# The association between dietary intake and breast cancer risk in black South African women.


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Mini-dissertation submitted in fulfilment of the requirements for the degree Master Science in Dietetics at the North West University

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# PREFACE

This mini-dissertation will be presented in article format. The *Magister Scientiae* (MSc) student, Ms I. Jacobs, performed statistical analysis and was the first author of the article: “Dietary intake and breast cancer risk in black South African Women: The SABC study”. This article was written in accordance with the authors guidelines of the *British Journal of Nutrition* to which the article has been submitted. The article has recently received a revised and resubmit decision from the *British Journal of Nutrition*. This article will soon be resubmitted for a final decision. The co-authors included C. Taljaard-Krugell, C. Ricci, H.H. Vorster, S. Rinaldi, H. Cubasch, R. Loubscher, T. Van Zyl, M. Joffe, S.A. Norris, I. Romieu,

Included is a statement from the co-authors, confirming their role in the article and providing permission for the inclusion of the article in this mini-dissertation. At the time of submission, Dr I. Romieu were out of office and could therefore not sign this declaration.

“I declare that I have approved the above-mentioned article, that my role in the study, is representative of my actual contribution and that I hereby give my consent that it may be published as part of the MSc mini-dissertation of Ms I. Jacobs”.

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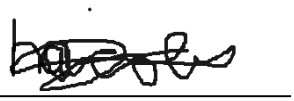
**Declaration of MSc student**

"I, Inarie Jacobs hereby declare that this MSc mini-dissertation is my own work and that this mini-dissertation has not been submitted to any other institution for examination."



I.Jacobs

**Acknowledgements**

**Dear God**

Let me stay in Your shadow.
Give that every earthly joy and fear, at last become insignificant to me.
I know all the branching paths, each time I lost my way.
Every time You came to fetch me.

Every day I devote my life, my thoughts, my heart and my soul to You.
Every earthly dream of wealth and fame, just a shadow against the wall.
What I am is a reflection of your indescribable mercy.
What I have is only borrowed.
Lord, I only yearn for Your waters of piece and rest.
Lead me, Lord, where my trust is without borders.

Lord,
Be my vision. Be my path, be my guide, be the centre of my life.
Be my source, be my light. Be the fire in my heart.
Be the wind in my sails. Be the reason that I live.

Disturb me, Lord, to dare more boldly, to venture on wilder seas where storms will show Your mastery. Push back the horizons of my hope.
I will never understand the depth of your love or the length of Your amazing grace.

***"Now all glory to God who is able with His mighty power at work within us, to accomplish infinitely more than we might ask or think."*** Ephesians 3:20

You are Lord of all! I trust in You.
I Love you! Forever and ever.

Love,
Your daughter
inarie

I owe my deepest gratitude towards the following people:

**My beloved parents**

Thank you for being my inspiration, for your constant love, prayer and support but most of all, thank you for believing in me! May I one day find the words to describe how blessed I am to have you as parents!

**My best friend and dearest sister**

Thank you for being the oldest, the one I look up to and the one who inspires me most. Your love, motivation and support kept me going. Thank you for being my biggest supporter. You will always be my person!

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**My supervisor:** Dr C. Taljaard-Krugell

What a phenomenal person to know, to be inspired by and to work with! I can only thank God for the privilege, honour and blessing to have you as my mentor and friend. You have tought me more than any book ever will. Thank you for being the giant who's shoulders I could stand on so I could see further.

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- Dr I. Romieu, Dr M. Joffe, Prof S.A. Norris, Dr H. Cubasch, Mrs R. Laubscher for their involvement in this study
- All fieldworkers from the CHBAH who contributed to data collection.
- The WCRF for funding of this master study.
- Participants of the SABC study.

# ABSTRACT

## Background

Breast cancer is the second leading diagnosed cancer in black South African women. The World Health Organization previously estimated that 30%-50% of all cancers, including breast cancer can be prevented by following a healthy diet, being physically active and maintaining a healthy body weight. However, previous research in South Africa showed that Westernised diets, high obesity rates and low physical activity levels are seen in South Africa and may contribute to an increased breast cancer risk. The main aim of this study was to investigate the association between dietary intake and breast cancer risk in black South African women residing in Soweto, Gauteng.

## Methods

This retrospective, population based, case-control study included 396 breast cancer cases and 396 matched controls, participating in the South African Breast Cancer study. A validated culture-specific quantitative food frequency questionnaire was used in combination with household utensils, food portion pictures and food models to determine habitual dietary intake. Energy dense intakes were used to create 12 food groups with the help of the Condensed Food Composition Tables for South Africa. Conditional logistic regression was applied to estimate odds ratios (OR) and 95% confidence intervals (CI) to determine breast cancer risk in relation with dietary intake.

## Results

Four out of five women (82%) in case and control participants were either overweight or obese. Low physical activity levels were noted in case (114 METs per week) and control (110 METs per week) participants. Additionally, nearly two thirds of women were postmenopausal and 86% of this sample earned less than R3 000 per month. After adjusting for confounding factors, inverse associations with breast cancer risk were noted in fresh fruit consumption (OR=0.3, 95% CI 0.12, 0.80, premenopausal) and in red and organ meat consumption (OR=0.6, 95% CI 0.40, 0.96, OR=0.6, 95% CI 0.47, 0.91). Savoury food consumption (sauces and soups) showed an increased breast cancer risk in postmenopausal women (OR=2.1, 95% CI 1.15, 4.07).

**Discussion and conclusion**

Fruit and organ meat contains possible protective factors against breast cancer and is less energy dense, contributing to a healthier body weight. Savoury foods may lack a variety of possible protective nutrients and are mostly energy dense. Red meat contains various nutrients that may protect against breast cancer risk. However, the association with red and organ meat consumption requires further investigation as the inverse association may be due to low consumption in this sample. Additionally, a Westernised diet and high obesity rates, co-existing with low physical activity levels in this sample are worrisome for it may contribute to an increased breast cancer risk. Therefore, inclusion of less energy dense and more nutrient rich foods (fresh fruit) is advised to be part of a balanced diet. Current health strategies should be prioritized to reduce obesity and breast cancer mortality rates in South Africa.

**Key terms:** Dietary intake; black women; breast cancer; South Africa; obesity; physical activity.

# OPSOMMING


### Agtergrond

Borskanker is die tweede grootste gediagnoseerde kanker onder swart vroue in Suid-Afrika. Die Wêreldgesondheidsorganisasie het voorheen geskat dat 30%-50% van alle kankers, borskanker inkluis, voorkom kan word deur 'n gesonde dieet te volg, fisies aktief te wees en 'n gesonde liggaamsgewig te handhaaf. Nietemin; vorige navorsing in Suid-Afrika het gewys dat verwesterse diëte, hoë obesiteitskoerse en lae vlakke van fisiese aktiwiteit kom voor in Suid-Afrika en kan bydra tot 'n verhoogde risiko in borskanker. Die hoofdoel van hierdie studie was om die verband tussen voedselinname en die risiko van borskanker in swart Suid-Afrikaanse vroue woonagtig in Soweto, Gauteng te ondersoek.

### Metodes

Hierdie retrospektiewe, bevolkingsgebaseerde, gevalle- en kontrolestudie het 396 borskankergevalle en 396 gepaste kontroles ingesluit wat aan die Suid-Afrikaanse Borskankerstudie deelgeneem het. 'n Geldige kultuur-georiënteerde kwantitatiewe voedsel-frekwensie vraelys is gebruik in kombinasie met huisgerei, prente van voedselporsies en voedselmodelle om gebruiklike voedselinname te bepaal. Innames wat hoog in energie is, is gebruik om 12 voedselgroepe te skep met behulp van die Verkorte Voedsel Samestellingstabelle (Condensed Food Composition Tables) vir Suid-Afrika. Voorwaardelike logistiese regressie is toegepas om kansverhoudings (odds ratio - OR) te skat en 95% vertrouensintervalle (confidence intervals - CI) om die risiko van borskanker in verhouding tot voedselinname te bepaal.

### Resultate

Vier uit vyf vroue (82%) wat deel uitgemaak het van die gevalle- en kontrolegroep was óf oorgewig óf obees. Lae fisiese aktiwiteitsvlakke is opgemerk in gevalle- (114 METs per week) sowel as kontrole-deelnemers (110 METs per week). Boonop was byna twee-derdes van die vroue post-menopousaal en verdien 86% van die steekproef minder as R3 000 per maand. Na aanpassing vir verwarrende faktore, is omgekeerde assosiasies met borskankerrisiko opgemerk ten opsigte van die verbruik van vars vrugte (OR=0.4, 95% CI 0.21, 0.97, pre-menopousaal) en in rooi- en orgaanvleis verbruik (OR=0.7, 95% CI 0.53; 0.94, OR=0.7, 95% CI 0.58; 0.91). Die verbruik van soutgeregte (souse en soppe) het 'n toename in die risiko vir borskanker in post-menopousale vroue getoon (OR=2.1, 95%CI 1.14, 4.07).

### Bespreking en slotsom

Vrugte en orgaanvleis bevat moontlike beskermende faktore teen borskanker en is laer in energie wat tot ’n gesonder liggaamsgewig bydra. Soutgeregte mag ’n tekort hê aan ’n variasie van moontlike beskermende nutriënte en is meestal hoog in energie. Rooivleis bevat verskeie voedingstowwe wat teen die risiko van borskanker kan beskerm. Nietemin, die verband met rooivleis, orgaanvleis en borskanker vereis verdere ondersoek aangesien die omgekeerde assosiasie toegeskryf kan word aan verlaagde rooivleis inname. Boonop is ’n verwesterse dieet en hoë obesiteitskoerse, wat met lae fisiese aktiwiteitsvlakke gepaardgaan, in hierdie steekproef kwellend aangesien dit tot ’n verhoogde borskankerrisiko kan bydra. Daarom word die insluiting van laer energiedigte, nutriënt-ryke voedselsoorte (vars vrugte) aanbeveel as deel van ’n gebalanseerde dieet. Huidige gesondheidstrategieë behoort geprioritiseer te word om obesiteit en borskanker sterftesyfers in Suid-Afrika te verlaag.

**Sleutelterme:** Dieetinname; swart vroue; borskanker; Suid-Afrika; obesiteit; fisiese aktiwiteite.

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# LIST OF ABBREVIATIONS

| | |
|---|---|
| AICR | American Institute for Cancer Research |
| ADSA | Association for Dietetics in South Africa |
| ASR | age-standardised rate |
| AMDR | acceptable macronutrient distribution range |
| BC | breast cancer |
| BMI | body mass index |
| CANSA | Cancer Association of South Africa |
| CHBAH | Chris Hani Baragwanath Academic Hospital |
| CHO | carbohydrate |
| CI | confidence interval |
| CRIBSA | Cardiovascular Risk in Black South Africans |
| CUP | Continuous Update Project |
| DDS | dietary diversity score |
| DEXA | dual energy x-ray absorptiometry |
| DNA | deoxyribonucleic acid |
| DRI | dietary reference intakes |
| EPIC | European Prospective Investigation into Cancer and Nutrition |
| ER | oestrogen receptor |
| $ER^+$ | oestrogen receptor positive |
| $ER^-$ | oestrogen receptor negative |

| | |
|---|---|
| FAO | Food and Agriculture Organisation |
| GLOBOCAN | Global cancer observatory |
| GICR | Global Initiative for Cancer Registry |
| HICs | High-income countries |
| HER2 | Human-Epidermal Growth Factor receptor 2 |
| HER2E | Human-Epidermal Growth Factor receptor 2 Enriched |
| HPCSA | Health Professions Council of South Africa |
| IARC | International Agency for Research on Cancer |
| IGF-1 | Insulin-like growth factor-1 |
| IHC | Immunohistolochemical |
| nm | not mentioned |
| NCD | non-communicable disease |
| METs | metabolic equivalents |
| MRC | Medical Research Council |
| LMICs | Low-income and middle-income countries |
| OR | odds ratio |
| PA | physical activity |
| PAHO | Pan American Health Organization |
| PR | progesterone receptor |
| PURE | Prospective Urban and Rural Epidemiological |
| QFFQ | quantified food frequency questionnaire |
| RDA | recommended daily allowance |

| | |
|---|---|
| RNA | ribonucleic acid |
| ROS | reactive oxygen species |
| SABC | South African Breast Cancer |
| SAFBDGs | South African Food Bases Dietary Guidelines |
| SAFL | Southern Africa Food Lab |
| SANCR | South African National Cancer Registry |
| SANHANES | South African National Health and Nutrition Examination Survey |
| SASAS | South African Social Attitude Survey |
| SD | standard deviation |
| THUSA | transition and health during urbanisation of South Africa |
| TNBC | Triple Negative Breast Cancer |
| US | United States |
| VAT | value added tax |
| WCRF | World Cancer Research Fund |
| WHO | World Health Organization |
| ZAR | South African Rand |

## LIST OF UNITS AND SYMBOLS

| | |
|---|---|
| g | gram |
| kg | kilogram |
| kg/m2 | kilogram divided by square meter (height) |
| % | percentage |
| > | greater than/above |
| ≥ | greater than and included |
| < | lower than/less |
| ≤ | lower than and included |
| kJ | kilojoule |
| m | meter |

# CHAPTER 1 INTRODUCTION

## 1.1 Background and motivation

Breast Cancer (BC) is an uprising concern since incidence and mortality rates are increasing globally. Worldwide, nearly 1.7 million new BC cases were diagnosed in 2012 (WCRF & AICR, 2017). The global cancer observatory (GLOBOCAN), predicted that one in every 18 women will die from BC in South Africa by the year 2025 (Edefonti *et al.*, 2009; Ferlay *et al.*, 2012). Compared to previous statistics from 2012 where one in every 26 South African women died from BC (Ferlay *et al.*, 2012), it is clear that BC mortality rates are rising in South Africa.

When BC is detected in early stages, better prognosis is made and BC may be more curable compared to BC diagnosed in late stages (stage III/IV) when cancer has spread to other body parts (Singh *et al.*, 2015). In contrast, high rates of late stage diagnoses are reported in black South Africans (Jedy-Agba *et al.*, 2016). Late stage diagnosis in South Africa may be due to a lack of awareness of BC, inadequate or costly healthcare and a lack of early screening interventions (Jedy-Agba *et al.*, 2016). Thus, late stage diagnoses in South Africa may contribute to high BC mortality rates. Prevention of BC would therefore be the most cost-effective strategy to reduce BC mortality and incidence rates in a low-to-middle income country like South Africa. Suitable alternative prevention methods that are affordable, simple and accessible to all South African citizens are needed to address the observed rising in BC mortality and incidence rates (Lynch-Kelly *et al.*, 2017).

Dietary components may act as promoting or inhibiting factors in BC development and is classified as a modifiable risk factor of BC (Kotepui, 2016; Singh *et al.*, 2015). The precise role of diet and the association thereof with BC, is still not clearly understood (Van Ryswyk *et al.*, 2016). However, research suggests that a third of all cancer cases are accredited to unhealthy dietary factors (Dwivedi *et al.*, 2014). In South Africa dietary intake in various populations have been studied broadly (Abrahams *et al.*, 2011; Kruger *et al.*, 2005; Vorster *et al.*, 2000; Vorster *et al.*, 2011; Vorster *et al.*, 2005). Hence, valuable insight has been obtained in South African's dietary intake. However, not much attention is drawn to BC risk and dietary intake in black South African women. Therefore, the need arises to investigate the association between dietary intake and BC risk in black South African women to contribute to simple, affordable and accessible BC dietary prevention guidelines in South Africa.

Dietary intake in South Africa is affected by the nutrition transition and urbanization (Steyn & Mchiza, 2014). The nutrition transition is defined as a shift in dietary intake and energy consumption (Abrahams *et al.*, 2011; Popkin, 1993). These changes occurred due to

agricultural, economical, epidemiological and demographic development over time (Abrahams *et al.*, 2011; Popkin, 1993). Previous research on the nutrition transition in South Africa reports of increased consumption of energy dense carbohydrates, processed meat products and high saturated fatty foods at lower costs in low-income groups of South Africa (McHiza *et al.*, 2015; Vorster *et al*., 2011; Vorster *et al*., 2005). This diet is associated with a westernised diet which tends to increase obesity prevalence (Steyn & Mchiza, 2014). Obesity is one of the major modifiable risk factors for postmenopausal BC (Vineis & Wild, 2014). This westernised diet is furthermore associated with a low fruit and vegetable intake/consumption (Steyn & Mchiza, 2014).

High fruit and vegetable intake/consumption are associated with a decreased risk for BC (WHO, 2017) and is less energy dense than processed foods and processed meat products that is higher in energy. Thus; a high consumption of energy dense foods leading to a higher risk for obesity together with a low consumption of fruit and vegetables may contribute to an increased BC risk in black South African women.

## 1.2 **Study design**

This MSc project is an affiliating study from the larger study, the South African Breast Cancer study (SABC) study, with the aim of investigating BC in relation to diet, physical activity and body size. This study was a retrospective, population-based case-control study conducted on African women from the Greater Soweto population within the Chris Hani Baragwanath Academic Hospital (CHBAH) referral network. Control participants in this study were selected from the same population source as the case participants and was matched on age ($\pm$ 5 years) and residential location of case participants. Control participants were non-blood relatives of case participants.

The CHBAH is the largest public hospital in South Africa; within 30 km, 80% of patients being referred via the public health sector. Therefore, CHBAH is representative of black South African women, diagnosed with BC. The cases aged ≥18 years were invasive primary BC patients newly diagnosed at the CHBAH Breast Unit prior to initiation of any treatment.

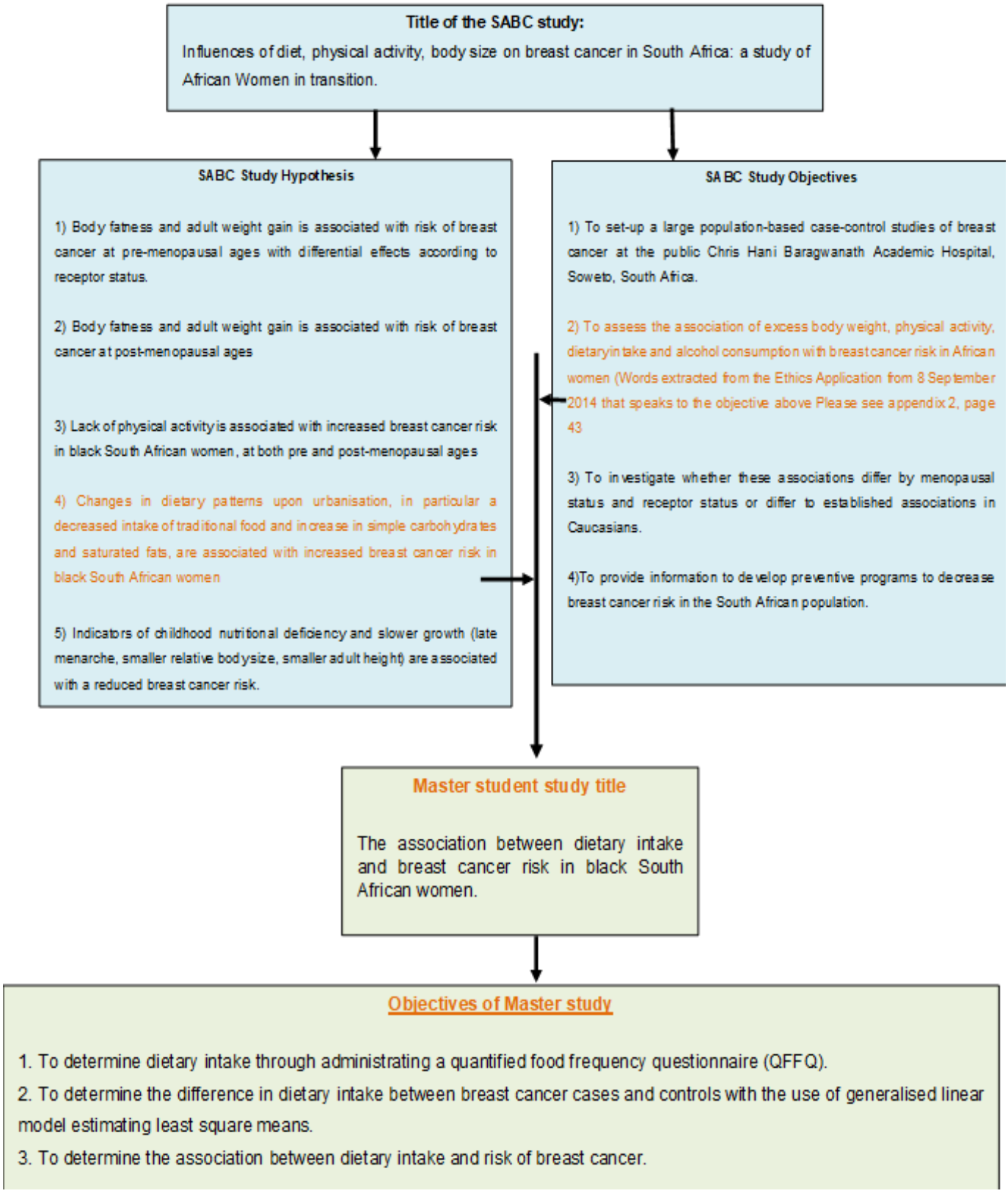


Figure 1-1: Conceptual framework of the large South African Breast Cancer study and the affiliating master study.

## 1.3 Aim, objectives and hypothesis

The main aim of this population-based case-control study was to determine the association between dietary intake and the risk of breast cancer in a population-based study of black South African women that was conducted in CHBAH, Soweto (December 2013 – June 2017).

To address the aim above, the following objectives were set:

1. To determine dietary intake through administrating a quantified food frequency questionnaire (QFFQ).
2. To determine the difference in dietary intake between BC cases and controls with the use of generalised linear model estimating least square means.
3. To determine the association between dietary intake and risk of BC.

This study tested the following hypotheses:

1. Dietary intake between cases and controls vary significantly.
2. Dietary intake from unhealthy more energy dense and nutrient poor food groups is positively associated with BC risk.
3. Dietary intake from healthy less energy dense and nutrient rich food groups is inversely associated with BC risk.

The role of dietary intake in BC was explored independently by known covariates of BC (family history of breast cancer, lactation/breast feeding, obesity, alcohol intake, smoking, physical activity, menopausal status, age of first pregnancy and age at menarche).

## 1.4 Research team and authors' contribution

**Table 1-1: Research team of the SABC study 2014-2017.**

| Team member | Partner name | Role and responsibility |
|---|---|---|
| Dr H Cubasch | Chris Hani Baragwanath Academic Hospital | Principal Investigator; surgeon co-responsible for diagnosing and recruiting subjects. |
| Prof S Norris | Chris Hani Baragwanath Academic Hospital | Director, MRC, Wits Developmental Pathways to Health Research unit. |
| Dr I Romieu | International Agency for Research on Cancer (IARC) | Principal Investigator of total study. |
| Dr S Rinaldi | International Agency for Research on Cancer | Overseer of total project with Dr I Romieu. |

| | | |
|---|---|---|
| Dr M Joffe | Witwatersrand University | South African coordinator of the SABC study. |
| Prof HH Vorster | North-West University | Advisor and trainer of QFFQ. |
| Dr C Taljaard-Krugell | North-West University | Supervisor and study leader for MSc student; QFFQ interviewer and data analysis leader for all food intake components of study. |
| Dr C Ricci | North-West University | Student co-study leader and statistician. |
| Dr T van Zyl | North-West University | Assistant supervisor and scientific input. |
| **Ms I Jacobs** | **North-West University** | **Full time MSc student; QFFQ interviewer; data capturing and analysis of dietary data; statistical analysis; article writing.** |

HPCSA - Health Professions Council of South Africa; MRC - Medical Research Council; SABC – South African Breast Cancer; QFFQ - quantified food frequency questionnaire

**Table 1-2: Level of involvement of the student and authors' contributors to the article to be submitted.**

| Team member | Affiliation | Role |
|---|---|---|
| Ms I Jacobs | CEN, NWU, Potchefstroom Campus | Full-time MSc student.<br>Protocol writing.<br>Statistical analysis.<br>Article writing. |
| Dr C Taljaard-Krugell | CEN, NWU, Potchefstroom Campus | Supervisor and study leader for MSc dissertation.<br>Provided guidance to the student during all stages of the project. |
| Dr C Ricci | CEN, NWU, Potchefstroom Campus | Co-supervisor of MSc dissertation.<br>Statistician.<br>Provided guidance to the student during all stages of the project. |
| Dr T van Zyl | CEN, NWU, Potchefstroom Campus | Assistant supervisor of MSc dissertation.<br>Provided scientific evidence. |
| Prof HH Vorster | Extraordinary Professor at the NWU, Potchefstroom Campus | Scientific input in dietary intake and food groups. |
| Dr I Romieu | Center for Research on Population Health, National Institute of Public Health, Cuernavaca, Morelos, Mexico. | Principal investigator (IARC).<br>Scientific input. |

| | | |
|---|---|---|
| | Hubert Department of Global Health, Emory University, Atlanta, GA, USA. | |
| Dr S Rinaldi | IARC, Section of Nutrition and Metabolism, Lyon, France. | Scientific input. |
| Dr H Cubasch | Department of Surgery, Faculty of Health Sciences, University of Witwatersrand, Johannesburg, South Africa.<br><br>Non-Communicable Diseases Research Division, Wits Health Consortium (PTY) Ltd, Johannesburg, South Africa. | Principal investigator.<br>Scientific input. |
| Ms R Laubscher | SAMRC, Cape Town, South Africa | Statistical analysis. |
| Dr M Joffe | Department of Surgery, Faculty of Health Sciences, University of Witwatersrand, Johannesburg, South Africa. | Scientific input. |
| Prof SA Norris | MRC Developmental Pathways to Health Research Unit, Department of Paediatrics, Faculty of Health Sciences, University of Witwatersrand, Johannesburg, South Africa. | Scientific input. |

CEN - Centre of Excellence for Nutrition; NWU - North-West University; SAMRC - South African Medical Research Council; IARC - International Agency for Research on Cancer; CHBAH - Chris Hani Baragwanath Academic Hospital

## 1.5 **Other study contributors**

The following persons who served as fieldworkers and assistants in anthropometric measurements, interviewers of QFFQs and women's health questionnaire are hereby acknowledged for their contribution to the SABC study:

Anthropometric measurements: Ms Yvonne Chaka

QFFQ interviewer: Sr Phindile Mathe

Women's health questionnaire: Mr Victor Shandukani, Ms Siphesihle Sibiya and Mrs Maria Sihlo

Laboratory Manager: Mrs Nontlatla Mkwanaz

## 1.6 Ethical clearance

Ethical approval for the larger SABC study was granted by the International Agency for Research on Cancer (IARC) and by the University of the Witwatersrand Committee for Research on Human Subjects (Ethical no: M140980) (see Annexure A). Permission to conduct research at Chris Hani Baragwanath Academic Hospital was obtained from the Gauteng Province Medical Advisory Committee (see Annexure B). This single dietary study obtained ethical approval from the Human Research and Ethics Committee of the North-West University (NWU-00118-17-S1) (see Annexure C).

## 1.7 Structure of this dissertation

Four chapters are presented in this mini-dissertation. All technical aspects of the dissertation, except for Chapter 3, adhere to the postgraduate manual guidelines of the North-West University (font Arial, size 11). Chapter 3 follows the authors' guidelines of the *British Journal of Nutrition* (font Times New Roman, 12-point type and 1.5 spacing). The decimal system was used for numbering with the exception of Chapter 3 where headings are not numbered. References, combined from chapter 1, 2 and 4 are presented in the Bibliography section and followed by the addenda.

Chapter 1 is an introduction to this study and briefly states the rationale for conducting this study. The study design stemming from the larger study is discussed followed by the aim and objectives. The roles and responsibilities of the research team are also acknowledged.

Chapter 2, the literature review, will follow the introductory chapter. Chapter 2 consists of recent published literature regarding BC and dietary intake globally but with the main focus on South Africa. The pathology of cancer and BC subtypes are explained for background on the complexity of the disease. Attention is drawn to modifiable risk factors, the Continuous Update Project report on BC and the possible role of physical activity, obesity and dietary factors in relation to BC risk. The nutrition transition, food insecurity and poverty influencing dietary intake in South Africa are broadly discussed. Finally, Chapter 2 concludes with a reflection on the possible influence of dietary intake in South Africa on BC risk.

Chapter 3 presents the main findings of this study as an article titled "Dietary intake and breast cancer risk in black South African women: The SABC study". Referencing follows the Vancouver reference style, as directed by authors' guidelines for the chosen journal, the *British*

*Journal of Nutrition*. A duplicate of the information for authors for the *British Journal of Nutrition* has been included in annexure I.

The last chapter, Chapter 4, completes this mini-dissertation and captures main findings and reflects on the objectives of this single study as well as limitations of the study. In addition, recommendations for further research have been made.

Other annexures include the compilation of the 12 food groups used in the study (annexure D), ethical approval letter for using the QFFQ (see Annexure E), the validated and reproducible QFFQ used for dietary assessment (annexure F). Informed consent was obtained by an independent registered nurse for case and control participants (see annexures G and H).

# CHAPTER 2 LITERATURE REVIEW

## 2.1 Introduction

Breast Cancer (BC) is globally the most common diagnosed cancer in women and the second leading cause of cancer mortality in various countries (WCRF & AICR, 2017; Castelló *et al.*, 2017; Guerrero *et al.*, 2017; Labadarios *et al.*, 2011). In 2017, an estimated annual mortality rate of 410 712 women were reported by the World Health Organization (WHO) (WHO, 2017). Furthermore, approximately 1 151 298 new BC cases are predicted by Global Cancer (GLOBOCAN) every year (IARC & WHO, 2012).

The WHO recently stated that 30%-50% of all cancers can be prevented through lifestyle changes (WHO, 2018). Additionally, previous research stated that women from a low BC risk country developed an increase BC risk upon immigration to high BC risk countries (Sieri *et al.*, 2008). This strengthens the possibility that BC is influenced by environmental and modifiable risk factors such as lifestyle factors and dietary intake (Dwivedi *et al.,* 2014; Sieri *et al.*, 2008). The possible impact of diet on BC risk has previously been studied worldwide (Hirko *et al.*, 2016). However, according to the Global Initiative for Cancer Registry Development (GICR) only one in five low to middle income countries (LMICs) have adequate cancer data to drive policies for cancer prevention strategies towards cancer (WHO & IARC, 2018). Even though dietary intake was previously studied in South Africa, insufficient attention is drawn to the association thereof with BC risk in black women. Genetic evidence suggests that BC tumour types and outcomes in black South African women might be different from black women in the United States (US) and possibly other countries as well (Bryc *et al.*, 2010). These genetic differences may occur due to geographical distances (Handley *et al*., 2007). Hence, difficulties may arise when results from studies of different ethnicities and geographical areas are compared to the black female population of South Africa to establish population specific prevention guidelines. Investigation of dietary intake and the association thereof with BC risk are therefore needed to obtain much needed information in the black female population of South Africa to establish guidelines for prevention.

The aim of this literature review is to provide an overview of the burden of increasing mortality and incidence rates of BC in South Africa. Risk factors associated with BC will be presented with a broad discussion on modifiable risk factors influencing BC development and outcome. Special attention will be given to dietary intake and associations with BC risk to this date. Finally, a broad discussion on influences of the nutrition transition on dietary intake in South Africa will be discussed to provide guidance towards preventative programs to decrease BC

risk in South Africa. This literature review will focus on black South African women, for the population-based case-control study of the South African Breast Cancer (SABC) study was conducted on black South African women.

## 2.2 The nutrition transition

### 2.2.1 Introduction of the nutrition transition

The nutrition transition was initially described by Popkin, who identified five stages in the nutrition transition (Popkin, 1993). The nutrition transition describes changes in dietary intake and physical activity (PA) related to agriculture development over time. The first stage (hunter-gatherer) represented high consumption of carbohydrates and fibre and low in saturated fat intake whilst obesity rates were low and PA levels were high. During the second stage, low dietary diversity was noted due to a period of famine where dietary intake shifted towards cultivation and settlements (first of crops, poultry and livestock) while PA levels remained high. In the third stage (receding famine) agriculture became more advanced. Dietary intake shifted to a decreased carbohydrate consumption and increased vegetable, fruit and protein consumption whilst decreased PA levels were noted. The fourth stage is associated with nutrition related non-communicable diseases and characterised by dietary intakes high in fat, sugar, refined grains and cholesterol. The fourth stage is further associated with low fibre consumptions and low levels of PA whilst increased obesity prevalence is noted. In the fifth stage changes in dietary intake will occur due to desired behavioural changes to prevent or delay degenerative diseases. Dietary intake will shift towards an increase in complex carbohydrates, vegetables and fruits, whilst a decreased consumption of fat, high fat meat, processed foods and dietary products are promoted (Popkin, 1993).

The stage of transition may differ in countries or regions within countries (Popkin, 1993). Urban and rural areas in the same country may represent different stages of the nutrition transition (Popkin, 1993). In addition, most high income countries (HICs) tend to be in the fifth stage of the nutrition transition, whilst most LMICs like South Arica, are not yet in the fifth stage of the nutrition transition (Abrahams *et al.*, 2011).

### 2.2.2 The nutrition transition within South Africa

The nutrition transition in South Africa has been studied expansively by various researchers (Abrahams *et al.*, 2011; Bourne *et al.*, 2002; Kruger *et al.*, 2005; MacIntyre *et al.*, 2012; Mciza *et al.*, 2005; Steyn & Mchiza, 2014; Vorster *et al.*, 2014) and contributed to a more comprehensive overview of dietary intake in South Africa. However, data on dietary intake within certain ethnic and age groups as well as certain demographic regions, is still limited.

Additionally, little attention is drawn to BC risk and dietary intake in South Africa as mentioned above. Therefore, difficulties arise when preventative nutrition related strategies are planned to reduce BC incidence in a diverse population like South Africa.

In 2001 the first South African food based dietary guidelines (SAFBDGs) were developed (Vorster *et al.*, 2001). In 2012 these SAFBDGs were updated and revised (Vorster *et al.*, 2013). The main aim of the SAFBDGs is to promote healthy eating for all people of South Africa (Vorster *et al.*, 2013). It is based on scientific evidence in relation to food and health and is mainly used as an educational tool to address the burden of chronic and non-communicable diseases such as obesity (Vorster *et al.*, 2013). These SAFBDGs are in line with the vision and mission of the WHO, Food and Agriculture Organisation (FAO) and Association for Dietetics in South Africa (ADSA) (DOH, 2003). In addition, the Cancer Association of South Africa (CANSA) also recommends a healthy diet in line with the SAFBDGs as preventative diet against cancer. These guidelines advise South Africans to follow a nutrient dense diet that is high in fruit, vegetables and low in energy dense, nutrient poor food such as fat, salt and sugar (Vorster *et al.*, 2013).

However, despite promotion of healthier, less energy dense and nutrient rich food in South Africa, a systematic review by the authors, Steyn and Mchiza (2014), stated that a more Westernised diet are being followed by the South African population. The nutrition transition and urbanization in South Africa might contribute to South Africans following a Westernised diet (Steyn & Mchiza, 2014). Westernised diets are characterised by high consumption of red and processed meats, potatoes, starches, refined grains, snacks and sweets (Castelló *et al.*, 2014). This diet can further be classified as a more energy dense and mostly nutrient poor diet (possibly lacking natural protective agents protecting against BC) that may result in an increased risk for obesity. Westernised diets were previously associated with a higher BC risk (Castelló *et al.*, 2014; Cottet *et al.*, 2009). Thus, the South African population might be at greater risk of developing BC when a Westernised diet is being followed.

The South African Department of Health has developed a National Strategy for the Prevention and Control of Obesity implemented from 2015 to 2020 (DOH, 2015). However, this strategy has had little impact up to date since obesity rates are still increasing (Tugendhaft *et al.*, 2016). Thus, highlighting the need for more effective intervention strategies to reduce obesity and adapt to dietary intake associated with the fifth stage of the nutrition transition to prevent degenerative diseases such as BC. In section 2.2.3 and 2.2.4 the focus will be on urbanization, dietary intake and dietary diversity as contributing factors of obesity in South Africa, a known risk factors for BC.

### 2.2.3 **Urbanization, obesity and South African dietary intake.**

A key hypotheses supported by the rural and urban comparison, is the abandoned traditional diet of the African population (Bourne *et al.*, 2002). A traditional diet is generally more nutritious than commercial food markets in urbanised settings associated with Westernised diets (Kuhnlein *et al.*, 2013). Traditional diets are further associated with a decreased prevalence of degenerative diseases, whereas Westernised diets are associated with higher prevalence of degenerative diseases (Bourne *et al.*, 2002). Urbanization also contributes to lifestyle changes such as decreases in PA levels (MacIntyre *et al.*, 2002).

A cross-sectional study of the transition and health during urbanisation of South Africa (THUSA) conducted by Vorster *et al.* (2000) demonstrated abundant differences between urban and rural populations. Differences were demonstrated in terms of dietary intake, an increase in BMI upon urbanisation and lack of PA in urban and rural areas. According to Popkin *et al.* (2012) urbanization contributes to decreased PA levels and increased obesity rates in the South African population.

Previously, excessive body weight was ranked as the fifth most contributing risk factor towards mortality rates in South Africa (Draper *et al.*, 2016). South African women tend to have the highest prevalence of obesity (42%) in sub-Saharan Africa, whilst combined incidence rates of overweight and obesity represented 69.3% of South African women (Ng *et al.*, 2014). Compared to only 27% of South African women being obese in 2003 (Tugendhaft *et al.*, 2016), emphasis is put on the rising obesity rates associated with time.

Previous research has shown that black South African women have a higher tolerance and preference for a bigger body size compared to white female populations (Draper *et al.*, 2016). In addition, former research conducted in South Africa found obesity in black women to be associated with perceived fortune, health and attractiveness (Mvo, 1999; Puoane *et al.*, 2005; Senekal *et al.*, 2001). Thus, overconsumption of energy dense and nutrient poor foods, together with increased inactivity and positive perceptions of obesity in the black female population of South Africa, may contribute to a higher BC risk in postmenopausal women (Draper *et al.*, 2016).

Various studies have been conducted on macronutrient, fibre and added sugar intake in South Africa (Wentzel-Viljoen *et al*., 2018; Vorster *et al*., 2014; Kolahdooz *et al*., 2013; Tydeman-Edwards, 2012; Nel & Steyn, 2002). These studies reported the effects of urbanization on dietary intake and are summarised in Table 2.1 (Wentzel-Viljoen et al., 2018; Mchiza *et al.*, 2015). Compared to rural populations, urban populations tend to follow a more Westernised

diet high in refined carbohydrates, added sugars, animal source products and saturated fats (Wentzel-Viljoen *et al.*, 2011). In addition, total energy intake is also one of the nutritional differences in urban and rural areas. According to Mchiza *et al.* (2015) and Wentzel-Viljoen *et al*. (2018) lower energy intake is reported in rural settings whilst higher energy intake is noted in urban regions. Thus, urban regions in South Africa might be at greater risk of being obese and postmenopausal women in these urban areas may therefore have an increased BC risk.

The Prospective Urban and Rural Epidemiology (PURE) study conducted after the THUSA study in the North West province of South Africa, showed notable differences in added sugar intake between urban and rural areas (Vorster *et al.*, 2014). Except for the concern of positive perceptions towards increased body size, added sugar consumption also raises concern regarding obesity and high consumption of nutrient poor foods. The SAFBDGs advise South Africans to use sugar, sugary foods and drinks sparingly (Vorster *et al.*, 2013). However, the Department of Health (2016) previously stated that South Africans are amongst the top 10 global consumers of sugary drinks. In addition, the median added sugar consumed by women in rural areas were 23.9 g in 2005 and doubled to 46.6 g in 2010 for the same rural areas (Wentzel-Viljoen *et al.*, 2018). Urban areas showed a median increased added sugar intake from 40.6 g in 2005 to 67.6 g in 2010 (Wentzel-Viljoen *et al*., 2018). Sugar was furthermore found to be the most consumed single food in the cross sectional study conducted by Tydeman-Edwards (2012) (see Table 2.8).

To decrease risk of NCDs such as obesity, added sugar consumption should not exceed 10% (25 g) of total daily energy intake but should preferably be below 5% of total energy intake (WHO, 2017). With time, added sugar intake of South Africans has increased above the recommended 10% (Vorster *et al.*, 2014). Worrisome, however; is the nutritional value of sugar. Sugar is defined as an energy dense, nutrient poor food and overconsumption of sugar may contribute to obesity. Vorster *et al.* (2014) further concluded that consumption of an excessive amount of sugar was positively associated with body weight, for changes in total energy intake was mostly affected. Thus, excessive sugar intake in South Africa may contribute to a higher risk for postmenopausal BC.

**Table 2.1: Macronutrient, sugar and fibre intake of South Africans based on the second dietary analysis of studies undertaken after 2000.**

| Dietary Reference Intakes (DRIs) Food and Nutrition Board | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | **Energy**: women of height 1,60 m with low activity and BMI= 22.5= 8465 kJ | | | | **Fat**: AMDR = 10 -35% | **Protein**: AMDR= 20-35% | **CHO**: AMDR= 45-65% | **Added Sugar**: < 10% or 25 g/day. Recommended by WHO | **Fibre**: RDA females= 25 g/day |
| **Comparison of rural and urban studies** | | | | | | | | | |
| **Study** | **Study design** | **Population** | **Race** | **Energy kJ** | **Fat % TE** | **Protein % TE** | **CHO % TE** | **Added Sugar † (g)** | **Fibre (g)** |
| **Nel & Steyn (2002)** | Secondary data analysis | Women-Rural & Urban | Black and White Africans | 7250 (3610) | 25.0 (12.2) | 14.3 (4.7) | 59.9 (14.1) | 45.4 (46.4) | 18.0 (12) |
| **‡ Wentzel-Viljoen *et al*., (2018). *PURE 2005** | Cohort study | Women-Rural | Black Africans | 6200 (5000; 7600) | 32.1 (23.2; 42.4)) | 40.4 (31.9; 51.0) | 243.5 (191.3; 295.6) | 23.9 (12.8; 36.5) | 17.3 (13.8; 22.1) |
| | | Women-Urban | Black Africans | 9000 (6900;12800) | 64.7 (45.9; 88.4) | 63.2 (47.4; 87.4) | 294.6 (209.8; 376.2) | 40.6 (24.1; 62.1) | 22.8 (15.1; 30.6) |
| **‡ Wentzel-Viljoen *et al*., (2018). *PURE 2010** | Cohort study | Women-Rural | Black Africans | 9100 (6500;11600) | 56.6 (36.6; 86.7) | 60.4 (44.6; 82.5) | 322.0 (240.9; 468.8) | 46.6 (24.2; 83.6) | 20.7 (14.9; 31.3) |
| | | Women-Urban | Black Africans | 11700 (8900; 14900) | 83.5 (58.3; 112.4) | 86.5 (64.2; 113.9) | 368.3 (274.9; 477.7) | 67.6 (32.6; 98.5) | 27.5 19.6; 37.8) |
| **Tydeman-Edwards (2012)** | Cross-sectional study | Women-Rural | Mostly black | 7755 | 25.9 | 16.9 | 60.3 | Na | Na |
| | | Women-Urban | Mostly black | 6621 | 22.8 | 17.7 | 63.3 | Na | Na |
| **Comparisons of different age group studies** | | | | | | | | | |
| **Jaffer (2009) CRIBSA study** | Cross-sectional study | Women (Urban) aged 19-44 | Black Africans | 7600 (2300) | 30.1 (12.7) | 12.4 (4.5) | 55.5 (12.5) | 54.4 (40.5) | 16.2 (8.5) |
| | | Women (Urban) aged 45-64 | Black Africans | 7100 (1800) | 27.6 (14.1) | 12.4 (4.9) | 57.3 (15.0) | 47.0 (36.3) | 16.8 (8.2) |
| **Kolahdooz et al., (2013)** | Cross-sectional study | Women (Rural) aged 19-50 | Not mentioned in article | 11650 | 17 (9) | 11 (2) | 67 (12) | 47.0 (24) | 47.0 (14) |
| | | Women (Rural) aged 51 + | Not mentioned in article | 11978 | 17 (7) | 12 (3) | 64 (11) | 47.0 (21) | 19.0 (9) |

*PURE - Prospective Urban and Rural epidemiological study designed to keep track of shifts in lifestyles, risk factors and chronic diseases amongst 150 000 people over 15 years in 17 high and low-income countries from major regions of the world.
† Added sugar included sugars (sucrose) inserted by adults or producers. Natural sugars (fructose) were excluded.
Data are presented as mean (SD)
‡ Data are presented as median (P25; P75)

BMI - Body Mass Index; AMDR - acceptable macronutrient distribution range; CHO - carbohydrate, WHO - World Health Organization; RDA - recommended daily allowance; SD - standard deviation; na - not available; TE - total energy; CRIBSA - Cardiovascular Risk in Black South Africans study invented to measure the nutritional consumption of the black urban population of Cape Town. Data adapted from Mchiza *et al.* (2015:8236)

### 2.2.4 **Dietary diversity in South Africa**

Dietary diversity can be defined as consumption of foods in different food groups within a specific time frame (FAO, 2010) and is often used to describe dietary intake of a population or individual (Steyn, 2013). Dietary diversity is described as an evaluation tool of food security at household level (FAO, 2010). Food security is described as adequate food availability at all times by all people (Nord & Prell, 2011:9). Dietary diversity scores are often used to analyse diet diversity and to determine food security within a population or household level (FAO, 2010). Dietary diversity scores are also useful to assess single food groups or to investigate dietary intake within a population. (FAO, 2010).

According to the cross-sectional studies of the South African National Health and Nutrition Examination survey (SANHANES) and South African Social Attitude Survey (SASAS), the black South African race had the lowest dietary diversity score of all ethnicities in South Africa (see Table 2.7) (Labadarios *et al.*, 2011; Shisana *et al.*, 2013). Furthermore, Steyn (2013) previously stated that low diet diversity scores may be a reflection of food insecurity and is often associated with a monotonous diet followed by the black South African population (Labadarios *et al.*, 2011). Monotonous diets are based on an increased consumption of energy dense carbohydrates (maize meal, bread, sugar and rice) and decreased consumption of fruit, vegetables and animal products (Steyn & Mchiza, 2014). Thus, a monotonous diet may be lacking a variety of nutrients that may protect against BC risk and is therefore worrisome as it may contribute to an increased BC risk.

In line with the above, overall health will be promoted if one's diet consists of various foods, containing various nutrients to increase dietary diversity (Steyn, 2013). However, since 2003, South Africa has legislated national fortification of staple foods such as wheat flour and maize meal products with various micronutrients. A cross-sectional study conducted by Tydeman-Edwards (2012) in South Africa, stated that maize meal and wheat flour products were under the top 10 most frequently consumed foods in that particular study (see Table 2.2). Fortification of these frequently consumed products will contribute to increase consumption of various micronutrients that would have otherwise not been consumed. However, single fortified foods still do not contain all necessary nutrients for optimal health (Labadarios *et al.*, 2011). Therefore, a diverse diet consisting out of various vegetables, fruit, whole grains, high fibre products, legumes, lean meat and low fat products are necessary for adequate nutrient intake and to promote health status in the individual (Labadarios *et al.*, 2011).

**Table 2-2: Dietary diversity scores of South Africa compared in urban and rural areas, different provinces and different ethnicities.**

| | 2012 SANHANES study (Shisana *et al*., 2013) | | | 2009 SASAS Study (Labadarios *et al*., 2011) | | |
|---|---|---|---|---|---|---|
| | *Mean DDS | | % DDS < 4* | *Mean DDS | | % DDS < 4* |
| | Mean | 95% CI | | Mean | 95% CI | |
| **Area** | | | | | | |
| Urban formal | 4.7 | 4.5-4.9 | 29.3 | 4.42 | 4.34-4.50 | 26 |
| Urban informal | 3.8 | 3.5-4.1 | 46.6 | 3.46 | 3.30-3.61 | 55.7 |
| Rural formal | 3.6 | 3.4-3.9 | 50.7 | 3.64 | 3.46-3.81 | 50.1 |
| Rural informal | 3.3 | 3.2-3.5 | 59.7 | 3.17 | 3.05-3.29 | 63.9 |
| **Race** | | | | | | |
| Black | 4 | 3.8-4.1 | 44.9 | 3.63 | 3.55-3.71 | 50 |
| White | 5.6 | 5.2-6.0 | 14.9 | 4.96 | 4.82-5.10 | 9 |
| Coloured | 4.5 | 4.2-4.7 | 30 | 4.43 | 4.30-4.56 | 26 |
| Asian | 4.1 | 3.7-4.6 | 31.6 | 4.44 | 4.29-4.58 | 26 |
| Total SA | 4.2 | 4.1-4.3 | 39.7 | 4.02 | 3.96-4.07 | 38 |

*Mean DDS based on nine food groups from data of two South African studies, SANHANES and SASAS, where a score of one is associated with a very weak diet diversity and nine an excellent diet diversity.

DDS- Diet diversity score. Data adapted from Mchiza *et al.* (2015:8241)

Mchiza *et al.* (2015) further report fruit, vegetables and dairy as the least common consumed food groups in South Africa in rural and urban areas. As discussed in section 2.2, fruit and vegetables may consist of protective factors against BC. In addition, the most common single foods eaten are reported in prior studies conducted in South Africa by Nel and Steyn (2002) and Tydeman-Edwards (2012) (see Table 2.3). Most often consumed items were tea, added sugar, brown bread, maize meal dishes, full cream milk, coffee, margarine, potatoes, white bread, fruit, vegetables and rice. Food intake did not differ much from the study conducted before 2000 (Nel & Steyn, 2002) and the study conducted in 2012 (Tydeman-Edwards, 2012). However, more energy dense and nutrient poor foods such as sweets, cookies and salt were consumed after 2000. As emphasised in section 2.2.2, overconsumption of energy dense and nutrient poor foods such as sugar and refined grains may contribute to increased obesity rates, which increases the risk for postmenopausal BC. Moreover, low intake of nutrient rich foods may lead to micronutrient deficiency and a decreased intake of possible protective nutrients against BC risk. Thus, there is a possible higher risk for BC in both pre- and postmenopausal women with overconsumption of energy dense and nutrient poor foods.

**Table 2-3: Comparison of 10 most frequently consumed single foods in South Africa between the study on secondary analyses of South Africa in 2000 (Nel & Steyn, 2002) and Bloemfontein women in 2012 (Tydeman-Edwards, 2012).**

| Study on Secondary Analyses (2000) | Bloemfontein Women (2012) |
|---|---|
| Maize porridge and dishes | Sugar |
| Sugar | Tea |
| Tea | Maize porridge |
| Brown bread | Stock/salt |
| White bread | Hard brick margarine/oil |
| Non-dairy creamer | Bread |
| Brick margarine | Full cream milk |
| Chicken meat | Vegetables |
| Full Cream milk | Fruit |
| Green leafy vegetables | Cold drinks |
| Potatoes | Chicken |
| Tomato and onion stewed | Eggs |
| Coffee | Sweets/chocolates |
| Eggs | Potato chips |
| Cabbage | Cakes/biscuits |

Data adapted from Mchiza *et al*. (2015)

### 2.2.5 Poverty, dietary intake and food security

Food insecurity can be defined as a state of being without reliable access to sufficient and affordable, nutritious food (FAO, 2010). Food insecurity in South Africa slightly decreased from 23.9% in 2010 to 22.3% in 2016 (STATS SA, 2016). Great contributions have been made by the Southern Africa Food Lab (SAFL) initiative to decrease food insecurity in South Africa (SAFL, 2016). The SAFL initiative aims to address food insecurity in South Africa and may therefore play a key role in decreasing food insecurity within South African households. Increased food security may promote overall health within households. However, even though decreased food insecurity rates are reported, 12,3 million South African citizens were still food insecure in 2016 (STATS SA, 2016). Worrisome is that food insecurity is associated with obesity and insufficient intake of diverse micronutrients needed for optimum health and prevention of degenerative diseases (Farrell *et al.*, 2017).

Previously, greater obesity rates have been associated with higher income countries than in lower income countries like South Africa (Popkin *et al.*, 2012). However, this pattern is changing and obesity among lower income groups in South Africa are increasing, despite food insecurity (Popkin *et al.*, 2012). This may be due to a simplified food system in South Africa (Du Plooy *et al*., 2017).

A simplified South African food system developed over time which mainly focuses on a limited selection of food products (Du Plooy *et al.*, 2017). These food products are high energy dense foods and are lower in cost. Hence, availability of cheap vegetable oils and fats from milk and meat has resulted in increased saturated fat consumption in South Arica (Popkin *et al.*, 2012). Even though saturated fat intake is not directly associated with BC risk (see Table 2.4), overconsumption of low cost, energy dense fats may contribute to a higher total energy intake/day, which may result a higher risk for obesity, a known BC risk factor in postmenopausal women.

Furthermore, the nutrition transition (phase four) also emphasise the increase in availability and accessibility of supermarkets, low-priced food chains and street food vendors selling more processed and energy dense foods (Steyn & Mchiza, 2014). It is common to find staple food such as refined starches (maize meal dishes, bread, and rice) and other food products with added sugar and fat within South African food-insecure households (Steyn & Mchiza, 2014). In addition, government initiatives subsidise staple foods such as samp, maize meal, bread, rice and vegetable oil, fruit and veg (Mchiza *et al.*, 2015). Thus, no Value Added Tax (VAT) is paid on these foods, making energy dense staple foods more affordable for low-income classes in South Africa. However, more energy dense VAT free foods (samp, maize meal, rice, bread, vegetable oil) are cheaper than fruit and vegetables. As mentioned earlier, even though these staple foods (maize and flour products) are fortified with some micronutrients, it still does not contain all nutrients needed for optimal health to lower the risk of degenerative diseases. Thus, a low-cost diet that is not diverse in nutrients (containing probable protective factors against BC) is therefore bothersome for it may contribute to an increased BC risk.

Buying food at low priced food chains or energy dense foods (mostly nutrient poor) in South Africa that are cheaper may not be by choice. It is rather a way of surviving due to the high Gini coefficient (62.8) of South Africa (The World Databank, 2018; Pisa & Pisa, 2017). A Gini coefficient is defined as a measure of deviation of income distribution amongst a household or individual within a specific country (World Databank, 2013). A Gini coefficient value of 100 represents absolute inequality, where 0 represents absolute equality (World Databank, 2013). Additionally, South Africa faced 27.6% of unemployment during 2016 while 44.5% of households in South Africa earned between R0 and R1583 ($120.69) per month (see Table 2.4) (STATS SA, 2016).

**Table 2-4: The estimated average annual and monthly income of the lowest to the upper income classes of South African households.**

| Annual income (ZAR) | Monthly income (ZAR) | Classification | Percentage contribution of income classification. |
|---|---|---|---|
| R0-19,00 | R0 - R1,583 | Lowest | 62.3% |
| R19,001-R86,00 | R1,584-R7,167 | Second lowest | |
| R86001-R197,000 | R7,168-R16,417 | Low emerging middle | 26.4% |
| 197,001-R400,000 | R16,418-R33,333 | Emerging middle | |
| R400,001-R688,00 | R33,334-R57,333 | Lower middle | |
| R688,001-R1,481,000 | R57,334-R123,417 | Upper middle | |
| R1,481,001-R2,360,00 | R123,418-R196,667 | Upper income/Emerging affluent | 1.3% |
| R2,360,001+ | 196,668+ | Affluent | |

Data adapted from Money South Africa (Hunter, 2016).

## 2.3 Breast Cancer

### 2.3.1 A global concern

In the following section BC will be discussed as a global concern with the focus on prevalence, incidence and mortality rates.

Mortality and incidence rates are constantly rising in developed and less developed countries (WHO, 2017). In 2012, approximately 1.7 million new BC cases were diagnosed worldwide which represented 25% of all cancer diagnoses (Bandera *et al.*, 2015). The WHO further predicted 2.1 million new global BC cases in 2025 (WHO & IARC, 2012). Higher incidence rates of BC are reported in HICs. Worrisome, however; is that incidence rates are increasing in LMICs (Jedy-Agba *et al.*, 2016). Research indicates that incidence rates of BC in LMICs are likely to increase even more in imminent decades due to population ageing and adoption of the lifestyle of HICs (Jedy-Agba *et al.*, 2016).

Adding to the above, the WHO recently stated that 70% of global BC deaths occurred in LMICs (WHO, 2018). Different incidence rates of BC in HICs and LMICs may be a reflection of variation in access of early BC screening and report practices in HICs together with different genetic, environment, lifestyle and healthcare factors (Bandera *et al.*, 2015).

Survival rates for BC differ worldwide, but in HICs early stage (stage I/II) BC diagnoses has an 80% to 90% survival rate, while advance stage (stage III/IV) BC diagnoses has a 24% survival rate (Ferlay *et al.*, 2012). According to the World Cancer Research Fund (WCRF) (2017) HICs in Europe and North America have the highest proportion of five-year survival rates compared to LMICs in Africa and Asia who have the lowest five-year survival rates for BC. Vanderpuye *et al.* (2017) further state that survival rates in African countries are rarely described or updated which contribute to the complexity of the survival statistics in Africa.

The WHO and Pan American Health Organization (PAHO) declared BC as a chronic non-communicable disease (NCD) that requires prevention and control strategies (PAHO & WHO, 2015). As indicated above, the latest mortality and incidence rates of BC emphasise an increasing burden on health organisations and societies. Cancer can largely be prevented because genetic predisposition and heredity only account for approximately 5% to 10% of all cancers, while risk factors and exposures to unhealthy lifestyles and environmental factors account for the rest (WCRF, 2018).

### 2.3.2 **A public health concern within South Africa**

Breast cancer has the highest age-standardised incidence rate (33.35/100 000 ASR) and the second highest age-standardised mortality rate (16.5/100 000 ASR) after cervical cancer in South African women (SANCR, 2014). In addition, BC is the second leading cancer in black South African women (18.01/100 000 ASR) (SANCR, 2014). Incidence rates of BC categorised by ethnicity (Black, White, Coloured and Asian/Indian) in South African women are presented in Figure 2.1. An increase in BC incidence rates is noted from 2000 to 2014 in all ethnicity groups.

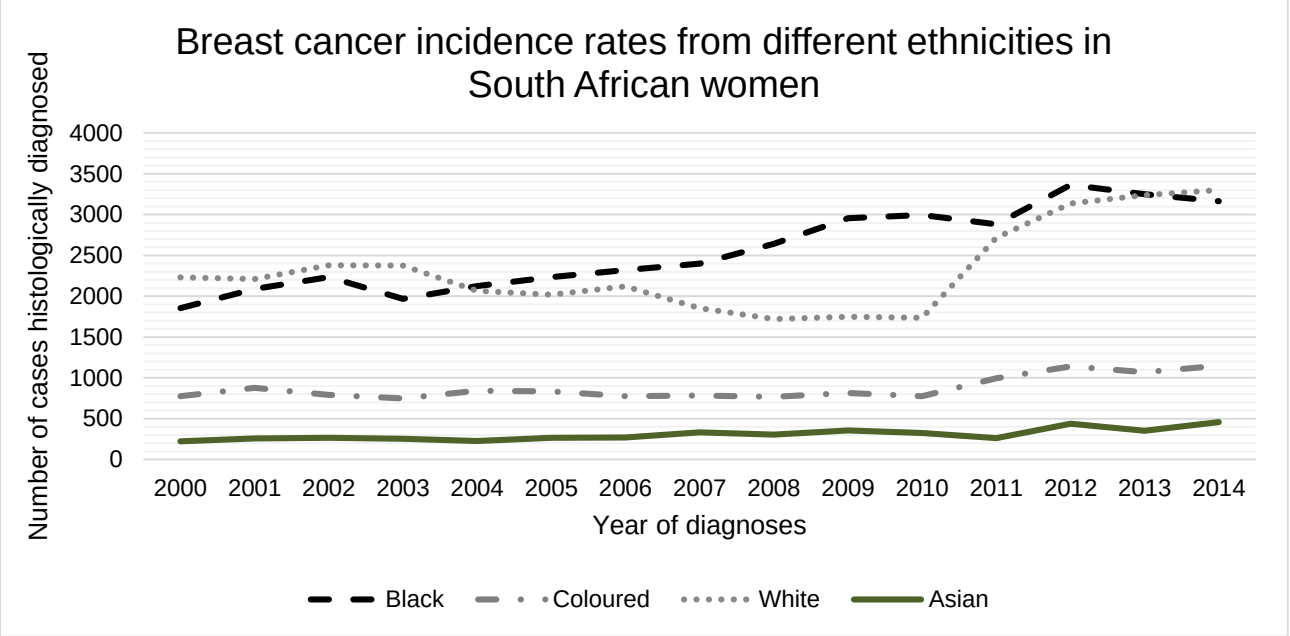


Figure 2-1: Incidence rates from different ethnicities in South African women.

Data adapted from the South African National Cancer Registry (2000-2014).

The South African National Cancer Registry (SANCR), the main pathology based cancer surveillance agency in South Africa, reported 33 956 black female BC cases between 1994 and 2009 (SANCR, 2014). However, scientists have reason to believe that not all BC cases in South Africa are reported in the SANCR (Singh *et al*., 2015a). Thus, incidence and mortality rates of BC in South Africa might be higher than previously and currently reported.

### 2.3.3 **Difficulties in breast cancer diagnoses**

Breast cancer is curable when it is detected in early stages (stage I and II) (Singh *et al.*, 2015a). Early stages of BC are referred to as spreading of cancer to nearby lymph nodes but not too distant parts of the body (WCRF & AICR, 2007). Therapeutic treatment (chemotherapy, hormone therapy and radiation) combined with early stage detection are major contributors in BC mortality reduction, especially in HICs (Jedy-Agba *et al.*, 2016). In contrast, higher late stage diagnoses are reported in black South African women compared to other ethnicities (74% to 91% vs 30% to 44%) (Jedy-Agba *et al.*, 2016). This is bothersome as late stage BC diagnoses are associated with poor prognosis.

Recently, the WHO stated that only 26% of LMICs have adequate pathology services for cancer screening and appropriate treatment available in the public sector (WHO, 2018). This is also true for South Africa. South Africa has limited organised population-based screening programmes for BC and opportunistic screening is restricted to only a small proportion of

higher socioeconomic women (Dickens *et al.*, 2016). The South African organisations, Pink Drive together with the Cancer Association of South Africa (CANSA), offer some of the limited BC screening programmes in South Africa (CANSA, 2018; Pink Drive, 2018). Both organisations have mobile health clinics and aim to provide free or low-cost health services to medically uninsured women in semi-urban and urban areas in South Africa (CANSA, 2018; Pink Drive, 2018). These health services focus on early BC detection and include screening of BC, physical examination and education towards BC risk factors (CANSA, 2018; Pink Drive, 2018). However, these mobile health clinics only reaches a small number of people over a period of time and late stage (stage III/IV) BC diagnoses still remain a major concern in South Africa.

The authors, Singh *et al.* (2015b:415) further report of a shortage of qualified healthcare professionals in South Africa (see Table 2.5). South Africa has 5.4 doctors per 10 000 population (Matsoso & Strachan, 2011:51). The oncology healthcare workers listed in Table 2.5 (Singh *et al.*, 2015b:415) are a combined list of the private healthcare system and the public healthcare system. Most of the South African population make use of public healthcare services (83%), while 57% of healthcare specialists are estimated to engage in private healthcare services (Matsoso & Strachan, 2011). South Africa's lack of healthcare professionals and inequality of specialists contribute to difficulties in diagnosing and treatment of BC in the early stages when prognosis is better. Thus, emphasizing the impact of inequalities in the healthcare system in South Africa, the burden thereof on BC and the need for alternative incidence reducing methods that focus on prevention rather than BC cure or treatment.

**Table 2-5: The Health Professions Council of South Africa (HPCSA) 2014 registered cancer-related specialists.**

| | Number | Per 10 000 population |
|---|---|---|
| Medical oncologists | 33 | 0.006 |
| Pathologists (anatomical) | 258 | 0.01 |
| Paediatric medical oncologists | 20 | 0.04 |
| Radiation oncologists | 201 | 0.05 |

Data adapted from (Singh *et al.*, 2015b:415)

## 2.4 Pathogeneses of breast cancer

Section 2.4 was added in this chapter to give an overview of the complexity of BC pathology. In addition, certain modifiable dietary risk factors for BC differ in subtypes and ethnicities and

are therefore important since this study is a population based study of the black female population of South Africa.

Cancer is characterised by uncontrolled cellular growth due to certain changes in genetic material of cells (WCRF & AICR, 2007:31). The division, differentiation and death of cells are regulated carefully within the human body (WCRF & AICR, 2007). Cancer growth begins as an individual cell that has lost the ability to control normal growth and regulation of the duplication processes (WCRF & AICR, 2007:31).

Progression of BC is influenced by hormones such as oestrogen and progesterone (WCRF & IARC, 2017). These hormones modulate growth and structure of epithelial tumour cells in breast tissue during puberty and breast maturation in pregnancy (WCRF & IARC, 2017). Oestrogens however, are involved in breast carcinogenesis through a proliferative effect on breast tissue (WCRF & IARC, 2017). High oestrogen levels (estradiol and oestrone) are associated with an increased risk for BC development (Petridou *et al.*, 2018). High oestrogen levels and uncontrolled cellular growth is often a result of exposure to environmental and dietary agents (Dwivedi *et al.*, 2014). Thus, dietary agents in combination with various other factors may contribute to BC development.

### 2.4.1 **Breast cancer subtypes**

Breast cancer is known to be a highly heterogeneous disease with different prognoses depending on intrinsic molecular subtypes (Dickens *et al.*, 2016). It can be distinguished by at least four different intrinsic molecular subtypes and up to 21 distinct histologic subtypes (DeSantis *et al.*, 2016). Subtype classification of BC is based on hormone receptor status, defined by oestrogen receptor (ER) and progesterone receptor (PR) status (Bandera *et al.*, 2015). Intrinsic molecular subtypes consist predominantly out of two positive hormone receptors (ER-positive/PR-positive) and two predominantly hormone-negative receptors (ER-negative/PR-negative) (Anderson *et al.*, 2014; Dickens *et al.*, 2014). Positive hormone receptors can further be divided into immunohistochemical subtypes of Luminal A and Luminal B and negative hormone receptors into immunohistochemical subtypes of human epidermal growth factor receptor 2 (HER2) enriched and basal-like factors (see Table 2.6) (Dickens *et al.*, 2016; Go *et al.*, 2016). They are associated with distinct risk factors and are biologically different in presentation, outcomes and response to treatment (Gershuni *et al.*, 2017). Breast tumours can further be classified based on expressions of oestrogen and progesterone receptors (Stricker *et al.*, 2017). Thus, emphasizing that BC is a complex disease.

**Table 2-6: Intrinsic breast cancer molecular subtypes**

| IHC-subtype | ER and/or PR | HER2 | Intrinsic subtype |
|---|---|---|---|
| Luminal A | Positive | Negative | Luminal A |
| Luminal B | Positive | Negative or positive | Luminal B |
| HER2 positive, non-luminal | Negative | Positive | HER2-enriched |
| Triple-negative | Negative | Negative | Basal-like |

*There are additional intrinsic molecular subtypes categorised into two predominantly HER2-positive subtypes (luminal B and HER2-enriched) and two predominantly HER2-negative
IHC - immunohistolochemical; ER - oestrogen receptor; PR - progesterone receptor; HER2 - Human-Epidermal Growth Factor Receptor 2.
subtypes (Luminal A and Basal-like). Data adapted from Anderson *et al.* (2014:5)

### 2.4.2 **Ethnicity, age and breast cancer subtypes**

Distribution of the four BC subtypes differ with age and race (Gershuni *et al.*, 2017). A wide variety of the distribution of subtypes across racial/ethnic groups is reported. Black and Hispanic ethnicities tend to be more susceptible to oestrogen receptor negative ($ER^-$) and Triple negative breast cancer (TNBC) than non-Hispanic white women (Bandera *et al.*, 2015). Certain BC subtypes such as $ER^-$ and TNBC tumours are more aggressive tumours and are associated with poorer prognosis, leading to higher mortality rates.

In addition, age also influences risk of certain BC subtypes (Parise *et al.*, 2010). The authors, Parise *et al.* (2010) state that black women of a younger age (< 41 years) are at higher risk for TNBC than older black women. Furthermore, an increase in age tends to be more associated with ER/PR-positive ($ER^+/PR^+$) tumours, while HER2-positive subtype incidence decreases with age (Parise *et al.*, 2010).

South Africa can be classified as a multi-racial country with a unique setting to investigate BC subtypes. The risk of developing BC in South Africa may vary according to ethnicity (Langenhoven *et al.*, 2016). Table 2.7 summarises various BC subtypes from four different studies conducted from urban areas (Soweto and Cape Town) in South Africa (Cubasch *et al.*, 2018; Cubasch *et al.*, 2013; Dickens *et al.*, 2016; Langenhoven *et al.*, 2016). Oestrogen receptor BC is the most prevalent BC subtype diagnosed in the studies conducted by Cubasch *et al.* (2013), Cubasch *et al.* (2018) and Langenhoven *et al.* (2016). These studies mentioned above, report of 50%, 55% and 49% of advance stage BC, respectively. Thus, more than half

or nearly half of the sample in all three studies mentioned above, were diagnosed in more advanced stage BC when prognosis is poor and may therefore contribute to high mortality rates in South Africa. Generally, BC prognosis is more favourable when detected in early stages compared to advanced BC diagnoses (Caplan, 2014). Additionally, these studies also show that the average age of BC diagnosed in black women ranged between 48 and 54.4 years. Thus, BC is mostly diagnosed in older black South African women.

**Table 2-7: Clinical trials reporting on advanced stages of BC and receptor status of studies conducted in South Africa.**

| Study | Sample size | Age at diagnoses | Population | Reported incidence of advanced stage BC (Stage III/IV) | Receptor status |
|---|---|---|---|---|---|
| Cubasch *et al.* (2013) | 1092 | 56% of sample ≥ 50+ years of age | Black women | 50% | ER: 58.0<br>PR: 47.0<br>HER2: 22.0<br>TNBC: 19.0 |
| Langenhoven *et al*. (2016) | 586 | 56 (not reported) | Mixed race | 55% | ER: 64.0<br>PR: 51.0<br>HER2: 36.0<br>TNBC: 16.5 |
| Cubasch *et al.* (2018) | 602 | 54.4±14.2 * | Mostly black (90.8%) | 49% | ER: 62.3<br>PR: 53.5<br>HER2: 24.0<br>TNBC: 21.7 |
| Dickens *et al.* (2016) | 6633 | 53 (43, 65) † | Black | Not mentioned | ER: 79.9<br>PR: 74.0<br>HER2:66.7<br>TNBC: 21.4 |

*Data reported as mean ± SD
†Data reported as median (25th percentile, 75th percentile)
ER - oestrogen receptor; PR - progesterone receptor; HER2 - Human-Epidermal Growth Factor receptor 2; TNBC - triple negative breast cancer.
Data adapted from Cubasch *et al.*, 2018:122; Dickens *et al.*, 2016:534; Vanderpuye *et al.*, 2017:4.

## 2.5 Risk factors of breast cancer

Boundless progress has been made in understanding the development of cancer and the extent to which endogenous and exogenous factors modify cancer risk (WCRF & AICR, 2007). Risk reduction methods and factors regarding nutrition, diet, physical activity (PA) and body weight associated with cancer are regularly updated by the Continuous Update Project (CUP) (WCRF & AICR, 2018). The CUP is a report on cancer survival and prevention led by WCRF international in partnership with the American Institution for Cancer Research (AICR) (WCRF & AICR, 2018). It is a reliable scientific aid which supports up-to-date policies and guidelines for prevention of cancer (WCRF & AICR, 2018).

In 2007, findings on all cancer survival and prevention were published in *Food, Nutrition, Physical Activity and the Prevention of Cancer: A Global Perspective* (second expert report of

2007) (WCRF & AICR, 2017). Findings on cancer are currently published in separate CUP reports for different cancers and are used to update cancer prevention recommendations (WCRF & AICR, 2018). The first CUP report on BC survival and prevention was published in 2010, followed by the second update report of 2017 and revised report of 2018 (WCRF & AICR, 2018). The CUP report on BC examines universal BC prevention factors and survival rates associated with nutrition, diet, physical activity and body weight (WCRF & AICR, 2018). This report aims to ensure that public members, health professionals and policymakers have access to the most recent research on BC risk reduction methods (WCRF & AICR, 2018).

Breast tissue differs at certain stages of life in response to environmental influences and hormonal status (WCRF & IARC, 2018). Thus, not all women have the same risk of developing BC (Cadmus-Bertram *et al.*, 2013). Risk factors for BC can be classified by endogenous hormone exposure and exogenous hormone exposures (WCRF & AICR, 2018). Endogenous hormone factors such as age, family history of BC, reproductive factors, genetic predisposition and exogenous hormone exposures such as environmental factors have all been associated with an increased risk for BC development (Shah *et al.*, 2014). Risk factors for BC can either be modifiable or non-modifiable and will be discussed as such in the next section (Cadmus-Bertram *et al.*, 2013).

### 2.5.1 **Non-modifiable risk factors (Other causes of BC)**

Breast tissue comprises largely out of fat, glandular tissue, ducts and connective tissue and mainly fat (WCRF & AICR, 2018). The prime periods of breast tissue development are during puberty, lactation or pregnancy (WCRF & AICR, 2018). Development of breast tissue is in response to hormones such as growth factors, insulin, oestrogen and progesterone (WCRF & AICR, 2018). Radiation and medication also influence endogenous and exogenous hormone exposure (WCRF & AICR, 2018). Cycles of endogenous oestrogen levels throughout a woman's lifetime are associated with developing of BC or protecting against BC (Shah *et al.*, 2014).

Early age at menarche (12 years of age) is classified as a risk factor for both pre- and postmenopausal women being diagnosed with BC (WCRF & AICR, 2018). The European Prospective Investigation into Cancer and Nutrition (EPIC) cohort showed that women who had an early menarche of younger than 13 years of age, had a twofold increase in risk of developing hormone receptor positive tumour BC (Ritte *et al.*, 2012). Late menarche (over 13 years of age) however, has shown to decrease lifetime exposure to oestrogen and progesterone hormone levels and may result in a decreased BC risk (WCRF & AICR, 2018).

Parity and age at first full term pregnancy also influences risk for BC development (Shah *et al.*, 2014). According to Shah *et al.* (2014), nulliparous women are at higher risk for developing BC compared to parous women. The CUP report further states that women over the age of 30 years who are nulliparous or who is pregnant for the first time may have a high risk of developing BC (WCRF & AICR, 2018). However, early child bearing age and pregnancies (< 30 years) are associated with inverse associations of BC development (WCRF & AICR, 2018).

Other life events such as an early onset of menopause are associated with a decreased risk of developing BC whilst a late onset of menopause (after 55 years of age) increases the risk for BC (WCRF & AICR, 2018).

Breast feeding is being described as a protective factor against BC (Shah *et al.*, 2014). Breast feeding may delay the return of some regular ovulatory cycles and causes reduction in endogenous sex hormone levels. High levels of testosterone tend to increase the risk of BC in postmenopausal women (Sieri *et al.*, 2009).

### 2.5.2 **Modifiable risk factors**

Lifestyle risk factors play an important role in developing BC and can be modified through behavioural changes (Shah *et al.*, 2014). Modifiable risk factors in relation with BC are physical inactivity, high alcohol intake, obesity and unhealthy dietary intake. A broad discussion of these modifiable risk factors will follow in the section to come.

**Physical activity as modifiable risk factor for breast cancer**

The latest CUP report concluded that vigorous PA probably protects against pre- and postmenopausal BC risk (WCRF & AICR, 2018). However, no significant associations between occupational activities or recreational PA and BC risk are reported (WCRF & AICR, 2018). PA is measured in metabolic equivalent minutes (METs). The WHO (2018) recommends at least 600 METs of PA per week for overall health benefits in adults age 18 to 64 years. This is approximately 150 minutes of brisk walking or 75 minutes of vigorous PA per week (WHO, 2018).

It has been hypothesised that an increase in PA tend to reduce body fat (Nomura *et al.*, 2016) which modify growth factors and endocrine profiles that may affect cancer growth susceptibility (WCRF & AICR, 2018). Moreover, the latest CUP report states that oestrogen and androgen levels are reduced with an increase in PA (WCRF & AICR, 2018). Thus, reduced oestrogen exposure during one's lifetime is associated with a low BC risk in pre- and postmenopausal women (WCRF & AICR, 2018). The CUP report further states that duration, intensity and type

of PA may affect the level of BC risk through different mechanisms (WCRF & AICR, 2018). Together with a possible reduced BC risk, a recent review also indicated that PA may improve health outcomes after BC diagnoses (Diggins *et al.*, 2017).

Inverse associations have been reported between higher PA and lower BC risk in various observational and experimental studies (Diggins *et al.*, 2017; Hong *et al.*, 2016; Nomura *et al.*, 2016; Steindorf *et al.*, 2013). These studies have been conducted in North America (California, North Carolina, New Jersey and Florida) Western Europe and Hawaii. Adding to the above, the systematic review of Kyu *et al.* (2016) with pooled data from studies in China, Ghana, India, Mexico, Russia, South Africa and North America, showed higher total PA levels (more than 8000 METs per week) were associated with a lower risk (14%) for BC compared to insufficiently active women (less than 600 METs per week). Thus, in agreement with the CUP report, these studies also indicated vigorous PA may be associated with a lower BC risk.

Approximately 43% to 49% of all South Africans over the age of 15 years does not meet the recommended moderate to vigorous PA METs/week (Micklesfield *et al.*, 2014). There is a lack of data on the possible role of physical inactivity as modifiable risk factor for BC in black South African female populations. Nevertheless, these high levels of inactivity are worrisome and the impact on higher incidence rates could have important implications on preventative measures. Thus, this level of inactivity may contribute to higher incidence rates of BC in South Africa.

**Alcohol as modifiable risk factor for breast cancer**

The latest CUP report concluded that consumption of alcohol is a probable cause for premenopausal BC and a convincing cause for postmenopausal BC (WCRF & AICR, 2018). Currently, no threshold for alcohol consumption in relation with BC risk has been set (WCRF & AICR, 2018). Furthermore, the IARC provided adequate scientific evidence to classify alcohol consumption as a group one carcinogen causing BC in women (Dwivedi *et al.*, 2014). Group one carcinogens are substances with strong scientific evidence that are proven to cause cancer (Dwivedi *et al.*, 2014).

The relationship between a higher BC risk and alcohol consumption may occur due to possible differences in dietary intake of people who consume alcohol, compared to those who don't (WCRF & AICR, 2018). Effects of alcohol mediate through certain impacts on lipid metabolism, production of lipid peroxidation, prostaglandins and generation of free radical oxygen species (ROS) (WCRF & AICR, 2018). Alcohol also enhances perforation of carcinogens into cells (WCRF & AICR, 2018). According to the IARC (2012), breast tissue metabolites alcohol to

acetaldehyde, leading to the production of ROS. ROS is associated with DNA damage and initiates cancer spurt (IARC, 2012). Alcohol increases circulating oestrogen levels which further affects the susceptibility to promote cancer growth (WCRF & AICR, 2018). Genetic factors may also regulate BC risk in a way of altered genes for alcohol, folate and methionine metabolism and repairing of DNA (WCRF & AICR, 2018).

Thomson (2012) found that increased alcohol consumption showed a significant association with an increased BC risk. Another study conducted by Danaei *et al.* (2005) estimated that globally, 21% of all BC deaths were attributable to alcohol consumption. Brennan *et al.* (2010) further states that convincing evidence has been reported for high alcohol consumption associated with an increased risk for BC. A study conducted of more than 1 280 000 middle aged British women concluded that for every additional drink regularly consumed every day, incidence of BC rises by 1.1% (Allen *et al.*, 2009). Williams *et al.* (2016) further states that the amount of alcohol consumed between puberty and first full-term pregnancy are proportional to BC risk. Thus, several studies in line with the CUP report concluded that alcohol is positively correlated with a higher BC risk.

**Obesity as modifiable risk factor for breast cancer**

High prevalence rates of overweight and obesity is a global concern (Draper *et al.*, 2016). Obesity is classified as a prognostic factor in BC risk (Gershuni *et al.*, 2017). Parekh *et al.* (2017) further states that obesity is declared as the most important BC risk factor for women of postmenopausal age (see Figure 2.2). The CUP report also concludes that greater weight gain and greater body fatness during adulthood contribute to convincing evidence of a higher BC risk in postmenopausal women (WCRF & AICR, 2018). According to Guerrero *et al.* (2017), 9% of BC cases are due to obesity in postmenopausal women. For postmenopausal BC risk, weight loss (> 5 kg) after 18 years of age tends to lower BC risk whilst weight gain after 18 years of age tend to increase BC risk (Andersen *et al.*, 2014). An increase in adiposity is associated with overlapping pathways of elevated aromatase-mediated oestrogen levels, increased circulating insulin-like growth factor-1 (ILGF-1) or insulin resistance which are linked to tumour promoting effects for BC (Bandera *et al.*, 2015; Gershuni *et al.*, 2017). Figure 2.3 shows probable adverse effects and the overlapping pathways associated with overweight and obesity on BC risk and survival (Bandera *et al.*, 2015:805). Overweight and obesity may also affect treatment of BC by influencing decisions regarding treatment and efficacy thereof (e.g. reduced dose of chemotherapy) (Bandera *et al.*, 2015).

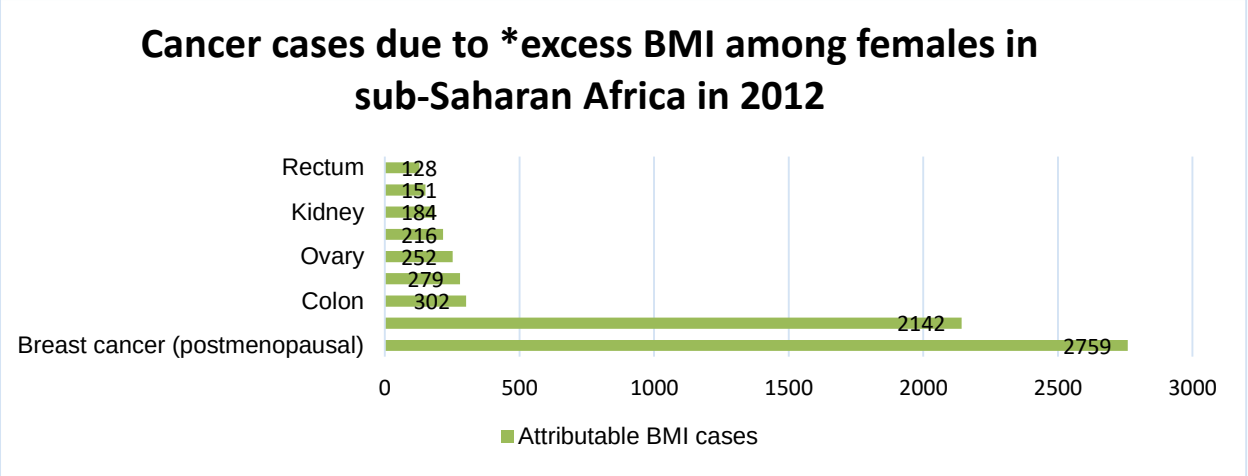


Figure 2-2: Overweight and obesity contribute to postmenopausal BC incidence cases in sub-Saharan Africa.

*Excess BMI refers to a BMI over 25 kg/m$^2$ and 29.9 kg/m$^2$ which is categorised by the WHO as overweight and obese respectively. Data adapted from online analysis for cancer and obesity (WHO & IARC, 2012).

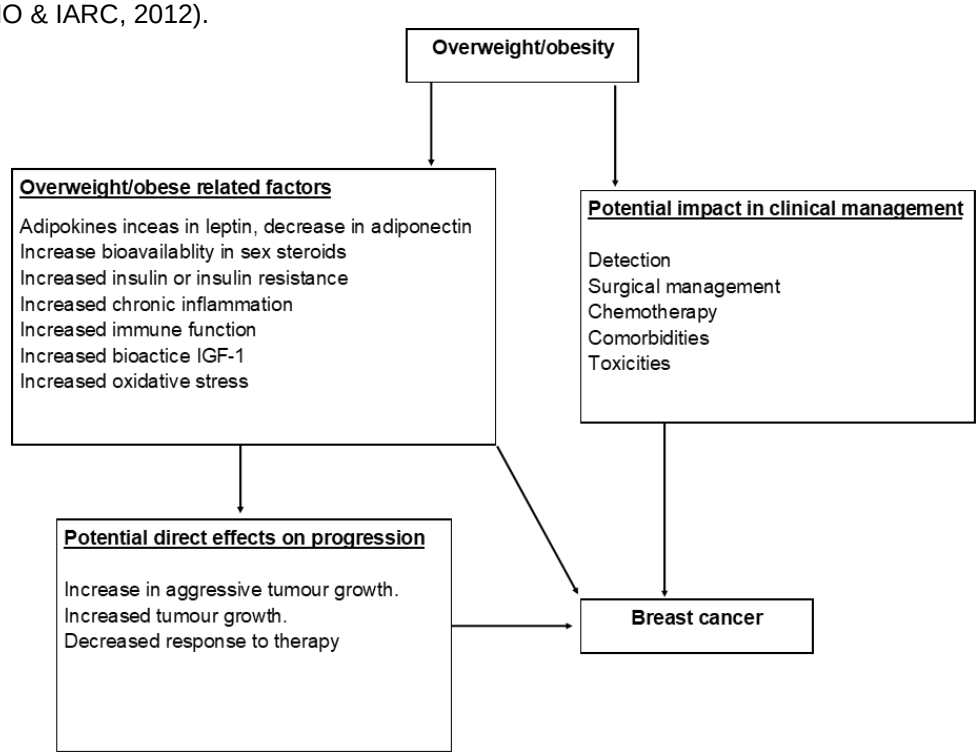


Figure 2-3: Possible adverse effects associated with overweight and obesity on postmenopausal BC risk and survival.

IGF-1, insulin-like growth factor I. Data adapted from (Bandera *et al*., 2015:805).

In contrast to obesity being a risk factor in postmenopausal women, premenopausal adiposity is inversely associated with BC risk (Rosner *et al.*, 2017). Childhood adiposity may influence growth and maturation and is related to decreased height growth velocity and early age at menarche, but does not influence attained height when fully grown (Rosner *et al.*, 2017). Probable relations with intermediate markers for BC risk such as breast density and benign breast tumours are also reported (Andersen *et al.*, 2014). Adiposity between the ages 5 and 10 years of age tend to show the most significant decrease in BC risk (Rosner *et al.*, 2017). Some studies also revealed inverse associations with BC risk at the age of 18 years (Rosner *et al.*, 2017).

Several studies conducted in urban areas of South Africa (multicentre study and Cape Town) reported on the average onset age of menopause in the black female population (Conradie *et al.*, 2014; Kabenkama *et al.*, 2018). The average onset age (mean ± SD) ranged between 46.0 ± 5.0 and 49.0 ± 5.0 years in the study conducted by Conradie *et al.* (2014) and the average onset age was 48.7 ± 2.9 in the study conducted by Kabenkama *et al.* (2018). Even though a higher body weight might be associated with a lower BC risk in premenopausal women, worrisome is that BC is mostly diagnosed in black women of older age in South Africa (Table 2.7) (Cubasch *et al.*, 2018; Cubasch *et al.*, 2013; Dickens *et al.*, 2014; Dickens *et al.*, 2016). Hence, these women are probably already in the onset of menopause or post menopause when diagnosed with BC. Obesity is therefore a major concern regarding BC risk in black South African women.

**Obesity, ethnicity and BC subtypes**

BC subtype distribution differs significantly in accordance to BMI status (Gershuni *et al.*, 2017). Thus, overweight or obese women may be more susceptible to develop BC of a specific subtype. The authors, Gershuni *et al.* (2017) report of the focus on the relationship between obesity and increased oestrogen production; thus, contributing to $ER^+$ BC pathogenesis. As mentioned in section 2.4, ER BC tumour type was mostly diagnosed in four individual studies in South Africa. Thus, black South African women who are obese from those regions (Soweto and Cape Town) might be more prone to develop ER type BC.

**Recommended dietary modification to reduce BC risk.**

Prevention of BC is the most cost-effective strategy for long-term cancer control (WHO, 2017). Modification of dietary factors forms part of effective approaches for BC control and prevention (WHO, 2017). As previously stated, 30% to 50% of all cancer cases may be prevented through behavioural changes such as a nutritive diet together with a healthy body weight and regular PA (WCRF, 2017; WHO, 2018). The WCRF (2017) currently promotes cancer prevention

recommendations where a diet high in whole grains, fruit, vegetables and dried beans and legumes? are encouraged whilst energy dense foods such as sugary drinks, alcohol and processed meat should be avoided. Furthermore, it is recommended that red meat consumption and salt intake should be limited (WCRF, 2017).

According to Parekh *et al.* (2017), BC patients do not have adequate knowledge about nutrition to reduce their risk for BC. Only 30% of BC patients are improving their habitual dietary intake after BC treatment (Costanzo *et al.*, 2011; Parekh *et al.*, 2017). A lack of health and nutrition literacy may contribute to high BC incidence and mortality rates (Hernandez, 2013).

Consumers are often left confused about the basic principles of diet and health and the association between BC risk, for they rely on recommendations of the food industry to make informed nutrition decisions (Costanzo *et al.*, 2011). A lack of knowledge on how to read food labels, which product to buy or how to interpret health claims on packaging are also reported to contribute to the confusion (Eicher-Miller *et al.*, 2015). According to Parekh *et al.* (2017), an environment of overeating and poor nutritional practices have been created by the food industry which contributed to the obesity epidemic. National strategies should be executed to increase awareness of a healthy lifestyle (WCRF, 2017). Diet modification through appropriate nutrition education may be a key approach to develop primary BC prevention programs.

## 2.6 Dietary intake

### 2.6.1 Dietary intake as contributing factor to breast cancer aetiology

Even though dietary intake in relation with BC risk has been studied comprehensively (Van Ryswyk *et al.*, 2016), the aetiology of BC and the relation with dietary intake is still not clearly understood (Dwivedi *et al.*, 2014). Mechanisms explaining carcinogenesis are provided (Table 2.4), but remain complicated, for several factors are interrelated in BC development (Ross, 2010). While it is not clear to what extent BC are specifically attributed to dietary factors, Dwivedi *et al.* (2014) suggest that a third of all cancer incidences are attributed to dietary factors. Dietary factors have shown effects that can contribute to the development of cancer by altering DNA or by altering how genetic messages in DNA are translated (WCRF & IARC, 2007). A functional human body depends on the availability of good nutrition (WCRF & IARC, 2007). The WCRF defines good nutrition as appropriate provision of nutrients from the level of whole organisms to cellular and intracellular level (WCRF & IARC, 2007). When a person is malnourished, either through over- or under-nutrition, physiological compromises in both cellular structure and function are made (WCRF and IARC, 2007).

Dwivedi *et al.* (2014) further states that the relation of an increased BC risk with dietary intake might be due to exposure to natural carcinogens such as heavy metals and aflatoxin in dietary components. Furthermore, low or insufficient intake of natural cancer protective components (phytochemicals and antioxidants) in one's diet may also contribute to an increased BC risk. Phytochemicals includes flavonoids, sterols, polyphenols and carotenoids and is found in various nutrient dense foods such as fruits and vegetables (Dwivedi *et al.*, 2014).

### 2.6.2 **Dietary intake in relation with breast cancer risk**

Dietary intake is a very broad term and is often associated with dietary patterns, population-based diets, single foods, macronutrients, micronutrients, food groups and dietary habits. These dietary components (mentioned above) and the association with BC risk have previously been investigated globally. However, in Chapter 3, the focus will be drawn to food groups for the purpose of investigating the association between dietary intake and BC risk. Therefore, findings from the latest CUP report and the association with food groups and BC risk will be discussed in the section to follow

Conclusions of the CUP report from several studies investigating specific food groups in relation to BC risk are summarised in Table 2.8. The CUP report currently concludes that there is limited, but suggestive evidence for a decreased BC risk in relation with non-starchy vegetables (in $ER^+$ BC tumour type), dairy products and carotenoid containing foods in pre- and postmenopausal women (WCRF & AICR, 2018). The CUP report further concludes that there is limited evidence with no conclusion for other food groups (cereal and cereal products, fruit, soya, total fat intake, red meat and processed meat) being investigated in relation with an increased or decreased BC risk (WCRF & AICR, 2018). Differences in populations, study designs and assessment methods may contribute to inconclusive or limited results in the CUP report. In addition, some studies did not separate between pre- and postmenopausal status and/or BC subtypes. Therefore, evidence is still lacking for some food groups to draw convincing conclusions in relation to risk or protection of BC. As research on dietary intake and BC risk are still lacking in South Africa, difficulties arise when the multi-cultural population of South Africa are to be compared with results from other ethnicities/populations to establish prevention diets against BC risk. The investigation of dietary intake in a population-based study may provide new insight in the role of diet in relation to BC risk in a South African context.

**Table 2-8: Food groups and the association with BC risk (unspecified*).**

| Food group | Compared to the CUP report 2017 | Mechanism |
|---|---|---|
| Non-starchy vegetables | No evidence for a significant dose-response relationship with a decreased BC risk. May possibly protect against $ER^-$ BC. | Phytochemicals present in vegetables have been hypothesised to reduce BC risk (especially ER-) (WCRF & AICR, 2017). |
| Carotenoid containing food | Limited, suggestive evidence that consumption of carotenoid containing foods decrease BC risk. | Beta-carotene, alpha-carotene and beta-cryptoxanthin are pro-vitamin A carotenoids and are metabolised to retinol. Retinol may influence nuclear receptor pathways that are involved in cancer growth (WCRF & AICR, 2017). |
| Milk and milk products (Dairy) | Limited, suggestive evidence of a significant decrease in BC risk. | Milk and milk products are a source of calcium which may be associated with protective effects. Rodent models with high calcium diets have shown reduced fat-induced mammary cell proliferation that might reduce carcinogenic effects (WCRF & AICR, 2017). |
| Cereals/ cereal products/ sugar | Limited evidence with no conclusion. | High circulating insulin may influence BC risk either directly, by stimulating insulin receptors in the breast tissue or indirectly by ILGF-1 through mitogenic effects (Romieu *et al.*, 2012). |
| Fruit | Limited evidence with no conclusion for a decreased BC risk. | Fruit is high in fibre that is hypothesised to reduce reabsorption of oestrogens in the gastrointestinal tract (Cohen, 1999). |
| Soya and soya products (Legumes, beans) | Limited evidence with no conclusion for a decreased BC risk. | Possible source of isoflavones (type of phytoestrogen) that may compete against oestrogen for the same binding sites. Thus, lowering oestrogen in the body. Isoflavones are also anti-oxidative and anti-inflammatory (Nagata, 2010). |
| Total dietary fat | Limited evidence with no conclusion. | Fatty acids present in fat may influence carcinogenic processes through mechanisms that changes cell membrane structures and alter metabolic effects (Albuquerque *et al.*, 2014) |
| Red meat | Limited evidence with no conclusion for decreased or increased BC risk. | Protein consumption may increase ILGF-1 that plays a key role in breast tissue development and tumour growth (Farvid *et al*., 2014). Protein foods differ in their nutrient content and may therefore have different BC risk outcomes (Farvid *et al.*, 2014). |
| Processed meat | Limited evidence with no conclusion. | |

*Menopausal status is not considered

$ER^-$ - oestrogen-receptor-negative; BC - breast cancer; insulin-like growth factor-1

## 2.7 **Summary**

Breast cancer is the most common cancer diagnosed in women world-wide and second leading cancer diagnosed in black South African women. In light of the literature presented above, South Africa is faced with worrisome evidence concerning modifiable risk factors for BC. Concerning modifiable risk factors include high obesity rates and low physical activity levels, leading to a possible increased BC risk. Together with these ongoing worrisome evidence, the nutrition transition and influence of urbanization in South Africa continues to impact dietary intake practices. However, high poverty rates seen in South Africa contribute to challenges in consumption of healthy foods recommended by the WCRF as prevention strategy to decrease BC incidence rates. Insufficient attention is drawn to dietary practices and BC risk to establish population based prevention strategies in South Africa. Therefore, investigation of the association between dietary intake and BC risk in black urban women in Soweto might give new insights towards affordable and accessible BC prevention guidelines.

## CHAPTER 3 ARTICLE

# Dietary intake and breast cancer risk in black South African women: The SABC study.

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**KEY WORDS** Dietary intake, black women, breast cancer, South Africa

**Shortened title:** Dietary intake and breast cancer risk


## ABSTRACT

Incidence rates of breast cancer (BC) are increasing in South Africa. The aim of this study was to investigate the association between dietary intake and BC risk in black South African women. The study population included 396 BC cases and 396 population-based controls, matched to the access on age and residence, participating in the South African Breast Cancer (SABC) study. Diet was assessed by using a validated quantified food frequency questionnaire (QFFQ) from which 12 energy adjusted food groups were formed and analysed. Odds ratios were estimated by using conditional logistic regressions, adjusted for confounding factors, comparing highest versus lowest median intakes. Fresh fruit consumption showed a decreased BC risk (OR= 0.3, 95%CI 0.12, 0.80) in premenopausal women whilst red and organ meat consumption showed inverse associations with BC risk (OR=0.6, 95%CI 0.49, 0.94 and OR=0.6, 95%CI 0.47, 0.91). Savoury food consumption (sauces, soup powders and salty snacks) were positively associated with BC risk in postmenopausal women (OR=2.1, 95%CI 1.15, 4.07). Based on these results, it is recommended that black South African women follow a diet with more fruit together with less energy dense, micronutrient poor foods such as savoury foods. More research is necessary to investigate the association between BC risk and red and organ meat consumption.


## Abbreviations

AICR, American Institute for Cancer Research; BC, breast cancer; CUP, Continues Update Project; DEXA, dual energy x-ray absorptiometry; $ER^+$, oestrogen positive; $ER^-$, oestrogen negative; SABC, South African Breast Cancer; PURE, Prospective Urban and Rural Epidemiological; QFFQ, Quantified food frequency questionnaire; SAFBDGs, South African Food Based Dietary Guidelines; WCRF, World Cancer Research Fund; WHO, World Health Organization.

## INTRODUCTION

Breast cancer (BC) is currently the most general cancer diagnosed in women and the second leading cause of cancer mortality globally [1]. Increased incidence rates in low-income and middle-income countries like South Africa are predicted in forthcoming years [2]. Modifiable lifestyle risk factors such as physical activity, body weight and dietary intake are key factors influencing BC risk [3,4].

The extent of dietary factors contributing to BC risk, is not yet fully known. However, the World Health Organization (WHO) previously estimated that 30-50% of all cancer cases could be prevented by avoiding a combination of risk factors including dietary factors [5]. Dietary intake in different population groups across South Africa has extensively been studied by various authors [6, 7, 8, 9, 10, 11]. Hence, valuable insight into South African dietary intake were obtained for health promotion interventions. The link however, between dietary intake and BC risk within black South African black women has not been given sufficient attention. Research investigating this specific association is lacking in South Africa. Therefore, evidence for guidelines towards a population specific diet to prevent BC is absent.

Prevention of BC would be the most cost-effective strategy for decreasing cancer incidence rates in a low- to middle income country like South Africa. Currently, modification towards a healthier diet (nutrient rich and less energy dense foods) is encouraged by the World Cancer Research Fund (WCRF) to promote prevention of various cancers [12]. In line with the WCRF, the South African Food Based Dietary Guidelines (SAFBDGs) also advises South Africans to follow a healthier diet as a strategy to reduce non-communicable diseases like obesity and cancer [13].

Despite the promotion of a less energy dense and more nutrient rich diet, a more Westernised diet is ever-increasingly being followed by black South African women [14]. A Westernised diet is defined by high intakes of energy dense foods such as refined grains, processed meats, added sugar and saturated fatty foods [15] and is frequently associated with a monotonous diet in South Africa. Monotonous diets are often a result of food insecurity and poverty that contributes to increase consumption of low cost, energy dense foods [14]. Increase consumption of energy dense foods might increase risk for obesity. The Continuous Update Project (CUP) report of BC risk and prevention acknowledges that obesity increases BC risk in post-menopausal women [4]. Thus, overconsumption of high energy dense foods and low physical activity levels together with

increasing obesity rates in the black female population of South Africa [14, 15] is worrisome risk factors for BC and raises concerns for health prevention strategies.

The aim of this study was to determine the association between dietary intake and breast cancer risk in a population-based study of black South African women within the SABC case-control study.

## SUBJECTS AND METHODS

### Study population

The SABC study is a matched population-based, case-control study conducted on black South African women from the greater Soweto population in Gauteng, South Africa.

Case participants (n=396), were women over the age of 18, with primary first, invasive, pathologically confirmed BC diagnosed at the Chris Hani Baragwanath Breast Unit in Soweto. Case participants were recruited, prior to any treatment, from December 2014 until June 2017. Control participants (n=396) were healthy, non-blood relatives of case participants matched by age (± 5 years), who lived in the same neighbourhood as the case, with no history of cancer diagnosis. The sample size was sufficient to obtain a power of 90% (type-II error rate $\beta$=10%) for odds ratio $\geq$ 1.3 when type 1 error was set to 5%.

### Dietary assessment

A validated and reproducible culture-specific QFFQ, was used in combination with food portion pictures, household utensils and food models together with the South African Food Composition Tables to determine dietary intake [16, 17, 18,19]. The QFFQ included 145 food items grouped together from the most frequently consumed staple foods to those foods consumed in small amounts. The food portion picture booklet comprised life-size colour photographs of 37 foods in three portion sizes and photographs of utensils to estimate portion sizes [20]. Women were asked about their intake over the past month to estimate their habitual dietary intake. The questionnaire was administered in English by registered dietitians, a trained nutritionist and a registered nurse who received training. Translation services for other languages were also offered by a registered nurse for participants who chose not to complete the QFFQ in English. The frequency included the number of time per day, per week, per month or seldom. The South African Food Composition Tables were used to code and calculate dietary intake from the frequency and portion size reported

on the QFFQ [19]. Household measurements were converted to grams by means of standardised tables [21]. The effects of seasonality were addressed by measuring dietary intakes throughout the year in all seasons.

**Non-dietary assessments**

Face-to-face interviews were conducted by trained fieldworkers and investigators. Self-reported demographics and socio-economic indicators such as level of education and income/month were obtained. Detailed information was collected regarding ethnicity, history of health, family history of BC, reproductive risk factors (age at menarche and at menopause for postmenopausal women only, age/year at each full term pregnancy, and its outcome, breast feeding history for each live birth, use of oral contraceptives and hormone replacement therapy, family history of cancer, breast health (previous breast lumps by breast laterality, breast pains), smoking habits and physical activity (household and recreational). Anthropometric measurements (weight, height, sitting height and waist circumference) were collected using standardized procedures accredited by Lohman's laws [22]. BMI was calculated using measured height and weight ($kg/m^2$). Waist circumference were adjusted for as a possible confounding factor as it is a better indication of body fat distribution/obesity than BMI. Questionnaires used to obtain above mentioned information was validated and proven to be reproducible in studies conducted in South Africa [23, 24].

**Ethical approval**

Ethical approval for the SABC study was granted by the International Agency for Research on Cancer (IARC) and by the University of the Witwatersrand Committee for Research on Human Subjects (Ethical no: M140980). Permission to conduct research at Chris Hani Baragwanath Academic Hospital was obtained from the Gauteng Province Medical Advisory Committee.

This single dietary study obtained ethical approval from the Human Research and Ethics Committee of the North-West University (NWU-00118-17-S1). Ethical approval was also granted for the use of the validated PURE (Prospective Urban and Rural Epidemiological) Quantified Food Frequency Questionnaire. All subjects gave written informed consent prior participation.

**Statistical analysis**

A total of 792 black female participants (396 cases and 396 controls) could be matched from the original 874 enrolled participants (415 cases and 459 controls). Unmatched case and control

participants were due to missing dietary data, incorrect data captured, unmatched geographical areas and withdrawal of participants. Baseline characteristics were described for BC cases and healthy controls. Normally distributed variables were presented as mean (SD) whilst variables with a skew distribution were presented as median, upper and lower quartiles. Categorical variables were presented as frequencies and percentages. Mean differences of normally distributed data between cases and controls were estimated using student's t test for independent samples, while skewed variables were tested by the Mann-Whitney U test. Categorical variables were compared using the Pearson's chi-square test. P-level for significance were $\leq 0.05$.

Energy-adjusted intake was used for analyses due to individuals whom generally alter their intake of nutrients and foods primarily by changing the composition of their diets, rather than the total amount consumed [25].

Dietary intake obtained from the QFFQs was divided into 12 food groups: cooked porridge (maize meal, oats, maltabella), starchy grains (breakfast cereals, pasta, bread, rice, cake flour, starchy vegetables), non-starchy vegetables (all other vegetables), fresh fruit, legumes (soy and beans), nuts and seeds, milk and milk products, animal protein (meat and meat products), fats and oils (mono-unsaturated, poly-unsaturated fat and saturated fats), added sugar (sweets, sugary drinks, jam and pudding), savoury snacks (sauces, potato crisps, spices, soup powders) and alcohol. Milk and milk products were separated from the animal protein food group as it contains some nutrients that meat and meat products does not contain such as added sugar in yoghurt, calcium. Animal protein were analysed separately from its original compilation to estimate the association with BC risk and different animal proteins (meat and meat products). The following sub groups were created from the animal protein (excluding milk and milk products) food group: red meat (mutton, beef and stews), organ meat (liver, kidneys, offal and curried offal from all animals), eggs (chicken eggs, fried, scrambled and poached), processed meat (ham, sausages and polony) and fish (hake, fish fingers and canned pilchards). Red meat is usually classified as mutton, beef, lamb, goat and pork including offal/organ meat thereof. Due to the differences in energy and nutrients, organ meat was separated from red meat in this sample. Missing information regarding food intakes (not captured) was imputed using the Expectation Maximization algorithm before performing analysis [26]. A generalised linear model was used to estimate differences of least square means, measured in kilojoules (kJ) of individual food groups (continuous variable) between cases and controls. The effect of potential confounders was tested by including additional variables into the generalised linear and conditional logistic regression models. The following confounders were examined:

ethnicity (Zulu/Pedi/Swazi, Xhosa, Sotho, Tshwane, Venda, Tsonga and Ndebele), individual income (R1-R3000, R3001-R6000 and R6001+), level of education (none/primary school, high school and college/post graduate/diploma), smoking (smokers and non-smokers), waist circumference (continuous data), habitual physical activity/day (active and less active), age at menarche (<15 years of age vs >15 years of age, ) full term pregnancy (yes/no), age at first pregnancy (<24 years of age vs >24years of age), age of menopause (<48 years of age vs >48 years of age), parity (≤3 children vs >3 children), ever breastfeeding (yes/no), use of exogenous hormones (hormonal birth control to avoid pregnancy (oral contraceptives and injections), or hormone replacement therapy), family history of BC (yes/no). Only menopausal status, ethnicity, waist circumference, physical activity, level of education, income/month, use of birth control, ever breast feeding, age at menarche, age of menopause onset, family history of breast cancer influenced crude analysis by more than 10%. All remaining food groups not used as the independent variable were adjusted for confounding effects since food groups are not eaten in isolation.

Conditional logistic regression was applied to estimate ORs and 95% confidence intervals (CIs) to measure the risk of BC in relation to highest vs lowest energy (kJ) intake (determined by median intake) of food groups. Adjustments for possible confounding factors were made in a sequential model. Unadjusted estimates between matched case and control participants were reported in model A whilst model B adjusted for the same confounding factors used in the generalised linear model. Analysis were also stratified according to menopausal status, oestrogen positive ($ER^+$) and oestrogen negative ($ER^-$) tumour types.

**Results**

The distribution of selected characteristics amongst cases and controls are reported in **Table 1**. As expected from the matched design, age was similar amongst cases and controls (54.68 ± 12.94 year, 54.70 ± 12.90 year) and ranged from 26 to 88 years. Weight and BMI had a similar distribution between case and control participants.

More than 80% of the study sample, cases (80.0%) and controls (82.3%), were either overweight or obese. High total energy intake/day were reported in both cases and controls, with a median of ($25^{th}$, $75^{th}$ percentile) 8 990 kJ (7 184 kJ, 10 284 kJ) in controls and 9 142 kJ (6 812 kJ, 9 759 kJ) in cases. In addition, low physical activity levels with little variation were noted. Neither cases nor controls' total weekly physical activity levels adhered to the recommended 600 METs/week [(4)].

**Table 1**
Distribution of baseline characteristics between controls and cases.

| Characteristics | Controls (n= 396) | Cases (n=396) | P |
|---|---|---|---|
| Age (years) | 54.6 (12.9) | 54.7 (12.9) | 0.9831 |
| Weight (kg) | 78.9 (17.7) | 77.5 (17.6) | 0.2660 |
| Height (cm) | 157.9 (6.3) | 157.5 (6.4) | 0.3427 |
| BMI (kg/m2) | 31.8 (6.9) | 31.4 (7.0) | 0.3090 |
| Underweight (n/%) | 5 (1.3) | 11 (2.8) | |
| Healthy BMI (n/%) | 63 (15.9) | 71 (17.9) | |
| Overweight BMI (n/%) | 93 (23.5) | 87 (22.0) | |
| Obese BMI (n/%) | 235 (59.3) | 227 (57.3) | |
| WC (cm) | 95.8 (13.7) | 93.3 (13.8) | 0.0113* |
| **Dietary intake (QFFQ)** | | | |
| TE (kJ/day) | 8990 (7184, 10284) | 9146 (6812, 9759) | 0.2631 |
| Protein (g/day) | 63.5 (49.2, 93.1) | 63.8 (47.4, 82.7) | 0.0831 |
| % of TE | 12.0 | 11.8 | |
| Animal protein (g/day) | 34.1 (22.9, 48.7) | 31.0 (20.6, 45.1) | 0.0057* |
| Plant Protein (g/day) | 29.5 (22.5, 40.2) | 29.6 (22.6, 39.7) | 0.9242 |
| Fat (g/day) | 64.4 (47.2, 95.7) | 64.8 (42.4, 91,9) | 0.1373 |
| % of TE | 27.2 | 26.9 | |
| Saturated fat (g/day) | 19.1 (12.6, 27.8) | 17.9 (11.4, 26.1) | 0.0499 |
| MUFA (g/day) | 20.6 (14.3, 31.7) | 20.5 (12.3, 28.3) | 0.0479* |
| PUFA (g/day) | 17.5 (11.70, 26.73) | 17.2 (11.1, 25.4) | 0.3934 |
| CHO (g/day) | 338.7 (147.3) | 330.8 (143.5) | 0.4412 |
| % of TE | 64.0 | 61.4 | |
| Added Sugar (g/day) | 67.9 (39.9, 109.7) | 65.3 (38.4, 105.5) | 0.3400 |
| % of TE | **12.0** | **12.1** | |
| Energy from alcohol (kJ/day) | 312 (288, 2204) | 79 (29, 1954) | 0.2007 |
| % alcohol contribution to TE | **3.4** | **0.8** | |
| PA (METs/week) | 110.2 (81.6, 149.7) | 114.0 (82.8, 163.1) | 0.1418 |
| **Ethnicity** | | | |
| Zulu and Pedi (n/%) | 26 (6.5) | 25 (6.4) | |
| Xhosa (n/%) | 22 (5.5) | 22 (5.6) | |
| Sotho (n/%) | 108 (27.4) | 144 (36.4) | |
| Tswana (n/%) | 19 (4.8) | 19 (4.8) | |
| Venda (n/%) | 40 (10.1) | 56 (14.1) | |
| Tsonga (n/%) | 65 (16.4) | 35 (8.8) | |
| Ndebele (n/%) | 116 (29.3) | 95 (23.9) | 0.004* |
| Smoking (n/%) | 44 (11.1) | 35 (8.8) | 0.286 |
| **Level of education** | | | |
| None/primary (n/%) | 71 (18.0) | 97 (24.5) | |
| High School (n/%) | 279 (70.5 | 257 (64.9) | |
| College/University/postgraduate (n/%) | 46 (11.6) | 42 (10.6) | 0.078* |

| Characteristics | Controls (n= 396) | Cases (n=396) | P** |
|---|---|---|---|
| **Individual income/month** | | | |
| R1-R3000 (n/%) | 335 (84.6) | 344 (86.9) | |
| R3001 - R6000$^{+}$ (n/%) | 61 (8.5) | 52 (8.6) | 0.364 |
| **Ever pregnant (n/%)** | 382 (96.5) | 377 (95.2) | 0.374 |
| **Number of children (children)** | 3 (2, 4) | 3 (2, 4) | 0.3739 |
| **Age at first pregnancy n/N (%)** | 24.5/32 (19.5, 26) | 23.5/26 (19, 28) | 0.567 |
| Full term pregnancy in parous women (n/%) | 382 (100) | 377 (100) | 0.3739 |
| **Ever breast fed n/N (%)** | 349/382 (91.3) | 339/377 (89.9) | 0.293 |
| Duration of breast feeding (1) (months) | 32 (12, 60) | 30 (8, 58) | 0.1868 |
| **Use of birth control (contraceptives)** | 215 (54,3) | 229 (57.8) | 0.355 |
| **Stage at BC diagnoses** | | | |
| I (n/%) | | 24 (6.5) | |
| II (n/%) | | 175 (44.8) | |
| III (n/%) | | 161 (40.8) | |
| IV (n/%) | | 31 (7.9) | |
| **BC Subtype** | | | |
| ER$^{+}$ (n/%) | | 312 (78.8) | |
| PR$^{+}$ (n/%) | | 281 (70.1) | |
| HER2 (n/%) | | 114 (28.8) | |
| **Receptor status** | | | |
| HER2 Enriched (n/%) | | 21 (5.3) | |
| Luminal A (n/%) | | 40 (10.1) | |
| Luminal B (n/%) | | 269 (67.9) | |
| TNBC (n/%) | | 66 (16.7) | |
| **Menopause status** | | | |
| Premenopausal (n/%) | 137 (34.6) | 140 (35.4) | |
| Postmenopausal (n/%) | 259 (65.4) | 256 (64.6) | 0.584 |
| Age at menopause (2) (years) | 48 (44, 50) | 47 (42, 50) | 0.7899 |
| **Family history of BC** (n/%) | 17 (4.3) | 25 (6.3) | 0.2046 |
| **Age at menarche** | 15 (13, 16) | 15 (13, 16) | 0.2485 |
| ≤15 years (n/%) | 182 (45.9) | 169 (42.6) | |
| >15 years (n/%) | 214 (54.1) | 227 (51.4) | 0.9407 |
| **Use of HRT (3)** | 2/259 (0.7) | 2/256 (0.7) | 0.134 |

WC, waist circumference: TE, total energy: MUFA, monounsaturated fatty acids: PUFA, poly-unsaturated fatty acids: CHO, Carbohydrates: PA, physical activity: BC, breast cancer: ER$^{+}$, oestrogen receptor positive: PR$^{+}$ progesterone receptor positive: HER2, Human-Epidermal Growth Factor-2; TNBC, Triple negative breast cancer; HRT: hormone replacement therapy.

Continues data are reported as mean (SD) if normally distributed and median (25th percentile, 75th percentile, categorical values are reported as n (%).

*Significant difference between case and control participants.

**Student t-test for independent variables, Mann-Whitney U test for skewed data and Pearson's chi$^2$ test for categorical variables. A P level of 0.05 were considered significant.

(1) In breast feeding women only
(2) Among postmenopausal women only
(3) In postmenopausal women only

In case participants, oestrogen receptor positive ($ER^+$) tumour type together with receptor type Luminal B were most prominent. Triple negative breast cancer (TNBC), the most aggressive BC tumour type, accounted for 16.7% of case participants.

Compared to controls, cases had a significant smaller waist circumference and lower animal protein-, saturated fat- and mono-unsaturated fat intake. Comparison between cases and controls differed significantly in ethnicity. Zulu, Pedi, Xhosa and Tswana speaking participants were evenly distributed amongst cases and controls. More Sotho and Venda speaking participants were noted in the case group whilst more Ndebele and Tsonga speaking participants were noted in the control group. No significant differences in the distribution of other macronutrients, level of education, individual income, menopausal status and smoking between cases and controls were observed.

Differences in mean energy (kJ) per day intake (adjusted for confounders mentioned above) between cases and controls in food groups are reported in **Table 2**. Significant differences between cases and controls were observed in all food groups except cooked porridge. The control group reported higher energy intakes from all food groups except cooked porridge.

**Table 2**
Adjusted mean* energy intake (kJ) from food groups in both controls (n=396) and cases (n=396)

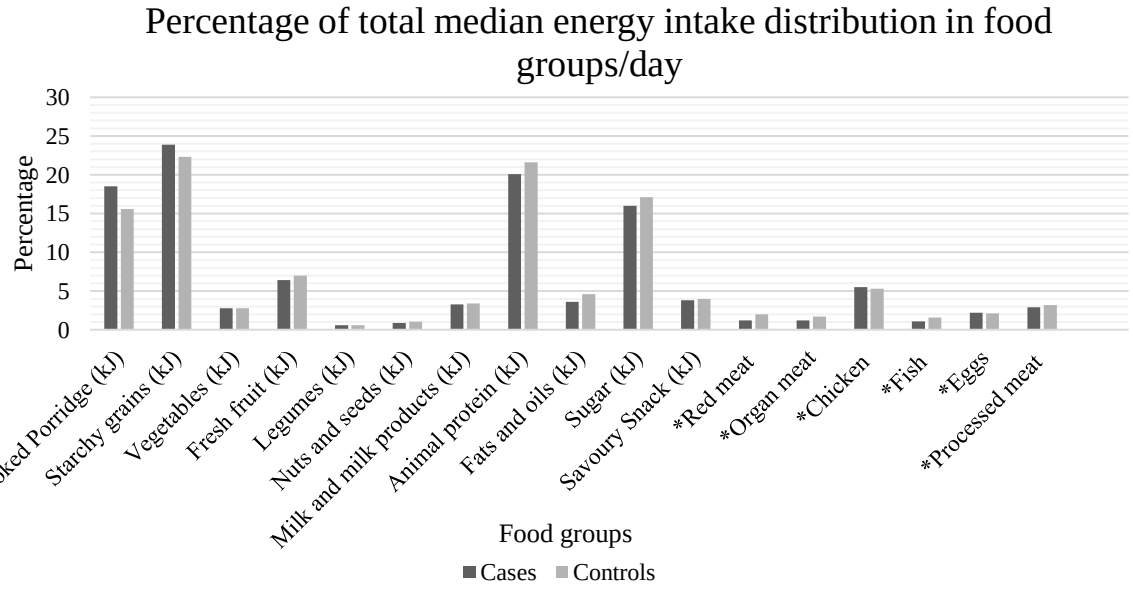
| | †Controls | Cases | |
|---|---|---|---|
| | **Mean (SE) (kJ)** | **Mean (SE) (kJ)** | **P for difference** ** |
| Cooked Porridge | 1842 (90.9) | 1825 (90.8) | 0.774 |
| Starchy grains | 3155 (162.4) | 2494 (162.4) | <0.001 |
| Vegetables | 667 (54.5) | 517 (54.7) | 0.013 |
| Fresh fruit | 949 61.5) | 737 (61.7) | 0.002 |
| Legumes | 215 (21.6) | 148 (21.6) | 0.003 |
| Nuts and seeds | 889 (101.1) | 620 (101.1) | 0.01 |
| Milk and milk products | 573 (40.9) | 378 (40.9) | <0.001 |
| Animal protein | 4551 (328.7) | 3209 (328.7) | <0.001 |
| Fats and oils | 1737 (164.1) | 1152 (164.3) | 0.001 |
| Sugar | 3009 (214.6) | 2195 (215.1) | <0.001 |
| Savoury Snack | 2064 (203.0) | 1336 (203.4) | 0.001 |

*Adjusted for menopausal status, ethnicity, waist circumference, physical activity, level of education, income/month, use of birth control (hormonal/oral contraceptives), ethnicity, ever breast feeding, age at menarche, age of menopause onset, family history of breast cancer. P value of what for significance were ≤ 0.05.
**Least square means based on total sum of squares for each food group and standard errors
†Comparison group
SE, standard error.

For the purpose of this study and using the SAFBDGs, vegetables, milk and milk products, legumes, fresh fruit, nuts and seeds were classified as more nutrient rich food groups, whilst

starchy grains, savoury foods, animal protein (high fat content), cooked porridge and sugar were considered to be more energy dense, nutrient poor food groups. **Supplementary Figure 1** presents the percentage distribution of median energy intake/day of food groups in case and control participants. Food groups that is likely to be more energy dense contributed to more than 75% of the total energy intake in both case and control participants. Less energy dense food groups accounted for 18.4% of total energy intake in controls and 14% in cases. Furthermore, high consumption of foods in the sugar (sugary drinks, added sugar products), animal protein (meat and meat products), starchy grains (refined and processed products) and cooked porridge food groups were noted. Low consumption of more traditional foods such as vegetables, sorghum, whole wheats and legumes were seen. Therefore, dietary intake in this study, was more in line with a Westernised diet as Westernised diets are known to be high in refined grains, meat and meat products and added sugar [(14).]

A total of 196/792 participants consumed alcohol in this sample whilst non-consumers accounted for 80.8% in case- and 69.7% in control participants and was therefore excluded as a food group in the analysis. The animal protein food group consisted out of red meat, organ and offal meat, fish, chicken, eggs and processed meat. The savoury snacks food group consisted out of soup powders, spices, potato crisps, sauces and salt biscuits.




**Supplementary Figure 1.** Percentage of total median energy intake distribution in food groups. *Animal food group compilation.

The association between dietary intake and breast cancer risk is reported in **Table 3**. After adjusting for confounding factors, inverse associations with BC risk were noted with fresh fruit consumption overall, and especially in premenopausal women (OR= 0.6, 95%CI 0.43, 0.94 and OR=0.3, 95%CI 0.21, 0.80, respectively). Inverse associations with BC risk were also found in the animal protein food group in overall, and especially in postmenopausal women (OR= 0.6, 95%CI 0.40, 0.96 and OR=0.5, 95%CI 0.28, 0.99, respectively) after adjusting for confounding factors.

Additional analyses within the animal protein food group (meat and meat products) indicated that the sub group "organ meat" showed a significant inverse association with BC risk in fully adjusted model (OR=0.6, 95%CI 0.49 0.93). "Red meat" showed a significant inverse association with BC risk in in all women (OR=0.6, 95%CI 0.49, 0.94) and especially in postmenopausal women (OR=0.5 95%CI 0.32, 0.88). Other subgroups in the animal food group (processed meat, fish, chicken and eggs) did not show any significant associations with BC risk.

After adjustment for confounders, savoury snack consumption showed a significant increased BC risk (OR=1.9, 95%CI 1.12, 2.43), especially in postmenopausal women (OR=2.1, 95%CI 1.15, 4.07).

Additionally, when exploring the association between BC risk and cancer subtypes, $ER^-$ tumour showed an inverse association with animal protein consumption (OR= 0.6, 95%CI 0.35, 0.98) whilst $ER^+$ stratification showed an inverse association with BC risk and nuts and seeds consumption (OR=0.2, 95%CI 0.58, 0.86).

**Table 3**

Association between food groups and breast cancer risk in cases and controls for daily median energy intake (highest vs lowest intake)

(Odds ratio and 95% confidence intervals)

| | **Model A (n=792)** | | **Model B (n=792)** | | ***ER$^+$ (n=312)** | | ***ER$^-$ (n=84)** | | **†Premenopausal (n=276)** | | **†Postmenopausal (n=516)** | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Food groups** | **OR (95% CI)** | **P** | **OR (95% CI)** | **P** | **OR (95% CI)** | **P** | **OR (95% CI)** | **P** | **OR (95% CI)** | **P** | **OR (95% CI)** | **P** |
| Cooked porridge (1518kJ) | 1.0(0.76, 1.40) | 0.859 | 0.9(0.73, 1.46) | 0.939 | 2.2(0.72, 6.92) | 0.173 | 0.9(0.62, 1.44) | 0.750 | 0.6(0.31, 1.34) | 0.183 | 1.2(0.82, 1.91) | 0.328 |
| Starchy grains (2655kJ) | 1.3(0.88, 1.97) | 0.058 | 1.3(0.86, 2.08) | 0.222 | 0.6(0.13, 2.71) | 0.521 | 1.5(0.84, 2.45) | 0.153 | 0.8(0.33, 2.07) | 0.604 | 1.5(0.82, 2.84) | 0.154 |
| Vegetables (275kJ) | 0.8(0.60, 1.29) | 0.047 | 0.9(0.64, 1.47) | 0.644 | 2.2(0.66, 8.64) | 0.265 | 0.8(0.53, 1.42) | 0.511 | 0.4(0.16, 1.28) | 0.090 | 1.2(0.76, 2.05) | 0.468 |
| Fresh fruit (673kJ) | 0.6(0.45, 0.94) | 0.004 | **0.6(0.43, 0.94)** | **0.022** | 0.8(0.13, 4.54) | 0.812 | 0.7(0.41, 1.12) | 0.108 | **0.3(0.12, 0.80)** | **0.026** | 0.7(0.44, 1.23) | 0.164 |
| Legumes (56kJ) | 0.9(0.73, 1.34) | 0.501 | 1.0(0.78, 1.47) | 0.872 | 0.5(0.14, 2.05) | 0.326 | 1.1(0.74, 1.76) | 0.488 | 1.9(0.93, 4.22) | 0.083 | 0.8(0.57, 1.35) | 0.344 |
| Nuts and seeds (104kJ) | 1.0(0.74, 1.37) | 0.355 | 1.1(0.85, 1.52) | 0.609 | **0.2(0.58, 0.86)** | **0.029** | 1.3(0.94, 1.82) | 0.249 | 1.1(0.52, 2.31) | 0.735 | 1.3(0.84, 2.04) | 0.323 |
| Milk and milk products (327kJ) | 0.7(0.55 ,1.03) | 0.937 | 0.8(0.61, 1.18) | 0.195 | 0.9(0.23, 3.82) | 0.951 | 0.8(0.51, 1.13) | 0.152 | 0.7(0.35, 1.66) | 0.449 | 0.8(0.53, 1.22) | 0.224 |
| Animal protein (1728kJ) | 0.6 (0.41, 0.95) | <0.001 | **0.6(0.40, 0.96)** | **0.040** | 1.0(0.95, 1.01) | 0.475 | **0.6(0.35, 0.98)** | **0.045** | 0.6(0.37, 1.68) | 0.351 | **0.4(0.28, 0.99)** | **0.029** |
| Fats and oils (453 kJ) | 0.7 (0.52, 1.02) | 0.004 | 0.7(0.52, 1.02) | 0.068 | 0.3(0.11, 1.14) | 0.068 | 0.8(0.54, 1.33) | 0.385 | 0.5(0.28, 1.19) | 0.089 | 0.8(0.53, 1.44) | 0.470 |
| Sugar (1668kJ) | 0.8 (0.57, 1.20) | <0.001 | 0.9(0.62, 1.48) | 0.667 | 1.3(0.34, 4.92) | 0.731 | 0.8(0.52, 1.37) | 0.460 | 1.9(0.86, 4.25) | 0.135 | 0.7(0.42, 1.37) | 0.299 |
| Savoury snack (388kJ) | 1.5 (1.02, 2.30) | 0.292 | **1.9(1.12, 2.43)** | **0.027** | 3.4(0.52, 24.32) | 0.216 | 1.5(0.91, 2.52) | 0.098 | 1.5(0.64, 4.22) | 0.389 | **2.1(1.15, 4.07)** | **0.017** |
| **‡Animal protein** | **OR (95% CI)** | **P** | **OR (95% CI)** | **P** | **OR (95% CI)** | **P** | **OR (95% CI)** | **P** | **OR (95% CI)** | **P** | **OR (95% CI)** | **P** |
| Red meat (190kJ) | 0.6(0.43, 0.78) | <0.001 | **0.6(0.49, 0.94)** | **0.029** | 2.0(0.51, 8.52) | 0.342 | **0.6(0.38, 0.86)** | **0.009** | 1.4(0.66, 3.35) | 0.384 | **0.5(0.32, 0.88)** | **0.018** |
| Organ meat (135 kJ) | 0.7(0.50, 0.88) | 0.005 | **0.6(0.47, 0.91)** | **0.022** | 1.8(0.43, 7.82) | 0.411 | **0.6(0.42, 0.91)** | **0.014** | 0.6(0.33, 1.21) | 0.144 | 0.8(0.56, 1.28) | 0.284 |
| Processed meat (316kJ) | 0.7 (0.52,0.94) | 0.012 | 0.9(0.61, 1.35) | 0.557 | 0.9(0.19, 4.10) | 0.885 | 0.9(0.57, 1.42) | 0.685 | 0.3(0.21, 1.02) | 0.071 | 1.1(0.68, 1.96) | 0.750 |
| Fish (154kJ) | 1.1 (0.94,1.00) | 0.280 | 0.7(0.56, 1.17) | 0.130 | 0.5(0.10, 2.41) | 0.388 | 0.7(0.44, 1.14) | 0.162 | 1.0(0.96, 1.17) | 0.934 | 0.7(0.45, 1.14) | 0.121 |
| Chicken (526kJ) | 0.6 (0.56,0.97) | 0.009 | 0.8(0.54, 1.25) | 0.281 | 0.5(0.08, 3.16) | 0.474 | 0.6(0.40, 1.05 | 0.080 | 0.4(0.29, 1.15) | 0.075 | 0.8(0.46, 1.47) | 0.374 |
| Eggs (208kJ) | 0.9 (0.92,1.04) | 0.093 | 1.0(0.95, 1.09) | 0.187 | 0.9(0.96, 1.02) | 0.434 | 0.8(0.53, 1.32) | 0.410 | 0.9(0.86, 1.27) | 0.637 | 1.0(0.91, 1.02) | 0.418 |

ER$^+$, oestrogen receptor positive: ER$^-$, oestrogen receptor negative

*Stratified by ER tumour type

†Stratified by menopausal status

‡Break down of original animal protein compilation.

Model A: Crude output

Model B: adjusted for menopausal status, ethnicity, waist circumference, physical activity, level of education, income/month, use of birth control (hormonal/oral contraceptives), ethnicity, ever breast feeding, age at menarche, age of menopause onset, family history of breast cancer

## Discussion

This study aimed to investigate the association between dietary intake and BC risk in black South African women. We found an inverse association with BC risk and consumption of fresh fruit in premenopausal women whilst subgroups of animal protein (red and organ meat) also showed inverse associations with BC risk. Savoury food consumption showed an increased BC risk in postmenopausal women. In addition, 4 out of 5 participants were either overweight or obese in both case and control participants.

Little attention is drawn to savoury foods in relation to BC risk possibly because savoury foods are more often associated with increased risk of gastric cancer [27]. A case control and cohort studies from various populations found no association with added salt or spices and BC risk [28, 29]. However, results from this study showed a strong increased BC risk with high savoury food consumption in Model B and in postmenopausal women. A possible reason for this positive association with BC risk might be due to a combination of the high salt content, processed preparation methods of soup powders, sauces and potato crisps, lack of anti-oxidants and phytochemicals (previously proven to reduce BC risk [4,30]) and high total energy content in this food group.

Unexpectedly, the results of our study showed the sub groups of animal protein, red meat and organ meat to be inversely associated with BC risk. The CUP report on BC states that there is limited evidence with no conclusions regarding an increased or decreased BC risk and consumption of animal protein [4]. Following on our findings, further analysis indicated that subgroups of animal protein, "red and organ meat", showed inverse associations with $ER^-$ tumour subtype. When results were stratified by menopausal status, only "red meat" showed an inverse association with BC risk in postmenopausal women.

Evidence investigating the association of BC risk with red meat and organ meat (as food groups) are lacking as consumption of organ meat in other countries may not be as much as in South Africa [31]. In South Africa red meat intake entails consumption of mostly organ and offal meat, as mutton, lamb and beef are mostly unaffordable for a large proportion of the South African population [32]. This was clearly observed in the information/data collected from the QFFQs.

Organ meat is less energy dense and a more nutrient rich protein (compared to red meat) and may contribute to explaining this inverse association with BC risk in black South African women [19].

Red meat however, is higher in energy due to a higher fat content and may increase the risk for obesity if over consumed. This is alarming since obesity is a known BC risk factor in postmenopausal women [4]. Furthermore, consumption of high amounts of red meat (120g per day) has previously been linked to an increased risk for other cancers (colorectal, lung and prostate) in various populations [33]. Hence, the WCRF and American Institute for Cancer Research (AICR) recommends limitation of red meat consumption (<500g cooked weight per week) as part of a cancer prevention diet [12]. Epidemiologic evidence for an increased BC risk with red meat consumption remain inconclusive, but is suggestive of an increased BC risk [33 34, 35].

Inverse associations with BC risk in this sample of both red and organ meat requires further investigation as no other case-control study has found an inverse association with BC risk. Given the case-control study design of this study, reverse causality is not likely to occur. However, we know that this population had low consumption of red and organ meat (total animal protein intake in cases accounted for <31g per day and <2% of total energy intake) and may contribute to the observed inverse association with BC risk. This in turn can be attributed to dietary recall bias and high rates (49%) of late stage BC diagnosis. In late stages of cancer, altered meat consumption (decreasing meat consumption) may occur due to taste alterations of progressive cancer symptoms [36]. The interpretation of the results presented above are further complicated by the coding methods currently used in South Africa. These will be discussed further more in the limitation section.

Less energy dense, nutrient rich foods such as fruits and vegetables are often associated with a decreased BC risk and is recommended by the WCRF and South African FBDGs for prevention of non-communicable diseases [12, 37]. These foods are lower in energy and rich in nutrients which contributes to maintaining a healthy body weight. Antioxidants and phytochemicals present in these less energy dense foods (fruit and vegetables) have also shown to reduce BC risk [30]. The CUP report states that there is currently limited evidence of a significant decrease BC risk associated with non-starchy vegetables and other less energy dense food groups [4]. In this sample, a significant protective association for decreased BC risk was found with a higher fruit consumption (673 kJ/ more than 1 ½ fruit servings/day) in $ER^-$ and premenopausal women. No significant associations were found for other less energy dense food groups such as vegetables. However, the portion sizes of vegetables eaten are usually very small. In this sample, vegetables accounted for 3% of the total energy intake in both case and control participants and may be an indication that the recommendation of the SAFBDG of 400g of fruit and vegetables/day was not met [13].

It is therefore important to investigate dietary intake in this sample as a whole. Energy dense foods from 4 food groups (cooked porridge, starchy grains, sugar and animal protein) accounted for more than 75% of the total energy intake whilst less energy dense food groups represented less than 18.5% in case and control participants. Dietary intake from this study are therefore in line with previous research on dietary intake in the black female population of South Africa where a monotonous diet (high in sugar, refined starches and fat from animal protein) associated with a Westernised diet were noted [12,13,14,15]. More energy dense staple foods such as maize meal and bread are fortified with micro-nutrients (Vitamin A, thiamine, riboflavin, niacin, pyridoxine, folic acid, iron and zinc) in South Africa. However, it is not known whether fortified food improve nutritional status of black South African women [38]. Thus, high consumption of mostly energy dense foods (generally also nutrient poor foods) in this sample is bothersome for a diet consisting mainly out of energy dense and nutrient poor foods, is not nutritionally adequate for optimal health [37] and prevention of BC.

Not all energy dense foods are unhealthy, but overconsumption of more energy dense foods may lead to a higher total energy intake/day, increasing the risk for obesity that is a known BC risk factor in postmenopausal women. Worrisome overweight and obesity rates mentioned above, together with high total energy intake per day and low physical activity, were noted in this study. Attention is thus also drawn to obesity as a possible risk factor that may contribute to increased BC risk in postmenopausal black South African women.

Moreover, it is acknowledged that healthier, less energy dense foods in South Africa are costlier than unhealthier more energy dense foods (mostly refined grains) such as cooked porridge, starchy grains, sugar, processed meat and fats [32, 38]. Previous studies conducted in rural areas in South Africa stated that dietary intake was directly linked to income in a social-economic restricted environment [32]. A low-income distribution was noted in this study where 85.8% of the sample earned less than R3001.00/month. Poverty may therefore contribute to lower intake of healthier less energy dense and nutrient rich foods that may protect against BC.

Control participants had a higher total energy consumption in almost all food groups and in total energy intake compared to case participants. Since control participants had a higher BMI and waist circumference these results were expected. Lower energy intakes seen in case participants may be due to BC diagnoses in late stages (stage III/IV) and altered dietary intake in case participants. During late stage BC (stage III/IV), patients often presents with decreased appetite and altered

taste acuity (dysgeusia, hypogeusia, ageusia) that can occur without any cancer treatment [36]. Additionally, the case-control study design may also influence these results.

Limitations

The sample size of this study was small, however data regarding diet and BC risk are lacking in South Africa. Therefore, results of this study is indicative of much needed data on dietary intake and BC risk in black South African women. The QFFQ was developed for a Tswana speaking population while this study population spoke several different languages (Venda, Xhosa, Sotho, Tswana). The coding method of single foods used in this study, using the South African food composition tables may have contributed to inaccurate grouping of foods within food groups. Some meals (stews), consisting out of two food groups (animal protein and starchy grains), were coded as a single food when in fact it could have been two separate single foods divided in different food groups. Underreporting and over reporting of certain foods may also be a limitation since dietary data are just an estimation of dietary intake and relies on the subject's memory. This study did not collect data on some risk factors associated with BC risk such as genetic mutations and time period form participants stopped breast feeding and BC diagnoses.

Strengths

This study had a population based and matched case-control study design which improved statistical precision. This study provided much needed evidence for an African population group in relation with BC risk since data on this topic are lacking. All questionnaires used to collect data was proven to be validated and data used in the analysis were highly standardized to improve precision and reduce statistical errors. All case participants were recruited prior to any BC treatment.

In conclusion, consumption of fresh fruit, red and organ meat showed an inverse association with BC risk whilst savoury food consumption showed an increased BC risk. However, no other studies have found an inverse association with BC risk and red or organ meat consumption. Therefore, further research is necessary to investigate the association with BC risk and red and organ meat. Moreover, dietary intake in this sample were in line with a Westernised diet whilst alarming overweight and obesity rates together with low physical activity levels were noted in this sample. A diet with foods lower in energy and higher in nutrients such as fresh fruit in combination with a decrease consumption of energy dense foods like savoury foods are advised as a possible

preventative diet for BC and strategy to reduce bothersome obesity rates in black South African women. However, poverty influences food choices and health interventions in South Africa should strive to implement affordable and accessible methods in line with these recommendations.

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Authorship

The authors' responsibilities were as follow-IJ: Performed statistical analysis and wrote the first draft of this manuscript; CTK: Revised the first draft, responsible for dietary intake and head of dietary intake components of study (Supervisor of single study); CR: Revised statistical analysis, gave scientific input (Co-supervisor of single study); HHV: was responsible for dietary data collection and coding QFFQ's, gave scientific input; TVZ: Gave scientific input (Assistant supervisor of single study); SR: Oversaw SABC study project, gave scientific input; HC: South African principle investigator of SABC study, co-responsible for diagnosing and recruiting subjects; RL: responsible for dietary intake analysis, gave scientific input; MJ; South African coordinator of the SABC study; SAN: Director of Wits Developmental pathways to Health Research unit; IR: Head principal investigator, gave scientific input.

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# CHAPTER 4 GENERAL DISCUSSION, CONCLUSION AND RECOMMENDATIONS

## 4.1 Introduction

The purpose of the final chapter is to provide a summary of the main findings of this research project as well as conclusions and recommendations for further research. The aim and objectives are listed below to provide a reference as to what was addressed in this mini-dissertation.

### 4.1.1 Research aim

This mini-dissertation investigated the possible associations between dietary intake and the risk of developing BC in the South African Breast Cancer study (SABC) (black women from the greater Soweto population).

### 4.1.2 Research objectives

I. To determine dietary intake through administrating a QFFQ.
II. To determine the difference in dietary intake between BC cases and controls with the use of a generalized linear regression model.
III. To determine the association between dietary intake and risk of BC.

## 4.2 Main findings

### 4.2.1 Determining dietary intake through administrating a QFFQ

A monotonous diet was noted in this sample as consumption of foods high in various nutrients such as vegetables, legumes, milk or milk products and nuts or seeds were low. Food groups such as such as sugar, cooked porridge (maize meal), starchy grains (rice, samp, pasta and bread) and animal protein (mostly high in fat or processed meat) accounted for 75% of total energy consumed. These foods mentioned above are often more energy dense and mostly nutrient poor.

In line with the above, dietary intake in this sample were similar to previous research conducted on South African populations that reported on a more Westernised diet being followed (MacIntyre *et al.*, 2002; Vorster *et al.*, 2005; Vorster *et al.*, 2011; Vorster *et al.*, 2014). This is worrisome since Westernised diets were previously associated with a higher BC risk (Castelló *et al.*, 2017).

Furthermore, Westernised diets are also associated with high obesity rates due to higher intakes of energy dense and mostly also nutrient poor foods (Castelló *et al.*, 2017).

Eighty percent of this sample were either overweight or obese in both case and control participants whilst the majority of this sample (65% in both case and control participants) were postmenopausal. Obesity in postmenopausal women is associated with a higher BC risk (WCRF & AICR, 2018). Therefore, high obesity rates noted in this sample are alarming for it might contribute to an increased BC risk in obese, postmenopausal women. Additionally, low PA levels were noted in this sample. Higher PA is associated with a decreased BC risk (WCRF & AICR, 2018). It is evident that high rates of overweight or obesity co-exist with low PA levels in our study sample and may contribute to an increased BC risk in black South African women.

In addition to the above, 86% of this study sample earned less than R3 000 per month. In South Africa, healthier foods (less energy dense and nutrient rich products) are pricier compared to more energy dense and often nutrient poor foods (Temple & Steyn, 2011). This might explain why lower cost foods such as sugar (sugar beverages, food with added sugars), starchy grains (rice and samp), cooked porridge (maize meal) and animal protein (chicken, processed meat) accounted for more than 75% of total energy intake in this sample.

### 4.2.2 **Differences in dietary intake between case and control participants**

Participants in the control group had a higher BMI and waist circumference compared to case participants. Therefore, it was not unexpected that total energy intake and energy intake within food groups were higher in control participants compared to case participants. Dietary intake in all food groups, except for cooked porridge, differed significantly between case and control participants. In case participants, lower total energy intake might be explained to some extent by the late stage of BC diagnosis amongst these women in this sample. Almost half (49%) of case participants were diagnosed in late stage BC (stage III or IV) when a decrease in appetite and altered taste sensitivity (resulting in decreased consumption in some foods) is known to occur as a symptom of progressive cancer growth (Cheung *et al.*, 2009). Since dietary intake data were collected within a few days of BC diagnoses, it might be possible that habitual dietary intake of case participants were already altered due to the possible influence of cancer on appetite (Thomas *et al*., 2017). Therefore, participants in the case group had a lower total energy intake and energy within food groups compared to participants in the control group.

### 4.2.3 The association between dietary intake and breast cancer risk.

Savoury food consumption (soup powders, sauces and potato chips) showed a positive association with BC risk in postmenopausal women of this sample. Foods in this food group are highly processed, high in salt, nutrient poor and more energy dense that may contribute to an increased risk for obesity if over consumed.

An inverse association with fresh fruit consumption and BC risk in premenopausal women were found whilst an inverse association were noted in the subgroups “red meat and organ meat”, within the animal protein food group. Fresh fruit is rich in nutrients and less energy dense that may contribute to maintaining a healthy body weight. Even though red and organ meat contains a variety of nutrients that may protect against BC risk, current research is rather favourable of an increased BC risk in relation with red meat consumption. Research supporting an increased or decreased BC risk in relation with red meat and organ meat consumption, grouped in food groups, are lacking. Therefore, this inverse association with BC risk in relation with red and organ meat may be due to low consumption and/or poverty and requires further investigation.

In line with the above, results from this study might indicate that the amount of nutrients in combination with the amount of energy present in food or foods is associated with an increased or decreased BC risk. Less energy dense foods combined with nutrient rich foods such as fresh fruit may protect against BC risk whilst more energy dense, nutrient poor foods (savoury foods) increase BC risk in this population. However, due to the monotonous diet, and delay in early BC diagnoses seen in this sample, true conclusions are difficult to make regarding dietary intake and the risk of developing BC in black South Africa women of the Soweto urban area.

## 4.3 Practical recommendations emanating from this study

- High obesity rates co-existing with low PA remain worrisome as it contributes to a higher BC risk in both pre- and postmenopausal women. Current prevention and control strategies on obesity and PA should be prioritized in South Africa. The Strategy for the Prevention and Control of Obesity in South Africa 2015-2020 is an example of such a strategy that should be prioritized (DOH, 2015). This strategy aims to reduce worrisome obesity rates and increase PA levels and may help reduce BC risk in both pre- and postmenopausal women. A multidisciplinary approach should be followed where the national Department of Health (DOH), provincial DOH, community workers and other allied health workers strive to implement this strategy on a national, provincial, district and sub-district level in rural and urban areas of South Africa. Additionally, children should be

taught from a young age about healthy food choices and the importance of being physically active.

- Poverty may contribute to low dietary diversity or a monotonous diet seen in this sample. Some most consumed single foods such as bread and maize meal are fortified with micronutrients as a strategy to increase micro-nutrient intake in South Africa. However, this strategy does not promote a diverse diet (like the WCRF and SAFBDGs) which is naturally high in various nutrients for optimal health and to reduce BC risk. Therefore, BC prevention strategies in South Africa should strive to establish new or promote existing lower cost diets that contain a variety of less energy dense and more nutrient rich foods. This lower cost diet should further strive to emphasize inclusion of foods on the list of zero VAT rated food items (dried beans, samp,maize meal, rice, brown bread, vegetables, fruits, vegetables oil, mealie rice, pilchards in tins, eggs, milk, lentils, milk powder, cultured milk and brown wheaten meal) in South Africa. Focus should be drawn to educate the population on a low cost prevention diet to reduce high energy and high carbohydrate (refined grains, sugar and added sugars) intake and to promote a diverse diet.
- Findings from this study support the current recommended cancer prevention diet, promoted by the WCRF and SAFBDGs. Therefore, savoury food or snacks that are highly processed, high in salt, energy and low in nutrients should be limited or avoided if possible. Less energy dense, nutrient rich food such as various fresh vegetables and fruit (400 g per day in total) should be part of a balanced diet as a possible strategy to reduce BC risk.
- Bothersome high rates of late stage BC diagnoses were seen in case participants from this study. BC is curable when detected in early stages. Therefore, early screening of BC should be made a priority in South Africa as a way to reduce high mortality rates in South Africa.

## 4.4 Limitations of this study

- The coding method used of foods consumed in this particular study with the use of the South African Food Composition tables did not separate certain foods that were captured as a meal. Pizza (frequently consumed in this study), for instance, contains meat, starchy grains, sauce, cheese and vegetables were coded as a single food since the code is adjusted for all macro and micro-nutrients. This made categorizing of such foods within a food group difficult.
- Due to the nature of this case-control study design, it is subject to bias. With regard to half of the case participants being diagnosed only in advance stage BC in this sample, a recall

bias might be possible since their appetite is already decreased. Habitual dietary intake of these case participants might therefore not be captured.

- Even though a validated and reproducible population specific QFFQ was used, using a QFFQ to collect dietary data may be subjected to underreporting and over reporting of portion sizes or dietary intake since data capturing relied on the participant's memory. The QFFQ used in this study was also developed for a Tswana speaking population whilst this study population spoke different languages.

## 4.5 Recommendations for future research

Breast cancer risk in relation with diet has extensively been studied globally. However, very little research has been conducted on dietary intake in relation with BC risk in South Africa. In conducting this project, lack of certain data was established in the literature available in South Africa and may be addressed by future research. Possible gaps include:

- In this study, foods with a high nutrient content (fruit) showed inverse associations with BC risk whilst food with a lower nutrient density (savoury food) showed positive associations with BC risk. Therefore, micro-nutrient intake in relation to BC risk should be investigated in South Africa. This might give new insight into protective factors within micro-nutrients of food that food groups in this study might have missed.
- Since very little attention is drawn to BC risk and dietary intake in South Africa, BC risk in relation to dietary intake should also be investigated in other South African ethnicities and in different geographical areas (urban coastal areas, rural coastal areas, etc.) for dietary intake or habits may vary in different areas and ethnicities.
- Given that single foods are not eaten in isolation, investigation of dietary patterns in relation with BC risk may sketch a better picture in understanding BC risk in relation to dietary intake. However, due to the monotonous diet seen in this sample, statistical difficulties may arise when dietary patterns are to be investigated due to high consumption of some food groups and low consumption of others. It is therefore recommended to investigate the development of statistical tools that aim to take monotonous diets into account.
- Explore dimension reduction techniques such as nutrient or dietary patterns with BC risk by revisiting the same data to make a conclusion about the inverse role of red and organ meat and BC risk.

- In line with the alarming obesity rates and high total energy intake per day seen in this sample, special attention should be drawn to portion sizes of foods or food groups. Portion sizes are directly proportional to the amount of energy (kJ) consumed and may lead to an increased risk for obesity. Therefore, more attention should be drawn to different portion sizes in food groups to able to establish thresholds of portion sizes in food groups. Quintile intakes of food can be used instead of investigating the highest versus the lowest energy intake as this study did. This might also be valuable to establish upper limit intakes of single foods or food groups that are protective of or increasing BC risk.
- Breast cancer is known to be a hormone related cancer (WCRF & AICR, 2018). Therefore, exogenous causes of elevated oestrogen levels in the female body such as xeno-oestrogens should be investigated to establish whether there is any association with BC risk. Xeno-oestrogens are found in plastic packaging of foods, plastic food containers, various food preservatives and foam cups or holders used to serve food in (Yang *et al*., 2011).
- A prospective cohort study design can also be used to investigate direct BC risk in relation with dietary habits over time.

To conclude, the aim and objectives of this study were reached. Findings of this study, regardless of the limitations, add much needed information to the literature regarding dietary intake and BC risk in the black female population of South Africa (Soweto).

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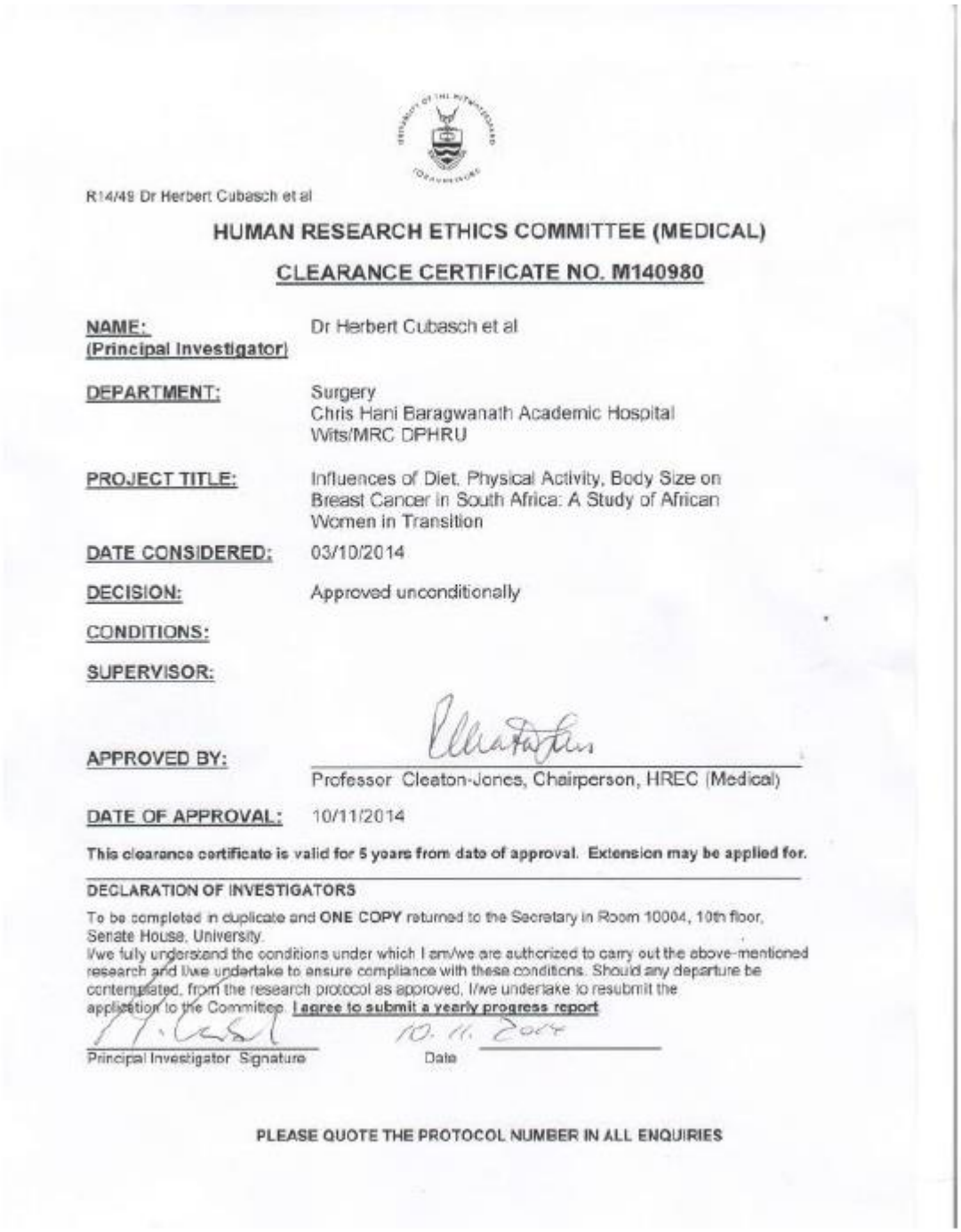
## ANNEXURES

## ANNEXURE A: ETHICAL APPROVAL LETTER, LARGE STUDY, UNIVERSITY OF THE WITWATERSRAND.



R14/49 Dr Herbert Cubasch et al

**HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)**

**CLEARANCE CERTIFICATE NO. M140980**

| | |
|---|---|
| **NAME: (Principal Investigator)** | Dr Herbert Cubasch et al |
| **DEPARTMENT:** | Surgery<br>Chris Hani Baragwanath Academic Hospital<br>Wits/MRC DPHRU |
| **PROJECT TITLE:** | Influences of Diet, Physical Activity, Body Size on Breast Cancer in South Africa: A Study of African Women in Transition |
| **DATE CONSIDERED:** | 03/10/2014 |
| **DECISION:** | Approved unconditionally |
| **CONDITIONS:** | |
| **SUPERVISOR:** | |
| **APPROVED BY:** | Professor Cleaton-Jones, Chairperson, HREC (Medical) |
| **DATE OF APPROVAL:** | 10/11/2014 |

**This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.**

**DECLARATION OF INVESTIGATORS**

To be completed in duplicate and **ONE COPY** returned to the Secretary in Room 10004, 10th floor, Senate House, University.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**

Principal Investigator Signature — Date: 10. 11. 2014

**PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES**

## ANNEXURE B: LETTER OF PERMISSION TO CONDUCT RESEARCH, CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL.

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

MEDICAL ADVISORY COMMITTEE
CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

**PERMISSION TO CONDUCT RESEARCH**

Date: 25 September 2014

TITLE OF PROJECT: Influence of diet, physical activity, body size on breast cancer in South Africa: a study of African women in transition

UNIVERSITY: Witwatersrand

Principal Investigator: H Cubasch

Department: Surgery

Supervisor (If relevant):

Permission Head Department (where research conducted): Yes

Date of start of proposed study: September 2014
Date of completion of data collection: December 2017

The Medical Advisory Committee recommends that the said research be conducted at Chris Hani Baragwanath Hospital. The CEO /management of Chris Hani Baragwanath Hospital is accordingly informed and the study is subject to:-

- Permission having been granted by the Committee for Research on Human Subjects of the University of the Witwatersrand.
- the Hospital will not incur extra costs as a result of the research being conducted on its patients within the hospital
- the MAC will be informed of any serious adverse events as soon as they occur
- permission is granted for the duration of the Ethics Committee approval.

Recommended
(On behalf of the MAC)
Date: 25 September 2014

Approved/Not Approved
Hospital Management
Date: 02/10/14

# ANNEXURE C: ETHICAL APPROVAL OF MSC STUDY, NORTH-WEST UNIVERSITY

NORTH-WEST UNIVERSITY
YUNIBESITI YA BOKONE-BOPHIRIMA
NOORDWES-UNIVERSITEIT

Private Bag X6001, Potchefstroom
South Africa 2520

Tel: 018 299-1111/2222
Web: http://www.nwu.ac.za

**Faculty of Health Sciences Ethics Office for Research, Training and Support**

**Health Research Ethics Committee (HREC)**

Tel: 018-285 2291
Email: Wayne.Towers@nwu.ac.za

09 April 2018

Dr C Taljaard
Dietetics-CEN

Dear Dr Taljaard

## APPROVAL OF YOUR APPLICATION BY THE HEALTH RESEARCH ETHICS COMMITTEE (HREC) OF THE FACULTY OF HEALTH SCIENCES

**Ethics number: NWU-00118-17-S1**

Kindly use the ethics reference number provided above in all future correspondence or documents submitted to the administrative assistant of the Health Research Ethics Committee (HREC) secretariat.

**Study title: The association between dietary patterns and the risk of breast cancer in black South African women**

**Study leader: Dr C Taljaard**

**Student: I Jacobs-24164399**

**Application type: Single study**

**Risk level: Minimal (monitoring report required annually)**

You are kindly informed that your ethics approval application has been successful and fulfils all requirements for approval. Your study is approved for a year and may commence from 09/04/2018. 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. A monitoring report should be submitted two months prior to the reporting dates as indicated i.e. annually for minimal risk studies, six-monthly for medium risk studies and three-monthly for high risk studies, to ensure timely renewal of the study. A final report must be provided at completion of the study or the HREC, Faculty of Health Sciences must be notified if the study is temporarily suspended or terminated. The monitoring report template is obtainable from the Faculty of Health Sciences Ethics Office for Research, Training and Support at Ethics-HRECMonitoring@nwu.ac.za. Annually, a number of studies may be randomly selected for an internal audit.

The HREC, Faculty of Health Sciences requires immediate reporting of any aspects that warrants a change of ethical approval. Any amendments, extensions or other modifications to the proposal or other associated documentation must be submitted to the HREC, Faculty of Health Sciences prior to implementing these changes. These requests should be submitted to Ethics-HRECApply@nwu.ac.za with a cover letter with a specific subject title indicating, "Amendment request: NWU-XXX-XXX". The letter should include the title of the approved study, the names of the researchers involved, the nature of the amendment/s being made (indicating what changes have been made as well as where they have been made), which documents have been attached and any further explanation to clarify the amendment request being submitted. The amendments made should be indicated in yellow highlight in the amended documents. The *e-mail*, to which you attach the documents that you send, should have a specific subject line indicating that it is an amendment request as well as the nature of the amendment e.g. "Amendment request: NWU-XXX-XXX". This submission will be handled via the expedited process.

Any adverse/unexpected/unforeseen events or incidents must be reported on either an adverse event report form or incident report form to Ethics-HRECIncident-SAE@nwu.ac.za. The *e-mail*, to which you attach the documents that you send, should have a specific subject line indicating that it is a notification of a serious adverse event or incident in a specific project e.g. "SAE/Incident notification: NWU-XXX-XXX". Please note that the HREC, Faculty of Health Sciences has the prerogative and authority to ask further questions, seek additional information, require further modification or monitor the conduct of your research or the informed consent process.

The HREC, Faculty of Health Sciences complies with the South African National Health Act 61 (2003), the Regulations on Research with Human Participants (2014), the Ethics in Health Research: Principles, Structures and Processes (2015), the Belmont Report and the Declaration of Helsinki (2013).

We wish you the best as you conduct your research. If you have any questions or need further assistance, please contact the Faculty of Health Sciences Ethics Office for Research, Training and Support at Ethics-HRECApply@nwu.ac.za.

Yours sincerely

Prof Wayne Towers
HREC Chairperson

Prof Minrie Greeff
Ethics Office Head

# ANNEXURE D: COMPILATION OF FOOD GROUPS

| | Food group | Sub group | Single foods |
|---|---|---|---|
| 1 | Cooked porridge | White porridge | Maize meal (stiff, soft or crumbly), E-pap, mageu, Ting |
| | | High fibre Porridge | Oats, mabella (sorghum/corn-rice) & Maltabella |
| 2 | Starchy grains | Breakfast cereals | Corn flakes, All bran, Weet bix and other |
| | | Refined grains | Rice, pasta, bread, samp, samp rice, vetkoek, dumpling, scones, provita, crackers, rusks, doughnut, Samp and beans, spaghetti bolognaise, cake flour, lasagne, |
| | | Whole grains | Brown rice, whole wheat bread, whole wheat scone, bulgar |
| | | Pies & Pizza's | Beef, steak and kidney, Cornish, chicken, sausage rolls, hamburger |
| | | Starchy vegetables | Potatoes, sweet potato, corn, sweet corn, beetroot, peas boiled |
| 3 | Vegetables | Green leafy vegetables | Spinach, cabbage, morogo, cauliflower, Broccoli, beetroot leaves, green beans, salad, coleslaw |
| | | Yellow vegetables and others | Pumpkin, carrots, tomato, onions, tomato gravy, mushrooms |
| 4 | Fresh fruit | Fruit | All fruits, fruit juice, dried fruit, Avocado, |
| 5 | Legumes | Legumes | Dried beans, peas, lentils, split peas, soups, soy and soy products |
| 6 | Nuts and seeds | Nuts and seeds | All nuts and seeds and peanut butter, peanuts |
| 7 | Milk and milk products | Milk | Whole milk, Fresh/longlife, skimmed, fat free, Powder. flavoured milk, |
| | | Milk products | Cheese, Yoghurt, cheese spread |

| | | | |
|---|---|---|---|
| 8 | Animal protein | Processed meat | Boerewors, other sausages, polony, cold meats, bacon, canned meats, canned mopanie worms. |
| | | Red meat | Beef, Mutton/lamb, pork, goat, offal, organ, sosaties, bacon |
| | | Chicken | All chicken meat, offal/organ meat and turkey |
| | | Fish | Pilchards, Fried fish, canned fish, Fish cakes, fish fingers, fish paste, fish cakes |
| | | Eggs | Boiled, Scrambled, Fried |
| 9 | Fats and oils | Hard brick butter | Brick margarine |
| | | Light margarine and soft margarines | PUFA soft spread |
| | | Oils | Salad dressing, Mayonnaise, sunflower, peanut oil |
| | | Other fats | Ice cream, instant pudding with milk |
| 10 | Sugar | Added sugar | Jam, syrup, honey, chocolates, candies, sweets, biscuits and cookies, cakes, tarts, sorbet, baked pudding, jelly, instant pudding, cheese cakes, muffins, canned fruits |
| | | Sugary drinks | Squash, fizzy drinks |
| 11 | Alcohol | Alcohol | Home brew beer, commercial beer, spirits, wine, |
| 12 | Savoury Snacks | Savoury Snacks | Marmite, fray bentos, Oxo, Potato crisps, cheese curls, niknaks, samoosas, Biscuits eg bacon kips, popcorn, tomato sauce, Worcester sauce, chutney, pickles, packet soups, soup powders pickles, atchar, chakalaka, Sandwich spread |

## ANNEXURE E: ETHIC APPROVAL LETTER FOR USING THE PURE QFFQ.

NORTH-WEST UNIVERSITY
YUNIBESITI YA BOKONE-BOPHIRIMA
NOORDWES-UNIVERSITEIT
POTCHEFSTROOM CAMPUS

Private Bag X6001, Potchefstroom
South Africa 2520

Tel: 018 299-1111/2222
Web: http://www.nwu.ac.za

**Faculty of Health Sciences**
Tel: 018 2992095
Fax: 018 2992088
Email: Annamarie.Kruger@nwu.ac.za

To whom it may concern

24 April 2013

Dear Prof. Vorster

**Additional Request: NWU-00016-10-A1**

Your request to use the validated PURE Food Frequency Questionnaire for the Chris-Hani-Baragwanath Hospital Breast Cancer Project has been approved by die Ethics Sub-Committee.

Yours sincerely

Prof. A. Kruger
Ethics Sub-Committee Chair

Original details: Prof. A. Kruger(10062416) C:\Users\13210572\Documents\ETIEK\2010 ETHICS\NWU-00016-10-A1 Additional Request 2.docm
24 April 2013

File reference: NWU-00016-A1 Additional Request

# ANNEXURE F: THE QFFQ USED IN THE SABC STUDY.

## SABC STUDY: DIETARY ASSESSMENT. THE PURE Quantitative Food Frequency Questionnaire (QFFQ)

Participant study number ☐☐☐☐☐☐☐☐☐☐☐☐☐

Participant initials ☐☐☐

1. Today's date: ☐☐☐☐ ☐☐ ☐☐ (year / month / day)

2. Interviewer name: _____ ☐

4.DOB: ☐☐☐☐ ☐☐ ☐☐ OR Age ☐☐ years

5. Have your diet and alcohol intake changed recently? How? Last month ☐ Last year ☐ No change ☐

| Age | Alcohol | Meat | Vegetables | Fruit |
|---|---|---|---|---|
| < 10 | | | | |
| 10 - 20 | | | | |
| 20 - 30 | | | | |
| 30 + | | | | |

6. **VITAMIN/MINERAL SUPPLEMENT CONSUMPTION**:
Have you taken multivitamin/minerals SUPPLEMENTS in the past year? Yes 1 / No 2

Combination of various vitamins/minerals? Yes 1 / No 2

7. **MULTIVITAMIN BRAND**: Indicate the brand of multivitamins/minerals that you have taken in the past year:
Multivitamins:.....Minerals:.....

8. **MULTIVITAMINS PER DAY**: How many tablets, spoons, etc. have you used per day in the past year? If you take for example 3 vitamin pills two times a day, you will have taken 6 pills per day.
☐ tablets ☐ spoons ☐ ..... ☐ ..... per day.

9. **MULTIVITAMINS TIMES PER WEEK**: Indicate how many times a week you have taken multivitamins/minerals in the past year. ☐ times per week

10. **MULTIVITAMINS MONTHS IN THE PAST YEAR**: Indicate how many months you have taken multivitamins in the past year. ☐ months in the last year

11. **WOULD YOU DESCRIBE THE FOOD THAT YOU ATE THE PAST MONTH AS TYPICAL OF YOUR USUAL FOOD INTAKE?**.....

12. Do you eat fat/margarine/? Yes 1 / No 2

Is it used in preparation of food? Yes 1 / No 2

If YES, what type do you have at home now? ☐ **HARD** (brick) Brand name .....

☐ **SOFT** (TUB) Brand name .....(Full fat, Medium or Light).....

☐ **MEAT FAT RECOOKED**

☐ Don't know

If brand name is given, do you usually use this brand? Yes 1 | No 2 | Don't know 3

**13. What type of salt do you use?**

Give brand names .....

Do you add salt to food while it is being cooked? Always 1 | Never 2 | Don't know 3

Do you add salt to your food after it has been cooked? Always 1 | Never 2

Do you like salty foods eg salted peanuts, crisps, chips, frito's, biltong, dried sausage, etc.

Very much 1 | Like it 2 | Not at all 3

**14. Do you eat maize meal porridge?** Yes 1 | No 2

If YES, what type do you have at home now?

Brand name: ..... 1

Don't know: ..... 2

Grind self: ..... 3

If brand name is given, do you usually use this brand? Yes 1 | No 2 | Don't know 3

Where do you get your maize meal from? (may answer more than one)

Shop ..... 1 ☐

Employer ..... 2 ☐

Harvest and grind self ..... 3 ☐

Other (specify) ..... 4 ☐

Don't know ..... 5 ☐

**15. How many persons eat in your household? .....**

Please think carefully about the food and drink you have consumed during the ***past month*** (four weeks). I will go through a list of foods and drinks with you and I would like you to tell me:

- If you eat the food

- How the food is prepared
- How much of the food you eat at a time
- How many times a day you eat it and if you do not eat it every day, how many times a week or a month you eat it.

To help you to describe the amount of a food you eat, I will show you pictures of different amounts of the food. Please say which picture is the closest to the amount you eat, or if it is smaller, between the sizes or bigger than the pictures.

***There are no right or wrong answers***. Everything you tell me is confidential.
Is there anything you want to ask now? Are you willing to go on with the questions?

## QUANTITATIVE FOOD FREQUENCY QUESTIONNAIRE (QFFQ)

**INSTRUCTIONS: Circle the answer. Fill in the amount and times eaten in the appropriate columns.**

I shall now ask you about the type and the amount of food you have been eating in the last month. Please tell me if you eat the food, how is it prepared, how much you eat, and how often you eat it.

| FOOD | DESCRIPTION | AMOUNT | TIMES EATEN | | | | CODE | AMOUNT / WEEK |
|---|---|---|---|---|---|---|---|---|
| | | | Per day | Per week | Per month | Never | | |
| PORRIDGE AND BREAKFAST CEREALS AND OTHER STARCH | | | | | | | | |
| **Maize-meal porridge** | Stiff (pap) Unfortified meal<br>Fortified meal | | | | | | 3400<br>4401 | |
| **Maize-meal porridge** | Soft (slap-pap) Unfortified<br>Fortified meal | | | | | | 3399<br>4400 | |
| **Maize-meal porridge** | Crumbly, Unfortified meal<br>Fortified meal | | | | | | 3401<br>4402 | |
| **Maltabella** | Corn-rice/sorghum | | | | | | 3437 | |
| **Maltabella** | Cooked porridge | | | | | | 3241 | |
| **Oats** | Cooked oatmeal porridge | | | | | | 3239 | |
| **Other cooked porridge** | Type: ..... | | | | | | | |
| **Breakfast cereals** | Brand name of cereals :<br>.....<br>Type of cereals<br>Corn flakes.....<br>All Bran.....<br>Weet Bix..... | | | | | | <br><br><br>3243<br>3242<br>3244 | |

| FOOD | DESCRIPTION | AMOUNT | TIMES EATEN | | | | CODE | AMOUNT / WEEK |
|---|---|---|---|---|---|---|---|---|
| | | | Per day | Per week | Per month | Never | | |
| Do you pour milk on your porridge or cereal? | | | | | | | Yes 1 | No 2 |
| If yes, what type of milk (whole fresh, sour, 1%, fat free, milk blend, etc) ..... | | | | | | | | |
| **If yes, how much milk** | Full cream | | | | | | 2718 | |
| | Low-fat (2%) | | | | | | 2772 | |
| | Fat-free | | | | | | 2775 | |
| Do you put sugar on your porridge or cereal? | | | | | | | Yes 1 | No 2 |
| **If yes, how much sugar** | Sugar with Porridge | | | | | | 3989 | |
| | Sugar with Cereal | | | | | | 3989 | |
| **Samp/maize rice** | Cooked | | | | | | 3250 | |
| **Samp and beans** | AMOUNT of samp with beans<br><br>Ratio of samp:beans : | | | | | | 3402<br>(1:1) | |
| **Samp and peanuts** | Samp and peanuts<br>Ratio: | | | | | | 3250<br>(samp) | |
| **Rice** | White | | | | | | 3247 | |
| | Brown | | | | | | 3315 | |
| | Maize Rice | | | | | | 3250 | |
| **Pasta** | Macaroni<br>Specify..... | | | | | | 3262 | |
| **Pasta** | Spaghetti<br>Specify..... | | | | | | | |
| **Pasta** | Other specify:<br>.....<br><br>..... | | | | | | | |

| FOOD | DESCRIPTION | AMOUNT | TIMES EATEN | | | | CODE | AMOUNT / WEEK |
|---|---|---|---|---|---|---|---|---|
| | | | Per day | Per week | Per month | Never | | |
| **Pizza** | Home made: Specify topping<br>.....<br>..... | AMOUNT | | | | | 3353 (base+ch) | |
| | Bought: Specify topping<br>.....<br>..... | | | | | | 3353 (base+ch) | |
| You are being very helpful. Can I now ask you about meat?<br><br>**CHICKEN, MEAT, FISH**<br><br>**How many times per week do you eat meat (beef, mutton, pork, chicken, fish)?** ..... | | | | | | | | |
| **Chicken (codes with skin)** | Boiled | | | | | | 2926 | |
| | Stewed with packet soup | | | | | | 4413 | |
| | Fried: in batter/crumbs<br>Eg Kentucky | | | | | | 3018 | |
| | Roasted: Bought: Chicken Licken, Nandos, etc. | | | | | | 2925 | |
| | Other:<br>..... | | | | | | | |
| **Do you eat chicken skin?** | | | | | | Always 1 | | Never 2 |
| **Chicken bones stew** | With tomato and onion<br>With packet soup | | | | | | 2985 | |
| **Chicken feet** | | | | | | | 2997 | |
| **Chicken offal** | Giblets<br>Liver | | | | | | 2998<br>2970 | |
| **BEEF:**<br>**Do you like your beef with fat, or fat trimmed?** | Fried. Specify oil (Reused or other type?)..... | | | | | | 2941 | |
| | Cooked/Stewed: Lean<br>Regular (with fat) | | | | | | 2921<br>2946 | |
| | Mince with tomato and onion | | | | | | 2987 | |

| FOOD | DESCRIPTION | AMOUNT | TIMES EATEN | | | | CODE | AMOUNT / WEEK |
|---|---|---|---|---|---|---|---|---|
| | | | Per day | Per week | Per month | Never | | |
| | Other: Specify | | | | | | | |
| **MUTTON/LAMB:** **Do you like your lamb with fat, or fat trimmed?** | Boiled | | | | | | 3041 | |
| | Fried in oil<br>Specify oil (Recooked meat fat or oil)..... | | | | | | | |
| | Stewed with vegetables | | | | | | 3040 | |
| | Grilled/Roasted | | | | | | 2947 | |
| | Other: Specify | | | | | | | |
| **Beef/Mutton Offal** | Intestines: boiled nothing added | | | | | | 3003 | |
| | Stewed with vegetables, curried | | | | | | 4377 | |
| | Liver | | | | | | 2920 | |
| | Kidney | | | | | | 2923 | |
| | Other: Specify | | | | | | | |
| **Pork** | Boiled/Braised | | | | | | 3044 | |
| | Spareribs, braised | | | | | | 3010 | |
| | Grilled / Roasted (Chop) | | | | | | 2930 | |
| **Goat meat** | Boiled | | | | | | 4281 | |
| | Stewed with vegetables | | | | | | | |
| | Grilled / Roasted | | | | | | 4281 | |
| **What type of vegetables is usually put into meat stews?** ..... **In what ratios?**..... | | | | | | | | |
| **Wors / Sausage** | | | | | | | 2931 | |
| **Bacon** | | | | | | | 2906 | |
| **Cold meats** | Polony | | | | | | 2919 | |
| | Ham | | | | | | 2967 | |
| | Vienna | | | | | | 2936 | |

| FOOD | DESCRIPTION | AMOUNT | TIMES EATEN | | | | CODE | AMOUNT / WEEK |
|---|---|---|---|---|---|---|---|---|
| | | | Per day | Per week | Per month | Never | | |
| | Other: Specify<br>.....<br>.....<br>..... | | | | | | | |
| **Canned meat** | Bully beef<br>Anything added? | | | | | | 2940 | |
| | Other: Specify<br>.....<br>..... | | | | | | | |
| **Meat pie**<br>Size? | Beef | | | | | | 2939 | |
| | Steak and kidney | | | | | | 2957 | |
| | Cornish | | | | | | 2953 | |
| | Chicken | | | | | | 2954 | |
| | Other | | | | | | | |
| **Hamburger** | Homemade<br>Bought<br>Which restaurant/menu item<br>..... | | | | | | 4418 | |
| **Dried beans/peas/lentils** | Soup | | | | | | 3145 | |
| | Salad | | | | | | 3174 | |
| **Soya products eg Toppers** | Brands at home now:<br>..... | | | | | | 3196 (Toppers) | |
| **Pilchards in tomato/chili/brine**<br>**(Circle which one)** | Whole | | | | | | 3102 | |
| | Mashed with fried onion | | | | | | 4420 | |
| **Fried fish**<br>**Specify oil/fat!!** | With batter/crumbs | | | | | | 3072 | |
| | Without batter/crumbs | | | | | | 3060 | |

| FOOD | DESCRIPTION | AMOUNT | TIMES EATEN | | | | CODE | AMOUNT / WEEK |
|---|---|---|---|---|---|---|---|---|
| | | | Per day | Per week | Per month | Never | | |
| **Other canned fish** | Tuna:Amount<br>In oil<br>or water?..... | | | | | | 3056 (oil)<br><br>3054 (water) | |
| | Pickled fish | | | | | | | |
| | Other: Specify<br>..... | | | | | | | |
| **Fish cakes** | Bought: Fried | | | | | | 3080 | |
| | Home made with potato | | | | | | 3098 | |
| **Fish fingers** | Bought | | | | | | 3081 | |
| **Eggs** | Boiled/poached | | | | | | 2867 | |
| | Scrambled: milk + fat (specify type of fat) | | | | | | | |
| | Fried: Fat (specify type of fat) | | | | | | | |
| Now we come to vegetables and fruit<br>**VEGETABLES AND FRUIT** | | | | | | | | |
| **Cabbage/ Cauliflower/ Broccoli** | How do you cook cabbage? | | | | | | | |
| | Boiled, nothing added | | | | | | 3756 | |
| | Boiled with potato and onion and brick margarine or with<br>Sunflower oil | | | | | | 3813<br>3815 | |
| | Fried with brick margarine<br>Fried with sunflower oil | | | | | | 3810<br>3812 | |
| | Other: | | | | | | | |
| | Coleslaw | | | | | | 3707 | |
| **Spinach/morogo/ beetroot leaves other green leafy vegetables** | How do you cook spinach? | | | | | | | |
| | Boiled, nothing added | | | | | | 3913 | |
| | Boiled with fat added<br>Type of fat ..... | | | | | | | |
| | With onion, tomato, potato | | | | | | | |
| | With peanuts | | | | | | | |
| | Other: | | | | | | | |
| | Don't know | | | | | | | |

| FOOD | DESCRIPTION | AMOUNT | TIMES EATEN | | | | CODE | AMOUNT / WEEK |
|---|---|---|---|---|---|---|---|---|
| | | | Per day | Per week | Per month | Never | | |
| **Tomato and onion gravy** | Home made with fat<br>Type of fat .....(SO) | | | | | | 4423 | |
| | Without fat | | | | | | 3925 | |
| | Canned | | | | | | 4192 | |
| **Pumpkin (yellow)/ Butternut?** | How do you cook pumpkin? | | | | | | | |
| | Boiled, nothing added | | | | | | 4164 | |
| | Cooked in fat and sugar<br>Fat ..... | | | | | | | |
| | Boiled, little sugar and fat<br>Fat ..... | | | | | | | |
| | Other | | | | | | | |
| | Don't know | | | | | | | |
| **Carrots** | How do you cook carrots? | | | | | | | |
| | Boiled, nothing added | | | | | | 3757 | |
| | Boiled, sugar and fat<br>Fat ..... | | | | | | | |
| | With potato and onion:<br>Fat..... | | | | | | | |
| | Raw, salad | | | | | | 3709 | |
| | Chakalaka | | | | | | 4412 | |
| | Other | | | | | | | |
| | Don't know | | | | | | | |
| **Mealies/ Sweet corn** | How do you eat mealies? | | | | | | | |
| | On cob – fat added<br>Fat ..... | | | | | | | |
| | On cob – no fat added | | | | | | 3725 | |
| | Creamed sweet corn / canned | | | | | | 3726 | |
| | Whole kernel/canned | | | | | | 3942 | |
| **Beetroot** | Salad | | | | | | 3699 | |
| | Boiled, nothing added | | | | | | 3698 | |
| **Green beans** | Boiled with margarine or oil | | | | | | 3788 or 3789 | |

| FOOD | DESCRIPTION | AMOUNT | TIMES EATEN | | | | CODE | AMOUNT / WEEK |
|---|---|---|---|---|---|---|---|---|
| | | | Per day | Per week | Per month | Never | | |
| **Green beans** | Cooked with potato, onion, and brick margarine or oil | | | | | | 3792 or 3794 | |
| **Potatoes** | How do you cook potatoes? | | | | | | | |
| | Boiled/baked with skin | | | | | | 4155 | |
| | Boiled/baked without skin | | | | | | 3737 | |
| | Mashed:<br>With milk?<br>With fat/margarine? | | | | | | | |
| | Roasted<br>Fat ..... | | | | | | | |
| | Potato salad with mayonnaise | | | | | | 3928 | |
| | French fries (chips) | | | | | | 3740 | |
| **Sweet potatoes** | How do you cook sweet potatoes? | | | | | | | |
| | Boiled/baked with skin | | | | | | 3748 | |
| | Boiled/baked without skin | | | | | | 3903 | |
| | Mashed<br>Fat..... | | | | | | | |
| | Other:<br>..... | | | | | | | |
| | Don't know | | | | | | | |
| **Salad vegetables** | Mixed salad: tomato, lettuce and cucumber | | | | | | 3921 | |
| | Raw tomato | | | | | | 3750 | |
| | Other salad vegetables:<br>..... | | | | | | | |
| **Salad dressing**.....<br><br>French<br>Mayonnaise..... | Homemade? (Give recipe)<br>.....<br>Bought. Brand and type?<br>..... | | | | | | <br><br>3487<br>3488 | |
| **Other vegetables, specify + preparation** | .....<br><br>..... | | | | | | | |

| FOOD | DESCRIPTION | AMOUNT | TIMES EATEN | | | | CODE | AMOUNT / WEEK |
|---|---|---|---|---|---|---|---|---|
| | | | Per day | Per week | Per month | Never | | |
| | ..... | | | | | | | |
| Do you like fruit? | | | | | | | Yes 1 | No 2 |
| Apples | | | | | | | 3592 | |
| Pears | | | | | | | 3582 | |
| Oranges | | | | | | | 3560 | |
| Naartjie | | | | | | | 3558 | |
| Banana | | | | | | | 3540 | |
| Grapes | | | | | | | 3550 | |
| Peaches | Fresh | | | | | | 3565 | |
| | Canned | | | | | | 3567 | |
| Apricots | Fresh | | | | | | 3534 | |
| | Canned | | | | | | 3535 | |
| Mangoes | | | | | | | 3556 | |
| Guavas | Fresh | | | | | | 3551 | |
| | Canned | | | | | | 3553 | |
| Avocado | | | | | | | 3656 | |
| Wild fruit/berries | Specify type:<br>..... | | | | | | | |
| Dried fruit | Types:<br>..Mixed..<br>Peach..... | | | | | | <br>3593<br>3568 | |
| PawPaw | | | | | | | 3563 | |
| Strawberries | | | | | | | 3573 | |
| Other fruit | ..... | | | | | | | |
| If participant eats canned fruit: Do you have custard with the canned fruit? | | | | | | | Yes 1 | No 2 |
| Custard | Home made: Milk | | | | | | 2716 | |

| FOOD | DESCRIPTION | AMOUNT | TIMES EATEN | | | | CODE | AMOUNT / WEEK |
|---|---|---|---|---|---|---|---|---|
| | | | Per day | Per week | Per month | Never | | |
| | Commercial eg Ultramel | | | | | | 2716 | |
| **BREAD AND BREAD SPREADS** | | | | | | | | |
| **Bread / Bread rolls** | White | | | | | | 3210 | |
| | Brown | | | | | | 3211 | |
| | Whole wheat | | | | | | 3212 | |
| Do you spread anything on the bread? | | | | | | Always 1 | Never 2 | |
| **Margarine** | What brand do you have at home now? | | | | | | | |
| | | | | | | | | |
| | | | | | | | | |
| | Don't know ..... | | | | | | | |
| **Peanut butter** | | | | | | | 3485 | |
| **Jam/syrup/honey** | | | | | | | 3985 | |
| **Marmite / Fray bentos / Oxo** | | | | | | | 4058 | |
| **Fish/meat paste** | | | | | | | 3109 | |
| **Cheese** | Type:<br>Processed (Parmalat).....<br>Spread, full fat.....<br>Cheddar.....<br>..... | | | | | | <br>2728<br>2730<br>2722 | |
| **Achar** | Mango/other | | | | | | 3117 | |
| **Other spreads** | Specify:<br>.....<br>..... | | | | | | | |
| **Dumpling** | | | | | | | 3210 | |
| **Vetkoek** | White flour | | | | | | 3257 | |

| FOOD | DESCRIPTION | AMOUNT | TIMES EATEN | | | | CODE | AMOUNT / WEEK |
|---|---|---|---|---|---|---|---|---|
| | | | Per day | Per week | Per month | Never | | |
| | Whole wheat flour | | | | | | 3324 | |
| **Filling of vetkoek?** | Specify..... | | | | | | | |
| **Bunny Chow** | White/brown bread | | | | | | | |
| **Filling** | Chips | | | | | | 3740 | |
| | Russian | | | | | | 4344 | |
| | Vienna | | | | | | 2936 | |
| | Cheese | | | | | | 2728 | |
| | Polony | | | | | | 2919 | |
| | Atchar | | | | | | 3117 | |
| Other? Specify | | | | | | | | |
| **Provita, crackers, etc.** | | | | | | | 3235 | |
| **Mayonnaise / salad dressing** | Mayonnaise | | | | | | 3488 | |
| **Specify:for self or family** | Other: Specify<br>..... | | | | | | | |
| **DRINKS** | | | | | | | | |
| **Tea** | English (normal) | | | | | | 4038 | |
| | Rooibos | | | | | | 4054 | |
| **Coffee** | | | | | | | 4037 | |
| **Sugar/cup tea or coffee** | Tea: | | | | | | 3989 | |
| | Coffee: | | | | | | 3989 | |
| **Milk/cup tea or coffee** | What type of milk do you use in tea and coffee? | | | | | | | |
| | Fresh/long life: whole/full | | | | | | 2718 | |
| | Fresh/long life: 2%/low fat | | | | | | 2772 | |
| | Fresh/long life: fat free | | | | | | 2775 | |
| | Whole milk powder<br>Brand:<br>..... | | | | | | 2721 (powder) | |

| FOOD | DESCRIPTION | AMOUNT | TIMES EATEN | | | | CODE | AMOUNT / WEEK |
|---|---|---|---|---|---|---|---|---|
| | | | Per day | Per week | Per month | Never | | |
| | Low fat milk powder<br>Brand:<br>..... | | | | | | 2825 (powder) | |
| | Skimmed milk powder<br>Brand:<br>..... | | | | | | 2825 (powder) | |
| | Milk blend<br>Brand:<br>..... | | | | | | 2770 (powder) | |
| | Whitener: type<br>..(**Such as CREMORA**).....<br>..... | | | | | | 2751 | |
| | Condensed milk | | | | | | 2714 | |
| | Evaporated milk | | | | | | 2715 | |
| | None | | | | | | | |
| **Milk as such** | Do you drink milk as such?<br>What type of milk | | | | | | | |
| | Fresh/long life: whole/full | | | | | | 2718 | |
| | Fresh/long life: 2%/low fat | | | | | | 2772 | |
| | Fresh/long life: fat free | | | | | | 2775 | |
| | Condensed milk | | | | | | 2714 | |
| | Sour/maas | | | | | | 2787 | |
| | Other:<br>.....<br>..... | | | | | | | |
| **Milk drinks**<br>**(Specify: made with milk or water, sugar added)** | Nestle:<br>..... | | | | | | | |
| | Milo:<br>..... | | | | | | | |

| FOOD | DESCRIPTION | AMOUNT | TIMES EATEN | | | | CODE | AMOUNT / WEEK |
|---|---|---|---|---|---|---|---|---|
| | | | Per day | Per week | Per month | Never | | |
| | Flavoured milk: ..... | | | | | | | |
| | Other: | | | | | | | |
| **Yoghurt** | Drinking yoghurt | | | | | | 2756 | |
| | Thick yoghurt | | | | | | 2734 | |
| | Low fat sweetened with fruit | | | | | | 2732 | |
| **Squash** | Sweet O | | | | | | 4027 | |
| | Six O | | | | | | | |
| | Oros/Lecol – with sugar | | | | | | 3982 | |
| | - artificially sweetener | | | | | | 3990 | |
| | KoolAid | | | | | | 4027 | |
| | Other: ..... ..... | | | | | | | |
| **Fruit juice** | Fresh/Liquifruit/Ceres | | | | | | 2866 | |
| | Tropica (Dairy –fruit juice mix) | | | | | | 2791 | |
| | Other: ..... ..... | | | | | | | |
| **Fizzy drinks Coke, Fanta, etc** | Sweetened | | | | | | 3981 | |
| | Diet | | | | | | | |
| **Mageu/Motogo** | | | | | | | 4056 | |
| **Ginger beer** | | | | | | | | |
| **Home brew beer: (Sorghum) Mild** | | | | | | | 4039 | |
| **Strong** | | | | | | | | |
| **Commercial Beer** | | | | | | | 4031 | |
| **Spirits** | | | | | | | 4035 | |

| FOOD | DESCRIPTION | AMOUNT | TIMES EATEN | | | | CODE | AMOUNT / WEEK |
|---|---|---|---|---|---|---|---|---|
| | | | Per day | Per week | Per month | Never | | |
| SPECIFY..... | | | | | | | | |
| Wine red | | | | | | | 4033 | |
| Wine White | | | | | | | 4033 | |
| Other specify | .....<br><br>..... | | | | | | | |
| Did you have 2 or more drinks in one session in the past month? YES NO<br><br>How many drinks did you have per session?<br><br>How many times did this happen? | | | | | | | | |
| **SNACKS AND SWEETS** | | | | | | | | |
| Potato crisps | | | | | | | 3417 | |
| Peanuts | Raw | | | | | | 4285 | |
| | Roasted | | | | | | 3458 | |
| Cheese curls, Niknaks, etc | | | | | | | 3267 | |
| Raisins | | | | | | | 3552 | |
| Peanuts and raisins | | | | | | | | |
| Chocolates | Name:<br>.Milk chocolate.....<br>Kit Kat.....<br>Chocolate coated bar.....<br><br>..... | | | | | | <br>3987<br>4024<br>3997 | |
| Candies | Sugus, gums, hard sweets, etc | | | | | | 4000 | |
| Sweets | Toffees, fudge, caramels | | | | | | 3991 | |
| Biscuits/cookies | Type:<br>Without filling.....<br>With filling.....<br><br>..... | | | | | | <br>3216<br>3217 | |
| Cakes and tarts | Type: | | | | | | | |

| FOOD | DESCRIPTION | AMOUNT | TIMES EATEN | | | | CODE | AMOUNT / WEEK |
|---|---|---|---|---|---|---|---|---|
| | | | Per day | Per week | Per month | Never | | |
| | Vanilla cake.....<br>Chocolate cake.....<br>.....<br>..... | | | | | | 3288<br>3289 | |
| **Scones** | | | | | | | 3237 | |
| **Rusks** | Type: .....<br>Home made/Bought<br>.....<br>Yeast or Butter milk..... | | | | | | | |
| **Savouries** | Sausage rolls | | | | | | 2939 | |
| | Samoosas: Meat filling | | | | | | 3355 | |
| | Samoosas: Vegetable filling | | | | | | 3414 | |
| | Biscuits eg bacon kips | | | | | | | |
| | Other specify:<br>Popcorn.....<br>..... | | | | | | 3332 | |
| **Jelly** | | | | | | | 3983 | |
| **Baked pudding** | Type:<br>.....<br>Sauce..... | | | | | | | |
| **Instant pudding** | Milk type:<br>..... | | | | | | | |
| **Ice cream** | Brand..... | | | | | | 3483 | |
| **Sorbet** | Brand..... | | | | | | 3491 | |
| **Other snacks/ sweets: specify** | .....<br>..... | | | | | | | |

| FOOD | DESCRIPTION | AMOUNT | TIMES EATEN | | | | CODE | AMOUNT / WEEK |
|---|---|---|---|---|---|---|---|---|
| | | | Per day | Per week | Per month | Never | | |
| | ..... | | | | | | | |
| SAUCES, GRAVIES AND CONDIMENTS | | | | | | | | |
| Tomato sauce | | | | | | | 3139 | |
| Worcester sauce | | | | | | | 4309 | |
| Chutney | | | | | | | 3168 | |
| Pickles | | | | | | | 3866 | |
| Packet soups<br>How many family members: | | | | | | | 3165 | |
| Other: | .....<br>..... | | | | | | | |
| WILD BIRDS, ANIMALS OR INCECTS (hunted in rural areas or on farms) | | | | | | | | |
| Wild fruit | | | | | | | | |
| | | | | | | | | |
| | | | | | | | | |
| | | | | | | | | |
| | | | | | | | | |
| | | | | | | | | |
| INDIGENOUS/TRADITIONAL FOODS/PLANTS/ANIMALS<br>Please tell me if you use any indigenous plants OR other indigenous foods like mopani worms, locusts etc. to eat | | | | | | | | |
| Mopani worms | | | | | | | | |
| | | | | | | | | |
| | | | | | | | | |
| | | | | | | | | |
| MISCELLANEOUS: Please mention any other foods used more than once/two times a month which are not listed: | | | | | | | | |
| Specify | | | | | | | | |
| | | | | | | | | |

# ANNEXURE G: INFORMED CONSENT FORMS FOR CASE PARTICIPANTS.

**Study Number**: SABC
**Study Title:** Influences of diet, physical activity, body size on breast cancer in South Africa: a study of African women in transition

**Sponsor:** World Cancer Research Fund

**Principal Investigator:** Dr Herbert Cubasch

**Institution:** Breast Unit, Chris Hani Baragwanath Academic Hospital

## STUDY INFORMATION SHEET- BREAST CANCER CASE

### Introduction

Good day, my name is _____ and I am a doctor/study interviewer at the Chris Hani Baragwanath Breast Unit (CHBBU). I would like to invite you to consider taking part in a research study entitled "**Influences of diet, physical activity, body size on breast cancer in South Africa: a study of African women in transition**" because you are a woman recently diagnosed with breast cancer at CHBBU

Before agreeing to take part, it is important that you read and understand the following explanation of the purpose of the study, study procedures, benefits, minor risks or discomforts and your right to withdraw from the study at any time. This information sheet is to help you decide if you would like to participate. You need to understand what is involved before you agree to take part in this study. It may contain words that you do not understand. Please ask the study doctor or the study staff to explain any words or information that you do not clearly understand.

The study will be performed at Chris Hani Baragwanath Academic Hospital at the Birth to Twenty Research Building. We will make sure to tell you how to get to this research building for your study visit should you agree to participate. 500 breast cancer patients and 500 age and neighborhood matched controls aged 18 years or older will participate in this study. There will be one visit only which will take 2-3 hours of your time.

### Purpose of study

We are doing this study because little is known about risk factors for breast cancer in a Black African population. We want to investigate if too much body weight; not enough exercise; poor eating habits; too much alcohol intake, having a family member who also has or had breast cancer is associated with an increased risk of developing breast cancer. We will also look at whether other diseases you might have such as diabetes, high blood pressure or HIV are associated with an increased risk of developing breast cancer. In addition, we want to find out if the risk factors are different between younger women who are still fertile (able to have babies) and older women who have stopped their monthly periods. We will compare our results against what is known mainly about white patients from other parts of the world. The results of this study may help us to develop treatments that can help to decrease breast cancer in our communities.

**Study Procedures**

If you agree to take part in this study, and you are of child bearing age and able to fall pregnant you will have to take a urine pregnancy test. If the pregnancy test is negative you will be eligible (allowed) to participate in the study. You will also first be asked questions to see if you qualify for the study.

We ask your permission to take approximately 45 ml (about 9 teaspoons) of your blood and a urine sample in order to test your blood levels of sugar (glucose), lipids (cholesterol and fats) and insulin (for glucose uptake). The urine sample is to measure hormones and food breakdown products. Both samples are to be stored for future testing

The test results can be different if you have eaten recently before the blood samples are taken so you have already signed a consent with the recruiter to fast for at least 6 hours. That means you cannot eat or drink anything after 12 o'clock at night on the night before your scheduled study visit, and that you have given me a copy of the signed fasting informed consent document.

We would like to keep your samples and a small piece of your breast tissue which was taken when we diagnosed your cancer, for future testing but we need your consent to do this. This is optional and if you don't want to agree – this will not stop you from taking part in the study. A separate consent will be given to you to sign if you are happy for us to keep your samples. Before we use any of your stored samples, we will get permission from the University of the Witwatersrand Human Research Ethics Committee (Medical) to do the research and we will make sure that all your information is kept confidential.

We will measure the size of your waist and hips with a tape measure. You will also need to have an ultrasound and a DEXA scan which is a special kind of X-ray which can measure where the fat sits throughout your body. The radiation produced by the DEXA scan is not harmful for adults, but it may be harmful to the unborn foetus (baby). So if you are of childbearing age and can still fall pregnant, you will need to take a pregnancy test to make sure you are not pregnant. We will give you a test kit to check your pregnancy status. If you are pregnant you will not be able to take part in the study.

If you agree to participate in this study you will be asked questions in two separate questionnaires that will take approximately 2 and a half hours of your time. The questions will be about:-

1. your body size and weight, now and in the past.
2. the type and amount of exercise you do.
3. your general health, where you stay, how you live, your education, if and where you work and income details, how you travel around, e.g. taxi or your own car, your ethnic group, languages you speak. Also where and how you lived as a child.
4. how many children you have had, how long you breast fed each child, if you are still fertile, your age at menopause (when you stopped to have the monthly bleed), if you used contraceptives and if any relative of yours had breast cancer

5. your eating habits.

When you attended the Breast Cancer Clinic and your cancer was diagnosed, you consented to have a HIV test as part of your clinical treatment. For this study, we ask your permission to use the results of the HIV test. However, if you do not give permission for your HIV test result to be used you can still participate in the study.

You will experience no harm or risks in taking part in this study. You will experience a mild discomfort or mild pain from the needle prick required to take your blood. There is no direct benefit from participating, but you might learn about some possible risk factors for breast cancer.

All information obtained during the course of this study, including hospital records, personal data and research data will be kept strictly confidential. Your identity will always be kept confidential and at all times only the study doctors and nurses will have access to your clinical records. All of your personal and study data will be identified by a study number and your initials. This data (it is called anonymised because you name is not shown anywhere on the information) will be used for analysis by the study team. We plan to present the results at research meetings and use the results to write articles in medical journals. Only anonymised data will be presented and your confidentiality will be maintained at all times.

There won't be costs involved for you to participate and we will cover your transport and refreshment costs for the single study visit at R150. This will be provided to you at the study visit.

If you have any questions, please do not hesitate to ask me or the study doctor. You should not agree to take part unless you are satisfied with all the procedures involved.

Your participation in this study is entirely voluntary and you can decline to participate, or stop at any time, without stating any reason. Your withdrawal will not affect your access to medical care in any way.

If you have any questions, please feel free to contact the study doctor, Dr Cubasch at 011 933 9267/8804.

This research has been approved by the University of the Witwatersrand Human Research Ethics Committee (Medical). If you have any queries related to the research you are free to contact the Chairman of the Ethics committee – Professor Cleaton-Jones on 011 717-2301.

If you decide to take part in this study, you will be asked to sign the consent document to confirm that you understand the study and agree to participate. You will be given a signed copy to keep.

Participant questions raised: _____

_____

**Informed Consent for participation in the study entitled :** Influences of diet, physical activity, body size on breast cancer in South Africa: a study of African women in transition

I, _____, hereby confirm that I have been informed by the study interviewer about the nature, conduct, benefits and risks of the study.

- I have received, read and understood the above written information (Participant Information Leaflet and Informed Consent) regarding the study.
- I am aware that the results of the study, including personal details regarding my sex, age, date of birth, initials and diagnosis will be anonymously processed into any research reports.
- In view of the requirements of research, I agree that the data collected during this study can be processed in a computerised system by the study team.
- I may, at any stage, without prejudice, withdraw my consent and participation in the study.
- I have had sufficient opportunity to ask questions and (of my own free will) declare myself prepared to participate in the study.
- I am aware that the results of the study, including my personal details and diagnosis will be kept confidential.
- I may, at any stage, without prejudice to myself and my future medical treatment, withdraw my consent to participate in this study. I have had sufficient opportunity to ask questions and hereby accept to participate in the study.
- I agree to all of the procedures and restrictions included in this Information Sheet.

**PARTICIPANT**

_____

Printed name Signature/mark/thumbprint Date

**INTERVIEWER**

I herewith confirm that the above participant has been fully informed about the nature, conduct and risks of the above study

_____

Printed Name Signature Date

**WITNESS STATEMENT (if appropriate):**

As an impartial third party, I witnessed the entire consent discussion and the participant's signature on the form. I attest that this entire form was read to the participant named above. This person had enough time to consider this information, had an opportunity to ask questions, and voluntarily agreed to be in this study.

_____

Printed Name Signature Date

***Participant received IC copy**: Signature* _____ *Date* _____

**Pregnancy Test result** □ **Negative** (MAY BE recruited)

□ **Positive** (may NOT be recruited)

□ **Not applicable** – not of child bearing age or capable of conceiving

Signed as verification of correctly recorded result

_____

Printed name of participant Signature of participant Date

_____

Printed name of authorized interviewer: Signature of Interviewer Date

# ANNEXURE H: INFORMED CONSENT FORM OF CONTROL PARTICIPANTS.

**Study Number**: SABC
**Study Title:** Influences of diet, physical activity, body size on breast cancer in South Africa: a study of African women in transition

**Sponsor:** World Cancer Research Fund

**Principal Investigator:** Dr Herbert Cubasch

**Institution:** Breast Unit, Chris Hani Baragwanath Academic Hospital

**STUDY INFORMATION SHEET -CONTROLS**

Good day, my name is _____ and I am a doctor/study interviewer at the Chris Hani Baragwanath Breast Unit (CHBBU). I would like to invite you to consider taking part in a research study entitled "**Influences of diet, physical activity, body size on breast cancer in South Africa: a study of African women in transition**" because you are a CONTROL, meaning you are a friend or non-blood relative invited to be considered to participate in this study by a woman patient recently diagnosed with breast cancer patient at CHBBU, living in the same residential area (neighborhood) as you, and of similar age (±5 years) to you. Or, you have been recruited by one of the study recruiters and you fulfill all recruitment criteria.

Before agreeing to take part in the research study,it is important that you read and understand the following explanation of the purpose of the study, study procedures, benefits, minor risks or discomforts and your right to withdraw from the study at any time. This information sheet is to help you decide if you would like to participate. You need to understand what is involved before you agree to take part.It may contain words that you do not understand so please ask the study doctor or the study staff to explain any words or information that you do not clearly understand.

The study will be performed at Chris Hani Baragwanath Academic Hospital at the Birth to Twenty Research Building. We will make sure to tell you how to get to this research building for your study visit should you agree to participate. 500 breast cancer patients and 500 age and neighborhood matched controls aged 18 years or older will participate. There will be one visit only which will take 2-3 hours of your time.

**Purpose of study**

We are doing this study because little is known about risk factors for breast cancer in a Black African population. We want to investigateif too much body weight; not enough exercise; poor eating habits; too much alcohol intake or a family member who also has or had breast canceris associated with an increased risk of developing breast cancer. We will also look atwhether other diseases you might have such as diabetes, high blood pressure, HIV are associated with an increased risk to develop breast cancer. In addition wewant to find out if the risk factors differ between younger women who are still fertile (able to have babies) and older women whohave

stopped their monthly periods. We will compare our results against what is known mainly about white patients from other parts of the world. The results of this study may help us to develop interventions that can help to decrease breast cancer in our communities.

**Study Procedures**

If you agree to take part in this study, you will first be asked questions to see if you qualify for this study.

We ask permission to take approximately 45 ml (about 9 teaspoons) of your blood and a urine sample in order to test your blood levels of sugar (glucose), lipids (cholesterol and fats) and insulin (for glucose uptake). The urine sample is to measure hormones and food breakdown products. Both samples are to be stored for future testing.

The test results can be different if you have eaten recently before the blood samples are taken so you have already signed a consent with the recruiter to fast for at least 6 hours. That means you cannot eat or drink anything after 12 o'clock at night on the night before your scheduled study visit, and that you have given me a copy of the signed fasting informed consent document.

We would like to keep your samples for future testing but we need your consent to do this. This is optional and if you don't want to agree – this will not stop you from taking part in the study. A separate consent will be given to you to sign if you are happy for us to keep your samples. Before we use any of your stored samples we will getpermission from the University of the Witwatersrand Human Research Ethics Committee (Medical) to do the research and we will make sure that all your information is kept confidential.

We will measure the size of your waist and hips with a tape measure. You will also need to have an ultrasound and a DEXA scanwhich is a special kind of X-raywhichcan measure where the fat sits throughout your body. The radiation produced by the DEXA scan is not harmful for adults but it may be harmful to the unborn foetus (baby). So if you are of childbearing age and can still fall pregnant, you will need to take a pregnancy test to make sure you are not pregnant. We will give you a test kit to check your pregnancy status. If you are pregnant you will not be able to take part in the study.

If you agree to participate in this study you will be asked questions in two separate questionnaires that will take approximately 2 and a half hours of your time. The questions will be about:-

1. your body size and weight, now and in the past.
2. the type and amount of exercise you do.
3. your general health, where you stay, how you live, your education, if and where you work and income details, how you travel around, e.g. taxi or your own car, your ethnic group, languages you speak. Also where and how you lived as a child.
4. how many children you have had, how long you breast fed each child, if you are still fertile, your age at menopause (when you stopped to have the monthly bleed), if you used contraceptives, if any relative of yours had breast cancer

5. your eating habits.

We ask permission to test your HIV status, but should you decline you may still participate in the study. If you agree to have the test, you will need to sign a separate Consent Form which is available from the Research interviewer.
You will experience no harm or risks in taking part in this study. You will experience a mild discomfort or mild pain from the needle prick required to take your blood. There is no direct benefit from participating, but you might learn about some possible risk factors for breast cancer. You will also receive a clinical breast examination with a referral to the breast unit at CHBAH for further investigation if needed.

All information obtained during the course of this study, including hospital records, personal data and research data will be kept strictly confidential. Your identity will always be kept confidential and at all times only the study doctors and nurses will have access to your clinical records. All of your personal and study data will be identified by a study number and your initials. It is called anonymised because you name is not shown anywhere on the information) will be used for analysis by the study team. We plan to present the results at research meetings and use the results to write articles in medical journals. Only anonymized data will be presented and your confidentiality will be maintained at all times.

There won't be costs involved for you to participate and we will cover your transport and refreshment costs for the single study visit at R150. This will be provided to you at the study visit.

If you have any questions, please do not hesitate to ask me or the studydoctor. You should not agree to take part unless you are satisfied with all the procedures involved.

Your participation in this study is entirely voluntary and you can decline to participate, or stop at any time, without stating any reason. Your withdrawal will not affect your access to medical care.

If you have any questions, please feel free to contact the study doctor, Dr Cubasch at 011 933 9267/8804.

This research has been approved by the University of the Witwatersrand Human Research Ethics Committee (Medical). If you have any queries related to the research you are free to contact the Chairman of the Ethics committee – Professor Cleaton-Jones on 011 717-2301.

If you decide to take part in this study, you will be asked to sign the consent document to confirm that you understand the study and agree to participate. You will be given a signed copy to keep.

Participant questions raised: _____
_____

**Informed Consent for participation in the study entitled :** Influences of diet, physical activity, body size on breast cancer in South Africa: a study of African women in transition

I_____, hereby confirm that I have been informed by the study interviewer about the nature, conduct, benefits and risks of the study.

- I have received, read and understood the above written information (Participant Information Leaflet and Informed Consent) regarding the study.
- I am aware that the results of the study, including personal details regarding my sex, age, date of birth, initials and diagnosis will be anonymously processed into any research reports.
- In view of the requirements of research, I agree that the data collected during this study can be processed in a computerised system by the study team.
- I may, at any stage, without prejudice, withdraw my consent and participation in the study.
- I have had sufficient opportunity to ask questions and (of my own free will) declare myself prepared to participate in the study.
- I am aware that the results of the study, including my personal details and diagnosis will be kept confidential.
- I may, at any stage, without prejudice to myself and my future medical treatment, withdraw my consent to participate in this study. I have had sufficient opportunity to ask questions and hereby accept to participate in the study.
- I agree to all of the procedures and restrictions included in this Information Sheet.
-

**PARTICIPANT**

_____

Printed name Signature/mark/thumbprint Date

**INTERVIEWER**

I herewith confirm that the above participant has been fully informed about the nature, conduct and risks of the above study

_____

Printed Name Signature Date

**WITNESS STATEMENT:**

As an impartial third party, I witnessed the entire consent discussion and the participant's signature on the form. I attest that this entire form was read to the participant named above. This person had enough time to consider this information, had an opportunity to ask questions, and voluntarily agreed to be in this study.

| Printed Name | Signature | Date |
|---|---|---|

***Participant received IC copy**: Signature* _____ *Date* _____

**Pregnancy Test result** ☐**Negative** (MAY BE recruited)

☐**Positive** (may NOT be recruited)

☐**Not applicable** – not of child bearing age or capable of conceiving

Signed as verification of correctly recorded result

| Printed name of participant | Signature of participant | Date |
|---|---|---|

| Printed name of authorized interviewer: | Signature of Interviewer | Date |
|---|---|---|

# ANNEXURE I: AUTHORS GUIDELINES - BRITISH JOURNAL OF NUTRITION.

## Directions to Contributors

*British Journal of Nutrition*
*(Revised September 2014)*

*British Journal of Nutrition* (BJN) is an international peer-reviewed journal that publishes original papers and review articles in all branches of nutritional science. The underlying aim of all work should be to develop nutritional concepts.

## SUBMISSION

This journal uses ScholarOne Manuscripts for online submission and peer review.

Complete guidelines for preparing and submitting your manuscript to this journal are provided below.

## SCOPE

The British Journal of Nutrition encompasses the full spectrum of nutritional science and reports of studies in the following areas will be considered for publication: Epidemiology, dietary surveys, nutritional requirements and behaviour, metabolic studies, body composition, energetics, appetite, obesity, ageing, endocrinology, immunology, neuroscience, microbiology, genetics, and molecular and cell biology. The focus of all manuscripts submitted to the journal must be to increase knowledge in nutritional science.

**The journal does NOT publish papers on the following topics:** Case studies; papers on food technology, food science or food chemistry; studies of primarily local interest; complementary medicine; studies on pharmaceutical agents or that compare the effects of nutrients to those of medicines; substances that are considered primarily as medicinal agents; studies in which a nutrient or extract is administered by a route other than orally (unless the specific aim of the study is to investigate parenteral nutrition) nor studies using non-physiological amounts of nutrients (unless the specific aim of the study is to investigate toxic effects).

### In vivo and in vitro models

Studies involving animal models of human nutrition and health or disease **will only be considered for publication** if the amount of a nutrient or combination of nutrients used could reasonably be expected to be achieved in the human population.

Studies involving *in vitro* models **will only be considered for publication** if the amount of a nutrient or combination of nutrients is demonstrated to be within the range that could reasonably be expected to be encountered in vivo, and that the molecular form of the nutrient or nutrients is the same as that which the cell type used in the model would encounter in vivo.

### Extracts

Studies involving extracts **will only be considered for publication** if the source of starting material is readily accessible to other researchers and that there are appropriate measures for quality control, that the method of extraction is described in sufficient detail with appropriate quality control measures, that the nutrient composition of the extract is characterised in detail and that there are measures to control the quality of the composition of the extract between preparations, and that the amount of extract used could reasonably be expected to be achieved in in the human population (or in animals if they are the specific target of an intervention).

Studies involving extracts in *in vitro* models **will only be considered for publication** if the above guidelines for studies involving extracts are followed, and that the amount and molecular form of the extract is the same as that which would be encountered by the cell type used in the model in vivo.

**Manuscripts submitted to BJN that are outside of the journal's scope or do not meet the above requirements will be rejected immediately.**

## REVIEW PROCESS

*British Journal of Nutrition* uses a single blind review process.

As part of the online submission process, authors are asked to affirm that the submission represents original work that has not been published previously, and that it is not currently being considered by another journal. Authors must also confirm that each author has seen and approved the contents of the submitted manuscript. Finally, authors should confirm that permission for all appropriate uses has been obtained from the copyright holder for any figures or other material not in his/her copyright, and that the appropriate acknowledgement has been made to the original source.

At submission, authors are asked to nominate at least four potential referees who may then be asked by the Editorial Board to help review the work. Manuscripts are normally reviewed by two external peer reviewers and a member of the Editorial Board.

When substantial revisions are required to manuscripts after review, authors are normally given the opportunity to do this once only; the need for any further changes should at most reflect only minor issues. If a paper requiring revision is not resubmitted within 2 months, it may, on resubmission, be deemed a new paper and the date of receipt altered accordingly.

## PUBLISHING ETHICS

*British Journal of Nutrition* considers all manuscripts on the strict condition that:

1) The manuscript is your own original work, and does not duplicate any other previously published work;
2) The manuscript has been submitted only to the journal - it is not under consideration or peer review or accepted for publication or in press or published elsewhere;
3) All listed authors know of and agree to the manuscript being submitted to the journal; and
4) The manuscript contains nothing that is abusive, defamatory, fraudulent, illegal, libellous, or obscene.

The Journal adheres to the Committee on Publication Ethics (COPE) guidelines on research and publications ethics.

Text taken directly or closely paraphrased from earlier published work that has not been acknowledged or referenced will be considered plagiarism. Submitted manuscripts in which such text is identified will be withdrawn from the editorial process. If a concern is raised about possible plagiarism in an article published in *British Journal of Nutrition*, this will be investigated fully and dealt with in accordance with the COPE guidelines.

## ARTICLE TYPES

*British Journal of Nutrition* publishes the following: Research Articles, Review Articles, Systematic Reviews, Horizons in Nutritional Science, Workshop Reports, Invited Commentaries, Letters to the Editor, Obituaries, and Editorials.

Research Articles, Reviews, Systematic Reviews, Horizons Articles, Letters to the Editor and Workshop Reports should be submitted to http://mc.manuscriptcentral.com/bjn. Please contact the Editorial Office on bjn.edoffice@cambridge.org regarding any other types of article.

### Review Articles

BJN is willing to accept critical reviews that are designed to advance knowledge, policy and practice in nutritional science. Current knowledge should be appropriately contextualised and presented such that knowledge gaps and research needs can be characterised and prioritised, or so that changes in policy and practice can be proposed along with suggestions as to how any changes can be monitored. The purpose or objective of a review should be clearly expressed, perhaps as question in the Introduction, and the review's conclusions should be congruent with the initial objective or question. Reviews will be handled by specialist Reviews Editors. Please contact the Editorial Office with any queries regarding the submission of potential review articles. All reviews, including systematic reviews and meta-analyses, should present the

uncertainties and variabilities associated with the papers and data being reviewed; in particular BJN cautions against uncritical acceptance of definitions and non-specific global terminology, the advice of advisory bodies, and reference ranges for example.

**Reviews**: These articles are written in a narrative style, and aim to critically evaluate a specific topic in nutritional science.

**Horizons in Nutritional Science**: These are shorter than Review articles and aim to critically evaluate recent novel developments that are likely to produce substantial advances in nutritional science. These articles should be thought-provoking and possibly controversial.

**Systematic Reviews and meta-analyses**: The journal endorses the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement, a guideline to help authors report a systematic review and meta-analysis (see British Medical Journal (2009) 339, b2535). A systematic review or meta-analysis of randomised trials and other evaluation studies should follow the PRISMA guidelines.

### Letters to the Editor

Letters are invited that discuss, criticise or develop themes put forward in papers published in BJN. They should not, however, be used as a means of publishing new work. Acceptance will be at the discretion of the Editorial Board, and editorial changes may be required. Wherever possible, letters from responding authors will be included in the same issue as the original article.

## DETAILED MANUSCRIPT PREPARATION INSTRUCTIONS

### Language

Papers submitted for publication must be written in English and should be as concise as possible. We recommend that authors have their manuscript checked by someone whose first language is English before submission, to ensure that submissions are judged at peer review exclusively on academic merit.

We list a number of third-party services specialising in language editing and / or translation, and suggest that authors contact as appropriate. Use of any of these services is voluntary, and at the author's own expense.

Spelling should generally be that of the *Concise Oxford Dictionary* (1995), 9th ed. Oxford: Clarendon Press. Authors are advised to consult a current issue in order to make themselves familiar with BJN as to typographical and other conventions, layout of tables etc. Sufficient information should be given to permit repetition of the published work by any competent reader of BJN.

Published examples of BJN article types can be found below:

Research Article
Review Article
Horizons Article
Letter to the Editor

### Authorship

The Journal conforms to the International Committee of Medical Journal Editors (ICMJE) definition of authorship, as described by P.C. Calder (*Br J Nutr* (2009) **101**, 775).

The contribution of individuals who were involved in the study but do not meet these criteria should be described in the Acknowledgments section.

### Ethical standards

The required standards for reporting studies involving humans and experimental animals are detailed in an Editorial by G.C. Burdge (*Br J Nutr* (2014) **112**).

***Experiments involving human subjects***

The notice of contributors is drawn to the guidelines in the World Medical Association (2000) Declaration of Helsinki: ethical principles for medical research involving human subjects, with notes of clarification of 2002 and 2004 (http://www.wma.net/en/30publications/10policies/b3/), the *Guidelines on the Practice of Ethics*

*Committees Involved in Medical Research Involving Human Subjects* (3rd ed., 1996; London: The Royal College of Physicians) and the Guidelines for the ethical conduct of medical research involving children, revised in 2000 by the Royal College of Paediatrics and Child Health: Ethics Advisory Committee (*Arch Dis Child* (2000) **82**, 177–182). Articles reporting randomised trials must conform to the standards set by the Consolidated Standards of Reporting Trials (CONSORT) consortium.

*Required disclosures:* A paper describing any experimental work on human subjects must include the following statement in the Experimental Methods section: "This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects/patients were approved by the [insert name of the ethics committee; a specific ethics number may be inserted if you wish]. Written [or Verbal] informed consent was obtained from all subjects/patients. [Where verbal consent was obtained this must be followed by a statement such as: Verbal consent was witnessed and formally recorded]." For clinical trials, the trial registry name, registration identification number, and the URL for the registry should be included.

**PLEASE NOTE:** From 1 October 2014, as a condition for publication, all randomised controlled trials that involve human subjects submitted to BJN for review must be registered in a public trials registry. A clinical trial is defined by the ICMJE (in accordance with the definition of the World Health Organisation) as any research project that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. Registration information must be provided at the time of submission, including the trial registry name, registration identification number, and the URL for the registry.

***Experiments involving the use of other vertebrate animals***
Papers that report studies involving vertebrate animals must conform to the 'ARRIVE Guidelines for Reporting Animal Research' detailed in Kilkenny *et al.* (*J Pharmacol Pharmacother* (2010) 1,94-99) and summarised at www.nc3rs.org.uk. Authors must ensure that their manuscript conforms to the checklist that is available from the nc3Rs website. The attention of authors is drawn particularly to the ARRIVE guidelines point 3b ('Explain how and why the animal species and model being used can address the scientific objectives and, where appropriate, the study's relevance to human biology', point 9c ('Welfare-related assessments and interventions that were carried out prior to, during, or after the experiment') and point 17a ('Give details of all important adverse events in each experimental group'). The Editors will not accept papers reporting work carried out involving procedures that cause or are considered likely to cause distress or suffering which would confound the outcomes of the experiments, or experiments that have not been reviewed and approved by an animal experimentation ethics committee or regulatory organisation.

*Required disclosures:* Where a paper reports studies involving vertebrate animals, authors must state in the Experimental Methods section the institutional and national guidelines for the care and use of animals that were followed and that all experimental procedures involving animals were approved by the [insert name of the ethics committee or other approving body; wherever possible authors should also insert a specific ethics/approval number].

## Manuscript Format

The requirements of BJN are in accordance with the Uniform Requirements for Manuscripts Submitted to Biomedical Journals produced by the ICMJE.

Typescripts should be prepared with 1.5 line spacing and wide margins (2 cm), the preferred font being Times New Roman size 12. At the ends of lines, words should not be hyphenated unless hyphens are to be printed. **Line numbering and page numbering are required.**

Manuscripts should be organised as follows:

***Cover Letter***
Papers should be accompanied by a cover letter including a brief summary of the work and a short explanation of how it advances nutritional science. The text for the cover letter should be entered in the appropriate box as part of the online submission process.

***Title Page***
The title page should include:
1. The title of the article;
2. Authors' names;

3. Name and address of department(s) and institution(s) to which the work should be attributed for each author;
4. Name, mailing address, email address, telephone and fax numbers of the author responsible for correspondence about the manuscript;
5. A shortened version of the title, not exceeding 45 characters (including letters and spaces) in length;
6. At least four keywords or phrases (each containing up to three words).

Authors' names should be given without titles or degrees and one forename may be given in full. Identify each author's institution by a superscript number (e.g. A.B. Smith[1]) and list the institutions underneath and after the final author.

If the paper is one of a series of papers that have a common main title followed by a subtitle specific to the individual paper, numbering should not be used to indicate the sequence of papers. The format should be 'common title: specific subtitle', with a short common title, e.g. 'Partitioning of limiting protein and energy in the growing pig: testing quantitative rules against experimental data'.

***Abstract***
Each paper must open with an unstructured abstract of **not more than 250 words**. The abstract should be a single paragraph of continuous text without subheadings outlining the aims of the work, the experimental approach taken, the principal results (including effect size and the results of statistical analysis) and the conclusions and their relevance to nutritional science.

***Introduction***
It is not necessary to introduce a paper with a full account of the relevant literature, but the introduction should indicate briefly the nature of the question asked and the reasons for asking it. It should be **no longer than two manuscript pages**.

***Experimental methods***
The methods section must include a subsection that describes the methods used for statistical analysis (see the section on statistical analysis in the appendix below) and the sample size must be justified by the results of appropriate calculations and related to the study outcomes.

For studies involving humans subjects or experimental animals, the Methods section must include a subsection that reports the appropriate ethical approvals for the study (see Ethical Standards above).

All analytical procedures must be accompanied by a statement of within and between assay precision.

*PCR analysis:* Where experiments involve measurement of mRNA including microarray analysis, for analysis of individual genes, mRNA should be measured by quantitative RTPCR. A statement about the quality and integrity of the RNA must be provided together with the results of eletrophoretic analysis of the purity of the PCR products. Unless published elsewhere, full details of the oligonuceoltide primers and of the PCR protocol must be stated either in the text or in Supplementary Material. The stability of reference genes used for normalisation of PCR data must be reported for the experimental conditions described. Where possible, analysis of mRNA levels should be accompanied by assessment of either protein levels or activities.

*Microarray analysis:* Studies involving microarray analysis of mRNA must conform to the "Minimum Information about a Microarray Experiment" (MIAME) guidelines including deposition of the raw data in an appropriate repository (the Access Code must be state din the Methods). All microarray experiments must be accompanied by appropriate validation by quantitative RTPCR.

***Results***
These should be given as concisely as possible, using figures or tables as appropriate. Data must not be duplicated in tables and figures.

***Discussion***
While it is generally desirable that the presentation of the results and the discussion of their significance should be presented separately, there may be occasions when combining these sections may be beneficial. Authors may also find that additional or alternative sections such as 'conclusions' may be useful. The discussion should be **no longer than five manuscript pages**.

***Acknowledgments***
Here you may acknowledge individuals or organizations that provided advice and/or support (non-financial). Formal financial support and funding should be listed in the following section.

***Financial Support***
Please provide details of the sources of financial support for all authors, including grant numbers. For example, "This work was supported by the Medical research Council (grant number XXXXXXX)". Multiple grant numbers should be separated by a comma and space, and where research was funded by more than one agency the different agencies should be separated by a semi-colon, with "and" before the final funder. Grants held by different authors should be identified as belonging to individual authors by the authors' initials. For example, "This work was supported by the Wellcome Trust (A.B., grant numbers XXXX, YYYY), (C.D., grant number ZZZZ); the Natural Environment Research Council (E.F., grant number FFFF); and the National Institutes of Health (A.B., grant number GGGG), (E.F., grant number HHHH)".

This disclosure is particularly important in the case of research that is supported by industry. Support from industry not only includes direct financial support for the study but also support in kind such as provision of medications, equipment, kits or reagents without charge or at reduced cost and provision of services such as statistical analysis; all such support must be disclosed here and if no such support was received this must be stated.
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***Conflict of Interest***
Please provide details of all known financial, professional and personal relationships with the potential to bias the work. Where no known conflicts of interest exist, please include the following statement: "None."

For more information on what constitutes a conflict of interest, please see the International Committee of Medical Journal Editors (ICMJE) guidelines.

***Authorship***
Please provide a very brief description of the contribution of each author to the research. Their roles in formulating the research question(s), designing the study, carrying it out, analysing the data and writing the article should be made plain.

***References***
Number references consecutively in the order in which they first appear in the text using superscript Arabic numerals in parentheses, e.g. 'The conceptual difficulty of this approach has recently been highlighted[1,2–4],. If a reference is cited more than once the same number should be used each time. References cited only in tables and figure legends should be numbered in sequence from the last number used in the text and in the order of mention of the individual tables and figures in the text.

Names and initials of authors of unpublished work should be given in the text as 'unpublished results' and not included in the References.

At the end of the paper, on a page(s) separate from the text, references should be listed in numerical order using the Vancouver system. When an article has more than three authors only the names of the first three authors should be given followed by '*et al*.' The issue number should be omitted if there is continuous pagination throughout a volume. Titles of journals should appear in their abbreviated form using the NCBI LinkOut page. References to books and monographs should include the town of publication and the number of the edition to which reference is made. References to material available on websites should include the full Internet address, and the date of the version cited.

Examples of correct forms of references are given below.

*Journal articles*
1. Setchell KD, Faughnan MS, Avades T *et al*. (2003) Comparing the pharmacokinetics of daidzein and genistein with the use of 13C-labeled tracers in premenopausal women. *Am J Clin Nutr* 77, 411–419.

2. Barker DJ, Winter PD, Osmond C *et al*. (1989) Weight in infancy and death from ischaemic heart disease. *Lancet* ii, 577–580.
3. Forchielli ML & Walker WA (2005) The role of gut-associated lymphoid tissues and mucosal defence. *Br J Nutr* 93, Suppl. 1, S41–S48.
4. Skurk T, Herder C, Kraft I *et al*. (2004) Production and release of macrophage migration inhibitory factor from human adipocytes. *Endocrinology* (Epublication ahead of print version).

*Books and monographs*
5. Bradbury J (2002) Dietary intervention in edentulous patients. PhD Thesis, University of Newcastle.
6. Ailhaud G & Hauner H (2004) Development of white adipose tissue. In *Handbook of Obesity. Etiology and Pathophysiology*, 2nd ed., pp. 481–514 [GA Bray and C Bouchard, editors]. New York: Marcel Dekker.
7. Bruinsma J (editor) (2003) *World Agriculture towards 2015/2030: An FAO Perspective*. London: Earthscan Publications.
8. World Health Organization (2003) *Diet, Nutrition and the Prevention of Chronic Diseases. Joint WHO/FAO Expert Consultation. WHO Technical Report Series* no. 916. Geneva: WHO.
9. Keiding L (1997) *Astma, Allergi og Anden Overfølsomhed i Danmark – Og Udviklingen 1987–199I* (*Asthma, Allergy and Other Hypersensitivities in Denmark, 1987–1991*). Copenhagen, Denmark: Dansk Institut for Klinisk Epidemiologi.

*Sources from the internet*
10. Nationmaster (2005) HIV AIDS – Adult prevalence rate. http://www.nationmaster.com/graph-T/hea_hiv_aid_adu_pre_rat (accessed June 2013).

***Figures***
Figures should be supplied as separate electronic files. Figure legends should be grouped in a section at the end of the manuscript text. Each figure should be clearly marked with its number and separate panels within figures should be clearly marked (a), (b), (c) etc. so that they are easily identifiable when the article and figure files are merged for review. Each figure, with its legend, should be comprehensible without reference to the text and should include definitions of abbreviations. The nature of the information displayed in the figures (e.g. mean (SEM)) and the statistical test used must be stated.

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***Tables***
Tables should be placed in the main manuscript file at the end of the document, not within the main text. Be sure that each table is cited in the text. Tables should carry headings describing their content and should be comprehensible without reference to the text. Tables should not be subdivided by ruled lines.

The dimensions of the values, e.g. mg/kg, should be given at the top of each column. Separate columns should be used for measures of variance (SD, SE etc.), the ± sign should not be used. The number of decimal places used should be standardized; for whole numbers 1.0, 2.0 etc. should be used. Shortened forms of the words weight (wt) height (ht) and experiment (Expt) may be used to save space in tables, but only Expt (when referring to a specified experiment, e.g. Expt 1) is acceptable in the heading.

Footnotes for table legends are given in the following order: (1) abbreviations, (2) superscript letters, (3) symbols. Abbreviations are given in the format: RS, resistant starch. Abbreviations in tables must be defined in footnotes in the order that they appear in the table (reading from left to right across the table, then down each column). Symbols for footnotes should be used in the sequence: *†‡§‖¶, then ** etc. (omit * or †, or both, from the sequence if they are used to indicate levels of significance).

For indicating statistical significance, superscript letters or symbols may be used. Superscript letters are useful where comparisons are within a row or column and the level of significance is uniform, e.g. '$^{a,b,c}$Mean values within a column with unlike superscript letters were significantly different ($P$<0·05)'. Symbols are useful for indicating significant differences between rows or columns, especially where different levels of significance are found, e.g. 'Mean values were significantly different from those of the control group: *$P$<0·05, **$P$<0·01, ***$P$<0·001'. The symbols used for $P$ values in the tables must be consistent.

***Supplementary material***
Additional data (e.g. data sets, large tables) relevant to the paper can be submitted for publication online only, where they are made available via a link from the paper. The paper should stand alone without these data. Supplementary Material must be cited in a relevant place in the text of the paper.

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## APPENDIX: MATHEMATICAL MODELLING, STATISTICS AND NOMENCLATURE

### Mathematical modelling of nutritional processes

Papers in which mathematical modelling of nutritional processes forms the principal element will be considered for publication provided: (a) they are based on sound biological and mathematical principles; (b) they advance nutritional concepts or identify new avenues likely to lead to such advances; (c) assumptions used in their construction are fully described and supported by appropriate argument; (d) they are described in such a way that the nutritional purpose is clearly apparent; (e) the contribution of the model to the design of future experimentation is clearly defined.

### Units

Results should be presented in metric units according to the International System of Units (see Quantities, Units and Symbols in Physical Chemistry, 3rd ed. (2007) Cambridge: RSC Publishing), and Metric Units, Conversion Factors and Nomenclature in Nutritional and Food Sciences (1972) London: The Royal Society – as reproduced in *Proceedings of the Nutrition Society* (1972) **31**, 239–247). SI units should be used throughout the paper. The author will be asked to convert any values that are given in any other form. The only exception is where there is a unique way of expressing a particular variable that is in widespread use. Energy values must be given in Joules (MJ or kJ) using the conversion factor 1 kcal = 4.184 kJ. If required by the author, the value in kcal can be given afterwards in parentheses. Temperature is given in degrees Celsius (°C). Vitamins should be given as mg or µg, not as IU.

For substances of known molecular mass (Da) or relative molecular mass, e.g. glucose, urea, Ca, Na, Fe, K, P, values should be expressed as mol/l; for substances of indeterminate molecular mass (Da) or relative molecular mass, e.g. phospholipids, proteins, and for trace elements, e.g. Cu, Zn, then g/l should be used. The 24 h clock should be used, e.g. 15.00 hours.

Units are: year, month, week, d, h, min, s, kg, g, mg, µg, litre, ml, µl, fl. To avoid misunderstandings, the word litre should be used in full, except in terms like g/l. Radioactivity should be given in becquerels (Bq or GBq) not in Ci. 1 MBq = 27·03 µCi (1Bq = 1 disintegration/s).

### Statistical treatment of results

Data from individual replicates should not be given for large experiments, but may be given for small studies. The methods of statistical analysis used should be described, and references to statistical analysis packages included in the text, for example: Statistical Analysis Systems statistical software package version 6.11 (SAS Institute, Cary, NC, USA). The description should provide enough information for a statistician with access to the data to reproduce the results presented. Information such as analysis of variance tables should be given in the paper only if they are relevant to the discussion. A statement of the number of replicates, their average value and some appropriate measure of variability is usually sufficient. Authors must state whether their data follow a Gaussian distribution or not, and the choice of statistical tests must be consistent with the distribution of the data.

***Justification for the sample size must be given***. If the study is based on a power calculation, details of this should be provided including the desired effect size and power as well as the estimate of variability that was used.

Comparisons between means can be made by using either confidence intervals (CI) or significance tests. The most appropriate of such measures is usually the standard error of a difference between means (SED) or the standard errors of the means (SEM). The SEM represents the uncertainty associated with the estimation of a given mean and is not directly related to the SED or comparisons among means in mixed models as it is in fixed effects models. The SED estimates the uncertainty associated with the difference between two means; because it is used in various mean comparisons tests, SED can be implied within the tests *per se*. The standard deviation (SD) is more useful only when there is specific interest in the variability of individual values and no treatment means are being compared. The sample size (n per treatment) should also be stated in text or in the table. Standard analysis of variance assumes homogeneous variance. Unless there is heterogeneous variance, as tested by an appropriate statistic, or there is unequal n, a pooled SEM or SED simplifies tables and is preferred. The number of decimal places quoted should be sufficient but not excessive. If data transformations are being used, text should clearly state which variables have been transformed in which way and how that was decision was reached (e.g., tests for normality, diagnostic plots).

Authors should consider whether their study is rather of explorative (hypothesis-generating) or confirmative (hypothesis-testing) nature. This is particularly important when results from multiple tests are being presented, which can be the case when various treatments are being compared, multiple endpoints are considered, or different subgroups are being analysed. Such multiple testing issues occur often in exploratory studies, and authors should take care not to overstate findings in these situations. At least the number of significant results should be compared to the number of tests compared, where 1 in 20 findings would be expected by chance alone. Methods that control certain error rates (experiment-wise error rate, false discovery rate, etc…) such as post-hoc tests can be used in this context, but are not obligatory, as long as the exploratory nature of the results is made clear. In confirmative studies, pre-planned comparisons or primary endpoints should be stated upfront and analysed by appropriate tools such as contrast testing for pre-planned comparisons. Unnecessary multiple testing corrections with respect to secondary comparisons or endpoints should be avoided to not compromise the power of the study.

Measurements on the same experimental unit over time or in different sections of tissue generally are not independent. If the repeated measures are taken from the same animal or human subject, which are expected to be randomly chosen to represent a population, an appropriate mixed model should be fitted while investigating the best covariance of error structures. All major statistical software packages offer a wide variety of structures; the one chosen should be stated.

If comparisons between means are made using CI, the format for presentation is, e.g. 'difference between means 0·73 (95 % CI 0·314, 1·36) g'. If significance tests are used, a statement that the difference between the means for two groups of values is (or is not) statistically significant should include the level of significance attained, preferably as an explicit *P* value (e.g. *P*=0·016 or *P*=0·32) rather than as a range (e.g. *P*<0·05 or *P*>0·05). It should be stated whether the significance levels quoted are one-sided or two-sided (when relevant). Where a multiple comparison procedure is used, a description or explicit reference should be given. Where appropriate, a superscript notation may be used in tables to denote levels of significance; similar superscripts should denote lack of a significant difference.

When the method of analysis is unusual, or if the experimental design is at all complex, further details (e.g., experimental plan, raw data, confirmation of assumptions, analysis of variance tables, etc.) should be included. Adequate detail should be provided for a subsequent reader to interpret and potentially repeat the approach used. For example, the statistical model should be provided or described in adequate detail, and all blocking factors and criteria should be provided. Regressions should provide appropriate estimates of parameter uncertainty (not necessarily provided by graphing software).

## Chemical formulas

These should be written as far as possible on a single horizontal line. With inorganic substances, formulas may be used from first mention. With salts, it must be stated whether or not the anhydrous material is used, e.g. anhydrous $CuSO_4$, or which of the different crystalline forms is meant, e.g. $CuSO_4.5H_2O$, $CuSO_4.H_2O$.

## Descriptions of solutions, compositions and concentrations

Solutions of common acids, bases and salts should be defined in terms of molarity (M), e.g. 0.1 M-$NaH_2PO_4$. Compositions expressed as mass per unit mass (w/w) should have values expressed as ng, µg, mg or g per kg; similarly for concentrations expressed as mass per unit volume (w/v), the denominator being the litre. If concentrations or compositions are expressed as a percentage, the basis for the composition should be specified (e.g. % (w/w) or % (w/v) etc.). The common measurements used in nutritional studies, e.g. digestibility, biological value and net protein utilization, should be expressed as decimals rather than as percentages, so that amounts of available nutrients can be obtained from analytical results by direct multiplication. See *Metric Units, Conversion Factors and Nomenclature in Nutritional and Food Sciences*. London: The Royal Society, 1972 (para. 8).

## Cell lines

The Journal expects authors to deposit cell lines (including microbial strains) used in any study to be published in publicly accessible culture collections, for example, the European Collection of Cell Cultures (ECACC) or the American Type Culture Collection (ATCC) and to refer to the collection and line or strain numbers in the text (e.g. ATCC 53103). Since the authenticity of subcultures of culture collection specimens that are distributed by individuals cannot be ensured, authors should indicate laboratory line or strain designations and donor sources as well as original culture collection identification numbers.

## Gene nomenclature and symbols

The use of symbols and nomenclature recommended by the HUGO Gene Nomenclature Committee is encouraged. Information on human genes is also available from Entrez Gene, on mouse genes from the Mouse Genome Database and on rat genes from the Rat Genome Database.

## Nomenclature of vitamins

Most of the names for vitamins and related compounds that are accepted by the Editors are those recommended by the IUNS Committee on Nomenclature. See *Nutrition Abstracts and Reviews* (1978) **48**A, 831–835.

| *Acceptable name* | *Other names** |
|---|---|
| *Vitamin A* | |
| Retinol | Vitamin $A_1$ |
| Retinaldehyde, retinal | Retinene |
| Retinoic acid (all-trans or 13-cis) | Vitamin $A_1$ acid |
| 3-Dehydroretinol | Vitamin $A_2$ |
| *Vitamin D* | |
| Ergocalciferol, ercalciol | Vitamin $D_2$ calciferol |
| Cholecalciferol, calciol | Vitamin $D_3$ |
| *Vitamin E* | |
| α-, β- and γ-tocopherols plus tocotrienols | |
| *Vitamin K* | |
| Phylloquinone | Vitamin $K_1$ |
| Menaquinone-n (MK-n)† | Vitamin $K_2$ |
| Menadione | Vitamin $K_3$, menaquinone, menaphthone |
| *Vitamin $B_1$* | |
| Thiamin | Aneurin(e), thiamine |
| *Vitamin $B_2$* | |
| Riboflavin | Vitamin G, riboflavine, lactoflavin |
| *Niacin* | |
| Nicotinamide | Vitamin PP |
| Nicotinic acid | |
| *Folic Acid* | |
| Pteroyl(mono)glutamic acid | Folacin, vitamin $B_c$ or M |
| *Vitamin $B_6$* | |
| Pyridoxine | Pyridoxol |
| Pyridoxal | |
| Pyridoxamine | |
| *Vitamin $B_{12}$* | |
| Cyanocobalamin | |
| Hydroxocobalamin | Vitamin $B_{12a}$ or $B_{12b}$ |
| Aquocobalamin | |
| Methylcobalamin | |
| Adenosylcobalamin | |
| *Inositol* | |
| *Myo*-inositol | *Meso*-inositol |
| *Choline* | |
| *Pantothenic acid* | |
| *Biotin* | Vitamin H |
| *Vitamin C* | |
| Ascorbic acid | |
| Dehydroascorbic acid | |

*Including some names that are still in use elsewhere, but are not used by BJN.
†Details of the nomenclature for these and other naturally-occurring quinones should follow the Tentative Rules of the IUPAC-IUB Commission on Biochemical Nomenclature (see *European Journal of Biochemistry* (1975) **53**, 15–18).

The terms **vitamin A**, **vitamin** C and **vitamin D** may still be used where appropriate, for example in phrases such as 'vitamin A deficiency', 'vitamin D activity'.

The term **vitamin E** should be used as the descriptor for all tocol and tocotrienol derivatives exhibiting qualitatively the biological activity of α-tocopherol. The term **tocopherols** should be used as the generic descriptor for all methyl tocols. Thus, the term **tocopherol** is not synonymous with the term **vitamin E**.

The term **vitamin K** should be used as the generic descriptor for 2-methyl-1,4-naphthoquinone (menaphthone) and all derivatives exhibiting qualitatively the biological activity of phylloquinone (phytylmenaquinone).

The term **niacin** should be used as the generic descriptor for pyridine 3-carboxylic acid and derivatives exhibiting qualitatively the biological activity of nicotinamide.

The term **vitamin $B_6$** should be used as the generic descriptor for all 2-methylpyridine derivatives exhibiting qualitatively the biological activity of pyridoxine.

Regarding **folate**, due to the wide range of C-substituted, unsubstituted, oxidized, reduced and mono- or polyglutamyl side-chain derivatives of pteroylmonoglutamic acid that exist in nature, it is not possible to provide a complete list. Authors are encouraged to use either the generic name or the correct scientific name(s) of the derivative(s), as appropriate for each circumstance.

The term **vitamin $B_{12}$** should be used as the generic descriptor for all corrinoids exhibiting qualitatively the biological activity of cyanocobalamin. The term **corrinoids** should be used as the generic descriptor for all compounds containing the corrin nucleus and thus chemically related to cyanocobalamin. The term **corrinoid** is not synonymous with the term **vitamin $B_{12}$**.

The terms **ascorbic acid** and **dehydroascorbic acid** will normally be taken as referring to the naturally-occurring L-forms. If the subject matter includes other optical isomers, authors are encouraged to include the L- or D- prefixes, as appropriate. The same is true for all those vitamins which can exist in both natural and alternative isomeric forms.

Weight units are acceptable for the amounts of vitamins in foods and diets. For concentrations in biological tissues, SI units should be used; however, the authors may, if they wish, also include other units, such as weights or international units, in parentheses. See *Metric Units, Conversion Factors and Nomenclature in Nutritional and Food Sciences* (1972) paras 8 and 14–20. London: The Royal Society.

## Nomenclature of fatty acids and lipids

In the description of results obtained for the analysis of fatty acids by conventional GLC, the shorthand designation proposed by Farquhar JW, Insull W, Rosen P, Stoffel W & Ahrens EH (*Nutrition Reviews* (1959), **17**, Suppl.) for individual fatty acids should be used in the text, tables and figures. Thus, 18 : 1 should be used to represent a fatty acid with eighteen carbon atoms and one double bond; if the position and configuration of the double bond is unknown. The shorthand designation should also be used in the abstract. If the positions and configurations of the double bonds are known, and these are important to the discussion, then a fatty acid such as linoleic acid may be referred to as *cis*-9,*cis*-12-18 : 2 (positions of double bonds related to the carboxyl carbon atom 1). However, to illustrate the metabolic relationship between different unsaturated fatty acid families, it is sometimes more helpful to number the double bonds in relation to the terminal methyl carbon atom, *n*. The preferred nomenclature is then: 18 : 3*n*-3 and 18 : 3*n*-6 for α-linolenic and γ-linolenic acids respectively; 18 : 2*n*-6 and 20 : 4*n*-6 for linoleic and arachidonic acids respectively and 18 : 1*n*-9 for oleic acid. Positional isomers such as α- and γ-linolenic acid should always be clearly distinguished. It is assumed that the double bonds are methylene-interrupted and are of the *cis*-configuration (see Holman RT in *Progress in the Chemistry of Fats and Other Lipids* (1966) vol. 9, part 1, p. 3. Oxford: Pergamon Press). Groups of fatty acids that have a common chain length but vary in their double bond content or double bond position should be referred to, for example, as $C_{20}$ fatty acids or $C_{20}$ PUFA. The modern nomenclature for glycerol esters should be used, i.e. triacylglycerol, diacylglycerol, monoacylglycerol *not* triglyceride, diglyceride, monoglyceride. The form of fatty acids used in diets should be clearly stated, i.e. whether ethyl esters, natural or refined fats or oils. The composition of the fatty acids in the dietary fat and tissue fats should be stated clearly, expressed as mol/100 mol or g/100 g total fatty acids.

## Nomenclature of micro-organisms

The correct name of the organism, conforming with international rules of nomenclature, should be used. If desired, synonyms may be added in parentheses when the name is first mentioned. Names of bacteria should conform to the current Bacteriological Code and the opinions issued by the International Committee on Systematic Bacteriology. Names of algae and fungi must conform to the current International Code of Botanical Nomenclature. Names of protozoa should conform to the current International Code of Zoological Nomenclature.

## Nomenclature of plants

For plant species where a common name is used that may not be universally intelligible, the Latin name in italics should follow the first mention of the common name. The cultivar should be given where appropriate.

## Other nomenclature, symbols and abbreviations

Authors should consult recent issues of BJN for guidance. The IUPAC rules on chemical nomenclature should be followed, and the recommendations of the Nomenclature Committee of IUBMB and the IUPAC-IUBMB Joint Commission on Biochemical Nomenclature and Nomenclature Commission of IUBMB in *Biochemical Nomenclature and Related Documents* (1992), 2nd ed., London: Portland Press (http://www.chem.qmul.ac.uk/iupac/bibliog/white.html). The symbols and abbreviations, other than units, are essentially those listed in *British Standard* 5775 (1979–1982), *Specifications for Quantities, Units and Symbols*, parts 0–13. Day should be abbreviated to d, for example 7 d, except for 'each day', '7th day' and 'day 1'.

Elements and simple chemicals (e.g. Fe and $CO_2$) can be referred to by their chemical symbol (with the exception of arsenic and iodine, which should be written in full) or formula from the first mention in the text; the title, text and table headings, and figure legends can be taken as exceptions,. Well-known abbreviations for chemical substances may be used without explanation, thus: RNA for ribonucleic acid and DNA for deoxyribonucleic acid. Other substances that are mentioned frequently (five or more times) may also be abbreviated, the abbreviation being placed in parentheses at the first mention, thus: lipoprotein lipase (LPL), after that, LPL, and an alphabetical list of abbreviations used should be included. Only accepted abbreviations may be used in the title and text headings. If an author's initials are mentioned in the text, they should be distinguished from other abbreviations by the use of stops, e.g. 'one of us (P. J. H.)...'. For UK counties the official names given in the *Concise Oxford Dictionary* (1995) should be used and for states of the USA two-letter abbreviations should be used, e.g. MA (not Mass.) and IL (not Ill.). Terms such as 'bioavailability' or 'available' may be used providing that the use of the term is adequately defined.

Spectrophotometric terms and symbols are those proposed in *IUPAC Manual of Symbols and Terminology for Physicochemical Quantities and Units* (1979) London: Butterworths. The attention of authors is particularly drawn to the following symbols: m (milli, $10^{-3}$), μ (micro, $10^{-6}$), n (nano, $10^{-9}$) and p (pico, $10^{-12}$). Note also that ml (millilitre) should be used instead of cc, μm (micrometre) instead of μ (micron) and μg (microgram) instead of γ.

Numerals should be used with units, for example, 10 g, 7 d, 4 years (except when beginning a sentence, thus: 'Four years ago...'); otherwise, words (except when 100 or more), thus: one man, ten ewes, ninety-nine flasks, three times (but with decimal, 2.5 times), 100 patients, 120 cows, 136 samples.

## Abbreviations

The following abbreviations are accepted without definition by BJN:

| | |
|---|---|
| ADP (GDP) | adenosine (guanosine) 5'-disphosphate |
| AIDS | acquired immune deficiency syndrome |
| AMP (GMP) | adenosine (guanosine) 5'-monophosphate |
| ANCOVA | analysis of covariance |
| ANOVA | analysis of variance |
| apo | apolipoprotein |
| ATP (GTP) | adenosine (guanosine) 5'-triphosphate |
| AUC | area under the curve |
| BMI | body mass index |
| BMR | basal metabolic rate |

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|---|---|
| bp | base pair |
| BSE | bovine spongiform encephalopathy |
| CHD | coronary heart disease |
| CI | confidence interval |
| CJD | Creutzfeldt-Jacob disease |
| CoA and acyl-CoA | co-enzyme A and its acyl derivatives |
| CV | coefficient of variation |
| CVD | cardiovascular disease |
| Df | degrees of freedom |
| DHA | docosahexaenoic acid |
| DM | dry matter |
| DNA | deoxyribonucleic acid |
| dpm | disintegrations per minute |
| EDTA | ethylenediaminetetra-acetic acid |
| ELISA | enzyme-linked immunosorbent assay |
| EPA | eicosapentaenoic acid |
| Expt | experiment (for specified experiment, e.g. Expt 1) |
| FAD | flavin-adenine dinucleotide |
| FAO | Food and Agriculture Organization (except when used as an author) |
| FFQ | food-frequency questionnaire |
| FMN | flavin mononucleotide |
| GC | gas chromatography |
| GLC | gas–liquid chromatography |
| GLUT | glucose transporter |
| GM | genetically modified |
| Hb | haemoglobin |
| HDL | high-density lipoprotein |
| HEPES | 4-(2-hydroxyethyl)-1-piperazine-ethanesulfonic acid |
| HIV | human immunodeficiency virus |
| HPLC | high-performance liquid chromatography |
| Ig | immunoglobulin |
| IHD | ischaemic heart disease |
| IL | interleukin |
| IR | infra red |
| Kb | kilobases |
| $K_m$ | Michaelis constant |
| LDL | low-density lipoprotein |
| MHC | major histocompatibility complex |
| MRI | magnetic resonance imaging |
| MS | mass spectrometry |
| MUFA | monounsaturated fatty acids |
| NAD+, NADH | oxidized and reduced nicotinamide-adenine dinucleotide |
| NADP+, NADPH | oxidized and reduced nicotinamide-adenine dinucleotide phosphate |
| NEFA | non-esterified fatty acids |
| NF-κB | nuclear factor kappa B |
| NMR | nuclear magnetic resonance |
| NS | not significant |
| NSP | non-starch polysaccharide |
| OR | odds ratio |
| PAGE | polyacrylamide gel electrophoresis |
| PBS | phosphate-buffered saline |
| PCR | polymerase chain reaction |
| PG | prostaglandin |
| PPAR | peroxisome proliferator-activated receptor |
| PUFA | polyunsaturated fatty acids |
| RDA | recommended dietary allowance |
| RER | respiratory exchange ratio |
| RIA | radioimmunoassay |
| RMR | resting metabolic rate |
| RNA, mRNA etc. | ribonucleic acid, messenger RNA etc. |
| rpm | revolutions per minute |
| RT | reverse transcriptase |

| | |
|---|---|
| SCFA | short-chain fatty acids |
| SDS | sodium dodecyl sulphate |
| SED | standard error of the difference between means |
| SFA | saturated fatty acids |
| SNP | single nucleotide polymorphism |
| TAG | triacylglycerol |
| TCA | trichloroacetic acid |
| TLC | thin-layer chromatography |
| TNF | tumour necrosis factor |
| UN | United Nations (except when used as an author) |
| UNICEF | United Nations International Children's Emergency Fund |
| UV | ultra violet |
| VLDL | very-low-density lipoprotein |
| $V_{O2}$ | $O_2$ consumption |
| $V_{O2max}$ | maximum $O_2$ consumption |
| WHO | World Health Organization (except when used as an author) |

Use of three-letter versions of amino acids in tables: Leu, His, etc.
CTP, UTP, GTP, ITP, as we already use ATP, AMP etc.

## Disallowed words and phrases

The following are disallowed by BJN:

- deuterium or tritium (use $^2H$ and $^3H$)
- c.a. or around (use approximately or about)
- canola (use rapeseed)
- ether (use diethyl ether)
- free fatty acids (use NEFA)
- isocalorific/calorie (use isoenergetic/energy)
- quantitate (use quantify)
- unpublished data or observations (use unpublished results)