of healthcare providers.

1.5.3 Benefits and risks of digital health in AD care

Digital health apps in AD constitute another major research field. Previous studies have demonstrated that no significant differences between them in regard to clinical outcomes and QoL outcomes comparing AD digital management with traditional in-person care models (97, 118, 119). An RCT compared online model and in-person care model for following up AD and concluded that equivalent improvement in clinical outcomes (118). Considering the substantial financial savings which digital health interventions in managing AD could reap, digital health could potentially be a promising substitute for in-person care (119).

Current technology for AD is still in its infancy; no reliable diagnostic apps are available in the market yet as there are a number of obstacles preventing them from being useable and marketable. Firstly, assessment of AD is a complex and multifaceted process, and so further assistance from clinical specialists is required. The algorithms within AD digital health app programs are complex and require extensive image database support. The second obstacle is that the highly nuanced changes in AD lesions development necessitate high-quality photos (in terms of angles, lighting, distance), and smartphone cameras might not be able to satisfy diagnostic requirements.

At present, mainstream AD apps in the market include mainly education apps and disease-tracking apps. Sensors such as scratch detection sensors have the potential to accurately quantify scratching over time. As well as allowing patients to record input, tracking apps can aid users by minimizing flare-up, and they can better inform doctors about disease progression and therefore help them develop effective management regimens (120).

1.5.4 Challenges facing digital health

While dermatology apps have been welcomed by the market, these aforementioned challenges remain unresolved.

i. Patient usability

Digital health apps must be reasonably user-friendly and should make medical diagnosis and tracking of dermatological ailments more convenient. There are three usability-related challenges, which need to be overcome. Firstly, an app should cater to the needs of the user. It is known that digital health developers often fail to fully incorporate the user's perspective, and even neglect users' basic needs. Secondly, developers need to understand the possible circumstances where the digital health app is going to be used. For example, if an app is designed for elderly patients, its design and use should not be complicated. Thirdly, the onboarding experience is another factor that affects the usability of the app. Disease management apps usually incorporate many features, but navigation between the features is not always clear. Users might navigate into a completely different interface accidentally, or might not be able to retrieve the information from the previous interface, and become frustrated quickly.

ii. Reliability and clinical relevancy

Digital health apps can be directly involved in the patient journey, and thus scientific evidence must be used to back up app developers' health-related claims. It is known that some app developers and marketers provide misleading information by making exaggerated and false claims, which may be placing users' health at risk. For example, in the United States in September 2011, the Food & Drug Administration fined the two companies behind the AcneApp and AcnePwnder apps for claiming that the red and blue lights emitted by the apps on an iPhone could clear acne (121). Therefore, in order to ensure the provision of reliable and quality apps on the market,

producers should be subject to thorough quality assessments, and regulatory authorities also need to rigorously supervise smartphone app developers.

iii. Data privacy

The rapid development of digital health apps has come at the cost to data privacy and security, with users being exposed to greater vulnerabilities and higher data breach risks. Based on the sample survey of domestic patient APP, about 80% of patients have a vulnerability in app usage, and 67% of them have high-risk vulnerabilities available for apps (122). In addition, many serious information leakage risks have been identified in third-party medical service platforms, with the risk of hackers obtaining patients' names, mobile phone numbers, ID cards, medical records, and laboratory test reports. People developing and administering digital health apps to patients should make every reasonable effort to ensure data privacy and security.

iv. Data integration

Data integration is the key prerequisite for developing a sustainable digital health ecosystem. However, at present, the data of major hospitals are almost isolated, and patient data is not integrated with each other. As for external wearable devices, there are still no uniform standards for various wearable devices in the market, and interface transmission conditions will differ among devices. At the same time, developments in backend services that make sense of digital health data have not kept up with digital health device development. As a result, there is a plentiful supply of devices actively collecting data from patients, but there is still more work to be done in making sense of such data.

1.6 Aim and objectives

1.6.1 Aim

By investigating the burden of childhood AD in Singapore and reviewing AD app landscape, this thesis aims to empower the app co-development solution in supporting AD self-management, and ultimately to accelerate the transition from traditional disease management routine to a digital platform.

1.6.2 Specific objectives

The objectives of my PhD research are to:

1. Provide updated knowledge of the perception of the quality of life among AD paediatric patients and their caregivers in the Singapore context and to investigate its explanatory factors.
2. Assess the family burden of paediatric AD patients in the Singapore population and to investigate its explanatory factors.
3. Explore the influencing factors involved in understanding patients' and healthcare professionals' perceptions by analysing concordance between physician-rated and caregiver perceived disease severity in children with AD.
4. Understand the app landscape by systematically assessing the functionalities and information of existing AD smartphone apps that could support AD management.
5. Propose a digital solution by co-designing a smartphone app using face-to-face workshops with caregivers, healthcare professionals, and researchers to incorporate their preferences and perceptions of AD management experience to app development process.

1.7 Content of the dissertation

Figure1.3 Overview of the PhD study

This dissertation explores the possibility of using a smartphone app to help patients and their caregivers manage AD. My thesis comprises of several interwoven studies in the following chapters (Figure 1.3):

Chapter 2 describes the Singaporean cultural and policy context, the AD patient journey in Singapore, and how digital health has integrated into people's life in Singapore. **Chapter 3** explains the rationale of choosing the mixed-method approach in achieving research objectives. It also describes the methodological approach, sources of data and analytical approaches.

Chapter 4 focusses on investigating the QoL among patients and their caregivers in Singapore. A cross-sectional study is therefore conducted to examine whether socio-demographic factors are associated with the quality of life indicators, and how different levels of AD severity impacts patients' and caregivers' QoL.

Chapter 5 provides an in-depth insight into the family burden of childhood AD and further explores the social and clinical factors potentially impacting family life and function.

Chapter 6 uses physician-rated and caregiver-perceived disease severity as a focus to provide evidence for understanding the patient-doctor concordance, given the fact that disease severity can seriously affect patient prognosis and compliance with treatment. A cross-sectional study is employed to explore the concordance between physician-rated and caregiver-perceived AD severity in paediatric patients and assess its potential explanatory factors.

Chapter 7 of the thesis is a systematic assessment of smartphone apps for AD management. In this chapter, according to international evidence-based guidelines, assessment criteria are established to understand the credibility, reliability, clinical relevancy of existing AD management apps through assessment of human-computer interaction.

Having acknowledged the QoL burden of targeted users and status quo of AD management apps in the market, I come to the phase of conceptualizing the content and features of the app. **Chapter 8** is followed with an app co-design exercise through a series of face-to-face workshops, among caregivers of children with AD, healthcare professionals and researchers, to propose a solution on supporting AD self-management with the help of the proposed smartphone app.

Key findings of this dissertation are summarised and discussed in **Chapter 9**. The strengths and limitations of this dissertation, policy and practice implications of the findings, and suggestions for future research, are also discussed.

Chapter 2

Study context

This chapter introduces Singapore's social background and the current status of AD care, and briefly describes the country's strategies in facing the rapid development of digital health. It also provides a background on Singaporean culture and healthcare, which places into context the methods used, and data discussed in subsequent chapters. The first section of this chapter details the researcher's personal background. An overarching introduction to Singapore is then provided in Section 2.2. Section 2.3 concerns the current situation of Singapore patient-centred care, and the provision of AD care and support to children in Singapore is described in Section 2.4. Section 2.5 describes Singapore's digital health ecosystem.

2.1 The PhD candidate's background

A variety of factors influence the interactions between researchers and their research studies. According to Råheim, *et al.* (2016), the background and position of the research will have an effect on the research scope, study angle, and methodology, as well as results interpretation (123). As such, it is necessary to describe the researcher's own background as it does affect their understanding of and attitudes in relation to the research subject:

I (the PhD candidate) was born in Tianjin, a coastal metropolis in Northern China, a city of over 15 million people. My educational background is in Medicine (MD): I received my medical training at Nankai University and the Chinese PLA General Hospital in Beijing, China. During my medical studies, I developed a comprehensive knowledge and understanding of disease concepts, and I gained insights in the quality and management of health services, which have proved invaluable to my PhD studies. I also had opportunities to develop good interpersonal skills with patients and doctors during the medical training, an aptitude which is relevant to patient recruitment

(discussed in Chapters 4, 5 and 6), as I managed to build a good rapport with the participants (discussed in Chapter 8).

Since the hospital placed an emphasis on training clinician-scientists, I gained experience in conducting clinical research using digital health intervention prior to commencing PhD project, and I witnessed the rapid growth of the digital health industry in China. I am fascinated by the ways in which digital health interventions provided by digital health now feature prominently in the lives of patients and doctors. It is my belief that digital health will profoundly improve healthcare service experience and healthcare management. This is the main reason why I have chosen digital health as the subject of my PhD project.

2.2 The healthcare system in Singapore

2.2.1 Overview of Singapore

Singapore is a city-state located in Southeast Asia. It is an island with a tropical maritime climate which is hot, humid and rainy all year round. The annual temperature range is 24 °C to 32 °C with an average humidity of 84.3%. Singapore covers an area of 710 square kilometres, and has a population of about 5.64 million people, comprising 74.3% ethnic Chinese, 13.4% Malays, and 9.0% Indians (124). The population density of Singapore is high, with 18,513 people per square mile (the country is the third-most densely populated country in the world) (125). Singapore's economic development has been remarkable: it is currently ranked among the best in the world (126). In the decades since gaining independence in 1965, the country has enjoyed exponential economic growth, with the standard of living increasing by five- to six-fold (126). Today, Singapore is among one of the most affluent countries in the world with a gross domestic product per capita of 64,578.77 USD (127). The country is also heavily urbanized, a feature which has contributed to the development of AD in Singapore (128).

2.2.2 Singapore's healthcare system

Singapore consistently strives to improve the availability, accessibility, affordability and the quality of healthcare by restructuring healthcare organisation and provision. According to Bloomberg Healthcare Efficiency Index 2018, the efficiency of the Singapore healthcare system is ranked second in the world (129). The achievement is ascribed mainly to careful governance and an efficient healthcare system. Singapore's healthcare model is provided by public and private organization concurrently and covers a wide healthcare spectrum, including primary care, comprehensive healthcare and long-term care services (130, 131).

It is estimated that 80% of primary care services are provided by private clinics, and 20% by government general clinics (131, 132). The government uses price levers to encourage people to see general clinics, and thus reduce the pressure on public tertiary hospitals. Integrated healthcare in Singapore is based mainly on its eight existing public tertiary hospitals. Each tertiary hospital provides inpatient treatment, specialist outpatient services, and 24-hour emergency services. There are also seven national specialist centres that represent the highest level of medical care in Singapore (133). In inpatient medical services, public hospitals provide 80% of the services, and the remaining 20% is provided by private hospitals (131). Intermediate and long-term care (ILTC) services are a range of healthcare services that patients need after their disease condition has become stable (134). For Singapore residents who need intermediate and long-term medical care, there are a variety of residential and community-based medical services available, including community hospitals, nursing home, hospice care institutions, and family medical care (131, 134).

The public and private hospitals, national medical centres and primary care clinics were merged into three regional health clusters, which oversee healthcare services to patients in the central, eastern, and western regions (135). Each cluster is led by the main hospital and aims to deliver integrated care to a geographically defined population. The network of regional service organizations is centred on the public tertiary hospitals, with medical clusters supported by surrounding comprehensive clinics, community hospitals, and nursing homes. Each cluster integrates services,

referrals, shared equipment, beds, and electronic medical records to bring about comprehensive effects and economies of scale (135). These measures have effectively improved the efficiency of medical services, and they ensure the rational distribution of medical resources (135).

2.2.3 Schemes and subsidies for healthcare in Singapore

Although Singapore provides a publicly funded healthcare system, it is different from that of the UK or United States, in that residents must take responsibility for their health by paying for medical expenses. The Singaporean government strikes a balance between high-quality healthcare and controllable costs by providing government subsidies only as a last resort. In 1983, the government announced the *National Health Care Plan* to provide affordable healthcare. The government devised a financing scheme termed the “3Ms”, which consist of Medisave, MediShieldLife, and Medifund (see Figure 2.1) (136, 137).

Figure 2.1 Singapore’s 3M financial schemes for healthcare

The Medisave Plan was announced in 1984. Under the plan, each Singapore permanent resident and citizen must deposit part of their monthly earnings into the Central Provident Fund (i.e. membership of CPF is compulsory), a portion of which is allocated to their Medisave account. A certain amount of contribution is also borne by the employer (138). CPF members can use their Medisave accounts to pay for local medical expenses for themselves or any immediate family members, for example, hospitalization costs and outpatient fees in public hospitals and approved private hospitals (139). The MediShieldLife Plan was implemented in an effort to protect people against higher expenditure on healthcare, particularly those with critical or chronic illnesses who may not be adequately covered through Medisave alone, e.g. long-term hospitalization or critical care. In addition, the Medifund Plan was introduced in April 1993 in order to assist a small proportion of residents who are unable to pay for medical expenses even after drawing upon the above financing schemes (140).

2.3 Patient-centred care in Singapore

Singapore is transforming from physician-centred to patient-centred care (141). Patient-centred care could potentially provide patients with high-quality, affordable medical services and maximize patient health benefits (142). In addition, interprofessional collaborations can enhance integrated care, information sharing, provide patients with a seamless, continuous and holistic healthcare service, minimize unnecessary treatment, and deliver cost-effective healthcare (143, 144). The National Healthcare Group Polyclinics (NHGP) initiated a teamlet model aiming to provide personalized, comprehensive care and support within the primary care setting for patient's medical, psychological and social needs (141). Patients within the community who need to be cared for by the teamlet are first identified, after which interdisciplinary teams then estimate each person's health risk, stratify these risks and devise plans to tailor healthcare resources to better meet individual needs. Subsequently, a teamlet member monitors and follows up patients by reviewing their digital dashboards on a regular basis, in order to identify patients' needs before each

upcoming appointment. The teamlet model enables healthcare providers to provide more customised, continuous and integrated care for patients (see Figure 2.2). Several similar patient-centred care programs have also been set up for the elderly and dementia patients who are dependent on the Singapore healthcare system; however, none of these patient-centred approaches has been used in AD management (145, 146).

Figure 2.2 Teamlet care model (107)

2.4 Atopic dermatitis care in Singapore

2.4.1 The high prevalence of atopic dermatitis in Singapore

The overall prevalence of AD across all age groups in Singapore is 13.1% and the prevalence of AD in children is much higher (20.6%). More than half of AD patients have their first disease onset before they reach 20 years of age (147). In 2002, Tay, *et al.* reported that 22.7% of 7-year-old children, 17.9% of 12-year-old children and

21.5% of 16-year-old children in Singapore have been diagnosed with AD ailments. Sex differences have also been observed in different age groups: among children aged 6-12, AD is more prevalent among boys than girls, whereas among children aged 12-16 it is more prevalent among girls. Ethnic differences have also been identified: Chinese and Malay people appear to be more susceptible to AD, whereas people of Indian origin and other races are less affected by AD (Chinese 21.6%; Malays 19.8%; Indians 16%; other races 14%) (148).

The high urbanization rate, which is associated with allergic illness, could be one of the explanations of the high prevalence of AD in Singapore. Residents living in conurbations like Singapore are exposed to pollutants from the urban environment (including smoke haze from forest fires, industrial emissions, animal dander, mould spores, etc.) chronically and repetitively, which could cause damage to the skin barrier (149, 150). In addition, modern lifestyles (such as increased stress, unhealthy diet, socioeconomic pressures, etc.) will also affect the development of and exacerbate AD (151, 152). Furthermore, the hot and humid environment in Singapore is an ideal habitat for the house dust mite (HDM). Although the role of HDM in the development of AD remains controversial, a higher HDM population is associated with a higher occurrence of allergic reactions and is said to be one of the reasons for the high prevalence of AD (153, 154). Another explanation could be that children in Singapore have fewer opportunities to be exposed to infectious agents during the early stage of life, partly due to good hygiene and healthcare standards in Singapore, which could be detrimental to immune tolerance (155, 156). Besides, the relatively low breastfeeding rate in Singapore could also partly explain the high prevalence of AD (157, 158).

2.4.2 Patient Journey in Singapore

Figure 2.3 maps out the Singaporean AD patient journey. The onset of AD is very early. The first symptoms occur among 60% of one-year-olds, and 85% are diagnosed with AD before the age of five (159). Under normal circumstances, parents will

require primary care for symptoms management guidance when they first become aware of the symptoms. Primary care doctors will give a timely diagnosis, treatment options and provide the necessary disease education. Caregivers will take care of their children and manage their symptoms daily. Meanwhile, caregivers will visit GP doctors intermittently to refill prescriptions or make changes to treatment plans. Between half and 60% of paediatric patients will recover fully from AD; the symptoms will disappear before they reach adulthood. However, some paediatric patients respond poorly to treatment and, when GP doctors deem the intervention necessary, they will then refer these patients to specialist hospitals for further treatment, or recommend hospitalization for systemic tests, treatment and education.

Figure 2.3 Patient Journey map

2.4.3 Challenges affecting AD care in Singapore

AD care in Singapore is facing several challenges. Although Singapore has a high AD prevalence rate, advocating for AD treatment and management may still be insufficient. Firstly, there is a need to raise awareness of AD as a serious public health issue. Patients with AD may not receive adequate attention and support in Singapore. Schoolchildren suffering from AD who have visible skin lesions are often marginalized and bullied (160). In addition, the lack of dedicated funds for AD management is another challenge faced by public sectors. Compared with more bounteous investments earmarked for other disease groups such as SGD\$300 million for mental health and SGD\$940 million for diabetes, investment in AD treatment and research is SGD\$30 million, which is 0.3% of the Ministry of Health's expenditure in 2017 (161). This is a cause for concern as the level of funding may not meet the growing demand for AD care in Singapore.

Besides, rigorous independent research is gradually decreasing as a result of over-commercialization in AD care (162, 163). Commercial conflicts of interest are common in the field of AD research, in which, according to the review findings in two publications, around half of earlier studies were found to be funded in full or in part by industry (164, 165). It is also worth noting that industry-sponsored studies are more likely to report biased results. There is evidence showing that industry-sponsored studies are more likely to compare an intervention against an inactive comparator, and to report results in favour of the product made by the sponsor's company (163, 166-169). Other forms of bias in industry-sponsored research include intentional avoidance of negative results (165). Such research does not inform clinicians appropriately, and could lead to over/mistreatment of AD patients.

Another challenge facing AD care is that healthcare services are fragmented. Although Singapore's healthcare system is moving towards integrated care, there is still a long way to go before integrated care, especially for patients with non-life-threatening diseases such as AD, can be implemented. The reasons for the fragmentation are summarized here: First, the current healthcare model is still predominantly reactive and centred on treatment. It is hard to establish a

comprehensive set of prevention and intervention mechanisms for patients, which weakens continuity in the medical service chain.

There is a lack of professional education on AD, and many AD sufferers have their misconceptions and receive misleading advice. Currently, there is one ‘eczema camp’, which is organized by healthcare providers to provide the necessary education to patients and their caregivers, and in which patients and caregivers can participate in educational activities (170). However, this is only an annual event, and so the support for AD patients is very limited and time-sensitive. The lack of professional management guidance and AD management plans also increase the possibility of AD recurrence, which pushes healthcare costs up (63, 171).

Another challenge is the doctor-patient relationship. The doctor might not fully understand the patient’s needs and experience and might not effectively detect AD and provide appropriate treatment and commonly not have sufficient time to help patients learn about their condition. The unclear curative effect leads to repeated medical treatment, and caregivers have to visit different clinics repeatedly in order to confirm a diagnosis; this further increases the fragmentation of healthcare services (172, 173).

2.5 Digital health ecosystem in Singapore

2.5.1 Singapore as a suitable setting for digital health implementation

Singapore is an ideal setting for implementing digital health services. First of all, Singapore has a well-established communication technology infrastructure, and high mobile phone penetration (174, 175). Meanwhile, Singapore also has an ageing population: according to the UN’s 2017 World Population Ageing report, it is predicted that nearly half (47%) of its total population will be at least 65 years old in the next three decades (176). Krishna, *et al.* (2014) state that there is also increasing demand for high-quality patient-centred healthcare, as traditional healthcare models can no longer meet growing demand (140). According to Jayaraman (2017), digital

health technologies can be leveraged to solve these problems (177). Digital health services, including telemedicine, can be used as ancillary services to increase the efficiency of Singapore's healthcare impact (178). In addition, Singapore provides an amenable business environment conducive to innovation, which can benefit research and development, and the implementation of digital health. Universities such as Nanyang Technological University and National University Singapore offer digital incubator programmes by providing start-up grants and guidance to help young entrepreneurs develop innovative biotech businesses (179, 180).

2.5.2 Singapore's transition to a 'smart nation'

The Lee Kuan Yew School of Public Policy and the National University of Singapore recently reported that Singapore is committed to transitioning into a 'smart nation': "In order to serve the public better, Singapore is building nation-wide data collection platforms, connecting and analysing infrastructure, and operating systems" (181). The core of the smart nation concept can be summarized in three dimensions: connection, collecting and understanding. The first phase of the smart nation platform is centred on 'Connection' and 'Collecting'. According to the Singapore Ministry of Health and the two aforementioned academic institutions, the goal of 'connection' is to provide a secure, high-speed, economical and scalable national communications infrastructure; 'collecting' refers to the assembly of better real-time data through sensor networks across the country, as well as efforts to protect, share and anonymize important data (181, 182). The dimension of 'understanding' relates to the collection of data – especially real-time data –for the purpose of establishing an effective sharing mechanism for the public; and, through the analysis of data, "to better predict the needs of the people and provide better public services" (181).

In their efforts to transition Singapore into a smart nation, the Integrated Health Information Systems Corporation (IHIS), a scientific institution under the Ministry of Health, has built a series of platforms which actualise the 'smart nation' in the field of healthcare (183). In recent years, the institution has cooperated with public

healthcare institutions to launch more than ten nation-wide technology platforms and systems (such as ‘Future Hospital’, and ‘Future Home Care’) (184, 185). It is anticipated that these new platforms will enable healthcare providers to establish closer partnerships with companies in other fields that provide information, medical devices, pharmaceuticals, and that promote a healthy lifestyle by providing nutrition guidance. Within the framework of digital health, Singapore is jointly developing new products and new business models; and, it aims to become an experimental platform for implementing new digital health solutions and systems in regional and global markets (185).

Chapter 3

Methodological considerations

This chapter describes the research design and analytical approach, which were adopted in an effort to fulfil the five research objectives of this PhD project. This chapter consists of three subsections. Section 3.1 presents the overarching rationale for the mixed methods research design. Section 3.2 explains the rationale of the quantitative approach used in this study. The rationale behind the systematic assessment of AD apps is described in Section 3.3. In Section 3.4, a statement justifying the selection of the qualitative approach for the app codesign workshops is provided, and this section also justifies the co-design approach, and details the workshop data collection and analysis methods.

3.1 Mixed methods rationale

Data gathered using multiple research methods are more detailed and reliable than that sourced using a single method (186-188). It is widely recognized that contextual particularities and challenges could subvert, neutralise, intensify or otherwise influence a research study (189). Therefore, contextual factors such as targeted populations and research sites are among some of the critical considerations that must be taken into account when selecting the most suitable methodological approaches. I should mention at this juncture that this thesis addresses a unique and complicated subject. Many AD patients in Singapore are young infants who cannot manage the disease themselves, and so my research has involved their caregivers in what is a multi-ethnic Asian city-state. In addition, this population is a relatively underrepresented and understudied one. These complications have been factored into the methodological approach adopted for this study.

The mixed-methods approach is a methodology which is commonly used for engaging complicated contexts encountered by the researcher directly, especially cross-cultural groups (187). For this dissertation, it was decided to employ the mixed

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methods approach in order to investigate in depth the relevant interconnected quantitative and qualitative components (187). The rationale is illustrated in Figure 3.1. A quantitative approach was needed to fulfil the research objectives of profiling the quality of life of the target audience, including paediatric patients, and their caregivers and relatives, via a cross-sectional study in a Singaporean context; and, to evaluate the factors influencing these individuals' lives and family functions. Secondly, a qualitative systematic assessment is required for assessing the landscape of the smartphone apps market in order to gain a better understanding of the apps' contribution to supporting AD self-management. Thirdly, the 'mix' happened after I have better ideas about the targeted users in Chapter 4 and 5 and landscape of the AD self-management apps market in Chapter 6 (Figure 3.1). The results, based on quantitative investigation and systematic assessment exploration, were combined to guide the following qualitative co-design section and to empower the participants with better knowledge in generating ideas in co-creating an AD self-management wireframe prototype (Chapter 7). The application of mixed method approach, as presented above, is helpful in elaborating and supplementing the findings in quantitative and systematic assessment studies and can also better address the aim of this dissertation.

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Figure 3.1 Mixed method research design

3.2 Rationale behind the quantitative approach

Chapter 4 to 6 concern cross-sectional studies with a sample of AD patients and their caregivers, who have attended paediatric tertiary dermatology clinics in Singapore. A cross-sectional study is considered a “snapshot” of the targeted population; it entails the collection of data at one point in time, and the drawing of conclusions only on a specific topic (190). This particular research method is considered necessary for this project for three reasons: (1) the cross-sectional design is a prevalent method in this research field, and can provide useful insights into the burden of disease among a subgroup of a population; (2) a cross-sectional study is usually conducted with a large pool of participants, and so can be used to detect and quantify relevant parameters even among subgroups; and, (3) the findings from cross-sectional studies can inform public health planning, monitoring, and resource allocation.

A societal perspective has been applied to the cross-sectional study detailed in chapters 4 and 5 in order to explore the humanistic burden of childhood AD in Singapore and its impact on children with AD, as well as on their caregivers and family relatives. The data collected in the study include health-related quality of life (HRQoL), family impact (DFI), and 36-item short-form survey (RAND 36) data concerning AD treatment and management (52, 191, 192). Chapter 6 uses the same dataset, but its focus is upon the extent of concordance between caregiver-reported and physician-rated severity of AD in paediatric patients in order to identify explanatory factors behind discordance. The cross-sectional studies could potentially serve as a baseline of future longitudinal studies.

3.3 Rationale for qualitative systematic assessment

The recent proliferation of smartphone apps offers opportunities for the delivery of self-management intervention. Apps are now being used for supporting an array of chronic disease conditions, including AD; however, to date, there have been few studies assessing the functionalities and quality of such apps (193, 194). At present, there is still no accepted method for app assessment. Whilst there is prior work in apps that provided some preliminary insights, conclusion to be drawn is limited as this line of work has only focused on apps with better user ratings or higher download numbers rather than a systematic assessment on all available apps (195). In addition, app stores release and update apps frequently, and so there is a high possibility that relevant apps, let alone the full panoply of apps, have not been considered or wholly examined in previous studies. In view of this, in order to gain a detailed, well-grounded knowledge of all relevant apps, it was decided to adopt a systematic review methodology, which could be used to assess the apps. Instead of reviewing articles, the app assessment ‘reviews’ smartphone apps. According to Cochrane (2011), “A systematic review is a review of primary studies on a particular research question that tries to identify, extract, synthesize and critically appraise all relevant evidence, and is regarded as an approach of producing more reliable and accurate evidence with less bias” (196).

The systematic app assessment using the systematic review framework was pursued as the best method to address the research objectives related to apps assessment. This systematic assessment is considered a qualitative approach as it relied on the subjective assessment of apps against pre-defined criteria. Even though the pre-defined criteria were derived from international AD guidelines, assessors often had to use a degree of subjective judgment when determining whether the app conformed to each criterion. For example, assessors were asked to record their overall impressions of this app and any other observations from this app testing in the criteria.

The use of evidence-based assessment criteria mitigated the risk of subjective biases of assessors. Assessors were asked to assess the app against the criteria in terms of clinical relevance and functionalities. In addition, assessors were asked to rate the authoritative, complementarity, privacy, attribution, justifiability, transparency, financial disclosure and advertising policy of the app according to the Health On the Net (HON) Code ¹(197). All apps were evaluated by assessors working in pairs, and any discrepancies were resolved through discussion with a third independent assessor in the team.

3.4 Rationale for qualitative co-design approach

Qualitative research provides meanings by exploring the manner in which people understand themselves, their feelings and the world around them. This research approach can be used to gain more detailed insights into the feelings and experiences of patients and their caregivers. The quantitative data obtained in this study was gathered via multiple-choice questions, which provide respondents with limited opportunity to share feedback and make additional comments. The qualitative approach can be used to collect information on people's immediate emotional feelings and their real-life experiences, via face-to-face, open-ended interviewing and dialogue. Rather than imposing an a priori set of frames within which participants fit their viewpoints, the qualitative approach used in this study allows participants to

¹ mobile Health On the Net (mHON) Code for apps was not released at the time when the research was conducted.

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choose topics upon which to comment in the workshops. Previous qualitative research studies have investigated targeted users' preferences and perceptions of chronic disease management (198, 199), and have contributed to the design of digital health tools such as digital platforms, and smartphone apps (200, 201).

The co-design approach is considered suitable for this PhD project for two reasons: (1) The co-design is an established approach and has been used in several previous studies. The findings of the first two focus groups provide direct observations of the stakeholders' (caregivers', health professionals' and researchers') own experiences of handling childhood AD. (2) The last co-development session brought together other stakeholders, who co-designed apps and provided actionable solutions for confronting the AD-related problems they observed when attending to children suffering from AD. When considering appropriate data analysis approaches, thematic analysis was chosen to analyse the transcriptions from the workshops (268). An inductive strategy was employed, which allowed for themes to be generated from the data, which were then organized into higher-order themes.

Different research approaches are listed in Table 3.1 below. The thought process for making suitable methodological choices regarding the analysis of qualitative data is as follows: Early on, it was decided to exclude the ethnography approach and discourse analysis approach as they do not meet the requirements of this project. The interpretative phenomenological analysis was also ruled out as it cannot capture new ideas and inspiration among all stakeholders during the co-design workshop. Grounded theory is a research methodology which analyses the data inductively: the data collected is reviewed repeatedly, and codes are then assigned to the data. The codes can be grouped into concepts and categories, whereby categories are merged with theory. However, the grounded theory approach is a time-consuming process, and novice researchers may tend to blur methodological lines by selecting purposeful instead of theoretical sampling, which can lead to methodological errors during the analysis. As thematic analysis is an ideal approach to figure out people's perspectives, views and experiences and it is usually applied in interview transcripts, it was decided

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to employ thematic analysis to analyse the qualitative data in the last chapter of the thesis (202, 203).

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Table 3.1 Selected qualitative analysis approaches (204-209)

	Ethnography	Grounded theory	Interpretative Phenomenological Analysis	Discourse analysis	Content Analysis	Thematic Analysis
Aim	Immersion in natural setting to gain insider experience	Generate theory from empirical data	Understand individual in-depth experience, e.g. experience of coping with AD	Capture nuances of text or public discourse, e.g. understanding social change and cultural contexts	Capture the meaning at descriptive level	Analyze narrative materials of life stories
Sampling and Methods	Observational studies	<ul style="list-style-type: none"> • Range of perspectives and stay true to research question; unstructured questionnaire • Theoretical sampling 	<ul style="list-style-type: none"> • Homogenous sample • Stay true to participants' stories • Unstructured questionnaire • Purposeful sampling 	<ul style="list-style-type: none"> • Documents, speeches, newspapers • Purposeful sampling 	<ul style="list-style-type: none"> • Documents like newspapers, mass media • Purposeful/convenience sampling 	a set of texts such as interview transcripts.
Analysis	<ul style="list-style-type: none"> • Data-driven • No fixed commitment to developing new theory 	<ul style="list-style-type: none"> • Data-driven • Constant comparison and iterative approach 	Identification of descriptive and interpretative themes that actively engage the researcher and participants	Detailed, thorough analysis of discourses-speeches, conversations and written text	<ul style="list-style-type: none"> • Deductive approach as categories are identified in advance • Involves counting of frequencies, i.e. number of times AD mentioned in social media 	<ul style="list-style-type: none"> • Description and interpretation • Deductive and inductive approach • Emphasizing context • No peer checking
Researcher's position	Neutral	Need to manage researcher's position	<ul style="list-style-type: none"> • Researcher's position is paramount • Importance of reflexivity 	High level of interpretation or abstraction expected	<ul style="list-style-type: none"> • Neutral • Inter-rater reliability often calculated 	Neutral

Chapter 4

Factors influencing quality of life in children with atopic dermatitis and their caregivers: a cross-sectional study

The challenge of AD can strongly affect patients and caregivers. Singapore, as a country with high prevalence of AD, has scope to improve the awareness of AD among the general population. The burden of AD should be documented to address the gaps in the evidence. Generating evidence for disease burden could also help us understand the target populations better, before embarking on developing interventions and digital apps to support them. Therefore, this chapter is conducted as the ‘first step’ to unravel needs of patients and caregivers and to guide support for future studies. This chapter focusses on understanding the quality of life among patients and their caregivers in Singapore. A detailed method of conducting this cross-sectional study is presented in Section 4.2. Findings on the quality of life burden of AD are detailed in Section 4.3 and the implications of the findings, limitations and future directions are discussed in Section 4.4.

4.1 Introduction

As mentioned in Chapter 1, AD is one of the most common chronic inflammatory skin conditions in children and burdens the quality of life of children and their caregivers (49, 52, 210, 211). The prevalence of AD in Singaporean school children aged seven to 12 years is 20.8% (212), which is relatively high compared to other developed countries and regions (US: 13%; Europe: 15%) (9, 13, 213, 214). A community-based study among Singaporeans demonstrated a high prevalence of AD as well as a low quality of life in adults and children compared with other skin conditions (214). A more recent study showed that Asian adolescents suffer significant psychosocial impact from this skin condition (213). Although clinicians

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are intuitively concerned whether more severe AD in a lower socioeconomic class family may lead to poorer quality of life, only limited studies have so far explored it: severity of AD is correlated with both patients and caregivers' quality of life showing that more severe AD associated with a pronounced adverse impact on both children and caregivers quality of life (36, 176). This finding addressed individual domains of quality of life but further analysis of social and clinical factors associated with quality of life in children and their caregivers was not performed in Singapore due to small sample size.

Better understanding of AD's effect on quality of life and the contributing factors can enhance current management and therapeutic strategies. Given the fact that one in five children are affected in Singapore (212), more empirical in-depth research needs to be conducted to examine factors associated with quality of life in children with AD and their caregivers. To address this gap, the purpose of this study is to investigate the impact of AD on quality of life in a high prevalence area and to assess its related factors.

4.2 Methods

4.2.1 Design and Participants

A cross-sectional survey was conducted from December 2016 to December 2017 at two paediatric dermatology clinics in Singapore: KK Women's and Children's Hospital and National Skin Centre. Children and their caregivers were invited to participate in this study. Patients were eligible if they were (i) 0 to 16 years of age and (ii) fulfilling the Hanifin and Rajka criteria (1980) for AD (215), (iii) able to understand English/Mandarin (Singapore has several official languages with the majority of the population speaking English or Chinese), (iv) had approved consent by their caregiver. Caregivers were included if they were: (i) equal to or older than 21 years of age, (ii) able to understand English/Mandarin, (iii) the legal guardian.

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4.2.2 Instruments

The following information and instruments were included in this cross-sectional questionnaire-based study (see Appendix 4.1):

i. Background questionnaire

Background questionnaire covers social demographic and clinical information of caregiver and child: Relationship of the person/s filling in this questionnaire (e.g. mother, father); caregiver's highest achieved qualification; caregiver's main daytime occupation; accommodation type; child's date of birth; child's sex; child's residential status; child's ethnic group; date of diagnosis first made; the number of children in the family and smoking in the family.

ii. 36-item short-form survey (RAND-36)

The RAND-36 is one of the most widely used health-related quality of life (HRQoL) instruments and has been validated in Singapore (216-218). Mental health and physical health of caregivers can be generated from health utility scores in eight domains, namely, physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional and mental health (216). RAND-36 is also a generic instrument enabling comparisons between caregivers of children with AD to other populations e.g. caregivers of children with other diseases or the general population. The score ranges from 0 to 100, with a lower score indicating poorer health or functioning (218). This questionnaire was answered by caregivers.

iii. The Infants' Dermatitis Quality of Life Index (IDQOL)

IDQOL questionnaire contains ten questions covering six areas of daily activities including symptoms and feelings, leisure, school or holidays, personal relationships, sleep, and treatment (219). Each question is answered on a 4-point Likert scale scored from 0 to 3. These are added to give a minimum score of 0 and a maximum score of 30. A higher score indicates a greater degree of QoL impairment (219). The severity banding for IDQOL scores: 0-1 = no effect on infant's life; 2-5 = small effect; 6-10

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= moderate effect; 11-20 = very large effect; 21-30 = extremely large effect (220). This questionnaire was answered by caregivers on behalf of their infant patients.

iv. The Children's Dermatology Life Quality Index (CDLQI)

The questionnaire contains ten questions covering six areas of daily activities including symptoms and feelings, leisure, school or holidays, personal relationships, sleep, and treatment (210). Each question is answered on a 4-point Likert scale scored from 0 to 3. These are added to give a minimum score of 0 and a maximum score of 30. A higher score indicates a greater degree of QoL impairment (210). The severity banding for CDLQI scores: 0-1 = no effect on child's life; 2-6 = small effect; 7-12 = moderate effect; 13-18 = very large effect; 19-30 = extremely large effect (210, 221). This questionnaire was answered by children.

4.2.3 Data collection procedure

For children under 4 years of age or who have not reached a suitable level of English language proficiency, health-related quality of life (HRQoL) was obtained through IDQOL. This was completed by the children's parents (219). For children who were of an adequate level of English proficiency, CDLQI, in text or cartoon version, was used. In cases when the child had difficulties to read the questionnaire themselves the research assistant at the study site or the parent assisted the child (210). The caregivers' HRQoL was obtained through RAND-36 (filled in by caregivers) (216).

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Figure 4.1 Data collection procedure

4.2.4 Disease severity assessment

AD severity was extracted from the electronic medical records. Medical records were recorded by a dermatologist during the clinics and contained: 1) disease severity and/or, 2) affected areas and symptoms. Disease severity mentioned in medical records was extracted (at the same time point as caregivers filled in the questionnaires). For those patients whose severity was not explicitly reported in the electronic medical records, symptoms and affected area were extracted from electronic medical records and assessed by an investigating physician-researcher using Eczema Area and Severity Index (EASI) calculator into mild (EASI score 1.1-7.0), moderate (EASI score 7.1–21.0) and severe (EASI score 21.1–50.0), very severe (EASI score 50.1-72) (30, 222). This score is calculated by the percentage of skin

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affected by AD for each body region and the intensity scores of four signs: redness; thickness; scratching; lichenification (30).

4.2.5 Statistical analysis

Since limited information regarding the study objectives relating to Singapore was published, I tried to generate baseline data using disease prevalence information. We mapped the required population of interest (i.e. paediatric AD cases) around two major hospitals in Singapore based on AD prevalence. Sample size was calculated in order to ensure sufficient precision in detecting disease burden outcomes (223). According to the sample size formula for a quantitative variable, the minimum required sample size was estimated by assuming a 20% prevalence of AD among children (age ≤ 18 years) in Singapore (147). Further, we have also considered a type-1 error rate of 5%, 80% power, a 5% permissible margin of absolute error, and a 10% non-response rate. Using the one-proportion hypothesis testing formula, the minimum required sample size was calculated to be 518 patients. Descriptive statistics for continuous variables are reported with mean $\pm$ SD, categorical variables are reported with frequencies and percentages (%). Normality of the continuous variables was tested by the Shapiro–Wilk test. The Wilcoxon rank-sum (or Mann–Whitney) test for two groups and Kruskal–Wallis test for more than two groups were used to find statistical associations between sociodemographic characteristics and RAND-36, CDLQI and IDQOL scores along with their subdomains. (A univariate model was calculated to inform the selection of influencing factors in multivariate regression, but it is not presented in this study as it provides no new information). Subsequently, as the distribution of CDLQI, IDQOL and RAND-36 was over-dispersed (i.e., the conditional variance exceeded the conditional mean), a negative binomial regression model was used to demonstrate the relationship between sociodemographic variables and CDLQI, IDQOL and RAND-36 measures. Univariable and multivariable incidence rate ratios (IRR) were calculated and reported with 95% confidence intervals (CIs). Statistical analysis was carried out using Stata 14.2 (StataCorp, College Station, TX, USA). Two-sided *p*-value less than

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0.05 was taken as statistically significant and the 95% confidence intervals (CIs) are presented.

4.2.6 Ethical approval and informed consent

The present study was approved by the Institutional Review Board of National Healthcare Group (NHG-DSRB: 2015/01228) and Nanyang Technological University (NTU IRB: IRB-2016-10-059-01). The methods were carried out following the relevant guidelines and regulations. Informed consent was obtained from all participants and their legal guardians. Identifiers were removed from all sections of the manuscript, including supplementary information. To protect the anonymity of their responses, no IP addresses, email addresses, or identifying information was collected.

4.3 Results

4.3.1 Patient characteristics

4. Factors influencing QoL in children with AD and their caregivers

Figure 4.2 Patient recruitment workflow

The characteristics of the participants are summarised in Table 4.1. In total, of 735 eligible children, 559 patients and their caregivers participated (76%). Reasons for rejection are listed in Figure 4.2. The study sample consists of 250 infants (age 0-4 years old) and 309 children (5-16 years old) (50% boys and 50% girls), with a mean age ($\pm$ SD) of 6.61 ± 4.55 years old. Disease severity was mild in 56.5% of the cases, moderate in 23.8% and severe in 11.5% (Disease severity was assessed using EASI score and in 46 cases, disease severity could not be retrieved). Seventy-two per cent of the participants were Chinese, Indian and Malay participants accounted for 15.9% and 5.9% respectively. A great majority of caregivers (81.6%) were educated to at least tertiary-level educational attainments. The majority were employed (80.9%), 19.1% were unemployed or retired.

4. Factors influencing QoL in children with AD and their caregivers

Table 4.1 Background characteristics of AD patients and their caregivers

Characteristics *	Total (n=559)	Sex		P-value
		Male (n= 282)	Female (n=277)	
Children's age (years) (Mean $\pm$ SD)	6.61 $\pm$ 4.55	6.91 $\pm$ 4.72	6.30 $\pm$ 4.36	0.11
Children's ethnicity, n (%)				0.42
Chinese	404(72.3)	195 (69.2)	209 (75.5)	
Indian	89 (15.9)	50 (17.7)	39 (14.1)	
Malay	33(5.9)	19 (6.7)	14 (19.1)	
Caucasian and others	33(5.9)	18 (6.4)	15 (5.4)	
Duration of disease (years) (Mean $\pm$ SD)	3.51 $\pm$ 3.62	3.75 $\pm$ 3.82	3.27 $\pm$ 3.40	0.12
Disease severity*, n (%)				0.45
Mild	316(56.5)	161(57.1)	155 (56.0)	
Moderate	133(23.8)	61 (21.6)	72 (26.0)	
Severe	64(11.5)	35 (12.4)	29 (10.8)	
Caregiver's highest achieved educational attainment, n (%)				0.55
Primary and secondary	103(18.4)	57 (20.2)	46 (16.6)	
Polytechnic and professional	181(32.4)	89 (31.6)	92 (33.2)	
University and above	275(49.2)	136 (48.2)	139 (50.2)	
Caregiver's employment status, n (%)				0.72
Employed	452(80.9)	231 (81.9)	221 (79.8)	
Unemployed/ retired	107(19.1)	51 (18.1)	56 (20.2)	
Type of housing*, n (%)				0.29
Public housing 1-3 rooms	68(12.2)	36 (12.8)	32 (11.6)	
Public housing 4-5 rooms	361(64.8)	189 (67.0)	172 (62.1)	
Private housing (condo, landed property)	128(23.0)	57 (20.2)	71 (25.6)	
Number of children in the family, n (%)				0.05
1	175(31.3)	97 (34.4)	78 (28.2)	
2	231(41.3)	120 (42.6)	111 (40.1)	
≥ 3	153(27.4)	65 (23.1)	88 (31.8)	
Smoking in family, n (%)				0.90
Yes	94(16.8)	48 (17.0)	46 (16.6)	
No	465(83.2)	234 (83.0)	231 (83.4)	

* Missing data: Disease severity, n=46; Living accommodation, n=2

4.3.2 Children's and their caregivers' quality of life

Mean scores of overall HRQoL were 8.76 ± 5.76 and 8.76 ± 5.46 for IDQOL and CDLQI respectively. Two quality of life subscales with a major impact on infants were itching and scratching (mean $\pm$ SD: 1.77 ± 0.84) and sleep disturbances (mean $\pm$ SD: 1.27 ± 0.82) (Figure 4.3). For CDLQI scales, symptoms and sleep disturbance were also the subscales with the largest impact (symptoms: mean $\pm$ SD: 1.22 ± 0.68 ; sleep disturbance: mean $\pm$ SD: 1.17 ± 1.07) (Figure 4.3). Significant differences in quality of life between different severity groups were observed among infants and children. Figure 4.3 shows that several IDQOL subdomain scores were increasingly impaired when disease severity increased (itching and scratching ($P < 0.001$), mood ($P = 0.002$), total time disturbed ($P = 0.013$), playing or swimming ($P = 0.031$), enjoying a family activity ($P = 0.002$), dressing uncomfortable (discomfort with clothing) ($P = 0.002$) and problems at bath time ($P < 0.001$)). CDLQI subscale domains were also increasingly impaired when the severity of the condition increased (symptoms and feelings ($P = 0.011$), leisure ($P = 0.007$), school or holidays disturbance ($P < 0.001$), personal relationship ($P = 0.022$), sleep affected ($P = 0.002$), and treatment ($P < 0.001$)).

Scores in the mental and physical health domains of the RAND-36 for the 559 caregivers were 38.52 ± 14.27 and 50.48 ± 9.69 respectively. Compared to RAND-36 scores in previous studies exploring the relationship between childhood disease and its impact on caregivers/parents, the data indicated that the mental health scores of caregivers looking after children with AD were poorer than those of caregivers of children with psychiatric disorders and equivalent to mothers looking after children with severe developmental disability and physical problems such as heart disease (224-226).

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Figure 4.3 Association between mean score of IDQOL and CDLQI reported subdomains and children's disease severity

A. IDQOL subdomains (X-axis: subdomains; Y-axis: mean score of IDQOL)

B. CDLQI subdomains (X-axis: subdomains; Y-axis: mean score of CDLQI)

* Significant differences in quality of life between different severity groups (missing data: n=46)
 IDQOL: The score ranges from 0 to 30. A higher score indicates a greater degree of quality of life impairment.
 CDLQI: The score ranges from 0 to 30. A higher score indicates a greater degree of quality of life impairment.

4.3.3 Factors related to children's quality of life

Univariate model and multivariate models were constructed to assess the relationship between sociodemographic variables and the HRQoL in children (Table 4.2). The model suggested that moderate and severe AD significantly decreases quality of life in IDQOL (moderate: IRR: 1.42, 95% CI: [1.20, 1.67], $P<0.001$; severe: IRR: 1.72, 95% CI: [1.32, 2.24], $P<0.001$). In CDLQI, moderate AD significantly decreases quality of life while no similar result was observed in severe cases (moderate: IRR: 1.08, 95% CI: [1.02, 1.14], $P=0.01$). Children's age was found to be associated with their quality of life with older children having better quality of life (IRR: 0.99, 95% CI: [0.98, 1.00], $P=0.02$). The remaining sociodemographic characteristics (ethnicity, educational attainment, number of children in the family and type of housing) did not demonstrate significance in the children's HRQoL model.

4. Factors influencing QoL in children with AD and their caregivers

Table 4.2 Multivariable regression analysis with factors associated with the children and caregivers' quality of life

Variables *	Children HRQoL						Caregivers RAND 36					
	IDQOL			CDLQI			Physical health			Mental health		
	IRR ^a	95%CI ^b	P-value	IRR	95%CI	P-value	IRR	95%CI	P-value	IRR	95%CI	P-value
Age of child (years)	1.02	[0.98, 1.06]	0.44	0.99	[0.98, 1.00]	0.02	1.01	[1.00, 1.01]	0.03	1.00	[0.99, 1.01]	0.44
Sex												
Male	1(Ref)											
Female	1.09	[0.93, 1.27]	0.31	0.99	[0.94, 1.05]	0.80	0.99	[0.96, 1.03]	0.69	1.00	[0.94, 1.06]	0.94
Disease duration (years)	1.01	[0.98, 1.05]	0.51	1.00	[1.00, 1.01]	0.16	1.00	[0.99, 1.00]	0.44	1.00	[0.99, 1.01]	0.60
Disease severity*												
Mild	1(Ref)											
Moderate	1.42	[1.20, 1.67]	p<0.001	1.08	[1.02, 1.14]	0.01	0.98	[0.94, 1.02]	0.35	0.97	[0.90, 1.05]	0.49
Severe	1.72	[1.32, 2.24]	p<0.001	1.05	[0.96, 1.15]	0.29	0.94	[0.89, 0.99]	0.03	1.03	[0.93, 1.15]	0.57
Ethnicity												
Chinese	1(Ref)											
Indian	1.12	[0.91, 1.38]	0.30	1.02	[0.95, 1.11]	0.56	0.93	[0.88, 0.97]	0.003	1.00	[0.90, 1.10]	0.97
Malay	1.28	[0.91, 1.80]	0.15	1.01	[0.94, 1.08]	0.82	0.95	[0.88, 1.02]	0.13	1.03	[0.89, 1.20]	0.65
Others	1.28	[0.90, 1.81]	0.17	1.03	[0.93, 1.14]	0.58	1.03	[0.96, 1.11]	0.41	1.04	[0.88, 1.23]	0.67
Educational attainment												
Polytechnic and professional	1(Ref)											
Primary and secondary	1.16	[0.90, 1.49]	0.27	1.01	[0.94, 1.09]	0.79	1.01	[0.96, 1.06]	0.72	0.99	[0.90, 1.08]	0.77
University	0.95	[0.79, 1.13]	0.54	0.99	[0.93, 1.05]	0.72	0.99	[0.95, 1.03]	0.58	0.99	[0.92, 1.07]	0.82
Number of children in family	1.00	[0.90, 1.11]	0.95	1.02	[0.98, 1.05]	0.42	0.99	[0.97, 1.01]	0.47	0.97	[0.93, 1.01]	0.19
Type of housing												
HDB 1-3 rooms	1(Ref)											
HDB 4-5 rooms	0.95	[0.71, 1.28]	0.76	1.01	[0.94, 1.10]	0.73	1.04	[0.98, 1.10]	0.21	1.09	[0.97, 1.23]	0.17
Private housing (condo, landlord)	1.01	[0.71, 1.44]	0.95	1.01	[0.92, 1.11]	0.84	1.09	[1.02, 1.17]	0.01	1.10	[0.96, 1.26]	0.19
Children's HRQoL ^c							0.99	[0.99, 1.00]	p<0.001	0.98	[0.97, 0.99]	p<0.001

* Missing data: Disease severity, n=46; Type of housing, n=2

^a IRR: incidence rate ratio; ^b CI: confidence interval

^c HRQoL: disease-specific HRQoL of patients with AD was measured using IDQOL and CDLQI

4.3.4 Factors related to children's quality of life subdomains

Table 4.3 presents a negative binomial analysis assessing the related sociodemographic and clinical factors in two subscales (sleep disturbance and symptoms and feelings) with the most impact on children in Figure 4.3. Age of infants and long disease duration may have an impact on the subdomain of symptoms and feelings (IDQOL age: IRR: 1.03, 95% CI: [1.01, 1.06], $P=0.02$; CDLQI disease duration: IRR: 1.02, 95% CI: [1.00, 1.04], $P=0.04$). Greater severity of AD was associated with a poorer quality of life in children for symptoms and feelings subdomain (moderate cases of IDQOL: IRR: 1.24, 95% CI: [1.10, 1.41], $P=0.001$; severe cases of IDQOL: IRR: 1.31, 95% CI: [1.07, 1.61], $P=0.01$; moderate cases of CDLQI: IRR: 1.20, 95% CI: [1.04, 1.40], $P=0.02$). Infants and children with high severity of disease suffered from significantly more severe sleep disturbance compared to those with lower disease severity (severe cases of IDQOL: IRR: 1.49, 95% CI: [1.19, 1.87], $P=0.001$; moderate cases of CDLQI: IRR: 1.63, 95% CI: [1.25, 2.13], $P<0.001$; severe cases of CDLQI: IRR: 1.97, 95% CI: [1.50, 2.60], $P<0.001$).

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Table 4.3 Multivariable regression analysis with factors associated with symptoms and feelings, and sleep disruption

Variables *	Symptoms and feelings						Sleep disturbance					
	IDQOL			CDLQI			IDQOL			CDLQI		
	IRR ^a	95%CI ^b	P-value	IRR	95%CI	P-value	IRR	95%CI	P-value	IRR	95%CI	P-value
Age of child (years)	1.03	[1.01, 1.06]	0.02	1.00	[0.97, 1.02]	0.78	0.99	[0.95, 1.03]	0.63	0.97	[0.94, 1.01]	0.13
Sex												
Male	1(Ref)											
Female	1.06	[0.94, 1.19]	0.35	1.11	[0.96, 1.27]	0.15	1.04	[0.89, 1.21]	0.61	1.02	[0.81, 1.28]	0.89
Disease duration (years)	1.01	[0.98, 1.04]	0.56	1.02	[1.00, 1.04]	0.04	0.99	[0.95, 1.04]	0.80	1.03	[1.00, 1.06]	0.05
Severity												
Mild	1(Ref)											
Moderate	1.24	[1.10, 1.41]	0.001	1.20	[1.04, 1.40]	0.02	1.11	[0.93, 1.33]	0.24	1.63	[1.25, 2.13]	p<0.001
Severe	1.31	[1.07, 1.61]	0.01	1.20	[0.98, 1.47]	0.08	1.49	[1.19, 1.87]	0.001	1.97	[1.50, 2.60]	p<0.001
Ethnicity												
Chinese	1(Ref)											
Indian	1.00	[0.85, 1.18]	0.97	1.07	[0.87, 1.30]	0.54	1.24	[1.02, 1.50]	0.03	1.06	[0.78, 1.45]	0.70
Malay	0.99	[0.75, 1.30]	0.93	1.08	[0.79, 1.46]	0.64	1.49	[1.18, 1.88]	0.001	1.34	[0.86, 2.07]	0.19
Others	1.12	[0.88, 1.42]	0.36	1.17	[0.87, 1.59]	0.30	1.18	[0.82, 1.69]	0.37	0.86	[0.46, 1.61]	0.63
Educational attainment												
Polytechnic and professional	1(Ref)											
Primary and secondary	1.04	[0.86, 1.25]	0.70	1.00	[0.85, 1.18]	0.98	1.35	[1.06, 1.72]	0.02	0.95	[0.71, 1.26]	0.72
University	0.96	[0.84, 1.11]	0.59	0.91	[0.77, 1.09]	0.32	0.97	[0.82, 1.15]	0.75	0.87	[0.65, 1.16]	0.35
Number of children in family	0.97	[0.90, 1.06]	0.54	0.95	[0.87, 1.03]	0.23	1.02	[0.92, 1.12]	0.76	1.04	[0.90, 1.19]	0.63
Type of housing												
HDB 1-3 rooms	1(Ref)											
HDB 4-5 rooms	1.07	[0.86, 1.33]	0.55	0.99	[0.82, 1.21]	0.93	0.97	[0.72, 1.30]	0.85	0.94	[0.70, 1.26]	0.67
Private housing (condo, landlord)	1.03	[0.80, 1.31]	0.84	0.78	[0.60, 1.01]	0.06	1.10	[0.77, 1.56]	0.61	0.93	[0.61, 1.42]	0.73

* Missing data: Disease severity, n=46; Type of housing, n=2

^a IRR: incidence rate ratio; ^b CI: confidence interval

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4.3.5 Factors related to caregivers' quality of life

Table 4.2 shows that poor health-related quality of life of children may also adversely affect their caregivers' mental and physical health (physical: IRR: 0.99, 95% CI: [0.99, 1.00], $P < 0.001$; mental: IRR: 0.98, 95% CI: [0.97, 0.99], $P < 0.001$). The scatterplot in Figure 4.4 demonstrated the relationship between children's HRQoL and their caregivers' physical and mental health. It showed that as children's HRQoL decrease, their caregivers' mental health and physical health could drop (a higher HRQoL score here meant a lower quality of life; higher physical/mental health meant better physical/mental health). Caregiver's physical health might be also associated with their children's age, with children with older age having a positive effect on their caregivers' physical health (IRR: 1.01, 95% CI: [1.00, 1.01], $P = 0.03$). Children with severe AD also had a significant impact on their caregiver's physical health while mild and moderate cases did not demonstrate such an influence (IRR: 0.94, 95% CI: [0.89, 0.99], $P = 0.03$).

Figure 4.4 Association between children's mean score of HRQoL and caregivers' physical and mental health (X-axis: mean score of HRQoL; Y-axis: mean score of physical health/mental health)

* HRQoL in this figure is a composite of IDQoL and CDLQI. A higher HRQoL in this figure indicates a lower health-related quality of life of children.

4.4 Discussion

This study has shown that disease severity, rather than sociodemographic factors affect the health-related quality of life for children. The severity of AD is significantly associated with patients' and caregivers' self-reported quality of life: more severe AD is related to a poorer quality of life. Another finding emerging from this study was that caregiver's mental and physical health was directly affected by their children's health-related quality of life. Poor quality of life in AD children could lead to poor mental and physical functioning among caregivers.

A meta-analysis published in 2016 has shown similar results to this study (227). Besides, when it is compared to prior studies in Singapore, this study reported better quality of life (lower CDLQI/IDQOL score) (213). The discrepancy may be because the sample size allowed us to detect a more accurate effect and participants recruited from dermatology specialist clinics with more severe AD (58, 228-230). The results above also suggest that sociodemographic factors, such as caregiver's educational attainment, may be of less influence on the treatment of children with AD than clinicians might intuitively think. In comparison to children, a relationship between caregiver's physical health and type of housing was found. As type of housing is considered as social class indicator in Singapore (231), this trend is in line with previous studies showing that social status may affect adults more than their children (232, 233). In research exploring the relationship between childhood AD and its impact on parents health similar conclusions have been described: a strong relationship was found between a greater disruption of sleep of the child with AD and higher levels of maternal anxiety and depression (224). Due to the burden of the condition and the impact of new routines imposed by continuous treatment, caregivers have to restructure their lives (234). Parents may spend hours to comfort their child and manage the disease. Adaptation to these changes also requires parents to be prepared mentally and physically for sleep disturbance, emotional distress, and exhaustion (235, 236). It is worrying that the negative impact on quality of life in these caregivers is more severe or comparable to prevalent paediatric chronic diseases, such as psychiatric disease and congenital heart disease (224-226). The

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results indicate the traditional scope in the treatment of AD should be broadened to include not only affected children but also their surrounding support system.

This in-depth study is the first to assess quality of life subdomains and related clinical and sociodemographic factors. Itching/scratching, emotional distress, and sleep disturbance were quality of life subdomains most reported, and their reporting increased with higher disease severity (Figure 2). This study showed that greater severity of AD leads to poorer health-related quality of life of the child. This might be explained by the fact that affected subdomains could be considered as a cluster issue. Symptoms such as intractable itching and scratching can consequently aggravate AD lesions resulting in significant sleep deprivation leading to exhaustion, unstable emotions and impaired functioning (237, 238). However, caregivers' quality of life is affected by multiple factors and could be directly affected by their children's quality of life instead of disease severity. As such, treatment strategies targeting specific AD symptoms should improve patient and caregiver quality of life.

Findings from this study have shown that the management and treatment routine of AD needs to be adapted to incorporate quality of life assessment in affected patients. In addition, preventing deterioration of the disease seems a key point in treatment. However, complete severity and symptom assessment and monitoring are not generally adopted in clinical routine, as this process is seen as too time-consuming. Disease tracking is an important factor in the treatment of AD, but self- or caregivers-assessment may be unreliable without appropriate guidance. Therefore, more convenient and efficient tools need to be deployed in the future to meet the current needs. Moreover, treatment should focus beyond the disease and more attention should be directed to the symptoms and feelings of children and their caregivers. Effective, evidence-based psychosocial assessment and intervention tools should be made available. For example, health apps could be tailored to target user's tracking needs as the diagnosis and management of AD are mainly based on visual examination (239). An app could also be valuable for keeping patients engaged, educate them and create awareness of their skin status. It would provide an

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opportunity for healthcare professionals to monitor and conduct (symptoms and feelings) interventions and guidance in real-time to a distance (110, 240).

It is interesting for us to find that moderate AD significantly decreased QoL while no similar results were observed in severe cases in CDLQI score. This finding appeared unexpected as clinical observations would suggest that individuals with more severe symptoms should be affected more than those with less severity. This could be explained: 1) Doctors prescribe stronger medications to treat the symptoms such as itchiness and sleep problems and therefore children with severe disease might be less affected by AD. 2) Severe patients and their caregivers may have better adherence to therapy and hence report to be less affected by severe AD. 3) More severe individuals might be getting used to the poor quality of life as well as have lower expectations than those with mild to moderate symptoms, and this would lead them to report better quality of life. Similar trends have been reported in the relation of quality of life to sleep and obsessive-compulsive disorder and other mental health issues (241, 242).

This study has several strengths. The high recruitment rate and the large study sample provide a good representation of children with AD in Singapore. According to the power calculation, the sample size of 559 participants is sufficient to capture the quality of life status accurately to allow subgroup analysis and to be generalised to other high prevalence countries. Secondly, this study is the first to employ a negative binomial model to test the social, clinical factors associated with paediatric AD patients' HRQoL. This model highlights how paediatric AD patients' health-related quality of life affects their caregivers' quality of life, which leads to a more complete understanding of the total burden. A weakness of this study is the lack of a non-AD control group. Therefore, we cannot compare AD patients and caregivers HRQoL with non-AD children and caregivers. I have however attempted to compare caregiver's quality of life for other chronic diseases. Secondly, the sample size calculation was not done separately for each study objective. This was due to limited disease burden information pertaining to AD patients in Singapore, and so we could only calculate the sample size based on prevalence of AD in Singapore. However, the sample size calculated using this method is considered to possess sufficient

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statistical power to reflect the disease burden in Singapore. Thirdly, a potential selection bias exists due to the large portion of patients excluded owing to the absence of a primary recruitment site (e.g. general practitioner clinics and primary care hospitals). Since participants were only recruited from tertiary hospitals, they might have been experiencing more severe disease conditions compared to those who visited primary care depots. However, this limitation could be compensated, to some extent, because of the particularity of pediatric diseases: parents have a tendency to turn towards tertiary care instead of visiting primary hospitals (e.g. visiting their GP) as they think paediatricians are generally better trained and equipped to diagnose diseases in children. As such, the major hospitals in this study cover the larger proportion of pediatric patients. Fourthly, a cross-sectional study may preclude concrete observations regarding the influence of AD over time. Lastly, the IDQOL scores may not accurately detect infants' HRQoL as their caregivers filled in the questionnaire on behalf of their infants.

4.5 Conclusion

This study provides an in-depth view of the AD-related quality of life among children and their caregivers in Singapore. It helps us understand the complex relationship between sociodemographic factors, disease severity, and quality of life in AD patients. More attention should be directed to AD symptoms and their effect on daily life. The correlation between disease severity and quality of life implicates that treatment should focus on prevention of severe AD. Future studies should investigate interventions to address factors associated with both the quality of life and the disease severity of children and their caregivers.

Chapter 5

Factors influencing family burden of the paediatric atopic dermatitis patient: a cross- sectional study

This chapter presents a study conducted to explore whether the focus of AD treatment should be broadened to include their family members not only the patients themselves but family as a unit. It concludes with important insights relevant for healthcare providers, policymakers and insurance companies. This chapter starts with an introduction in Section 5.1. A detailed method of conducting this cross-sectional study is subsequently presented in Section 5.2. Findings on the family burden of AD are detailed in Section 5.3 and the implications of the findings, limitations and future directions are discussed in Section 5.4.

5.1 Introduction

As presented in the previous chapters, AD contributes to behavioural and social impairment in paediatric AD patients, and can also affect family members, resulting in symptoms such as daytime drowsiness, poor concentration and poor work output (52, 220, 229, 236, 243-245). Family functioning can greatly influence patient-related outcomes. In Asia, both the nuclear and extended family structure are strongly embedded in the culture, with family members often residing together and having a strong sense of responsibility to provide care (57, 246-249). A sick child can markedly affect normal family life, mental and social wellbeing of other family members (250): Financial expenditure and demanding treatment of child's AD can further increase burden on the family (60). Families may also experience the feelings of helplessness regarding their child's symptoms and high-stress levels associated with the guilt of not managing their child 'well' (60, 243).

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Previous studies confirmed a significant relationship between severity of childhood AD and family quality of life (DFI) showing that more severe AD might be related to greater impact on DFI (243, 251, 252), and yet, limited quantitative information was revealed on the other factors, such as social and clinical factors, associated with DFI. Considering the high prevalence of AD, understanding the impact of AD on DFI can lead to a better understanding of how the management of disease could improve patient and family-related outcomes. As such, based on previous findings, this study sought to provide an in-depth insight into the family burden of paediatric AD and to explore the social and clinical factors potentially impacting family life and function (DFI).

5.2 Methods

5.2.1 Design and participants

Please refer to Section 4.2.1 Design and participants.

5.2.2 Instruments

The following information and instruments were included in this cross-sectional questionnaire-based study:

i. Background questionnaire

Please refer to Section 4.2.2 Instruments in Chapter 4.

ii. Dermatitis Family Impact (DFI)

DFI questionnaire is a disease-specific measure to assess the impact of AD on family life and function. It captures information on the degree of impact AD has on the family, in areas such as housework, cooking and feeding, sleep, leisure, shopping, expenditure, tiredness, distress, relationship and overall life (191). This questionnaire

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is filled in by caregivers. DFI has been widely validated in many countries including Singapore (253). DFI questions are scored on a four-point Likert scale ranging from 0 (not at all) to 3 (very much) so that the total DFI score ranges from 0 to 30 (2).

iii. **36-item short-form survey (RAND-36)**

Please refer to Section 4.2.2 Instruments in Chapter 4.

iv. **Children's health-related quality of life (HRQoL)**

Infants' Dermatitis Quality of Life Index (IDQOL) in infants and Children's Dermatology Life Quality Index (CDLQI) in children were merged into the children's HRQoL score to evaluate AD-related quality of life among paediatric patients with AD (3, 5). Please find information and scoring system of IDQOL and CDLQI in Section 4.2.2 Instruments in Chapter 4.

5.2.3 Data collection procedure

Information about the impact of childhood AD on the family was collected through DFI (filled in by caregivers) (191). For children under 4 years of age or have not reached a suitable level of English language proficiency, children's HRQoL was obtained through IDQOL. This was completed by the child's parent (219). For children who were of an adequate level of English proficiency, CDLQI, in text or cartoon version, was used. In cases when the child had difficulties in reading the questionnaire themselves the research assistant at the study site or the parent assisted the child (210). The caregivers' HRQoL was obtained through RAND-36 (filled in by caregivers) (216). Procedure for questionnaires data collection was detailed in Figure 5.1.

5. Factors influencing family burden of children with AD

Figure 5.1 Questionnaires data collection procedure

5.2.4 Disease severity assessment

Please refer to Section 4.2.4 Disease severity assessment in Chapter 4.

5.2.5 Statistical analysis

We estimated the minimum required sample size by assuming a 20% prevalence of AD among children (age ≤ 18 years) in Singapore (214). Further, we considered the type-one error rate to 5%, 80% power, a 5% permissible margin of absolute error and a 10% nonresponse rate. Then using the one proportion hypothesis testing formula, the minimum required sample size was calculated to be 518 patients. Descriptive statistics for continuous variables are reported with mean $\pm$ SD and categorical

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variables are reported with frequencies and percentage (%). Normality of the continuous variables was tested by the Shapiro–Wilk test. Wilcoxon rank-sum (or Mann–Whitney) test for two groups and Kruskal Wallis test for more than two groups were used to finding the statistical association between socio-demographic characteristics (ethnicity, education, occupation, housing accommodation) and DFI score along with their subdomains. As the distribution of DFI was over-dispersed (i.e., the conditional variance exceeded the conditional mean), a negative binomial regression model was used to find associated factors with DFI. However, Poisson regression was used for DFI subscales (i.e., sleep disturbance, emotional distress and tiredness/exhaustion) as conditional variances were similar to its conditional means. As such, a negative binomial regression model and Poisson model were used to demonstrate the relationship between socio-demographic variables and DFI measures. Univariable and multivariable incidence rate ratios (IRR) were calculated and reported with 95% confidence intervals (CIs). Statistical analysis was carried out using Stata software version 14.2 (StataCorp, College Station, TX, USA). A two-sided p-value less than 0.05 was taken as statistically significant.

5.2.6 Ethics approval and informed consent

Please refer to Section 4.2.6 Ethical approval and informed consent.

5.3 Results

5.3.1 General characteristics of the family life and function

The demographic characteristics of the included families are provided in Table 5.1. In total, of 735 eligible family member-child referred by clinicians, 559 participated (76%). Reasons for rejection are listed in Figure 4.2 in the previous chapter. The ages of paediatric patients in the families ranged from 1 month to 16 years with a mean 6.61 ± 4.55 years. Key demographic and other patient and family member characteristics are presented in Table 5.1.

5.3.2 Dermatitis family impact and its subdomains

More than 94% of families reported that their family life and function (DFI) were affected by their child's AD (DFI > 0). The mean score for DFI in affected families was 9.19 ± 7.28 , sleep disturbance, emotional distress and tiredness/exhaustion were the subscales with the largest impact (sleep time: mean $\pm$ SD = 1.16 ± 1.01 ; emotional distress: mean $\pm$ SD = 1.16 ± 0.95 ; tiredness/exhaustion: mean $\pm$ SD = 1.19 ± 0.98) (Figure 5.2). Significant difference among different disease severity groups was observed in overall DFI score as well as in nine out of ten subdomains (marked as * in Figure 5.2) including housework ($P < 0.001$), food preparation and feeding ($P = 0.021$), sleep deprivation ($P < 0.001$), shopping ($P = 0.048$), expenditure ($P < 0.001$), tiredness ($P < 0.001$), emotional distress ($P < 0.001$), relationship ($P < 0.001$) and helping with treatment ($P < 0.001$) indicating that family life and function (DFI) whose child with more severe AD affected more by the disease on almost all subdomains.

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Table 5.1 Social and Demographic Characteristics of Patients and Their Families

Characteristics *	N	% / Mean $\pm$ SD
Children's Age (years) (Mean $\pm$ SD)	559	6.61 $\pm$ 4.55
Sex		
Male	282	50.45%
Female	277	49.55%
Ethnicity (n, %)		
Chinese	404	72.27%
Indian	89	15.92%
Malay	33	5.90%
Others	33	5.90%
Duration of disease (years) (Mean $\pm$ SD)	559	3.51 $\pm$ 3.62
Disease severity (n, %) (n= 513)		
Mild	316	56.53%
Moderate	133	23.79%
Severe	64	11.45%
Parent's highest achieved qualification (n, %)		
Polytechnic and professional	181	32.38%
Primary and secondary	103	18.43%
University	275	49.19%
Parent's employment status (n, %)		
Employed	452	80.86%
Unemployed/ retired	107	19.14%
Mother's allergic history (n, %)		
Eczema	162	28.98%
Asthma	80	14.31%
Hay fever	6	1.07%
Living accommodation (n, %) (n= 557)		
Government flat 1-3 rooms	68	12.21%
Government flat 4-5 rooms	361	64.81%
Private housing (condo, landlord)	128	22.98%
Number of children in the family (n, %)		
1	175	31.31%
2	231	41.32%
≥ 3	153	27.37%
Families reported affected by AD ^a	526	94.10%

* Missing data: Disease severity, n=46; Living accommodation, n=2

^a Families reported affected by AD refers to those family with DFI>0

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Figure 5.2 Association between mean score of DFI reported subdomains and children's disease severity (X-axis: DFI subdomains; Y-axis: Mean score of dermatitis family impact)

* Significant differences in dermatitis family impact between different severity groups (missing data: n=46)

5.3.3 Factors related to DFI and its subdomains

Univariate model and multivariate models were employed to analyse the factors associated with family life and function (Table 5.2). Families with older children were less affected by their child's AD (IRR: 0.97, 95%CI: [0.96, 0.99], P=0.002). Disease duration and severity also affects DFI. Having AD for longer seems to affect family life and function more than in those families where children had it for a shorter period (IRR: 1.02, 95%CI: [1.00, 1.04], P=0.019). Families with children with moderate and severe AD had poorer family life and function than those with mild disease (moderate: IRR: 1.23, 95%CI: [1.09, 1.40], P=0.001; severe cases: IRR: 1.26, 95%CI: [1.06, 1.49], P=0.008). Family members' QoL also affects family life and function. As for the caregivers' QoL, both mental health and physical health of caregivers can affect family life and function. Better mental and physical health among caregivers reported less impaired family life and function (physical health: IRR: 0.99, 95%CI: [0.98, 0.99], P<0.001; mental health: IRR: 0.99, 95%CI: [0.99, 0.99], P<0.001). A family whose child has a poorer HRQoL will have a poorer family life and function score (DFI) (IRR: 1.04, 95%CI: [1.03, 1.05], P<0.001).

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As sleep disturbance, emotional distress and tiredness/exhaustion were the most frequently affected DFI subdomains (Figure 5.2), a Poisson analysis was used to assess their relationship with demographic characteristics, HRQoL, and RAND-36 (Table 5.3). Sleep disturbance and tiredness/exhaustion were significantly affected by the severity of AD (sleep disturbance: IRR: 0.64, 95%CI: [0.47, 0.88], $P<0.01$; tiredness and exhaustion: IRR: 0.71, 95%CI: [0.56, 0.91], $P<0.01$). Emotional distress showed a significant sex difference, with families with an affected female child less affected by AD compared to those with an affected male child (IRR: 0.85, 95%CI: [0.73, 0.98], $P=0.02$). In addition, the model was also demonstrated that children suffering from longer disease duration was related to increasing family exhaustion (Disease duration: IRR: 1.03, 95%CI: [1.00, 1.05], $P=0.03$). Type of residential accommodation was significantly associated with decreasing sleep disturbance and family exhaustion indicating that families who live in government flat 4-5 rooms might be less affected by children's AD compared with those families live in government flat 1-3 rooms (Sleep disturbance (government flat 4-5 rooms): IRR: 0.78, 95%CI: [0.61, 0.98], $P=0.03$; family exhaustion (government flat 4-5 rooms): IRR: 0.79, 95%CI: [0.64, 0.98], $P=0.03$).

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Table 5.2 Relation between Dermatitis family overall impact and demographic characteristics, HRQoL and RAND36 in univariate and multivariate models

Variables*	Dermatitis Family Impact ^c					
	Univariate model			Multivariate model		
	IRR ^a	95% CI ^b	p-value	IRR	95% CI	P-value
Age of child (years)	0.99	[0.97, 1.00]	0.038	0.97	[0.96, 0.99]	p<0.01
Sex of child						
Male	1(Ref)					
Female	0.95	[0.84, 1.07]	0.386	0.93	[0.83, 1.05]	0.236
Ethnicity						
Chinese	1(Ref)					
Indian	1.24	[1.05, 1.45]	0.009	1.13	[0.96, 1.31]	0.133
Malay	1.15	[0.86, 1.55]	0.349	1.02	[0.80, 1.30]	0.865
Caucasian and others	1.43	[1.17, 1.75]	p<0.001	1.33	[1.10, 1.60]	p<0.01
Qualification						
Polytechnic and professional	1(Ref)					
Primary and secondary	1.01	[0.85, 1.20]	0.896	0.88	[0.76, 1.02]	0.099
University	0.87	[0.76, 1.00]	0.053	0.99	[0.87, 1.14]	0.93
Number of children in family	1.02	[0.94, 1.11]	0.679	0.99	[0.91, 1.06]	0.712
Accommodation						
Government flat 1-3 rooms	1(Ref)					
Government flat 4-5 rooms	0.81	[0.69, 0.95]	0.011	0.91	[0.78, 1.06]	0.235
Private housing (condo, landlord)	0.68	[0.56, 0.83]	p<0.001	0.81	[0.66, 0.99]	p<0.05
Disease duration (years)	1.00	[0.99, 1.02]	p<0.001	1.02	[1.00, 1.04]	0.019
Severity						
Mild	1(Ref)					
Moderate	1.38	[1.20, 1.59]	p<0.001	1.23	[1.09, 1.40]	0.001
Severe	1.50	[1.26, 1.79]	p<0.001	1.26	[1.06, 1.49]	0.008
HRQoL ^d	1.06	[1.05, 1.07]	p<0.001	1.04	[1.03, 1.05]	p<0.001
RAND 36 ^e						
Physical health	0.98	[0.97, 0.98]	p<0.001	0.99	[0.98, 0.99]	p<0.001
Mental health	0.98	[0.98, 0.99]	p<0.001	0.99	[0.99, 0.99]	p<0.001

*Missing data: Disease severity, n=46; Living accommodation, n=2

^a IRR: incidence rate ratio; ^bCI: confidence interval

^c DFI: The score ranges from 0 to 30. A higher score indicates a greater degree of QoL impairment.

^d HRQoL: disease-specific HRQoL of children with AD was measured using IDQoL and CLDQI

^e RAND 36: The score ranges from 0 to 100, with a lower score indicating poorer health or functioning

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Table 5.3 Relation between sleep disturbance, emotional distress, tiredness and exhaustion and demographic characteristics, HRQoL and RAND36

Variables *	DFI subdomains								
	Sleep disturbance			Emotional distress			Tiredness and exhaustion		
	IRR ^a	95% CI ^b	P-value	IRR	95%CI	P-value	IRR	95%CI	P-value
Age of child (years)	1.02	[1.00, 1.04]	0.11	1.01	[0.99, 1.03]	0.44	1.00	[0.99, 1.02]	0.71
Sex of child									
Male	1(Ref)								
Female	0.87	[0.75, 1.01]	0.07	0.85	[0.73, 0.98]	0.02	0.88	[0.77, 1.01]	0.08
Ethnicity									
Chinese	1(Ref)								
Indian	1.01	[0.82, 1.25]	0.91	1.11	[0.90, 1.36]	0.32	1.02	[0.84, 1.25]	0.81
Malay	1.18	[0.89, 1.57]	0.24	1.05	[0.79, 1.39]	0.72	1.05	[0.79, 1.41]	0.74
Caucasian and others	0.89	[0.63, 1.26]	0.51	1.07	[0.82, 1.41]	0.62	0.91	[0.66, 1.24]	0.55
Qualification									
Polytechnic and professional	1(Ref)								
Primary and secondary	0.97	[0.79, 1.20]	0.81	1.18	[0.98, 1.43]	0.08	0.97	[0.79, 1.18]	0.75
University	0.95	[0.79, 1.14]	0.58	1.06	[0.89, 1.27]	0.51	0.95	[0.80, 1.13]	0.58
Number of children in family	0.91	[0.83, 1.01]	0.08	0.98	[0.89, 1.08]	0.71	0.97	[0.88, 1.06]	0.49
Accommodation									
Government flat 1-3 rooms	1(Ref)								
Government flat 4-5 rooms	0.78	[0.61, 0.98]	0.03	0.94	[0.75, 1.18]	0.61	0.79	[0.64, 0.98]	0.03
Private housing (condo, landlord)	0.86	[0.66, 1.13]	0.28	1.12	[0.85, 1.47]	0.42	0.94	[0.74, 1.21]	0.65
Disease duration (years)	1.02	[0.99, 1.04]	0.18	1.01	[0.99, 1.03]	0.47	1.03	[1.00, 1.05]	0.03
Severity									
Mild	1(Ref)								
Moderate	1.08	[0.91, 1.28]	0.37	1.13	[0.96, 1.33]	0.13	1.11	[0.95, 1.31]	0.19
Severe	0.64	[0.47, 0.88]	p<0.01	0.84	[0.66, 1.07]	0.15	0.71	[0.56, 0.91]	0.01
HRQoL ^c	0.99	[0.98, 1.01]	0.35	1.00	[0.98, 1.01]	0.81	0.99	[0.98, 1.01]	0.50
RAND 36 ^d									
Physical health	1.00	[0.99, 1.01]	0.91	1.00	[0.99, 1.01]	0.78	1.00	[0.99, 1.01]	0.98
Mental health	1.00	[0.99, 1.00]	0.11	1.00	[1.00, 1.01]	0.63	1.00	[0.99, 1.01]	0.92

*Missing data: Disease severity, n=46; Living accommodation, n=2

^a IRR: incidence rate ratio; ^bCI: confidence interval

^c HRQoL: disease-specific HRQoL of children with AD was measured using IDQOL and CLDQI

^d RAND 36: The score ranges from 0 to 100, with a lower score indicating poorer health or functioning

5.4 Discussion

The purpose of this study was to provide a more in-depth insight into the impact of paediatric AD on families. This study revealed that 94% of families reported that their family life and function were affected by their children's AD with most commonly affected domains being sleep disturbance, emotional distress, and tiredness/exhaustion. In addition, the severity of the child's AD was found to be significantly associated with dermatitis family impact and its subdomains, indicating that severe AD causes more severe impairment of family functioning. Univariate and multivariate models showed that patient's age, disease severity and disease duration worsen family life and function. This study also found that self-reported HRQoL in paediatric patients and mental and physical health of caregivers contributed to impaired family life and function (DFI).

Impact of childhood AD on family life and function is very large. It has been reported that the family life and function got more impaired than those of families with psoriasis patient (DFI: mean and SD: 5.6 ± 5.8) and is even comparable with those of families with congenital ichthyosis patients (DFI: mean: 9.0) (254, 255). Worldwide, similar impacts on families with children with AD were shown in European countries while Asian countries reported greater impairment (Korea (DFI mean and SD: 11.2 ± 6.0) and Malaysia (DFI mean and SD: 9.4 ± 5.3)). An earlier study in Singapore found a lower family impact of AD compared to this study (219, 245, 252, 256-258). I postulate that this difference may be because this study captured a more varied spectrum of disease severity, with children hospitalized for AD to those only in outpatient follow-up. This sample size was also large enough to assess the effect of dermatitis family impact.

The most affected dermatitis family impact subdomains (sleep disturbance, emotional distress and tiredness/exhaustion) were fitted into a regression model and found families whose child has severe AD might be less affected by lack of sleep or tiredness even after adjustment of disease duration, child's age, etc by the model. This finding appeared unexpected as clinical observations would suggest that individuals with more severe symptoms should be affected more than those with less

severity. Similar trends have been reported in the relation between sleep and obsessive-compulsive disorder and other mental health issues (241, 242). One of the reasons may be because doctors may pay more attention to severe patients' itchiness and sleep problems and therefore prescribe stronger medications to treat the symptoms. In addition, it could be expected that severe patients and their family members may have better adherence to therapy and hence report less affected in the severe AD. Another reason could be families with more severe individuals get used to the poor sleep quality and tiredness as well as have lower expectations than those with mild to moderate symptoms, and this would lead them to report less affected by sleep disease disturbance and tiredness.

Sleep disturbance secondary to the pruritus of AD can not only affect patients themselves but can adversely affect other family members. Further research in the development of anti-pruritic medications and sleep aids can go a long way to improve the QoL of AD patients and their family members (259, 260). In addition, this analysis also shows that psychological impairment is commonly affected in family members of AD children. In clinical practice, doctors typically focus more on managing the skin condition of AD patients and often overlook the psychological problems of the child, less so of their family members (224, 261). Besides, doctors are likely to be unaware of the association between AD severity, psychological status and poor family function. Currently, there are limited interventions available to clinicians to address these important issues. Further research to focus on psychosocial interventions and support is needed to address the psychosocial health of AD patients and their families (213, 245, 262).

This study has several advantages. As family support plays a significant role in the treatment of AD, this study provides a unique perspective to understand the family burden of AD (57). In comparison to the limitations in previous work, I used statistical models to identify the associated with factors of family impact which could benefit treatment and intervention decisions in clinical practice. Besides, this sample incorporates 559 families with Chinese, Indian, Malay population which could be generalized in Singapore and other multi-ethnic countries. Moreover, several study

limitations merit attention. First, the family impact was reported by parents and may not represent all family members' point of view. In some of the participating families, it is grandparents or domestic helpers who take care of the children with AD instead of their parents. Secondly, there is no healthy control group included in this study which precludes us from calculating the comparison with healthy families. Thirdly, participants were only recruited from tertiary hospitals where patients might have been experiencing more severe disease conditions compared to those who visited primary care hospitals.

5.5 Conclusion

In clinical practice, doctors typically focus more on managing the skin condition of AD patients and often overlook the psychological problems of the child, less so of their family members. However, I reported that more than 94% of the families' life and function was affected by their children's diseases. Social and clinical factors, as well as the self-reported QoL of patients and their caregivers, contribute to impaired family functioning. Thus, to improve the overall family QoL, the focus of AD treatment should not be limited to the patients, but the scope should be broadened to include their family members.

Chapter 6

Concordance between physician-rated and caregiver-perceived disease severity in children with atopic dermatitis: A cross-sectional study

It is difficult for caregivers to accurately assess their children's disease condition. Even though they realize their children's disease condition worsens, it is still problematic to accurately detect the real disease severity changes. Therefore, I used physician-rated and caregiver perceived disease severity as a focus to provide evidence for understanding the patient-doctor concordance since it can seriously affect treatment compliance. This chapter explores the concordance between caregiver-reported and physician-rated severity of AD. Followed by introducing the background information in Section 6.1, a description of the study methods is presented in Section 6.2. Results are presented in Section 6.3. I then discuss the results with reference to prior studies, its strengths, limitations and observations of the recruitment in Section 6.4. Recommendations for future research are discussed before concluding the chapter.

6.1 Introduction

Previous chapter has shown that the severity of the disease often predicts the health status, with more severe AD associated with lower quality of life (22, 52, 118, 236). Therefore, rating the severity of AD is an important step in understanding the level of ill-health and establishing a baseline, which can be used to plan for the provision of appropriate disease management and alleviation of the accompanying burdens (263). Current severity scoring systems for AD are based on various scales and relies on the health professionals' medical expertise and knowledge of assessing the

intensity of signs and symptoms (30, 80, 264). However, this clinical opinion may differ substantially from patients' and caregivers' subjective assessment of the severity of AD (80).

Caregivers often assess the degree of severity of their child's condition based on their own subjective feelings and observations and often includes symptoms beyond clinical grading scales and physician's medical assessment while physicians often make an assessment based on one visit (263, 265). Therefore, it is common that physicians and caregivers have different views of the children's AD, a divergence that potentially could affect caregivers' approach to treatment and disease management (266).

Understanding discrepancies between physicians and caregivers can shed light on when parental understanding of severity is differently understood which is an important step in improving adherence to treatment recommendations (267, 268). This study, therefore, aims to explore the concordance between caregiver-reported and physician-rated severity of AD in paediatric patients as well as investigate potential explanatory factors.

6.2 Methods

6.2.1 Design and participants

Please refer to Section 4.2.1 Design and participants in Chapter 4.

6.2.2 Instrumentation and outcome measures

Included patients and caregivers completed a questionnaire that included background information such as sociodemographic data as well as questions about weekly out-of-pocket expenses related to the child's AD for purchases of non-medical products and services e.g. over-the-counter moisturizers, laundry services, and special diet food. Those costs were attributed to the cost year of 2017 and re-calculated to

represent the annual cost per child. The questionnaire also obtained caregiver reported time spent on informal caregiving (hours per week) due to the child's condition.

6.2.3 Disease severity assessment

Severity assessment by physicians and caregivers was reported differently since there are substantial inconsistencies in pre-understandings about the severity of AD and how it is valued (e.g. parents taking psychosocial aspects into account while physicians strictly clinically assess the condition of the child's skin). AD severity was therefore assessed from a medical viewpoint (physician's) versus a subjective and cognitive perception based on daily observations of the child's condition (caregiver's).

Physician-rated disease severity: Please refer to Section 4.2.4 Disease severity assessment in Chapter 4. The information was collected at the same time point when caregivers filled in the questionnaires.

Caregiver-perceived disease severity: Caregiver-perceived disease severity was collected when they visited the dermatology clinic. Caregivers were required to respond whether they perceived their child's AD severity as mild, moderate or severe. Caregivers were advised to answer this question based on how they perceived their child's current condition rather than the overall impression of the disease.

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6.2.4 Statistical analysis

Descriptive statistics for continuous variables are reported with mean $\pm$ SD, categorical variables are reported with frequencies and percentages (%). Agreement between physician-rated severity and caregiver perceived severity was assessed with Cohen's Kappa (269). The Kappa statistics (k) was interpreted as "slight agreement" (0.01 to 0.20), "fair agreement" (0.21 to 0.39), "moderate agreement" (0.40 to 0.60),

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“substantial agreement” (0.61 to 0.80) and “almost perfect agreement” (0.81 to 1.00) (270).

Multivariable logistic regression analyses were performed to estimate factors associated with both the underestimation and overestimation of the severity of the condition in relation to the physicians rating. Underestimation of children’s disease severity was defined as caregiver-perceived disease severity is less severe than physician-rated disease severity while overestimation of children’s disease severity was defined as caregiver-perceived disease severity is more severe than physician-rated disease severity (see Figure 6.1). Odds ratios (OR) were calculated for each variable and reported with 95% confidence intervals (CIs). The fitted regression model was explored for associations between all variables (number of children in family and type of housing; education and employment and type of housing) and p-value less than 0.05 was considered as significant collinearity. The overall goodness-of-fit for the logistic model was assessed by model discrimination (c-statistics) and calibration (Hosmer-Lemeshow test p-value) measures. All statistical analyses were undertaken by using Stata version 14.2 (StataCorp, College Station, TX, USA). A two-sided p-value less than 0.05 was considered as statistically significant.

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Figure 6.1 Illustration of underestimation and overestimation assessment

	Physician-rated disease severity			
		Mild	Moderate	Severe
Caregiver-perceived disease severity	Mild	Concordance	<u>Underestimation</u>	<u>Underestimation</u>
	Moderate	<u>Overestimation</u>	Concordance	<u>Underestimation</u>
	Severe	<u>Overestimation</u>	<u>Overestimation</u>	Concordance

6.2.5 Ethics approval and informed consent

Please refer to Section 4.2.6 Ethical approval and informed consent in Chapter 4.

6.3 Results

6.3.1 Social demographic and baseline data

The characteristics of the participants are summarised in Table 6.1. A total of 434 patients with an equal sex distribution (50.0% females and 50.0% males) were included in the study ². Of the sample, 22.3% of the children were 0-2 years of age, 17.3% were 2-4 years of age and 60.4% were 4-16 years of age. The majority of the

² As caregiver-perceived disease severity could not be retrieved in 125 participants, the sample size of this study (n=434) is smaller than the sample size of previous two chapters (n=559).

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participants were Chinese (71.2%), followed by Indians (17.7%), Malays (5.8%) and Caucasian and others (5.3%). Caregivers with professional degrees or university education accounted for 81.3% of the sample, while 18.7% had primary or secondary school qualification. Most caregivers were employed (80.2%). The most common housing type was government flats (public housing 1-3 rooms: 13.6%; public housing 4-5 rooms: 65.4%), followed by private housing (21.0%). With regards to family size, 31.3% of families had one child, 42.6% had two children and 26.1% had more than two children.

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Table 6.1 Study participants and their caregiver's characteristics by AD severity degree

Characteristics	N (%)	Physicians assessed severity		
		Mild	Moderate	Severe
Total participants	434 (100.0)	265	110	59
Sex				
Female	217 (50.0)	130	60	27
Male	217 (50.0)	135	50	32
Child's age (years) (%)				
0-2	97 (22.3)	72	19	6
2-4	75 (17.3)	50	18	7
4-16	262 (60.4)	143	73	46
Ethnicity, n (%)				
Chinese	309 (71.2)	183	78	48
Indian	77 (17.7)	53	15	9
Malay	25 (5.8)	17	7	1
Caucasian and others	23 (5.3)	12	10	1
Duration of disease				
0-6 months	114 (26.3)	70	31	13
6 months-2 years	98 (22.6)	68	23	7
> 2 years	222 (51.1)	127	56	39
Caregiver's highest achieved educational qualification, n (%)				
Polytechnic and professional	142 (32.7)	87	38	17
Primary and secondary	81 (18.7)	47	18	16
University and above	211 (48.6)	131	54	26
Caregiver's employment status, n (%)				
Employed	348 (80.2)	209	94	45
Unemployed/retired	86 (19.8)	56	16	14
Type of housing*, n (%)				
Public housing 1-3 rooms	59 (13.6)	36	15	8
Public housing 4-5 rooms	284 (65.4)	170	72	42
Private housing (condo/landed property)	91 (21.0)	59	23	9
Number of children in the family, n (%)				
1	136 (31.3)	83	33	20
2	185 (42.6)	107	53	25
>2	113 (26.1)	75	24	14
Costs related to atopic dermatitis (mean $\pm$ SD)				
Time spend on personal care	4.87 $\pm$ 7.91	4.30 $\pm$ 7.08	5.44 $\pm$ 6.95	6.34 $\pm$ 12.01
Time spend on accompanying to healthcare visits	0.54 $\pm$ 2.23	0.48 $\pm$ 2.03	0.67 $\pm$ 2.99	0.61 $\pm$ 1.24
Time spend on companionship and emotional support	3.55 $\pm$ 9.60	2.80 $\pm$ 7.35	3.51 $\pm$ 7.11	7.00 $\pm$ 18.25
Time spend on specially prepared food	1.61 $\pm$ 5.16	1.81 $\pm$ 6.05	1.08 $\pm$ 2.99	1.70 $\pm$ 3.81
Total cost for out-of-pocket expense ^a	2962.07 $\pm$ 6581.46	2335.19 $\pm$ 4480.67	2787.43 $\pm$ 4891.70	6103.33 $\pm$ 13233.70

^a Out-of-pocket expenses related to the child's AD for purchases of non-medical products and services e.g. over-the-counter moisturizers, laundry services, and special diet food. Those costs were attributed to the cost year of 2017 and re-calculated to represent the annual cost per child

6.3.2 Agreement of severity rating

Overall concordance between caregiver-perceived AD severity in patients and the severity rating by physicians was 61.5% cases. There are 38.5% discordance reported and among which, 27.7% of caregivers underestimated their children's disease severity compared to the physicians' ratings while 10.8% of caregivers overestimated their child's AD severity. Crude agreement and kappa statistics for concordance and discordance are displayed in Table 6.2. Type of housing is an indicator of socioeconomic status in Singapore, this study showed that participants living in smaller government flats had the lowest concordance (k: 27.2%) compared to caregivers residing in bigger government flats (k: 39.5%) and private housing (k: 34.8%). With regards to the duration of disease, there was a fair agreement in AD severity grading between caregivers and physicians if their child's duration was between 6 months and 2 years or more than 2 years. There was a moderate agreement in patients with disease duration less than 6 months (k: 44.4%). For children's age, there was a moderate agreement in subjects between 0 to 2 years of age, but fair agreement in children older than 2 years of age (age of the child: 0-2 years old: k: 44.3%; 2-4 years old: kappa statistic=30.0%; 4-16 years old: k: 35.3%). Caregivers of Indian and primary and secondary school education showed a moderate agreement with physician-rated severity (Indian: k: 40.0%; primary and secondary school education: k: 41.0%). For the employment status of caregivers, those that were currently employed had higher concordance than unemployed or retired caregivers (employed caregivers: kappa=38.1%; unemployed/retired: k: 31.0%). With regards to family size, there was higher concordance in families with one child (k: 39.8%) and a similar trend was detected for lower concordance for families with more children (two children k: 36.2%; more than two children k: 34.6%).

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Table 6.2 Concordance and discordance in physician and caregiver rated severity of the child's AD

Characteristics	N	Crude agreement (%)	Kappa statistic (%) 95% CI
Overall	434	61.5	36.8 [30.1, 43.5]
Sex			
Female	217	61.3	40.0 [30.2, 49.8]
Male	217	61.8	40.0 [30.7, 49.3]
Child's age (years)			
0-2	97	70.1	44.3 [29.6, 59.0]
2-4	75	58.7	30.0 [14.0, 46.0]
4-16	262	59.2	35.3 [26.7, 43.9]
Ethnicity			
Chinese	309	59.5	34.8 [26.9, 42.7]
Indian	77	67.5	40.0 [23.6, 56.4]
Malay	25	60.0	30.9 [1.6, 60.2]
Others	23	69.6	47.2 [16.5, 77.9]
Duration of disease			
Less than 6 months	114	67.5	44.4 [30.6, 58.2]
6 months to 2 years	98	63.3	36.5 [22.2, 50.8]
More than 2 years	222	57.7	32.8 [23.6, 42.0]
Caregiver's highest achieved educational attainment			
Polytechnic and professional	142	61.3	35.3 [23.2, 47.4]
Primary and secondary	81	63.0	41.0 [25.8, 56.2]
University and above	211	61.1	35.9 [26.2, 45.6]
Caregiver's employment status			
Employed	348	62.4	38.1 [30.5, 45.7]
Unemployed/ retired	86	58.1	31.0 [16.6, 45.4]
Type of housing*			
Government flats 1-3 rooms	59	55.9	27.2 [8.9, 45.5]
Government flats 4-5 rooms	284	62.5	39.5 [31.2, 47.8]
Private housing (condo, landed property)	91	62.6	34.8 [19.4, 50.2]
Number of children in the family			
1	136	63.2	39.8 [27.8, 51.7]
2	185	61.6	36.2 [25.5, 46.9]
>2	113	59.3	34.6 [22.3, 47.0]

6.3.3 Multivariable regression analyses

The multivariable regression analyses for underestimation of children's disease severity can be seen in Table 6.3. Through the multivariable regression analysis, it was found that caregivers to children between 4 and 16 years of age (OR: 5.50, 95% CI: [1.36, 22.21], $p=0.017$) and caregivers to children with a disease duration of 6 months to 2 years (OR: 0.24, 95% CI: [0.06, 0.94], $p=0.04$) were more likely to underestimate their child's disease severity. Another statistically significant factor associated with caregivers underestimating their child's AD severity was disease-related out-of-pocket expenses (e.g. moisturizing creams, special hygiene products, additional costs for laundry etc.) (OR: 1.00005, 95% CI: [1.00001, 1.00009], $p=0.011$). Approximately 14.7% of the caregivers who underestimated their child's severity also had out-of-pocket expenses $\geq$ US\$10,000 per year (95% CI: [10.2, 19.2]). Sociodemographic characteristics (Sex, ethnicity, educational attainment, caregiver's employment status, number of children in the family and type of housing) did not reveal any significance in the model. Overall goodness-of-fit for the logistic model was acceptable (c-statistic: 0.79; and Hosmer-Lemeshow p -value: 0.642). The multivariable regression analyses were also conducted for overestimation of children's disease severity (Table 6.4). However, there are no significant associations found for any factors when tested for overestimating AD severity.

6. Concordance between physician-rated and caregiver perceived disease severity in children with AD

Table 6.3 Multivariable logistic regression analysis of factors associated with underestimation the severity of AD

Variables	N	Odds Ratio	95%CI	P-value
Sex				
Female	217 (50.0)	1(Ref)	-	-
Male	217 (50.0)	0.72	[0.37, 1.40]	0.327
Child's age (years)				
0-2	97 (22.3)	1(Ref)		
2-4	75 (17.3)	4.20	[0.92, 19.08]	0.063
4-16	262 (60.4)	5.50	[1.36, 22.21]	0.017
Ethnicity				
Chinese	309 (71.2)	1(Ref)	-	-
Indian	77 (17.7)	0.53	[0.20, 1.39]	0.552
Malay	25 (5.8)	0.14	[0.01, 1.73]	0.331
Duration of disease				
6 months	114 (26.3)	1(Ref)	-	-
6 months to 2 years	98 (22.6)	0.24	[0.06, 0.94]	0.040
> 2 years	222 (51.1)	0.77	[0.32, 1.86]	0.563
Caregiver's highest achieved educational attainment				
Polytechnic and professional	142 (32.7)	1(Ref)	-	-
Primary and secondary	81 (18.7)	0.78	[0.29, 2.09]	0.620
University and above	211 (48.6)	0.72	[0.32, 1.62]	0.428
Caregiver's employment status				
Employed	348 (80.2)	1(Ref)	-	-
Unemployed/ retired	86 (19.8)	1.21	[0.52, 2.82]	0.664
Type of housing				
Public housing 1-3 rooms	59 (13.6)	1(Ref)	-	-
Public housing 4-5 rooms	284 (65.4)	0.45	[0.18, 1.11]	0.084
Private housing (condo, landed property)	91 (21.0)	0.50	[0.16, 1.56]	0.231
Number of children in the family				
1	136 (31.3)	1(Ref)	-	-
2	185 (42.6)	1.33	[0.62, 2.83]	0.464
≥3	113 (26.1)	0.60	[0.23, 1.58]	0.300
AD-related cost categories				
Time spend on personal care (hours)	-	1.01	[0.98, 1.05]	0.449
Time spend on accompanying to healthcare visits (hours)	-	0.62	[0.34, 1.10]	0.103
Time spend on companionship and emotional support (hours)	-	1.01	[0.98, 1.04]	0.624
Time spend on specially prepared food (hours)	-	1.04	[0.95, 1.13]	0.393
Total cost for out-of-pocket expenses (USD)	-	1.00005	[1.00001, 1.00009]	0.011

6. Concordance between physician-rated and caregiver perceived disease severity in children with AD

Table 6.4 Multivariable logistic regression analysis of factors associated with overestimation the severity of AD

Variables ^a	N	Odds Ratio	95%CI	P-value
Sex				
Female	217 (50.0)	1(Ref)	-	-
Male	217 (50.0)	1.006	[0.64, 1.58]	0.979
Child's age (years)				
0-2	97 (22.3)	1(Ref)	-	-
2-4	75 (17.3)	1.38	[0.65, 2.96]	0.402
4-16	262 (60.4)	1.08	[0.54, 2.14]	0.826
Ethnicity				
Chinese	309 (71.2)	1(Ref)	-	-
Indian	77 (17.7)	0.83	[0.44, 1.58]	0.570
Malay	25 (5.8)	1.56	[0.63, 3.85]	0.335
Duration of disease				
6 months	114 (26.3)	1(Ref)	-	-
6 months to 2 years	98 (22.6)	1.44	[0.74, 2.83]	0.287
> 2 years	222 (51.1)	1.17	[0.61, 2.24]	0.643
Caregiver's highest achieved				
Polytechnic and professional	142 (32.7)	1(Ref)	-	-
Primary and secondary	81 (18.7)	0.70	[0.34, 1.43]	0.330
University and above	211 (48.6)	1.17	[0.68, 1.99]	0.567
Caregiver's employment status				
Employed	348 (80.2)	1(Ref)	-	-
Unemployed/ retired	86 (19.8)	1.03	[0.57, 1.84]	0.933
Type of housing				
Public housing 1-3 rooms	59 (13.6)	1(Ref)	-	-
Public housing 4-5 rooms	284 (65.4)	0.93	[0.47, 2.00]	0.928
Private housing (condo, landed property)	91 (21.0)	0.60	[0.33, 1.89]	0.600
Number of children in the family				
1	136 (31.3)	1(Ref)	-	-
2	185 (42.6)	0.90	[0.53, 1.53]	0.689
≥3	113 (26.1)	1.43	[0.80, 2.55]	0.234
AD-related cost categories				
Time spend on personal care (hours)	-	1.00	[0.97, 1.03]	0.905
Time spend on accompanying to healthcare visits (hours)	-	1.03	[0.91, 1.16]	0.660
Time spend on companionship and emotional support (hours)	-	1.00	[0.97, 1.03]	0.918
Time spend on specially prepared food (hours)	-	0.97	[0.91, 1.03]	0.325
Total cost for out-of-pocket expenses (USD)	-	1.00	[0.99996, 1.00003]	0.662

^a Overall goodness-of-fit for the logistic model was assessed by model discrimination (c-statistics=0.60) and calibration (Hosmer-Lemeshow test p-value=0.248).

6.4 Discussion

Our findings revealed an overall discordance of 38.5% between caregiver perceived severity of AD compared to physician-rated severity (100% - crude agreement%). There was also a trend towards an increased discordance with more severe AD. The result showed that caregivers tended to rate their child's AD severity lower than the physician (27.7%). This result is similar to a study assessing the discordance between self-reported and physician-rated AD severity in adults, which showed a 31.4% discordance with patients rating their disease severity lower than physicians (271). Knowing that as much as 27.7% of caregivers underestimate their child's AD severity may have important clinical implications for treatment adherence.

Caregivers play a key role in managing their child's AD and their perception of the child's AD severity can affect treatment motivations and further decide their treatment behaviour. If caregivers are unable to differentiate between various degrees of severity and symptoms thereof, and not properly knowing how and when to e.g. medicate or to consult healthcare professionals (282). More importantly, if parents underestimate the severity of their child's AD, this may lead to the suboptimal treatment of the condition, e.g. neglecting to apply topical steroids and emollients, and not following dietary restrictions (272, 273). There is also a risk that some caregivers may resort to their own forms of treatment for their child's AD, without involving a physician (272). Therefore, concordance between caregivers and physicians as to the severity of AD in a patient is important as AD, being a chronic disease, requires self-involvement in terms of severity recognition and adherence to physician-recommended treatments, so as to achieve better treatment outcomes (274).

Both the physician's severity rating and caregiver's assessments are also required to guide future therapeutic decisions and treatment pathways. The findings showed that discordance was associated with an older age of the child (age 4-16 years of age) as well as a moderate disease duration of 6 months to 2 years. We speculate that this potentially could be associated with increased desensitization to a chronic condition over time or that AD may appear subjectively worse in infants compared to older children (since it may cover more skin area, the child may cry more). A third possible

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explanation is that older children with AD may manage their treatment with less caregiver involvement, hence the parent is not as aware of the condition status (for older children). Besides, the association between caregiver underestimation of AD and out-of-pocket expenses cannot be explained by this study as the analysis did not include testing for casualties. It could, however, be argued that parents not perceiving their child's condition as severe are more prone to self-treat with over the counter (OTC) alternatives. As seen in one study where caregivers bought OTCs such as non-medical moisturisers, coconut oil and herbal remedies believing that would cure, be sufficient management for AD or a "safer" alternative to medical drugs (266).

Limitations of this study include multiple sources of potential bias and imprecision since all study subjects were recruited from specialized healthcare. As such, the sample may not be representative of the patients and caregivers in primary care or other healthcare settings. Another aspect to consider is that other explanatory factors not captured in the questionnaire could have affected the discordance between the caregiver and physician rating of the disease severity in AD. I also acknowledge that using different tools for physicians and caregivers is somewhat problematic since a proper comparison cannot be made. One assessment comes with detailed instructions, whilst another might be based on subjective perception. However, as previously reported are physicians and parents' perspectives are different and they value different aspect in making severity judgements: physicians are likely to rely on evaluating visual signs, and supplemented by a brief history while caregivers are prone to evaluate symptoms/complaints from their child as well as their visual signs. Hence this limitation could be explained as this study tried to capture the measures from a real-life perspective (266). This also reflects that caregivers may have a potentially better understanding of severity and physicians might overestimate AD severity given that they only see the child during clinic visits and therefore, physicians need to take caregiver's perceived disease severity into consideration which could potentially help make a precise clinical decision.

6.5 Conclusion

In conclusion, discordance in physicians rating and caregivers' perception of disease severity for paediatric AD shows a tendency amongst caregivers to underestimate the disease severity. The information has clinical implications, in that disease severity self-assessment might be omitted in current patient education materials. Concordance in the assessment of disease severity between caregivers and physicians should be underscored as their conflicting perceptions of a child's AD severity can impede treatment motivations and further affect treatment outcomes. Future research in this area should include more potentially explanatory variables and have larger sample sizes to generate more robust findings.

Chapter 7

Atopic dermatitis apps conformance with clinical guidelines: A systematic assessment of functions, tools and content

Chapter 7 is a qualitative systematic assessment of smartphone apps for AD management. In this chapter, I try to understand apps for disease management, clinical relevancy (e.g. whether the app follows existing evidence-based guidelines) as well as features and functionality aspects. Followed by an introduction presented in Section 7.1, methods are then detailed in Section 7.2. Findings of the app assessments are shown in Section 7.3. Implications of the findings, limitations and future directions are discussed in Section 7.4.

7.1 Introduction

As I discussed in the introduction chapter, self-management plays a pivotal role in improving the quality of life among AD patients (275). Understanding of the disease increases patient satisfaction with the treatment and results in improved outcomes and adherence (276). Well-educated patients have significant improvements in their disease severity scores compared with controls (95). For timely recognition of flares and informed treatment decisions during clinic visits, guidelines advocate tracking of the disease by (a) monitoring possible triggers (e.g. allergens), (b) recording disease severity including specific symptoms and signs (c) response to therapy (277). There is an increasing need for various monitoring means to support patients, their caregivers and healthcare professionals in managing the disease.

Smartphone apps can increase patients' and caregivers' knowledge of the disease, support self-management and empowerment by, for example, giving patients insight

into their health condition, enabling them to make informed choices and engaging them in self-care activities and potentially diminishing the need for face to face contact with their health care professionals (278). Dermatological conditions are deemed suitable for smartphone-supported management, as clinical diagnosis and assessment of severity partly rely on visualization. This is reflected by the number of dermatology-related mobile apps which have more than doubled in the past years (9). Studies have, however, found diagnostic inaccuracy of smartphone applications and several other reports have also suggested that the app marketplace has much to improve (279). For apps to be used and recommended to patients and their healthcare providers, accuracy and reliability are essential. Incorrect information and recommendations, in addition to privacy issues, are some of the key challenges of current apps (280).

Research has not yet focused on AD smartphone apps. Given the hypothetical benefits and challenges, quality and comprehensiveness of available AD self-management apps should be evaluated to guide clinicians and patients in recommending and using the most appropriate apps. To assess the global marketplace, apps available in the most spoken languages (English, Chinese, and Spanish) will provide a comprehensive overview covering a population of nearly two billion people (281). This study systematically assesses the self-management functionalities of all available apps accessible to English, Chinese and Spanish speaking patients or caregivers of AD patients.

7.2 Methods

7.2.1 Search strategy

This cross-sectional study reviewed all AD self-management apps for patients/caregivers available from July to November 2018. The app selection and identification were conducted using a systematic approach to minimize bias. Apps were identified using specific search terms and subsequently reviewed for suitability based on app store descriptions. Suitable apps were downloaded for testing against

pre-defined criteria. Apps that appeared across multiple platforms were assessed separately. Apps with in-app purchases were assessed with and without the full purchase of additional features/functionalities. If apps were translated into another language, apps were also assessed individually.

English, Chinese and Spanish language smartphone apps were searched for using 42matters, an app search engine that retrieves apps from most widely used smartphone stores (Google Play Store and Apple App Store iOS) which covers apps from 55 countries in both above-mentioned operating systems (282). As Chinese apps are not available in Google Play in mainland China, Chinese Android apps were searched through the platforms used by more than 95% of the users in China(283): ‘Tencent MyApp’, ‘360 Mobile Assistant’, ‘Baidu Mobile Assistant’, ‘Huawei App Market’, ‘Oppo Software Store’, ‘MIUI App Store’, ‘VIVO App store’, ‘Sogou Mobile Assistant’, ‘PP Assistant’ and ‘Wandoujia’ platform. Search terms “atopic dermatitis”, “AD”, “dermatitis”, “rash”, “dermatology”, “skin disease” and Chinese and Spanish translations of these terms were used. English search terms: 1) eczema, 2) atopic dermatitis or dermatitis, 3) dermatology or derma*, 4) skin disease or skin; Chinese search terms: 1) 湿疹, 2) 红疹 or 疹, 3) 皮炎, 4) 癣, 5) 皮肤病; Spanish search terms: 1) dermatitis atópica, 2) eccema or eccemas atópicos, 3) dermatitis, 4) rash or rash cutáneo or erupción cutánea , 5) dermatología, 6) enfermedad de la piel or enfermedades de la piel or enfermedad cutánea or enfermedad dermatológica or dermatopatía or dermatopatías" or dermatopatías eccematosas. To assure the terms were conceptually equivalent to the English terms forward- and back-translations were used.

If apps were downloadable and accessible, they were assessed for inclusion using predetermined inclusion and exclusion criteria.

Inclusion criteria:

- 1) Smartphone or tablet app available on Google Play Store, Apple App (iOS) Store and Chinese Android App Stores
- 2) Dermatology related app with an AD section

- 3) English/Chinese/Spanish language
- 4) Free or paid
- 5) Content or tools addressing one or more aspects of AD diagnosis, management, monitoring or support as either the sole function or in a way that AD-related elements can be isolated from the rest of the content
- 6) Target patients with AD or caregivers of children with AD

Exclusion criteria:

- 1) Targeted solely at healthcare providers
- 2) App explicitly disclaims that it is intended for health-related purposes
- 3) App has no other function apart from teleconsultation for AD
- 4) App only includes alternative medicine/homoeopathy/home remedies
- 5) App cannot be used due to technical problems after two attempts
- 6) Outdated – incompatible with current operating systems (iOS 11.4.2 and Android 8.0.0)

7.2.2 Assessment

AD-specific app assessment criteria were developed to review the range of features and functions that support management of AD and the extent to which the apps are consistent with international AD guidelines. To establish the criteria American Academy of Dermatology Guideline (22, 63), The National Institute for Health and Care Excellence (NICE) Guideline (2007) (64), Guidelines for the Management of Atopic Dermatitis in Singapore (284), Guidelines for the Management of Atopic Dermatitis in China (湿疹诊疗指南), and the Argentinean Atopic Dermatitis National Consensus (Consenso Nacional de Dermatitis Atópica 2013) were used, subsequently, they were reviewed by co-authors who are all physicians and two experienced dermatologists. Self-management was divided into the apps' tracking and educational (information-providing) function. In terms of app functionality,

Health on the Net (HONcode) principles³ were adapted to assess the reliability of information based on citations, justifications of claims and authority of information, as well as adherence to ethical standards of transparency, privacy and advertising policies (108, 280). An example of two criteria and their assessment is listed in Table 7.1 (the full assessment criteria can be found in Appendix 7.1).

³ mobile Health On the Net (mHON) Code for apps was not released at the time when the research was conducted.

Table 7.1. Example of app assessment criteria (Please refer to Appendix 7.1 to access the full criteria)

Field	Description	Justification/Evidence	Options
Treatment management	Does the app provide any information on disease management?	<p>Patients should be given instructions on the needs to safely and effectively self-manage their medicines. [NICE Clinical Guideline 76 (CG76)(285)]</p> <p>Healthcare professionals should spend time educating children with atopic eczema and their parents or caregivers about atopic eczema and its treatment. They should provide information in verbal and written forms, with practical demonstrations, and should cover:</p> <ul style="list-style-type: none"> - How much of the treatments to use - How often to apply treatments - When and how to step treatment up or down - How to treat infected atopic eczema. [NICE Clinical Guideline 57 (CG57)(64)] 	<p>Yes/No</p> <p><u>Yes-if the app contains any information with eczema management in any form (video/text/game/quiz).</u></p> <p><i>Example. An app (app code EI12) (286) has games to teach users to apply moisturizer.</i></p> <p><u>No-if the app does not provide any of the above information.</u></p>
Psychological factors	Does the app provide any information on psychological management?	<p>During an assessment of psychological and psychosocial wellbeing and quality of life, healthcare professionals should take into account the impact of atopic eczema on parents or caregivers as well as the child and provide appropriate advice and support. [NICE Clinical Guideline 57 (CG57)(64)]</p>	<p>Yes/No</p> <p><u>Yes-if the app contains any information with eczema psychological management in any form (video/text/game/quiz)</u></p> <p><i>Example. An app (app code EI19) (287) asks users to assess their mood on a daily basis.</i></p> <p><u>No-if the app does not contain above information.</u></p>

App assessment was performed on an iPhone 7 (iOS 11.4.1) and a Sony XPERIA XZs (Android 8.0.0). To establish standardization of interpretation and application of the assessment criteria, 24% of English and Chinese apps were first assessed individually by one pair of assessors, and differences were discussed and resolved through consensus. Assessment of remaining apps was performed by reviewers in pair (English and Chinese speaking assessors reviewed English and Chinese apps; English and Spanish speaking assessors reviewed Spanish apps) independently assessing each app in random order. Discrepancies were resolved through discussion with a third independent reviewer in the team.

7.2.3 Data analysis

Cohen's Kappa was used to calculate the inter-rater agreement between two reviewers at initial screening and assessment process. An agreement between 60-80% represents a reasonably good agreement between the reviewers. Apps were profiled according to types, functions, and quality of included apps using descriptive statistics (frequencies and percentages). No further statistical analysis was deemed relevant. The units of analysis are the platform-specific app and target user group. Subgroup analysis for AD-specific assessment and HON Code principles was done using Stata software version 14.2 (StataCorp, College Station, TX, USA).

7.3 Results

7.3.1 App selection

The flowchart of app selection is shown in Figure 7.1. The initial search yielded 1522 potential apps in English (938 Android apps and 584 IOS apps), 255 Chinese apps in IOS (Android Chinese apps were assessed manually because Chinese Android apps are not available in Google Play in mainland China), and 676 in Spanish (422 Android apps and 254 iOS apps). Two-hundred and thirty-six apps were downloaded for full assessment after the primary screening (136 English apps, 81 in Android and

55 in IOS; 21 Chinese IOS apps and 79 Spanish apps, 48 in Android and 31 in iOS). After downloading, 98 apps were included for final assessment (67 English, 22 Chinese, 9 Spanish). Eight apps (8/98, 8%) present in both iOS and Android were assessed as separate apps, four apps (4/98, 4%) were assessed twice (free and paid). There were four (4/98, 4%) apps translated from English to Spanish. Thirty-one per cent (28/89) of English and Chinese apps were assessed by two assessors with mean Cohen's kappa of inter-rater reliability of 0.796. Forty-four per cent (4/9) of the Spanish apps were assessed by both assessors, the Cohen's kappa for the Spanish apps was 0.650. All apps assessed in pairs were discussed after the initial assessment, where after consensus was reached. The list of assessed apps is available from the authors (see Appendix 7.2).

Figure 7.1 Flowchart of app selection process

*Not included are the manually searched Chinese Android apps on the platforms²⁵, these were not retrievable through a search engine and therefore primary screening was not undertaken for these apps

7.3.2 App characteristics

Table 7.2 presents the basic app characteristics. Amongst the 98 assessed apps, 84% (82/98) provided educational information, 39% (38/98) had disease tracking functions, and 13% (13/98) did both. Most apps targeted adult users (76/98, 78%), followed by caregivers (19/98, 19%) and children (below age 13) (3/98, 3%). Fifteen per cent (15/98) required payment (or contained an in-app purchased domain) with a median cost of \$2.99 USD (range \$0.99-\$8.68). Technical errors (such as crashing, freezing or getting stuck during use) were found in three of the assessed apps (3/98, 3%). Eight apps (8/98, 8%) offered games and three apps (3/98, 3%) provided reward programs. Thirteen apps (13/98, 13%) allowed users to share the record with social media. Seventeen apps (17/98, 19%) protected user's privacy by requiring a password to login the app. Twelve apps offered (12/98, 12%) direct access to a healthcare professional by, for example, a video or audio consultation. Eight apps (8/98, 8%) helped users connect to an AD support group.

Table 7.2 App characteristics

Characteristics	Description	Total, n (%) 98 (100)	App platform, n (%)	
			Android, n (%) 62 (63)	IOS, n (%) 36 (37)
App language	Primary language of the app			
<i>English</i>		67 (68)	45 (73)	22 (61)
<i>Chinese</i>		22 (22)	11 (18)	11 (28)
<i>Spanish</i>		9 (9)	6 (10)	3 (8)
Governmental bodies partnership during the app development process	Is the app created/commissioned/partnered by any governmental bodies / government-affiliated companies, hospitals or universities?	18 (18)	9 (15)	9 (25)
Cost	Cost to download the app			
<i>Free</i>		83 (85)	56 (90)	27 (75)
<i>Paid</i>		15 (15)	6 (10)	9 (25)
Location restriction	Is this app limited to certain locations/countries/regions?			
<i>Only US</i>		5 (5)	2 (3)	3 (8)
<i>Only China</i>		8 (8)	7 (11)	1 (28)
<i>Only India</i>		1 (1)	1 (2)	0 (0)
<i>No restriction</i>		84 (86)	52 (84)	32 (89)
Target users n, %	What is the target user of the app?			
<i>Children (age below 13)</i>		3 (3)	1 (2)	2 (6)
<i>Caregivers</i>		19 (19)	11 (18)	8 (22)
<i>Adults (age 13 and above)</i>		76 (78)	48 (77)	28 (78)
Technical errors n, %	Does the app get stuck, crash or frozen more than once when using	3 (3)	1 (2)	2 (56)
Education features n, %	Does the app have any function related to providing information on disease pathophysiology / treatment / psychological factors / environmental factors?	82 (84)	55 (89)	27 (75)
Tracking features n, %	Does the app have any function related to tracking of disease / treatment / QOL / environmental factors?	38 (39)	19 (31)	19 (53)
Supporting attributes n, %				
<i>Rewards</i>	App provides a reward programme for users	3 (3)	1 (2)	2 (6)
<i>Games</i>	Does the app contain any games?	8 (8)	4 (6)	4 (11)
<i>Password protected</i>	App requires a personal login and password	17 (17)	8 (13)	9 (25)

7. AD apps assessment

<i>Share to social media</i>	Does the app allow recorded data of the patient to be shared on social media (e.g. Facebook/twitter?)	13 (13)	8 (13)	5 (14)
<i>Data export</i>	Does the app allow data to be exported (e.g. PDF/Excel, email, cloud, etc.)?	21 (21)	13 (21)	8 (22)
Access to healthcare professionals	Does the app include a health professional who is accessible to the user (without users inputting any health provider/health professional information)?	12 (12)	6 (10)	6 (17)
Support group	Can the app connect the user to a community/support group of other users/caregivers with eczema?	8 (8)	5 (81)	3 (8)
Advertisement	Does adverts interfere with the functioning of the app (if any?). Answer "Yes" if you feel bothered by the adverts, answer "No" if there are no adverts.	28 (29)	22 (35)	6 (17)

7.3.3 AD specific educational information criteria

Table 7.3 shows the assessed content and function for the apps providing educational information (n=82), none of the apps provided all listed information. However, more than two-thirds (64/82, 78%) provided information on pharmacological management. Sixty-five (65/82, 79%) provided instruction on application of topical creams such as calcineurin inhibitors and corticosteroids, and 39 (39/82, 48%) provided information on side-effects of medication. Only 15% (12/82) provided a valid source for pharmacological information (sources were considered valid if they were reported by certified doctors, cited peer-reviewed papers, international guidelines, or referred to government websites or websites with another validated source). Sixty-four (64/82, 78%) offered education on non-pharmacological therapies such as moisturizer application and bath habits, 13 of these (13/82, 16%) provided the valid source for non-pharmacological therapies. The minority (21/82, 26%) provided information on environmental allergens, and fifteen (15/82, 18%) provided food allergy-related information. In terms of customization of AD management, twenty apps (20/82, 24%) mentioned the role of an action plan and the prioritization of management goals.

Content in more than one-third (28/82, 34%) of apps providing educational information was not in agreement with international guidelines. The inconsistency was largely related to use of topical steroids. Ten apps (10/82, 12%) discouraged the long-term use of topical steroids while several guidelines recommend them as maintenance medication in moderate to severe disease (22, 63, 64, 277). Twelve per cent (10/82) advised on home remedies without disclaiming these are non-evidence-based therapies (e.g. vitamin supplements and probiotics). Inaccurate information on the pathophysiology and mechanisms of AD was found in 13% (11/82), focusing only on certain contributing factors such as allergies and not mentioning the multifactorial nature of the disease. Nine out of 82 apps (9/82, 11%) failed to mention mainstay therapies such as the use of emollients and moisturizers. Other inconsistencies found during the assessment were inappropriate recommendations on commercial bath additives (1/81, 1%), home dust mite covers and massages (1/81, 1%) as well as

misguidance on dietary changes (1/81, 1%) and shower and bath behaviour (1/81, 1%).

Table 7.3 Educational information assessment criteria (n=82)

Assessment criteria	Total n (%) 98 (100)	Targeted users n (%)		
		Children 3 (3)	Caregivers 19 (19)	Adult 76 (78)
Information on disease mechanism and course	64 (65)	2 (66)	16 (84)	46 (61)
Information on symptoms	68 (69)	3 (100)	19 (100)	46 (61)
Information on pharmacological therapies	65 (66)	1 (33)	15 (79)	49 (63)
<i>Topical application</i>	65 (66)	1 (33)	15 (79)	49 (63)
<i>Side-effects</i>	39 (40)	1 (33)	11 (58)	27 (36)
Provided valid source of pharmacological information	12 (12)	0 (0)	9 (47)	3 (4)
<i>Certified doctors</i>	7 (7)	0 (0)	7 (14)	0 (0)
<i>Peer reviewed papers and international guidelines</i>	4 (4)	0 (0)	1 (5)	3 (4)
<i>Authorised online sites (governmental support websites, evidence-based websites, etc.)</i>	1 (1)	0 (0)	1 (5)	0 (0)
Information on non-pharmacological therapies	64 (65)	3 (100)	16 (84)	45 (59)
<i>Bath practice</i>	60 (61)	3 (100)	14 (74)	43 (57)
<i>Moisturizer application</i>	49 (50)	2 (66)	14 (74)	33 (43)
<i>Wet wrap</i>	20 (20)	1 (33)	5 (26)	14 (18)
<i>Using non-soap cleansers, bath additives, acidic spring water</i>	44 (45)	2 (66)	12 (63)	30 (39)
<i>Side-effects</i>	6 (6)	0 (0)	4 (21)	2 (3)
Provided valid source of non-pharmacological information	13 (13)	1 (33)	8 (41)	4 (5)
<i>Certified doctors</i>	6 (6)	0 (0)	6 (32)	0 (0)
<i>Peer reviewed papers and international guidelines</i>	4 (4)	0 (0)	1 (5)	3 (4)
<i>Authorised online sites</i>	3 (3)	1 (33)	1 (5)	1 (1)
Information on the goals of management	20 (20)	0 (0)	7 (37)	13 (17)
Information on psychological /QoL	36 (37)	1 (33)	8 (42)	27 (36)
Information on food allergy	15 (15)	1 (33)	2 (11)	12 (16)
Information on aeroallergens	21 (21)	1 (33)	16 (84)	4 (5)
App provides all above information	0 (0)	0 (0)	0 (0)	0 (0)

7.3.4 AD specific tracking function criteria

Table 7.4 demonstrates the tracking functions available in the apps (n=38). None of the apps contains all the features listed in Table 7.4. Thirty-one out of 38 apps (82%) provided a function to track disease status of which 12 (12/38, 32%) used a validated scoring system such as POEM, SCORAD, and PEST (22, 288, 289). Fourteen (14/38, 37%) allowed users to set reminders to record the status of the disease. Thirteen (13/38, 34%) checked the users' psychological status regularly for example by the level of sleep disturbance, stress, and mood, with advice such as how to manage stress or seek counselling. Most (34/38, 89%) apps provided a disease management tracking function; thirteen (13/38, 34%) helped users record oral medicine intake (e.g. cyclosporine, azathioprine, methotrexate), sixteen (n=16/38, 42%) provided a topical application record function for users. Less than half (17/38, 45%) allowed users to set reminders for treatment management and only four apps (4/38, 11%) provided advice if the skin condition worsened. Thirteen out of 38 apps (34%) provided tracking functions on environmental factors by real-time environmental condition tracking (e.g. pollens, humidity, temperature through passive data collection) and recording potential environmental triggers. Eleven apps (11/38, 29%) had a food diary function for patients and caregivers on documenting any foods that may trigger AD. None of the apps allowed users to set goals based on their own needs.

Table 7.4 Tracking function assessment criteria (n=38)

Assessment criteria (Does the app allow users)	Total (n=98) N (%)	Targeted users		
		Children 3 (3)	Caregivers 19 (19)	Adult 76 (78)
Track disease status	31 (32)	1 (33)	0 (0)	30 (39)
<i>Record current disease status</i>	27 (28)	1 (33)	0 (0)	26 (34)
<i>Monitor disease based on recommended validated scoring systems (SCORAD, EASI, POEM)</i>	12 (12)	0 (0)	0 (0)	12 (16)
<i>Set reminders to record eczema status</i>	14 (14)	0 (0)	0 (0)	14 (18)
<i>Diagnostic functions</i>	5 (5)	0 (0)	1 (5)	4 (5)
<i>Track of psychological factors</i>	13 (13)	0 (0)	0 (0)	13 (17)
Track disease management	34 (35)	1 (33)	1 (5)	32 (42)
<i>Record oral medicine intake (e.g. Cyclosporine, azathioprine, methotrexate, etc.)</i>	13 (13)	0 (0)	0 (0)	13 (17)
<i>Record topical application (e.g. topical calcineurin inhibitors, topical corticosteroids etc.)</i>	16 (16)	0 (0)	0 (0)	16 (21)
<i>Key in frequency and dose for each medication (oral medicine, topicals)</i>	13 (13)	0 (0)	0 (0)	13 (17)
<i>Record non-pharmacologic treatment management (moisturizers application, bath practice, wet wrap etc.)</i>	19 (19)	1 (33)	0 (0)	18 (24)
<i>Key in frequency and notes for non-pharmacologic treatments</i>	14 (14)	1 (33)	0 (0)	13 (17)
<i>Set reminders for treatment management</i>	17 (17)	1 (33)	0 (0)	16 (21)
<i>Provide information on step-up or step-down treatment</i>	1 (1)	0 (0)	0 (0)	1 (1)
<i>Provide advice if skin condition becomes worse</i>	4 (4)	0 (0)	0 (0)	4 (5)
<i>Set specific goals of management</i>	2 (2)	0 (0)	0 (0)	2 (3)
Track trigger factors	13 (13)	0 (0)	0 (0)	13 (17)
<i>Provide real-time environmental conditions (e.g. Pollens, humidity, temperature, etc.)</i>	5 (5)	0 (0)	0 (0)	5 (7)
<i>Record environmental triggers of eczema</i>	11 (11)	0 (0)	0 (0)	11 (14)
<i>Contains a food diary</i>	11 (11)	0 (0)	0 (0)	11 (14)
App has all above features	0 (0)	0 (0)	0 (0)	0 (0)

7.3.5 Health on Net (HON) code principles

Figure 7.2 displays the percentage of apps which complied with the Health on the Net principles (108). None of the included apps met the terms of all eight principles. Most of the apps (78/98, 80%) had contactable developers (transparency principle) and provided a financial disclosure (69/98, 70%). Few apps (15/98, 15%) indicated the qualifications of the specific individuals who developed the app or contributed to the information provided (authoritative principle). Thirty-one per cent of the apps (30/98) indicated privacy and/or confidentiality clause in the app. Additionally, I assessed whether the app treated the data gathered from children separately as children may need to use the app under their caregiver's supervision. Only several apps (i.e. app code EI12) differentiate between user profiles (286). Some apps (i.e. app code CI05, app code CI04, etc.) designed for caregivers mentioned that those below 18 must use the app under parental supervision (290, 291). The app (app code CI03) directed users to pass the phone to parents to enter personal information (292).

Figure 7.2 HONcode principles ^a

^a Advertising policy - App distinguishes advertorials from content;

Financial disclosure - App indicates funding sources;

Transparency - App developers are contactable (by e-mail); Justifiability - App backs up claims relating to the benefits and performance by evidence;

Attribution - App cited information sources;

Privacy - App has privacy and/or confidentiality clause;

Complementarity - App has a disclaimer stating the information provided and/or app function do not replace healthcare providers advice;

Authoritative - App indicates the qualifications of specific individuals who developed the app or contributed to the information provided.

7.4 Discussion

I systematically assessed all available AD self-management apps for patients and their caregivers in the three most widely spoken languages. Available AD apps (n=98) most common function is information provision (n=82, 84%), followed by disease tracking (n=38, 39%). Evaluated apps had diverse functionalities with varying quality. Most apps failed to cite their source of educational information, and even apps with cited claims or information provided by qualified doctors contained content inconsistent with guidelines. This is concerning, particularly with regards to

steroid use where balanced information about appropriate use, dosing, and side effects should be sufficiently explained, as concerns about steroid side-effects are a common reason for their underuse and a major barrier to appropriate AD management (293, 294). Since apps covering all assessment domains were not found, this chapter only shows assessment criteria instead of recommending specific AD apps in order to avoid misleading potential users and healthcare professionals. These assessment criteria (Appendix 7.1) could also potentially serve as a reference for developers in the future when they develop/update AD apps.

Frequent tracking is the cornerstone of effective AD self-management (64, 277). Therapy is needed on a daily basis and patients with more severe AD require intensive, individualized management and monitoring. Currently, only 38 apps (38/98, 39%) provide disease tracking functions and only one in eight (12/98, 12%) allow users to directly access a healthcare provider via a fee-based teleconsultation (I did not assess the apps which were merely designed for teleconsultation). Another gap in apps functionality was incomprehensive tracking of AD triggers such as possible allergens in food and environment, which could help prevent flares (295). A clear description of the app's functionalities when downloading the app could align patients' and healthcare professionals' needs when a patient, for example, is just looking for allergen tracking some of the apps might be better than others.

Information on psychological impacts and interventions was not provided in the majority (46/82, 56%) of apps. This is concerning since AD has serious psychological implications and is an independent risk factor for psychiatric conditions like affective and stress-related disorders (179, 262). Moreover, stress may also be an aggravating factor (296), perpetuating a vicious cycle. Nevertheless, recording physical and mental health information is sensitive (297) and poor security and transparency may impede a user's willingness to input such information (298). I found 35% of the apps failed to provide a proper privacy policy (Figure 7.2).

Inconsistency of provided information was also identified in insulin calculation (193), smoking cessation and asthma self-management apps in previous studies (193, 299, 300). Likewise, in other dermatology apps, concerns of efficacy and accuracy

of diagnostic tools in skin cancer screening and early melanoma detection have been expressed (301, 302). Investigated smartphone apps detecting melanoma lesions have shown low sensitivity with a seemingly inaccurate assessment potentially resulting in giving patients a false reassurance (303, 304). Moreover, established quality standards or regulatory oversight of mobile medical apps mainly focus on apps connected to medical devices. The exclusive focus on these misses opportunity for positive impact and impedes safeguards of minimizing harm for the users of the majority of medical apps which are not connected to devices. Consulting incorrect or incomprehensive app resources, for information about disease conditions instead of seeking the care of healthcare professionals could pose a risk on patients and their caregivers (303).

This study has several merits. First, with covering all apps available in the three worldwide most widely spoken languages, this study is the first to provide a comprehensive overview of AD apps. Apps included in this review cover more than 1.8 billion of the world's population (281). The results are a reference to patients and health professionals who aim to recommend to their patients' AD self-management apps. Secondly, guideline-derived assessment criteria provide a validated rational basis from a clinical and technical point of view. Thirdly, this study adopted a systematic assessment methodology using my team's experience, which reduces the possible bias compared to other assessment and reviews (193, 299, 300).

The scope of the study is however limited as assessment was not able to cover the entire spectrum of apps related to AD management due to overlapping functionalities hidden within other apps. For example, general health-tracking apps may be used to monitor AD, and specific information may be found in general dermatology apps. This limitation should not affect the purpose of this review since the search specifically focused on AD apps to support self-management. Teleconsultation apps, which constituted 21.0% of dermatology apps available in 2017, were also excluded (110). Future studies could investigate the quality of teleconsultation and general health apps in supporting AD self-management. Other important areas that are not reported in this study are the usability and the appropriateness of in-app adverts.

However, there are still limited validated measures to reliably assess usability for health apps from different users' perspectives. While it is ideal to have multiple functions built into an app, the ease of use of an app will determine its adoption by patients and its resultant benefits. As such, apps must be customized taking into consideration a patient's lifestyle and level of comprehension such that it integrates into a patient's routine way of life. A final caveat is that the study does not evaluate the extent to which information was understandable for the specific age groups. Information relating to the average reading age of people accessing apps could not be traced, and so it might be not possible to assess whether the information can be understood by its users in this study. Future study can collaborate with app companies and collect average reading age by conducting a short survey when users register their account in the app.

Digital health could bridge health literacy and health outcomes (305, 306). By delivering multi-media education, digital health tools could equip patients with better knowledge and make them actively engage in the healthcare process. Data collected from an app could also help healthcare providers understand their patients better and help build an integrated healthcare ecosystem. Digital health tools also have the potential to address health inequalities (307, 308). They can be used to promote healthcare and cultivate healthcare behaviours across the population (309). Caregivers could enjoy equal access to information, irrespective of local jurisdiction and healthcare facilities. Access to healthcare apps enhances autonomy and help users take control of their own health care (310). For example, by using the app, caregivers and their children can assess AD severity more precisely, and can quantify the frequency of medication application and cultivate the good bathing practice.

Even though dermatology-related apps have been developed at unprecedented speed and volume, systematic assessment of their safety and efficacy is lagging behind (110). However, the under-investigated reliability and accuracy of these tools obscure their efficiency or even bring unpredictable risk to the targeted users. I found that patients should use the available AD self-management apps with caution. Meanwhile, healthcare professionals should be aware of the issues, direct patients to selected apps

with comprehensive tracking functions and validated information and could alternatively consider advocating the use of other reliable information resources such as accredited webpages or disease-specific educational leaflets (311, 312). Also, regulation, certification or similar quality assurance mechanisms of medical smartphone apps should adequately keep pace. Policymakers may need to review the developer's qualifications before any healthcare-related apps are offered to the patients and the public and increase the threshold for entering the market by setting evidence-based app quality controls and implementing user-friendly accreditation programs (280). During the development process, innovative models such as co-design could ensure all stakeholders are consulted frequently to assure the accuracy, efficacy, and user-friendliness of apps.

7.5 Conclusion

The assessed AD self-management apps had shortcomings; however, certain apps did provide appropriate functions with accurate information and comprehensive tracking of AD-related factors. The large variance in assessed quality of available AD apps underlines the need for the published recommendation of apps or guides to aid clinicians in advocating appropriate apps for AD patients and caregivers. With room for further development of quality, the field of mobile health has great potential to better patient care and self-management of AD, address major unmet needs, and open new modalities to supplement traditional models of care, provided that appropriate measures are taken to improve the quality standards.

Chapter 8

Creating a smartphone app for atopic dermatitis self-management: A participatory co-design approach with caregivers, healthcare professionals and researchers

After I have a better understanding of the targeted users and existing apps in the market, it comes to the phase of conceptualizing the content and features of the app. Co-design is one of the approaches that help us better understand stakeholders' perceptions and preferences. This chapter describes an app co-design exercise with carers of children with AD, healthcare professionals, researchers and developers through a series of face-to-face workshops to propose a solution by applying their preferences and perceptions to smartphone app features. I present this chapter by justifying the needs for co-design in introduction (Section 8.1) and then describe the method used for conducting the co-design workshops (Section 8.2). The findings were presented in Section 8.3. This chapter is ended by discussing the strengths and limitations, recommendations for future research in Section 8.4.

8.1 Introduction

In the previous introduction chapter, I have discussed that AD, especially childhood AD, requires skilled self-management including coping with a complex regime: caregivers need to help their children apply creams on a daily basis and, at the same time, in order to reduce recurrence, they also need to modify their children's daily routine and diet in order to avoid aggravating triggers. Therefore, caregivers may have unaddressed needs and concerns when managing their children's AD. Lack of support leaves caregivers not feeling confident, or even failing to manage and provide disease management support for their children's condition in between visits to the

clinic. As such, it is necessary for caregivers to be equipped with supporting tools which help them to properly manage patients' condition on a continuous basis (215).

Smartphone apps are increasingly being leveraged to increase patient engagement and facilitate disease self-management for conditions such as diabetes, asthma, dementia and cancer (101, 250, 278, 313, 314). Evidence as to their effectiveness is mixed (315). While many studies document the benefits of smartphone apps in terms of supporting users to monitor, treat and follow up disease conditions, the quality of apps is a cause for concern as lack of clinical evidence in proving the effectiveness of apps. The reason could be because many of the apps are not tailored to user's needs which may explain the low adoption rate in clinical practice (110, 315). Working in partnership with stakeholders in the design process can better serve app development. By doing so, developers can more easily identify desirable features for an app as well as obstacles hindering long-term usage; together, app developers and stakeholders could improve the viability, usability, and effectiveness of apps in healthcare services (316-318).

The co-design approach is considered one of best ways to understand the user's needs. The co-design approach has been used to build self-management apps for chronic diseases such as heart failure, dementia, etc (9, 201). User-centred design has been employed in AD app development before, but relevant information online is so sparse that previous experiments cannot easily be repeated by other researchers. Given the fact that self-management is crucial to tackling AD among children, an app involving all stakeholders with detailed procedures is needed. The objectives of this study are to better understand the needs of and challenges confronting caregivers and healthcare professionals (HCPs) who care for children with AD, and to explore the desirable features and content that smartphone app should offer in supporting AD self-management.

8.2 Methods

8.2.1 Study design and settings

Data were collected across three co-design workshops conducted in a specialist hospital in Singapore from September 2018 to March 2019 across two phases (Table 8.1). The workshops were designed to bring together multiple stakeholders, including caregivers and HCPs and researchers, and thus allowed different stakeholders to voice their unique experiences and perspectives (see Appendix 8.3).

Table 8.1 Co-design workshop

Variables	Phase 1		Phase 2
	Caregivers session	Healthcare professionals session	Design session
Participants	Caregivers of paediatric AD patients (n=14)	Paediatrics dermatologists (n=8) Pharmacists (n=2)	Caregivers (n=6), Researchers (n=4)
Content	<ul style="list-style-type: none"> •Share their problems and difficulties encountered in their daily life •Propose their needs •Discuss how the app can be used in their daily life and what features can be adopted by smartphone app 	<ul style="list-style-type: none"> •Share their problems and difficulties encountered in their daily life •Propose their needs •Discuss how the app can be used in their daily life and what features can be adopted by smartphone app 	<ul style="list-style-type: none"> •Briefing the need and proposed feature discussed in the previous caregivers' journey sessions •Top needs were assigned to the participants •Individual crazy eights exercise to sketch their own prototype •Team Sketches •Revisions •Present the wireframe to the entire group

Phase 1: Workshops one and two adopted a focus group discussion format. Workshop one was a focus group discussion with caregivers: two researchers facilitated the group discussion (Researcher KG: Professor. Female. Health Psychology / Behavioural Medicine; Researcher WS: Analyst. Female. Public

health). Additional field notes were collated to capture relevant contextual information. Semi-structured questions were used to guide the focus group discussions. In order to better serve the research objectives, the semi-structured questions used in the previous AD quality of life study were designed to address both subjective feelings and objective findings regarding the most disturbing aspects of childhood AD. Questions were piloted within internal team. The topics raised during Workshop one were as follows:

Q1. What were your needs the first 6 months after the symptoms started, from 6-months to a year, or later? Did you feel well informed, especially with respect to (1) disease status, (2) treatment and management guidance (3) emotional support?

Q2. Where do you get the information? Are you satisfied with your knowledge of taking care of your child's AD? What is the source of the information?

Q3. Previous experience in app usage: Has anyone used a smartphone app to manage AD?

Q4. If there is a smartphone app to help you manage your child's AD, please list the top features that you want to have in the app.

Q5. If there would be a smartphone app with all the information and features you need; what frequency do you think you will use it? What are the possible barriers that would keep you from consistent usage?

Besides, during Workshop One, caregivers were also asked to write down desirable features they would like to see in an AD app and pass on their recommendations to the researcher (Researcher XM: PhD student/Medical doctor. Female. Public health). The researcher subsequently sorted those features provided by the caregivers and combined these with the other features summarized from the app assessment in Chapter 7 and started a real-time online voting session with the caregivers. The caregivers were asked to vote for 'must-have' features and 'nice to have' features they would expect to see when using a smartphone to manage their children's AD.

Workshop Two was a focus group discussion involving HCPs; two researchers facilitated the group discussion (Researcher JC: Medical doctor and professor. Male. Public health; Researcher KG: Professor. Female. Health Psychology / Behavioural Medicine). Additional field notes were taken to capture relevant contextual information. Semi-structured questions were used to guide focus group discussions. The semi-structured questions were designed based on the feedback of caregivers in Workshop one. They were as follows:

Q1. How do you educate your patients (their caregivers) during the clinic? Are you satisfied with the results?

Q2. What do caregivers need the first 6 months after the symptoms started, from 6-months to a year, or later? Does the education need to change according to (1) different severity (2) duration of diseases (3) child age?

Q3. Have you considered using smartphone apps to educate your patients (and their caregivers)?

Q4. What features should an app have to address those problems?

Q5. Would you mind providing teleconsultation service to your patients?

Phase 2: After completion of Phase One, a final co-design workshop was conducted with caregivers and researchers in an effort to design the wireframe prototype and to elicit their feedback. After the participants outlined various design requirements in workshops one and two, the facilitator asked participants to design the interface of the app themselves (Researcher JC: Medical doctor and professor. Male. Public health; Researcher; XM: PhD student/Medical doctor. Female. Public health). The app had to address at least one of the top needs mentioned in the previous workshops. The workshop groups discussed and explored the ideas from the drawings and came to an agreement on the top features or ideas they wanted to include in one consolidated master sketch. Groups sketched a single layout that incorporates the top ideas. The teams regrouped and critiqued the wireframe prototype. After the feedback

and revision session, the groups discussed and explored the ideas from the drawings and came to an agreement during the development of the consolidated master sketch.

8.2.2 Participant recruitment

Purposive sampling was used when I recruited participants. Eligible participants were recruited among those of a baseline cohort in a prior study, who had provided consent to be re-contacted for participation in this study. Caregivers had to meet the following inclusion criteria: (1) Adults providing unpaid care/assistance to youth/children with AD; and, (2) prior experience with using a smartphone app to manage health-related issues. The exclusion criterion was as follows: Caregivers who did not own a smartphone nor had any knowledge of mobile applications. HCPs were recruited from the Dermatology Department at the KK Women's and Children's Hospital in Singapore. Researchers were recruited from Lee Kong Chian School of Medicine, Nanyang Technological University.

8.2.3 Instruments

The following questionnaires were administered during the co-design workshops (see Appendix 8.1):

i. Demographic questionnaire

Caregiver participants were asked to fill in the demographic questionnaire in workshops one and three including their date of birth, sex, residential status, highest qualification earned, and main daytime occupation; and, the child's date of birth, child's sex, date of the first diagnosis, and the biggest concern relating to the management of the child's AD.

ii. Technology acceptance questionnaire

Caregiver participants were asked to fill in the technology acceptance questionnaire during workshops one and three. The questionnaire was developed by the study team adopting the technology acceptance model (319, 320). The list of questions tested individuals' knowledge of healthcare apps usage, acceptability, and usability; and, it is addressed perceived ease of use, perceived usefulness, user satisfaction, and usability (319, 320).

iii. Workshop evaluation form

At the end of each workshop, the participants were asked to fill in the evaluation form and provide feedback. Three questions were asked in the evaluation form: (1) a rating of the workshop, (2) the most helpful aspect of the workshop, and (3) any suggestions for improving the workshops.

8.2.4 Data collection and analysis

Workshops were audio-recorded, transcribed and managed using QSR NVIVO software (version 11) (321, 322). The transcript data were first broken down into concepts and reorganized in order to summarize key issues from each workshop. I (XX), KG and JC reviewed and discussed concepts immediately after each workshop so that emerging issues could be explored in subsequent workshops. I transcribed the audio recordings, and processed the observation logs, photos and written products in order to contextualize and gain more details about the discussion. Thematic analysis was chosen to analyse the transcriptions from the workshops (202). An inductive strategy was employed, which allowed for themes to be generated from the data, which were then organized into higher-order themes. The Nvivo software program was used to store and code the transcript. First cycle coding was performed on the raw data. After that, researchers met and compared each other's codes. An Inter-Rater Reliability (IRR) test was performed between the researchers' findings; whenever an acceptable IRR was not achieved, the inconsistencies were jointly discussed until a consensus was reached.

All eligible participants provided informed consent prior to the workshops. Ethical approval was sought with the Institutional Review Board of Nanyang Technological University prior to the commencement of the study (NTU IRB:2018-09-053). The reporting follows Consolidated criteria for reporting qualitative studies (COREQ) checklist (Appendix 8.4 COREQ checklist).

8.3 Results

8.3.1 Participants' characteristics

The participant recruitment procedure and reasons for exclusion are listed in Figure 8.1. The characteristics of the caregivers are summarised in Table 8.2. Out of a total of 270 eligible caregivers, eighteen caregivers participated (6.7%). The caregivers' sample included a diverse range of demographics (see Table 8.2): the majority of them were women (77.8%), the mean age of the participants was 37.87 ± 7.81 years old, and the children's disease duration was 4.72 ± 4.57 years. Paediatrics dermatologists ($n=8$) and pharmacists ($n=2$) were recruited for the second workshop: their mean age was 35.50 ± 6.69 and their mean practice time was 9.76 ± 6.57 . Four public health researchers with a mean age of 37.80 ± 8.12 years attended the third workshop.

The caregivers' perceptions of using self-management smartphone apps were assessed in order to test perceived usefulness, ease of use and user satisfaction (Table 8.3). Eighty-nine per cent of the participants found it easy to get mobile tracking on children's disease, and 89% of them felt confident in using a smartphone app to manage children's AD. Seventy-eight per cent of the participants believed that using a smartphone app to manage AD would increase the caregiver's quality of life.

Figure 8.1 Participants recruitment process⁴

⁴ Caregivers (n=2) were repetitive recruited and have participated two workshops (the first workshop and the third workshop)

Table 8.2 Demographic characteristics of caregiver participants

Variables	Characteristics	N	% / Mean $\pm$ SD
Caregiver	Sex		
	Female	14	77.8%
	Male	4	22.2%
	Age	18	37.87 $\pm$ 7.81
	Qualification		
	Bachelor's degree and above	10	55.6%
	Diploma	4	22.2%
	O level and below	4	22.2%
	Children's disease duration	18	4.72 $\pm$ 4.57
Healthcare Professional	Sex		
	Female	8	80%
	Male	2	20%
	Age	10	35.50 $\pm$ 6.69
	Specialization		
	Paediatrics dermatology	8	80%
	Pharmacy	2	20%
	Practice duration	10	9.76 $\pm$ 6.57
Researcher	Sex	4	37.80 $\pm$ 8.12
	Female	2	50%
	Male	2	50%
	Age	4	37.80 $\pm$ 8.12
	Specialization		
	Public health	4	100%

Table 8.3 Perceived usefulness, ease of use and user satisfaction of smartphone app among caregivers

Items	Strongly agree	Agree	Neutral	Disagree	Strongly disagree
Are you aware of the availability of health apps (applications) for smartphones	67%	33%	0%	0%	0%
A smartphone self-management app will enable me to get information quickly	28%	56%	17%	0%	0%
A smartphone self-management app will allow my doctor to follow up the disease from outside of the hospital	24%	53%	24%	0%	0%
A smartphone self-management app will save the time of doctors and nurses	7%	40%	40%	0%	13%
I would find it easy to get mobile tracking on my child's disease	22%	67%	11%	0%	0%
Using a health app will be clear and understandable.	24%	59%	12%	0%	6%
It would be easy for me to become familiar with using a smartphone self-management app	24%	59%	12%	0%	6%
I feel confident in using a smartphone app to manage my child's AD	11%	78%	11%	0%	0%
I believe using a smartphone app to manage AD will increase my quality of life	17%	61%	22%	0%	0%
I think that I would like to use a smartphone self-management app on a daily basis	18%	65%	18%	0%	0%

8.3.2 Thematic analysis

Eight primary themes were identified that reflected caregivers' and HCPs' needs and concerns for AD self-management support: (1) understanding of causes, triggers, and symptoms of AD, (2) understanding the disease course and the complications related to AD, (3) which medication to choose and when to use it, (4) generic instruction vs specific instruction, (5) alternative treatments preferable to steroids, (6) guilt and frustration, (7) self-esteem, (8) the duty to make their child feel better. I then subsequently grouped the primary themes into three superordinate themes: *empowerment by education*, *confusion overtreatment*, and *emotional impact* are

foundational issues for support caregivers when helping them to manage a child's AD. Each superordinate theme is further explained below.

1) Empowerment by education

Both the caregivers and HCPs believed that education enables patients and their caregivers to handle AD and live with AD. The caregiver's perception of diseases often shapes their attitude in relation to self-management and affects their adherence and capability of engaging themselves in self-management following a medical consultation. Two aspects were highlighted during the discussion: (1) understanding of causes, triggers and symptoms of AD; and, (2) understanding disease course and the complications related to AD.

i. Understanding of causes, triggers, and symptoms of AD

The caregiver participants expressed a desire to understand more about AD, especially those caregivers whose children were newly diagnosed with AD. They experienced much confusion during the first few months after the first diagnosis, especially in relation to **cause and triggers**, and **symptoms** aspects. They wanted to know what environments or temperatures would prevent them from triggering flare-ups, and were concerned as to whether existing symptoms were 'normal'. The two quotes below represent their anxieties:

'We're talking about temperature...sometimes it gets too cold [when] using the aircon...[which]...actually triggers the AD itself, so it will make the skin very, very dry and that's when it gets terrible for him also. So, what kind of temperature is actually good for him? It's always a question, makes me wonder.'

(Caregiver 01, Female)

'Even the doctor, he will diagnose this and tell you it's a typical AD, but [when] this thing came, I didn't [know] whether it's normal.'

(Caregiver 02, Female)

ii. Understanding the disease course and the complications related to AD

Caregivers also described their confusion about the **disease course** and the **complications** related to AD. They claimed that existing support and education received during the consultation might be not enough and sometimes may not suit their needs. According to one caregiver, *‘No one told them what happened and what happened next.’* Some caregivers did not realize the importance of disease course until they have discovered that their child was following another child’s disease pattern. One mother said:

‘Nobody tells you...I mean, the way it changes. I just so happened to come to this outing thing, and I saw, I mean, supposed to get AD trip outing and I saw a different one and I wasn’t given an education. It was later on [when I found out] he just had the same thing - just shed, shed, his skin just shed.’

(Caregiver 03, Female)

They also reported that lack of awareness and understanding of the complications related to AD could throw them into uncertainty. Therefore, relevant knowledge should be provided in the first place so as to prepare the caregivers mentally, and to help them successfully and smoothly pass the most helpless stage. One mother mentioned:

‘When my son first had it, I know that he suddenly had lumps, so I wasn’t sure what was it. I brought him to see a doctor. At that time, he got blisters all over. I didn’t know what it was. So, I found that link? It apparently, it’s linked with AD. I don’t know why it’s linked but it’s linked. So, for me, that was very scary cause it’s just one of links, and stuff like that. So, for six months I didn’t know what was happening - it was very frightening. If there is a way to let me know it beforehand, I will definitely be better prepared.’

(Caregiver 03, Female)

HCPs also highlighted the need for a greater understanding of causes and triggers for patients and their caregivers. One doctor mentioned:

'I think that information will come in, [i.e.] to recognize...the flare. In a way, if we could teach them [about the] cause [of and] how to identify the flare-up, that [would be] better. That is [the] key point of providing information. And most importantly, [teach them] to use their own language.'

(Doctor 01, Female)

However, they also underlined that the caregivers should lower their expectations and accept the truth that their children need to live with the disease. Otherwise, they could develop an irrational attitude, which could hinder them from treating AD properly, particularly if they spend most of the time trying to find a 'cure' for AD. One doctor said:

'One thing that bothers me a lot is...the psychology of the parents. Because they don't, they're unable to accept that their kids have AD, that there is no cure, that there are many triggers. So...they try to find different and different ways to treat the AD. And no matter what your app is doing, [it has] to address...this fear or uncertainty that they have. Which is going to make it very difficult to, I don't know, live [with] that treatment.'

(Doctor 03, Male)

2) Confusion over treatment

There was also a consensus that confusion over AD treatment could be another barrier to patients and their caregiver's proper self-management, one which could have a cascading effect on the outcomes of the AD. Caregivers and patients can feel confused over (1) which medication to choose and when to use it, and (2) receiving general instructions from a doctor, and (3) treatments that might be preferable to steroids.

i. Which medication to choose and when to use it

Caregivers, especially first-time parents, can feel overwhelmed with all the information available to them when they are selecting medication. There were too many brands for them to choose in the market, and they did not know precisely which medication to choose and when to use it. One mother mentioned:

'What kind of salt [should] we use for them? What do they use to shower? When should I apply this cream? The shower creams. I cannot just buy any of the shower [creams]. We end up with having over ten tubes of cream at home, wish it was a little clear which one to use and when to use.'

(Caregiver 01, Female)

Confusion in selecting medication was also observed among doctors. Caregivers received different prescriptions from doctors when they switched doctors. One mother mentioned:

'Different doctors' prescriptions, different medications. That's also one of the problems we face. My son is actually two years old. So, I brought him to the PD, initially, and he was prescribed with one cream which [contains] 1% steroid... Then when I brought him to another doctor, the doctor was like, "Your child is only a baby, two months old. How can you apply this cream on him? It's too strong for him." So, another cream came, and that one came through this doctor and another cream came and we end up with all many, many, different steroid creams and totally no idea which one to use. Plus, different doctors have different knowledge...[and] tackle...problems differently.'

(Caregiver 01, Female)

ii. Generic instruction vs specific instruction

Having to administer multiple creams also contributes to the treatment-related burden and confusion experienced by caregivers. While the administering of lotions itself was not found to be a major issue (as caregivers have usually worked out a routine),

they still had pending questions relating to the treatment timing, sequence and amount, i.e. of **applying the creams**. They reported that the doctors always give them guidance in general, but that self-management in daily life is more detailed and difficult. For example, even with the same patient, the severity of AD lesions can vary widely, and so confusion over which cream should be applied to which specific lesion can arise. One caregiver said:

'I think about how to apply the cream and everything. Plus, when we go to the doctor, they don't show us how to apply [it]. They just tell you, "This is the cream, you apply." Any knowledge that is this sufficient? Am I [applying] too much, am I too little? How should I apply? Do I have to rub it? What? All [that information is] totally missing.'

(Caregiver 01, Female)

iii. Alternative treatments preferable to steroids

The option of using less aggressive treatments was discussed during both the caregiver session and HCP session. Some parents worried about the side-effects of steroids in children and mentioned that they preferred to seek out alternative forms of treatment (e.g. traditional Chinese medicine, ayurvedic medicine) which are deemed safer. One mother said:

'I [keeping looking] for professional help; however, they always say that steroids [are] ...the best treatments for AD. But I think there are other products as well, but they [insist on] staying on the steroids [and won't talk about other] products. A lot of people [are choosing] organics, natural products and they think [they are] useful.'

(Caregiver 03, Female)

HCPs, on the other hand, expressed concerns over so-called alternative medications. They claimed that they may contain stronger steroids, and that some patients may miss the best treatment opportunities either because they are avoiding or over-applying steroids. One doctor said:

'... 'cause the community is very pushed back by steroids. You know, they say "it's bad", "it doesn't work", "everything else works". We're fighting [this] war.'

(Doctor 03, Female)

3) Emotional impact

Peeling and erythema of the skin affect children's appearance and can be detrimental to their social life. When the skin condition is relapsed, the children's mood becomes irascible and their irritable emotions will induce them into irritating the skin and making their skin condition even worse. Three subthemes relating to the emotional impact of AD were identified during the workshops. These were (1) guilt and frustration, (2) self-esteem, and (3) the duty to make their child feel better:

i. Guilt and frustration

The feeling of **guilt** was repeatedly mentioned by caregivers whenever they talked about their child's illness. It was difficult for some of the parents to express the feeling of guilt, especially the subtler form of guilt, which found expression in the form of questions. One mother stated:

'But you should say the guilt says that you never take care of your kids, probably. That's why you have this thing. Because you never do this thing that causes problems. Where is the guilt initially? I had it.'

(Caregiver 08, Female)

When the parents reflected on their situation, ***they sometimes regretted things they had done at an earlier stage in life:***

'I think people [keep] criticizing, [saying], "There must be something that you're doing during a pregnancy which resulted that your child having AD," [or], "I probably shouldn't be eating this kind of stuff, shouldn't be doing this during pregnancy." So, the whole process starts from the day you're pregnant and you're

guilty until [the child is] born and then you're guilty. Now if you do a C section, they say, "Yes, that's also partly why your child has AD, plus, they didn't go through the birth canal," [or], "Ah, everything's your fault."'

(Caregiver 01, Female)

The guilt may also stem from ***applying strong medicines on a young child***. Some felt worried over "putting their kid through something that was not necessary" and the risk that "there is a side effect after the child grows up". One parent said:

'People always tell me that don't put steroids on your son because it brings you the bad thing, so I always feel guilty of putting him steroid every single time. So, whenever I visit the doctor, I keep asking doctors about steroid, steroid, how bad it can be like that at the same time. So, being a mother, you want to try to listen to other people advices. The guilt, it's the guilt.'

(Caregiver 02, Female)

The problem of unhelpful 'helpful' advice by others was raised up repeatedly by the caregivers during the workshop, which could be another cause of feelings of guilt among them. Such advice includes doctors and peers prescribing overusing of steroids, as well as unspoken blame and judgement imposed by families, friends and HCPs. One participant mentioned:

'Because I will have people come [to] me, [saying]: "Why you give your son this kind of food? You should put him on a vegetable diet, a gluten-free diet." As a parent initially, we go on a guilt trip, like, "Oh, we should have done this, maybe he would get better." But initially, I'm sure it's frustrating.'

(Caregiver 04, Female)

ii. Self-esteem

Children experiences the same emotional impact as their parents, sometimes even to bigger degrees. Parents often reflected that when their children get older, changes in

their appearance could affect their self-esteem. Children might find it frustrating when the skin lesions recur and show as anger eventually. One mother mentioned:

'My child [is] always very angry. I mean I'm sure it started with frustration because the skin conditions are on and off - but it shows as anger. It affects my child's self-esteem...harm his self-esteem.'

(Caregiver 08, Male)

iii. The duty to make their child feel better

In addition to experiencing guilt and self-esteem, the parents also expressed a strong responsibility to make their children feel better, and felt concerned that their children would become more self-aware as they grow older, and that AD would affect their emotional health in the long run. According to one parent:

'I think the main thing that I want [is] to make my child feel better, even though with myself I struggled a lot in the early stage. When my child [is] getting older and aware of herself...it starts to affect [her] emotional...health. My child currently is 2 years old, she doesn't feel anything yet, but on a longer-term, she will start to get aware of herself and how others view her, and I think it will be another challenge that we need to meet as well. Not just the physical part, [but also] the physiological part.'

(Caregiver 02, Female)

8.3.3 Ideas and features of the AD self-management app

During the workshops, various functionality requirements were discussed among participants. The most prevalent requirement across the groups was knowledge of the symptoms, and on managing the symptoms, medication usage and triggers. They also expressed a desire to brief caregivers and children about the issues that they might face in the future following diagnosis.

The HCPs also emphasized that such information should be provided in the right amount in the local language. Excessive information provided during medical consultations may overwhelm both patients and their caregivers. However, inadequate information may also leave them feeling directionless, a feeling which induces them into “*going online for relevant information which could lead doctors to spend more consultation time in correcting the wrong online [information]*” (Doctor 02, Female). The goal is to make sure users fully understand the requirements, and thus reduce confusion over information. To accomplish this, features such as podcasts, chatbots, or online lectures were proposed as the potential modes for delivering such information. HCPs also highlighted that the apps should provide other patients’ stories or feedback in order to debunk the myths concerning or against steroids.

The other requirement discussed during the workshop was the need for patients and caregivers to communicate with HCPs. In this context, participants proposed that technology could be used throughout the whole process of the healthcare journey, from preparation for the clinical consultation, facilitation of clinical consultation, disease status follow-up, to real-time management after medical consultation. Here, the main goal of the technology would be to help caregivers identify and manage flare-ups, to mitigate confusion, and, at the same time, facilitate HCPs into gaining a better understanding of patients’ needs and limitations.

Participants also opined that the technology should enable the user to provide support to others, in this case by sharing knowledge and experiences with their peers in Singapore. They suggested that apps should be designed to provide social support and facilitate connectedness with others. For example, when other caregivers encounter difficulties when managing flare-ups, their peers could support them and detail their own experiences. In addition, peers can also comfort caregivers emotionally by recognizing their efforts and mitigating their guilt. This might be accomplished using an online forum with messaging, chat or call functions.

Also, both caregivers and HCPs suggested that the app should be personalized. The personalization should embody two aspects: (1) features and content should be

tailored to each individual's needs; and, (2) features and content should suit the local context. In this way, the app could help them with prioritizing and making new choices, and with defining their own goals and the small steps necessary for reaching these goals. One doctor mentioned:

'As they keep clicking that app, for example, [when] researching the triggers, after a while, the app...[should] push all the information related to triggers to the users, and eventually, it becomes interactive. The app will "know" the user.'

(Doctor 01, Male)

Image analysis was also mentioned during the workshop. It was recommended that caregivers could take photographs and use the app to analyse each photograph in order measure the severity. They also advised that the app should give advice or suggestions corresponding to the extent and severity of the skin condition, so that clients can get "immediate help without seeing the doctor".

8.3.4 Wireframe prototype development

The wireframe prototype contained features designed for addressing the challenges and confusions mentioned in the previous workshops. The 'must-have' features include: (1) knowledge on medication use and their side effects, (2) knowledge on the symptoms and appropriate management, (3) knowledge on the external triggers leading to AD flares, (4) monitoring of skin conditions, (5) communication channels with HCPs, and (6) monitoring of external triggers that may lead to AD flares.

The 'nice to have' features recommended by participants (caregivers in workshop one) include: (1) debunking the myths about AD, (2) knowledge on the natural history and development of AD, (3) reminders for topical application and medication-taking, (4) peer support from other caregivers or patients, (5) monitoring of caregivers' and children's emotions, and (6) emotional support with interactive app features.

As shown in the master sketch of the prototype (Figure 8.2), the prototype allows users to record lesions of AD in different body parts, and provides instructions relating to treatment, symptoms, triggers, as well as people's emotions. The 'Journal' section enables caregivers to track the patient's disease condition, and could prove useful to their doctor during a visit to the clinic.

Another core feature of the prototype is the education element. Participants designed both the chatbot feature and forum feature, both of which are for educational purposes (Figure 8.2). The chatbot allows users to access relevant information quickly and easily, which is presented in a clear, understandable format. The forum feature builds a bridge between caregivers and their peers by letting them exchange local information and, to some extent, allowing peers to provide information and emotional support to users. Participants also designed a notification feature, through which the prototype can remind users to avoid the possible triggers around them and decrease AD relapse.

8.3.5 Workshop evaluation feedback

The workshop evaluation comments (Appendix 8.2) indicated that the co-design workshop was successful in creating and generating new ideas and content for smartphone app development. All of the participants agreed that the workshop was organized, that its aims were clear, and its activities had been carefully prepared. All the participants felt that the workshop methods used were appropriate for the audience, and said that they enjoyed the workshop. However, some issues were also identified in the evaluation feedback: 21% of participants highlighted the need to improve workshop time management, and felt that the time should be better utilized.

Figure 8.2 The master sketch of wireframe prototype

8.4 Discussion

8.4.1 Summary

A series of co-design workshops were organized in this Chapter. Caregivers, doctors, pharmacists and researchers jointly explored their needs, preferences, and perceptions on AD self-management and proposed self-management app prototype. Findings of this chapter showed that co-design interaction can encourage social

interaction between people, which would stimulate creativity and engage more introverted participants, and thus help developers/researchers to articulate the root of the clinical problems (323, 324).

8.4.2 Comparison with existing literature

Findings of this study are aligned with previous evidence: twenty-eight families whose children were suffering from AD were interviewed in a previous study: they expressed the same frustrations with both medical care and AD treatments. The conflict between caregivers and healthcare professionals has also been captured in a previous study, which matches the findings in this chapter (272). Participants in previous studies have also expressed similar concerns and uncertainties: Batchelor, et al. (2013) gathered information from 493 participants and found that treatment-related uncertainties centred mainly around topical steroids, food allergy and moisturizer (325). In addition, Teasdale, et al. (2017) conducted 27 online forum-based discussions with 98 caregivers and identified a need for more detailed and reliable information on topical corticosteroids usage (326). This is in line with the results in this chapter, which reports that caregivers in Phase One were keen on looking for alternative medicines so as to avoid using steroids (325-327). In addition, this chapter goes further in exploring personal experiences, emotional needs and feelings among both caregivers and healthcare professionals, and considering how their points of view could be linked to features of smartphone apps.

8.4.3 Research implications

Some issues were identified and should be addressed in future studies. Firstly, it is important to ensure that all the participants fully understand and can keep pace with workshop information and activities – or, to use the colloquialism, “read off the same page”. The participants may interpret questions or tasks differently, and there is a risk of digressing the topic or narrating the same topic repeatedly, which can lead to the

workshop being less productive in terms of producing the ideas or thoughts anticipated.

Secondly, at the start of 3rd workshop, a briefing presentation of current research and technology used for AD management was delivered, in an effort to encourage the participants to allow their own needs and challenges to guide app co-design. However, it should be mentioned that the briefing presentation might have limited their thinking and they may have been inclined to follow the information shared during the briefing session.

Thirdly, the voice of every participant should be heard during the workshops. It should be highlighted that the selection of participants in any applied study should ensure a good representation of the relevant population. Besides, since the final wireframe prototype is designed by both researchers and caregivers, it is difficult for us to differentiate caregiver's perspective and researcher's opinion in Phase Two. Future studies should design additional co-design exercises to engage with researchers and fielded the opinions of different roles more carefully.

Lastly, forms of AD management support can be delivered in a number of different models according to the local healthcare system context and policy (328). Information on users' needs and challenges collected in Phase One can be widely applied not only to the content design of apps, webpages and leaflets but also to the design of the operating model. The operating model need not be limited to patients/caregivers; it could be extended to doctors and even healthcare providers. Potentially, we can deliver different models such as the 'app-only model' or the 'HCPs webpage/leaflets + patients/caregivers app' model (doctors can use leaflets to educate their patients and employ a webpage portal to manage/follow-up their patients, while patients can use a smartphone app to receive updated, trustworthy disease knowledge and disease management guidance, and also to tele-consult with their doctors) (329).

This wireframe prototype is the first draft of the wireframe. In future developments, workflow pathways need to be designed subsequently in order to allow the app to be used in a full range of application scenarios. Feedback from internal team members and users will be sought so as to identify any logical breaks and technical inconsistencies. In the meantime, efforts to revise the wireframe prototype will be continued, whereby the wireframe will be repeatedly tested in an effort to realize a healthcare app with the features discussed in the workshops. Following further wireframe development, app skins will be designed via collaboration with app design professionals, prior to real app development (330, 331).

8.4.4 Strengths and Limitations

Both the co-design approach and the findings from this study can inform future research studies into co-designing smartphone apps for and with the stakeholders affected by chronic diseases. However, this has been an explorative study, and so any generalizations should be treated with caution.

First of all, it must be acknowledged that data were derived from interviews with a relatively small group of participants, and so their views are not necessarily generalizable to all caregivers and healthcare professionals. In particular, caregivers were only recruited from a tertiary public hospital, and so their children might be suffering from relatively more severe manifestations of AD.

The scope of the study is also limited as the target audience of the app consists entirely of caregivers whose children have AD. However, that limitation alone does not preclude us from being able to satisfy the aims of this study since the content and features caregivers mentioned are to some extent interchangeable. Some of the issues and features caregivers mentioned can also be favoured for both children and adults. The app developed according to this workshop findings could be considered as the first version of the app, which is mainly targeted at caregivers whose children have AD. Future studies should engage and incorporate different perspectives from children and adults in order to further increase representativeness.

Another caveat of this study is that only caregivers were asked to vote for desirable features. Therefore, we do not know how healthcare professionals might have ranked the features, and cannot compare rankings between healthcare professionals and the caregivers. We have, however, attempted to address this knowledge gap by interviewing healthcare professionals and asking them to describe desirable features. Information collected from both sides has been used to inform the final wireframe prototype. Besides, the thematic saturation of the workshops was probably less than satisfactory; other themes might have emerged had I conducted more workshops.

8.5 Conclusion

Three workshops were conducted to field stakeholders' needs and challenges in managing AD and co-design activities were employed to jointly create an AD self-management wireframe prototype. Participant recruitment-based and logistical issues were also identified which could be addressed in future studies. This chapter could be a novel contribution to the canon of literature on engagingly designing digital health tools.

Chapter 9

Discussion and Conclusions

This discussion chapter comprises eight sections. In Section 9.1, the key findings are presented from chapters 4 to 8 and considered in the light of wider relevant literature, by way of commencing the discussion on the research subject. Section 9.2 synthesises the findings and constructs a broad overview from this. Section 9.3 discusses the potential implications of the findings on public health practice. The significance and contribution of this project's findings to the knowledge are discussed in Section 9.4. In Section 9.5, the limitations of this PhD project, its methods and results, are considered. In view of these, Section 9.5 also proposes recommendations for further research, as well as for clinical practice optimization. Section 9.6 is a personal reflection of the achievements and lessons learned during the course of the PhD project. Finally, Section 9.7 summarizes the pertinent points in this chapter.

9.1 Summary of findings

In the preceding eight chapters, this dissertation has explored the possibility of using a smartphone app to help AD patients and their caregivers, specifically children and their caregivers in Singapore. A mixed-method approach was selected in order to address this issue from several angles to better inform and conceptualize the required functions of an AD self-management app. The key finds of earlier chapters are summarized below:

Healthcare professionals, patients and their caregivers need to fully understand the effects of AD on patients' quality of life (QoL). **Chapter 4** investigated the impact of AD on people's QoL in Singapore and related factors, and provided an insight into the current level of knowledge among AD paediatric patients and their caregivers in Singapore. This cross-sectional study included 559 children with AD and their caregivers. Itching/scratching, emotional distress and sleep disturbance were most reported by the participants, and these increased with higher disease severity. This

study has shown that disease severity, rather than sociodemographic factors (Sex, ethnicity, educational attainment of carers, number of children) affect the Health-Related Quality of Life (HRQoL) of children with AD. The severity of AD is significantly associated with patients' and caregivers' self-reported quality of life: more severe AD corresponds to a poorer quality of life. Another finding emerging from this study was that a caregiver's mental and physical health was directly affected by their children's HRQoL. Poor QoL in AD children could lead to poor mental and physical functioning among caregivers. Current AD diagnostics and treatment need to consider the factors influencing both children and their caregivers' quality of life. More attention should be directed to AD symptoms and their effects on daily life.

The following **Chapter 5** featured a cross-sectional study, the purpose of which was to further understand how childhood AD affects family life. The sample comprised 559 families, of which 94.1% reported that family life was being affected by their children's AD. Sleep deprivation, emotional distress, and tiredness were the most frequently reported reactions. The multivariable analysis results revealed that children's HRQoL and caregiver's quality of life (QoL) were both predictors for Dermatitis Family Impact (DFI). Other factors affecting family QoL included children's age, ethnicity, disease duration, disease severity, and family accommodation. Therefore, disease status and social factors, as well as the diminished QoL among patients and their caregivers, contribute to impaired family functioning.

Chapter 6 explored the concordance between caregiver-reported and physician-rated severity of AD in paediatric patients and investigated the potential explanatory factors behind the degree of concordance. Physician-reported severity of AD data was retrieved from medical records, while caregiver-reported disease severity and sociodemographic data were obtained via a survey conducted at the same time point. Findings revealed a 38.5% disparity between physician-rated and caregiver-perceived severity data. Data sets for diseases with a duration shorter than 6 months shared a higher concordance, compared to that between data sets for diseases with a duration of 6 months or more. It was found that 28.0% of the caregivers underestimated the severity of their child's condition, while 10.8% overestimated the

severity. Factors associated with the underestimation of disease severity included the child's age, the disease duration, and out-of-pocket expenses. Therefore, there is a tendency for caregivers to underestimate severity. This information may have clinical implications for treatment outcomes if caregivers neglect to adhere to physicians' medical advice.

Having identified and made the case for a step change in care of children with AD the next phase of my PhD research focused on exploring the role ubiquitous mobile phones and apps could play in helping to improve care. To begin with, in order to provide a comprehensive overview of AD smartphone apps in the global app market, **Chapter 7** systematically evaluated all available AD self-management apps for patients and their caregivers in the three most widely spoken languages (English, Chinese and Spanish). The assessment criteria were based on app conformance with international AD guidelines. The following domains were assessed: consistency and comprehensiveness of AD specific educational information; quality and comprehensiveness of AD specific tracking functions; and, compliance with health information best practice principles. After assessing available AD apps in English, Chinese and Spanish, a number of issues were raised concerning the reliability and consistency of apps. The majority did not conform to guidelines concerning health information or provided sufficient evidence of their benefits as regards AD self-management. Information accompanying most apps failed to cite trustworthy educational information sources, and even apps which were apparently recommended or contained instructions provided by qualified doctors contained content which was inconsistent with guidelines. This chapter shines a torch on the smartphone app landscape by systematically assessing the functionalities and information of existing AD smartphone apps that could support AD management, and its findings informed the co-design workshops, which were reported in Chapter 8.

The aim behind **Chapter 8** was to try and find a solution by co-designing a smartphone app during a series of face-to-face workshops with caregivers, healthcare professionals (HCPs) and researchers who in turn were asked to describe their preferences and perceptions when taking care of children with AD. Three themes that reflected caregivers' needs for AD self-management support were identified during

the sessions: ‘empowerment by education’, ‘confusion over treatment’, and ‘emotional impact’. Various functionality requirements were raised and discussed by the participants. The wireframe prototype was designed during the final facilitation workshop. The co-design approach was shown to better engage participants as they were more collaborative, efficient and creative in the workshops. The framework used in the co-design workshops was successful in that it encouraged the generating of new ideas and content for future smartphone app development.

9.2 Overall Discussion

9.2.1 Improving the QoL of children with AD

Chapters 4 and 5 showed that the children’s QoL affected their caregivers’ mental health, and family life and functioning. Therefore, improving their QoL is not only crucial to the patients themselves, but also to the people involved in their lives and struggles with the disease. Several strategies should be taken into consideration:

First, focus on early detection before symptoms appear or worsen. For example, healthcare providers can use social media to educate the general public with basic knowledge of the different type of skin condition. This service can help patients better prepared for the disease and also reduce the pressure on healthcare system. Secondly, there is a need for a continuous AD education program after diagnosis that provides structured courses for patients, especially for teenagers in school who are engaged in self-management. The course could also provide mental health support for patients, teaching them how to address stigma and emotional challenges, issues which are not being currently addressed in clinical consultations. The shared knowledge and skills help children better cope with the challenges ahead of them. A digital solution that includes an app could play an important role in this.

9.2.2 Support for Caregivers: Who is Taking Care of the Caregiver?

Caregivers also experience physical and psychological burdens and may become patients as a result of caring. Both quantitative and qualitative results reported in chapters 4 and 8 have shown that poor QoL among children with AD has a negative effect on the mental and physical well-being of their caregivers, and that its impact is relatively large compared to that in relation to other paediatric chronic conditions (225, 226). There is substantial evidence indicating that the caregiver of a child with AD experiences feelings of desperation and depression (332, 333).

Little support is provided to caregivers for coping with their children's disease technically and emotionally. In clinical practice, it is difficult for healthcare professionals to provide guidance adequately during a consultation. Healthcare professionals have insufficient time for disease education during the tightly scheduled consultations, and there is limited training for them in the provision of disease education. According to a study by Kessels (2003), more than half of the patients and their caregivers failed to recall the health information provided only one week after visiting the clinic (334). On the other hand, health educational materials provided in the hospital setting are sometimes not appropriate and not tailored to the population they serve. The feeling of "being abandoned" is even stronger when caregivers return home, as their children have been "discharged to the family". The paediatric AD patient population, although sizeable, is also scattered, and many patients and caregivers receive little or no peer support. A study by Naylor (2002) reinforced the importance of continuous support from hospital to home, and highlighted that breakdowns in care support may lead to negative patient-related outcomes (335). The findings from the co-design study in this PhD project show how participating parents expressed their need for continuous support from healthcare professionals and the community.

This presents an opportunity for the development of new, innovative support which could deploy digital technologies. According to previous research on "Caregivers and Digital Health" survey, despite the growing array of digital health tools that might help support caregivers, a majority of them (58%) are simply not aware of digital

health tools available to help while 56% of caregivers have difficulty in finding a digital health tool to addresses their specific needs (336). Therefore, it is necessary to understand the technologies which caregivers really need. Two needs could be addressed using digital health solutions. The first objective is to directly reduce caregivers' emotional distress so as to improve their mental health and overall quality of life. Counselling appears to be an effective way of mitigating distress and has been demonstrated to be an effective means of improving the mental health and wellbeing of caregivers in relation to other chronic diseases, including caregivers of children with developmental disabilities and juvenile rheumatoid arthritis (337, 338). With a broad and easy-to-access user base, digital health apps could provide a tele-counselling service and bring caregivers some psychological relief (339, 340). They can also assist the caregiver by enabling a smooth transition following a consultation, and they empower caregivers in managing their children's disease by making them feel competent and capable. According to a previous survey (336), caregivers reported that apps can help reduce stress by easing communication, decreasing complexity, and improving organization needs. For example, by employing a smartphone app, healthcare providers can set up a caregiver caring plan for providing continuous support after each consultation (i.e. by scheduling a follow-up teleconsultation regularly (at a time convenient to the caregivers) to provide real-time information and help them manage their children's current skin condition).

9.2.3 Digital Health: Is It Good Enough?

i. Existing health information might not be trustworthy

Previous chapters raised several concerns regarding the quality, consistency and comprehensiveness of digital health tools and information source is an important determinant of the credibility of health information (341, 342). Credentials of the writers, operators and funders need to be investigated when evaluating the trustworthiness of digital health information (343). Another important of getting health advice is online forums. These platforms offer opportunities for people to ask questions or to raise concerns with advice being received within a short period (344).

However, there is still the risk of spreading inaccurate information. For example, an opinion leader within a forum may provide inaccurate or even biased (advertising-orientated) information (342, 345).

ii. New approaches to quality assurance of digital health solutions are required

As mentioned back in Chapter 7, most of the apps are designed for assisting non-medical trained users in understanding health issues or identifying their needs for further professional medical attention. However, these apps are not subject to any sort of verification or regulation. The FDA does not regulate most of these apps, and the FDA's website suggests that it does not intend to expand regulation to non-medical device apps. Therefore, most of the digital health apps disclaim that they are only intended for educational purposes or even entertainment purposes in order to avoid FDA regulation (346). As such, the information given by poor quality apps may mislead users, influence their judgments of disease severity, and delay treatment, resulting in negative health outcomes (347, 348). In addition, current digital health platforms lack strong empirical evidence and a unified fiduciary standard, resulting in the inability to form a more consistent standard within the industry.

iii. The mismatch between 'supply' and 'demand'

The development, distribution and quality testing of digital health technologies require collaboration from both the supply-side and demand-side. The supply-side is analogous to the technology development phase and involves digital health companies or research institutions, while the demand-side concerns the user's needs. Translation of new technology is considered a 'success' when the supply-side and demand-side exactly match each other, i.e. applying technology to the real needs of the users and then generating economic and social value in the market. But it is a common observation that the connection between the two sides is always mismatched, leading to a break in the innovation chain. This is of great concern to digital health practitioners: the supply-side does not adequately understand targeted users' perspective; hence, the technology designed does not fully meet user needs leading to the low usage rate of the technology. On the other side, targeted users have many

unanswered questions during clinical encounters but often do not receive adequate technical support. Therefore, to solve this problem, relevant institutions should promote the use of multi-party collaborations to jointly design the product and transform from ‘technology-driven’ to ‘demand-driven’.

iv. The right role for industry involvement in digital health

Homogenization and over-commercialization are risks of which researchers should be mindful when cooperating with industry bodies. Similar to the previous studies in relation to challenges in AD care mentioned in Chapter 2, a large number of similar AD experiments may have led to overtreatment and unnecessary waste (162, 163, 169). This is more obvious in a field where there is considerable industry investment.

Digital health is a field into which ‘hot money’ is being injected. Over-commercialization occurs where digital health product development is being staggered by several merchandising tie-ins. For example, digital health apps developed/funded by pharmaceutical companies are likely to provide health advice which prioritizes the company’s interests over clinical efficacy. Such information may overly serve the interests of pharmaceutical companies and lead to over/mistreatment, which can produce different adverse symptoms among patients.

Another problem is homogeneity among apps. According to one recent report, most apps are similar in terms of content and function, in that they concentrate mainly on appointment registration, consultation, patient education, and medication assistance. Such homogeneity is common, rendering it difficult for consumers to discern the authority and credibility of each digital health app; as a result, people feel discouraged, and are less likely to download and use them (349). Therefore, the right role for industry involvement in digital health needs to be explored more closely in future.

9.3 Implications for public health practice

Since AD is not a life-threatening disease, policymakers may not give it the same priority as other high-profile non-communicable diseases (such as diabetes and

dementia). However, Chapters 4 and 5 have demonstrated that AD affects the QoL of patients, caregivers and patients' family life and functioning as much as some other paediatric chronic diseases which are perceived as more severe, such as psychiatric disease and congenital heart disease (224-226). Therefore, I hope that my study will contribute to the policy considerations to address the challenges associated with AD. With the assistance of policymakers and funding bodies, care of AD could be done in a more effective, cost-efficient way.

First of all, the importance of AD should be recognized by the general public. Health literacy of AD needs to be promoted and to make the public aware of the impact of AD on individuals and families. Secondly, continuing education needs to be provided to primary care doctors. Healthcare providers can train those doctors with better communication skill and teach them how to cope better with AD patients (350, 351). Thirdly, holistic AD care programs also need to be developed as similar programs have been demonstrated to reduce patient return visits and to effectively relieve the burden on healthcare system (215, 262, 351).

The findings in Chapter 7 and Chapter 8 highlighted the following issues concerning app development: (1) reliability and validity of the health content/information disseminated by the apps; (2) evidence-based features of the app; and (3), the involvement of stakeholders in the app development process. The findings together with the app assessment criteria could be put forth as a checklist by app developers to ensure the development of high-quality AD self-management apps. These strategies may also benefit healthcare professionals by helping them identify good apps for their patients. A more generic 'layman' checklist should also be developed for patients and caregivers in order to help them find suitable apps themselves.

"Smartphone app clearinghouses" is a concept, which was raised in a previous study conducted by Boudreaux, *et al.* (2014) (352). According to Spaulding (2017): "Clearinghouses take the opposite position of each side of a trade. When two parties agree on the terms of a transaction, a clearinghouse sits in the middle, acting as both the buyer and the seller" (353). The term is supposed to be used as a financial instrument; however, in this case, 'clearinghouse' is referred to as a middleman who

ensures that all apps have been validated against a series of evidence-based criteria and, therefore, pose fewer risks for target users. If a clearinghouse is established for digital health smartphone apps, it may be easier for patients to find the app they need. This quality assurance will also greatly reduce the burden on healthcare professionals who want to prescribe apps, but who are concerned about the effectiveness and lack of adequate supervision. A clearinghouse could also be more conducive to government regulation.

In addition to a smartphone app checklist and clearinghouse, in order to facilitate digital health development, government and industry regulators also need to take action in response to the overtreatment and homogeneity phenomena associated with the current digital health industry. Industry regulators might need to formulate related public health policies in order to regulate commercial involvement in the development of digital health products. For example, regulators could instruct app companies to declare commercial involvement prior to releasing the products on the market. In addition, industry regulators could potentially raise more funds from non-conflict of interest institutions, including government departments, universities, or non-profit organizations, so as to reduce dependence on commercial organizations. Moreover, researchers and clinicians also need to research the landscape of the industry in an effort to identify the areas that need more input from the government; this will hopefully guide future directions into digital health support for AD.

9.4 Contributions of this research project

This thesis contributes to the fields of dermatology and digital health in the following ways:

To the best of my knowledge, the work described in Chapters 4 and 5 constitute one of the largest AD and QoL-based studies performed in children with AD, their caregivers and family units as a whole. The large sample size is a good representation of the societal burden of childhood AD; and, since the study population comprises multiple ethnic groups (Chinese, Indian, and Malay populations), the findings can be

generalized to other multi-ethnic countries. Besides, the studies were adequately powered to accurately capture the QoL status for subgroup analysis and extension to other high prevalence countries. Furthermore, the model presented in chapters 4 and 5 highlights how children, caregivers, and family QoL could affect one other. This model also helps to build a more holistic understanding of childhood AD burden.

The cross-sectional study conducted in Chapter 6 reflects what happens in real life. Physicians only see patients once every few months whereas caregivers see their children every day. Therefore, physician perceptions of severity are based on measures from the only one-time point, whereas the caregiver perspective encompasses the experience of caring for an AD patient over a long period.

Systematic review methodology in Chapter 7 makes an original and significant contribution to the field. By leveraging more efficient inclusion and exclusion criteria and more comprehensive app databases, the study reduces possible selection bias, and it encompasses a wider range of available apps compared to other app assessment reviews which have often been based solely on researchers' subjective judgements and consensuses (240, 348, 354). Chapter 7 also maps out the landscape of existing smartphone apps in the three most widely spoken languages worldwide (covering more than 1.8 billion of the world's population). The findings should benefit both AD patients and health professionals who are searching for suitable AD self-management apps, as well as app developers who are seeking applicable assessment criteria which can guide the development of high-quality AD self-management apps.

During the co-design workshops in Chapter 8, the stakeholders proposed desirable features and content for the AD self-management app. Participants' perceptions and preference identified in the workshops form an original contribution to literature in the field of smartphone apps design. The co-design framework could also be adapted for future studies addressing other health issues. The findings from this study could also help stakeholders develop and utilize AD self-management apps, which can potentially reduce the burden of childhood AD and empower caregivers to carry out self-management more effectively.

9.5 Limitations of this study, and recommendations for future research

9.5.1 Limitations

There are several limitations to the scope, design and results generated in this project:

- i. There was no non-AD control group in Chapter 4-6, and so it is not possible to compare the circumstances of children with AD, plus their caregivers and family relatives, with those of children, caregivers and family members who are unaffected by AD. Attempts were made to compare the caregiver's QoL when attending to children with AD, to that of caregivers attending to patients with other chronic diseases.
- ii. Participants (Chapter 4-6) were recruited from specialist clinics, where the patients may suffer from more severe AD than those seen in primary care. In addition, parents who filled out the questionnaire on behalf of the patient (e.g. infants or children) will have provided their own perspectives, which might not have accurately reflected the infant/child's point of view. With some participating families, although the parents who filled in the questionnaire identified themselves as the children's "caregivers", it is the grandparents or domestic helpers who are actively caring for the children.
- iii. Chapter 7 was not able to cover the entire spectrum of apps related to AD management in the market; given the sheer number of developers and the ease of uploading new apps online, it is likely that some apps may have been missed. Also, there are overlapping functionalities with other apps. For example, general health-tracking apps may be used to monitor AD, and specific information may be lacking in general dermatology apps. These limitations should not affect the purpose of this review since this PhD project has specifically focused on AD apps to support self-management.
- iv. Level of content saturation retrieved from phase one workshops in Chapter 8 is likely acceptable as it was deemed sufficient for designing the wireframe prototype in the phase two co-design workshop. However, new themes would

have emerged had more workshops been conducted. Also, the workshops were designed to ensure that the voices of all stakeholders were heard; however, it was observed that researchers and developers tended to defer to the opinions of parents and patients, and rarely voiced opinions drawn from their own expertise, and thus their perceptions and preferences have not been emphasized.

9.5.2 Recommendations for future research

There are a number of issues which deserve greater attention in future research. Firstly, longitudinal cohort on childhood AD in Singapore needs further study in the future. The cross-sectional design just gives a snapshot and do not show the long term QoL burden and there is a large likelihood that the patients approached for participation had a flare-up. Since the HRQoL for Childhood AD at flare-ups are probably quite different compared to a non-flare up period, the longitudinal study can capture the social-economic burden during both flare-up and non-flare up period. Moreover, future research could potentially extend its research scope to adult AD patients which could provide a broader view of disease burden and contribute to the establishment, implementation and monitoring of evidence-based policies for both children and adults' patients in Singapore.

Secondly, future research should work on the alignment of management, assessment and monitoring of AD. At the crux of this challenge is the lack of a consistent standard for evaluating the severity of the disease (33). Researchers should work with policymakers, medical professionals, and patient support groups in order to establish consistent, effective AD severity measurement tools. Consistency in data capture would also enable researchers to more easily compare studies, and to communicate using a 'common language'(33). Such tools could also provide valuable data to pave the way for future advanced research studies.

Thirdly, future research studies should assess the appropriateness and effectiveness of apps for different target groups. Different user groups should have different requirements regarding app functions and content. Besides, further evaluation of the

availability and appropriateness of in-app advertising is needed, and future research studies should also focus on best practices for ensuring long-term usage of such apps. It is ideal to have multiple functions built into an app, but ease-of-use will determine whether the user is likely to use it for a long time. Therefore, the behaviours of users of different target groups must be studied to ensure that they can benefit from using these apps in the long run.

Fourthly, feasibility trials should be conducted in the future. There is still no robust evidence of the benefits of smartphone app usage among AD patients, including paediatric patients. Therefore, there is a need for evaluating the usability of smartphone-based interventions, which precedes randomized control trials, which in turn should facilitate comparisons with usual care. A feasibility trial could also help to identify whether the prototype app developed could potentially provide automated, tailored support for treatment among paediatric patients with AD.

Fifthly, future research should give attention to the best ways of integrating digital health information system (355). Researchers can analyse and evaluate various risks that may arise in the process of information system integration, and further explore the ways of managing the system effectively, thus ultimately ensuring the success of the integration (355).

Future research can also focus on establishing user privacy protection models (356). Technically, the privacy protection should be built according to access users' security level. By limiting users' access scope and read permissions, privacy protection models can prevent unauthorized use of resources and potential information leakage. Besides, further research should also help healthcare providers develop specific laws or legislative framework on collecting privacy information and thus, to adapt the needs of the fast development of digital health (279).

Lastly, further research could also be aimed at the optimization of clinical pathways in AD care. By constructing an organizational management system, developing a clinical pathway strategy, and evaluating and analysing clinical pathway effects, future research can better understand medical behaviour, shorten the average days of

hospitalization, reduce medical expenses, and can ensure healthcare quality, and improve patient satisfaction in the long run.

9.6 Impacts of the research on the researcher

I worked as a doctor for three years before commencing this PhD project, which in turn has been a considerably different experience to the ‘study-exam preparation-exam’ cycle which I encountered in medical school. I have enhanced my quantitative analysis skills, especially when I learned how to do statistical modelling from scratch, and I have gained in-depth insights in my efforts to fulfil the study aims. In addition, I recollect with fondness the generosity of the participants at the co-design workshops, who gave up their time, and who were willing to share their experiences, insights and ideas. Their contributions towards developing the AD self-management app prototype have been essential. Personally, I believe that the qualitative research not only complemented my quantitative research skills but also helped me develop a more subjective perspective. By using a mixed-method approach, I learned to perceive the world through different lenses.

During the course of this PhD trajectory, I have met many AD patients and their caregivers in the clinic, and have witnessed their suffering with my own eyes. This experience has made me question my priorities in life: when I commenced the project, my chief aim was to execute and complete this PhD project successfully in order to earn my doctor title; whereas now, I believe that I should use my medical knowledge and research skills to help people in need. I hope that everything I have learned during the course of this project might help AD patients and their caregivers, even slightly, to make their lives easier and to reduce the burden of living with AD. To be honest, before I started my PhD journey, as a young doctor I sometimes found routine clinical work tiring. This is not easy for me to acknowledge, but for a long time, I showed a diminished empathy towards my patients. These past four years of PhD study have given me an opportunity to reconnect with patients, reflect on the meaning and need for empathy, and to assess what I should be doing in the future.

I will close this section with a famous Chinese saying:

愿你出走半生 归来仍是少年

Years can wrinkle our skin but never wrinkle our soul.

9.7 Concluding remarks

Current models of health care delivery for AD treatment do not optimally support self-/caregiver-management of the condition, nor take into account the variability of the disease in-between consultations. The strong shift from the ‘traditional health model’ to ‘patient-centred digital health model’ reflects an acknowledgement of the need for continued monitoring of disease symptoms, health treatment and the psychological and physical experiences of both patients and caregivers outside the health clinic. Although digital health is increasingly being applied in healthcare, robust scientific exploration is lagging behind the curve.

In this thesis, the quantitative research findings on factors influencing the QoL of childhood AD patients and their caregivers provide a window into their needs and how an AD self-management app should address those needs. By identifying the social burden of childhood AD, the quantitative studies focus on the most troublesome factors affecting the QoL of patients and caregivers, and provide new ideas which inform self-management smartphone app development. By evaluating the AD self-management app landscape, the systematic assessment further narrowed the scope and honed in on the concerns surrounding the safety and practicality of these apps. The causes of these concerns and the gaps in the existing system were identified.

The qualitative co-design workshops complemented the quantitative studies by investigating stakeholders’ needs, perspectives and perceptions in relation to caring for children with AD. This dissertation also focused on the areas where current AD-management may have been overlooked or underestimated; and, it has highlighted the importance of patient education, social support for AD patients and caregivers, as well as proper regulation of digital health tools.

Several steps should be taken before a new digital health app is released. First, the conceptualization of the app should be based on an in-depth investigation of the patient’s burden. Second, the features of the app should be tailored to stakeholders’ needs and the local context. Third, the contents of the app should be theoretically supported, and users should be provided with instructions that are user-friendly and

conveyed in layman's terms. Only when these steps are completed will the app provide safe and effective support to children with AD and their caregivers.

This dissertation is a pioneering effort in the evaluation of digital health interventions to improve AD self-management. Issues emphasized in this dissertation have potentially far-reaching implications. Future research should work on integrating digital health in current clinical practices for AD treatment in order to provide holistic, patient-centred AD care.

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Section A. Patient's Information

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Section B. Socio-demographic Information**Section B: Socio-demographic Information**

Important, section B consists of questions in relation to the parent/carer, not the child with atopic dermatitis.

1. Relationship of the person/s filling in this questionnaire (e.g. mother, father).

Relation:

2. What is your highest achieved qualification?

- 1 ☐ No qualification 2 ☐ Primary school 3 ☐ Lower secondary 4 ☐ Secondary school
 5 ☐ Post-secondary Pre-university 6 ☐ Polytechnic 7 ☐ Professional qualification 8 ☐ University

3. What is your main daytime occupation?

- 1 ☐ Employed 2 ☐ Unemployed 3 ☐ Retired

If employed: What is your occupation?

4. What is your current main accommodation type?

- 1 ☐ HDB dwellings, 1-3 room 2 ☐ HDB dwellings, 4-5 rooms 3 ☐ Condominium
 4 ☐ Landed property 5 ☐ Other (please, describe)

Section C. Background Information

Section C: Background Information

1. What was the mother's age when the child was born (years)?

1 ☐ 14-19 2 ☐ 20-24 3 ☐ 25-29 4 ☐ 30-34 5 ☐ 35-39 6 ☐ >40

2. Does the child's mother ever have any of the following diseases? (tick as many boxes as apply)

1 ☐ Asthma 2 ☐ Hay fever 3 ☐ Eczema

3. Was the child ever breast-fed (or bottled fed with breast milk)?

1 ☐ Yes 2 ☐ No

If yes, for how long?

1 ☐ Less than 1 week 2 ☐ 1-6 weeks 3 ☐ 6 weeks to 6 months 4 ☐ More than 6 months

4. Was the child introduced to solid food before age of 4 months?

1 ☐ Yes 2 ☐ No

5. Was the child born by natural delivery or a caesarean section?

1 ☐ Natural delivery 2 ☐ Caesarean section

6. Has the child ever accepted any form of antibiotic treatment before 1 years of age?

1 ☐ Yes 2 ☐ No

7. Does the child have any older sibling(s)?

1 ☐ Yes 2 ☐ No If yes, how many?

8. Does the child have any younger or equally old sibling(s)?

1 ☐ Yes 2 ☐ No If yes, how many?

9. Has the ever child attended a formal child-care (e.g. pre-school, nursery school, professional child-carer)?

1 ☐ Yes 2 ☐ No

10. Does the child's household have furry pets at present or/and during the first year of the child's life?

1 ☐ Yes 2 ☐ No

11. Does anybody, at present, smoke inside the child's home?

1 ☐ Yes 2 ☐ No

If yes, how many cigarettes (or similars) in total are smoked per day in the child's home? (e.g. mother smokes 4 + father smokes 5 + other persons smoke 3 = 12 cigarettes)

1 ☐ Less than 10 cigarettes 2 ☐ 10-20 cigarettes 3 ☐ More than 20 cigarettes

Section D. Client Service Receipt Inventory

Section D: Client Service Receipt Inventory

1. Please record any hospitalisation into public general hospital or private hospital (SGH, TTSH, NUH, Mount Alvernia, Mount Elizabeth, Raffles Hospital, KKH etc.) in the last 12 months.

Inpatient admissions	Reason for stay	Speciality (e.g. Paediatrics)	No. of nights in hospital in the last 12 months
1.			
2.			
3.			

2. Please record any visits to out-patient hospital services over the last 6 months due to atopic dermatitis and for other reasons respectively.

Outpatient hospital services	Number of attendances due to atopic dermatitis	Number of attendances for other reasons
24hrs emergency department visits		
National speciality centre attendances eg., National Skin Centre		
Clinical specialities eg., internal medicine		
Allied health departments eg, dietetics		
Other (please, describe);		
Other (please, describe);		

3. Please record any use of primary care services over the last 6 months due to atopic dermatitis and for other reasons respectively.

Primary care	Number of attendances due to atopic dermatitis	Number of attendances for other reasons
General practitioner/family doctor/ polyclinic		
Nurse (e.g. dressing)		
Medical follow up after discharge from hospital		
Patient care education		
Diagnostic (e.g. laboratory test, x-ray, allergy test, skin prick test, patch test)		
Other (please, describe);		
Other (please, describe);		

4. In the last month, what medication has been taken because of the atopic dermatitis (by the person with the disease)? Include all kind of medicines, e.g. western prescription medications, vitamins, Chinese medicine, homeopathic, herbal medicines, topical medicines.

Name of drug	Dosage (if known)	Dosage frequency
1.		
2.		
3.		
4.		

5. Children with atopic dermatitis may need extra care and support provided by their parents, other relatives or friends. For how many hours are parents, other relatives and friends providing this kind of help in an average week? Please give estimates of the numbers of hours per week that is due to the atopic dermatitis and that reduces paid working hours or time for leisure on the following tasks.

Activity	Average <u>numbers of hours of help per week</u> due to the atopic dermatitis
Personal care, e.g. Daily application of cream	
Accompanying to healthcare visits	
Companionship and emotional support	
Specially prepared homemade food	
Other (please, describe);	
Other (please, describe);	

6. If your child would not have had atopic dermatitis, how much time do you think that you and other informal carers would have spent in other activities? Please give estimates of the numbers of hours per weekday and weekend day for every carer, their relation to the child and type of activity.

Carer 1. Relation: (e.g. mother)

Average numbers of hours that are estimated to have been spent in other activities if the child would not have had AD, by activity		
Activity	Average numbers of hours per weekday	Average numbers of hours per weekend day
Paid work		
Un-paid work (e.g. housework)		
Other activities such as leisure		

Carer 2. Relation: (e.g. mother)

Average numbers of hours that are estimated to have been spent in other activities if the child would not have had AD, by activity		
Activity	Average numbers of hours per weekday	Average numbers of hours per weekend day
Paid work		
Un-paid work (e.g. housework)		
Other activities such as leisure		

Carer 3. Relation: (e.g. mother)

Average numbers of hours that are estimated to have been spent in other activities if the child would not have had AD, by activity		
Activity	Average numbers of hours per weekday	Average numbers of hours per weekend day
Paid work		
Un-paid work (e.g. housework)		
Other activities such as leisure		

7. Over the past 6 months, have parents, relatives and friends lost income because they provide care and support for the person with atopic dermatitis, e.g. reduced number of paid working hours?

1 ☐ Yes 2 ☐ No

8. What is your usual mode of transportation to doctor because of your child's condition of atopic dermatitis? Indicate wherever applicable.

1 ☐ Public transport 2 ☐ Taxis 3 ☐ Privately owned vehicles

4 ☐ Other:

9. Have parents, other relatives or friends had extra expenses over the last 6 months as a consequence of the care and support for the person with atopic dermatitis? If yes, please fill in the table below with the estimated extra expenses in an average week.

	Total out-of-pocket expenses in an average week the last 6 months, \$SGD per week
Moisturizing creams	
Hygiene products e.g., body wash	
Extra laundry cost	
Clothing or textiles	
Humidifier	
Water filter	
Special diet	
Other (please, describe);	
Other (please, describe);	

(You can provide more information about expenditure not stated above in the box below)

10. If there is anything that we have not covered related to service utilisation and expenses but that might be of importance, please use the space on the back of this page.

[illegible]

Section E. Dermatitis Family Impact Questionnaire

Section E: Dermatitis Family Impact Questionnaire

The aim of this questionnaire is to measure how much your child's skin problem has affected you and your family **OVER THE LAST WEEK**. Please tick one box for each question.

1.	Over the <u>last week</u> , how much effect has your child having eczema had on housework, e.g. washing, cleaning.	Very much
A lot
A little
Not at all	☐
☐
☐
☐
2.	Over the <u>last week</u> , how much effect has your child having eczema had on food preparation and feeding.	Very much
A lot
A little
Not at all	☐
☐
☐
☐
3.	Over the <u>last week</u> , how much effect has your child having eczema had on the sleep of others in family.	Very much
A lot
A little
Not at all	☐
☐
☐
☐
4.	Over the <u>last week</u> , how much effect has your child having eczema had on family leisure activities, eg swimming.	Very much
A lot
A little
Not at all	☐
☐
☐
☐
5.	Over the <u>last week</u> , how much effect has your child having eczema had on time spent on shopping for the family.	Very much
A lot
A little
Not at all	☐
☐
☐
☐
6.	Over the <u>last week</u> , how much effect has your child having eczema had on your expenditure, eg costs related to treatment, clothes, etc.	Very much
A lot
A little
Not at all	☐
☐
☐
☐
7.	Over the <u>last week</u> , how much effect has your child having eczema had on causing tiredness or exhaustion in your child's parents/carers.	Very much
A lot
A little
Not at all	☐
☐
☐
☐
8.	Over the <u>last week</u> , how much effect has your child having eczema had on causing emotional distress such as depression, frustration or guilt in your child's parents/carers.	Very much
A lot
A little
Not at all	☐
☐
☐
☐
9.	Over the <u>last week</u> , how much effect has your child having eczema had on relationships between the main carer and partner or between the main carer and other children in the family.	Very much
A lot
A little
Not at all	☐
☐
☐
☐
10.	Over the <u>last week</u> , how much effect has helping with your child's treatment had on the main carer's life.	Very much
A lot
A little
Not at all	☐
☐
☐
☐

Section F. RAND 36

Section F: RAND-36

This survey includes a wide variety of questions about your health and your life. We are interested in how you feel about each of these issues.

Important, section F consists of questions in relation to the parent/carer, not the child with atopic dermatitis.

	Excellent	Very good	Good	Fair	Poor
	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

1. In general, would you say your health is:
Somewhat worse now than one year ago

	Much better now than one year ago	Somewhat better now than one year ago	About the same	Somewhat worse now than one year ago	Much worse now than one year ago
	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

2. Compared to one year ago, how
would you rate your health in general
now?

The following items are about activities you might do during a typical day. Does your health now limit you
in these activities? If so, how much?

	Yes, Limited a lot	Yes, Limited a little	No, Not limited at all
--	--------------------	-----------------------	------------------------

3. Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports	1 ☐	2 ☐	3 ☐
4. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	1 ☐	2 ☐	3 ☐
5. Lifting or carrying groceries	1 ☐	2 ☐	3 ☐
6. Climbing several flights of stairs	1 ☐	2 ☐	3 ☐
7. Climbing one flight of stairs	1 ☐	2 ☐	3 ☐
8. Bending, kneeling, or stooping	1 ☐	2 ☐	3 ☐
9. Walking more than a mile	1 ☐	2 ☐	3 ☐
10. Walking several blocks	1 ☐	2 ☐	3 ☐
11. Walking one block	1 ☐	2 ☐	3 ☐
12. Bathing or dressing yourself	1 ☐	2 ☐	3 ☐

During the past 4 weeks, have you had any of the following problems with your work or other regular daily
activities as a result of your physical health?

	Yes	No
--	-----	----

13. Cut down the amount of time you spent on work or other activities	1 ☐	2 ☐
14. Accomplished less than you would like	1 ☐	2 ☐
15. Were limited in the kind of work or other activities	1 ☐	2 ☐
16. Had difficulty performing the work or other activities (for example, it took extra effort)	1 ☐	2 ☐

During the past 4 weeks, have you had any of the following problems with your work or other regular daily
activities as a result of any emotional problems (such as feeling depressed or anxious)?

	Yes	No
--	-----	----

17. Cut down the amount of time you spent on work or other activities	1 ☐	2 ☐
18. Accomplished less than you would like	1 ☐	2 ☐
19. Didn't do work or other activities as carefully as usual	1 ☐	2 ☐

20. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours, or groups?
Not at all	Slight	Moderately	Quite a bit	Extremely
1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
21. How much bodily pain have you had during the past 4 weeks?
None	Very mild	Mild	Moderate	Severe	Very severe
1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐
22. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?
Not at all	Slight	Moderately	Quite a bit	Extremely
1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
23. Did you feel full of pep?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐
24. Have you been a very nervous person?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐
25. Have you felt so down in the dumps that nothing could cheer you up?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐
26. Have you felt calm and peaceful?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐
27. Did you have a lot of energy?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐
28. Have you felt downhearted and blue?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐
29. Did you feel worn out?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐
30. Have you been a happy person?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐
31. Did you feel tired?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐

These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling.

How much of the time during the past 4 weeks?

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
32. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐

How TRUE or FALSE is each of the following statements for you.

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
33. I seem to get sick a little easier than other people.	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
34. I am as healthy as anybody I know	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
35. I expect my health to get worse	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
36. My health is excellent	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

Section G. Children's Dermatology Life Quality Index

Important, this instrument is to be completed by the child with atopic dermatitis.

Children's Dermatology Life Quality Index

The aim of this questionnaire is to measure how much your skin problem has affected you **OVER THE LAST WEEK**. Please tick one box for each question.

1.	Over the last week, how itchy, "scratchy", sore or painful has your skin been?		Very much	☐
			Quite a lot	☐
			Only a little	☐
			Not at all	☐
2.	Over the last week, how embarrassed or self conscious, upset or sad have you been because of your skin?		Very much	☐
			Quite a lot	☐
			Only a little	☐
			Not at all	☐
3.	Over the last week, how much has your skin affected your friendships?		Very much	☐
			Quite a lot	☐
			Only a little	☐
			Not at all	☐
4.	Over the last week, how much have you changed or worn different or special clothes/shoes because of your skin?		Very much	☐
			Quite a lot	☐
			Only a little	☐
			Not at all	☐
5.	Over the last week, how much has your skin trouble affected going out, playing, or doing hobbies?		Very much	☐
			Quite a lot	☐
			Only a little	☐
			Not at all	☐
6.	Over the last week, how much have you avoided swimming or other sports because of your skin trouble?		Very much	☐
			Quite a lot	☐
			Only a little	☐
			Not at all	☐
7.	<u>Last week</u>
was it
school time?		If school time: Over the last week, how much did your skin problem affect your school work?	Prevented school ☐
	OR			Very much ☐
	was it
holiday time?		If holiday time: How much over the last week, has your skin problem interfered with your enjoyment of the holiday?	Quite a lot ☐
				Only a little ☐
				Not at all ☐
8.	Over the last week, how much trouble have you had because of your skin with other people calling you names, teasing, bullying, asking questions or avoiding you?		Very much	☐
			Quite a lot	☐
			Only a little	☐
			Not at all	☐
9.	Over the last week, how much has your sleep been affected by your skin problem?		Very much	☐
			Quite a lot	☐
			Only a little	☐
			Not at all	☐
10.	Over the last week, how much of problem has the treatment for your skin been?		Very much	☐
			Quite a lot	☐
			Only a little	☐
			Not at all	☐

Please check that you have answered EVERY question. Thank you.

© Children's Dermatology Life Quality Index. M.S. Lewis-Jones, A.Y. Finlay, May 1993.

Section H. Children's Dermatology Life Quality Index (Cartoon version)

Trouble with Skin

The aim of the questionnaire is to measure how much your skin problem has affected you **OVER THE LAST WEEK**. Please tick one box for each question.

OVER THE LAST WEEK

1

Very much
☐
Quite a lot
☐
A little
☐
Not at all
☐

How itchy, scratchy, sore or painful has your skin been?

2

Very much
☐
Quite a lot
☐
A little
☐
Not at all
☐

How upset or embarrassed, self conscious or sad have you been because of your skin?

3

Very much
☐
Quite a lot
☐
A little
☐
Not at all
☐

How much has your skin affected your friendships?

4

Very much
☐
Quite a lot
☐
A little
☐
Not at all
☐

How much have you changed or worn different or special clothes/shoes because of your skin?

5

Very much
☐
Quite a lot
☐
A little
☐
Not at all
☐

How much has your skin trouble affected going out, playing or doing hobbies?

6

Very much
☐
Quite a lot
☐
A little
☐
Not at all
☐

How much have you avoided swimming or other sports because of your skin trouble?

Section I. Infant's Dermatitis Quality of Life Index

Infant's Dermatitis Quality of Life Index		
<p>Important, this section is to be answered by parent/carer in relation to child with atopic dermatitis. The aim of this chart is to record how your child's dermatitis has been. Each question concerns THE LAST WEEK ONLY.</p>		
<p>Dermatitis Severity</p>		
Over the last week, how severe do you think your child's dermatitis has been?; i.e. how red, scaly, inflamed or widespread.	Extremely severe	☐
	Severe	☐
	Average	☐
	Fairly good	☐
	None	☐
<p>Life Quality Index</p>		
1. Over the last week, how much has your child been itching and scratching?	All the time	☐
	A lot	☐
	A little	☐
	None	☐
2. Over the last week, what has your child's mood been?	Always crying, extremely difficult	☐
	Very fretful	☐
	Slightly fretful	☐
	Happy	☐
3. Over the last week approximately how much time on average has it taken to get your child off to sleep each night?	More than 2 hrs	☐
	1 - 2 hrs	☐
	15mins - 1 hr	☐
	0-15mins	☐
4. Over the last week, what was the total time that your child's sleep was disturbed on average each night?	5 hrs or more	☐
	3 - 4 hrs	☐
	1 - 2 hrs	☐
	Less than 1 hour	☐
5. Over the last week, has your child's eczema interfered with playing or swimming?	Very much	☐
	A lot	☐
	A little	☐
	Not at all	☐
6. Over the last week, has your child's eczema interfered with your child taking part in or enjoying other family activities?	Very much	☐
	A lot	☐
	A little	☐
	Not at all	☐
7. Over the last week, have there been problems with your child at mealtimes because of the eczema?	Very much	☐
	A lot	☐
	A little	☐
	None	☐
8. Over the last week, have there been problems with your child caused by the treatment?	Very much	☐
	A lot	☐
	A little	☐
	None	☐
9. Over the last week, has your child's eczema meant that dressing and undressing the child has been uncomfortable?	Very much	☐
	A lot	☐
	A little	☐
	None	☐
10. Over the last week how much has your child having eczema been a problem at bathtime?	Very much	☐
	A lot	☐
	A little	☐
	None	☐
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Appendix 7.1 App assessment criteria

1. Basic App information				
Ref	Field	Description	Justification/Evidence	Options
1-1	App ID	A unique ID number generated for each app for easy identification and merging of data. The initial list of apps is identified from listing apps that meet the inclusion criteria based on the search terms, calibrated by two researchers.	App ID number is for research tracking purposes	Alpha-numeric
1-2	App Name	The given name/title of the app.	Extracted from app store	Free text
1-3	Developer name	The company of the app developer. If there is no name, note the developer's name.	Extracted from app store	Free text
1-4	Platform	Is this app tested on Android or iOS?	Apps available on both Android and iOS platforms will be assessed on both	Android/iOS
1-5	App version number	List the latest version of the app during assessment	Extracted from app store	Alpha-numeric
1-6	User rating	State user ratings if applicable on a scale of 5. Leave blank if information is not available	Extracted from app store	Numeric
1-7	Number of people who rated	State the number of people who provided ratings for the app at the point of assessment. Leave blank if information is not available	Extracted from app store	Numeric
1-8	Cost (App or in-app purchase)	Cost to download the app. Specify the actual price in SGD paid to access the app/app feature	Documented while app was purchased	Numeric
1-9	Assessor	Reviewer's initials. Each reviewer is to use consistent initials.	For documentation	Free text

1-10	Assessment date	Date the app is reviewed.	For documentation	dd/mm/yyyy
1-11	Language	What is the primary language of the app?	For screening	English/Chinese/Malay/Tamil/Hindi
1-12	Accessible region	Is this app limited to certain locations/countries/regions?	For documentation	Free text
1-13	Target user of the app	Who is the target user of the app?	Information should be tailored to suit patients [SG guideline]	Child patient/Caregivers/Adult patient/All
1-14	Tracking and Monitoring function	Does the app have any function related to tracking of disease/treatment/ QOL / environmental factors?		Yes/No
1-14-1	Treatment and management	Does the app have any functions related to tracking of treatment management E.g. record pills/cream/moisturizer	Physicians should be aware of the treatment/ management plan when appropriate [AAD guideline]. Topical is recommended for AD-affected individuals who have failed to respond to good skin care and regular use of emollients alone [AAD guideline].	Yes/No
1-14-2	Disease status	Does the app have any disease tracking functions? e.g. record skin conditions, disease severity, etc.	Key intervention for AD self-management.	Yes/No
1-14-3	Psychological factors	Does the App have functions related to tracking of psychological factors or QOL? E.g. record or track psychological status (questionnaires)	Psychological intervention resulted in decreased disease severity. Physicians should be aware of and assess for conditions associated with atopic dermatitis, such as sleep disturbance, depression, and other neuropsychiatric conditions [AAD guideline]. During an assessment of psychological and psychosocial wellbeing and quality of life, healthcare professionals should take into account the impact of atopic eczema on parents or carers as well as the child and provide appropriate advice and support. [NICE guidelines]	Yes/No

1-14-4	Environmental factors	Does the app have functions relating to the tracking of environmental factors? e.g. food allergy, house dust mites, pollens, animal dander, and fungi	When clinically assessing children with atopic eczema, healthcare professionals should seek to identify potential trigger factors including <ul style="list-style-type: none"> - Irritants, for example, soaps and detergents (including shampoos, bubble baths, shower gels, and washing-up liquids) - Skin infections - Contact allergens - Food allergens - Inhalant allergens. [NICE guidelines CG57]	Yes/No
1-15	Information education function	Does the app have any function related to providing information on disease pathophysiology/treatment/ psychological factors / environmental factors?		Yes/No
1-15-1	Treatment management	Does the app provide any information on disease management?	Patients should be given instructions on the needs to safely and effectively self-manage their medicines [NICE guidelines CG76] Healthcare professionals should spend time educating children with atopic eczema and their parents or carers about atopic eczema and its treatment. They should provide information in verbal and written forms, with practical demonstrations, and should cover: <ul style="list-style-type: none"> - How much of the treatments to use - How often to apply treatments - When and how to step treatment up or down - How to treat infected atopic eczema. [NICE guidelines CG57]	Yes/No
1-15-2	Psychological factors	Does the app provide any information on psychological management?	During an assessment of psychological and psychosocial wellbeing and quality of life, healthcare professionals should take into account the impact of atopic eczema on parents or carers as well as the child and provide appropriate advice and support. [NICE guidelines]	Yes/No
1-15-3	Environmental factors	Does the app provide any information on environmental factors that may pose as triggers or allergens?	Increased knowledge of disease mechanisms and course, the appropriate use of therapies, and the goals of management can improve treatment adherence and lessen fears and misconceptions. Educational methods vary	Yes/No

			greatly in scope, intensity, frequency, setting, and personnel used. [AAD guidelines]	
1-15-4	Symptoms, disease course & pathophysiology	Does the app provide any information on symptoms, disease course or pathophysiology?	Educational programs are recommended as an adjunct to the conventional therapy of atopic dermatitis [AAD guideline]. Increased knowledge of disease mechanisms and course, the appropriate use of therapies, and the goals of management can improve treatment adherence and lessen fears and misconceptions. Educational methods vary greatly in scope, intensity, frequency, setting, and personnel used. [AAD guidelines]	Yes/No
2. Tracking and Monitoring function				
S/N	Criterion statement		Justification/Evidence	Options
2-1. Tracking of disease management				
2-1-1	Does the app record pharmacologic treatment management (oral medicine, topical applications, etc.)?		Physicians should be aware of the treatment/management plan when appropriate [AAD guideline]. Topical is recommended for AD-affected individuals who have failed to respond to good skin care and regular use of emollients alone [AAD guideline].	Yes/No/NA
2-1-1-1	If yes, does the app allow the user to record oral medicine intake (e.g. cyclosporine, azathioprine, methotrexate, etc.)?			Yes/No/NA
2-1-1-2	If yes, does the app allow the user to record topical applications (e.g. topical calcineurin inhibitors, topical corticosteroids etc.)?			Yes/No/NA

2-1-1-3	If yes, does the app allow the user to key in frequency and dose for each medication (oral medicine, topical)?	Treatment dose and frequency are important components in patient's education [SG guideline].	Yes/No/NA
2-1-2	Does the app record non-pharmacologic treatment management (moisturizers application, bath practice, wet-wrap etc.)?	The application of moisturizers should be an integral part of the treatment of patients with AD as there is strong evidence that their use can reduce disease severity and the need for pharmacologic intervention [AAD guideline].	Yes/No/NA
2-1-2-1	If yes, does the app allow the user to key in frequency and notes for non-pharmacologic treatments?	Treatment dose and frequency are important components in patient's education [SG guideline].	Yes/No/NA
2-1-3	Can the user set reminders for treatment management?	This will serve as a time point at which a patient should accept the treatment, of which, failure to do so will trigger a reminder alarm.	Yes/No/NA
2-1-4	Any other comments on treatment management related functions? (free text)	To record any significant but missing information	Free text
2-2. Tracking of disease status			
2-2-1	Can the user record or capture current atopic dermatitis status/changes?	Desirable feature to help the patient evaluate the efficiency of their treatment and to choose	Yes/No

2-2-1-1	If yes, how does the app record or capture a patient's status/changes?	where best to apply the treatment in relation to their eczema, it's important to assess AD severity between consultations. Physicians should be aware of and assess for conditions associated with atopic dermatitis, such as rhinitis/rhinoconjunctivitis, asthma, and it is recommended that physicians discuss them with the patient as part of the treatment/management plan when appropriate [AAD guideline].	manual entry/shooting pictures/recording the impact on daily activities (leisure activities attendance, social activities, etc.)/ recording certain symptoms (itchiness, dryness, redness, etc.)/self-assessment tool (SCORAD scoring system, Eczema Area and Severity Index (EASI), Investigator Global Assessment (IGA), etc.)/Others (free text)/NA
2-2-2	Is the monitoring of disease based on recommended validated scoring systems (SCORAD, EASI, POEM)	The available literature suggests that the SCORAD index, the EASI score, and the Patient-Oriented Eczema Measure (POEM) severity scale have been adequately tested and validated; therefore, their use can be considered when practical [AAD guideline].	Yes/No
2-2-3	Can the user set reminders to record atopic dermatitis status?	This will serve as a time point at which a patient should monitor disease status, of which, failure to do so will trigger a reminder alarm.	Yes/No
2-2-4	If the skin condition becomes worse (e.g. Crusting or oozing sores, Severe scratch marks, Widespread rash, Severe discoloration of the skin, Fever that is accompanied by a rash, Painful cracks on the hands or fingers, signs of bacterial infection etc.). Does the app come up with corresponding advice?	Important function to protect patient's safety	Yes/No
2-2-5	If yes, how does the app provide advice (screenshot)?	Healthcare professionals should spend time educating children with atopic eczema and their parents or carers about atopic eczema and its treatment. They should provide information in verbal and written forms, with practical demonstrations, and should cover... when and how to step treatment up or down... how to treat infected atopic eczema [NICE guidelines]. The Eczema Action Plan can help caregivers	Screenshot

2-2-6	If yes, what is the advice?	know how to treat their child as the eczema changes [AAD guideline].	Free text
2-2-7	If yes, is the advice in accordance with major guidelines for atopic dermatitis? (AAD, NICE, Singapore guidelines)		Yes/No/inconsistent/NA
2-2-8	If yes, what alarm condition will activate the advice (multiple choice)?		Crusting or oozing sores/Severe scratch marks/Widespread rash/Severe discoloration of the skin/Fever that is accompanied by a rash/Painful cracks on the hands or fingers/Signs of bacterial infection/Others (free text)/NA
2-2-9	Does the app have the ability to provide information on step-up or step-down treatment?	Step-up or step-down treatment is an important component for patient education [AAD guideline].	Yes/No
2-2-9-1	If yes, in what way does the app provide the above information?		By text/doctor consultation
2-2-10	Does the app have diagnostic functions for atopic dermatitis?	Desirable functionality	Yes/No
2-2-11	Any other comments on disease monitoring related functions?	To record any significant but missing information	Free text
2-3. Tracking of psychological factors / QOL			
2-3-1	What instrument does the app employ (e.g. psychological questionnaires, quality of life questionnaires, how AD affect daily life mood, depression, anxiety, etc.)?	Psychological intervention resulted in decreased disease severity. Physicians should be aware of and assess for conditions associated with atopic dermatitis, such as sleep disturbance, depression, and other neuropsychiatric conditions [AAD guideline].	Free text
2-3-1-1	If yes, what the frequency of the assessment?		Daily/Weekly/Monthly/As needed
2-3-2	Any other comments on psychological/quality of life-related functions?	To record any significant but missing information	Free text

2-4. Tracking of environmental factors & allergens			
2-4-1	Does the app provide real-time environmental conditions monitoring (e.g. Pollens, humidity, temperature, etc.)?	Desirable functionality	Yes/No
2-4-2	Does the app allow the user to record any food may trigger AD?	Desirable functionality	Yes/No
2-4-3	Does the app allow user record environmental triggers of AD?	Desirable functionality	Yes/No
2-4-4	Any other comments on allergen related functions? (free text)	To record any significant but missing information	Free text
3. Information education function			
S/N	Criterion statement	Justification/Evidence	Options
3-1. Information on disease treatment			
3-1-1	Does the app provide instruction/information on pharmacologic treatment management?	Patients should be given instructions the person needs to safely and effectively self-manage their medicines [CG76].	Yes/No
3-1-1-1	If yes, does the app provide instruction/information on topical applications (e.g. topical calcineurin inhibitors, topical corticosteroids etc.)?	Patients should be given instructions the person needs to safely and effectively self-manage their medicines [CG76].	Yes/No/NA
3-1-1-2	If yes, does the app provide information on side-effects of the medication?	Patient fears of side effects associated with the use of topical corticosteroids for AD should be recognized and addressed to improve adherence and avoid undertreatment [AAD guideline].	Yes/No/NA
3-1-1-3	If yes, is the source of the information provided?	An important criterion for assessing the reliability and validity of information provided	Yes/No/NA

3-1-1-4	If yes, is the source provided valid? What is the source?	An important criterion for assessing the reliability and validity of information provided	Yes/No/NA/Free text
3-1-2	Does the app provide any information on the appropriate use of non-pharmacologic therapies?	It is recommended that physicians discuss them with the patient as part of the treatment/management plan, when appropriate [AAD guideline].	Yes/No
3-1-2-1	If yes, does the app provide any information on bath practice?	Recommendations for the use of topical therapies in the treatment of atopic dermatitis (recommendation strength C; level of evidence III) [AAD guideline].	Yes/No/NA
3-1-2-2	If yes, does the app provide any information about moisturizer applications?	Recommendations for the use of topical therapies in the treatment of atopic dermatitis (recommendation strength B; level of evidence II) [AAD guideline] Emollients should be used during active disease flares in conjunction with topical anti-inflammatory agents, and also as maintenance therapy. Apply before and after swimming or bathing while the skin is still moist (within 5 min) [SG guideline].	Yes/No/NA
3-1-2-3	If yes, does the app provide any information on wet wrap?	Recommendations for the use of topical therapies in the treatment of atopic dermatitis (recommendation strength B; level of evidence II) [AAD guideline]	Yes/No/NA
3-1-2-4	If yes, does the app provide any information on using non-soap cleansers, bath additives, acidic spring water?	Recommendations for the use of topical therapies in the treatment of atopic dermatitis (recommendation strength C; level of evidence III) [AAD guideline]	Yes/No/NA

3-1-2-5	If yes, does the app provide information on side-effects of the non-pharmacological therapies?	Patient fears of side effects associated with the use of topical corticosteroids for AD should be recognized and addressed to improve adherence and avoid undertreatment [AAD guideline].	Yes/No/NA
3-1-2-6	If yes, is the source of the information provided?	An important criterion for assessing the reliability and validity of information provided	Yes/No/inconsistent/NA
3-1-2-7	If yes, is the source provided valid? What is the source?	An important criterion for assessing the reliability and validity of information provided	Yes/No/NA/inconsistent/Free text
3-1-2-8	If yes, is the information in accordance with major guidelines for atopic dermatitis? (AAD, NICE, Singapore guidelines)	An important criterion for assessing the reliability and validity of information provided	Yes/No/inconsistent/NA
3-1-3	Does the app provide any information on the goals of management?	The often-protracted nature of AD necessitates setting several long-term treatment goals: the prevention of continued outbreaks, the management of comorbidities and secondary complications that arise, and minimizing adverse effects while trying to maximize positive outcomes [AAD guidelines].	Yes/No
3-1-4	Does the app allow users to set goals of management?	A feature encourages patients to maintain adherence to treatment regime.	Yes/No

3-1-5	Any other comments on treatment management related functions? (free text)	To record any significant but missing information	Free text
3-2. Information on psychological factors / QOL or psychological intervention			
3-2-1	Does the app provide quality of life-related information (psychological information, quality of life information, etc.)?	Psychological intervention resulted in decreased disease severity. Physicians should be aware of and assess for conditions associated with atopic dermatitis, such as sleep disturbance, depression, and other neuropsychiatric conditions [AAD guideline]. Healthcare professionals should be aware that all categories of severity of atopic eczema, even mild, can have a negative impact on psychological and psychosocial wellbeing and quality of life. This should be taken into account when deciding on treatment strategies [NICE guidelines]	Yes/No
3-2-2	Does the app provide psychological intervention (e.g. autogenic training, biofeedback, brief dynamic psychotherapy, cognitive behavioral therapy, habit reversal behavioral therapy, and a stress management program)?	Psychological interventions have also been used to help with coping with AD [AAD guideline].	Yes/No
3-2-2-1	If yes, what intervention does the app employ (e.g. Questionnaires, games)?		Questionnaires/Games/Text/Others (free text)/NA
3-2-3	Any other comments on psychological/quality of life-related functions?	To record any significant but missing information	Free text
3-3. Information on environmental factors & allergens			
3-3-1	Does the app provide food allergy related information?	Children with moderate to severe AD should be considered for food allergy evaluation for milk, egg, peanut, wheat, and soy if at least 1 of the following is met: (A) persistent AD in spite of optimized treatment or (B) having a reliable history of immediate reaction after ingestion of a specific food [AAD guideline].	Yes/No

3-3-2	Does the app provide aeroallergens related information (e.g. house dust mites, pollens, animal dander, and fungi, and higher rates of sensitization, etc.)?	Common aeroallergens include house dust mites, pollens, animal dander, and fungi, and higher rates of sensitization are noted in those with moderate to severe AD [AAD guideline].	Yes/No
3-3-3	Any other comments on allergen related functions?	To record any significant but missing information	Free text
3-4. Information on symptoms, disease course & pathophysiology			
3-4-1	How is education information provided?	Important criterion as how information is presented may affect user's understanding	Via text/game/Q&A/others (free text)
3-4-2	Does the app have atopic dermatitis related education (disease mechanisms and course, symptoms)?	Increased knowledge of disease mechanisms and course, the appropriate use of therapies, and the goals of management can improve treatment adherence and lessen fears and misconceptions [AAD guideline].	Yes/No
3-4-2-1	If yes, is education/information about symptoms provided (e.g. patients and caregivers should be informed that in patients with more pigmented skin AD may temporarily cause the skin to lighten or darken)?	Patients and caregivers should be informed that in patients with more pigmented skin AD may temporarily cause the skin to lighten or darken [SG guideline].	Yes/No/NA
3-4-2-2	If yes, is education/information about disease mechanisms and course provided?	Increased knowledge of disease mechanisms and course, the appropriate use of therapies, and the goals of management can improve treatment adherence and lessen fears and misconceptions [AAD guideline].	Yes/No/Na
3-4-3	Is the information provided in accordance with major guidelines for atopic dermatitis? (AAD, NICE, Singapore guidelines)	An important criterion for assessing the reliability and validity of information provided	Yes/No/inconsistent/NA
3-4-4	Specify any other atopic dermatitis related education (free text)	To record any significant but missing information	Free text
3-4-5	Any other comments on education-related functions? (free text)	To record any significant but missing information	Free text

4. Other attributes			
S/N	Criterion statement	Justification/Evidence	Options
4-1	Can the app create user profiles?	Information should be tailored to suit patients [SG guideline]	Yes/No
4-2	Does the app provide user with rewards for completing treatment management/education/disease monitoring?	Desirable functionality to encourage patients to maintain adherence to treatment regimen	Yes/No
4-2-1	If yes, elaborate on what (e.g. treatment adherence, education, skin condition record, etc.) is being rewarded		Free text
4-2-2	If yes, elaborate on the type of reward (e.g. Stars, motivational messages, etc.).		Free text
4-3	Does the app contain any games?	Desirable functionality	Yes/No
4-3-1	If yes, what is/are the purpose of the game(s)?		Free text
4-4	Does the app get stuck, crash or frozen more than once when using? (Answer "Yes" if app hangs for more than 3s in two occasions)	App will frustrate user if it keeps hanging	Yes/No
4-5	Does adverts interfere with the functioning of the app (if any?). Answer "Yes" if you feel bothered by the adverts, answer "No" if there are no adverts.	Desirable not to have adverts as it may prevent the proper functioning of the app	Yes/No

4-6	Is the app created/commissioned/partnered by any governmental bodies / government-affiliated companies, hospitals or universities?	It is desirable that the information source provided by the commission body is accredited (reliable)	Yes/No	
4-6-1	If Yes, which body created/commissioned/partnered the app?		Free text	
4-7	Is the account password protected?	Desirable functionality for privacy to personal health information	Yes/No	
4-8	Does the app allow recorded data of the patient to be shared on social media (e.g. Facebook/twitter?)	Desirable functionality for added support	Yes/No	
4-9	Does the app allow data to be exported (e.g. PDF/Excel, email, cloud, etc.)?	Desirable functionality for user to restore data collected from app	Yes/No	
4-10	Does the app include a health professional who is accessible to the user (without users inputting any health provider/health professional information)?	Desirable functionality for added support	Yes/No	
4-11	Can the app connect the user to a community/support group of other users/caregivers with AD?	Eczema workshops and nurse-led programs may be useful as an adjunct to conventional therapy [AAD guideline]. Practitioners should be aware of educator and lay-led management resources, such as the educational information and support groups provided by organizations [AAD guideline].	Yes/No	
4-12	Please record your overall impressions of this app and any other observations from this app testing.	To record any significant but missing information	Free text	
5. HON principles				
S/N	Criterion statement	Description	Justification/Evidence	Options

5-1	Does the app indicate the qualifications of specific individuals who developed the app or contributed to the information provided?	Authoritative: The qualifications of the authors are indicated	HON principles are essential standards for information governance	Yes/No
5-2	Is there a disclaimer stating or which implies that the information provided and/or app functions do not replace the healthcare provider's advice? (places to look: disclaimer within the app, under the Terms & Conditions in the app, on the app developer's website, in the app store's description of the app).	Complementarity: Information should support, not replace, the doctor-patient relationship	HON principles are essential standards for information governance	Yes/No/Advice given by a healthcare provider
5-3	Is there a privacy and confidentiality clause in the app? (Answer NA if no data collected)	Privacy: Respect the privacy and confidentiality of personal data submitted to the site by the visitor	HON principles are essential standards for information governance	Yes/No/NA
5-3-1	Does the app take caution regarding the collection or processing of data from children?	How shall I treat any data gathered from children? (UK Apps developer code of conduct) With regard to apps which, because of their design or functionality, are particularly aimed at children under the age of 16 or which are particularly likely to be used by such children, you must pay attention to the age limit defining children or minors in national legislation, choose the most restrictive data processing approach in full respect of the principles of		Yes/No/NA (no data collected/no user identifiers, e.g. age, name, user ID, photos/not targeting children)
5-3-2	If yes, how does the app do so?			Free text (e.g. stated in privacy clause, pop-up before data is keyed in...)

			data minimization and purpose limitation, and refrain wherever possible from collecting data through children in relation to their relatives and/or friends. Parental involvement is crucial for such apps. Therefore, you must undertake reasonable efforts to verify that consent is given or authorized by the holder of parental responsibility for the processing of health data of minors.	
5-3-3	If no, what patient identifiers may be collected?			Free text (e.g. name, age, date of birth, user ID, email, photographs)
5-4	Are information sources in the app cited?	Attribution: Cite the source(s) of published information, date medical and health pages	HON principles are essential standards for information governance	Yes/No/NA
5-5	Are the claims relating to benefits and performance in the app description (e.g. description in the app store) backed up by evidence? Options: Yes (claims are backed up by evidence), no (claims not backed up by evidence), NA (no claims)	Justifiability: Site must back up claims relating to benefits and performance	HON principles are essential standards for information governance	Yes/inconsistent/No/NA
5-6	Are the developers contactable by email? (the email may be found in the app, the app store, app developer's website, etc).	Transparency: Accessible presentation, accurate email contact	HON principles are essential standards for information governance	Yes/No

5-7	Does the app indicate any funding sources? ("Yes" if the app is managed by a registered commercial company and "No" if it is by an individual developer without funding information)	Financial disclosure: Identify funding sources	HON principles are essential standards for information governance	Yes/No
5-8	Are advertorials distinguishable from the content of the app?	Advertising policy: Clearly distinguish advertising from editorial content	HON principles are essential standards for information governance	Yes/No/No advertising

Appendix 8.1 Questionnaire for eczema smartphone app co-design workshop

Questionnaire for eczema smartphone app co-design workshop

Workshop I&II

PART A: Demographic data

1. What's your date of birth: / / (dd/mm/yy)
2. Gender: ☐ Male ☐ Female
3. Residential status: ☐ Singapore citizen ☐ Permanent resident ☐ Non-resident
4. What is your highest achieved qualification?
5. What is your main daytime occupation?
6. What is your child's date of birth: / / (dd/mm/yy)
8. Your child's gender: ☐ Male ☐ Female
9. When was a diagnosis of atopic dermatitis first made?
Date: / / (mm/yy)
10. What's your biggest concern when you take care of your child's eczema?
.....
.....
.....
11. If you want to use smartphone app to assist you in managing your child's eczema, please tick 3 features that you would like to have in the app.

☐ Disease education ☐ Disease monitoring ☐ Pharmacological guidance

☐ Communication with healthcare workers ☐ Communication with other caregivers

☐ Psychological support ☐ Others. Please specify.....

Ref: Abu-Dalboh (2013). A QUESTIONNAIRE APPROACH BASED ON THE TECHNOLOGY ACCEPTANCE MODEL FOR MOBILE TRACKING ON PATIENT PROGRESS APPLICATIONS. Journal of Computer Science, 9(6), pp.763-770.

PART B:

1. Are you aware of the availability of health apps (applications) for smartphones?

☐ Yes ☐ No

2. What type of applications do you download?

☐ Games

☐ Education

☐ Books

☐ News

☐ Social

☐ Health and Lifestyle

☐ Business

☐ Other

3. If you download a health app, what type of app do you download?

☐ BMI/alcohol unit

☐ Smoking cessation

☐ Vascular risk assessment

☐ Fitness

☐ Diet and nutrition

☐ Strongly agree ☐ Agree ☐ Neutral ☐ Disagree ☐ Strongly disagree

Perceived ease of use

1. I would find it easy to get mobile tracking on my child's disease

☐ Strongly agree ☐ Agree ☐ Neutral ☐ Disagree ☐ Strongly disagree

2. Using a health app will be clear and understandable.

☐ Strongly agree ☐ Agree ☐ Neutral ☐ Disagree ☐ Strongly disagree

3. It would be easy for me to become familiar with using a smartphone self-management app.

☐ Strongly agree ☐ Agree ☐ Neutral ☐ Disagree ☐ Strongly disagree

User satisfaction

1. I feel confident in using a smartphone app to manage my child's eczema.

☐ Strongly agree ☐ Agree ☐ Neutral ☐ Disagree ☐ Strongly disagree

2. I believe using a smartphone app to manage eczema will increase my quality of life.

☐ Strongly agree ☐ Agree ☐ Neutral ☐ Disagree ☐ Strongly disagree

Attribute of usability

1. I think that I would like to use a smartphone self-management app on a daily basis

☐ Strongly agree ☐ Agree ☐ Neutral ☐ Disagree ☐ Strongly disagree

Perceived usefulness

1. A smartphone self-management app will enable me to get information quickly.

☐ Strongly agree ☐ Agree ☐ Neutral ☐ Disagree ☐ Strongly disagree

2. A smartphone self-management app will allow my doctor to follow up the disease from outside of the hospital

☐ Strongly agree ☐ Agree ☐ Neutral ☐ Disagree ☐ Strongly disagree

3. A smartphone self-management app will save the time of doctors and nurses.

Appendix 8.2 Workshop evaluation form

Workshop Evaluation Form

Workshop III

1. Please rate the following from 1 to 5 where 1=strongly disagree, 2=disagree, 3=neutral, 4=agree, and 5=strongly agree.

1. The workshop was very organized.	1	2	3	4	5
2. The workshop began on time and used the time well.	1	2	3	4	5
3. The workshop was clear.	1	2	3	4	5
4. The presenter was well prepared.	1	2	3	4	5
5. The presenter was responsive to the questions.	1	2	3	4	5
6. The workshop methods used were appropriate for the audience.	1	2	3	4	5
7. I enjoyed the workshop.	1	2	3	4	5
8. I understand the concepts as presented in the workshop.	1	2	3	4	5

2. What did you find most helpful about the workshops?

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3. List any suggestions to improve the workshops.

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Thank you for your feedback. We appreciate your participation.

Ref: Abu-Dalboh (2013). A QUESTIONNAIRE APPROACH BASED ON THE TECHNOLOGY ACCEPTANCE MODEL FOR MOBILE TRACKING ON PATIENT PROGRESS APPLICATIONS. *Journal of Computer Science*, 9(6), pp.763-770.

Appendix 8.3 Scripts for co-design workshops

Smartphone app co-design workshop I

Register

Xiaomeng will be outside the conference room and make sure they sign the consent form, have name tag, fill the questionnaires

Welcome and introduction

The facilitator should introduce themselves and make it clear that they are not part of the clinical team that directly provides (or provided) the participants' care, and that their role is as a facilitator of the discussion.

Provide practical details, including:

- tea/coffee/water facilities
- location of toilets
- duration of discussion (approximately 2 hours).

Beginning of the workshop

Thank you for participating in this workshop. The reason we invited you is that we want to develop a smartphone app for a (grand)parent like you to manage your child's eczema. You were all in our previous quality of life eczema study. I guess most of your children suffered or are still experiencing problems with eczema. Therefore, we would like to know the problems you meet when you take care of your child as well as your perceptions and preferences when you use a smartphone app.

This discussion is built around certain questions. I will ask you a few questions and I would like to hear from all of you. Please note that anything you want to say is important.

The session will be confidential, and whatever is said today must stay in the room.

Besides, I would like to introduce Xiaomeng who will be the note-taker. The discussion will also be audiotaped but your name will be anonymized in the record and following analysis. You can feel free to talk openly.

Ask participants to introduce themselves.

Ask if there are any questions.

Before leaving today, please make sure you filled in the questionnaires and voucher log. We are very interested in your feedback so please don't forget to fill out the feedback form as well.

Facilitating the workshop

Session	Key questions
Challenge session	Q1: How eczema affect you and your child's life? Q2(optional): What do you normally do when you take care of your child at home?

<p>Challenge session</p> <p><i>Materials: A1 paper, Marker pen.</i></p> <p><i>Time: 10-15mins</i></p>	<p>Q1: How eczema affect you and your child's life?</p> <p>Q2(optional): What do you normally do when you take care of your child at home?</p> <p>*** This will be an open question. You can write down their answer in the A1 paper.</p>
<p>Need session</p> <p><i>Materials: Sticky notes (3 colours), A1 paper, Marker pen.</i></p> <p><i>Time:25-30mins</i></p>	<p>Q1 (activity): What were your needs the first 6 months after the symptoms started, from 6-months to a year, or later? Did you feel well informed, especially with respect to 1) disease status, 2) treatment and management guidance 3) emotional support</p> <p>*** The second activity will talk about the information you need. We can ask them to write it down and stick the challenges in the A1 paper (see picture above). A1 paper can be divided into 1) disease status, 2) treatment and management plan 3) emotional support.</p> <p>Q2: Where do you get the information? Are you satisfied with your knowledge of taking care of your child's eczema? What is the source of the information?</p> <p>*** This will be an open question. You can write down their answer in the A1 paper</p>
<p>Break (10 mins)</p> <p><i>Collect the questionnaires and sign the voucher log (Xiaomeng)</i></p>	
<p>App experience session</p> <p><i>Material: Sticky notes (3 colours), A1 paper, Marker pen, Kahoot</i></p>	<p>Q1: Previous experience in app usage. Have anyone used a smartphone app to manage eczema?</p> <p>*** This will be an open question. You can write down their answer in the A1 paper.</p>

<p>App experience session</p> <p><i>Material:</i> Sticky notes (3 colours), A1 paper, Marker pen, Kahoot online polling system</p> <p><i>Time: 45 mins</i></p>	<p>Q1: Previous experience in app usage. Have anyone used a smartphone app to manage eczema?</p> <p>*** This will be an open question. You can write down their answer in the A1 paper.</p> <p>Q2(activity): If there is a smartphone app to help you manage your child's eczema, please list the top features that you want to have in the app.</p> <p>*** The third activity will talk about the topic you want to cover in the smartphone app. The participant will write the topic they are interested in and stick them to the corresponding section in the A1 paper. A1 paper can be divided into 1) education 2) monitor 3) communication. After that, we can sort them and together with the other topics we had, we will start real-time online polling (eg. http://www.easypolls.net/poll.html?p=5c5e96e4e4b000f8f0a03574. I will share the link via WhatsApp). You can see the result straight away after they vote and then we can identify top 3 needs within each category.</p> <p>Q3(optional): If there would be a smartphone app with all the information and features, you need; what frequency do you think you will use it? What are the possible barriers that would keep you from consistent usage (eg. your child's disease gets better? Too complicated? Privacy concerns?)?</p>
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Closing the workshop

Please make sure you have completed your evaluation forms and get your 20SGD NTUC voucher.

Smartphone app co-design workshop II

Participant arrival

Keep in mind that some participants are likely to arrive early, so it is important to be at the venue and have the room set up in advance to be available to greet participants.

When focus group participants arrive:

- welcome them
- offer light refreshments, for example tea, coffee, water, and a snack
- take time to develop rapport
- obtain consent
- hand out the questionnaires and ask them to fill in before workshop starts
- ask the participants to download the apps/show apps

Opening the workshop

Welcome

The facilitator should introduce themselves and make it clear that they are not part of the clinical team that directly provides (or provided) the participants' care, and that their role is as a facilitator of the discussion.

Housekeeping

Provide practical details, including:

- tea/coffee/water facilities
- location of toilets
- duration of discussion (approximately 2 hours).

Overview of the project

Before starting, give the group an overview of the project and the purpose of the discussion based on the written information previously provided. Use a conversational tone. (present slides/screenshot of the app)

Beginning of the discussion

Thank you for participating in the workshop. The reason for inviting you is that we would like to develop a smartphone app for parents to manage their child's eczema and we would like to know your experience as a healthcare professional. We also want to know your perceptions and preferences when you use/introduce a smartphone app to your patients.

This discussion is built around certain questions. I will ask you a few questions and I would like to hear from all of you about your experience when you educate and treat your patients in the clinic. Please note that anything you want to say is important.

The session will be confidential, and that discussion must stay in the room.

Besides, I would like to introduce XXX who will be the note-taker. The discussion will also be audiotaped but your name will be anonymized in the record and following analysis. You can feel free to talk openly.

Ask if there are any questions.

Facilitating the discussion

Q1. How do you educate your patients (their caregivers) during clinic? Are you satisfied with the results?

If yes, what do you normally do?

If no, how to improve? How do you think education should be effectively delivered?

Probes:

Has anybody else had a similar experience?

Does anybody have anything different to discuss?

Q2. What are caregivers need the first 6 months after the symptoms started, from 6-months to a year, or later? Does the education need to change according to 1) different severity 2) duration of diseases 3) child age?

Probes:

Does anybody have anything different to discuss?

Q3. Have you considered using smartphone apps to educate your patients (and their caregivers)?

If yes, how will you select the app in the market? What features you value most?

If no, what is your concern?

Probes:

Does anybody have anything different to discuss?

Q4. What features should an app have in order to address those problems?

Probes:

Does anybody have anything different to discuss?

Q5. Would you mind providing teleconsultation service to your patients?

If yes, what're your concerns?

If no, why?

Probes:

Does anybody have anything different to discuss?

Smartphone app co-design workshop III

Before the workshop

Materials: slides, a3 paper, feedback grid paper, audio recording devices, sticky notes, pen, markers, participants name list, questionnaires and evaluation forms, voucher log sheets, timers

Seminar room 1

Layout of the workshop

Register

Xiaomeng will be outside the conference room and make sure they sign the consent form, have name tag, fill the questionnaires.

Welcome and Introduction

The facilitator should introduce themselves and make it clear that they are not part of the clinical team that directly provides the participants' care, and that their role is as a facilitator of the discussion.

Provide practical details, including:

- tea/coffee/water facilities
- location of toilets
- duration of discussion (approximately 2 hours).

Beginning of the workshop

Thank you for participating in this workshop. The reason we invited you is that we want to develop a smartphone app for a parent like you to manage your child's eczema. You were all in our previous quality of life eczema study and some of you also participated in our previous workshop. In the previous workshop, we have already discussed the problems you meet when you take care of your child as well as your perceptions and preferences when you use a smartphone app. Based on the previous workshops, in this workshop, we will design the interface of the eczema app together.

The session will be confidential, and whatever is said today must stay in the room.

Besides, I would like to introduce Xiaomeng who will be the note-taker. The discussion will also be audiotaped but your name will be anonymized in the record and following analysis. You can feel free to talk openly.

Ask participants to introduce themselves.

Ask if there are any questions.

Facilitating the workshop

Session	Key information
Introduction <i>Materials: Slides</i> <i>Time: 10-15mins</i>	<ul style="list-style-type: none"> ▪ Overview of the eczema apps (slides) ▪ Top needs (slides)

<p>Individual crazy eights exercise</p> <p><i>Materials: Slides A3 paper, Marker pen.</i> <i>Time: 30 mins</i></p>	<p>Now we are moving to the first activity of today: I will let you to design the interface of the app yourself. The app must cover at least one of the top needs listed in the slides.</p> <ul style="list-style-type: none"> Working as individual Have each person fold an 8x11 piece of paper into eight panels. (Or four, double-sided, if you want more space.) Set a timer for 12 minutes Use those 12 minutes to scribble out a sketch or idea in a single panel. It can be a button, a feature, a user scenario, a tagline... wherever your mind goes. You'll fill out eight panels (hence the crazy and the eight), front and back. Your ideas will be bad, obvious, simple, messy and confusing. That's the point. <ul style="list-style-type: none"> At the end, look at what you drew, and start the timers again, with another set of 8 panels. Expand, explore, push, scribble, generate, play. It'll make sense later.
<p>Team Sketches</p> <p><i>Materials: Slides A3 paper, Marker pen, name tag.</i> <i>Time: 30 mins</i></p>	<p>We will now break <u>in</u> to smaller groups for sharing. Everyone now has your own wireframe prototype. Teams now come together and compare their Crazy Eights drawings.</p> <p>For the <u>break out</u> groups, please notice the coloured dots on your name tags. You will go to the <u>break out</u> group indicated by your colour. Let's change the seats and find the right colour.</p> <p>Groups discuss and explore the ideas from the drawings and come to an agreement on the top features or ideas they want to include in one consolidated master sketch. Groups sketch a single layout that incorporates the top ideas (You can draw an outline of a smartphone to serve as the frame.).</p>
<p>Break (10 mins) <i>Collect the questionnaires and send out the workshop feedback form (Xiaomeng)</i></p>	
<p>Flamethrower Rounds</p> <p><i>Material: Sticky notes (3 colours), A3 paper, feedback grid paper, Marker pen, timer.</i> <i>Time: 15 mins</i></p>	<p>Ok. Welcome back. Now it is time to create a space for speed-critiques. We are now doing 3 rounds of flamethrower Rounds (3 rounds) (10*3mins)</p> <p>A member from each group is sent to another group.</p> <ol style="list-style-type: none"> The host group has 3 minutes to present and pitch their sketch The visitor has 3 minutes to ask any questions The hosts turn their back and take notes as the visitor "flame-throws," tearing the idea apart critically, mentioning any bad ideas they notice.

	+ What worked	Δ What could be improved	While feedback is being given, host teams record feedback on a “feedback grid”: a quadrant with each square labelled Plus, Minus, Ideas and Questions.
	? Questions	! Ideas	
Revisions <i>Time: 10mins</i>	<ul style="list-style-type: none"> Now everyone come back to their seats. The teams regroup and share your insights and feedback from the Flamethrower found. Making any changes they see to be <u>necessary</u>, the group redraws their product idea as a master sketch. 		
Pitches <i>Materials: Timer</i> <i>Time: 20mins</i>	<p>Welcome back. We will now have 5 minutes of pitches for each group. Each group will have 5 minutes to share. Who would like to start us off?</p> <ul style="list-style-type: none"> Present the wireframe to the entire group Teams now pitch their wireframe to the entire group, in 5-minute pitches. It's important to keep to this time limit. 		

Closing the workshop

Before leaving today, please make sure you filled in the questionnaires and voucher log. We are very interested in your feedback so please don't forget to fill out the feedback form as well.

Appendix 8.4 Consolidated criteria for reporting qualitative studies (COREQ): 32-item checklist

No. Item	Guide questions/description	Reported on Page #
Domain 1: Research team and reflexivity		
<i>Personal Characteristics</i>		
1. Interviewer/facilitator	Which author/s conducted the interview or focus group?	Page 140-142
2. Credentials	What were the researcher's credentials? E.g. PhD, MD	Page 140-142
3. Occupation	What was their occupation at the time of the study?	Page 140-142
4. Sex	Was the researcher male or female?	Page 140-142
5. Experience and training	What experience or training did the researcher have?	Page 140-142
<i>Relationship with participants</i>		
6. Relationship established	Was a relationship established prior to study commencement?	N/A
7. Participant knowledge of the interviewer	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	N/A
8. Interviewer characteristics	What characteristics were reported about the interviewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	N/A
Domain 2: study design		
<i>Theoretical framework</i>		
9. Methodological orientation and Theory	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	Page 144
<i>Participant selection</i>		
10. Sampling	How were participants selected? e.g. purposive, convenience, consecutive, snowball	Page 143
11. Method of approach	How were participants approached? e.g. face-to-face, telephone, mail, email	Page 143
12. Sample size	How many participants were in the study?	Page 145-146
13. Non-participation	How many people refused to participate or dropped out? Reasons?	Page 145-146
<i>Setting</i>		
14. Setting of data collection	Where was the data collected? e.g. home, clinic, workplace	Page 144-145

15. Presence of non-participants	Was anyone else present besides the participants and researchers?	Page 140-143
16. Description of sample	What are the important characteristics of the sample? e.g. demographic data, date	Page 145-148
<i>Data collection</i>		
17. Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?	Page 141-142
18. Repeat interviews	Were repeat interviews carried out? If yes, how many?	No. I didn't carry out repeat interviews
19. Audio/visual recording	Did the research use audio or visual recording to collect the data?	Page 144-145
20. Field notes	Were field notes made during and/or after the interview or focus group?	Page 141-142
21. Duration	What was the duration of the interviews or focus group?	Page 140-143
22. Data saturation	Was data saturation discussed?	Methods
23. Transcripts returned	Were transcripts returned to participants for comment and/or correction?	N/A
Domain 3: analysis and findings		
<i>Data analysis</i>		
24. Number of data coders	How many data coders coded the data?	Page 144-145
25. Description of the coding tree	Did authors provide a description of the coding tree?	N/A
26. Derivation of themes	Were themes identified in advance or derived from the data?	Page 144-145
27. Software	What software, if applicable, was used to manage the data?	Page 144-145
28. Participant checking	Did participants provide feedback on the findings?	Page 159-160
<i>Reporting</i>		
29. Quotations presented	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	Page 148-158
30. Data and findings consistent	Was there consistency between the data presented and the findings?	Page 148-160
31. Clarity of major themes	Were major themes clearly presented in the findings?	Page 148
32. Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	Page 148-158