Skin barrier function of White and Black African nursing students

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"In all seriousness, people think that it's the ideas that are important. Well, everyone has ideas, all the time. I tend to write mine down and remember them, but at some point you have to apply the bum to the seat and knock out about sixty five thousand words" – Terry Pratchett.

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ABSTRACT

Title: Skin barrier function of White and Black African nursing students.

Background: Nursing students are required to complete a minimum of 2000 practical hours in healthcare facilities during their four years of tertiary education. They are required to frequently wash and disinfect their hands during a practical shift to prevent nosocomial infections in patients. These routines involving frequent hand washing in combination with skin occlusion from wearing latex or nitrile gloves may have a negative impact on the skin condition of their hands. Transepidermal water loss (TEWL), stratum corneum (SC) hydration and skin surface pH are common parameters included in assessing the effect of frequent hand washing and wet work on skin condition. However, limited published literature exists on the long-term effects of nursing student practical training on skin barrier function and how skin barrier function compares between White and Black African nursing students. International studies have focused on investigating hand dermatitis as a consequence of these workplace conditions in nursing students, however prevalence and severity of hand dermatitis have not been investigated among a South African nursing student population. Natural moisturising factor (NMF) has been used recently to establish the risk of developing skin diseases such as dermatitis associated with low NMF. Quantifying NMF in a nursing student population may provide valuable insight into their potential susceptibility for skin conditions associated with low NMF. Evaluating skin barrier function in nursing students provides the opportunity to not only investigate early changes in these biophysical parameters, during their practical training, but may also provide the means to identify early interventions that may protect their skin health already at the start of their career.

Aims and objectives*:* The aim of this thesis was to quantify and compare skin barrier function, NMF content and hand dermatitis prevalence and severity between South African White and Black African nursing students during their tertiary education. The specific objectives were (i) to compare baseline skin barrier function between White and Black African nursing students, (ii) to compare NMF content of the skin on the hands between White and Black African nursing students, (iii) to evaluate the skin barrier function of White and Black African nursing students during the progression of their tertiary education and (iv) to quantify hand dermatitis prevalence and severity among tertiary nursing students.

Methods*:* Skin barrier function parameters including TEWL, SC hydration and skin surface pH were measured in female nursing students (63 White, 42 Black African) three times a year and

repeated for two years, before the COVID-19 pandemic. Baseline skin barrier function was established by measuring TEWL, SC hydration and skin surface pH in first-year White and Black African nursing students prior to the commencement of their practical training. Skin barrier function parameters were measured on the dorsal aspects and palms of both hands and additionally on both volar forearms. Tape strip samples were collected from participants' dominant dorsal hands and NMF content was measured, including histidine (HIS), pyrrolidone carboxylic acid (PCA), trans-urocanic acid (t-UCA) and cis-urocanic acid (c-UCA), as well as cytokines interleukin-1 α (IL-1α) and interleukin-1 receptor antagonist (IL-1RA). NMF components HIS, PCA, t-UCA, c-UCA and total NMF (tot-NMF which is the sum of individual components) were determined by High Performance Liquid Chromatography after extraction with water. A dermatologist clinically evaluated the skin of the participants to diagnose the prevalence and severity of dermatitis among the participants. The presence of erythema, oedema, oozing/crusts, excoriation, lichenification and dryness of the affected skin area were evaluated and a severity score (None = 0; Mild = 1; Moderate = 2; Severe = 3) was designated for each of the six clinical signs (Maximum score = 18). These evaluations were performed at the start of the South African academic year (January) and at the end of the year (November) to assess any change in dermatitis severity.

Results*:* No significant difference in TEWL was established between the White and Black African nursing students. SC hydration was significantly lower ($p \leq 0.05$), and skin surface pH was significantly higher ($p \leq 0.0001$) in Black African nursing students when compared to White students. No statistically significant differences in PCA, t-UCA, c-UCA, IL-1α or IL-1RA were found between Black African and White nursing students. HIS was significantly ($p = 0.001$) higher in White nursing students when compared to Black African students. The ratio of tot-UCA/HIS was significantly higher in Black Africans ($p = 0.0002$), while the ratio of c-UCA/tot-UCA was significantly ($p = 0.0001$) lower when compared to White nursing students. TEWL and SC hydration significantly ($p < 0.001$) decreased over two years in the first-year students, while only specific differences were established for senior students. Skin surface pH varied significantly ($p < 0.001$) over the two years with significant increases (p < 0.031) in the winter months. The only significant difference between White and Black African students was established in skin surface pH, where Black African students had significantly higher ($p < 0.001$) skin surface pH on the dorsal hands. Hand dermatitis prevalence increased with 11% for White and 12% for Black African nursing students after one year of training. Hand dermatitis scores increased significantly ($p < 0.04$) between the start and end of one year of practical training in both racial groups. Black

African nursing students had the highest severity index of 6 at the end of one year of practical training.

Conclusions*:* Black African nursing students had significantly lower baseline SC hydration and higher baseline skin surface pH. Whereas skin barrier function trends over a period of two years and NMF content did not differ significantly between the racial groups, Black African nursing students still had higher hand dermatitis prevalence and severity scores after one year of practical training. The impact of nursing student practical training on skin health was demonstrated among a South African nursing student population, providing valuable and novel findings for a high-risk population of nursing students.

Key terms: Transepidermal water loss, stratum corneum hydration, skin surface pH, natural moisturising factor, trans-urocanic acid, cis-urocanic acid, pyrrolidone carboxylic acid, practical training, tertiary education, hand dermatitis, occupational skin disease, White, Black African, healthcare workers.

OPSOMMING

Titel: Velgrensfunksie van Wit en Swart Afrikaan verpleegkunde studente.

Agtergrond: Daar word van verpleegkunde studente vereis om 'n minimum van 2000 praktiese ure in gesondheidsorgfasiliteite te voltooi gedurende hul vier jaar van tersiêre opvoeding. Daar word van hulle verwag om gereeld hul hande te was en te ontsmet tydens 'n praktiese skof om hospitaal verworwe infeksies by pasiënte te voorkom. Hierdie roetines wat gereelde hande was insluit, in kombinasie met velafskerming deur die dra van lateks of nitriel handskoene, kan 'n negatiewe impak hê op die vel toestand van hul hande. Transepidermale waterverlies (TEWV), stratum korneum (SK) hidrasie en veloppervlak pH is algemene parameters wat ingesluit word by die assessering van die effek van gereelde hande was en velafskerming op die veltoestand. Daar is egter beperkte gepubliseerde literatuur oor die langtermyn effekte van verpleegkunde studente se praktiese opvoeding op velgrensfunksie en hoe velgrensfunksie vergelyk tussen Wit en Swart Afrikaan verpleegkunde studente. Internasionale studies het gefokus op die ondersoek van handdermatitis as 'n gevolg van hierdie toestande by verpleegkunde studente, maar die voorkoms en erns van handdermatitis is nog nie ondersoek in 'n Suid-Afrikaanse verpleegkunde studente populasie nie. Natuurlike bevogtigingsfaktor (NBF) is onlangs gebruik om die risiko vir die ontwikkeling van veltoestande soos dermatitis wat verband hou met lae NBF, te bepaal. Die kwantifisering van NBF in 'n verpleegkunde studente populasie kan waardevolle insig gee met betrekking tot hul potensiële vatbaarheid vir veltoestande wat verband hou met lae NBF. Die evaluering van velgrensfunksie by verpleegkunde studente bied die geleentheid om nie net vroeë veranderinge in hierdie biofisiese parameters tydens hul praktiese opleiding te ondersoek nie, maar kan ook die hulpmiddels verskaf om vroeë intervensies te identifiseer wat hul velgesondheid alreeds aan die begin van hul loopbaan kan beskerm.

Doelstellings en doelwitte: Die doel van hierdie proefskrif was om velgrensfunksie, NBF-inhoud en die voorkoms van handdermatitis tussen Wit en Swart Afrikaan verpleegkunde studente gedurende hul tersiêre opvoeding te kwantifiseer en te vergelyk. Die spesifieke doelwitte het ingesluit (i) om basislyn velgrensfunksie tussen Wit en Swart Afrikaan verpleegkunde studente te vergelyk, (ii) om NBF-inhoud op die vel van die hande tussen Wit en Swart Afrikaan verpleegkunde studente te vergelyk (iii) om die velgrensfunksie van Wit en Swart Afrikaan verpleegkunde studente gedurende die vordering van hul tersiêre opvoeding te evalueer en (iv) om die voorkoms en erns van hand dermatitis onder tersiêre verpleegkunde studente te kwantifiseer.

Metodes: Velgrensfunksie parameters insluitend transepidermale waterverlies (TEWV), stratum korneum (SK) hidrasie en veloppervlak pH is drie keer per jaar in vroulike verpleegkunde studente (63 Wit, 42 Swart Afrikaan) gemeet en vir twee jaar herhaal, voor die COVID-19 pandemie. Basislyn velgrensfunksie is vasgestel deur TEWV, SK hidrasie en veloppervlak pH in eerstejaar Wit en Swart Afrikaan verpleegkunde studente te meet voor die aanvang van hul praktiese opleiding. Velgrenfunksie parameters is op die dorsale aspekte van beide hande gemeet en ook op beide volêre voorarms. Plakker monsters is van deelnemers se dominante dorsale hand versamel en NBF-inhoud is gemeet, insluitend histidien (HIS), pyrrolidoonkarboksiel suur (PKA), trans-urokaniese suur (t-UKA) en cis-urokaniese suur (c-UKA), sowel as sitokiene interleukien-1 α (IL-1α) en interleukien-1 reseptor antagonis (IL-1RA). NBF-komponente HIS, PKA, t-UKA, c-UKA en totale NBF (tot-NBF wat die som van individuele komponente is) is bepaal deur vloeistof chromatografie na ekstraksie met water. 'n Dermatoloog het die vel van die deelnemers klinies geëvalueer om die voorkoms en erns van dermatitis onder die deelnemers te diagnoseer. Die teenwoordigheid van eriteem, edeem, vloeiing/korse, ekskoriasie, likenifikasie en droogheid van die geaffekteerde velarea is geëvalueer en 'n ernstigheidstelling (Geen = 0; Lig = 1; Matig = 2; Ernstig = 3) is vir elk van die ses kliniese tekens (Maksimum telling = 18) toegeken. Hierdie evaluasies is aan die begin van die Suid-Afrikaanse akademiese jaar (Januarie) en aan die einde van die jaar (November) uitgevoer om enige verandering in die ernstigheid van dermatitis te beoordeel.

Resultate: Geen betekenisvolle verskil in TEWV is tussen die Wit en Swart Afrikaan verpleegkunde studente vasgestel nie. SK hidrasie was betekenisvol laer ($p \leq 0.05$) en veloppervlak pH was betekenisvol hoër ($p \leq 0.0001$) in Swart Afrikaan verpleegkunde studente in vergelyking met Wit studente. Geen statistiese betekenisvolle verskille is gevind in PKA, t-UKA, c-UKA, IL-1α of IL-1RA tussen Swart Afrikaan en Wit Suid-Afrikaanse verpleegkunde studente nie. HIS was betekenisvol ($p = 0.001$) hoër in Wit studente in vergelyking met Swart Afrikaan studente. Die verhouding van tot-UKA/HIS was betekenisvol hoër in Swart Afrikane ($p = 0.0002$), terwyl die verhouding van c-UKA/tot-UKA betekenisvol ($p = 0.0001$) laer was in vergelyking met Wit verpleegkunde studente. TEWV en SK hidrasie het betekenisvol ($p < 0.001$) afgeneem oor twee jaar by die eerstejaarstudente, terwyl slegs spesifieke verskille vir senior studente vasgestel is. Veloppervlak pH het betekenisvol ($p < 0.001$) gevarieer oor die twee jaar met betekenisvolle toenames ($p < 0.031$) in die wintermaande. Die enigste betekenisvolle verskil is bevind tussen Wit en Swart Afrikaan studente in veloppervlak pH, waar Swart Afrikaan studente se vel oppervlak pH betekenisvol ($p < 0.001$) hoër was op hulle dorsale hande. Handdermatitis voorkoms het met 11% vir Wit en 12% vir Swart Afrikaan verpleegkunde studente toegeneem na een jaar se opleiding. Handdermatitis ernstigheidstellings het betekenisvol (p < 0.04) toegeneem tussen die begin en einde van een jaar se praktiese opleiding in beide rassegroepe. Swart Afrikaan verpleegkunde studente het die hoogste ernstigheidsindeks van 6 gehad aan die einde van een jaar se praktiese opleiding.

Gevolgtrekkings: Swart Afrikaan verpleegkunde studente het betekenisvolle laer basislyn SK hidrasie en hoër basislyn veloppervlak pH gehad. Alhoewel velgrensfunksie tendense oor 'n tydperk van twee jaar en NBF-inhoud nie betekenisvol verskil het tussen die rassegroepe nie, het Swart Afrikaan verpleegkunde studente steeds hoër handdermatitis voorkoms en ernstigheidstellings gehad na een jaar se praktiese opleiding. Die impak van verpleegkunde studente se praktiese opleiding op velgesondheid is in 'n Suid-Afrikaanse verpleegkunde student populasie gedemonstreer, wat waardevolle en nuwe bevindinge vir 'n hoë-risiko populasie soos verpleegkunde studente verskaf.

Sleutelterme: Transepidermale waterverlies, stratum korneum hidrasie, vel oppervlak pH, natuurlike bevogtigende faktor, trans-urokaniensuur, cis-urokanien suur, pyrrolidoon karboksielsuur, praktiese opleiding, tersiêre opleiding, handdermatitis, beroepsverwante vel siekte, Wit, Swart Afrikaan, gesondheidsorgwerkers.

PREFACE

This thesis is submitted in article format and written according to the requirements of the NWU manual for postgraduate studies and conforms to the requirements preferred by the appropriate journals. The thesis is written according to UK English spelling, with the exception of institutional or organisational names and references that were used as published. Three articles and one short communication are included in this thesis:

Article I: Transepidermal water loss, stratum corneum hydration and skin surface pH of female African and Caucasian nursing students.

Article II: Natural moisturising factor constituents in South African nursing students.

Article III: Skin barrier function of Black African and White nursing students.

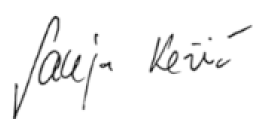
Short communication: Hand dermatitis prevalence and severity in a population of South African nursing students.

The *American Psychological Association* (APA) style is used throughout the main text of the thesis, with the exception of Chapters 3 and 4 which are written according to the AMA referencing style as required by the respective journals. References were compiled with the Endnote™ x8.2 (PDF Tron™ Systems Inc, Philadelphia) software and were checked for consistency with the large language model software Bing AI (Microsoft Corporation, Redmond WA). Details on the requirements of the reference styles can be found at the beginning of Chapters 3 to 6 of this thesis.

For the purpose of this thesis the term race is used for groups of people with similar physical features and skin colour (Anand S.S., 1999. Using ethnicity as a classification variable in health research: perpetuating the myth of biological determinism, serving socio-political agendas, or making valuable contributions to medical sciences? Ethnic Health; 4:241-244). White is used for participants with light pigmented skin and Black African for participants with dark pigmented skin. However, at the time of publication of Article I (Chapter 3) in 2019, Caucasian and African were the accepted terms for participants with light pigmented and dark pigmented skin respectively and were used as such. When discussing other published literature, the racial terms would be used as published.

The contributions of the listed co-authors and their consent for use in this thesis are given in Table 1. The relevant editors or publishers granted permission for the use of the published material, and proof thereof is given in the Annexure C.

Table 1: Contributions of the different authors and consent for use.

Author	Contributions of co-authors	Consent*
M.M. Young	Responsible for the planning of the experimental method and design of the study under supervision. Responsible for data collection by performing experimental studies. Responsible for data analysis and interpretation of results. First author of articles included in Chapters 3 to 6. Responsible for writing the thesis.	
A. Franken	As Promoter planned and designed the study in collaboration with the candidate (student) and other promoters. Assisted with data interpretation and supervised the writing of articles and thesis.	
J.L. Du Plessis	As Co-promoter assisted in planning the study in collaboration with the candidate and other promoters. Assisted with data interpretation and supervised the writing of articles and thesis.	
L. Reichert	Responsible for clinical evaluation and diagnosing skin conditions of the participants of the study. Gave a critical review of the article included in Chapter 6 as co-author.	
S. Kezic	Responsible for NMF and cytokine analyses and assistance with data interpretation. Gave a critical review of the article included in Chapter 4 of the thesis as co-author.	
I. Jakasa	Responsible for NMF and cytokine analyses and assistance with data interpretation. Gave a critical review of the article included in Chapter 4 of the thesis as co-author.	

* I declare that I have approved the chapter/article(s) and that my role in the study as indicated above is representative of my actual contribution, and that I hereby give my consent that it may be published as part of the thesis of Miss. M.M. Young.

The outline of the thesis is as follows:

- Chapter 1 – General introduction with background, research aims and objectives, and hypotheses.
- Chapter 2 – A literature study on topics relevant to this thesis.
- Chapter 3 – Article I entitled: Transepidermal water loss, stratum corneum hydration, and skin surface pH of female African and Caucasian nursing students, published in *Skin Research and Technology*.
- Chapter 4 – Article II entitled: Natural moisturising factor constituents in South African nursing students. Submitted to Contact Dermatitis for publication.
- Chapter 5 – Article III entitled: Skin barrier function of Black African and White nursing students. Submitted to *Journal of Dermatology Nurses' Association* for publication.
- Chapter 6 – Short communication entitled: Hand dermatitis prevalence and severity in a population of South African nursing students. Submitted to *Workplace Health & Safety* for publication.
- Chapter 7 – The conclusion with recommendations, limitations and recommendations for future studies.
- Annexures A to E – Ethics approval, turn-it in reports, permission for use of copyright material, evidence of submission of articles to peer-reviewed journals and declaration of language editing.

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF UNITS

%	percent/percentage
a.u.	arbitrary units
°C	degrees Celsius
$g \cdot m^{-2} \cdot h^{-1}$	grams per square metre per hour
mmol/g protein	millimoles per gram of protein
N	Newton force
µg/ml	micrograms per millilitre
t	time interval

LIST OF ABBREVIATIONS

≤	less than or equal to
<	less than
>	more than
CI	Confidence intervals
COVID-19	Coronavirus disease of 2019
FLG	Filaggrin gene
GM	Geometric mean
HIS	Histidine
IL	Interleukin
IL-1α	Interleukin-1 alpha
IL-1RA	Interleukin-1 receptor antagonist
Ig-E	Immunoglobulin type E
JDNA	Journal of Dermatology Nurses’ Association
MCI	methylchloroisothiazolinone
MRSA	methicillin-resistant *Staphylococcus aureus*
NMF	Natural moisturising factor
NRF	National Research Foundation
PCA	Pyrrolidone carboxylic acid
SANC	South African Nursing Council

LIST OF ABBREVIATIONS (CONTINUED)

SC	Stratum corneum
SLS	Sodium Lauryl Sulphate
SDS	Sodium Dodecyl Sulphate
TEWL	Transepidermal water loss
Tot-NMF	Total natural moisturising factor
Th-1	T-helper cells type 1
Th-2	T-helper cells type 2
TSLP	Thymic stromal lymphopoietin
t-UCA	Trans-urocanic acid
c-UCA	Cis-urocanic acid
UCA	Urocanic Acid
UV	Ultra-violet radiation
UV-B	Ultra-violet B radiation

CHAPTER 1 GENERAL INTRODUCTION

1.1 Introduction

Skin barrier function of nursing students has garnered significant interest during the span of the previous decade (Held *et al.*, 2001; Hachem *et al.*, 2002; Schmid *et al.*, 2005). Following the COVID-19 pandemic, the investigation of skin barrier function and occupational skin diseases of nursing students and healthcare workers has been conducted with increased rigor and depth (Babić *et al.*, 2022; Šakić *et al.*, 2022). This is due to the irritant and allergic effects associated with the conditions that healthcare workers are experiencing during their practical training and subsequent career at healthcare facilities (Lee *et al.*, 2013). These include wet work tasks such as bathing patients, frequent cleansing and disinfecting their hands with soaps and alcohol-gel rubs, and skin occlusion when wearing latex and nitrile medical gloves to prevent nosocomial infections (Department of Health, 2020).

Frequent hand washing, skin occlusion and wet work have been established to significantly affect skin barrier function (Fartasch, 1997; Fartasch *et al.*, 2012). These include elevated transepidermal water loss (TEWL), decreased stratum corneum (SC) hydration and elevated skin surface pH (Barel *et al.*, 2001; Gloor *et al.*, 2004), which indicate compromised skin barrier function. Research on these conditions has been expanded towards the molecular mechanisms behind the compromised skin barrier function and subsequent skin diseases including atopic and contact dermatitis, which included investigations on changes in natural moisturising factor (NMF). NMF is comprised of hygroscopic amino acids and their derivatives which act as osmolytes by drawing water into the SC (Monteiro-Riviere, 2010). NMF therefore not only plays a critical role in maintaining SC hydration, but also one of the NMF components, urocanic acid (UCA) is responsible for maintaining SC pH (Elias & Schmuth, 2009). As with skin barrier function, skin occlusion, Sodium Lauryl Sulphate (SLS) and n-propanol exposure significantly decrease NMF content (Angelova-Fischer *et al.*, 2016).

The development of occupational skin diseases in healthcare workers is consistent with expectations due to the compromised skin barrier function and reduction of NMF associated with exposure to detergents, wet work and skin occlusion (Angelova-Fischer *et al.*, 2016; Babić*et al.*, 2022). Significant risk factors to develop occupational contact dermatitis were identified in Ethiopian healthcare workers including hand wash frequency, number of pairs of gloves used per day, personal allergy and lack of health and safety training (Mekonnen *et al.*, 2019). Frequent hand washing, young age, history of atopic dermatitis and duration of glove wearing were also identified as risk factors for hand eczema in Korean healthcare workers. This study identified hand eczema symptoms in 75.6% of the participants, but only 31% of participants self-reported hand eczema (Lee *et al.*, 2013). Hand eczema prevalence was established to be higher among nurses, with 68% of healthcare workers that self-reported hand eczema, and of these 76% were nurses (Longuenesse *et al.*, 2017). In Croatia, 49% of final year apprentice nurses had clinical symptoms of hand eczema, while only 46% were self-reported by the participants (Šakić *et al.*, 2022). Apprentice nurses' hand eczema prevalence increased from 23% to 31% after three years of practical training in Dutch healthcare facilities (Visser *et al*., 2014)

Studies on hand eczema prevalence among nurses and nursing students have been conducted worldwide, but currently there are limited published literature on skin barrier function and occupational skin diseases among South African nursing students. Furthermore, the nursing workforce of South Africa is predominantly composed of Black African females (South African Nursing Council [SANC], 2022), and literature on how skin barrier function compare between White and Black African skin remains contradictory and inconclusive (Darlenski & Fluhr, 2012; Alexis *et al.*, 2021). Most of the opposing findings on racial differences in skin barrier function is the result of different methodologies employed including different instrumentation and anatomical positions measured by the studies (Alexis *et al.*, 2021). Two studies that measured baseline TEWL on the volar forearms of White and Black African participants established no significant difference between the racial groups (Berardesca *et al.*, 1991; Warrier *et al.*, 1996). However, these studies were conducted on a small number of participants more than 20 years ago and newer research with modern equipment would be necessary before any conclusions can be drawn on racial variation in skin barrier function. It is noteworthy to mention that most studies that investigated racial variation in skin barrier function were conducted among African Americans and White Americans (Wesley & Maibach, 2003; Alexis *et al.*, 2021), and skin compensatory mechanisms related to environmental and geographical factors may play a significant role when comparing international studies. For example, low ambient environmental humidity levels significantly affect TEWL and SC hydration (Chou *et al.*, 2005). It is therefore imperative to consider environmental factors such as ambient relative humidity during the studies before drawing any conclusions on racial variation in skin barrier function, and published findings of skin barrier function in a South African population are limited.

Considering the integral role that NMF plays in maintaining SC hydration and SC pH, insight into how NMF content compares among racial groups in a South African population is crucial before assessing the skin condition of a specific population under conditions that may alter skin barrier function and NMF. NMF content has been quantified in a South African population, but is limited to two studies (Thawer-Esmail *et al.*, 2014; Raj *et al.*, 2016). Thawer-Esmail *et al.* (2014) investigated associations between NMF content, loss-of-function mutations on the filaggrin gene (FLG) and atopic dermatitis, while Raj *et al.* (2016) compared facial SC NMF content between South African ethnicities and established higher NMF content in Black Africans. These studies did not evaluate a population that is frequently exposed to detergents and wet work, and Raj *et al.* (2016) did not measure NMF content on an anatomical position that is frequently exposed to these conditions. As it has been established that NMF content is affected by skin occlusion, SLS and n-propanol exposure (Angelova-Fischer *et al.*, 2016), further research is necessary in a high risk population such as nursing students.

South African nursing students are required to complete 2000 working hours in healthcare facilities during their four years of tertiary (university) education (SANC, 2005). During their practical training in healthcare facilities, they are required to frequently wash and disinfect their hands to prevent nosocomial infections. There is no published information available on how skin barrier function compares between White and Black African South Africans. There is no information available on how skin barrier function changes with the progression of nursing students' tertiary education, specifically for those with dark pigmented skin. Compromised skin barrier function in nursing students, may have a substantial influence on their quality of life as it may precede occupational skin diseases such as hand dermatitis. Studies on hand dermatitis prevalence in nursing students have been conducted worldwide, but no data exists for South African nursing students. Furthermore, nursing students with intrinsically low NMF content may be more susceptible to hand dermatitis but NMF content has not been evaluated before in a South African nursing student population. Quantification of nursing students' skin barrier function and NMF content, may contribute towards preventing occupational skin diseases in nursing students.

For the purpose of this thesis the term race is used for groups of people with similar physical features and skin colour (Anand, 1999), where White is used for participants with light pigmented skin and Black African for participants with dark pigmented skin. Racial terms would be used as published when discussing other published literature.

1.2 Research aims and objectives

1.2.1 General aim

The general aim of this study is to quantify and compare skin barrier function, NMF content and hand dermatitis prevalence between South African White and Black African nursing students during their tertiary education.

1.2.2 Specific objectives

The specific objectives of this study are:

1. To compare baseline skin barrier function between White and Black African nursing students.
2. To compare NMF content of the skin on the hands between White and Black African nursing students.
3. To evaluate the skin barrier function of White and Black African nursing students during the progression of their tertiary education.
4. To quantify hand dermatitis prevalence and severity among tertiary nursing students.

1.3 Hypotheses

Hypothesis 1: TEWL is the accepted and primary parameter to evaluate skin barrier function (Pirot & Falson, 2004). However, controversy still exists in literature on how baseline TEWL compare between the racial groups, due to variation in methodology and anatomical positions measured (Alexis *et al.*, 2021). Two studies that measured baseline TEWL on the volar forearms of participants, established no significant difference in TEWL between White and Black Africans (Berardesca *et al.*, 1991; Warrier *et al.*, 1996). Therefore, it is hypothesised that no significant difference exists in baseline skin barrier function (based on TEWL) between White and Black African nursing students.

Hypothesis 2: NMF content has been measured on the facial stratum corneum of a South African population and it was observed that Black Africans had higher NMF content when compared to Caucasians (Raj *et al.*, 2016). It is hypothesised that NMF content is higher on the hands of Black African nursing students when compared to White nursing students.

Hypothesis 3: Nurses are subjected to wet work and skin occlusion, which have been identified as risk factors for compromised skin barrier function (Fartasch *et al.*, 2012). Babić *et al.* (2022) established elevated TEWL in apprentice nurses during the COVID-19 pandemic. It is, therefore, hypothesised that skin barrier function on the hands of White and Black African nursing students deteriorate, as measured by an increase in TEWL, over a two-year period during the progression of their tertiary education.

Hypothesis 4: Visser *et al.* (2014) established an increase of hand eczema cases in nursing students during the progression of their studies. It is hypothesised that hand dermatitis in White and Black African nursing students increases in prevalence and severity within a one-year period of their tertiary education.

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CHAPTER 2 LITERATURE STUDY

2.1 Introduction

Skin barrier function refers to the skin's natural defence mechanism to protect the body against endogenous water loss and exogenous influences from the environment (Bouwstra, 1997). However, when the skin's natural defences are overwhelmed by environmental insults, it may result in skin diseases (Bouwstra & Ponec, 2006). This is especially prevalent in the healthcare sector where healthcare workers are expected to frequently wash their hands and perform wet work tasks. These conditions disrupt skin barrier homeostasis and may result in occupational skin diseases (Hachem *et al.*, 2002; Symanzik *et al.*, 2022a). Occupational skin diseases are generally considered to be under-reported in South Africa (Carman & Kruger, 2008). However, South African workers have spent between R20 to R900 per month to treat their occupational skin diseases (Rose & Rees, 2014). A recent review of national occupational disease statistics in South Africa revealed one case each of irritant contact dermatitis and allergic contact dermatitis between 2015 and 2020. This review included data from the national compensation fund and selected companies' voluntary corporate social responsibility disclosures (Rikhotso *et al.*, 2022a). Statistics from the national compensation fund showed a decreasing trend in occupational skin diseases with 217 cases compensated for in 2001 and 45 cases compensated for in 2009. After 2009 no occupational skin disease cases were compensated for. The authors noted that in the absence of a functional national health surveillance system, it was difficult to estimate the number of occupational diseases in South Africa (Rikhotso *et al.*, 2022b).

South African nursing students are required to complete 2000 hours of practical training in hospitals during their tertiary degree studies (South African Nursing Council [SANC], 2005). Wet work, exposure to chemicals and frequent hand washing may disrupt their skin barrier function or even cause skin disease before their career starts as a healthcare worker. Nursing students, as a study population, provides an opportunity to investigate the risk of occupational skin diseases caused by frequent hand cleansing and wet work in a South African population. This chapter discusses the available information on skin barrier function, the effect of frequent hand cleansing and wet work on skin barrier function, natural moisturising factor (NMF), as well as the occupational skin diseases prevalent in nursing students and the published literature on the skin care intervention of these diseases.

For the purpose of this thesis the term race is used to groups of people with similar physical features and skin colour (Anand, 1999), where White is used for participants with light pigmented skin and Black African for participants with dark pigmented skin. Racial terms would be used as published when discussing other published literature.

2.2 Skin barrier function

The skin's barrier function primarily resides in the stratum corneum (SC) which consists of flattened enucleated corneocytes embedded in a lipid matrix (Bouwstra & Ponec, 2006). These components protect against endogenous water loss in two ways: Firstly, the enucleated corneocytes form a protein meshwork with tonofilaments and keratohyalin aggregated by filaggrin. Filaggrin is also metabolised into pyrrolidone carboxylic acid (PCA) and urocanic acid (UCA) which are hygroscopic amino acids, thus attracting water to keep the skin naturally hydrated. These amino acids are the major constituents of the natural moisturising factor (NMF) of the skin. Secondly, the lipid matrix forms a hydrophobic barrier which prevents transdermal diffusion of water (Tagami, 2010; Voegeli & Rawlings, 2023). This transdermal diffusion of water is used to measure the state of the skin barrier function, namely transepidermal water loss (TEWL). TEWL excludes water loss through perspiration and therefore represents the condition of the skin's barrier (Pirot & Falson, 2004). Skin barrier function is further discussed by describing the formation of the SC, endogenous and exogenous factors influencing skin barrier function, and racial differences in skin barrier function.

2.2.1 Formation of the stratum corneum

The stratum corneum is formed through a process known as keratinisation, when the keratinocytes from the stratum basale differentiate and move upward to the stratum corneum. During this process, the volume of the keratinocytes increases while lamellar vesicles, tonofilaments, and keratohyalin are formed. The lamellar vesicles contain glycosphingolipids, phospholipids, free sterols and catabolic enzymes. As the cytoplasm volume increases, the nuclei disintegrate, and the lamellar vesicles discharge their content into the extracellular space. The tonofilaments and keratohyalin form a protein meshwork which is aggregated into tight bundles by filaggrin. The end result is protein enriched cells filled with the tonofilaments and keratohyalin, surrounded by the lipids secreted by the lamellar vesicles. These protein enriched cells i.e. corneocytes, are interlinked by corneodesmosomes that help protect against mechanical stress and are essential for the desquamation process of the SC. The lipids secreted by the lamellar vesicles are broken down to non-polar lipids including ceramides, cholesterol and free fatty acids (Proksch *et al.*, 2008; Monteiro-Riviere, 2010). These lipids lie parallel to the cell surface of the corneocytes and are covalently bound to involucrin, further enhancing the impermeability of the SC (Nemes *et al.*, 1999; Proksch *et al.*, 2008). The process of SC formation is important to understand how it is influenced by various endogenous and exogenous factors that may result in a perturbed skin barrier function.

2.2.2 Factors influencing skin barrier function.

There are numerous endogenous or exogenous factors that may have an impact on skin barrier function by altering the protein component or the lipid matrix. Skin barrier function is often described according to TEWL; however, a multi-parametric approach is recommended to describe the state of the barrier function in its entirety (Darlenski *et al.*, 2009). Therefore, factors influencing TEWL are discussed as well as factors influencing SC hydration and skin surface pH.

2.2.2.1 TEWL

Endogenous factors that influence TEWL include age, anatomical position, circadian rhythm, race and skin health amongst others (du Plessis *et al.*, 2013). TEWL is only influenced by age after 60 years when TEWL gradually decreases (Wilhelm *et al.*, 1991; Farinelli & Berardesca, 2006). This may be due to enlarged corneocytes and increased thickness of the SC observed in elderly persons that may be related to an impaired desquamation process after the age of 60 (Farinelli & Berardesca, 2006).

Evidence of the influence of circadian rhythm on TEWL remains inconclusive as there is limited published literature available. Higher TEWL values have been measured during the evening (≈ 20:00) and lower TEWL during the morning between 08:00 and 10:00 (Yosipovitch *et al.*, 1998). However, another study found that the diurnal variation is related to the change in skin temperature (Spruit, 1971). The Spruit (1971) study was limited to two time points, whereas Yosipovitch *et al.* (1998) monitored TEWL every two hours for 24 hours.

TEWL varies on different anatomical positions as skin thickness and physiology vary between these positions (Pinnagoda *et al.*, 1990; Farinelli & Berardesca, 2006). SC thickness on different anatomical body positions may not be a simple inverse proportional relationship (decrease in TEWL as SC thickness increases), as there are other physiological factors that play a role, e.g., eccrine sweat gland activity (Pinnagoda *et al.*, 1990). For example, TEWL is higher on the palms, where the SC is generally thicker, when compared to TEWL measured on the dorsum of the hand. Furthermore, low TEWL values have been measured on the ventral forearms, the scalp, spinal area and the calf, while high TEWL have been measured on the palms, arch of feet and axillae (Kleesz *et al.*, 2011). All these areas vary in SC thickness and eccrine sweat gland activity and exposure to the environment. Recently, a significant positive non-linear correlation was established between SC hydration and TEWL, once SC hydration exceeds a threshold level. However, this relationship was only established on the palms of participants and may contribute to the anatomical variation of TEWL (Mayrovitz, 2023). Variation of TEWL between anatomical positions is therefore a combination of these factors rather than a single determinant (Farinelli & Berardesca, 2006; Kleesz *et al.*, 2011).

As mentioned above, SC hydration has also been established to influence TEWL, as a positive non-linear relationship has been established between TEWL and SC hydration when a threshold level of SC hydration (> 60 a.u.) was exceeded. However, this relationship was only determined on the palmar thenar eminence of male participants, as SC hydration did not exceed the proposed threshold level in female participants nor on the volar forearms of the participants (Mayrovitz, 2023). It has been proposed that the diffusion coefficient for SC water increases as the SC water content increases (Blank *et al.*, 1984). This principle of water diffusion through the SC may be applied to the opposite phenomenon where extremely low SC water content might cause low TEWL. A study that evaluated apprentice hairdressers' skin barrier function for three years established a decrease in TEWL after work-related exposure to wet work (John *et al.*, 2000), which is opposite to what is expected as an increase in TEWL is normally associated with a surfactant irritation and wet work (Gloor *et al.*, 2004; Fartasch *et al.*, 2012).

Discrepancies in literature on TEWL variation between racial groups emerge when studies with different methodologies (e.g., anatomical position measured, interventions used) are compared to each other. Therefore, racial differences in TEWL are discussed by only comparing studies with similar methodologies i.e., *in vivo* human studies, TEWL as measured on the volar forearm and only baseline TEWL values will be compared. In a study conducted with 15 Africans, 12 Caucasians and 12 Hispanics, no significant difference in TEWL was determined at the baseline between the racial groups (Berardesca *et al.*, 1991). These results were later substantiated by a study conducted with 30 African women and 30 Caucasian women, establishing no significant difference in TEWL as measured on their forearms. However, it is noteworthy that TEWL was lower in African women although not statistically significant (Warrier *et al.*, 1996). No difference in TEWL does not necessarily indicate that the structure and physiological processes of African and Caucasian skin are the same. African skin, for instance, have more cell layers, a greater overall lipid content in the SC, but a lower number of ceramides (Berardesca & Maibach, 2003). Even though ceramide content has been established to inversely correlate with TEWL, it does not automatically point towards an elevated TEWL in Africans as observed in the *in vivo* studies discussed. This suggests that there are other compensating mechanisms at play that might enhance their skin barrier function e.g., increased cell layers in the SC (Weigand *et al.*, 1974). A higher rate of spontaneous desquamation was also revealed in African skin which suggests a higher recovery rate of the SC and altered intercellular cohesion (Corcuff *et al.*, 1991). These results have been replicated in a more recent study that determined a higher barrier recovery rate in Africans after tape stripping. This study also established higher cohesion in African skin as more tape strips were required to disrupt their barrier function to the same extent as that of Caucasian participants (Gunathilake *et al.*, 2009).

Exogenous factors influencing TEWL include, skin washing and wet work, skin occlusion, skin damage, cigarette smoking and environmental factors such as air convection, temperature, relative humidity, direct light, and seasons (du Plessis *et al.*, 2013). TEWL of non-smokers was found to be significantly lower than smokers' TEWL and no difference in TEWL was determined between active and passive smokers (Muizzuddin *et al.*, 1997).

Skin health generally deteriorates during winter as SC lipids, sebum and SC hydration all decrease, SC stiffness and scaliness are higher (Engebretsen *et al.*, 2016). Consequently, skin barrier function also declines during winter indicated by increased TEWL (Black *et al.*, 2000). However, when low ambient temperature and relative humidity's effect on TEWL are examined separately, contradicting results emerge. Low ambient temperature does not significantly change TEWL (Roure *et al.*, 2012), while low relative humidity decreases TEWL (Chou *et al.*, 2005), indicating towards an improvement of skin barrier function. This may be an adaptation mechanism as SC thickness, synthesis of lamellar bodies and lipids all increased in a study conducted on hairless mice (Denda *et al.*, 1998). Similar compensatory mechanisms were seen in a study conducted on factory workers exposed to ultra-dry working environments. TEWL significantly decreased within half a month of exposure to the ultra-dry working environments (relative humidity = 1.5%), for 12 hours a day. The workers' TEWL slowly recovered after ten months of working in the factory but was still lower than the control group's TEWL after 20 months (Chou *et al.*, 2005). This may be of interest for South African workers especially in the North-West province where the average relative humidity ranges between 39 – 45%, as calculated for 2017 and 2018 (World Weather Online, 2018). People living and working in these environmental conditions may have adapted to these conditions through the compensatory mechanisms explained, and this should be kept in mind when comparing their skin barrier function with international results.

Skin cleansing with common hand wash soaps which include active ingredients such as Sodium Lauryl Sulphate (SLS) and Sodium Dodecyl Sulphate (SDS) or with alcohol gel rubs may cause significant morphological changes in the skin affecting its barrier function (Fartasch, 1997). Surfactants such as SLS or SDS induce changes in the lamellar arrangement of lipids in the SC or alters the keratinisation process (Fartasch, 1997; Törmä *et al.*, 2008). These morphological changes maybe the cause of an increase of TEWL observed after SLS treatment, indicating a disturbed barrier function for up to seven to nine days after treatment (Gloor *et al.*, 2004). Elevated TEWL was also observed in participants exposed to water for 7 days (Fartasch *et al.*, 2012), while skin occlusion alone does not significantly alter TEWL (Fartasch *et al.*, 2012; Weistenhofer *et al.*, 2015). Long term exposure to water causes hyperhydration of the SC, characterised by enlarged corneocytes, corneodesmolysis and larger intercellular spaces (Antonov *et al.*, 2012). Skin occlusion alone may not increase TEWL, however in circumstances where co-exposure to water and soaps exists, the effects may be worse than exposure to only one of these factors. One explanation may be the reservoir effect that soaps have on the skin when occlusive gloves are worn after the skin cleansing. Lodén *et al.* (2003), established that the quantity of soap that remained on the skin after rinsing is enough to induce barrier impairment. These conditions are especially prevalent in healthcare settings where healthcare workers are expected to frequently wash their hands and wear occlusive gloves to prevent nosocomial infections (Pittet, 2001). The combined influence of these factors was evident when a group of nursing staff's TEWL was compared to that of administrative workers. The nurses' TEWL was significantly higher on all test sites when compared to the administrators (Hachem *et al.*, 2002). The pathology during these circumstances is discussed in more detail in Section 2.4.1.

TEWL is affected by skin health as numerous skin diseases are characterised by increased TEWL such as ichthyotic disorders, atopic and contact dermatitis, burns and psoriasis (Rogiers, 2001; Babić *et al.*, 2022). Not surprisingly, this is due to skin homeostasis that is disrupted during these diseases that result in an alteration in the lipid bilayers or corneocyte cohesion (Boguniewicz & Leung, 2011). Skin barrier function will therefore also be compromised in occupational skin diseases, when working conditions overwhelm the skin's natural defence mechanisms and result in a pathological condition e.g., irritant or contact dermatitis (Antonov *et al.*, 2012). The specific working conditions of healthcare workers and the resulting skin conditions are discussed further in Section 2.4.

2.2.2.2 SC hydration

Age, race, anatomical region, circadian rhythm, and skin health are endogenous factors that influence SC hydration (du Plessis *et al.*, 2013). SC hydration naturally decreases with age, although this varies between anatomical regions. The difference in SC hydration in elderly people is more pronounced on anatomical regions exposed to the environment e.g., sun exposed skin (Farinelli & Berardesca, 2006). A study which evaluated skin biophysical parameters between two age groups (29 years and 74 years) established SC hydration to be lower in the older age group on the upper eyelid and perioral area, but significantly higher on the forearm (Marrakchi & Maibach, 2007). SC hydration also varies between different anatomical regions within the same age group, with the lowest values measured on the scalp and the highest values on the spinal area, elbow flexure, cheek, axilla and on the forehead (Kleesz *et al.*, 2011). This variation can also be explained by the variation in skin structure and function of the various anatomical regions as explained in Section 2.2.2.1 where TEWL was discussed. Evidence on the influence of circadian rhythm in SC hydration is still unclear (du Plessis *et al.*, 2013). Yosipovitch *et al.* (1998), detected no circadian rhythm for SC hydration while Le Fur *et al.* (2001) indeed detected a circadian rhythm. However, Le Fur *et al.* (2001) only detected rhythmicity when SC hydration was evaluated within an 8-hour period as no significant rhythmicity was established for a 24 hour period, similar to the Yosipovitch *et al.* (1998) study which could not establish significant rhythmicity of SC hydration over a 24 hour period (Yosipovitch *et al.*, 1998; Le Fur *et al.*, 2001).

Racial differences in SC hydration are also still inconclusive (Wesley & Maibach, 2003). Berardesca *et al.* (1991) established that Africans have higher SC hydration than Caucasians as measured on their dorsal forearm. Warrier *et al.* (1996) and Manuskiatti *et al.* (1998) could not determine a significant difference in SC hydration on any of the measured anatomical regions (including the forearms), between Africans and Caucasians at baseline. A key difference between these studies is that the Berardesca *et al.* (1991) study used conductance to measure SC hydration while (Warrier *et al.*, 1996) and (Manuskiatti *et al.*, 1998) both used capacitance to measure SC hydration (Berardesca *et al.*, 1991; Warrier *et al.*, 1996; Manuskiatti *et al.*, 1998). As these instruments use different measuring principles and measure at different frequencies it should be taken into consideration when comparing studies (Berardesca *et al.*, 1997). The findings of the studies that determined no significant difference in SC hydration between racial groups correspond with the same studies that also determined no significant difference in TEWL between the racial groups evaluated (Berardesca *et al.*, 1991; Warrier *et al.*, 1996). However, there are circumstances where the relationship between TEWL and SC hydration might be misleading. As seen in a study conducted under ultra-low humidity levels, TEWL significantly decreased (indicating an improvement of skin barrier function), while SC hydration also significantly decreased (Chou *et al.*, 2005). This is an important consideration when comparing the skin biophysical parameter of racial groups in South Africa where inland regions' ambient relative humidity levels are below 60% (World Weather Online, 2018). In South Africa the cultural and socioeconomic status of the racial groups must also be considered when assessing their skin condition. SC hydration might be influenced by the socioeconomic status of participants as this determines the type and frequency of cosmetic products purchased. Caucasian women with a higher occupational status were established to be more likely to buy expensive cosmetic products (Chao & Schor, 1998). Cultural habits in South Africa, for example, include Africans being raised to use petrolatum for dry skin (as determined from the questionnaires of the present study) which may have an impact on their overall skin health and therefore SC hydration.

Similar to TEWL, SC hydration is influenced by exogenous factors including cigarette smoking, skin occlusion, skin washing and wet work, as well as environmental factors such as air convection, temperature, relative humidity, direct light and seasons (du Plessis *et al.*, 2013). The skin hydration of women smoking between 11 and 20 cigarettes a day was significantly lower than that of non-smokers (Wolf *et al.*, 1992). Seasonal variation of SC hydration is well established, as skin hydration decreases during the dry months of winter (Engebretsen *et al.*, 2016). SC water content has been determined to decrease at low temperatures, however the relationship was stronger when relative humidity levels were below 60% (Spencer *et al.*, 1975).

The relationship between SC water content and relative humidity levels depends on three characteristics of the SC i.e., the hydrophobic barrier formed by the lipid bilayers, the water-holding capacity of the SC through hygroscopic amino acids and the corneodesmosomes that are responsible for the SC's tortuosity that determines the water distribution in the SC (Tagami, 2010; Vyumvuhore *et al.*, 2013). These factors respectively determine the diffusibility of water in the SC as well as the ratio of water molecules bound to hygroscopic amino acids and the free water molecules. The optimal lipid arrangement and ratio of bound and unbound water were determined at relative humidity levels of approximately 60%, corresponding to the maximum binding capacity of the SC (Vyumvuhore *et al.*, 2013). As discussed in Section 2.2.2.1, low ambient relative humidity levels may have a significant impact on skin health. Persons living in regions with low ambient relative humidity levels may have decreased SC hydration as the ratio of bound and unbound water may be distorted.

Exposure to skin cleansers with active ingredients such as SLS or SDS decreases skin hydration by either removing the lipids from the SC (Ananthapadmanabhan *et al.*, 2013) or by degrading the protein structures in the SC (Fartasch, 1997), thus compromising the water holding capacity of the SC. In the Fartasch (1997) study, molecular changes in the SC were evaluated after SDS and acetone treatment respectively. They established that after SDS treatment, the upper lipid bilayers remained intact, while significant damage was done to the nucleated cells of the epidermis. Furthermore, acetone treatment resulted in compromised intercellular lipids at all levels of the SC (Fartasch, 1997). This corresponds to a study conducted on lipid removal by surfactants that determined that only small amounts of lipids were removed after SLS and Alkyl Benzene Sulfonate (LAS) treatment (Froebe *et al.*, 1990). However, fatty acids were released at a higher rate than the other lipids, suggesting that fatty acids, which form part of the lower fluid portion of the SC lipid bilayers, are more extractable than the lipids in the upper bilayers of the SC (Froebe *et al.*, 1990; Ananthapadmanabhan *et al.*, 2013).

Another mechanism of dehydration after surfactant exposure is the penetration of anionic surfactants which bind to corneocyte proteins. This process enhances the hyperhydration of the SC, resulting in swelling of corneocytes. After surfactant treatment the subsequent diffusion of the water molecules to the surrounding environment results in rapid dehydration of the SC if the ambient humidity is low. As this happens at a rapid rate rather than a normal diffusion rate, it causes the bonds between corneocytes and the lipid matrix to loosen, which compromises the diffusional barrier and subsequently causes dry skin (Ananthapadmanabhan *et al.*, 2013). Nevertheless, numerous studies conducted on surfactant induced damage concluded that it results in decreased SC hydration (Fulmer & Kramer, 1986; Boyce *et al.*, 2000; Gloor *et al.*, 2004; Ananthapadmanabhan *et al.*, 2013). When different cleansing regimens are compared to evaluate their effect on skin hydration, interesting findings emerge. For instance, when a soap and water routine is compared to alcohol hand gel, the soap and water routine significantly decreased SC hydration while alcohol gel rub had no significant impact (Boyce *et al.*, 2000). Evidence also exists that exposure to water alone may disrupt the internal environment of the SC. As described earlier, exposure to water causes hyperhydration of the SC, swelling of corneocytes and disruption of the lipid bilayers (Warner *et al.*, 2003). However, the compounding effect of soap and water should be considered. If hyperhydration occurs (due to water exposure) and the lipid bilayers are compromised by subsequent degradation of covalent bonds between the corneocytes and the lipid matrix, cracks are formed that enable surfactants to induce more damage in the deeper layers of the SC (Warner *et al.*, 2003; Ananthapadmanabhan *et al.*, 2013). The same principle applies to skin occlusion. Skin occlusion alone does not significantly affect SC hydration (Wetzky *et al.*, 2009; Fartasch *et al.*, 2012) and interestingly clinical studies found that the combination of skin occlusion, wet work and SLS irritation also did not significantly alter SC hydration (Fartasch *et al.*, 2012). However, when skin hydration is evaluated in a non-clinical setting such as in a population that is occupationally exposed to these conditions, the impact on SC hydration is observed. The SC hydration of hospital workers was assessed in a cross-sectional study and was significantly lower when compared to office workers (Hachem *et al.*, 2002).

SC hydration is altered by skin health as numerous skin diseases such as atopic and contact dermatitis, ichthyosis vulgaris are the result of impaired molecular pathways responsible for hydrating the skin causing an inflammatory response associated with these diseases (Elias & Schmuth, 2009; Boguniewicz & Leung, 2011). One of these pathways is when a null mutation occurs on the FLG gene encoding filaggrin. This leads to a decreased natural moisturising factor (NMF) including urocanic acid (UCA) and pyrrolidone carboxylic acid (PCA) which are hygroscopic amino acids responsible for attracting water molecules to keep the SC hydrated (Boguniewicz & Leung, 2011). The detailed mechanism of filaggrin and NMF is discussed in Section 2.3, but it is worth discussing the implications on SC hydration. A study which measured SC hydration and TEWL in 44 children with atopic dermatitis, established that the SC hydration is significantly lower than that of the control group and TEWL significantly higher (Hon *et al.*, 2008). Individuals with low NMF content due to a genetic predisposition are vulnerable to skin diseases characterised by low SC hydration including atopic dermatitis and contact dermatitis (Eberlein-Konig *et al.*, 2000). SC hydration provides an objective measure of the skin's ability to retain moisture and is a critical parameter when assessing skin health, particularly during cases of contact and atopic dermatitis.

2.2.2.3 Skin surface pH

Skin surface pH is influenced by endogenous factors such as anatomical region, gender, age, race, skin health, circadian rhythm and exogenous factors including wet work, skin cleansing and environmental factors i.e. seasons (Stefaniak *et al.*, 2013). Circadian rhythmicity was determined for skin surface pH as skin surface pH tends to be higher in the afternoon (between 14:00 and 16:00) and lower during the evening (20:00). This diurnal variation of skin surface pH may be indicative of the circadian rhythmicity of SC enzymes (Yosipovitch *et al.*, 1998), as there are numerous pH dependant enzymes in the SC (Schmid-Wendtner & Korting, 2006). As with TEWL and SC hydration, skin surface pH also varies between anatomical regions as the structure and function of the skin varies between anatomical regions (Farinelli & Berardesca, 2006; Stefaniak *et al.*, 2013). Skin surface pH was established to be lowest on the forehead and highest on the dorsal hand (Kleesz *et al.*, 2011). Results on gender differences in skin surface pH are contradicting (Stefaniak *et al.*, 2013). One study found no significant difference in skin surface pH between males and females as measured on their foreheads and cheeks (Zlotogorski, 1987). Another study found that women had significantly higher skin surface pH than men as measured on the forearms (Jacobi *et al.*, 2005). Although these studies differ in anatomical regions measured, studies available with similar methodologies are sparse (Stefaniak *et al.*, 2013), and more data on gender related differences in skin surface pH are required to clarify the discrepancies. Age related differences in skin surface pH have been established as skin surface pH measured in an older population was higher as measured on the forehead, chin and forearm (Marrakchi & Maibach, 2007). Another study determined that a significant difference in skin surface pH only presented in the age group over 80 years (Zlotogorski, 1987).

Evaluating racial differences in skin surface pH should be approached in the same way that racial differences in TEWL were evaluated. Discrepancies emerge when studies are compared that measured skin surface pH on different anatomical regions and utilised different interventions. Two studies established no significant difference in skin surface pH between African and Caucasian participants as measured on the volar forearm at baseline (Warrier *et al.*, 1996; Berardesca *et al.*, 1998). Differences in skin surface pH are present when various interventions are employed or when different anatomical regions are measured. For example, the Berardesca *et al.* (1998) study established lower skin surface pH in Africans after tape stripping, while no significant difference was established at baseline. Warrier *et al.* (1996) also established lower skin surface pH in Africans, but the difference was measured on the cheeks of the participants and skin surface pH did not differ significantly on the volar forearms. Comparing skin surface pH during interventions or on anatomical regions where variability of skin biophysical parameters is well known, is challenging, because the difference in skin surface pH cannot be attributed to race with certainty as it may rather be a combination of various factors that may play a role in skin surface pH variability.

Natural skin surface pH i.e., skin surface pH measured when refraining from skin cleansing and use of cosmetic products, is approximately 4.7 (Lambers *et al.*, 2006). The use of alkaline soaps and detergents to cleanse skin generally raises skin surface pH as the pH of soaps ranges from 9 to 11 depending on the type of soap (Dlova *et al.*, 2017). However, this effect only seems to present in the long term. Evaluation of skin surface pH with bioengineering methods determined no significant difference 24 hours after cleansing with a standard soap (Symanzik *et al.*, 2022a), while another study found a small but significant increase in skin surface pH after 10 weeks of daily use of standard soap (Barel *et al.*, 2001). Similar results were established in a study that compared the bathing of intensive care unit (ICU) patients with a standard cleanser and with an acidic cleanser (pH of 5.5), where the skin surface pH was higher in patients washed with standard soap (Duncan *et al.*, 2013). Interestingly no significant difference was determined between the standard soap and acidic cleanser's effect on micro-flora of the skin (Duncan *et al.*, 2013). The most recent study that investigated the long-term effect of skin occlusion on skin surface pH was Wetzky *et al.* (2009) which found that skin surface pH increased after seven days of skin occlusion with natural rubber latex gloves (Wetzky *et al.*, 2009). This corroborates earlier studies that also established an increase in skin surface pH after skin occlusion (Aly *et al.*, 1978; Hartmann, 1983).

The significance of skin surface pH in the context of skin conditions is currently a subject of contention. Initial research indicated an elevation in skin surface pH associated with atopic and contact dermatitis (Stefaniak *et al.*, 2013; Proksch, 2018). This was corroborated recently by a study that also demonstrated higher skin surface pH in patients with lesional and non-lesional atopic dermatitis when compared to controls (Jurakic Toncic *et al.*, 2020). The physiological mechanism underlying the elevated skin surface pH observed in atopic dermatitis is linked to low levels of NMF (Kezic *et al.*, 2011), as UCA (a component of NMF) is a known acidifier of the SC (Elias, 2010). However, a Spanish research team determined no significant difference in skin surface pH between healthy people and patients with atopic dermatitis (Montero-Vilchez *et al.*, 2021), whereas Cannavò *et al.* (2017) established lower skin surface pH in patients with psoriasis (Cannavò *et al.*, 2017). Elevated skin surface pH is also observed in irritant contact dermatitis (Schmid-Wendtner & Korting, 2006). Elevated skin surface pH was measured on the cheeks of participants who have skin that is objectively sensitive and prone to irritation, when compared to healthy volunteers (Seidenari *et al.*, 1998). Elsner *et al.* (1990) also found that skin surface pH increased on the forearms of participants two and three days after SLS irritation. The study also established that skin surface pH and blood flow were the best predictors for vulvar irritant contact dermatitis (Elsner *et al.*, 1990). Exposure to alkaline detergents such as SLS causes irritant contact dermatitis by raising skin surface pH which increases serine proteases activity e.g., KLK5 and KLK7 which are enzymes that affect desquamation and lipid synthesis (Jakasa *et al.*, 2018). Desquamation is affected by serine proteases due to the breakdown of DSG1, a structural protein responsible for corneodesmosomes formation (Elias & Schmuth, 2009). Whereas an increase in serine proteases activity causes the degradation of beta-glucocerebrosides and acidic sphingomyelinase, two enzymes responsible for lipid processing in the SC (Holleran *et al.*, 1994).

These enzymatic changes during conditions of elevated skin surface pH were confirmed in a study that assessed serine proteases activity after a prolonged increase in skin surface pH in male Skh1/Hr mice (Hachem *et al.*, 2005). The evidence of increased skin surface pH associated with skin diseases such as atopic and contact dermatitis is compelling, with numerous studies establishing this finding, and the physiological mechanisms supporting the premise. However, the two studies that contradicted these findings (Cannavò *et al.*, 2017; Montero-Vilchez *et al.*, 2021) still bring into question if more research is necessary or if a standardised protocol should be established when measuring skin surface pH in clinical research.

2.3 Natural moisturising factor (NMF)

Natural moisturising factor (NMF) is a collective term for hygroscopic amino acids and their derivatives that act as osmolytes by drawing water into the SC (Harding & Rawlings, 1999). This function of NMF hydrates the SC and together with the hydrophobic barrier created by SC lipids are the two main mechanisms of natural hydration of the SC (Monteiro-Riviere, 2010). Two main components of NMF used in clinical research are pyrrolidone carboxylic acid (PCA) and urocanic acid (UCA), the metabolites of filaggrin (Tagami, 2010). UCA also plays a role in maintaining SC pH in the optimum acidic range of 4.5 to 5.6 (Schmid-Wendtner & Korting, 2006; Elias & Schmuth, 2009). NMF is formed when filaggrin is hydrolysed during cornification above the stratum compactum to produce arginine, glutamine, and histidine. Arginine is then converted to citrulline, glutamine to PCA and histidine is deaminated to produce trans-urocanic acid (t-UCA). Ultraviolet-B (UV-B) radiation causes photoisomerisation of t-UCA to cis-UCA, which functions as an endogenous sunscreen (Elias & Schmuth, 2009; Elias, 2010).

Decreased NMF levels hold serious implications for skin health as low NMF levels are associated with skin diseases characterised by decreased SC hydration and increased skin surface pH, viz. atopic dermatitis and contact dermatitis (Eberlein-Konig *et al.*, 2000). To understand the intricate immune pathways and consequences of low NMF content, this section first discusses the genetic predisposition associated with atopic dermatitis. These principles are then applied to the conditions caused by environmental factors and the implications thereof for contact dermatitis. Atopic dermatitis, asthma, and allergic rhinitis are generally associated with the genetic predisposition to produce increased immunoglobulin-E (Ig-E) in response to hapten exposure (Boguniewicz & Leung, 2011). Atopic dermatitis has been strongly associated with a loss-of-function mutation on the filaggrin gene (FLG) (O'Regan *et al.*, 2009). A loss-of-function mutation on FLG leads to a compromised skin barrier, and consequently increases the risk of hapten penetration (Breuer & Werfel, 2012).

As mentioned, non-functional filaggrin and consequential decrease of NMF content cause low SC hydration and elevated skin surface pH as illustrated in Figure 2-1. Elevated skin surface pH increases serine proteases activity and breaks down corneodesmosomes and lipid processing enzymes compromising the structural integrity of the SC and increasing hapten penetration. This activates the production of primary cytokines namely interleukin-1α (IL-1α) and IL-1β which contributes to the inflammation associated with atopic dermatitis (Elias & Schmuth, 2009). Hapten exposure also stimulates thymic stromal lymphopoietin (TSLP) secretion which is a T-helper cell type 2 (Th-2) attracting cytokine. Th-2 cells secrete IL-4 and IL-13 which are cytokines that are not only associated with impaired barrier function but may also be responsible for the immune dysregulation in atopic dermatitis (Boguniewicz & Leung, 2011). IL-4 inhibits ceramide secretion and the expression of structural proteins including filaggrin and desmoglein-3 (Howell *et al.*, 2008; Kabashima, 2013). Furthermore, IL-4 and IL- 13 also downregulate IL-17 and antagonise the IL-17 induced expression of anti-microbial peptides such as human β-defensin (He *et al.*, 2009; Nograles *et al.*, 2010). A Th-2 mediated response stimulates cytokines that elicits pruritus / itching, which will create further physical barrier disruption due to scratching. Elevated skin surface pH and decreased human β-defensin decrease the antimicrobial defence of the skin. This positive feedback loop and consequences of loss-of-function mutation on FLG are illustrated in Figure 2-1 (next page).

Due to the decrease in microbial defence of the skin during these conditions, methicillin-resistant *Staphylococcus aureus* (MRSA) infections were found to be more prevalent among nurses with atopic dermatitis (Brans *et al.*, 2016). It has been observed that MRSA exhibits a stronger affinity towards corneocytes with low NMF. This is attributed to the corneocytes that are enveloped by a thick layer of nanoscale villus protrusions (Feuillie *et al.*, 2018). This affects the spread of pathogens in hospitals, as nurses with atopic dermatitis are more likely to harbour MRSA bacteria on their hands, posing a higher risk of transmission to patients. In addition, nurses with occupational skin diseases such as hand eczema may not adhere to proper hand hygiene protocols as it may exacerbate the skin condition (Pittet, 2001). This may be either a contributing factor or worsen the fact that the most common route for MRSA transmission is through skin contact (Solberg, 2000).

The preceding section discussed the immune dysregulation and the implications of a loss-of-function mutation on FLG in relation to atopic dermatitis. However, this immune pathway is not exclusive to a loss-of-function mutation on FLG. Environmental factors that result in a decrease in NMF would hold similar consequences i.e., elevation of skin surface pH, decreased microbial defence and SC hydration, (as illustrated in Figure 2-1).

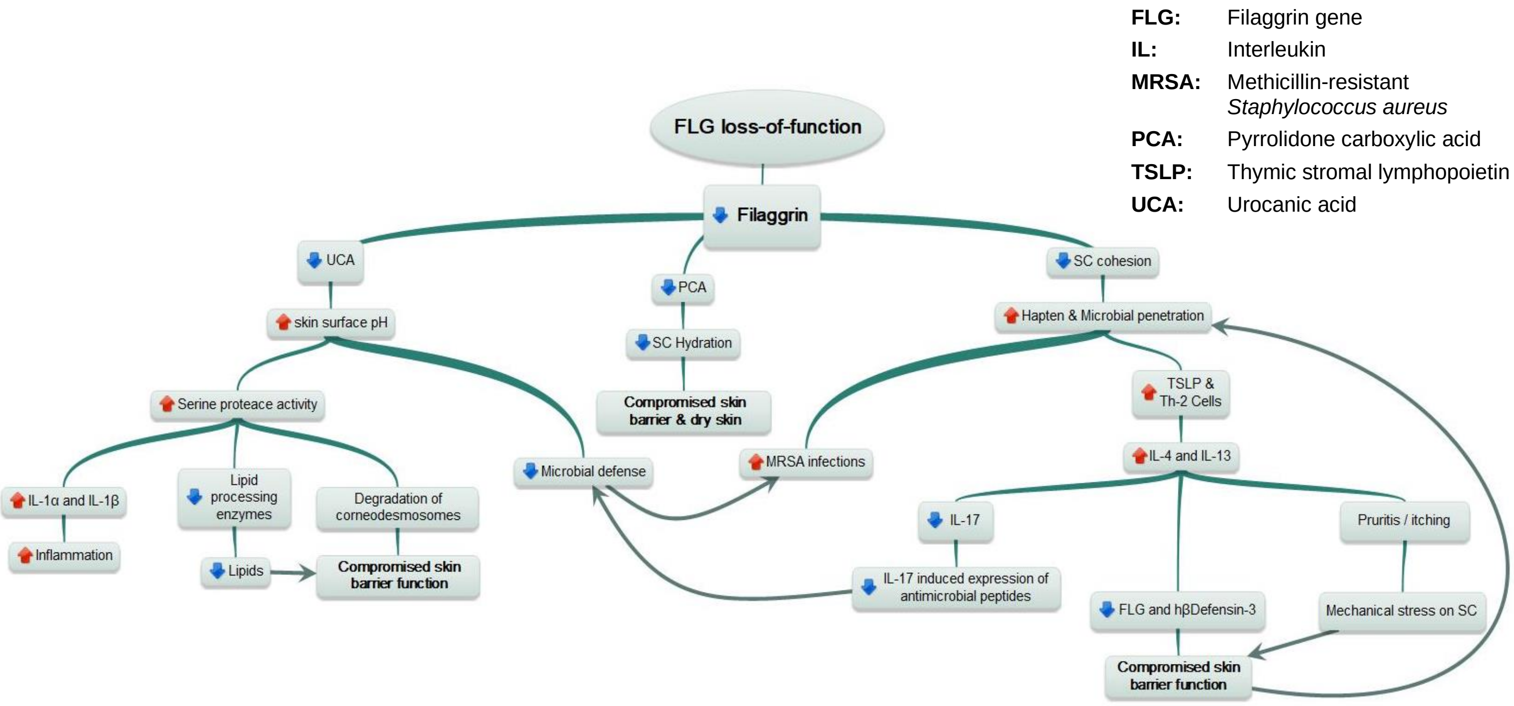

Figure 2-1: Flow diagram of FLG loss-of-function consequences and immune dysregulation during atopic dermatitis (Adapted from: He *et al.,* 2009; Boguniewicz & Leung, 2011; Kabashima, 2013).

A study that assessed the effect of common skin sensitisers on NMF, established that SLS and methylchloroisothiazolinone (MCI), a preservative used in personal care products, reduced NMF significantly after 3 days (Koppes *et al.*, 2017). These findings were corroborated in another study that investigated the effect of skin occlusion, n-propanol and SLS on NMF content. NMF decreased significantly after exposure to n-propanol and SLS, while skin occlusion significantly worsened the effect of the irritants on NMF (Angelova-Fischer *et al.*, 2016). However, these findings have not been replicated in occupational settings. NMF levels were not able to predict the development of hand eczema in metal workers in a two-year prospective cohort study (Reich *et al.*, 2020). Another study could also not establish an association between NMF content and improvement of contact dermatitis in healthcare workers after the 12 month follow up (Soltanipoor *et al.*, 2019). This was corroborated by Visser *et al.* (2014a), who could not establish a direct correlation between hand eczema risk and FLG mutations. However, this study did find that the risk of hand eczema increased if the nursing students had a history of atopic dermatitis (Visser *et al.*, 2014a). This once again emphasises the complex interaction between the inflammation associated with atopic dermatitis and contact dermatitis that arises from frequent exposure to hand soaps, skin occlusion and wet work prevalent in healthcare settings and is discussed further in Section 2.4.1.

Racial differences in NMF content may implicate different susceptibility to skin diseases associated with low NMF. In an American population, FLG loss-of-function mutations were found in 27.5% of white participants compared to only 5.8% of African American participants (Margolis *et al.*, 2012). Interestingly, the prevalence of atopic dermatitis in an American population was significantly higher in African Americans even though their FLG loss-of-function mutations were six times less than European Americans (Brunner & Guttman-Yassky, 2019). This may suggest that other factors play a role in the pathogenesis of atopic dermatitis in individuals of African ancestry. An *in vitro* study determined that filaggrin was more expressed and processed in Caucasian epidermis when compared to Black African epidermis. This study also indicated that several enzymes involved in processing filaggrin were differently modulated in Caucasian and Black African skin, which may result in different NMF levels in the two groups (Girardeau-Hubert *et al.*, 2019). Different modulation of filaggrin processing enzymes may be one possible explanation for higher atopic dermatitis prevalence in African Americans that loss-of-function FLG mutations alone cannot explain. When comparing *in vivo* NMF levels, one study established that Black Africans have significantly higher PCA levels than Caucasians (Raj *et al.*, 2016) which could be related to the higher prevalence of FLG loss-of-function mutations in Caucasians. This suggests that racial differences in skin health and disease susceptibility may be influenced by factors beyond FLG loss-of-function mutations, including variations in NMF content and the modulation of enzymes involved in filaggrin processing.

In South African amaXhosa patients with atopic dermatitis, similar results were observed, where the patients had no FLG mutations but still had lower PCA and UCA levels. The authors hypothesised that there might be an interplay between systemic Th-2 cell inflammation and FLG suppression in this population (Thawer-Esmail *et al.*, 2014), as illustrated in Figure 2-1. Based on the available literature, there have been only two studies (Thawer-Esmail *et al.*, 2014; Raj *et al.*, 2016) conducted within the South African population that have measured NMF levels. Given the limited published literature, it is evident that further research in this area is necessary. This will not only fill the existing knowledge gap but also potentially contribute to improved health outcomes in the South African population.

2.4 Skin barrier function of nursing students

The previous sections discussed specific factors that influence skin barrier function. This section elaborates on the conditions specifically prevalent in healthcare settings and how these conditions affect the skin barrier function of nursing students. Skin barrier function of nursing students has been extensively investigated internationally (Held *et al.*, 2001; Visser *et al.*, 2014b; Šakić *et al.*, 2022), not only to identify the genesis of the skin pathology associated with healthcare workers, but also to identify the potential of early intervention on nursing students' skin health (Moldovan *et al.*, 2021). Furthermore, younger age has been identified as a risk factor for occupational skin diseases (Ibler *et al.*, 2012; Lee *et al.*, 2013), as hand eczema prevalence was higher in assistant nurses below the age of 40 (Flyvholm *et al.*, 2007). NMF increases with age (Howard *et al.*, 2022), further contributing to the age-related risk for developing occupational skin disease, and low NMF has been associated with atopic dermatitis risk (Thawer-Esmail *et al.*, 2014). The importance of investigating nursing students' skin health and skin barrier function is apparent and available literature on this topic is reviewed in the following section.

2.4.1 Skin pathophysiology of nursing students

Nursing students' skin barrier function is affected during their practical training in healthcare facilities as they are required to frequently wash their hands with soap and water, disinfect with alcohol gel rubs and perform wet work tasks as part of their duties. All these factors affect skin barrier function parameters including TEWL, SC hydration and skin surface pH, as discussed in previous sections. A study that investigated self-reported symptoms of hand dermatitis and concurrent TEWL in apprentice nurses, found that self-reported hand dermatitis increased from 36.5% to 43.3% after three years of practical training. TEWL also significantly increased after three years with the nurses that had hand dermatitis symptoms in the final follow-up. However, nurses without hand dermatitis symptoms did not show changes in TEWL in three years (Schmid *et al.*, 2005). In another cross-sectional study, TEWL was significantly higher and SC hydration significantly lower in nurses when compared to hospital administrative workers (Hachem *et al.*, 2002).

These changes in skin barrier function parameters due to the exposure to hand soaps, skin occlusion and wet work are substantiated by studies that investigated skin disease prevalence in healthcare workers. Occupational-related contact dermatitis prevalence among Ethiopian healthcare workers was 31.5%. This study identified that hand washing frequency, number of pairs of gloves used per day, personal history of allergy and lack of health and safety training to be significant contributors to hand dermatitis risk in the population (Mekonnen *et al.*, 2019). Similar risk factors were identified in the healthcare staff of a hospital in Taiwan, where individuals with a history of atopic dermatitis had a 3.76-fold risk of developing hand dermatitis. This study also identified frequency of hand washing as a significant risk factor for hand dermatitis (Lan *et al.*, 2011). Hand eczema prevalence among healthcare workers in a Denmark hospital was 21% and was positively associated with working hours, history of atopy, younger age and male sex (Ibler *et al.*, 2012). In a Korean hospital, the self-reported prevalence of hand eczema was 31%, and it was associated with factors such as young age, a history of atopic dermatitis, frequent hand washing, and the duration of glove wearing. It's noteworthy that in this study, hand eczema symptoms were clinically diagnosed in 75.6% of the participants. However, only 31% of participants self-reported having hand eczema (Lee *et al.*, 2013). In France, 68% of healthcare workers reported hand dermatitis at the Nantes University Hospital. Among this group, nurses were particularly affected, with a notably higher prevalence rate of 76% (Longuenesse *et al.*, 2017). These concerning findings are also prevalent in apprentice or student nurses who just started their career in healthcare. In a three-year longitudinal study, the prevalence of hand eczema in apprentice nurses was 23% in the first year, 25% in the second year and 31% in the third year of the study (Visser *et al.*, 2014b). A study conducted during the COVID-19 pandemic established that 49% of final year apprentice nurses were clinically diagnosed with hand eczema, while only 46% of the participants self-reported hand eczema (Šakić *et al.*, 2022).

The challenges faced by healthcare personnel, particularly nurses, due to their duties are universal. Numerous studies (Lee *et al.*, 2013; Longuenesse *et al.*, 2017; Šakić *et al.*, 2022) have highlighted an alarmingly high prevalence of hand eczema among nursing staff, emphasising the significant occupational health issue this represents in the healthcare sector. Furthermore, there is a significant discrepancy between self-reported hand eczema and clinically diagnosed hand eczema. From these studies it appears that the incidence of self-reported hand eczema tends to be much lower than that of clinically diagnosed cases, highlighting the potential for underreporting of hand eczema in healthcare workers.

2.4.2 Skin care intervention for nursing students

Numerous intervention studies have been conducted to prevent hand eczema prevalence in healthcare workers. These studies focussed on providing education and training in appropriate hand hygiene routines, correct glove use and the use of moisturisers and emollients during the working shift. Studies that focussed solely on education and training, found significant beneficial changes in skin barrier function and hand eczema severity scores in the intervention groups. Held *et al.* (2001) established no significant change in TEWL in the intervention group of student nurses who was given an educational programme, while the control group had a significant increase in TEWL after 10 weeks. Another study which provided an educational programme for nurses working in geriatrics found that hand eczema significantly decreased (from 26% to 17%) after 12 months in the intervention group (Dulon *et al.*, 2009). When emollients and an educational programme were provided to healthcare workers, no new hand eczema cases were observed in the intervention group, while 12 new cases were identified in the control group after six months. This study also reported lower hand eczema scores in the intervention group than in the control group (Symanzik *et al.*, 2022b). Two studies (Soltanipoor *et al.*, 2019; Moldovan *et al.*, 2021) evaluated the effectiveness of the use of emollients to reduce hand eczema prevalence in healthcare workers. In their study design, both the intervention and control group received educational materials and lectures on hand hygiene routines and the use of emollients, but only the intervention group received additional access to emollients to use during their shift. Soltanipoor *et al.* (2019) assessed the healthcare workers Hand Eczema Severity Index (HECSI) scores and NMF levels and found no change in NMF levels after one year. However, HECSI scores decreased in the intervention group from 6.2 points to 4.2 points after one year (Soltanipoor *et al.*, 2019). Moldovan *et al.* (2021) assessed HECSI scores, TEWL and SC hydration in nursing students. Hand eczema reduced from 19.1% to 11.34% in the intervention group and increased from 19.6% to 59.52% in the control group. TEWL decreased after three months in the intervention group and increased in the control group. In addition, SC hydration increased in the intervention group and decreased after three months in the control group (Moldovan *et al.*, 2021).

Based on the published literature, both educational programmes and the use of emollients significantly improve the skin health outcomes for healthcare workers. Burke *et al.* (2018) evaluated which factors influence nurses to use moisturisers during a work shift. Their study observed that the use of moisturisers during work, improved when nurses believed that it is part of their professional duty to apply hand moisturiser frequently. Ninety-six percent of the participants were aware that dermatitis increased the risk of skin pathogens and 76% of the participants agreed that moisturisers reduced the risk of dermatitis. Despite their awareness, the use of moisturisers remained low as only 15% of nurses reported the use of moisturisers. The authors were unable to determine the cause of low moisturiser use, as the consensus is that a lack of knowledge may be the cause, but the study showed a high level of knowledge and understanding (Burke *et al.*, 2018).

Recently, the South African Department of Health and the National Institute for Communicable Diseases (NICD), published a practical manual for infection prevention and control to be implemented in healthcare facilities. This manual contains practical instructions to prevent healthcare associated infections, as well as guidelines for healthcare workers to protect their skin health. Healthcare facilities are therefore, required to provide hand soaps, alcohol-based hand disinfectants and emollients for healthcare workers to use during their working shift, under these guidelines (Department of Health, 2020). Furthermore, the Occupational Health and Safety Act 85 of 1993 requires employers to provide information, instruction, and training to employees regarding the health risks associated with their duties and how to use control measures to prevent these risks (Occupational Health and Safety Act 85 of 1993). Healthcare facilities which require their employees to frequently wash and disinfect their hands, as well as perform wet work tasks, are legally required to provide information, instruction, and training to their employees regarding the dermatitis risk and the importance of emollient use during a work shift. This would not only benefit the employees' skin health, but also protect the patients in their care. Hand dermatitis increases the risk of transmission of skin pathogens, as MRSA bacteria were established to be more prevalent on the hands of nurses with atopic dermatitis (Brans *et al.*, 2016). The maintenance of skin barrier function and prevention of hand dermatitis among healthcare professionals are therefore imperative for infection control in healthcare facilities and to protect the health of employees.

2.5 Conclusion

Numerous studies illustrated that the conditions experienced by nursing students during their practical training in healthcare facilities, affects their skin barrier function including TEWL, SC hydration and skin surface pH. Due to the nature of their work, nursing students are a high-risk population to develop occupational skin diseases. Studies that investigated occupational skin diseases in a nursing student population have been done world-wide, however literature in the South African population is limited. There are discrepancies in literature on how NMF is affected in an occupational setting where frequent hand washing, and wet work are prevalent. Additional discrepancies exist on how TEWL, SC hydration, skin surface pH and NMF content differ between White and Black Africans. Longitudinal studies on how skin barrier function changes during nursing students' practical training have not been done before in dark pigmented/African skin. Understanding key changes in skin barrier function and NMF content in a South African nursing student population is imperative before practical intervention can take place.

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CHAPTER 3 ARTICLE I.

Young, M.M., Franken, A., Du Plessis, J.L. Transepidermal water loss, stratum corneum hydration, and skin surface pH of female African and Caucasian nursing students. 2019. Skin Research and Technology; 25:88-95. https://onlinelibrary.wiley.com/doi/10.1111/srt.12614

3.1 Background

Conflicting evidence exists on how skin barrier function compare between White and Black African skin and more fundamental research is necessary to clarify some of the contradictory findings. In South Africa most of the nursing workforce is Black African, and research on the racial differences in skin barrier function is required before any skin care recommendations can be made to improve their occupational skin health. The prevalence of occupational skin diseases tends to increase during the tertiary education of nurses (as their practical training hours increase) and research on their skin barrier function may elucidate the physiological development of the disease. This article investigated how skin barrier function compares between Black African and White nursing students, prior to their practical training and was published in Skin Research and Technology (15 Citations according to Wiley as on 8/11/2023), which is the official journal of International Society for Bioengineering and the Skin (ISBS). Preliminary findings of this article were also presented at the Society of Cosmetic Chemists (CosChem) annual conference during 2018. Title of oral presentation: Interaction between skin surface pH and skin hydration in African and Caucasian nursing students.

3.2 Instructions for authors (excerpt)

Skin Research and Technology is a clinically oriented journal on biophysical methods, imaging, skin pharmacology and radiation therapy techniques and how they are used in dermatology, plastic surgery and in cosmetic and pharmaceutical sciences.

Conflict of Interest: The journal requires that all authors disclose any potential sources of conflict of interest. Any interest or relationship, financial or otherwise that might be perceived as influencing an author's objectivity is considered a potential source of conflict of interest. These must be disclosed when directly relevant or directly related to the work that the authors describe in their manuscript. Potential sources of conflict of interest include but are not limited to: patent or stock ownership, membership of a company board of directors, membership of an advisory board or committee for a company, and consultancy for or receipt of speaker's fees from a company. The existence of a conflict of interest does not preclude publication. If the authors have no conflict of interest to declare, they must also state this at submission. It is the responsibility of the corresponding author to review this policy with all authors and collectively to disclose with the submission ALL pertinent commercial and other relationships.

Manuscript structure: Structured abstract; Introduction; Materials and Methods; Results; Discussion; Conclusion Acknowledgements; References; Tables; List of figure captions*; List of supporting information legend.

Figure Legends: Legends should be concise but comprehensive – the figure and its legend must be understandable without reference to the text. Include definitions of any symbols used and define/explain all abbreviations and units of measurement.

Figures: Although authors are encouraged to send the highest-quality figures possible, for peer-review purposes, a wide variety of formats, sizes, and resolutions are accepted.

References: All references should be numbered consecutively in order of appearance and should be as complete as possible. In text citations should cite references in consecutive order using Arabic superscript numerals:

Journal article

1. Nedelec B, Forget NJ, Hurtibise T, et al. Skin characteristics: normative data for elasticity, erythema, melanin, and thickness at 16 different anatomical locations. Skin Res Technol 2016;22:263-275.

Book

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Internet Document

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3.3 Transepidermal water loss, stratum corneum hydration, and skin surface pH of female African and Caucasian nursing students.

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ORIGINAL ARTICLE

WILEY

Transepidermal water loss, stratum corneum hydration, and skin surface pH of female African and Caucasian nursing students

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Abstract

Background: Conflicting evidence exists on how skin barrier function compares between Africans and Caucasians. This study measured skin barrier function of South African first year nursing students before their practical training started to compare skin barrier function between the racial groups.

Methods: Transepidermal water loss (TEWL), stratum corneum (SC) hydration, and skin surface (SS) pH was measured on female first year nursing students (19 African and 31 Caucasian; age range 18-40 years). Geometric means and ranges were calculated and the influence of anatomical areas and racial differences were evaluated respectively.

Results: No significant difference in TEWL was established between the racial groups. SC hydration was significantly lower ($P \le 0.05$) and SS-pH was significantly higher ($P \le 0.0001$) in African nursing students when compared to Caucasians. African nursing students had significantly lower ($P \le 0.05$) SC hydration on their palms when compared to the other anatomical areas.

Conclusion: Stratum corneum hydration and SS-pH differed significantly between African and Caucasian skin, while no difference was found for TEWL, the primary parameter used to evaluate skin barrier function. Low SC hydration and high SS-pH of African nursing students prior to their practical training, may suggest a higher risk for developing occupational skin diseases.

KEYWORDS

nursing students, racial differences, Skin barrier function

1 | INTRODUCTION

Skin barrier function refers to the ability of the skin to protect against environmental assaults and to prevent endogenous water loss.[1] This barrier function primarily resides in the stratum corneum (SC), which is organised in the commonly known "brick-and-mortar" structure. The "brick-and-mortar" model describes the components of the stratum corneum as proteins ("bricks") embedded in a lipid matrix ("mortar").[2] The protein component consists of enucleated corneocytes filled with keratin filaments and water, which is surrounded by the second component, that is, lipids; including ceramides, free fatty acids, and cholesterol.[3] These lipids are arranged parallel to the corneocytes and provide a hydrophobic barrier, preventing endogenous water loss, and the proteins act as osmolytes by attracting water, thus creating two defences against endogenous water loss.[4] Skin barrier function is assessed by measuring the amount of endogenous water that diffuses outward through the SC, and with an intact barrier the transepidermal water loss (TEWL) is limited.[1]

On the volar forearm healthy baseline TEWL ranges between 13 g m^{-2} h^{-1} and 25 g m^{-2} h^{-1} but varies on other anatomical positions.[5] Other skin surface biophysical measurements may also provide more information on the condition of the SC. For example, SC hydration describes the current hydration of the SC, and may be an indication if the hydrophobic barrier and water-holding capacity of the SC are functioning optimally.[6] SC hydration values above 40 a.u. are considered as an indication of healthy skin.[7] Furthermore, skin surface pH describes the pH environment on the skin surface and consequently, if the lipid-processing enzymes are functioning within the optimum acidic pH range necessary to synthesise the lipid matrix.[8] The optimal skin surface pH range is between 4.5 and 5.9 for healthy skin,[5,8] however, this range may differ between males and females as the influence of gender is still inconclusive.[9] For this study, skin barrier function is described according to these three parameters.

There are numerous factors that influence skin barrier function, which should be considered when investigating skin barrier function. Exogenous factors to consider include smoking, skin damage, skin washing, skin occlusion, solvents/surfactant exposure, and environmental conditions.[9,10] Low environmental humidity and temperature negatively affects skin barrier function, as increased TEWL and decreased SC hydration have been measured during the winter months.[11] Smoking, exposure to solvents/surfactants and skin washing decrease skin barrier function by increasing TEWL and decreasing SC hydration.[9] Skin washing and occlusion increase skin surface pH,[10] while skin occlusion and prolonged exposure to water increase SC hydration or may even cause hyperhydration of the SC.[12]

Endogenous factors influencing TEWL and SC hydration include age (decrease with age), anatomical position (varies at different anatomical locations), skin health (TEWL increase and SC hydration decrease in diseased skin), skin temperature, and sweating (TEWL and SC hydration increase with elevated skin temperature and sweating).[9] The endogenous factors influencing skin surface pH are age (increase with age),[13,14] anatomical position (varies at different anatomical locations), and skin health (increase in diseased skin).[10] It is unclear if circadian rhythm affects TEWL or SC hydration as there are currently inconclusive supporting evidence.[9] There are also conflicting evidence on the difference of these three parameters between males and females and between racial groups.[9,10]

For this publication only the opposing literature on the difference in skin barrier function between racial groups are discussed. The term race is used here referring to groups with similar physical features and skin colour,[15] where Caucasian is used for light pigmented skin and African for dark pigmented skin. The contradictory findings on the racial differences in skin barrier function may be due to the small number of participants included in studies, different sexes being compared between studies, or different anatomical positions measured.[16] The majority of studies reported higher TEWL in Africans than in Caucasians, however, TEWL was measured on different anatomical positions and different interventions were used in the studies.[17-22]

No significant difference in SC hydration was established between racial groups by two studies, which performed the measurements on the same anatomical regions on female participants and both used the same capacitance measurement method.[23,24] Discrepancies in SC hydration difference between racial groups only present itself if studies are compared that performed SC hydration measurements with different measurement methods (capacitance vs conductance).[16]

Few studies have evaluated racial differences in skin surface pH, however, the findings are also contradictory.[16,25] Berardesca et al[21] found no significant difference in skin surface pH on the volar forearms of Africans and Caucasians, while Warrier et al[23] and Gunathilake et al[25] established lower skin surface pH on the cheeks and forearms of Africans when compared to Caucasians.

Due to the opposing findings in published literature on racial differences in skin barrier function, more fundamental research is necessary to clarify some of the contradictory findings. In South Africa, the majority of the nursing workforce is African,[26] and research on the racial differences in skin barrier function is required before any skin care recommendations can be made to improve their occupational skin health. The prevalence of occupational skin diseases tends to increase during the tertiary education of nurses[27] (as their practical training hours increase) and research on their skin barrier function may elucidate the physiological development of the disease. The aim of this study was to compare skin barrier function between African and Caucasian nursing students, prior to their practical training and subsequent wet work in the hospitals.

Table 1. Participant skin colour classifications according to self-reported race, L^*a^*b colour space value (L^*) and skin pigment types

Race	N	L^* value range	Skin pigment type[26]
Caucasian	31	58.68-70.46	II-III
Indian/Mixed race	4	47.79-59.59	III-IV
African	19	40.88-55.99	IV-VI

2 | METHOD

This study was approved by the Health Research Ethics Committee of the North-West University, South Africa (Ethics approval number: NWU-00337-16-A1).

2.1 | Study population

Female first year nursing students from the North-West University were recruited to participate in this study. Participants were recruited prior to their practical training in the hospitals in order to measure skin barrier function before any influence of daily occupational hand hygiene practices. After obtaining informed consent, 4 Indian/Mixed race, 19 African, and 31 Caucasian first-year nursing students participated in this study. All of the participants were

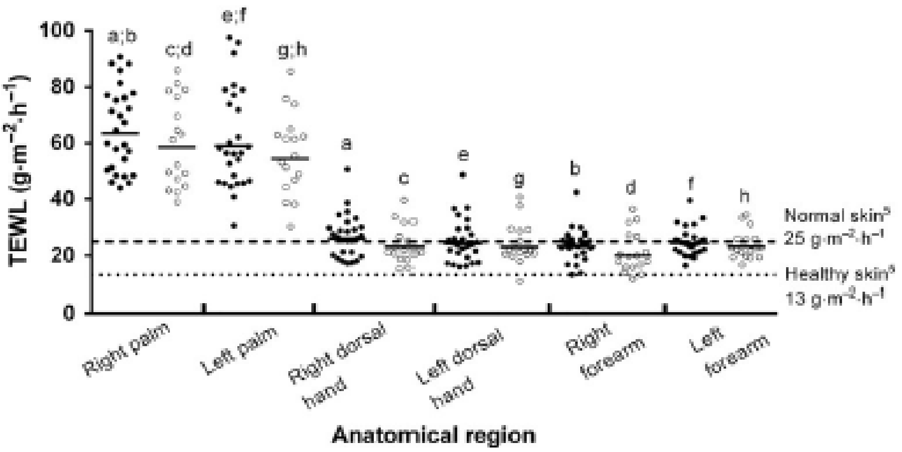

Figure 1. TEWL (GM indicated with solid line) according to anatomical areas for (●) Caucasian and (○) African nursing students. [a-h]Significant differences ($P \leq 0.0001$) in TEWL between indicated anatomical areas

nonsmokers and between the ages 18 and 40 years. The participants were grouped into self-reported racial groups and corresponding skin pigment types (Fitzpatrick scale)[28] as well as colour space values of the Commission International d'Eclairage (CIE) represented by L^*a^*b coordinates, as summarised in Table 1. The L^* value indicates the lightness of the skin (0 = black and 100 = white), the a^* value indicates the range between green and red (green < 0 < red), and the b^* value the range between blue and yellow (blue < 0 < yellow). These values were measured on the volar forearm of the nondominant forearms of the participants with a Colorimeter (CL-400) manufactured by Courage and Khazaka (CK) electronic GmBH, Germany.

2.2 | Skin barrier function measurements

Participants were instructed not to wash and apply any cosmetic products on their hands and forearms 12 hours prior to the measurements. Skin barrier function was measured according to previously published methods[29] and are summarised in this study according to three parameters, that is, TEWL, skin surface pH, and SC hydration. TEWL measurements were performed with a Tewameter® (TM 300), skin surface pH with a skin pH meter (PH 905) and SC hydration with a Corneometer (CM 825), all manufactured and calibrated by Courage and Khazaka (CK) electronic GmBH, Germany.

Participants were allowed to acclimatise for 20 minutes in a climate-controlled room (21-22°C; relative humidity 40-60%). Skin barrier function parameters were measured on the palmar and dorsal aspects of both hands and additionally on both volar forearms. Participants' hands and forearms were chosen as these regions will be subjected to frequent hand washing when the nursing students' practical training starts. These values will, therefore, be comparable with future studies investigating the potential longitudinal changes in skin barrier function of nursing students. An average for each of the skin barrier function parameters were calculated from three consecutive measurements, measured adjacently on the designated anatomical areas. Skin surface pH averages were calculated by using the logarithm of the average of the hydrogen ion concentration.

Additionally, participants were clinically evaluated by a dermatologist to diagnose any pre-existing skin diseases. Participants diagnosed with a skin disease or using oral contraceptives or retinoid medication were excluded from the study, as it has been proven to alter sebum gland activity[30,31] and will therefore influence the skin barrier function measurements. After this exclusion criterion was applied, a total of 27 Caucasian, 17 African, and 3 Indian/Mixed race nursing students' skin barrier function data remained. Skin barrier function data of Indian/Mixed race nursing students were excluded, as there were too few participants of this racial group to enable comparisons with sufficient statistical power.

2.3 | Statistical analyses

The skin barrier function data were not normally distributed, and are therefore, reported as geometric means (GM) and range. The difference in skin barrier function between African and Caucasian nursing students was evaluated with nonparametric Mann-Whitney U tests and the corresponding effect sizes were calculated. Effect sizes are used in empirical research to establish the importance of the statistical significant ($P \leq 0.05$) differences between groups evaluated.[32] Effect sizes were calculated from the Z value divided by the square root of total number of samples. This value represents the proportion of the variance that is accounted for by the independent variable (categorical), that is, small effect ≤0.1; medium effect ≈0.3 or large effect ≥0.5.[33] Spearman rank correlations were used to evaluate monotonic relationships between TEWL, SC hydration, and skin surface pH in the respective racial groups. Correlations were significant if $P \leq 0.05$ and the strength of the relationship were categorised as weak if $r_s = 0.00$-0.39, moderate if $r_s = 0.40$-0.59, and strong if $r_s = 0.60$-1.0[34]

Statistical analyses were performed with Statistica version 13.2 (Statsoft Inc. Palo Alto, California) and figures generated with GraphPad Prism® version 7 (GraphPad Software San Diego, California).

3 | RESULTS

Skin barrier function parameters, that is, TEWL, SC hydration, and skin surface pH were measured for African and Caucasian

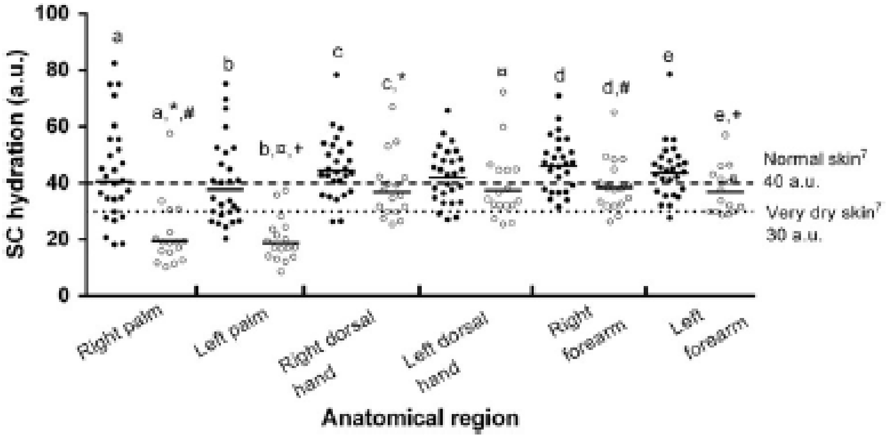

Figure 2. SC Hydration (GM indicated with solid line) according to anatomical area for (●) Caucasian and (o) African nursing students. [a-e]Significant differences ($P \le 0.05$) in SC hydration between two racial groups [*,#,¤,+]Significant differences ($P \le 0.05$) in SC hydration between anatomical areas

nursing students and were grouped according to the anatomical areas (palm, dorsal hand, and volar forearm of both arms). Measurements were conducted in room conditions with a relative humidity between 40 and 60% and room temperature of 21-22°C. Room temperature and relative humidity had no significant influence ($P > 0.05$) on any of the measured parameters. The influence of age and which hand is dominant (Right or Left) in the nursing students also did not have any significant influence ($P > 0.05$) on the measurements.

The TEWL of Caucasian nursing students ranged from 23.22 g $m^{-2} h^{-1}$ to 63.45 g $m^{-2} h^{-1}$, with the lowest TEWL measured on the right volar forearm and the highest on the right palm. African nursing students' TEWL ranged from 20.07 g $m^{-2} h^{-1}$ on the right volar forearm to 58.60 g $m^{-2} h^{-1}$ measured on the right palm (Figure 1). Both racial groups had significantly higher ($P \le 0.0001$) TEWL on both palms than on the other anatomical areas. No significant difference ($P > 0.05$) in TEWL was established between Caucasian and African nursing students.

The SC hydration ranged between 37.71 a.u. and 45.94 a.u. in Caucasian nursing students and between 18.71 a.u. and 38.37 a.u. in African students as measured, respectively, on the right volar forearm and left palm of both racial groups. The geometric mean SC hydration measured on the different anatomical areas were in descending order; right volar forearm > right dorsal hand > left volar forearm > left dorsal hand > right palm > left palm, in both racial groups, except in African students where SC hydration on the left dorsal hand was higher than on the right hand (Figure 2). In African nursing students, SC hydration was significantly lower on both palms ($P \le 0.05$) than on the other anatomical areas. No significant difference in SC hydration was established between the anatomical areas measured in Caucasian nursing students.

The SC hydration was significantly higher ($P \le 0.05$) in Caucasian nursing students when compared to African nursing students on all anatomical areas, except on the left dorsal hand. Effect sizes were calculated for the significant difference in SC hydration between the racial groups and a large effect (0.63) was established for the SC hydration difference on the palms, and a medium effect (0.3) for race as measured on the forearms and right dorsal hand.

In African nursing students a negative correlation ($r_s = -0.519$, moderate effect) was established between TEWL and SC hydration, if anatomical areas were not considered in the analysis. However, if TEWL and SC hydration of African nursing students were grouped into the specific anatomical areas, no significant correlation existed. In Caucasian nursing students no significant correlation was established between TEWL and SC hydration.

Skin surface pH in Caucasian nursing students ranged between 4.53 and 4.73 measured on the right volar forearm and right dorsal hand. In African nursing students, skin surface pH ranged between 5.14 and 5.35 as measured on the left volar forearm and left palm. Anatomical area had no significant influence on skin surface pH in either of the two racial groups. Significant differences were, however, established between the two racial groups (Figure 3). African nursing students had significantly higher ($P \le 0.0001$) skin surface pH than Caucasian nursing students on all anatomical areas which were substantiated by a large effect size (0.71).

4 | DISCUSSION

Skin barrier function was measured in female South African first year nursing students aged between 18 and 40 years, prior to their practical training in order to compare skin barrier function between African and Caucasian nursing students. First year nursing students were recruited before their practical training started in the hospitals to compare skin barrier function between the racial groups. Nursing students were selected due to their high risk for occupational skin diseases during their nursing career, and this study forms part of a larger longitudinal study investigating skin barrier function changes in South African nursing students. The age range selected for participating in this study is wide for university students, however, it ensured that more students could participate in the study since skin barrier function parameters will only be influenced at ages above

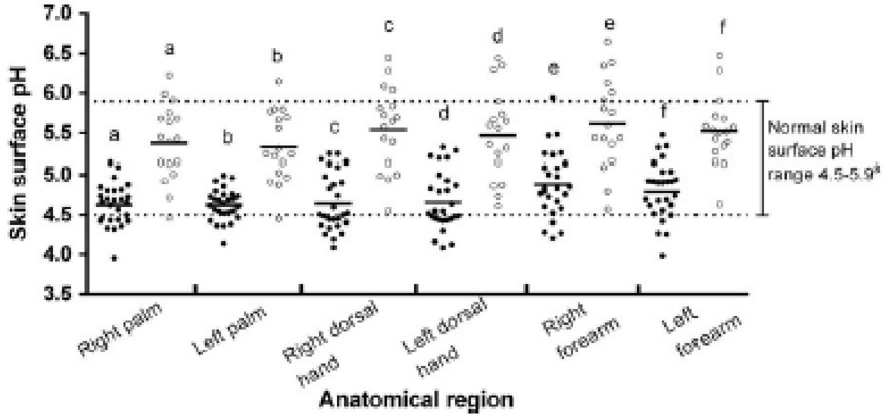

Figure 3. Skin surface pH (GM indicated with solid line) according to anatomical area (•) Caucasian and (o) African nursing students. [a-f]Significant differences ($P \leq 0.0001$) in skin surface pH between two racial groups on all anatomical areas

60 years.[9,35] Three parameters (TEWL, SC hydration, skin surface pH) were chosen to represent skin barrier function, and were measured on both hands and volar forearms.

The TEWL was approximately three times higher on the palms compared to the other anatomical areas, in both racial groups. It is well established that TEWL is higher on the palms, as numerous studies documented the anatomical variance in TEWL,[9,29,36] specifically higher TEWL on the palms, because of the increased activity and number of eccrine sweat glands on the palms.[5,37] In this study, no significant difference in TEWL was established between Caucasian and African nursing students. These results are substantiated by Warrier et al[23] who measured TEWL on 30 African and 30 Caucasian women, and also found no significant difference in TEWL on the volar forearms. The only significant difference in TEWL between racial groups was measured on the cheeks of the women (lower in Africans).[23] However, these findings contradict previous studies which reported significantly higher TEWL in Africans compared to Caucasians.[16,18,20] These studies measured TEWL on numerous anatomical areas, included different interventions in their methodology, and did not report gender, and are, therefore, not comparable to the present study. The significant difference in TEWL between the anatomical areas (eg palm > cheek > dorsal hand > palm)[5,36] may explain the opposing literature on racial differences in TEWL between the different studies, if TEWL measurements were compared with each other without considering anatomical areas.

There was less variation in SC hydration values between anatomical areas. The only significant difference between the anatomical areas in SC hydration was established in African nursing students, with significantly lower SC hydration on the palms (51% lower than other areas). Low SC hydration on the palms is consistent with a study that measured SC hydration on 16 anatomical areas, unfortunately this study did not report the participants' race.[5] However, the extent of low SC hydration on the palms of African nursing students in this study is well below that of healthy SC hydration values, as proposed by the German Society for Scientific and Applied Cosmetics (DGK), characterising very dry skin <30 a.u.[7] Accordingly, the SC hydration on the palms of the African nursing students (18.71-19.5 a.u.) in this study was approximately 53% lower than the recommended 40 a.u. Furthermore, 15 of the 17 African participants' SC hydration was below 30 a.u. characterising very dry skin in 88% of the African participants included in this study. The recommended values by the DGK were based on 349 participants, unfortunately racial groups were not reported in the study.[7] As race is not reported for the DGK values, comparing SC hydration of African participants with the DGK values might not be a reflection of the true SC hydration status of African participants. There are, however, no recommended SC hydration values for African participants and this may be an opportunity for future research.

Contrary to previous studies which did not establish a racial difference in SC hydration on any anatomical areas,[22-24] SC hydration in African nursing students was approximately 26% lower than that of Caucasian nursing students in this study. Warrier et al[23] and Manuskiatti et al[24] both measured SC hydration on various anatomical areas (including forearms with capacitance) but did not establish any significant racial differences in SC hydration. Warrier et al[23] noted that the change in SC hydration after occlusion with the capacitance probe was higher in Caucasians than Africans (on the legs and forearms) and concluded that SC water content was higher in Caucasians. In this study, SC hydration was higher in Caucasians, however, the severely low SC hydration in Africans have not been described before. The low SC hydration of African nursing students, in conjunction with the increased TEWL on the palms (established with the moderate negative correlation), may be an indication of a compromised skin barrier function and not necessarily be due to variation in eccrine sweat gland activity. This inverse relationship found between SC hydration and TEWL in African nursing students, in this study is consistent with literature,[6,38,39] which indicates a compromised skin barrier function in this group. These values were obtained after participants with pre-existing skin diseases and using medications such as oral contraceptives or retinoid medication were excluded. Severely low SC hydration and compromised barrier function in African nursing students may be ascribed to decreased ceramides in African skin[40] as lipid content has been linked to SC water-holding capacity and barrier function.[41] Inherent dry skin in

African nursing students may increase their risk for developing occupational skin diseases once their practical training starts, as the frequency of wet work and skin occlusion increase during their tertiary training.[27]

Another possible explanation may be the socioeconomic status of the students which influences the type of cosmetic products the students prefer and can afford to buy. Income, occupational status, and race are important factors determining the type of cosmetic products that consumers will buy. A study investigating consumption of cosmetics established that Caucasian women with a higher occupational status are more likely to buy expensive brand cosmetic products.[42] Cultural and personal habits may also play a role in determining the type of cosmetic product that students prefer. African nursing students may have been influenced by South African culture in which they were raised to use, for example, petrolatum for dry skin. Personal habits of the students may influence the quantity cosmetic product that they apply as well as the application frequency. A recent study established that nurses understood the benefits of frequently using moisturisers, but the frequency of use was still low.[43] This may be because of the impracticality of using moisturisers during a shift, however, the study also established that the frequency of use may improve with the belief that it was part of nurses' professional responsibility to protect their skin health. The socioeconomic status, cultural, and personal habits of the students may impact their skin health as it determines the type and therefore, quality, of cosmetic products that they will buy.

Skin surface pH was not significantly different between the anatomical areas in either of the two racial groups. Skin surface pH of Caucasian nursing students was in a pH range between 4.5 and 5.9. However, African nursing students had significantly higher skin surface pH on all anatomical areas when compared to the Caucasian nursing students. In terms of the actual hydrogen ion concentration (ie higher hydrogen ion concentration equals lower pH), the hydrogen ion concentration was four times higher in Caucasian nursing students than in African nursing students.

The higher skin surface pH of African nursing students corresponds with the dehydrated SC, as higher skin surface pH has been associated with low SC hydration values.[44] This may be due to the various pH-dependant enzymes which are responsible for synthesis of the lipid barrier.[8] However, these findings are not consistent with a previous study that established lower skin surface pH in Sri Lankan female nurses (classified as dark pigment IV-V skin, mean age 25 years) compared to light pigmented I-II skin (German female nurses, mean age 29 years).[25] The relationship between higher skin surface pH and low lamellar body density was established in the above mentioned study, although it was only measured on light pigmented skin.[25] Warrier et al[23] also established lower skin surface pH in Africans, although skin surface pH was only measured on the cheeks and legs of the participants and, therefore, not directly comparable to the findings of the present study. Berardesca et al[21] established no significant difference in skin surface pH between Africans and Caucasians on the volar forearms prior to sodium lauryl sulphate (SLS) induced irritation, however, only 10 Caucasian and 8 African subjects participated in their study.

The higher skin surface pH in African nursing students in this study unfortunately contributes to the contradictory evidence on the racial difference in skin surface pH, but it demonstrates that the pH-regulated mechanisms may not be as simple as previously thought. Skin surface pH for instance may not be solely dependent on the pigment of the skin but may also rely on the impact of socioeconomic factors on skin care products used[42] as discussed previously.

If only TEWL was considered to assess skin barrier function, it would have indicated no significant difference in skin barrier function between African and Caucasian nursing students. However, SC hydration and skin surface pH were significantly different between racial groups and should be included in the evaluation of skin barrier function. SC hydration was severely low, and skin surface pH high in African nursing students, which may be an indication of compromised skin barrier homeostasis. This study suggests that TEWL alone is not sufficient to assess skin barrier function and a more comprehensive assessment of skin barrier function should include parameters such as SC hydration and skin surface pH.

The limitations of this study included the inability to compare African nursing students' SC hydration values to an appropriate guideline such as the DGK values, as race was not reported in the DGK study. Future studies may investigate the correlation between skin surface pH and skin surface sebum in African and Caucasian participants. This may illustrate the interaction between elevated skin surface pH and dry skin. More research on SC hydration of African skin is necessary to establish relevant guideline SC hydration values. A study investigating the efficiency of different moisturisers on the severely dry skin in African participants that were established in this study, will provide valuable information to improve the skin health of South African nursing students.

5 | CONCLUSION

Skin barrier function was compared between African and Caucasian nursing students. No significant difference was established in TEWL between the two racial groups. African nursing students' SC hydration was significantly lower (indicating dry skin) and skin surface pH significantly higher when compared to Caucasian nursing students. Caucasian nursing students, therefore, had a healthier skin barrier function as all three biophysical parameters (TEWL, SC hydration, skin surface pH) were within normal ranges. SC hydration in African nursing students was below the recommended value and with accompanying elevated skin surface pH it may indicate disrupted skin barrier homeostasis. Pre-existing, compromised skin barrier homeostasis of African nursing students may affect their skin health once their practical training starts, as the frequency of wet work and skin occlusion will increase, consequently increasing their risk for developing occupational skin diseases.

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CHAPTER 4 ARTICLE II

Young, M.M., Du Plessis, J.L., Kezic, S., Jakasa, I., Franken, A. Natural moisturising factor constituents in South African nursing students. Submitted to *Contact Dermatitis* for consideration of publication.

4.1 Background

Natural moisturising factor (NMF) in human skin is one of the key components in maintaining skin barrier homeostasis. NMF mainly consist of free amino acids and their derivatives that act as humectants in the stratum corneum (SC) by attracting water molecules and hydrating the skin. The majority of South African healthcare workers are Black Africans with dark pigmented skin, however studies on how natural moisturising factor (NMF) compare between dark and light pigmented skin are limited. Investigating NMF content in nursing students during practical training may provide insight on the potential development of skin disease during their tertiary education. This article quantified and compared NMF content between Black African and White nursing students, to contribute to the limited evidence of racial variances in NMF content. This article was submitted to *Contact Dermatitis* and the reviewers have recommended possible publication. At the time of submission of this thesis the rebuttal was still in process.

4.2 Instructions for authors (excerpt)

Contact Dermatitis is designed primarily as a journal for clinicians who are interested in various aspects of environmental dermatitis. This includes both allergic and irritant (toxic) types of contact dermatitis, occupational (industrial) dermatitis and consumers' dermatitis from such products as cosmetics and toiletries.

Conflict of interest: Authors will be asked to provide a conflict of interest statement during the submission process. For details on what to include in this section, see the section ‘Conflict of Interest’ in the Editorial Policies and Ethical Considerations section below. Submitting authors should ensure they liaise with all co-authors to confirm agreement with the final statement.

Article structure: Contact Dermatitis now offers Free Format submission for a simplified and streamlined submission process. However, the content of your manuscript must conform to the guidelines described in the Article Types. This is particularly important for Contact Points. **1. Introduction** - Present the background briefly, but do not review the subject extensively. Give only pertinent, current (if possible) references. State the specific questions you want to answer. **2. Patients, Methods/Materials or Methods** - Describe selection of patients or experimental animals, including controls. Do not use patients' names or hospital numbers. Identify methods, apparatus (manufacturer's name and address; for US companies, please include spelled-out state, but do not add "U.S.A.") and procedures in sufficient detail to allow other workers to reproduce the results. Provide references and brief descriptions of methods that have been published. When using new methods, evaluate their advantages and limitations. Indicate whether the procedures were approved by a properly constituted Ethics Committee in your country, or in accordance with the current Helsinki Declaration. Drug trials must be logged on a public register, the register and the registration number must be stated in the text. **3. Results** - Present results in logical sequence in tables and illustrations. In the text, explain, emphasise, or summarise the most important observations. When appropriate, data should be statistically evaluated, and the appropriateness of the statistical methodology explained. Estimates (proportions, means, risk quotients etc.) should include confidence intervals. Authors are encouraged to seek advice from a statistician. **4. Discussion** - Do not repeat in detail data given in the Results section. Emphasise the new and important aspects of the study. Relate the observations to other relevant studies. On the basis of your findings (and those of others), discuss possible implications/conclusions. Limitations, as well as strengths, of your study should be discussed, however, avoiding sweeping generalisations. When stating a new hypothesis, clearly identify it as such.

References: All references should be numbered consecutively in order of appearance. In text citations should cite references in consecutive order using Arabic superscript numerals.

For more information about this reference style, please see the AMA Manual of Style.

Reference examples follow; list up to 6 authors, while, if more than 6, list the first 3 followed by "et al".

Journal article

Malmberg P, Guttenberg T, Ericson MB, Hagvall L. Imaging mass spectrometry for novel insights into contact allergy - a proof-of-concept study on nickel. Contact Dermatitis. 2018;78(2):109-116.

Book

Voet D, Voet JG. Biochemistry. New York: John Wiley & Sons; 1990. 1223 p.

Internet Document

American Cancer Society. Cancer Facts & Figures 2003. http://www.cancer.org/downloads/STT/CAFF2003PWSecured.pdf. Accessed March 3, 2003.

4.3 Natural moisturising factor constituents in South African nursing students.

4.3.1 Abstract

Background: The majority of South African healthcare workers are Black Africans with dark pigmented skin. Studies on how the markers of skin barrier function and natural moisturising factor (NMF) compare between dark and light pigmented skin are limited. Quantifying NMF in a nursing student population during their practical training at university may provide valuable insight into their potential susceptibility for skin conditions associated with low NMF.

Objectives: The objectives of this study were to quantify and compare NMF content of Black African, Mixed Race and White nursing students from their dominant dorsal hand.

Methods: Forty-nine White, 32 Black African and 5 Mixed Race nursing students participated in this study. Tape strip samples were collected from the participants' dominant dorsal hand and NMF content was measured, including histidine (HIS), pyrrolidone carboxylic acid (PCA), trans-urocanic acid (t-UCA) and cis-urocanic acid (c-UCA), as well as cytokines interleukin-1 alpha (IL-1α) and interleukin-1 receptor antagonist (IL-1RA).

Results: No statistically significant differences in PCA, t-UCA, c-UCA, IL-1α or IL-1RA were found between Black African and White nursing students. HIS was significantly (p = 0.001) higher in White nursing students when compared to Black African students. The ratio of tot-UCA/HIS was significantly higher in Black Africans (p = 0.0002), when compared to White nursing students.

Conclusion: No significant differences were established in NMF content between White and Black African nursing students, other than HIS which was significantly higher in White students than in Black African students. Different HIS levels between the racial groups suggests variation in histidase activity which may be related to skin pH and pigmentation. This finding may suggest that nursing students at the beginning of their career may have similar susceptibility to skin diseases related to NMF.

Key words: trans-urocanic acid, cis-urocanic acid, pyrrolidone carboxylic acid, natural moisturising factor, tertiary education

4.3.2 Introduction

Natural moisturising factor (NMF) in human skin is one of the key components in maintaining skin barrier homeostasis. NMF mainly consist of free amino acids and their derivatives that act as humectants in the stratum corneum (SC) by attracting water molecules and hydrating the skin.[1] NMF components including urocanic acid (UCA) and pyrrolidone carboxylic acid (PCA) are products from the hydrolysis of the SC structural protein, filaggrin. Filaggrin is hydrolysed to arginine, glutamine and histidine (HIS), amongst others, during cornification above the stratum compactum, where a high quantity of water is still present. As the water content decreases in the outer layers of the SC, histidase is activated and HIS is deaminated to trans-urocanic acid (t-UCA), and PCA is produced from glutamine while arginine is converted to citrulline.[2, 3] Finally, photoisomerization of t-UCA to the c-UCA isomer takes place under ultraviolet-B (UV-B) radiation and serves as an endogenous sunscreen.[2] NMF components are hygroscopically active and by drawing water to the SC, they play a key role in maintaining SC hydration. Furthermore, t-UCA is a known acidifier of the SC and is therefore important for maintaining the pH gradient in the SC.[2-4]

Loss-of-function mutations in the filaggrin gene (*FLG*) has been strongly associated with the development of atopic dermatitis, and has a strong correlation with the severity and onset of the disease.[3-5] This is due to the cascading effect that low filaggrin content has on the skin condition as it results in low NMF content, which causes low SC water content and increased skin surface pH.[6, 7] An increase in skin pH may cause the activation of serine proteases causing degradation of extracellular lipid processing enzymes, consequently leading to compromised SC integrity.[3] Impaired SC barrier due to the *FLG* loss-of-function mutation may increase hapten penetration and the accompanying inflammatory response.[3, 4]

FLG null mutations and atopic dermatitis have been associated with an increased risk for developing hand eczema.[8] Healthcare workers are required to follow a strict hand hygiene regimen to prevent nosocomial infections in healthcare settings.[9] This however increases their exposure to wet work and irritants such as water and hand soap, as well as allergens such as latex rubber which increases the probability of developing contact dermatitis.[10] Several studies showed that skin irritants reduce NMF levels in the skin[11, 12] Healthcare workers are especially vulnerable to these irritants, because of a possible compromised SC integrity caused by low NMF.

A study comparing African and Caucasian skin *in vitro* found that filaggrin was more expressed and processed in Caucasian epidermis than in African epidermis. The study also suggested that the modulation of most enzyme genes differed between the two skin types, indicating that the production of NMF could vary between them.[13] PCA concentration was measured in South African albino Africans, Black Africans and Whites in 2016. PCA levels were higher in albino Africans than in Black Africans and Whites, while Black Africans had significantly higher PCA levels than Whites.[14] NMF content was also measured in South African amaXhosa patients with atopic dermatitis to investigate the relationship between atopic dermatitis, NMF content and *FLG* loss of function mutations. PCA and UCA levels were established to be significantly lower in patients with atopic dermatitis when compared to patients in the control group. However, these results were established in patients without a *FLG* mutation suggesting that there is an interplay between systemic T-helper 2 cell (Th-2) inflammation and *FLG* suppression in South African amaXhosa patients.[15] The majority of South African healthcare workers are Black African,[16] and NMF content studies on dark pigmented skin are limited to these two studies, which did not include a high risk population such as nursing students.

This study aimed to quantify and compare NMF content of Black African and White nursing students. Investigating NMF content in nursing students during practical training may provide insight on the potential development of skin disease during their tertiary education.

4.3.3 Method

This study was conducted in accordance with the Helsinki Declaration[18] and approved by the Health Research Ethics Committee of the North-West University, South Africa (Ethics approval number: NWU-00337-16-A1).

4.3.3.1 Study population

Female nursing students from the North-West University, South Africa were recruited to participate in this study. For the purpose of this publication the term race refers to groups with similar physical features and skin colour[18] where White is used for light pigmented skin and Black African for dark pigmented skin. After obtaining written informed consent, 49 White, 32 Black African and 5 Indian / Mixed race nursing students (second to fourth year undergraduate students) participated in this study. All of the participants were non-smokers and between the ages 18 and 40 years.

The participants were grouped into self-reported racial groups and corresponding skin pigment types (Fitzpatrick scale)[19] as well as colour space values of the Commission International d'Eclairage (CIE) represented by L*a*b coordinates, as summarised in Table 4-1. The L* value indicates the lightness of the skin (0 = black and 100 = white), the a* value indicates the range between green and red (green < 0 < red) and the b* value the range between blue and yellow (blue < 0 < yellow). These values were measured on the volar wrist of the non-dominant forearms[20] of the participants with a Colorimeter (CL-400) manufactured by Courage and Khazaka (CK) electronic GmBH, Germany.

Table 4-1: Participant skin colour classifications according to self-reported race, L*a*b colour space value (L*) and skin pigment types.

Self-reported race	N	L* value range	Skin pigment type[20]
White	49	58.68 – 70.46	II – III
Indian / Mixed race	5	47.79 – 59.59	III – IV
Black African	32	40.88 – 55.99	IV – VI

4.3.3.2 Natural moisturising factor collection and analyses

Sequential tape stripping was used to collect NMF from the upper layers of the participants' SC at the beginning of the academic year (January / February), during 2018. Participants were asked not to apply any cosmetic products to their hands 12 hours prior the NMF sample collection.

Six tape strips were applied to the same marked skin area on the dominant dorsal hand of the participants with standardised force (10 N) using a disc pressure applicator (Cuderm, Texas). The first three tape strips were discarded to correct for any residual cosmetic products still present on the skin and the remaining three samples stored at - 80 °C until further analysis. The total SC protein content on the tape strips were measured by determining the optical density at 850 nm with the D-Squame Scan 850A (Monaderm, Monaco). NMF components HIS, PCA, t-UCA, c-UCA and total NMF (tot-NMF which is the sum of individual components) were determined by High Performance Liquid Chromatography after extraction with water as described elsewhere.[21] The values were normalised according to the total amount of SC proteins determined with the optical density measurements of the tape strip and expressed as mmol per gram of proteins.[22] The analyses of cytokines IL-1α and IL-1RA on the tape strips were performed by Mesoscale multiplex immunoassay (MESO QuickPlex SQ 120 assay, MSD, Rockville, Maryland). The cytokine concentrations were normalised for protein amount determined with Pierce Protein Assays (Thermo Fischer Scientific).

The metabolism of HIS to t-UCA is expressed as a ratio tot-UCA/HIS, and the conversion of t-UCA to c-UCA is expressed as the ratio of c-UCA/tot-UCA.

4.3.3.3 Statistical analyses

Statistical analyses were performed with Statistica 64 version 13.3 (Statsoft Inc. Palo Alto, California) and figures generated with GraphPad Prism® version 7 (GraphPad Software San Diego, California).

A normal distribution of the data was assumed according to the central limit theorem,[23] as the sample sizes used in parametric tests were above 30 and constant variance of the data were tested with Levene's test and confirmed ($p > 0.05$). Statistical outliers were detected with a Grubbs' test[24] and a total of four outliers were removed from the data prior to the analyses. Descriptive results are presented as Geometric Means (GM) and Confidence Intervals (CI: 95%). One-way Analysis of Variance (ANOVA) was used to determine if NMF constituents significantly differed with age and independent t-tests for differences in hand dominance (Right or Left). Statistical analyses were not performed on Mixed Race student data, due to the small number of students that participated in the study, however descriptive statistics are reported.

Differences in NMF constituents between the racial groups were tested with independent t-tests (significant if $p \leq 0.05$). Effect sizes were calculated as Cohen's d test statistic [*(Mean $_{(group\ 2)}$ - Mean $_{(group\ 1)}$)/pooled standard deviation*] and interpreted as follow: small effect d = 0.2; moderate effect d = 0.5 and large effect d = 0.8.[25] Pearson correlations were used to test for significant correlations between the NMF constituents and the relationship between NMF constituents is displayed in linear regression graphs. Correlations were significant if $p \leq 0.05$ and the strength of the relationship were categorised as weak if $r = 0.00 – 0.39$; moderate if $r = 0.40 – 0.59$; and strong if $r = 0.60 – 1.0$.[26]

4.3.4 Results

NMF tape strip samples were collected from female nursing students (mean age 20 ± 2.42) at the beginning of the academic year. NMF tape strip samples were collected from the dominant dorsal hand of participants, and the influence of hand dominance (Right or Left) had no significant influence ($p > 0.05$) on the results. Participant age also had no significant influence on the results ($p > 0.05$).

NMF components and cytokine results are presented in Table 4-2. Geometric means of total protein content for White nursing students was 79.48 µg/ml (CI 37.72, 138.94) and 65.34 µg/ml (CI 26.04, 155.09) for Black African nursing students, while Mixed Race students' total protein content was 87.50 µg/ml (CI 67.42, 134.33). The total NMF (tot-NMF) of White nursing students was 0.65 mmol/g protein (CI 0.25, 1.18) and 0.55 mmol/g protein (CI 0.28, 1.02) for Black African nursing students, while Mixed Race students' tot-NMF was 0.48 (CI 0.17, 1.00). Levels of NMF components ranged between 0.004 and 1.37 mmol/g protein, with t-UCA and c-UCA both with the lowest concentrations (0.004 mmol/g protein) and PCA with the highest concentration (1.37 mmol/g protein) in all the racial groups. GM IL-1α in all the racial groups were 0.03 ng/µg protein (CI 0.01, 0.10), while GM IL-1RA ranged from 0.14 ng/µg protein (White students) to 0.21 ng/µg protein (Mixed Race students).

No significant differences (*p* > 0.05) were established in total protein content, t-UCA, c-UCA, PCA, tot-NMF or in the cytokines IL-1α and IL-1RA between Black African and White nursing students. A significant difference was, however, found in HIS concentration. HIS concentration was significantly lower (*p* = 0.001) in Black African nursing students (GM 0.09; CI 0.04, 0.24) when compared to White nursing students, (GM 0.15; CI 0.04, 0.32) with a large effect size of 0.84.

Table 4-2: NMF constituents (mmol/g protein) and cytokines (ng/µg protein) of White, Black African and Mixed Race nursing students (N = 84).

NMF Constituents (mmol/g protein)	**White (n = 47)**		**Black Africans (n = 32)**		**Mixed Race (n = 5)**	
	GM	**CI 95%**	**GM**	**CI 95%**	**GM**	**CI 95%**
Tot-Protein (µg/ml)	79.48	37.72, 138.94	65.34	26.04, 155.09	87.50	67.42, 134.33
HIS	**0.15** [a]	0.04, 0.32	**0.09** [a]	0.04, 0.24	0.10	0.04, 0.24
t-UCA	0.03	0.01, 0.06	0.03	0.02, 0.07	0.02	0.01, 0.05
c-UCA	0.05	0.01, 0.13	0.05	0.03, 0.09	0.03	0.01, 0.08
tot-UCA	0.08	0.02, 0.19	0.08	0.04, 0.15	0.06	0.02, 0.12
PCA	0.41	0.17, 0.77	0.38	0.19, 0.76	0.31	0.11, 0.64
tot-NMF	0.65	0.25, 1.18	0.55	0.28, 1.02	0.48	0.17, 1.00
tot-UCA/HIS	**0.56** [b]	0.20, 1.37	**0.91** [b]	0.31, 2.16	0.56	0.39, 1.22
c-UCA/tot-UCA	**0.64** [c]	0.57, 0.69	**0.60** [c]	0.51, 0.66	0.58	0.48, 0.66
Cytokines (ng/µg protein)						
IL-1α	0.03	0.01, 0.09	0.03	0.01, 0.10	0.03	0.01, 0.06
IL-1RA	0.14	0.04, 0.42	0.16	0.03, 0.35	0.21	0.05, 0.15

[a – c] Significant differences (*p* = 0.001) between racial groups in NMF constituents.
Total protein content (Tot-Protein), histidine (HIS), trans-urocanic acid (t-UCA), cis-urocanic acid, (c-UCA), total urocanic acid (tot-UCA), pyrrolidone carboxylic acid (PCA), total natural moisturising factor (tot-NMF), total urocanic acid per histidine (tot-UCA/HIS), cis-urocanic acid per total urocanic acid (c-UCA/tot-UCA), interleukin-1 alpha (IL-1α), interleukin-1 receptor antagonist (IL-1RA).

Significant strong positive correlations exist between t-UCA and c-UCA in both racial groups (Whites *r* = 0.99, *p* ≤ 0.05; Black Africans *r* = 0.97, *p* = 0.001). The metabolism of HIS to UCA were assessed with t-UCA and c-UCA combined as total-UCA (tot-UCA) per HIS. Linear regression graphs were used to illustrate this relationship between HIS and tot-UCA in White nursing students (Figure 4-1a) and Black African nursing students (Figure 4-1b). Correlations between HIS and tot-UCA were significant (p = 0.001) in both racial groups, with a weak positive correlation in White students (r = 0.29) and a moderate positive correlation in Black African students (r = 0.46).

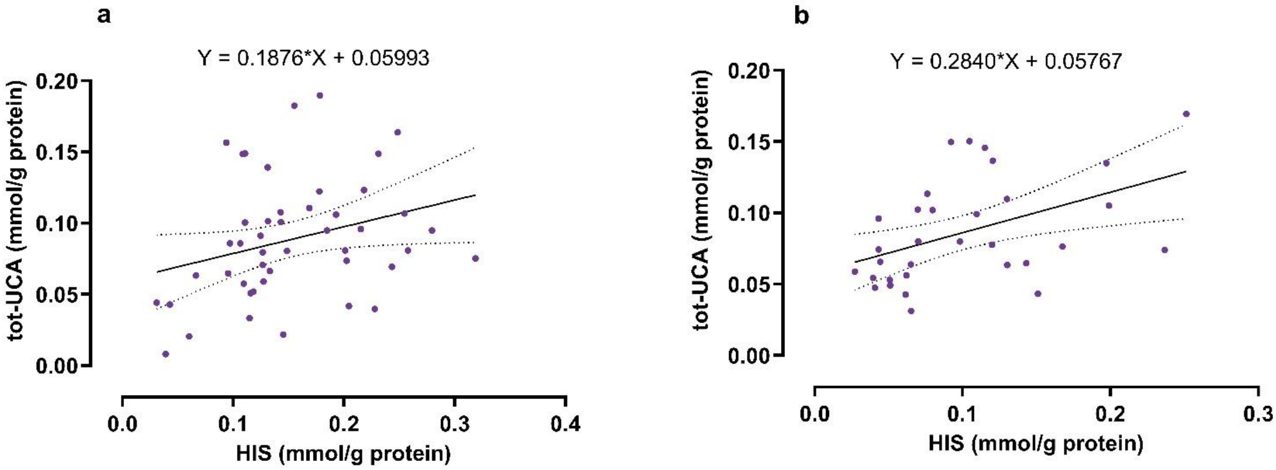

Figure 4-1: Linear regression graphs of HIS (mmol/g protein) and tot-UCA (mmol/g protein) in White (a) and Black African (b) nursing students with 95% Confidence Intervals (dotted lines).

Although no significant differences were established in tot-UCA between the racial groups, a difference in the pathway of HIS to UCA is however present, as the ratio calculated between these metabolites (tot-UCA/HIS) differed significantly between the racial groups. The ratio of tot-UCA/HIS was significantly lower (p = 0.0002) in White students (GM ratio 0.56, CI 0.20, 1.37) than in Black African students (GM ratio 0.91, CI 0.31, 2.16) with a moderate effect size of 0.45. However, the ratio of c-UCA/tot-UCA was significantly higher (p = 0.0001) in White students (ratio GM 0.64, CI 0.57, 0.69) when compared to Black African students (ratio GM 0.60, CI 0.51, 0.66) with a moderate effect size of 0.52.

4.3.5 Discussion

NMF constituents were measured in Black African, White and Mixed Race nursing students (mean age 20 ± 2.42) at the start of an academic year. As part of their training, nursing students are required to complete practical training in hospitals, where they are subjected to a high amount of wet work including frequent hand washing, which may increase their risk of developing contact dermatitis. Wet work and frequent hand washing are known to decrease NMF that may lead to a compromised skin barrier and skin irritation.[11] This may be due to Sodium Lauryl Sulphate (SLS) that causes denaturation of the proteins in the conrnified envelope, which may cause leakage of NMF components from the corneocytes.[27] An individual with intrinsically lower NMF levels e.g. due to skin phototype or *FLG* mutations it may increase their susceptibility for contact dermatitis. Therefore, measuring NMF may aid in determining if these students are susceptible to skin diseases associated with low NMF levels. NMF components that were measured included HIS, t-UCA, c-UCA, PCA and their sum was expressed as total NMF (tot-NMF). Furthermore, total protein content, and cytokines (IL-1α and IL-1RA) were also quantified. The ratio of tot-UCA/HIS was calculated to illustrate the metabolism of HIS to UCA by the enzyme histidase and the c-UCA/tot-UCA ratio to illustrate t-UCA conversion to c-UCA by UV-B radiation.[2, 3]

Only five Mixed Race students participated in this study, and were, therefore, not included in the statistical comparison analyses, but descriptive statistics were reported. No significant differences were established for tot-NMF, t-UCA, c-UCA and PCA, between Black African and White nursing students. These results are contradictory to the findings of a previous study which found a significant difference in PCA concentrations between Black African and Whites in a South African population.[14] These conflicting results may be due to anatomical variation in the sampling sites as the present study collected tape strips from the dorsal hands of participants, while Raj *et al.*[14] collected tape strip samples from the cheeks of participants. Another possible explanation may be that there are age-related differences in NMF levels between the present study and the study by Raj *et al.*[14] as the mean age in this study was 20 ± 2.42 years compared to 41 ± 2.77 years in the study conducted by Raj *et al.*[14] Recently Howard *et al.*[28] established that NMF content increases with age in healthy subjects.

We found, however that HIS was significantly (p = 0.001) lower in Black African students when compared to White students. HIS is one of the filaggrin degradation products, which is deaminated by the enzyme histidase to form t-UCA.[2] The significantly higher ratio of tot-UCA per HIS found in Black African students, suggests that a proportion of the HIS metabolised to t-UCA is higher in Black African students which might explain their lower HIS levels. This difference in HIS conversion to tot-UCA may be due to the activity of histidase that differs between the two groups.[13]

HIS is deaminated to t-UCA by histidase which functions optimally at acidic pH. The dendrites of melanocytes in dark pigmented skin (IV-V) have been found to be more acidic than those in lightly pigmented skin (I-II) and contributed to a higher activity of histidase in dark pigmented skin.[29] Higher activity of histidase may therefore increase the production of t-UCA from HIS.[3]

Similar t-UCA levels in both racial groups suggests that skin surface pH should be similar in both racial groups, and therefore similar susceptibility to skin pH related skin diseases e.g. atopic dermatitis,[6] because t-UCA is a known acidifier of the SC.[2-4] However, the skin surface pH of the participants of the present study have been investigated previously, and the skin surface pH of Black African nursing students was significantly higher than that of White nursing students (Skin surface pH average of 5.35 for Black African nursing students, and 4.73 for White nursing students, as measured on the volar forearm).[30] Higher skin surface pH of Black African nursing students, may support the hypothesis that personal habits contribute to the higher skin surface pH in this group. The type of cosmetic products the students use at home may play a role in maintaining their skin surface pH. In our larger study it was determined from participant questionnaires that Black African nursing students used petrolatum for dry skin which may have influenced the skin surface pH in this group. Another reason might be difference in the amount of other skin components which are known to influence skin pH, such as sphingoid bases and free fatty acids. [31, 32]

Similar NMF content in racial groups may suggest a similar susceptibility to skin diseases associated with NMF content. Atopic dermatitis prevalence in the United States was determined to be higher in African American participants when compared to European Americans, even though *FLG* loss-of-function mutations were six times less common in African Americans.[33] However, in a study that tested irritant contact dermatitis susceptibility between African Americans and Caucasians, the threshold for irritancy was significantly higher in African Americans which indicated that Caucasians were more susceptible to irritant contact dermatitis.[34] The literature on the prevalence of skin diseases between different racial groups are contradicting and the susceptibility to skin diseases is determined by numerous factors, of which NMF is only one. The results of this study have shown that there is no significant difference in NMF content between the two racial groups this early in the nursing students' career. If only considering the role of NMF in the susceptibility of skin diseases, the results indicated similar NMF content, and therefore a similar susceptibility. However, a person's susceptibility to skin diseases is determined by various factors.

Future studies may investigate the influence of different types of cosmetic products on NMF content in participants. More research on the anatomical variation of NMF content is also necessary as occupational skin diseases such as contact dermatitis often start on the anatomical site most exposed e.g., the hands.

One limitation of this study was that NMF content could only be measured at a single anatomical region and not on the cheeks of participants which prevented accurate comparison of the findings of this study to published research. NMF was measured on the dorsal aspect of participants' hands to quantify NMF at the site most exposed to frequent hand cleansing and wet work in a nursing student population. NMF was measured on participants hands in order for this data to be used in a larger study to determine the susceptibility of nursing students to occupational skin diseases.

4.3.6 Conclusion

NMF content in this study generally did not differ between the two racial groups, as the only significant difference was established in the HIS concentration and HIS to tot-UCA metabolism. Increased ratio between HIS and its metabolite UCA in Black African nursing students may indicate higher activity of histidase in this group. However, tot-UCA content did not differ significantly between the two racial groups. The observation of similar Natural Moisturizing Factor (NMF) content between the racial groups suggests similar hygroscopic properties between the groups. This may indicate that the intrinsic susceptibility to skin diseases related to NMF content does not differ significantly between these groups this early in their career. However, this study also illustrated that more research is necessary on NMF content comparisons between racial groups as the findings of this study contradicted previous studies. More research would be necessary before interventions based on NMF content differences between dark- and light pigmented skin can be recommended. This study contributed valuable data on NMF quantity in a high-risk group and the comparison of NMF between two racial groups in South Africa.

4.3.7 Acknowledgements

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CHAPTER 5 ARTICLE III.

Young, M.M., Franken, A., Du Plessis, J.L. Skin barrier function of Black African and White nursing students. Submitted to *Journal of Dermatology Nurses' Association* for consideration of publication.

5.1 Background

Nursing students in South Africa are required to complete a minimum of 2000 working hours during their four years of tertiary (university) education. They are circulated through the different departments of hospitals during their practical training, and are trained in proper hand hygiene routines to prevent nosocomial infections between patients. These routines involving water in combination with skin occlusion from wearing latex or nitrile gloves may all have a negative impact on the skin condition of their hands. Assessment of skin biophysical parameters in a South African nursing population may provide insight in long term changes in their skin condition in a practical setting. This article investigated changes in skin barrier function parameters over a period of two years, in nursing students completing their tertiary education. This article was submitted to *Journal of Dermatology Nurses' Association,* which is the is the official journal of the Dermatology Nurses' Association (DNA). The format of this article is written with Arial Font 11, and 1.5 line spacing for uniformity of the thesis, however an excerpt of the instructions for authors is included below.

5.2 Instructions for authors (excerpt)

Journal of Dermatology Nurses' Association (JDNA) provides a forum for multidisciplinary discussions related to all aspects of dermatology nursing and practice, including clinical practice, education, research, prevention, public health, health administration, international health, legal-ethical issues, social issues, health equity, and public policy. We invite original articles that focus on a broad spectrum of issues related to dermatology nursing, from the perspectives of nursing, public health, behavioral health, and medicine. Submissions are welcomed from nurses and other healthcare professionals, as well as from multidisciplinary teams.

Ethical / Legal considerations: *JDNA* is a peer-reviewed journal that follows publishing standards set by the American Psychological Association (APA; http://apa.org/) and the Committee on Publication Ethics (COPE; http://publicationethics.org/). A submitted manuscript must be an original contribution not previously published in print or online (except as an abstract, preliminary report, thesis, dissertation, or preprint). If an abstract from a poster or presentation has been published in conference proceedings, the abstract and manuscript submitted to *JDNA* must be substantially different and provide new information for readers. A preprint may have been posted anytime and anywhere, including on scholarly collaboration networks. If the manuscript is accepted, to ensure that readers can find and cite the final published version, we encourage researchers to add the digital object identifier (doi) to the posted preprint version.

English language standards: Please compose your manuscript in English with United States spelling, grammar, and punctuation conventions. A clear, concise, academic writing style is required.

Manuscript preparation: Manuscripts should use a 12-font Time New Roman, double-spaced, with one inch margins. JDNA follows the style of the Publication Manual of the American Psychological Association (APA), 7th edition.

Article structure: Submissions should include the following: (a) title page; (b) manuscript body that includes, in this order: abstract and 3-6 key words (on first page), title (on page 2, centered and not bolded), manuscript text (with appropriate headers), references and key considerations, (c) tables, if applicable; and (d) figures if applicable.

References: The style of references is the 6th edition of the *Publication Manual of the American Psychological Association* (APA). References used in the text are cited by author's name and date of publication in parentheses (Smith, 2000), with page numbers cited for direct quotations. All references cited in the text must be included on the reference list and authors are responsible for bibliographic accuracy and must check every reference in manuscript and proofread again in page proofs. The reference list must be arranged alphabetically by first author's last name.

Examples of correct forms of references:

*Standard journal article:*Schmelzer, M., Case, P., Chappell, S., & Wright, K. (2000). Colonic cleansing, fluid absorption, and discomfort following tap water and soapsuds enemas. *Applied Nursing Research*, *13*(2), 83–91.

Chapter in a book: Hixon, M. E. (2000). Professional development: Socialization in advanced practice nursing. In J. V. Hickey, R. M. Ouimette, & S. L. Venegoni (Eds.). *Advanced practice nursing: Changing roles and clinical applications* (2nd ed.), (pp. 46–65). Philadelphia: Lippincott Williams & Wilkins.

Online (Electronic) document: Follow guidelines at www.apastyle.org/elecref.html Centers for Disease Control & Prevention (CDC). (2001). Twinrix®. Combined Hepatitis A and Hepatitis B Vaccine. Retrieved October 30, 2001, from http://www.cdc.gov/ncidod/diseases/hepatitis/twinrix.htm.

5.3 Skin barrier function of Black African and White nursing students

5.3.1 Abstract

Aims: Assessment of skin biophysical parameters in a South African nursing population may provide insight in long term changes in their skin condition in a practical setting. This study aimed to investigate changes in skin barrier function parameters over a period of two years, in nursing students completing their tertiary education.

Methods: Transepidermal water loss, stratum corneum hydration and skin surface pH were measured in female nursing students (63 white, 42 Black African) three times a year and repeated for two years. Linear mixed models and Bonferonni post-hoc tests were performed to test changes over time in skin barrier function parameters.

Results: Transepidermal water loss and stratum corneum hydration significantly ($p < 0.001$) decreased over two years in the first-year students, while only specific differences were established for senior students. Skin surface pH significantly ($p < 0.001$) varied over the two years with significant increases ($p < 0.031$) in the winter months. The only significant difference ($p < 0.001$) between white and Black African students was established in skin surface pH.

Conclusion: This study demonstrated the variability of skin barrier function parameters, specifically seasonal variation in skin surface pH. This study also revealed possible long-term changes in skin condition through the recovery of the SC in a practical setting.

Key words: Practical training, skin surface pH, stratum corneum hydration, tertiary education, Transepidermal water loss.

5.3.2 Introduction

Nursing students in South Africa are required to complete a minimum of 2000 working hours during their four years of tertiary (university) education. They are circulated through the different departments of hospitals during their practical training and are trained in proper hand hygiene routines to prevent nosocomial infections between patients (Pittet, 2001; SANC, 2005). Hand hygiene routines traditionally consist of a combination of washing with soap and water and using alcohol gel rubs. Additionally, nursing students are expected to conduct wet work tasks, such as washing/bathing patients and prolonged glove wearing, as part of their daily duties. These routines involving water in combination with skin occlusion from wearing latex or nitrile gloves may all have a negative impact on the skin condition of their hands (Jungbauer *et al.*, 2004). The impact of these working conditions on skin condition have been extensively studied in healthcare settings (Held *et al.*, 2001; Jungbauer *et al.*, 2004; Larson *et al.*, 1997; Visser *et al.*, 2014).

Transepidermal water loss (TEWL), stratum corneum (SC) hydration and skin surface pH are common parameters included in assessing the effect of frequent hand washing and wet work on skin condition (Held *et al.*, 2001; Jungbauer *et al.*, 2004; Larson *et al.*, 1997; Visser *et al.*, 2014). Efforts to prevent changes in skin condition and occupational skin diseases in healthcare workers were intensified during and following the coronavirus (COVID-19) pandemic (Darlenski *et al.*, 2021; Desai *et al.*, 2020; Symanzik *et al.*, 2022), due to an increase in hand washing frequencies and longer durations of hand washing during the pandemic (Balato *et al.*, 2020). This again highlighted the importance of assessing skin barrier function parameters in healthcare workers to provide accurate and effective interventions.

Skin barrier function refers to the ability of the skin to protect against exogenous toxins and preventing endogenous water loss through the stratum corneum (SC). This is evaluated by measuring the amount of water vapor above the SC, apart from perspiration, which is known as TEWL (Pirot & Falson, 2004). Low TEWL values are indicative of an intact skin barrier and a healthy physiological skin condition (Darlenski *et al.*, 2009; Fartasch, 1997; Rawlings *et al.*, 2008). The hydration status of the SC influences TEWL, as it is a measure of the water content that stays behind in the SC (Darlenski *et al.*, 2009). Physiologically, TEWL and SC hydration are influenced by the lipid arrangement in the SC and the protein component known as the Natural Moisturizing Factor (NMF) (Monteiro-Riviere, 2010). NMF consists of hygroscopic amino acids, which hydrates the SC by drawing water into the SC (Harding & Rawlings, 1999). Lipid arrangement in the SC forms a hydrophobic barrier preventing endogenous water loss or TEWL (Elias, 2010). The lipid arrangement is influenced by skin surface pH as the lipid metabolizing enzymes in the SC are pH dependent and functions optimally in an acidic range between 4.5 and 5.9 (Kleesz *et al.*, 2011; Schmid-Wendtner & Korting, 2006).

Occupational exposure to wet work and frequent hand cleaning may alter these parameters by either hyperhydrating the SC or by delipidation of the SC directly from hand wash soaps and alcohol rubs, or by increasing the skin surface pH and consequential altered lipid metabolizing enzyme activity (Ananthapadmanabhan *et al.*, 2013; Fartasch, 1997; Fartasch *et al.*, 2012; Jungersted *et al.*, 2010). These effects were illustrated by a study comparing TEWL, SC hydration and clinical evaluation of dermatitis between administrative staff and nurses at a hospital. TEWL values were significantly higher and SC hydration was significantly lower in nurses when compared to administrative staff. Irritant contact dermatitis was also diagnosed on the hands of nurses (Hachem *et al.*, 2002). In another study, the prevalence of hand eczema in apprentice nurses, increased by 23% in the first year of training and 31% in the third year with frequent hand washing as one of the risk factors (Visser *et al.*, 2014). Hand washing frequency was also identified as one of the significant risk factors for developing irritant contact dermatitis in a nursing population at the Kaohsiung Medical University Hospital in Taiwan (Lan *et al.*, 2011). Behavioral changes associated with high prevalence of hand eczema in nurses included washing their hands more frequently, while stopping the use of alcohol gel rubs (Longuenesse *et al.*, 2017). While alcohol gel rubs may elicit a stinging sensation on pre-irritated skin, it has been determined to be less irritating to the skin than frequent washing with surfactants (Löffler & Kampf, 2008). Furthermore, the use of soap and water alone is not an effective disinfectant measure, as hand hygiene guidelines recommend the use of alcohol gel rubs after washing with soap and water in cases where non-enveloped viruses might be present (Hillier, 2020). Nurses reported reasons for non-compliance to disinfection measures to be inaccessible supplies, insufficient time, wearing gloves, interference with worker-patient relations and pre-irritated skin (Pittet, 2001). Chronic hand eczema not only impacts infection control in hospitals, but also the quality of life of healthcare professionals. It is estimated that a 25% increase in medical costs is associated with chronic hand dermatitis, while it also significantly impairs work productivity and daily activities (Fowler *et al.*, 2006).

Assessing biophysical parameters such as TEWL, SC hydration and skin surface pH in a university nursing student population may provide insight into the development of hand dermatitis. Evaluating skin barrier function in nursing students provides the opportunity to not only investigate early changes in these biophysical parameters, during their practical training, but may also provide the means to identify early interventions for future studies that may protect their skin health at the start of their career. Research on long term changes in these parameters in an African population is limited. In South Africa, most of the nursing workforce is Black African (Wildschut & Mqolozana, 2008), and a deterioration of these parameters during their tertiary education may have significant long term implications for their career as healthcare professionals. This study aims to investigate changes in TEWL, SC hydration and skin surface pH in white and Black African university nursing students in a two-year cohort study.

5.3.3 Methods

5.3.3.1 Ethical Statement

This study was approved by the Health Research Ethics Committee of the North-West University, South Africa (Ethics approval number: NWU-00337-16-A1).

5.3.3.2 Study population

Female nursing students (Academic year one to four) from the North-West University were recruited to participate in this study. All participants were non-smokers and between the ages of 18 and 40 years. Participants diagnosed with a skin disease or using oral contraceptives or retinoid medication were excluded from the study, as it has been proven to alter sebum gland activity (Orfanos & Zouboulis, 1998; Zouboulis *et al.*, 2007) and will therefore influence the skin barrier function measurements. After this exclusion criterion was applied, a total of 63 white, 42 Black African and 5 Indian / Mixed race nursing students participated in the study. Skin barrier function data of Indian / Mixed race nursing students were excluded in data analyses, as there were too few participants of this group to enable comparisons with sufficient statistical power.

Participants were only recruited during the first phase of the study and were grouped according to the academic year group they were enrolled in when they started the study. Participants were identified according to the initial year group classification throughout the study although they continued their tertiary education during the study. For example, first year students were enrolled in their first year at the start of the study, and in their second year during the second year of the study but were identified as first year students throughout the study.

The participants were grouped into self-reported racial groups and corresponding skin pigment types (Fitzpatrick scale) (Fitzpatrick, 1988) as well as color space values of the Commission International d'Eclairage (CIE) represented by L*a*b coordinates, as summarized in Table 5-1. The L* value indicates the lightness of the skin (0 = black and 100 = white), the a* value indicates the range between green and red (green < 0 < red) and the b* value the range between blue and yellow (blue < 0 < yellow). These values were measured on the volar forearm of the non-dominant forearms of the participants with a Colorimeter (CL-400) manufactured by Courage and Khazaka (CK) electronic GmBH, Germany.

Table 5-1: Participant skin color classifications according to self-reported race, L*a*b color space value (L*) and skin pigment types.

Race	N	L* value range	Skin pigment type[32]
White	63	58.68 – 70.46	II – III
Indian / Mixed race	5	47.79 – 59.59	III – IV
Black African	42	40.88 – 55.99	IV – VI

5.3.3.3 Skin barrier function measurements

Participants were instructed not to wash and apply any cosmetic products on their hands and forearms 12 hours prior to the measurements. Skin barrier function was measured according to previously published methods (Darlenski *et al.*, 2009) and are summarized in this study according to three parameters i.e., TEWL, SC hydration and skin surface pH. TEWL measurements were performed with a Tewameter® (TM 300), SC hydration with a Corneometer (CM 825) and skin surface pH with a skin pH meter (PH 905), all manufactured and calibrated by Courage and Khazaka (CK) electronic GmBH, Germany.

Participants were allowed to acclimatize for 20 minutes in a climate-controlled room (21 – 22 °C; relative humidity 40 – 60%). Skin barrier function parameters were measured on the dorsal aspects of both hands and additionally on both volar forearms. Participants' hands and forearms were chosen as these regions will be subjected to frequent hand washing and wet work during the nursing students' practical training. An average for each of the skin barrier function parameters were calculated from three consecutive measurements, measured adjacently on the designated anatomical areas. Skin surface pH averages were calculated by using the logarithm of the average of the hydrogen ion concentration.

The skin barrier function parameters were measured prior to the coronavirus (COVID-19) pandemic before hand hygiene regimens intensified. Skin barrier function measurements were performed three times per year, at the beginning of the academic year (January/February), during South African winter months (June/July) and at the end of the academic year, during the start of the South African summer (October/November). These measurements were repeated for two years.

5.3.3.4 Statistical analyses

Statistical analyses were performed with SPSS version 27 (IBM Corp. Armonk, NY) and illustrated with GraphPad Prism® version 7 (GraphPad Software San Diego, California).

Normality of the data was tested with residual plots conducted with each association tested. Residuals were determined to have a normal distribution indicated by $p > 0.05$. Statistical outliers were detected with Grubbs' test (Grubbs, 1950) and a total of 11 outliers were removed from the data prior to the analyses. Differences between the left and right anatomical regions and the influence of room conditions (relative humidity and temperature) were tested with multiple regression.

Linear mixed models were performed to test if skin barrier function measurements differed significantly over the two years for the two racial groups (significant if $p \leq 0.05$). Specific differences between the skin barrier function measurement at any of the time points and between the two racial groups were tested with Bonferonni post-hoc tests.

Effect sizes were for the differences between any of the time points were calculated as follow:

$$(Mean\ 1 - Mean\ 2)/\sqrt{(Residual\ Variance + Intercept\ Variance)}.$$

Effect sizes were interpreted as small effect $r = 0.2$; moderate effect $r = 0.5$ and large effect $r = 0.8$ (Fritz *et al.*, 2012).

5.3.4 Results

Only skin barrier function parameters as measured on the dorsal aspect of the hands are included in the results, as this region was more exposed to wet work and frequent hand washing. Data from the volar forearms which demonstrated normal skin condition are included in supplementary tables for reference. No significant difference ($p > 0.05$) in skin barrier function measurements between right and left hand were detected and therefore averages of measurements of the right and left hand are presented in Figure 5-1 a – f. First year students' data are presented separately to illustrate skin barrier function data from a participant group with no prior practical experience in hospitals and clinics. Participant fall-out for the first-year students were 10.3% and 10.5% for the white and Black African students respectively. Whereas participant fall-out for the senior students were 32.4% and 60.9% for the white and Black African students respectively. These included students completing their tertiary education who no longer could participate in the study.

Baseline skin barrier function parameters were measured on the first-year students prior to their practical training in hospitals and is represented by the t_0 values. Black African first-year students' mean TEWL was 24.61 $g{\cdot}m^{-2}{\cdot}h^{-1}$ (CI: 22.62; 26.61), while white students' baseline mean TEWL was 26.19 $g{\cdot}m^{-2}{\cdot}h^{-1}$ (CI: 24.57; 27.81) as illustrated in Figure 5-1a. Mean baseline SC hydration (Figure 5-1b) was 39.49 a.u. (CI: 35.75; 43.23) for Black African students and 44.94 a.u. (CI: 41.85; 48.03) for white students, whereas mean baseline skin surface pH was 5.50 (CI: 5.27; 5.72) for Black African students and 4.66 (CI 4.48; 4.85) for white students as illustrated in Figure 5-1c.

For first year students, the mean TEWL measured at t_0 was significantly higher ($p < 0.001$) than in the subsequent time intervals with the lowest mean TEWL measured at the t_2 interval (white 13.88 $g{\cdot}m^{-2}{\cdot}h^{-1}$ and Black Africans 12.51 $g{\cdot}m^{-2}{\cdot}h^{-1}$) with a large effect size of 1.09 for Black African students and 1.13 for white students (Figure 5-1a). TEWL in both racial groups were significantly ($p < 0.004$) higher at t_4 and t_5 when compared to t_2, with large effect sizes in both racial groups between t_2 and t_4 (Black African, 1.22 and white students, 0.96) as well as between t_2 and t_5 (Black African, 1.37 and white students, 1.01). However, the trend of TEWL over two years significantly ($p < 0.001$) decreased in both racial groups (established with linear mixed models). TEWL did not significantly differ between white and Black African students over the two years.

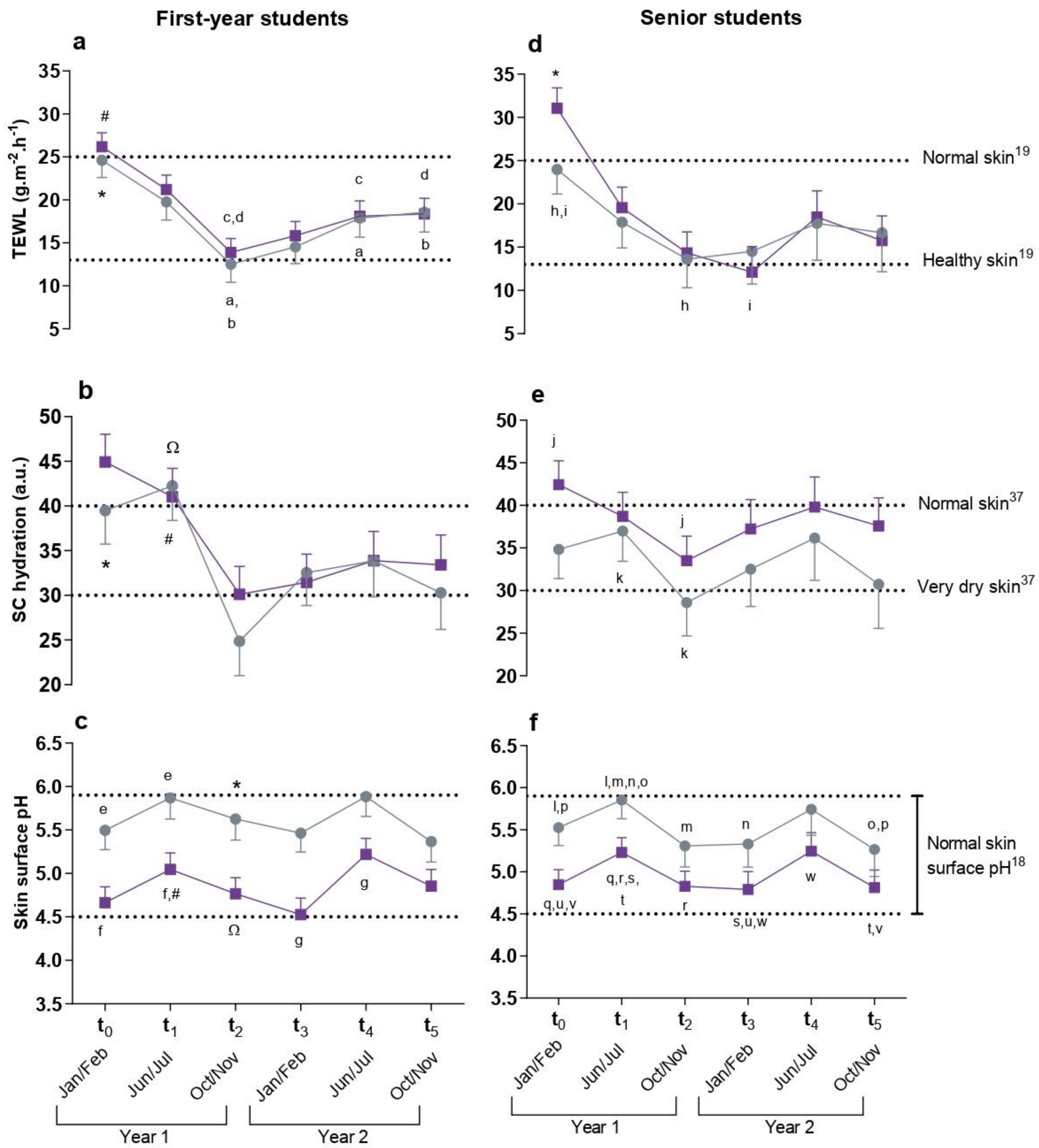

Figure 5-1: Mean skin barrier function parameters (TEWL, SC hydration and skin surface pH) for Black African nursing students (grey, •) and white nursing students (purple, ■) measured on dorsal hand, three times a year for two years (t0 – t5). Confidence intervals (CI 95%) indicated by whiskers.

***,#,Ω Significant differences ($p < 0.001$) tested with linear mixed models and Bonferonni post-hoc tests in the skin barrier function parameters for all subsequent times.**

a - w Significant differences ($p < 0.001$) in skin barrier function parameters between specific time intervals, indicated adjacent the black (•) data line for Black African students and adjacent the grey (■) data line for white students

Mean SC hydration for the first year students was the highest at t_0 and t_1 for both racial groups (Figure 5-1b), after which mean SC hydration was significantly ($p < 0.001$) lower in the subsequent time intervals with the lowest mean SC hydration measured at t_2 (Black Africans = 24.87 a.u. and white = 30.12 a.u.) with large effect sizes for both white students (1.29), and Black African students (2.05). Linear mixed models determined that the trend of SC hydration significantly ($p < 0.001$) decreased over the two years in both racial groups. SC hydration was not significantly different between white and Black African students.

The lowest mean skin surface pH was measured at t_3 for white first year students (4.53) and t_5 for Black African first year students (5.37), while the highest skin surface pH was measured during t_4 (Black Africans = 5.89 and white = 5.22) for both racial groups of first year students (Figure 5-1c). Significant differences ($p < 0.001$) in skin surface pH were established at t_0 and t_1 for both racial groups. Skin surface pH for white students significantly ($p < 0.001$) increased at t_4, when compared to t_3. Effect sizes for skin surface pH differences of Black African students ranged between a large effect between t_0 and t_1 (0.74) and a small effect size between t_2 and t_3 (0.32). Effect sizes for skin surface pH differences of white students ranged with a large effect between t_1 and t_3 (1.03) to a small effect size between t_2 and t_5 (0.17). Skin surface pH differed significantly ($p < 0.001$) between the racial groups and skin surface pH significantly ($p < 0.001$) varied over time in both racial groups (established with linear mixed models).

The first skin barrier function measurements for senior students were performed at the start of the academic year and are represented by t_0 as illustrated in Figure 5-1d – f. However senior students have had practical experience at this point and are therefore not a true representation of baseline skin barrier function parameters. Mean TEWL at t_0 for senior Black African students was 23.99 $g \cdot m^{-2} \cdot h^{-1}$ (CI: 21.13; 26.85) and 31.07 $g \cdot m^{-2} \cdot h^{-1}$ (CI: 28.72; 33.42) for white students. Mean SC hydration at t_0 was 34.83 a.u. (CI: 31.42; 38.24) for Black African students and 42.44 a.u. (CI: 39.65; 45.23) for white students, while skin surface pH was 5.53 (CI: 5.31; 5.74) and 4.85 (CI: 4.68; 5.03) for Black African and white students respectively. In Black African students TEWL were significantly ($p = 0.001$) lower at t_2 and t_3 when compared to t_0 (effect sizes t_2, 1.49 and t_3, 1.36) as illustrated in Figure 5-1d. white students' TEWL measured during t_0 was significantly ($p < 0.001$) higher than the subsequent time intervals with the largest effect size between t_0 and t_3 (2.72), however no other significant differences in TEWL were established for this group in the remainder of the time intervals (Figure 5-1d). Linear mixed models determined the trend of TEWL significantly ($p < 0.001$) decreased over two years in both racial groups, however TEWL did not significantly differ between the racial groups.

Mean SC hydration of Black African senior students was 34.83 a.u. (CI: 31.42; 38.24), and 42.44 a.u. (CI: 39.65; 45.23) for white senior students at t_0 (Figure 5-1e). Mean SC hydration ranged between 36.83 a.u. and 28.58 a.u. for Black African students and, 42.44 a.u. and

33.51 a.u. for white students. SC hydration of Black African senior students was significantly ($p = 0.006$) lower at the t_2 interval when compared to t_1 (large effect, 1.01), while white senior students' SC hydration was significantly ($p < 0.001$) lower at the t_2 interval when compared to t_0 (large effect, 1.07). No other specific differences in SC hydration between time intervals were established in the two racial groups, however time had a significant ($p < 0.001$) overall effect on both racial groups (established with linear mixed models). SC hydration was not significantly different between the two racial groups.

Mean skin surface pH at t_0 was 5.53 (CI: 5.31; 5.74) for Black African students, and 4.85 (CI: 4.68; 5.03) for white students (Figure 5-1f). Skin surface pH significantly ($p < 0.001$) increased at t_1 when compared to t_0 for both racial groups established with medium effect sizes (Black African, 0.63 and white, 0.73). Skin surface pH was subsequently significantly ($p < 0.001$) lower at t_2, t_3 and t_5 when compared to t_1, with large effect sizes in the Black African group (t_2, 1.05; t_3, 1.00; t_5, 1.13) and medium to large effect sizes for the white group (t_2, 0.77; t_3, 0.84; t_5, 0.80) Skin surface pH increased during t_4 when compared to t_3 in both racial groups, however the increase was only significant ($p < 0.001$) in white students with a large effect size of 0.87. Skin surface pH significantly ($p < 0.001$) varied over time, overall, in both racial groups and skin surface pH differed significantly ($p < 0.001$) between the two racial groups as established with linear mixed models.

5.3.5 Discussion

This study aimed to investigate changes in skin barrier function on the hands of South African nursing students over a period of two years, to investigate the long-term effect of nursing students' practical training which would include frequent hand washing, skin occlusion and wet work on their skin physiology. TEWL, SC hydration and skin surface pH were measured on the hands and volar forearms of white and Black African nursing students (Academic Years one to four), however only data collected from the dorsal aspect of the hand were illustrated in Figure 5-1. These skin barrier function parameters were conducted at the beginning of the academic year and repeated after four months, for two years in total. Participant fall-out was quite high for the senior students (Academic Years two to four), however this included students completing their tertiary studies who could therefore no longer participate in the study.

Baseline TEWL, as measured at t_0 for first year students, were measured prior to any practical training in healthcare facilities and ranged from 26.19 $g \cdot m^{-2} \cdot h^{-1}$ (white students) to 24.61 $g \cdot m^{-2} \cdot h^{-1}$ (Black African students). Normal TEWL measured on healthy skin generally range from 13 $g \cdot m^{-2} \cdot h^{-1}$ to 25 $g \cdot m^{-2} \cdot h^{-1}$ on the dorsal aspect of the hands (Kleesz *et al.*, 2011). The baseline TEWL of first year students as measured in this study, therefore falls into the higher range of normal TEWL with white students' baseline TEWL 4% above the normal range, which may be due to higher SC hydration also measured at baseline. TEWL did significantly decrease

($p < 0.001$) over the two years in both racial groups of first year students, however this decrease in TEWL only dropped below the lower limit of healthy TEWL (13 $g{\cdot}m^{-2}{\cdot}h^{-1}$) (Kleesz *et al.*, 2011). during t_2 for Black African students with the lowest TEWL measured (mean: 12.51 $g{\cdot}m^{-2}{\cdot}h^{-1}$). Measurements conducted during t_2, were taken at the end of their first academic year, during which the lowest TEWL was measured in both racial groups (white students mean: 14.34 $g{\cdot}m^{-2}{\cdot}h^{-1}$ and Black African students mean: 12.51 $g{\cdot}m^{-2}{\cdot}h^{-1}$). During the first academic year, first year students started their practical training in healthcare centers, and lower TEWL indicate an improvement of skin barrier function, however if TEWL is evaluated concurrently with SC hydration it may suggest the opposite, as the lowest SC hydration was also measured at t_2 for both racial groups. If TEWL and SC hydration are considered together it may suggest that low SC hydration can lead to low TEWL as there would be less water content available in the SC to diffuse through the epidermis.

TEWL marginally increased in their second academic year, with a significant increase ($p < 0.004$) at t_4 and t_5 for both racial groups. In their second year of practical training nursing students from the North-West University focus on wound dressing and taking patient vital signs (established in participant questionnaires). The variability of TEWL in the long term has been established previously, in a study that followed apprentice nurses for three years. TEWL was significantly higher after one year of vocational training and significantly higher after three years, when compared to the first measurement. However, no significant difference was established between the one-year follow-up measurement and the final measurement after three years (Schmid *et al.*, 2005), even though there were two years in between the first follow-up measurement and the final measurement. Similar variability in TEWL was established in this study for the senior students where significant differences ($p \leq 0.001$) was established between the initial measurement at t_0 and the following measurements, however no significant differences were established between the follow up measurements (t_2 to t_5). Furthermore, a decrease in TEWL after work-related exposure to wet work was established in a study that followed junior hairdressers for three years (John *et al.*, 2000), which corroborates with the findings of this study which showed significant ($p < 0.001$) lower TEWL in both first year and senior students after two years. Seasonal influence on TEWL did not seem to play a significant role in the data, as no significant differences were established between t_0 and t_1, nor between t_3 and t_4 in both racial groups, with t_1 and t_4 measured during June and July which is the winter months in the southern hemisphere.

The baseline SC hydration of first-year students at the start of the study (t_0) and at t_1 were close to the normal range for healthy skin (40 a.u.) (Heinrich *et al.*, 2003) on the dorsum of the hands. After t_1 SC hydration significantly decreased in the intervals that followed, with the lowest SC hydration measured at t_2, which were taken after one year of practical training, for both racial groups (white students 30.12 a.u.; Black African students 24.87 a.u.). SC hydration at t_0 and t_1

were both significantly higher than at later time points. This suggests that even after one and two years of training, SC hydration levels did not reach the same levels as at the start of the study or during the first winter. Dry skin is characterized with SC hydration values equal to or lower than 30 a.u (Heinrich *et al.*, 2003) and SC hydration for the first-year students from t_2 and the following intervals all kept fluctuating around 30 a.u. indicating dry skin in the students. A decrease in SC hydration from long term exposure to work-related wet work and frequent hand washing was not established previously in a study that followed apprentice nurses for three years (Schmid *et al.*, 2005), nor in the study that followed apprentice hairdressers for three years (John *et al.*, 2000). However, SC hydration levels of senior students in this study did support the findings of previous research (John *et al.*, 2000; Schmid *et al.*, 2005), which did not show a long-term decrease in SC hydration. In this study, only specific differences in SC hydration were established among senior students. Although lower SC hydration levels were expected during winter months (t_1 and t_4), the data did not show a clear seasonal influence for either first-year or senior students. The only exception was a significant decrease in SC hydration from t_1 to t_2 for first year and Black African senior students. No significant differences were found between t_4 and the intervals immediately before (t_3) and after (t_5) it.

A decrease in SC hydration after exposure to frequent cleansing could not be established previously in clinical settings (Fartasch *et al.*, 2012; Symanzik *et al.*, 2022), however SC hydration measured on the hands of nurses that followed a soap and water regimen significantly decreased after two weeks (Boyce *et al.*, 2000). The latter study required the nurses to only use soap and water in between patient care and did not allow the use of moisturizers or emollients for the two weeks (Boyce *et al.*, 2000). These studies illustrate the different findings between studies conducted in a clinical setting and studies that are performed in a practical setting. Furthermore, the decrease of SC hydration in the short term, without the use of any skin care products, illustrates the negative impact that soaps and wet work have on the skin, but excluded factors that may influence the recovery of the SC in practice. This was demonstrated by the studies that found no significant decrease in SC hydration after three years for apprentice nurses (Schmid *et al.*, 2005) or apprentice hairdressers (John *et al.*, 2000). Longitudinal studies, by design, have factors out of the control of investigators that may impact the findings of the studies, such as the use of moisturizers and emollients by participants. However, this can be considered as an advantage of longitudinal studies as the findings would be more representative of real-world conditions (white & Arzi, 2005).

Mean skin surface pH measured at t_0 for first year students were 4.66 for white students and 5.50 for Black African students which falls into the healthy range for skin surface pH between 4.5 and 5.9 (Schmid-Wendtner & Korting, 2006). Skin surface pH fluctuated throughout the two years for both racial groups with significant increases at t_1 and t_4, however all skin surface pH measurements were still within the normal range for first year students and senior students. Skin surface pH of senior students also showed significant increases at t_1 and t_4. These measurements (t_1 and t_4) were taken mid-year during the winter months (June / July) of South Africa, and similar results were determined in previous studies that established that skin surface pH increases during winter months (Jiang *et al.*, 2022; Song *et al.*, 2015). Senior students' skin surface pH frequently fluctuated (indicated by l to w on Figure 5-1-f) throughout the two years. Fluctuations in skin surface pH over the two years did not show a pattern of practical significance other than the seasonal variation in this study. The study that investigated skin bioengineering methods in apprentice hairdressers for three years also did not determine practical significant differences in skin surface pH (John *et al.*, 2000).

Black African students' skin surface pH was significantly higher than that of white students for both the first year and senior students. These findings are not consistent with previous studies which established lower skin surface pH in dark pigmented (Type IV-V) when compared to light pigmented skin (Type I-II) (Gunathilake *et al.*, 2009; Warrier *et al.*, 1996). However, the aforementioned studies were conducted on Sri-Lankan (skin Type IV-V) and German nurses (skin Type I-II) and for the second study on African American (skin Type IV-V) and white (skin Type I-II) female subjects. However, a recent study conducted on a South African population found similar results to those presented in this study. Skin surface pH of Black African females was significantly higher than white female subjects from Pretoria (South Africa), although these measurements were performed on the facial skin (Voegeli *et al.,* 2019). Based on this evidence geographical location may play a more important role on skin physiology than skin pigmentation.

This study aimed to investigate any significant changes in skin barrier function while nursing students complete their tertiary education and training. Furthermore, as most of the nursing workforce in South Africa is Black African (Wildschut & Mqolozana, 2008), this study additionally aimed to investigate changes in skin barrier function in a Black African nursing student population. While no significant differences were established between white and Black African students' TEWL and SC hydration over the two years, the fact that both racial groups had a similar pattern in their skin barrier function parameters indicates that regardless of race, exposure to frequent hand washing and wet work affected their skin condition. The significant decline in TEWL in both racial groups might be seen as an improvement of skin barrier function, coupled with TEWL that were within the normal range for all groups over the two years, apart from white students' (TEWL was 4% above normal at baseline). However, if the significant decline in SC hydration is also taken into consideration, it may indicate otherwise. Low SC hydration may lead to low TEWL due to lower water content available in the SC which may cause lower water evaporation above the SC. Therefore, TEWL considered solely may not be an accurate representation of skin condition. Future studies may be able to investigate the role that interventions can play in preventing low

SC hydration in healthcare workers and which intervention would be practical and effective in a South African nursing population. Specifically, if hygroscopic or lipid rich moisturizers would be effective and practical in a South African nursing population, considering the overall dry climate and high ultra-violet (UV) index of South Africa (World Bank Group, 2021).

Limitations of this study were that the skin care regimens of the participants and the type of cleansing routines used in the hospitals could not be taken into consideration. Nursing students' practical training is based on a rotational basis between different hospitals using different hand soaps and alcohol gel rubs. In some cases, soap dispensers would not have a label which made it difficult to determine the type of soap they used. Furthermore, the fact that many of the hospitals are short staffed, students' practical training is often under high pressure and fast paced which made the carrying of hand hygiene regimen diaries impractical. Another limitation of this study was that the normal ranges for TEWL and skin surface pH were based on studies conducted on white males (Kleesz *et al.*, 2011), while the gender and race was not reported in the study for SC hydration mapping (Heinrich *et al.*, 2003). Further research is required to establish normal ranges for females and for Black African skin.

5.3.6 Conclusion

The skin barrier function of nursing students in this study was significantly affected by their practical training over a period of two years. TEWL and SC hydration significantly decreased over two years in the first-year students, while only specific differences in TEWL and SC hydration could be established between the time intervals for the senior students. Skin surface pH significantly varied over the two years with significant increases in the winter months. No significant differences were determined between white and Black African students in TEWL and SC hydration, while skin surface pH differed significantly between white and Black African first year and senior students, with significantly higher skin surface pH values found in Black African students when compared to white students. This study illustrated the variability of skin barrier function parameters and the possible recovery of the SC in a practical setting. A multi-parameter approach is recommended when investigating skin condition / barrier function, as illustrated with the interaction between TEWL and SC hydration in this study.

5.3.7 References

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CHAPTER 6 SHORT COMMUNICATION

Young, M.M., Du Plessis, J.L., Reichert, L., Franken, A., Hand dermatitis prevalence and severity in a population of South African nursing students. Submitted to *Workplace Health & Safety* for consideration of publication.

6.1 Background

Hand dermatitis is a common occurrence among healthcare workers as they are required to frequently perform wet work tasks and cleanse their hands to prevent nosocomial infections in healthcare facilities. Studies on hand dermatitis incidence in South African healthcare workers with dark pigmented skin are limited, although the majority of healthcare workers are Black Africans. In South Africa the most prevalent dermatological condition is eczema, accounting for one third of the cases reported. However, occupational skin diseases are considered under reported in South Africa when compared to international data. Hand eczema prevalence tends to be higher among student nurses when compared to professional nurses, as younger age has been associated as a risk factor for dermatitis. This article evaluated the prevalence and severity of hand dermatitis in a population of South African nursing students, after one year of practical training and provided new data on the pathology in a South African context. This article was submitted to *Workplace Health & Safety*, which is an internationally refereed journal. The format of this article is written with Arial Font 11, and 1.5 line spacing for uniformity of the thesis, however an excerpt of the instructions for is included below.

6.2 Instructions for authors (excerpt)

Workplace Health & Safety (WH&S) is the official journal for the American Association of Occupational Health Nurses, Inc. (www.AAOHN.org). WH&S is published by Sage Publishing. WH&S welcomes the submission of original manuscripts of interest to occupational and environmental health nurses that includes original research, literature reviews, professional practice (evidence-based practice updates, clinical case reports and clinical updates, leadership and management, legal/regulatory, successful programs), current topics, editorials, and letters to the editor.

Research ethics: All papers reporting animal and human studies must include whether written approval to conduct the study was obtained from the Ethics Committee or Institutional Review Board of the author's institution. Please ensure that you have provided the full name and institution of the review committee, as well as the Ethics Committee reference number. We accept manuscripts that report on human and/or animal studies for publication only, if it is made clear that the investigations were carried out in accordance with high ethical standards. Studies using humans, which might be interpreted as experimental (e.g., controlled trials), should conform to the Declaration of Helsinki https://www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/, and the typescripts must include a statement that the research protocol was approved by the appropriate ethical committee. In line with the Declaration of Helsinki 1975, revised in Hong Kong 1989, we encourage authors to register their clinical trials (and other suitable databases identified by the ICMJE, http://www.icmje.org).

Brief Report for Research or Professional Practice: This article format is ideal for presenting Pilot or small research studies (e.g., with smaller sample sizes) or pilot or small professional practice programs. These are short reports in which the findings are preliminary and/or narrowly focused. Please refer to the descriptions for Professional Practice and Original Research for more details on the manuscript outline and approach. The article should be structured per the instructions provided for the Research or Professional Practice article descriptions provided above. This manuscript format includes the Insert Box. Insert Box titled "Applying Research to Occupational Health Practice" and “Implications for Occupational Health Nursing Practice or Implications for Occupational Health Practice”: This should provide the reader with information regarding how the study findings are relevant to current occupational and environmental health practice, including how the findings can be reasonably applied to the frontline occupational health nurse or other occupational health practitioner. This includes a 150-word summary that provides a brief overview of the findings and how the findings apply to occupational health nursing practice or general occupational health practice. This is different from the Abstract and does not include sub-headings. The Insert/Box is a brief narrative description of the project.

Typing: Text, tables, and figures must be in Arial font, pt. 11 throughout. The main text must be double-spaced throughout with left margin alignment, including acknowledgments, abstract, text, references, and figure legends. The tables should be single spaced. All pages should be numbered.

Length of manuscripts: Brief reports should contain a structured abstract (250 words) and the text word count should be 1 500 to 2 500 words.

References: Authors are expected to provide accurate and proper sourcing throughout their documents. Primary sources should be used. Manuscripts must conform to the guidelines for manuscript preparation as per the Publication Manual of the American Psychological Association, 7th ed. (2020). Additional details can be found in the APA Blog. The authors are responsible for the accuracy of references. The following includes examples of in-text APA citations, followed by APA formatting for the reference list.

APA In-text Citations:

Work by one author:First and subsequent citations: Author (year); parenthetical (Author, year)

Work by two authors: First and subsequent citations: Smith and Walker (1997); parenthetical (Smith & Walker, 1997)

Work by three or more authors:First citation: Smith et al. (1997); parenthetical (Smith et al., 1997)

Subsequent citation: Smith et al. (1997); parenthetical (Smith et al., 1997)

Examples:

Journal article:

More than 20 authors: Wiskunde, B., Arslan, M., Fischer, P., Nowak, L., Van den Berg, O., Coetzee, L., Juárez, U., Riyaziyyat, E., Wang, C., Zhang, I., Li, P., Yang, R., Kumar, B., Xu, A., Martinez, R., McIntosh, V., Ibáñez, L. M., Mäkinen, G., Virtanen, E., . . . Kovács, A. (2019). Indie pop rocks mathematics: Twenty One Pilots, Nicolas Bourbaki, and the empty set. Journal of Improbable Mathematics, 27(1), 1935–1968. https://doi.org/10.0000/3mp7y-537

Book:

Voet, D., & Voet, J. G. (Eds.). (1990). Basic biochemistry (3rd ed.). J. Wiley.

(No publisher location details required)

Chapter in a book:

Kuret, J. A., & Murad, F. (1976). Hormones. In A. G. Gilman & P. Taylor (Eds.), The pharmacological basis of therapeutics (8th ed., pp. 1334-1360). Grune & Stratton.

Paper at conference:

Eisenberg, J. (1995, October 28-30) Market forces and physician workforce reform. Paper presented at the annual meeting of the Association of American Medical Colleges, Washington, DC.

Maddox, S., Hurling, J., Stewart, E., & Edwards, A. (2016, March 30-April 2) If mama ain't happy, nobody's happy: The effect of parental depression on mood dysregulation in children [Paper presentation]. Southeastern Psychological Association 62nd Annual Meeting, New Orleans, LA, United States

Web site:

Food and Drug Administration (FDA) Resources Page. (n.d.). http://vm.cfsan.fda.gov/;aplrd/sodium.txt

6.3 Hand dermatitis prevalence and severity in a population of South African nursing students

6.3.1 Abstract

Background: Studies on hand dermatitis incidence in South African healthcare workers with dark pigmented skin are limited, although the majority of healthcare workers are Black Africans. This study evaluated the prevalence and severity of hand dermatitis of nursing students after one year of practical training.

Methods: Forty-nine White and 32 Black African nursing students participated in this study. The skin of the participants was clinically evaluated by a dermatologist and a hand dermatitis severity score was determined at the start and end of one year of practical training.

Findings: Hand dermatitis prevalence increased with 11% for White and 12% for Black African nursing students after one year of training. Hand dermatitis scores increased significantly ($p = 0.03$, small effect size 0.33, White students and $p = 0.04$, moderate effect size 0.44, Black African students) between the start and end of one year of practical training in both racial groups. Black African nursing students had the highest severity index of 6 at the end of one year of practical training.

Conclusion: Severity and prevalence of hand dermatitis increased in both racial groups after one year of practical training. This is indicative that nursing students' practical training had a significant impact on their skin health after one year.

6.3.2 Background

Hand dermatitis is a common occurrence among healthcare workers as they are required to frequently perform wet work tasks and cleanse their hands to prevent nosocomial infections in healthcare facilities (Diepgen, 2012). In South Africa the most prevalent dermatological condition is eczema, accounting for one third of the cases reported (Hartshorne, 2003). This has serious implications for healthcare workers including increased health costs, prolonged sick leave and diminished quality of life (Cvetkovski et al., 2005; Fowler et al., 2006). Moreover, a Danish study has shown that female healthcare workers are more likely to take prolonged sick leave due to hand dermatitis (Cvetkovski et al., 2005), further exacerbating the issue as the majority of nurses in South Africa are female (South African Nursing Council [SANC], 2022) Younger age has been associated as a risk factor for developing occupational skin diseases (Ibler et al., 2012; Lee et al., 2013), and a Danish study found that hand eczema prevalence is higher in apprentice nurses when compared to nurses (Flyvholm et al., 2007). The incidence of hand eczema also increased during vocational training with a Dutch study that reported 81 new cases of hand eczema after a 1-year follow-up (Visser et al., 2014).

This study evaluated the prevalence and severity of hand dermatitis in a population of South African nursing students including White and Black African students, after one year of practical training and may provide new data on the pathology in a South African context.

6.3.3 Method

6.3.3.1 Ethical considerations

This study was approved by the Health Research Ethics Committee of the North-West University, South Africa (Ethics approval number: NWU-00337-16-A1). Participants were briefed on the study's purpose and risk-benefit ratio and provided informed consent prior to participation in the study. Personal information was not used, and the database was anonymised before data analyses.

6.3.3.2 Methodology

Female nursing students (Academic Year 1 to 4) from the North-West University, South Africa were recruited to participate in this study. The participants were grouped into self-reported racial groups and corresponding skin pigment types (Fitzpatrick scale) (Fitzpatrick, 1988), i.e. White and Black African. All of the participants were non-smokers and between the ages of 18 and 40 years. A dermatologist clinically evaluated the skin of the participants to diagnose the prevalence and severity of dermatitis among the participants. The presence of erythema, oedema, oozing/crusts, excoriation, lichenification and dryness of the affected skin area were evaluated and a severity score (None = 0; Mild = 1; Moderate = 2; Severe = 3) were assigned for each of the six clinical signs (Maximum score = 18). Percentage change of severity scores was calculated as follow:

$$\frac{Severity\ Score\ (end\ of\ year) - Severity\ Score\ (start\ of\ year)}{Severity\ (start\ of\ year)} \times 100$$

These evaluations were performed prior to the COVID-19 pandemic at the start of the South African academic year (January, 2018) and at the end of the year (November, 2018) to assess any change in dermatitis severity.

6.3.3.3 Statistical analyses

Statistical analyses were performed with Statistica 64 version 13.3 (Statsoft Inc. Palo Alto, California) and figures generated with GraphPad Prism® version 7 (GraphPad Software San Diego, California). Hand dermatitis prevalence and severity scores are reported as percentage of nursing students who participated in the study. A normal distribution of the data was assumed according to the central limit theorem (Le Cam, 1986), as the sample sizes used in parametric tests were above 30 and constant variance of the data were tested with Levene's test and confirmed ($p > 0.05$). A significant change in hand dermatitis scores between the start and end of the year were tested with dependent t-tests and the corresponding effect sizes were calculated (Ellis, 2010).

6.3.4 Results

Hand dermatitis prevalence and severity scores were evaluated at the start and end of the year to establish any change after one year of practical training of nursing students (mean age 20 ± 2.42). Hand dermatitis prevalence and severity indices of the nursing students are illustrated in Figure 1.

In January, 87% of White nursing students and 72% of Black African students had no indication of dermatitis (indices = 0). The prevalence of hand dermatitis increased after one year with 11% new cases for White and 12% new cases for Black African nursing students. The severity of hand dermatitis scores significantly increased between January and November for White students (Figure 1a) ($p = 0.03$, small effect size 0.33) and Black African students (Figure 1b) ($p = 0.04$, moderate effect size 0.44). The percentage of White nursing students that were diagnosed with a severity score of 2 increased from 6% to 15%, while severity score of 3 increased from 2% to 6% between January and November.

Black African students showed similar results with the severity score of 2 that increased from 11% to 31%, and severity scores of 3 and 6 that were 0% in January increased with 3% in November. Consequently, severity scores of 1 decreased between January and November for both racial groups (6% to 2% for White students and 17% to 0% for Black African students). While higher severity scores of 2 and 3 all increased in prevalence between January and November for both racial groups (Figure 1c).

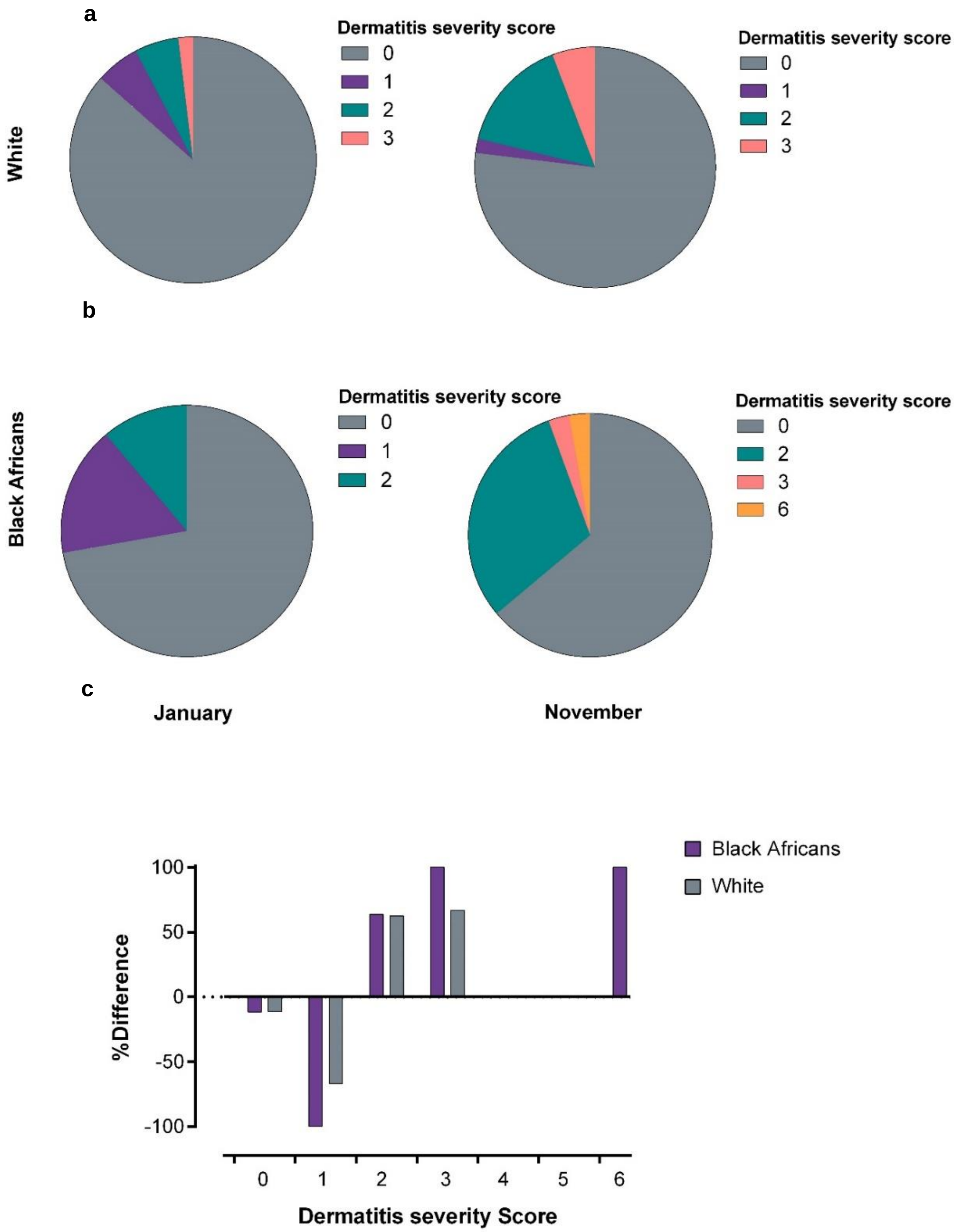

Figure 6-1: Severity indices of White (a) and Black African (b) nursing students assessed during January and November and the percentage change (c) in the dermatitis severity score between January and November.

6.3.5 Discussion

As part of their training, nursing students are required to complete practical training in hospitals, where they are subjected to frequent hand washing and wet work, which may increase their risk of hand dermatitis. The severity of hand dermatitis was determined among the participants at the start and end of an academic year of nursing students (mean age 20 ± 2.42).

After one year of practical training, hand dermatitis prevalence increased with 11% in White nursing students and 12% for Black African nursing students. The severity of dermatitis also increased significantly ($p \leq 0.04$) in both racial groups between the start and the end of the academic year. The prevalence of dermatitis severity scores of 2, 3 and 6 increased in Black African nursing students, while only severity scores 2 and 3 increased significantly in White students in November. A severity score of 6 would either indicate a score of 1 in all six clinical signs evaluated or it would mean scoring a 2 or 3 in severity in two or more of the clinical signs. In both cases it would have a significant impact on the quality of life of the participants without intervention.

Black African nursing students' skin condition significantly deteriorated with a moderate effect size (0.44), compared to a smaller effect size of 0.33 observed in White students. This is consistent with the findings of another study that observed increased hand eczema prevalence within the first apprenticeship year of nursing students (Visser et al., 2014). Considering that these changes took place after only one year of practical training, and that the duration of the South African tertiary nursing degree extends over a period of four years, it is anticipated that the incidence and severity of hand dermatitis would be considerably exacerbated after completion of their education. Moreover, it is important to note that the practical training hours of nursing students are not comparable to the hours of a full-time healthcare professional. Consequently, continuous exposure to wet work throughout their professional career may have a significant impact on their quality of life.

In the absence of more recent data, the number of occupational skin diseases (OSD) cases reported in South Africa during 2008 were approximately 30 times lower when compared to international data, mainly due to underreporting (Carman & Kruger, 2008). Occupational skin diseases are considered under reported especially when considering the results from the present study conducted only on student nurses, which showed a significant increase in hand dermatitis prevalence and severity after only one year of practical training. Training on the use of hand moisturisers during a shift had beneficial effects on UK nurses' skin condition (Burke et al., 2018), and could be included in the training of student nurses. In South Africa the Occupational Health and Safety Act (Act 85 of 1993) requires employers to provide information, instruction and training to employees regarding the health risks associated with their employment, as well as control measures that may reduce the risks (Occupational Health and Safety Act 85 of 1993). Healthcare providers and tertiary institutions are therefore, legally required to provide instruction and training to healthcare workers on how to minimise occupational skin diseases.

6.3.5.1 Limitations

A limitation of this study was that the skin care regimens of the participants and the type of cleansing routines used in the hospitals could not be taken into consideration. The rotational nature of nursing students' training across various hospitals, each using different hand soaps and alcohol gel rubs, added complexity. Unlabelled soap dispensers and the impracticality of maintaining hand hygiene diaries due to high-pressure, fast-paced training environments in understaffed hospitals further compounded this issue.

6.3.6 Conclusion

The prevalence of hand dermatitis increased after one year with 11% new cases for White and 12% new cases for Black African nursing students. Dermatitis severity increased in both racial groups after one year of practical training with Black African nursing students having the highest severity score of 6 out of 18 at the end of the year. This study provided valuable insights on the development of skin disease in nursing students, as the severity of dermatitis was higher in Black African nursing students at the end of the academic year. Black African nursing students may therefore be more vulnerable to the development of dermatitis during their tertiary education. It is recommended that education programmes for healthcare workers should include skin care regimens as part of their training and possibly apply specific training for vulnerable groups as identified in this study.

Applying Research to Occupational Health Practice

The irritant and allergic effects associated with the duties of healthcare workers during their practical training and subsequent career at healthcare facilities have a significant impact on their skin health. This has been illustrated by the findings of this study that showed significant increases in hand dermatitis prevalence and severity in South African nursing students after one year of practical training. Moreover, Black African nursing students had the highest severity of hand dermatitis after the one-year follow up. As the majority of the South African nursing workforce consist of Black African females, measures to protect their skin health should be refocused and enforced. This study provided novel findings on hand dermatitis prevalence within a South African nursing student population, however it is important to note that the practical training hours of nursing students are not comparable to the hours of a full-time healthcare professional.

Implications for Occupational Health Nursing Practice

This study reported the increase in the incidence and severity of hand dermatitis of nursing students after only one year of practical training. This illustrates the impact of hand hygiene and wet work on the skin health of nursing students and the potential impact of continuous exposure. For the frontline occupational health nurse, it is important to understand the influence of hand hygiene practices on their skin health, as well as the methods that should be followed to protect their skin health during their nursing career.

6.3.7 References

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CHAPTER 7 CONCLUDING CHAPTER

This chapter discusses the conclusions drawn from the study, with particular emphasis on the aims, objectives and hypotheses postulated in this thesis. Recommendations are made to prevent or minimise skin barrier function deterioration in South African nursing students and consequential hand dermatitis risk. Finally, the limitations of skin barrier function assessments are discussed, and possible future studies recommended.

7.1 Conclusions

Skin barrier function has been compared between racial groups in numerous studies conducted over the span of the past two decades (Berardesca *et al.*, 1991; Warrier *et al.*, 1996; Wesley & Maibach, 2003; Alexis *et al.*, 2021). It is important to understand baseline skin barrier function differences among racial groups, if any. Thereafter, it is possible to determine the influence of certain conditions that may compromise skin barrier function in a specific population. Previous studies that investigated racial differences in skin barrier function, measured as transepidermal water loss (TEWL), determined no significant difference between African and Caucasian skin (Berardesca *et al.*, 1991; Warrier *et al.*, 1996). However, as these studies were conducted among a small number of participants, more than 20 years ago and measured skin barrier function in an American population, it was necessary to evaluate skin barrier function variation amongst South African racial groups.

Therefore, for the purpose of this thesis, baseline skin barrier function was measured of White and Black African first-year nursing students before their practical training commenced at healthcare facilities. Skin barrier function as measured with TEWL, and other parameters including stratum corneum (SC) hydration and skin surface pH were compared between White and Black African nursing students, achieving the first objective of this study. This was published in *Skin Research and Technology* (MM Young, A Franken, JL du Plessis. Transepidermal water loss, stratum corneum hydration and skin surface pH of female African and Caucasian nursing students. Skin Res Technol. 2019;88-95) and is included in Chapter 3 of the thesis. No significant difference in baseline TEWL between White and Black African nursing students was established. The first hypothesis that: *No significant difference exists in baseline skin barrier function (based on TEWL) between White and Black African nursing students,* is therefore accepted. Skin barrier function, primarily defined by TEWL, is the skin's ability to prevent endogenous water loss (excluding perspiration) (Pirot & Falson, 2004). White and Black African nursing students included in this study, therefore, had similar endogenous water loss (measured as TEWL), but the other skin parameters measured, differed significantly between the racial groups. SC hydration was significantly lower and skin surface pH significantly higher in Black African nursing students. SC hydration of Black African nursing students was far below the recommended corneometrical values proposed by the German Society for Scientific and Applied Cosmetics (DGK). Unfortunately, the racial groups of participants were not reported in this multicentre DGK study (Heinrich *et al.*, 2003), and might therefore not be comparable to a South African population. However, the low SC hydration established in Black African nursing students may be associated with the elevated skin surface pH found in this group. Elevated skin surface pH increases serine proteases activity, which causes the breakdown of enzymes responsible for lipid synthesis (Jakasa *et al.*, 2018). A compromised lipid matrix would negatively affect the water holding capacity of the SC as the hydrophobic lipid barrier is one of the key components of maintaining SC hydration (Voegeli & Rawlings, 2023).

A second component of maintaining SC hydration is Natural Moisturising Factor (NMF), which forms part of the hydrophilic protein component of the SC and maintains SC hydration by attracting water in the SC (Voegeli & Rawlings, 2023). Due to the integral role that NMF plays in maintaining SC hydration and skin surface pH, racial differences in NMF content have been investigated to provide some clarity on structural and physiological differences of the skin between racial groups. Previous studies measured NMF content in a South African population and established higher NMF levels in Black Africans when compared to Caucasians (Raj *et al.*, 2016). However, Raj *et al.* (2016) measured NMF on the cheeks of participants which is not as frequently exposed to washing as the hands.

In order to assess NMF levels in a nursing student population who are required to frequently cleanse their hands, NMF was collected from the dorsal hands of White and Black African nursing students and the findings were submitted for publication in *Contact Dermatitis* (Chapter 4 of this thesis). The second objective has been achieved when no significant difference was established in most of the NMF amino acids and their derivatives between White and Black African nursing students, collected from their hands. The only difference between the racial groups was established for histidine which was significantly higher in White students. Histidine is enzymatically broken down to form trans-urocanic acid (t-UCA) which is one of the primary free amino acids evaluated to determine NMF content (Elias, 2010). While a significant difference was established in histidine between the racial groups, t-UCA did not differ significantly between White and Black African nursing students. The second hypothesis of: *NMF content is higher on the hands of Black African nursing students when compared to White nursing students,* is therefore rejected.

Published literature on NMF in a South African population is limited to two studies (Thawer-Esmail *et al.*, 2014; Raj *et al.*, 2016), while the NMF comparison between South African racial groups is limited to the findings published by Raj *et al.* (2016). As with skin barrier function, NMF content may vary between anatomical positions which may be a possible explanation for the contradictory results, as NMF was collected from the dorsal hands for this study while Raj *et al.* (2016) evaluated facial NMF content. Furthermore, NMF content increases with age in healthy subjects (Howard *et al.*, 2022), and the mean age of participants included in this study was 20 ± 2.42 years compared to 41 ± 2.77 years in the study conducted by Raj *et al.* (2016), which may further contribute to the contradictory results. Due to the discrepancies in participants' ages and anatomical positions where NMF was collected from, the results reported in Chapter 4 of this thesis may not be comparable to that of Raj *et al.* (2016). However no other published studies on NMF content of different racial groups are available. Similar NMF content between White and Black African nursing students indicates similar SC hygroscopic properties between the groups. When considering these results together with the results reported in Chapter 3, it substantiates the theory that the low SC hydration observed in Black African nursing students may be related to the compromised lipid hydrophobic barrier and not due to decreased hygroscopic properties of their SC.

Occupational exposure to wet work and frequent hand washing may affect skin barrier function, as detergents may directly remove SC lipids or increase skin surface pH, thereby altering the activity of lipid processing enzymes (Fartasch, 1997; Jungersted *et al.*, 2010). A compromised hydrophobic lipid barrier may increase TEWL and subsequently decrease SC hydration (Boyce *et al.*, 2000; Jungersted *et al.*, 2010). As healthcare workers are occupationally exposed to wet work and frequent hand cleansing and disinfecting regimens, the changes that may occur in the skin barrier function parameters are of particular significance to them. Studies on skin barrier function and occupational skin diseases have been conducted specifically on nursing students internationally (Held *et al.*, 2001; Visser *et al.*, 2014; Šakić *et al.*, 2022), as younger age has been identified as a risk factor for occupational skin diseases (Ibler *et al.*, 2012). While there are numerous studies available on the effects of nursing student practical training on their skin barrier function, as mentioned above, there are no published literature available on how skin barrier function of Black African nursing students is affected. For the purpose of this thesis, skin barrier function of White and Black African nursing students was assessed over a period of two years during their tertiary education and the findings submitted for publication in the *Journal of Dermatology Nurses' Association* (Chapter 5 of this thesis). TEWL significantly decreased over a period of two years indicating an improvement in skin barrier function in both White and Black African nursing students. The third objective of this study was achieved when White and Black African nursing students' skin barrier function was evaluated with the progression of their tertiary education. The third hypothesis stated: S*kin barrier function on the hands of White and Black African nursing students deteriorate, as measured by an increase in TEWL, over a two-year period during the progression of their tertiary education.* This hypothesis is rejected, as a significant decrease in TEWL was established over a period of two years in White and Black

African nursing students. The decrease in TEWL in both racial groups indicates that skin barrier function of White and Black African nursing students has improved with the progression of their tertiary education. However, SC hydration of first-year nursing students, also significantly decreased over two years. When TEWL and SC hydration are evaluated together, it can be discerned that the observed decrease in TEWL may potentially be attributed to low SC hydration. The diffusion coefficient for SC water is dependent on the water content present in the SC (Blank *et al.*, 1984), and during conditions where low SC hydration is present, TEWL may also be low. This phenomenon was also observed in apprentice hairdressers, where a decrease in TEWL was established after three years of exposure to wet work (John *et al.*, 2000). The results in Chapter 5 of this thesis showed that a multiparameter approach should be followed when interpreting TEWL, as it may be affected by other skin parameters such as SC hydration.

The practical training in healthcare facilities had a discernible impact on the skin condition of South African nursing students. This was evidenced by the significant decrease in TEWL and SC hydration with the progression of their studies, with the lowest SC hydration established for Black African first-year nursing students at the end of the first year. No significant differences were established between White and Black African nursing students' TEWL and SC hydration trends over the period of two years. This indicated that regardless of race, exposure to frequent hand washing and wet work affected their skin condition, illustrated by the significant decrease in TEWL and SC hydration. Skin surface pH was significantly different between the racial groups however, no significant trends were detected over the period of two years. The significant difference in skin surface pH between White and Black African nursing students established after two years of practical training (Chapter 5 of this thesis), corroborated the findings of baseline skin surface pH differences between the racial groups reported in Chapter 3. The observed difference in baseline and longitudinal skin surface pH between the racial groups, emphasises the necessity of targeted interventions focused on recovering skin surface pH of Black African nursing students to a normal acidic pH.

Following the significant effect that occupational exposure to wet work and frequent hand washing have on skin barrier function, various studies focussed on determining the prevalence of occupational skin diseases in nursing students and the associated risk factors. A Danish study established a significantly higher prevalence of hand eczema in apprentice nurses when compared to professional nurses (Flyvholm *et al.*, 2007). During the COVID-19 pandemic a Croation study determined that 49% of final year apprentice nurses had hand eczema (Šakić *et al.*, 2022). High prevalence of hand dermatitis among nursing students is universal and studies have been conducted worldwide. However limited published sources are available on hand dermatitis prevalence among Black African nursing students. One study that investigated occupational contact dermatitis among healthcare workers in Ethiopia established self-reported contact dermatitis in 31.5% of the healthcare workers in a hospital in Gondor town (Mekonnen *et al.*, 2019). However, as the majority of participants in the study conducted by Mekonnen *et al.* (2019) were male, limited data on hand dermatitis prevalence in Black African female nursing students still exist. South African nurses are predominantly Black African females (SANC, 2022), and the prevalence and severity of hand dermatitis were investigated among South African nursing students, achieving the fourth objective. The findings were submitted for publication in *Workplace Health & Safety* (Chapter 6 of this thesis). Hand dermatitis prevalence increased with 11% for White and 12% for Black African nursing students after one year of practical training. Furthermore, hand dermatitis severity scores also significantly increased after one year in both racial groups. The fourth hypothesis of: *Hand dermatitis in White and Black African nursing students increases in prevalence and severity within a one-year period of their tertiary education*, is therefore accepted. It was found that hand dermatitis scores of 2, 3 and 6 increased in prevalence among Black African students, while only scores of 2 and 3 increased in prevalence among White students. This indicates that prevalence and severity of hand dermatitis were higher in Black African nursing students when compared to White students. Considering that these results were only determined after one-year of practical training, exposure to wet work during full-time occupation may have a significant impact on their quality of life as healthcare professionals.

The results presented in this thesis showed that Black African nursing students had significantly lower baseline SC hydration and higher baseline skin surface pH. Whereas skin barrier function trends over a period of two years and NMF content did not differ significantly between the racial groups, Black African nursing students still had higher hand dermatitis prevalence and severity scores after one year of practical training. This illustrated the impact of low baseline SC hydration and elevated skin surface pH on Black African students' skin health prior to starting their tertiary education. Therefore, the baseline skin condition of Black African nursing students may have predisposed them to have a higher risk for developing skin diseases during their practical training. The relationship between TEWL and SC hydration was demonstrated as well as the importance of interpreting TEWL and skin barrier function with a multiparameter approach. A significant decrease in SC hydration, as well as an increase in prevalence and severity of hand dermatitis was established in both racial groups with the progression of their practical training. This finding confirmed that the wet work conditions prevalent during nursing student tertiary education affected both racial groups' skin condition. The impact of nursing students' practical training on skin health was demonstrated in a South African nursing student population, providing valuable and novel findings for a high-risk population such as nursing students.

These findings were established during the tertiary education of nursing students before they started their career as professional nurses. Intervention to protect nursing students' skin health should therefore be implemented during their tertiary education to minimise the risk of developing occupational skin diseases. Interventional studies that focused on education and training of proper hand hygiene routines during a working shift of healthcare workers illustrated the success of reducing the risk of hand dermatitis (Held *et al.*, 2001; Dulon *et al.*, 2009). It is therefore necessary to include training on proper hand hygiene routines during nursing students' tertiary education to minimise their risk to develop occupational skin diseases.

7.2 Recommendations

Recommendations for nursing students and skin barrier function research based on the findings of Chapters 3, 4, 5 and 6 are discussed in the following section.

7.2.1 Recommendations for nursing students and healthcare workers

Educational programmes on appropriate hand hygiene routines, correct glove use, and moisturiser usage reduce the risk of hand dermatitis in nursing students (Held *et al.*, 2001; Dulon *et al.*, 2009). South African employers are legally required to provide information, instruction, and training to their employees regarding any health risks associated with their occupation (Occuptional Health and Safety Act 85 of 1993). **Recommendation 1:** South African healthcare facilities and tertiary institutions should not only incorporate training on the risk of hand dermatitis and measures to reduce the risk, into their educational programmes, but also instruct healthcare workers to follow the proper hand hygiene protocols published by the Department of Health (Department of Health, 2020). These protocols should be enforced by health and safety representatives, and refresher training should be provided at intervals recommended by the health and safety committee (Occuptional Health and Safety Act 85 of 1993) or when new research is published that significantly impacts these protocols. Furthermore, educational material and informative posters should be posted at healthcare facilities (refer to Figure 7-1). Recommendations on informative posters can include that jewellery should not be worn during a practical shift (Department of Health, 2020) as the metals from jewellery may increase the risk of sensitising and allergic reactions, and washing hands with lukewarm water as hot water may increase the irritant capacity of detergents (Ohlenschlaeger *et al.,* 1996), and using gloves during wet work to protect against the irritant effects of water (Wilke *et al.,* 2018). The importance of thoroughly rinsing and drying hands after washing with soap and water to remove any residual soap and water from the skin may minimise the risk of dermatitis (Held *et al.,* 2001). The recommendation for when to use alcohol sanitisers and when to wash with soap and water is included in recommendation 2, while moisturiser use is included in recommendation 3 of this section.

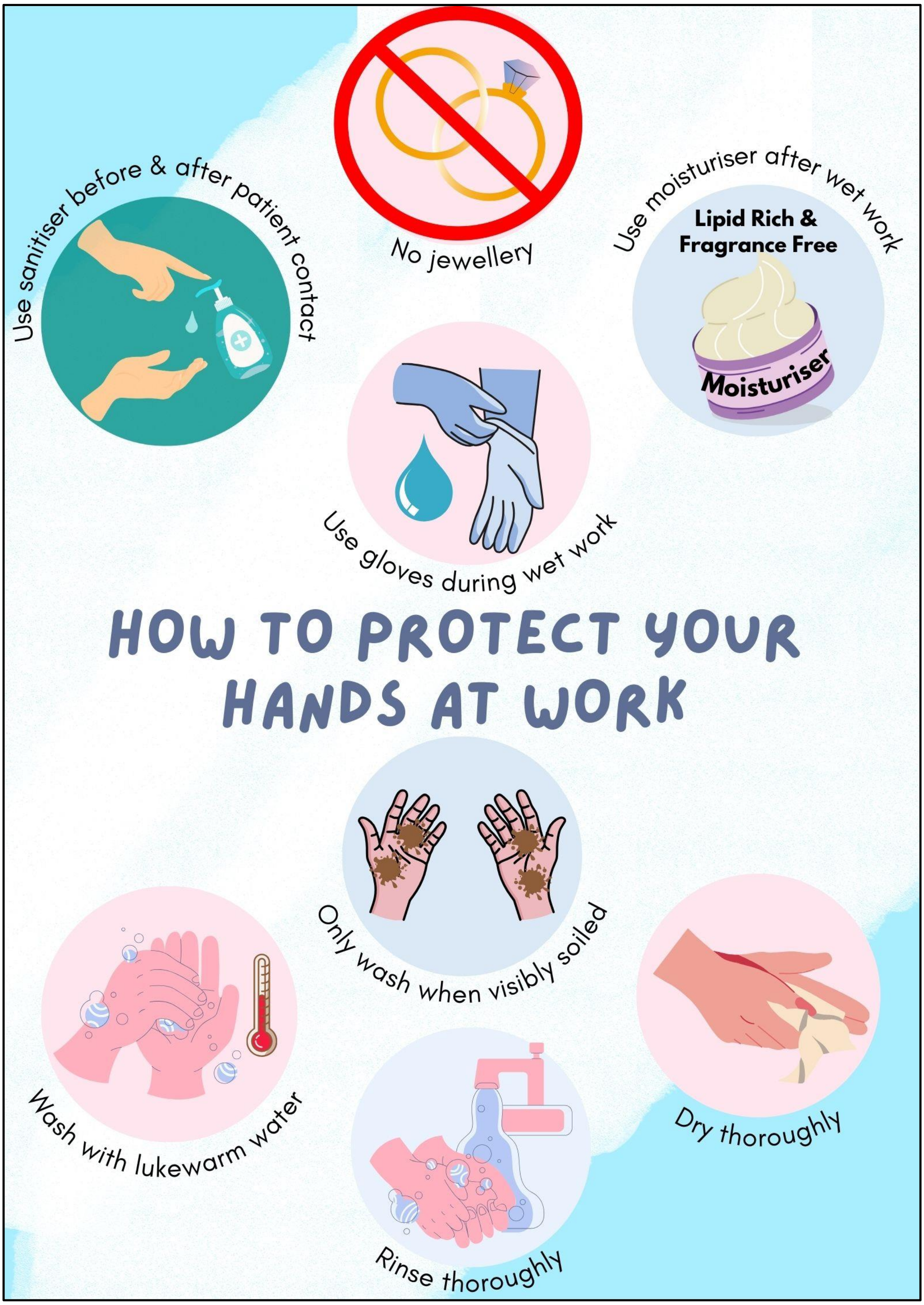

Figure 7-1: Example of an educational poster with evidence based recommendations to minimise the risk of hand dermatitis in healthcare workers (Original image using the following sources; Ohlenschlaeger *et al.,* 1996; Held *et al.,* 2001; Dulon *et al.,* 2009; Wilke *et al.,* 2018; Soltanipoor *et al.,* 2019; Department of Health, 2020).

Soap and water cleansing routines significantly decrease SC hydration, whereas alcohol gel rubs do not have a significant impact on SC hydration (Boyce *et al.*, 2000). **Recommendation 2:** Educational programmes on proper hand hygiene routines for healthcare workers should include training on when to use soap and water to wash their hands and when alcohol gel rubs are sufficient. The practical manual for infection prevention and control in South African healthcare facilities recommends using alcohol gel rubs before and after patient contact; and soap and water when hands are visibly soiled (Department of Health, 2020).

The use of emollients has been established to be an effective control measure to reduce hand dermatitis incidence among healthcare workers and nursing students (Soltanipoor *et al.*, 2019; Moldovan *et al.*, 2021). Furthermore, the provision of emollients in healthcare facilities reduced hand dermatitis incidence even further (Moldovan *et al.*, 2021). The results presented in this thesis found that the SC hydrophilic properties were similar between White and Black African nursing students. However, SC hydration was still significantly lower in Black African nursing students. **Recommendation 3:** Lipid rich moisturisers containing ceramides or triglycerides, may therefore be more effective in replenishing the lipid matrix and preventing low SC hydration of Black African skin. Healthcare facilities should provide access to emollients and encourage the use of emollients during a work shift for healthcare workers and nursing students. Emollients should contain a combination of humectants (e.g., glycerine or urea) and lipids or ceramides (e.g., ceramide NP or triglycerides) (Danby *et al.*, 2022). Emollients should be applied after washing hands and exposure to wet work (Dulon *et al.*, 2009), covering all surfaces of the hands, including in between fingers, fingertips and back of the hands (Wigger-Alberti *et al.*, 1997).

Proof of significantly higher skin surface pH that was established with Black African nursing students is found in Chapters 3 and 5 of this thesis. Skin surface pH have been found to be higher after skin cleansing with standard soaps, when compared to acidic cleansers (Duncan *et al.*, 2013). **Recommendation 4:** The use of acidic cleansers with a label e.g., “pH balanced”, may be more beneficial for Black African skin to prevent skin surface pH elevation and the skin changes associated with elevated skin surface pH. These cleansers often contain citric acid or lactic acid which is designed to balance skin surface pH (Lukić *et al.*, 2021).

7.2.2 Recommendations for skin barrier function research

When evaluating racial variances in skin barrier function between different studies, consideration should be given to instrumentation used, interventions employed and anatomical positions measured as these may have an impact on the results of the studies (Kleesz *et al.*, 2011; Alexis *et al.*, 2021). **Recommendation 5:** Only the results of studies with similar methodology and anatomical positions measured should be compared to draw accurate conclusions on how skin barrier function compares between racial groups. For example, to compare baseline skin barrier function between racial groups, the best approach is to compare *in-vivo* human studies that measured TEWL on the volar forearms, prior to interventions implemented, such as surfactant exposure, or no interventions employed at all.

Recommendation 6: The influence of endogenous and exogenous factors should be taken into consideration when designing skin barrier function studies, as there are numerous factors that might influence TEWL, SC hydration and skin surface pH and its measurement (du Plessis *et al.*, 2013; Stefaniak *et al.*, 2013). Endogenous factors that should be considered when designing a skin barrier function study include age, race, gender, anatomical position, circadian rhythm, and skin health. Exogenous factors include skin washing and wet work, solvents or surfactants, skin occlusion, skin damage, smoking, and environmental factors such as air convection, ambient temperature, relative humidity, direct light, and season (du Plessis *et al.*, 2013; Stefaniak *et al.*, 2013). These factors should be applied to the inclusion and exclusion criteria of participants and to the skin barrier function measurement conditions.

Recommendation 7: A multiparameter approach should be followed when measuring and interpreting skin barrier function, as TEWL is dependent on SC water diffusion coefficient (Blank *et al.*, 1984) and is therefore influenced by SC hydration (Mayrovitz, 2023). Furthermore, TEWL only provides information on endogenous water loss (Pirot & Falson, 2004) and not the overall skin condition.

Recommendation 8: Skin exposure to detergents and short-chain aliphatic alcohols influence NMF content (Angelova-Fischer *et al.*, 2016), and care should be taken when interpreting results from anatomical positions where exposure to these are prevalent such as the hands of participants. Particular attention should be given when comparing results from studies that collected NMF from other anatomical positions where the same exposure might not be as prevalent.

7.3 Limitations

Limitations of the study based on the findings of Chapters 3, 4, 5 and 6 are discussed in the following section.

7.3.1 Limitations of the study

Skin care regimens of the participants and cleansing routines used in the hospitals could not be taken into consideration. Nursing students are rotated between different healthcare facilities during their practical training where different hand soaps and alcohol gel rubs are provided. In some cases, soap dispensers were not labelled making it difficult to determine the type of soap they used. Furthermore, hospitals are often short staffed and nursing students' practical training is often under high pressure and fast paced, which made it impractical for the participants to keep hand hygiene regimen diaries.

Participant fall-out of first-year students was 10.5% and 60.9% for the senior students. Participant fall-out for the senior students included the students that completed their tertiary education and could no longer participate in the study. Furthermore, nursing students have a full academic schedule including theoretical contact sessions and practical training in healthcare facilities which made it difficult for some of the participants to participate in the study.

The number of Black African nursing students who participated in the study were approximately 30% less than White nursing students. This may be attributed to sociocultural variables that influenced their decision to participate or that the recruitment process did not effectively reach this demographic. The recruitment process of this study started at the beginning of the academic year, during the registration period of students, and some of the students may have registered later in the academic year. Due to the study design, there was a limited period when baseline skin barrier function could be measured before the students started their practical training, and students who registered later in the year could not be included in the study.

NMF content was only measured at a single anatomical position and not on the cheeks of participants, which prevented accurate comparison of the findings to previous studies (Raj *et al.*, 2016). NMF was collected from the dorsal hands of participants for the purpose of this thesis to quantify NMF on the site most exposed to frequent hand washing among a nursing student population.

7.3.2 Limitations of available research

International guidelines on standard SC hydration values were published 20 years ago and racial groups were not reported. These guidelines were also based on SC hydration measured on the volar forearm (Heinrich *et al.*, 2003). These values for interpreting SC hydration may therefore not be applicable in a South African population as presented in Chapter 3, where baseline SC hydration values for Black African nursing students were reported to be significantly lower than that of White students before their practical training commenced. Black African nursing students' SC hydration on the palms were also far below the guidelines proposed by Heinrich *et al.* (2003) that investigated SC hydration on the volar forearms.

The normal range established for skin surface pH are based on a study conducted on White male participants (Kleesz *et al.*, 2011). These ranges may not be applicable to a South African female nursing student population as gender has been established to significantly affect skin surface pH (Stefaniak *et al.*, 2013).

7.4 Future studies

Future studies should investigate the relationship between skin surface pH and SC sebum content between Black African and White nursing students. This may explain the relationship between low SC hydration identified in Black African nursing students and elevated skin surface pH. Confirmation of this relationship will enable recommendations to be made for this population to use specific moisturisers to replace SC lipids.

A study comparing the efficiency of lipid rich moisturisers and hygroscopic active moisturisers among a South African healthcare worker population will provide confirmation on which moisturisers would be most effective to improve the skin health of nursing students and healthcare workers.

A multicentre study investigating skin barrier function, SC hydration and skin surface pH in healthy volunteers would assist in elucidating some of the discrepancies in literature on the differences between racial groups. It would also assist in establishing guidelines and accurate reference values of these parameters for different racial groups if applicable.

Thus far studies on NMF content have focused on the relationship between filaggrin gene mutations, NMF content and atopic dermatitis prevalence (Kezic *et al.*, 2008; O'Regan *et al.*, 2009). More research is necessary on NMF content in healthy volunteers to establish reference values which can be used in comparison when NMF content is altered in intervention studies.

Further research on the possible link between skin disease, SC hydration and NMF content specifically is required. Previous research focussed on NMF content and skin disease (Soltanipoor *et al.*, 2019), however SC hydration have not been included in the investigations. This may elucidate the relationship between low NMF content and consequential low SC hydration and related skin diseases.

Currently no published literature is available on NMF content variation between anatomical areas. Future studies comparing NMF content on different anatomical positions will provide valuable insights. These will include insight on NMF content variation between anatomical positions that are frequently subjected to cleansing, such as the hands, and regions that are consistently exposed to solar ultra-violet radiation such as facial areas.

The influence of participants' socio-economic status regarding the type of cosmetic products that they buy and the effect on their skin barrier function and NMF content may be investigated. This may determine the potential socio-economic influences on skincare choices and the subsequent impact on skin health.

An observational study on current hand hygiene protocols in South African healthcare facilities may assist in identifying potential causes of skin condition deterioration among South African nurses. This may also investigate the practicality of international interventions such as emollient dispensers in healthcare facilities within a South African context.

Investigating the impact of an educational programme intervention on the skin health of South African nurses may provide insight on the effectiveness of skin health education in a South African population. Educational intervention has been successful in international studies (Held *et al.*, 2001; Dulon *et al.*, 2009), but this has not been investigated in a South African population.

7.5 References

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ANNEXURES

Annexure A: Ethics approval

The original ethics approval and most recent continuation letter are included on the next page.

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Institutional Research Ethics Regulatory Committee

Tel: +27 18 299 4849
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ETHICS APPROVAL CERTIFICATE OF STUDY

Based on approval by **Health Research Ethics Committee (HREC)** on **25/11/2016** after being reviewed at the meeting held on **20/10/2016**, the North-West University Institutional Research Ethics Regulatory Committee (NWU-IRERC) hereby **approves** your study as indicated below. This implies that the NWU-IRERC grants its permission that provided the special conditions specified below are met and pending any other authorisation that may be necessary, the study may be initiated, using the ethics number below.

Study title: **Skin barrier function of Caucasian and African nursing students.**

Study Leader/Supervisor: **Prof A Franken**
Student: **M Young**

Ethics number:

N	W	U	-	0	0	3	3	7	-	1	6	-	A	1
Institution				Study Number						Year			Status	

Status: S = Submission; R = Re-Submission; P = Provisional Authorisation; A = Authorisation

Application Type: Single study
Commencement date: 2016-11-25 **Risk:** **Minimal**

Continuation of the study is dependent on receipt of the annual (or as otherwise stipulated) monitoring report and the concomitant issuing of a letter of continuation up to a maximum period of three years.

Special conditions of the approval (if applicable):

- Translation of the informed consent document to the languages applicable to the study participants should be submitted to the HREC (if applicable). Any research at governmental or private institutions, permission must still be obtained from relevant authorities and provided to the HREC.Ethics approval is required BEFORE approval can be obtained from these authorities.

General conditions:

While this ethics approval is subject to all declarations, undertakings and agreements incorporated and signed in the application form, please note the following:

- The study leader (principle investigator) must report in the prescribed format to the NWU-IRERC via HREC:
  - annually (or as otherwise requested) on the monitoring of the study, and upon completion of the study
  - without any delay in case of any adverse event or incident (or any matter that interrupts sound ethical principles) during the course of thestudy.
- Annually a number of studies may be randomly selected for an external audit.
- The approval applies strictly to the proposal as stipulated in the application form. Would any changes to the proposal be deemed necessaryduring the course of the study, the study leader must apply for approval of these amendments at the HREC, prior to implementation. Wouldthere be deviated from the study proposal without the necessary approval of such amendments, the ethics approval is immediately and automatically forfeited.
- The date of approval indicates the first date that the study may be started.
- In the interest of ethical responsibility the NWU-IRERC and HREC retains the right to:
  - request access to any information or data at any time during the course or after completion of the study;
  - to ask further questions, seek additional information, require further modification or monitor the conduct of your research or the informedconsent process.
  - withdraw or postpone approval if:
    - any unethical principles or practices of the study are revealed or suspected,
    - it becomes apparent that any relevant information was withheld from the HREC or that information has been false or misrepresented,
    - the required amendments, annual (or otherwise stipulated) report and reporting of adverse events or incidents was not done in a timelymanner and accurately,
    - new institutional rules, national legislation or international conventions deem it necessary.
- HREC can be contacted for further information or any report templates via Ethics-HRECApply@nwu.ac.za or 018 299 1206.

The IRERC would like to remain at your service as scientist and researcher, and wishes you well with your study. Please do not hesitate to contact the IRERC or HREC for any further enquiries or requests for assistance.

Yours sincerely

Linda du Plessis

Digitally signed by Linda du Plessis
DN: cn=Linda du Plessis, o=NWU, ou=Vaal Triangle Campus, email=linda.duplessis@nwu.ac.za, c=ZA
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31 October 2023

Prof A Franken
OHHRI

Dear Prof Franken

FEEDBACK ON NWU-HREC ANNUAL MONITORING REPORT: NWU-00337- 16-A1

We would like to thank you for submitting the annual monitoring report for your project entitled, ***"Skin barrier function of Caucasian and African nursing students"***, to the North-West University Health Research Ethics Committee (NWU-HREC) in a timely manner. Please f ind below the decision of the NWU-HREC regarding the continuation of your project.

Classification	Mark with X	Comment	
Clarification			
Completion (Final report)			
Suspended			
Continuation	X	**Date of next monitoring report:**	31 October 2024
Termination			

Should you have any further queries, please feel f ree to contact Mr Buti Majola at your earliest convenience (E-mail: Ethics-HRECMonitoring@nwu.ac.za; Tel: 018 299 2197). We wish you well in your future endeavours.

Yours sincerely

Chairperson: NWU-HREC

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Annexure B: Turn-it in Reports

Turn-it in reports for Chapters 1, 2 and 7 are included on the next page.

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20	Sané Jansen van Rensburg, Anja Franken, Johannes Lodewykus Du Plessis.	<1 %

"Measurement of transepidermal water loss, stratum corneum hydration and skin surface pH in occupational settings: A review", Skin Research and Technology, 2019
Publication

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Annexure D: Evidence of submission of articles to peer-reviewed journals

Article II submission to *Contact Dermatitis*

From: Contact Dermatitis <no-reply@atyponrex.com>
Sent: Monday, October 16, 2023 11:17 AM
To: Anja Franken <Anja.Franken@nwu.ac.za>
Subject: Manuscript submitted to Contact Dermatitis

Dear Anja Franken,

Your manuscript "Natural moisturising factor constituents in South African nursing students" has been successfully submitted and is being delivered to the Editorial Office of *Contact Dermatitis* for consideration.

You will receive a follow-up email with further instructions from the journal editorial office, typically within one business day. That message will confirm that the editorial office has received your submission and will provide your manuscript ID.

Thank you for submitting your manuscript to *Contact Dermatitis*.

Sincerely,
The Editorial Staff at Contact Dermatitis

By submitting a manuscript to or reviewing for this publication, your name, email address, and affiliation, and other contact details the publication might require, will be used for the regular operations of the publication, including, when necessary, sharing with the publisher (Wiley) and partners for production and publication. The publication and the publisher recognize the importance of protecting the personal information collected from users in the operation of these services and have practices in place to ensure that steps are taken to maintain the security, integrity, and privacy of the personal data collected and processed. You can learn more by reading our data protection policy. In case you don't want to be contacted by this publication again, please send an email to codedoffice@wiley.com.

Article III submission to *Journal of Dermatology Nurses' Association*

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From: em.jdna.0.85178b.88bfe87d@editorialmanager.com <em.jdna.0.85178b.88bfe87d@editorialmanager.com> On Behalf Of JDNA
Sent: Wednesday, August 2, 2023 7:25 PM
To: Anja Franken <Anja.Franken@nwu.ac.za>
Subject: A manuscript number has been assigned to your JDNA submission

08-02-2023

Dear Prof Franken,

Your submission entitled "Skin barrier function of Black African and White nursing students" has been assigned the following manuscript number: JDNA-D-23-00029.

You will be able to check on the progress of your paper by logging on to Editorial Manager as an author.

https://www.editorialmanager.com/jdna/

Your username is: anja.franken@nwu.ac.za https://www.editorialmanager.com/jdna/l.asp?i=71496&l=QJKAHK2O

Thank you for submitting your work to The Journal of the Dermatology Nurses' Association.

With kind regards,

Melissa Derby, *
Managing Editor
The Journal of the Dermatology Nurses' Association

Short communication submission to *Workplace Health & Safety*

Submission Confirmation

Thank you for your submission

Submitted to	Workplace Health & Safety
Manuscript ID	WHS-23-0368
Title	Hand dermatitis prevalence and severity in a population of South African nursing students
Authors	Young, Monica Du Plessis, Johannes Reichert, Lize Franken, Anja
Date Submitted	17-Nov-2023

Annexure E: Declaration of language editing

Venita de Kock
BA HONS. • PEG
084 588 5008
venita.dekock@gmail.com

23 November 2030

LANGUAGE EDITING STATEMENT

I, Jannetje Levina De Kock,
hereby declare that the thesis submitted
for the degree Doctor of Philosophy in
Health Sciences in Occupational Hygiene (OHHRI)
at the North-West University
with the title

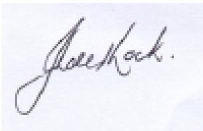
Skin barrier function of White and Black African nursing students

by

Monica M Young
22170685

- has been edited for language correctness and spelling.
- has been edited for consistency (repetition, long sentences, logical flow)

No changes have been made to the document's substance and structure (nature of academic content and argument in the discipline, chapter and section structure and headings, order and balance of content, referencing style and quality).



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