

Factors influencing delay in presentation and their impact on cancer stage in women with a diagnosis of breast cancer in South Africa

Factors influencing delay in presentation in women with a diagnosis of breast cancer in South Africa and their impact on cancer stage at presentation – [original title]

A thesis submitted to the Faculty of Health Sciences, University of Witwatersrand,
in fulfilment of the requirements for the degree of Doctor of Philosophy

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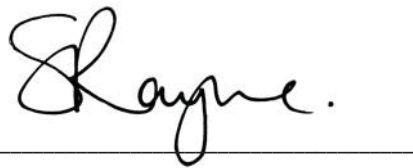
Johannesburg, 2018

Declaration

I, Sarah Louise Rayne, declare that the work contained in this thesis is my own work, except to the extent indicated in the acknowledgement sections.

This thesis is being submitted for the degree of Doctor of Philosophy, at the University of Witwatersrand, Johannesburg, South Africa.

This work has not been submitted for any other degree or examination in this or any other university.

A handwritten signature in black ink, reading "Rayne.", is positioned above a horizontal line. The signature is written in a cursive style with a prominent initial 'R'.

Sarah Louise Rayne (PHD Candidate)

Thursday, 31 January 2019

Publications

The following peer reviewed publications are included as part of this thesis (order of publication):

1. Rayne S, Schnippel K, Wright K, Kruger D, Firnhaber C, Benn C. Fear of Treatments Surpasses Demographic and Socioeconomic Factors in Affecting Patients With Breast Cancer in Urban South Africa. *J Glob Oncol* 2016;3:125–34. doi:10.1200/JGO.2015.002691.
2. Rayne S, Schnippel K, Benn C, Kruger D, Wright K, Firnhaber C. The Effect of Access to Information on Beliefs Surrounding Breast Cancer in South Africa. *J Cancer Educ* 2017. doi:10.1007/s13187-017-1234-3.
3. Rayne S, Schnippel K, Kruger D, Benn C, Firnhaber C Delay to diagnosis and breast cancer stage in an urban South African breast clinic. Submitted to *South African Medical Journal* *S Afr Med J* 2019;109(3): doi:10.7196/samj.2019.v109i3.13283
4. Rayne S, Schnippel K, Grover S, Kruger D, Benn C, Firnhaber C The effect of beliefs about breast cancer on stage and delay to presentation: Results from a prospective study in urban South Africa. Submitted to *South African Journal of Surgery* *In press*
5. Rayne S, Schnippel K, Grover S, Fearnhead K, Kruger D, Benn C, Firnhaber C. Unraveling the South African Breast Cancer Story: The Relationship of Patients, Delay to Diagnosis, and Tumor Biology With Stage at Presentation in an Urban Setting. *Journal of Surgical Research*. 2019 Mar 1;235:181-9. doi: 10.1016/j.jss.2018.09.087

Presentations

The following reviewed abstracts have been accepted for presentation as part of this thesis (order of meeting):

1. **Rayne, S.**, Kruger, D., Wright, K., and Benn CA. “Under-estimating psycho-social issues in young women with breast cancer in South Africa, may seriously impact their ability to make informed treatment choices”
Winner of best oral presentation (student): Wits Health Sciences Research Day, September 2014
2. **Rayne, S.**, Kruger, D., Wright, K., and Benn CA. “Under-estimating psycho-social issues in young women with breast cancer in South Africa, may seriously impact their ability to make informed treatment choices” European School of Oncology Breast Cancer in Young Women Conference, Dublin, November 2014
3. **Rayne, S.**, Schnippel, K., Kruger, D., Wright, K., Firnhaber, C., and Benn, C. “Understanding the fears expressed by patients with a breast cancer diagnosis in urban South Africa” AORTIC (African Organisation for Research and Training in Cancer) conference, Marrakesh, Morocco, November 2015
4. **Rayne S.**, Schnippel K, Kruger D, Benn C, Wright K, and Firnhaber C. “The effect of access to information on beliefs of breast cancer patients toward their disease in urban South Africa: A cross-sectional descriptive study” Bert Myburgh Research Forum, November 2016
5. **Rayne, S.**, Schnippel, K., Benn, C., Kruger, D., Wright, K. and Firnhaber, C., "Attitudes and beliefs of breast cancer patients toward their disease in urban South Africa: A cross-sectional descriptive study" European Cancer Congress, Amsterdam, January 2017
6. **Rayne, S.**, Schnippel, K., Benn, C., Kruger, D., Wright, K. and Firnhaber, C., "Attitudes and beliefs of breast cancer patients toward their disease in urban South Africa: A cross-sectional descriptive study" Wits Cancer Research Symposium 2017
7. **Rayne S.**, Schnippel K, Fearnhead K, Grover S, Kruger D, Benn C, Firnhaber C “Unravelling the South African breast cancer story: the relationship of patients, delay to diagnosis and stage with tumour biology in an urban setting.” 11th European Breast Cancer Conference, Barcelona 2018

Regulations

Formatting and language

As prescribed by the Faculty of Health Sciences style guide the references are presented using the Vancouver format and are numbered in ascending order in the text and are listed in that order in the references. The references are referred to in the text by a number in square parenthesis (i.e. [2]). The references are not listed at the end of every chapter but a complete list is at the end of the thesis.

The results chapters are the published articles and are presented as they were on acceptance / submission. The text formatting has been adapted to match that of thesis, but the structure is that prescribed by the journal. For clarity all tables and figures are embedded, but the thesis has been referenced as one body of work.

The journal articles were submitted in English (United Kingdom) and for consistency this is carried through the thesis.

Permission to publish

There were five journal articles included in the thesis. Where the journal articles are currently published in open access journals with Creative Commons Attribution license they do not require additional permission to be reused or included in this thesis. Where permission is required, it has been sought and obtained (Appendix E). The remaining journal articles are currently under review and permission will be sought once they are accepted if required.

Abstract

Background

Breast cancer is the most common cancer in women in most low- and middle-income countries, and often presents at an advanced stage affecting prognosis irrespective of the care available. Studies from sub-Saharan Africa concerning patients with breast cancer are often presented as a homogeneous group with lack of education, awareness and access commonly cited as reasons for late stage and delay to presentation.

Study Rationale

This study was designed to explore this uniform characterisation of patients with breast cancer in three parts: first define the relationship of their demographic and socio-economic characteristics with their attitudes, fears and beliefs held regarding breast cancer and its treatment; then determine the relationship of socio-economic and psychosocial characteristics with a patient's stage at presentation, and delay to presentation; and finally investigate and understand the heterogeneity of breast cancer molecular biology in this population, and assess its independent contribution to late-stage disease.

Methods

A questionnaire was designed for distribution to breast cancer patients. It included questions about their characteristics, socio-economic circumstances, education, and ability to access care as well as their agreement to statements of knowledge and beliefs about breast cancer. In a pilot study, the questionnaire was distributed to 263 breast cancer patients at two sites (one government and one private health care facility) in Johannesburg.

Using a modified questionnaire including time to access care, patients attending the urban government open-access breast unit over a 14-month period with a new diagnosis of breast cancer were then recruited. The stage at presentation and molecular subtype for participants was recorded. The relationship of clinical stage and delay to presentation to demographic variables, beliefs and molecular subtypes were assessed through univariate and multivariate modified Poisson's regression methods of calculating odds ratio with 95% confidence intervals.

Results

The pilot study found that fears related to treatments were far stronger than those related to socio-economic barriers, and higher in young women under 40 years. Access to information was protective from adverse beliefs about cancer but positive expressions of cure and beating cancer were found equally in all women. Socio-economic status was a strong confounder of race and explained most of the racial differences in levels of fear.

In the final study, 252 women diagnosed with a new breast cancer completed the survey (response rate of 70.8%). Stage 3 (56.0%) was most common at presentation and nearly one third of all patients presented with T4 cancer. Total delay to present at the breast clinic was associated with locally advanced stage at presentation ($p=0.021$) and most delay occurred between acknowledging a breast symptom and seeking care. Self-reported transport difficulties predicted both advanced stage at presentation and delay to presentation of more than six months.

Invasive ductal carcinoma was most common (92.7%), and the most common subtype was Luminal B (57.9%) followed by Luminal A (21.5%), triple negative (13.9%) and HER2 positive (6.7%). HER2 overexpression remained an independent risk factor for late stage at presentation.

Conclusions

Participant's beliefs about their new breast cancer diagnosis and breast cancer in general were most commonly appropriate, and showed a low level of fatalism, in contrast to other studies in sub-Saharan Africa. Few beliefs or socio-economic factors influenced delay to presentation or stage at presentation, however this study found that tumour biology has a compelling place in understanding the aetiology of late-stage disease.

This thesis has contributed information to the complex interplay that exists between the patient, her environment and the breast tumour biology. It helps us address the issues of access to care, in both patients-related and treatment availability.