

Systems Delays in the Management of Malignant Breast Disease

by

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Declaration

I, Dr E Dalwai, hereby declare that the work on which this dissertation/ thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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Signature Ebrahim Dalwai

Date ...07th December 2015

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Abbreviations used in this document

WHO:	World Health Organisation
USA:	United States of America
ASIR:	Age Standardised Incidence Ratio
MDT:	Multi-disciplinary Team
SA:	South Africa
SPSS:	Statistical Program for Social Sciences
GP:	General Practitioner
OPD:	Out patients department (clinic setting)
SOPD:	surgical out patients department
FNAC:	fine needle aspiration cytology
WLE:	wide local excision
CXR:	Chest x-ray
GDP:	Gross Domestic Product
USD:	United States Dollar

Glossary of terms used in this document

Patient Delay: These are delays experienced before engaging with the health care system from time of onset of symptoms.

Systems Delays: These are delays experienced after engaging with the health care system. Also referred to as doctor delays

Modified Radical Mastectomy	An operation to remove the breast whilst preserving the pectoral muscles and up to level II nodes (Auchincloss variation)
Sentinel Lymph Node Biopsy	An operation to remove 2 or 3 identified lymph nodes using radiolabelled isotope or blue dye to assess whether the breast cancer has spread to the axilla
Breast Conserving Surgery	An operation to treat breast cancer with preservation of a cosmetically acceptable breast mound. The tumour with a surrounding cuff of normal breast tissue is excised. It always requires radiotherapy
Neo-adjuvant Therapy	A form of therapy that occurs before surgery. It may include any of chemo, radio, hormonal or biologic therapy
Adjuvant Therapy	Any form of therapy that occurs after surgery. It may include any of chemo, radio, hormonal or biologic therapy
Gross Domestic Product	The gross domestic product (GDP) represents the total value of all goods and services produced over a specific time period often used to assess the size of the economy.

PART A

Protocol

1. Title of study

System Delays in the management of Malignant Breast Disease

2. Investigators

E Dalwai, I Buccimazza

3. Introduction

Malignant breast disease remains a major health concern. It is the most common cancer in women worldwide and although more common in industrialized countries, the WHO reports increasing breast cancer trends worldwide ⁽¹⁾.

The annual incidence rate in the USA is 101 per 100 000⁽²⁾. In South Africa the overall age standard incidence ratio (ASIR) of breast cancer in 2010 was 25.86 per 100 000 compared to 25.1 per 100 000 in the previous report (1993-1995)^(3,4). A racial disparity remains between women in South Africa with incidence rates in SA Black women at 18.33 per 100 000 which are comparable with those reported in developing countries. Incidence rates in SA white women are 83.72 per 100 000 which are comparable with rates in industrialized countries Rates in SA Indian women are almost double those reported in Bombay, India ⁽³⁾

In under resourced countries like South Africa the disease initially comes to the attention of the general surgeon, usually at secondary level hospitals, where the diagnosis is confirmed and initial work-up commenced prior to presentation to the multidisciplinary team. In centers of excellence this is a seamless process involving radiology, pathology and nuclear medicine. In the state sector in South Africa this process is challenging, as it involves lengthy delays due to shortage of specialized staff in the above-mentioned disciplines.

At a secondary level hospital in 2008, it was noted that a considerable system delay in the diagnosis and work-up of breast cancer patients existed.

This observation was the stimulus for the study: to quantify the delays and use the information to improve service delivery in the management of breast cancer.

4. Aims

Primary Aim

Document the time delay and reasons from initial presentation at a secondary level hospital to initial assessment at the multi-disciplinary breast clinic at a tertiary level hospital.

Secondary Aims

- a. Document intervals between specific care steps in breast cancer diagnosis and treatment so as to identify unique problems
- b. Propose viable policy changes to decrease delay

5. Patients and Methods

A retrospective audit of all adult patients with histologically proven malignant breast disease referred from R K Khan's Hospital to the multi-disciplinary breast oncology clinic at Inkosi Albert Luthuli Central Hospital between Jan 2008 and Jan 2009. Data will be collected from hospital folders at both sites and cross referenced with an electronic database at Albert Luthuli Hospital. Data collected will include basic demographics along with dates for the initial visit, mammograms, tissue sampling, staging investigations and combined breast oncology clinic. This allows a total system delay and intermediate delays to be calculated. Data will be analysed using SPSS version 15.0 (SPSS Inc., Chicago, Ill, USA). Quantitative data including time in days between dates of entry and exit from the cohort and between intermediate dates will be summarized using mean, standard deviation and range, or median and inter-quartile range as appropriate. Sample size is estimated at 50-60 patients for the study period.

6. Exclusion criteria

Individuals whose folders cannot be located will be excluded. Those that default during work-up will be excluded from the overall analysis. Where it is possible they will be included in the relevant subset analysis.

Patients who were admitted for their work-up will be excluded from the formal analysis. These patients would complete radiological investigations sooner and were fast tracked to the multi-disciplinary clinic decreasing the average time delay.

7. Study Limitations

The main limitation is the inability to confirm that our patients are being upstaged by the delay in their work-up. This would have implications on their treatment and prognosis. It was found that patients were not being accurately staged at their initial presentation. Therefore, no conclusions can be made on effects of the system delay documented in this study.

The sample size is small, and could be seen as a limitation. However, it is a descriptive study attempting to identify a trend in a select group of patients.

8. Ethical considerations

The study has been approved by both the University of Kwazulu Biomedical Research Ethics Committee and University of Cape Town Human Research Ethics Committee. The electronic data files will be password protected and no identifying data will be reported. The investigators are part of the surgical team managing the study population ensuring no breach of confidentiality. This study has no bearing on clinical management decisions during the duration of the study period.

There are no conflicts of interest, and no funding from any source to disclose.

9. References

1. World Health Organisation. Executive summary. In: National Cancer Control Programmes: Policies and Managerial Guidelines. Geneva, Switzerland: WHO, 2002:i-xxiv

<http://www.who.int/cancer/media/en/414.pdf>

2. CDC WONDER United States cancer statistic, 1999-2005 mortality archive request. Atlanta, GA: Centres for Disease Control and Prevention, US Department of Health and Human Services; 2008.

3. Somdyala NI, Bradshaw D, Gelderblom WC, et al. Cancer incidence in a rural population of South Africa, 1998 - 2002. *Int J Cancer* 2010;127(10):2420-2429. [<http://dx.doi.org/10.1002/ijc.25246>]

4. Cancer in South Africa 2010 Full Report. National Cancer Registry. National Institute for Occupational Health.

http://www.nioh.ac.za/?page=cancer_statistics&id=163

10. Appendix A

Clinical Audit Data Sheet

Name Age

First Consultation

GP

OPD

SOPD

Imaging

Mammogram

Ultrasound Breast

Histology	procedure	results
FNAC		
Core needle biopsy		
WLE		

Further Investigations

Bloods

CXR

Ultrasound Abdomen

Admitted for work-up

Other

Breast Clinic

Multidisciplinary Breast Oncology Clinic

PART B

Literature Review

1. Introduction and Objectives

Breast Cancer is a common malignancy in South Africa with a reported incidence of 1 in 29 ⁽¹⁾. The management requires many disciplines working together to ensure successful outcomes. In resource poor settings ensuring affordable, quality healthcare is a challenge. This literature review serves to gain insights into the current literature on health systems delays in breast cancer and whether outcomes are affected. Health systems with resource constraints will be of specific interest as in South Africa costs are a limiting factor. The international literature will be used as a reference point to compare our data.

2. Breast Cancer Treatment

The management of breast cancer has historically been predominantly surgical. This has evolved with time to a multi modal treatment approach including chemotherapy, radiotherapy and hormonal therapy. The surgical options have similarly evolved from modified radical mastectomy and axillary clearances to include breast conserving therapy and sentinel lymph node biopsy. The main reason for this evolution towards less aggressive surgery has been population based screening and identification of early lesions. As management has evolved, decision-making has become more complex and the resources required have escalated.

The average female with breast cancer would require multiple visits to complete her triple assessment consisting of clinical examination, pathological diagnosis and radiological imaging ⁽²⁾. Once the diagnosis is confirmed, decisions regarding management have to be taken and effected. Delays to surgery or initial treatment affect both patients and their treating physicians. After recovery from surgery most patients will require adjuvant therapy with 6 cycles of chemotherapy that lasts for approximately 5 months. After breast conserving surgery radiotherapy is mandatory and will last for 4-6 weeks. Radiotherapy may also be offered to

patients with a high risk of local recurrence, irrespective of the type of surgery performed. Thereafter, females that have estrogen receptor positive tumours will require hormonal therapy for 5 years ⁽³⁾. Younger patients may consider risk-reducing surgery in the form of bilateral oophorectomies to induce menopause. The treatment program is often individualised, requires input from various disciplines and continues for an extended period of time, which is challenging for both our patients and our health systems.

3. Challenges with health systems research

There are a number of challenges when considering health systems research.

3.1 Lack of standardized end-points

The current literature has varying end-points when determining the delay in service delivery ^(4,5). Most will commence with the first presentation to the health service. Some commence from the date of screening mammography, positive histology or definitive surgery. Similarly the end-points are scattered between

- a. Confirmed diagnosis of malignancy
- b. Commencement of definitive oncological management
- c. Completion of various oncological treatments
- d. Definitive surgical intervention

These differences make it difficult to directly compare the current research and respective health systems. The main reason for this plethora of standardized end points relates to how the data gets collected. These data points are retrospectively audited from clerical/ oncology databases explaining the variations in reporting.

3.2 Regional Variations

A further challenge in comparing health systems research is that every country has a different health care system making direct comparisons difficult. Similarly solutions are not transferable. Variations are also noted within national systems

when comparing different districts/provinces. This is a strong argument for conducting this type of research.

3.3 Acceptable delay

There is a lack of evidence supporting an acceptable time delay in the diagnosis and work-up of breast malignancy. The suggested timelines, therefore, are figures derived from consensus and experience rather than medical evidence. The European Guidelines were published in February 2008 in the Annals of Oncology and currently recommend the following timelines in working days ⁽⁶⁾

Defined Care Step	Time in working days
Screening mammography and result	15
Symptomatic mammography and result	5
Result of screening mammography and offered assessment	5
Result of diagnostic mammography and offered assessment	5
Assessment and issuing of results	5
Decision to operate and date offered for surgery	15

Table 1 European Guidelines for quality assurance in breast cancer – 4th edition

An overall delay of less than 30 working days is recommended from date of symptomatic mammogram to date offered for surgery in the case of operable

breast cancer. This equates to 6 weeks. The guidelines suggest that “women should be fully assessed in three visits or less” and that women with “symptoms and signs suggestive of breast cancer must be offered an appointment within 2 weeks” ⁽⁶⁾. This document therefore provides us with a benchmark from which to work in the management of breast disease.

4. A case study: The experience in the United Kingdom

The United Kingdom has the fifth largest national economy in the world with a gross domestic product of 3.115 trillion USD ⁽⁷⁾. It is a developed economy with a publically funded health care system. In the United Kingdom waiting times in the NHS are constantly in the spotlight. In 2000 the NHS Cancer Plan was published in which the Labour Government pledged to spend £10 million per annum to decrease all cancer waiting lists ⁽⁸⁾. This document covered the management of various regions regarding the management of these diseases. A 2-week rule was introduced specifically in the management of breast disease. All patients with suspected malignant breast disease had to be seen at a specialist’s clinic within 2 weeks. A timeline for further work-up of patients or intervention was set at one month. This provided a total acceptable time delay of 6 weeks, which are loosely based on the European Guidelines, listed above.

Many audits assessed the impact of this newly adopted protocol in an attempt to either justify or vilify the guidelines. The Yorkshire Cancer Registry is a large database that serves the north of England. The data from 1976–1995 are listed below and show average delays well within the guidelines ⁽⁹⁾.

Delays	Time in days
Family physician to first hospital visit	10.25
First hospital visit to first treatment	9.25
Family physician to first treatment	23.5

Table 2. Yorkshire Cancer Registry 1976-1995 ⁽⁹⁾

Although certain areas were already within the goal waiting periods, many areas/districts were not within these goals. This is where the new waiting period guidelines were successful. The approach to the work-up of cancer had been standardized thereby ensuring that everybody has access to the same level of care. The guidelines were shown to be imperative in ensuring a certain level of care was achieved and maintained.

A follow on from the NHS Cancer Plan 2000 was published in 2007 called the Cancer Reform Strategy ⁽¹⁰⁾. Further commitments have been made to improve the care provided to all patients diagnosed with cancer. The following points pertain specifically to breast disease

1. Extended breast screening to under 50's
2. All breast symptoms to be seen in 14 days (not only those suspicious of cancer)
3. Decrease radiotherapy waiting times to less than 31 days

These are further efforts to decrease the delay in the work-up and management of breast disease with the ultimate aim of decreasing the mortality associated with malignant breast disease.

5. Average Delays

In Table 3 the waiting times are noted for the various papers reviewed. They all have different end-points and as such cannot be compared directly. The country of origin has also been listed to provide some bearing on the results.

Study	Location	Sample Size	End Points	Median Delay
Katz S J et al 1993 ⁽⁵⁾	Washington, USA	369	Symptom delay – first symptom to first consult Diagnosis delay – first consult to diagnosis Surgery delay – diagnosis to initial surgery	9.5 days 16.5 days 8 days
Sainsbury R, et al 1999 ⁽⁹⁾	Huddersfield, United Kingdom	36 222	GP referral to first treatment	23.5 days
National Cancer Registry 1999 ⁽¹¹⁾	United Kingdom (incl Ireland)	2424	GP referral to first treatment	26.4 days
Montella M, et al 2001 ⁽¹²⁾	Naples, Italy	644	System delay – first consult to hospital admission for surgery	1-3m 422 (65%) 3-6m 102 (16%) >6m 120 (19%)

Bardell T et al 2006 ⁽¹³⁾	Kingston Canada	9502	Surgery delay - diagnosis to admission for surgery - surgery within 2weeks of diagnosis	26.9 days 43%
Jack R H, et al May 2007 ⁽¹⁴⁾	London, United Kingdom	35 354	Time to radiotherapy from diagnosis/ previous treatment (whichever was shorter)	52 days
Rayson D et al Jan 2007 ⁽¹⁵⁾	Nova Scotia Canada	637	Surgery delay– diagnosis to initial surgery Oncology delay – surgery to first therapy Total delay	36 days 52 days 96 days

Table 3: Summary of delays

It is important to note that most of the research originates from developed countries with well-funded health care systems. Healthcare inflation within these systems are concerning as they are at rates above inflation. Taxpayers need to be convinced that their money is being spent wisely and the healthcare is of a sufficient standard. This can be achieved with regular audits of the existing service thereby ensuring best practice and cost effectiveness.

6. Resource constraint settings

South Africa is defined as a middle income, emerging market economy by the International Monetary Fund with an estimated gross domestic product of 350 billion USD for 2013 ⁽⁷⁾. We have a publically funded health care system that is responsible for health care of approximately 80% of the population. Only 18.4 % of the population belongs to a medical insurance scheme and access health care in the private sector. In 2014/15, 163 billion Rand was spent on public sector health care with 162 billion Rand being spent in the private sector. This provides insight into the disparity with our current healthcare system ⁽¹⁶⁾.

There is no data on the systems delays in our healthcare network, which makes improvements difficult to achieve and confirm. Data on systems delays in similar emerging market economies are not universally available. We have included data from Nigeria and Kenya, which focuses on the patient delay to presentation with breast cancer. Furthermore, we have information on the breast cancer services in Asia, Eastern Europe and Central America.

The data from Africa focus only on patient delay to access health care services for breast cancer. These were questionnaire based studies conducted at the respective tertiary hospitals with patient estimates of delay. Otieno and his Kenyan colleagues found that 73.1% of patients presented more than 3 months after noticing the breast mass. The majority (24.1%) were reassured that it was harmless when consulting medical personnel, while 23.5% felt the mass was not a concern as they were painless ⁽¹⁷⁾. Similar findings were shown by Ukwenya and his colleagues in Nigeria, who concluded that the delays were due to a combination of local beliefs that were not accepting of western treatment and inadequate health care ⁽¹⁸⁾.

In a recent article, Breast Care in Developing Countries, Agarwal and colleagues looked at the breast cancer care in India, Mexico and Croatia ⁽¹⁹⁾. While delays

were not specifically discussed insights into breast cancer care in resource constraint settings were forthcoming.

In India, the majority of patients present with locally advanced or metastatic disease with 5-year survival rates between 48 and 62%. There is no population based screening system in place and mammography is not easily available or affordable. Diagnosis is made on clinical examination alone, with up to 40% of patients undergoing an inadequate surgical procedure as treatment for breast cancer. Adjuvant radio or chemotherapy is costly, requires multiple treatment sessions and has a social stigma attached to it affecting compliance. Breast conservation and sentinel lymph node biopsies are offered to less than 1% of all patients diagnosed with breast cancer. This is due to the limited availability of radiotherapy and nuclear medicine expertise.

Mexico is the eleventh largest economy globally ⁽⁷⁾, yet has an ever increasing gap between the wealthy and the poor. Breast cancer has become the second most common female malignancy after cervical cancer and is routinely diagnosed a decade earlier than in developed countries. Mexico introduced a screening mammography service in the 1990's with 508 screening units servicing 12 million women over the age of 40 years. Further improvements are needed in the treatment of these patients as the public hospitals are overwhelmed, with delays in diagnosis and management commonplace, causing disease progression.

Croatia is a country of 4.5 million people, which has radically improved its breast cancer service over the last 25 years. At that stage 40% of breast cancers were locally advanced. This improvement was achieved with a public education program, introduction of mammographic screening (including mobile units), establishing a centralized Oncology Breast Unit and a Division of Plastic and Breast Surgery. Currently almost half of all breast cancers are less than 10mm in size with a 5year survival of 89%.

One of the countries where data on systems delays is available is Thailand, which is classified as a middle income country with a GDP of 373 billion USD ⁽⁷⁾. This compares favourably with South Africa's economy and serves as a good comparator for this study. Poom and colleagues completed a cross-sectional questionnaire based study on 180 patients and found a median patient delay of 12 days and system delay of 21 days ⁽²⁰⁾. These were patient reported time frames, which were corroborated with patient records where possible. They found an increased system delay in younger patients, those with previous breast complaints, lower education and family income levels. A delay of more than 3 months was noted in 17% of the cohort which compares with quoted European data. Thonsukai and colleagues looked at 94 women and found that the systems delay was a median of 4 weeks ⁽²¹⁾. Almost 25% of patients experienced a delay of more than 3 months. The factors associated with an increased delay included being single and consulting at a peripheral hospital as opposed to the university hospital. These factors highlight the need for a unified breast disease awareness program and implementation of certain care standards in the management of breast cancer.

7. Effects of delay

One of the main reasons for health systems research is assessing the impact of these delays on patients. The perception is that a long delay increases mortality, but proving this remains a challenge.

A meta-analysis done by Richards et al in 1999 analysed 87 studies linking delay and mortality ⁽²²⁾. Their findings suggest that delays of 3-6 months were associated with an increased mortality rate. This is the accepted thinking when dealing with the work-up of breast disease and any delay longer than six months is unacceptable.

A number of smaller studies have showed no survival difference ^(11, 23). The main reason for this anomaly was that these studies were all done retrospectively and

medical practitioners would fast track patients with late-stage disease. Hence the paradoxical relationship between increased mortality and a shorter delay in these studies.

In summary, there are a number of variables that make health systems research challenging. It is imperative that we continuously assess our health system to ensure an effective and sustainable service. In this manner we will identify shortcomings and institute measures to improve the care afforded to our patients.

8. References

1. Cancer in South Africa 2010 Full Report. National Cancer Registry. National Institute for Occupational Health. (Accessed July 2013)
http://www.nioh.ac.za/page=cancer_statistics&id=163
2. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology: breast cancer. Version1.2010. 2009 October (accessed April 2016)
http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf
3. Maughan KL, Lutterbie MA, Ham PS. Treatment of Breast Cancer *Am Fam Physician* 2010;81(11):1139-1346
4. Ivo A. Olivotto, Christina Bancej, Vivek Goel, Judy Snider, Ronald G. McAuley, Brenda Irvine, Lisa Kan, Doug Mirsky, Margaret J. Sabine, Renée McGilly, Judy S. Caines Waiting times from abnormal breast screen to diagnosis in 7 Canadian provinces *CMAJ* 2001;165(3):277-83
5. Steven J. Katz, T. Greg Hislop, David B. Thomas, Eric B. Larson Delay from Symptom to Diagnosis and Treatment of Breast Cancer in Washington State and British Columbia *Medical Care*, 1993;31(3):264-268
6. N. Perry, M. Broeders, C. de Wolf, S. Tornberg, R. Holland, L. von Karsa European guidelines for quality assurance in breast cancer screening and diagnosis. Fourth edition—summary document *Annals of Oncology* 2008;19: 614–622
7. International Monetary Fund. World Economic Outlook Database: Country Information (accessed April 2015)
<https://www.imf.org/external/pubs/ft/weo/2015/01/weodata/co.pdf>

8. The NHS Cancer Plan. 2000
<http://www.doh.gov.uk/cancer> 48–9.
9. Sainsbury R, Johnston C, Haward B. Effect on survival of delays in referral of patients with breast-cancer symptoms: a retrospective analysis *The Lancet* 1999 Apr;353:1132-35
10. Cancer Reform Strategy 2007
<http://www.nhs.uk/NHSEngland/NSF/Documents/CancerReformStrategy.pdf>
11. Comber H, Cronin DP, Deady S et al. Delays in treatment in the cancer services: impact on cancer stage and survival *Irish Medical Journal* 2005 Sep;98(8):238-9
12. Montella M, Crispo A, Botti G et al. An assessment of delays in obtaining definitive breast cancer treatment in Southern Italy *Breast Cancer Research and Treatment* 2001 Apr; 66(3): 209-215
13. T. Bardell, P. Belliveau, W. Kong, W. J. Mackillop Waiting Times for Cancer Surgery in Ontario: 1984-2000 *Clinical Oncology* (2006) 18: 401-409
14. Jack RH, Davies EA, Robinson D et al. Radiotherapy waiting times for women with breast cancer: a population based cohort study *BMC Cancer* 2007 May; 7:71
15. Daniel Rayson, Nathalie Saint-Jacques, Tallal Younis et al. Comparison of elapsed times from breast cancer detection to first adjuvant therapy in Nova Scotia in 1999/2000 and 2003/04 *CMAJ* Jan 30, 2007;176(3):327-332
16. National Treasury Fiscal Review - Health Expenditure in the public and private sectors 2010/11 – 2016/17

<http://www.treasury.gov.za/publications/igfr/2015/prov/Chapter20420-20Health.pdf>

17. Otieno ES, Micheni JN, Kimende SK et al. Delayed Presentation of Breast Cancer Patients *East Afr Med J* 2010 April;87(4):147-50
18. Ukwanya AY, Yusufu LMD, Nmadu PT et al. Delayed treatment of symptomatic breast cancer: The experience from Kaduna, Nigeria *SAJS* 2008 Nov;46(4):106-10
19. Agarwal G, Ramakant P, Sanchez Forgach ER et al. Breast Cancer Care in Developing Countries *World J Surg* 2009;33:2069-2076
DOI 10.1007/s00268-009-0150-z
20. Poum A, Promthet S, Duffy SW et al. Factors associated with delayed diagnosis of breast cancer in northeast Thailand *J Epidemiol* 2014;24(2):102-108
21. Thongsuksai P, Chongsuvivatwong V, Sriplung H. Delay in breast cancer care: a study in Thai women *Med Care* 200 Jan;38(1):108-114
22. Richards MA, Westcombe AM, Love SB, Littlejohns P, Ramirez AJ. Influence of delay on survival in patients with breast cancer: a systematic review *Lancet* 1999;353:1119-1126
23. Neave LM, Mason BH, Kay RG et al. Does delay in diagnosis of breast cancer affect survival? *Breast Cancer Res Treat* 1990 Feb;15(2):103-8

Part C

Journal Article

System delays in breast cancer

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Abstract

Background

Centralised multidisciplinary management of breast cancer occurs in KwaZulu-Natal, South Africa and requires a diagnostic and staging pathway at the referring hospital. Delays in this pathway are unknown. This study, conducted at a referring hospital, R K Khan (RKK), quantifies and analyses these delays

Methods

A retrospective folder review included all patients with breast cancer diagnosed at RKK from January 2008 to January 2009. Data extraction included demographic data, time to diagnosis and initial staging using a standardised data sheet. Specific care steps were identified, namely delays to initial imaging with mammography, pathology confirmation, staging workup and eventual referral to a centralised breast clinic.

Results

A total of 45 patients were included with 43 females and 2 males. The average age was 56 years (Range 38 – 82 years). The mean individual care step delays were 18.3 days to initial imaging, 21.2 days to pathological confirmation, 9.2 days to initial staging and 22.7 days to review at the centralised breast clinic. The delays were sequential with a mean total delay of 70.1 days or 10 weeks with an interquartile range of 48 - 82 days.

Conclusion

This study confirmed significant delays in the care pathway, which are almost double the international recommendations of 6 weeks. Steps to reduce delays at all phases have been instituted with specific care step targets leading to the establishment of a breast cancer registry with an audit capability. We suggest targeting an 8 week period for the work-up and staging of every patient with

breast cancer. The establishment of a breast cancer registry and regular audits thereof are essential in maintaining care standards and achieving best practice.

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Introduction

In South Africa, breast cancer is the 4th most common cause of death from all malignancies.^[1] In South Africa, we notice a discrepancy in incidence rates between various ethnic/race groups. African women have rates similar to those in other developing countries. Caucasian women have rates that are comparable with industrialised countries. In women of Indian origin the rates are almost double those reported in India.^[1]

In most developing countries, including South Africa, breast cancer initially comes to the attention of the general surgeon, usually at a secondary level hospital, where the diagnosis is confirmed and surgery is performed. An oncology opinion is usually sought in the postoperative period. This system is changing and multidisciplinary teams (MDTs) are being formed to manage breast cancer. These teams involve surgical, oncology, radiology, pathology, nuclear medicine and plastics and reconstructive surgery disciplines. The MDTs consider the treatment options and patient preference before deciding on appropriate management. Such a system has evolved in the Durban Metropole based at Inkosi Albert Luthuli Central Hospital (IALCH). This is not an open access breast service and requires a diagnostic and staging pathway at the referring hospital. This study conducted at a referral hospital, R K Khan (RKK), quantifies and analyses these delays.

The primary objective of the study was to quantify the total time delay between initial presentation at RKK and eventual review at the multidisciplinary breast clinic at IALCH. The secondary objectives were to document the time intervals between specific care steps, identify the reasons for these delays and propose policy change to improve the situation.

Methods

RKK is a regional hospital and services a population of approximately 1.5 million people.^[2] Around 60 new breast cancer cases are diagnosed annually in the surgery department. A retrospective folder review included patients with histologically proven breast cancer seen at RKK and referred to the MDT at IALCH from January 2008 to January 2009. Patients were excluded if they were admitted for work-up and management or if folders were inaccessible for data collection.

Care pathway

The care pathway timeline is illustrated in Fig.1, which shows the experience of the average patient at this referring hospital. The initial consultation was followed by a delay to the mammography/ultrasound (D1 – initial imaging delay). At the second visit the mammography or ultrasound was reviewed and a biopsy performed followed by a delay awaiting histology results (D2 – pathology delay). The third visit consisted of confirming these results and booking a metastatic work-up including an abdominal ultrasound, chest radiograph and liver function tests (D3 – staging delay). Finally, the fourth visit reviewed these investigations and a multidisciplinary breast clinic appointment at IALCH was booked (D4 – referral delay). This was the best-case scenario, as some patients would require repeat biopsy or additional radiological investigations leading to further delays.

Demographic data captured during the folder review included age, gender and address. A timeline was generated for each case by capturing dates of the first consultation, mammogram, histology report, abdominal ultrasound, chest radiograph and IALCH multidisciplinary breast clinic. The individual care step delays were quantified and any reasons sought to explain excessive delays were noted during the folder review.

Data analysis was conducted using SPSS for Windows, Version 15.0 (Chicago SPSS Inc.). Quantitative data including time in days between dates of entry and

exit from the cohort and between intermediate dates have been summarised using mean delay and interquartile range.

Results

The cohort included 45 patients with 43 females and 2 males with a mean age of 56 years. The mean delay, interquartile range and range are illustrated in Table 1. These delays were sequential with the referral delay being a week longer than the others. If we combine all radiology based delays, i.e. D1 and D3, it totals 27.5 days which is the longest delay and underscores their importance in breast cancer services. The pathology delay (D2) was 3 weeks with six patients requiring multiple biopsies to confirm the diagnosis. The final phase of delay (D4) was referral to the MDT breast clinic, which averaged 22.7 days. This led to a mean total delay of 10 weeks with nine patients who waited over 3 months.

Discussion

This study confirmed significant delays in the care pathway for breast cancer at a regional hospital. An appropriate delay remains a challenge to quantify due to lack of an evidence base. Current guidelines are derived from consensus statements and experience gained largely from well resourced, publicly funded health systems in Europe and North America.^[3-8] The delays in these studies are tabulated in Table 2 and provide some perspective when interpreting our results. It is easy to appreciate that none of the studies conform to standardised reporting of delays. The average delay was 5 - 6 weeks for most patients, which is half our delay. It is important to note that some of the studies do not have full datasets, thus preventing direct comparisons. These audits provide an insight into the delays in other health systems and serve as guidelines in determining an acceptable delay.

The European Guidelines published in February 2008 recommended an overall delay of less than 25 working days from date of symptomatic mammogram to date offered for surgery in the case of operable breast cancer. This equates to a

maximum acceptable delay of 5 weeks. Furthermore, 'women should be fully assessed in three visits or less' and 'women with symptoms and signs suggestive of breast cancer must be offered an appointment within 2 weeks.'^[9]

In 2010, the European Society of Breast Cancer Specialists published an updated position statement on quality indicators in the management of breast cancer. Their recommendation is a waiting time of less than 6 weeks from initial diagnostic visit to definitive treatment. This time frame has to be achieved in at least 75% of patients as a minimum standard.^[10]

In the UK, waiting times in the National Health Service (NHS) are constantly in the spotlight. In 2000, the NHS Cancer Plan was published in which the Labour Government pledged to spend £10 million per annum to decrease all cancer waiting lists.^[11] A 2-week rule was introduced specifically in the management of breast cancer. All patients with suspected malignant breast disease had to be seen at a specialist clinic within 2 weeks. A timeline for further work-up of patients or intervention was set at a further 4 weeks, providing a total delay of 6 weeks.

A follow on from the NHS Cancer Plan was published in 2007 called the Cancer Reform Strategy.^[12] Breast screening was extended to ages under 50 years and over 70 years with all patients with breast cancer symptoms to be seen within 2 weeks. These guidelines have been successful in improving waiting times with 99.2% of patients with breast cancer starting treatment within 1 month of diagnosis.^[13]

The underlying concerns with these delays are whether it correlates with an increased mortality. A meta-analysis by Richards *et al.*^[14] in 1999 analysed 87 different studies looking at delay and mortality in breast malignancy. Their findings suggest that delays exceeding 3 months were associated with an increased mortality rate.^[14] A more recent article gathered information from the

National Cancer Registry in the UK and found a median delay of 22 days from diagnosis to treatment. In contrast, they found no difference in mortality in patients who waited more than 25 days.^[15]

The consensus is that an acceptable delay is less than 6 weeks from first presentation to commencement of treatment. In comparison, our service showed a 70 day/10 week mean delay. This is difficult to compare with the guidelines discussed above as the end points differed. In our study, our patients were seen at a MDT breast clinic within 10 weeks, but were no closer to definitive treatment by that stage. We did not discuss patient delay from time of symptoms to first contact with the health system as we were unable to quantify this accurately. The study had further limitations in that it was a single centre review with no comparative data and relatively small numbers.

The initial imaging delay (D1) involved accessing a mammogram and/or an ultrasound of the breast. At most regional level hospitals in South Africa there are limited radiology and mammography services. This study site had a full time radiologist reporting on all mammograms, and yet the radiology delay was a major concern. The staging delay (D3) included the delay to an abdominal ultrasound, chest radiograph and certain blood tests with the rate limiting step being the abdominal ultrasound. If we combine these delays (D1 and D3) they total 27.5 days, which is the longest delay. The single radiologist has an overwhelming workload, contributing to the delay.

The pathology service is a vital component in our breast cancer service, as histology remains the mainstay of diagnosis. In certain instances the specimens were inadequate and this reflects the experience of the clinician performing the biopsy. The surgical clinic was staffed with a variety of medical personnel from surgeons, registrars, medical officers and interns. The need to repeat biopsies was thought to be a reason for additional delay to diagnosis. . The second component of this delay relates to the delay in processing and reporting the

specimen at the pathology laboratory, which services the entire province and has staff and resource limitations.

Having identified these delays, meetings were arranged with all the major stakeholders including the radiology and pathology services. We sensitised them to our concerns regarding the delay and welcomed feedback and logistical changes to improve the service. All parties were keen to use this research to motivate for additional funding and staff and indicated the need for regular audits of the service.

In the surgical clinic, a focal liaison was identified that would expedite the referrals of all our patients with breast malignancy to the MDT breast clinic. Protocols were also agreed upon to minimise unnecessary mammograms, thus alleviating the workload on the radiology department. In patients who had obviously suspicious mammograms the radiologist would expedite the metastatic work-up by doing the abdominal ultrasound at the same time, thereby decreasing the delay.

The data suggests that a central, open access breast clinic might be better suited to decreasing the delay and improving overall care for these patients. Anecdotal evidence exists in the South African setting that this type of service decreases delays in the work-up of breast malignancy.

Developing local guidelines

There are no guidelines regarding acceptable delays for breast cancer in resource poor settings. We have attempted to set some norms for acceptable delays based on data generated in this review. The recommendations in Table 3 would need to be achieved in 75% of patients as a minimum standard.

The establishment of a breast cancer registry is essential in ensuring timeous management. The registry can be the responsibility of an experienced nurse and

the process overseen by a clinician with experience in the management of breast cancer. Regular and ongoing audits of the system are imperative to ensure minimum standards are achieved.

Conclusion

Breast cancer remains a major public health concern, testing our health care model in South Africa. The discussion around acceptable and attainable system delays is important and needs input from all stakeholders responsible for managing this disease. We look forward to further research and developments on this topic.

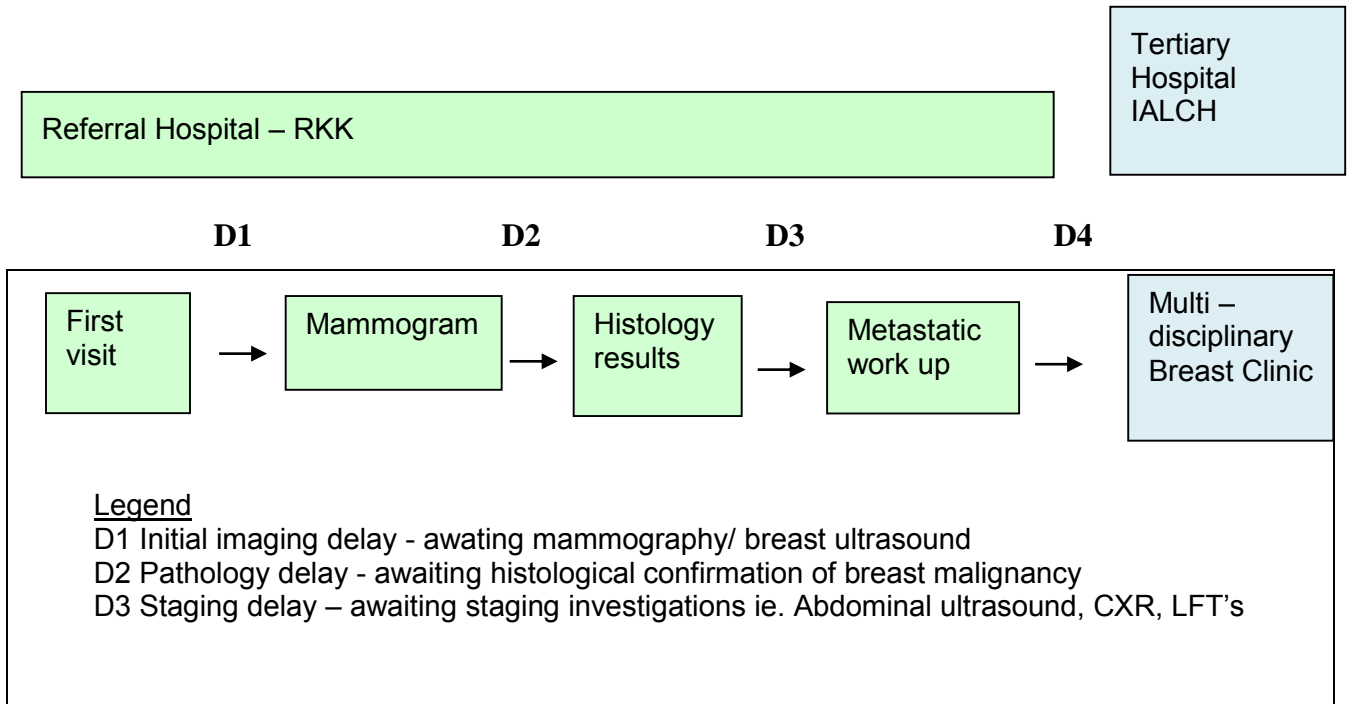


Figure 1 – Care pathway timeline illustrating consultations and time delays between care steps during the diagnosis and staging of breast cancer

	Care steps	Mean delay	Inter Quartile Range (IQR)	Range
D1	Initial Imaging	18.3	8.5 – 21.75	2 - 81
D2	Pathology	21.2	14 – 29	7 - 87
D3	Staging	9.2	1 – 17	1 - 40
D4	Referral	22.7	10.75 – 32	1 - 49
	Total Delay	70.1	47.75 – 82.25	32 - 199

Table 1: Results of individual care steps and total delay presented as mean delay, interquartile range and range. All results are in days.

Study	Location	No	Patient delay (weeks)	Imaging Delay (weeks)	Histology Delay (weeks)	Staging Delay (weeks)	MDT Delay (weeks)	Treatment Delay (weeks)	Total Delay (weeks)
Katz 1993 ^[3]	Canada	174	1	2 ½				1	4
Montella 2001 ^[4]	Italy	644	65% in 4 *	68% in 4 11% in 12 *					39% > 12 *
Olivotto 2001 ^[5]	Canada	139 58		2 ½	3 ½	7 to diagnosis NOT treatment			
Bardell 2006 ^[6]	Canada	950 2					3 ½		4 43% in 2 **
Rayson 2007 ^[7]	Canada	637		2		3			5
Poum 2013 ^[8]	Thailand	180	2	3		5 to diagnosis NOT treatment			
This study	South Africa	45		2 ½	3	1 ¼	3		10

Table 2 – Summary of delays in various studies. It represents the various reporting standards and end points indicating the difficulty in making direct comparisons.

Legend

- Shaded blocks indicate no data available for specific delays in those datasets. The total delay column refers to totals for available datasets and not necessarily mean delay to treatment/surgery commencement.
- * Montella et al presented the delay in this format ie the percentage of patients completed within a certain time frame, and did not provide mean delays
- ** Bardell et al only looked at delay to treatment and did not present data on diagnosis and staging delay
- Olivotto & Poum' studies looked at time to diagnosis only and provided no data on staging or treatment delays

	Time	Total Delay
Surgical Clinic	1 week	
Diagnosis Radiology & Pathology delay	4 weeks	5 weeks
Definitive Management Neo-adjuvant chemo OR Surgery	3 weeks	8 weeks

Table 3 Guidelines for Breast Cancer Delays

References

1. Somdyala NI, Bradshaw D, Gelderblom WC, et al. Cancer incidence in a rural population of South Africa, 1998 - 2002. *Int J Cancer* 2010;127(10):2420-2429. [http://dx.doi.org/10.1002/ijc.25246]
2. Subben P. RK Khan Hospital Commemorating 40 Years 2010. <http://www.kznhealth.gov.za/RKKhan/anniversary.pdf> (accessed January 2009)
3. Katz SJ, Hislop TG, Thomas DB, et al. Delay from symptom to diagnosis and treatment of breast cancer in Washington State and British Columbia. *Med Care* 1993;31(3):264-268. [http://dx.doi.org/10.1097/00005650-199303000-00007]
4. Montella M, Crispo A, Botti G, et al. An assessment of delays in obtaining definitive breast cancer treatment in Southern Italy. *Breast Cancer Res Treat* 2001;66(3):209-215.
5. Olivotto IA, Bancej C, Goel V, et al. Waiting times from abnormal breast screen to diagnosis in 7 Canadian provinces. *CMAJ* 2001;165(3):277-283.
6. Bardell T, Belliveau P, Kong W, et al. Waiting times for cancer surgery in Ontario: 1984-2000. *Clin Oncol* 2006;18(5):401-409. [http://dx.doi.org/10.1016/j.clon.2006.02.012]
7. Rayson D, Saint-Jacques N, Younis T, et al. Comparison of elapsed times from breast cancer detection to first adjuvant therapy in Nova Scotia in 1999/2000 and 2003/2004. *CMAJ* 2007;176(3):327-332. [http://dx.doi.org/10.1503/cmaj.060825]
8. Poum A, Promthet S, Duffy SW, et al. Factors associated with delayed diagnosis of breast cancer in Northeast Thailand. *J Epidemiol* 2014;24(2):102-108. [http://dx.doi.org/10.2188/jea.JE20130090]

9. Perry N, Broeders M, de Wolf C, et al. European guidelines for quality assurance in breast cancer screening and diagnosis. 4th edition--summary document. *Ann Oncol* 2008;19(4):614-622.
[<http://dx.doi.org/10.1093/annonc/mdm481>]
10. Del Turco MR, Ponti A, Bick U, et al. Quality indicators in breast cancer care. *Eur J Cancer* 2010;46(13):2344-2356.
[<http://dx.doi.org/10.1016/j.ejca.2010.06.119>]
11. Department of Health. The NHS Cancer Plan 2000:1-98.
http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_4014513.pdf (accessed February 2008).
12. Department of Health. Cancer reform strategy. *Clin Oncol* 2008; 20(4) 271-274
[<http://dx.doi.org/10.1016/j.clon.2008.01.014>]
13. Aveyard E, Pottage C, McDonnell P, et al. Waiting times for suspected and diagnosed cancer patients, 2012-2013 Annual Report. 2013: 3-5.
<http://www.england.nhs.uk/statistics/wp-content/uploads/sites/2/2013/07/Cancer-Waiting-Times-Annual-Report-2012-13-amended.pdf> (accessed July 2014).
14. Richards MA, Westcombe AM, Love SB, et al. Influence of delay on survival in patients with breast cancer: A systematic review. *Lancet* 1999; 353(9159):1119-1126.
15. Redaniel MT, Martin RM, Cawthorn S, et al. The association of waiting times from diagnosis to surgery with survival in women with localised breast cancer in England. *Br J Cancer* 2013;109(1):42-49.
[<http://dx.doi.org/10.1038/bjc.2013.317>]

Appendix C

South African Journal of Surgery Author Guidelines

Accepted manuscripts that are not in the correct format specified in these guidelines will be returned to the author(s) for correction, and will delay publication.

AUTHORSHIP

Named authors must consent to publication. Authorship should be based on substantial contribution to: (i) conception, design, analysis and interpretation of data; (ii) drafting or critical revision for important intellectual content; and (iii) approval of the version to be published. These conditions must all be met (uniform requirements for manuscripts submitted to biomedical journals; refer to **www.icmje.org**)

CONFLICT OF INTEREST

Authors must declare all sources of support for the research and any association with a product or subject that may constitute conflict of interest.

RESEARCH ETHICS COMMITTEE APPROVAL

Provide evidence of Research Ethics Committee approval of the research where relevant.

PROTECTION OF PATIENT'S RIGHTS TO PRIVACY

Identifying information should not be published in written descriptions, photographs, and pedigrees unless the information is essential for scientific purposes and the patient (or parent or guardian) gives informed written consent for publication. The patient should be shown the manuscript to be published.

Refer to www.icmje.org.

ETHNIC CLASSIFICATION

References to ethnic classification must indicate the rationale for this.

MANUSCRIPTS

Shorter items are more likely to be accepted for publication, owing to space constraints and reader preferences.

Original articles not exceeding 3 000 words, with up to 6 tables or illustrations, are usually observations or research of relevance to surgery. References should preferably be limited to no more than 15. Please provide a structured abstract not exceeding 250 words, with the following recommended headings: *Background, Objectives, Methods, Results, and Conclusion.*

Scientific letters/short reports, which include case reports, side effects of drugs and brief or negative research findings should preferably be 1500 words or less, with 1 table or illustration and no more than 6 references. Please provide an accompanying abstract not exceeding 150 words.

Editorials, Opinions, etc. should be about 1000 words and are welcome, but unless invited, will be subjected to the SAJS peer review process.

Review articles are rarely accepted unless invited.

Letters to the editor, for publication, should be about 400 words with only one illustration or table, and must include a correspondence address.

Obituaries should be about 400 words and may be accompanied by a photograph.

MANUSCRIPT PREPARATION

Refer to articles in recent issues for the presentation of headings and subheadings. If in doubt, refer to 'uniform requirements' - www.icmje.org.

Manuscripts must be provided in **UK English**.

Qualification, affiliation and contact details of ALL authors must be provided in the manuscript and in the online submission process.

Abbreviations should be spelt out when first used and thereafter used consistently, e.g. 'intravenous (IV)' or 'Department of Health (DoH)'.

Scientific measurements must be expressed in SI units except: blood pressure (mmHg) and haemoglobin (g/dl). Litres is denoted with a lowercase 'l' e.g. 'ml' for millilitres). Units should be preceded by a space (except for %), e.g. '40 kg' and '20 cm' but '50%'. Greater/smaller than signs (> and <) should be placed immediately preceding the relevant number, i.e. 'women >40 years of age'. The same applies to \pm and $^{\circ}$, i.e. '35 \pm 6' and '19 $^{\circ}$ C'.

Numbers should be written as grouped per thousand-units, i.e. 4 000, 22 160...

Quotes should be placed in single quotation marks: i.e. The respondent stated: '...'

Round **brackets** (parentheses) should be used, as opposed to square brackets, which are reserved for denoting concentrations or insertions in direct quotes.

General formatting The manuscript must be in Microsoft Word or RTF document format. Text must be single-spaced, in 12-point Times New Roman font, and contain no unnecessary formatting (such as text in boxes, with the exception of Tables).

ILLUSTRATIONS AND TABLES

If tables or illustrations submitted have been published elsewhere, the author(s) should provide consent to republication obtained from the copyright holder.

Tables may be embedded in the manuscript file or provided as '**supplementary files**'. They must be numbered in Arabic numerals (1,2,3...)

and referred to consecutively in the text (e.g. 'Table 1'). Tables should be constructed carefully and simply for intelligible data representation. Unnecessarily complicated tables are strongly discouraged. Tables must be cell-based (i.e. not constructed with text boxes or tabs), and accompanied by a concise title and column headings. Footnotes must be indicated with consecutive use of the following symbols: * † ‡ § ¶ || then ** †† ‡‡ etc.

Figures must be numbered in Arabic numerals and referred to in the text e.g. '(Fig. 1)'. Figure legends: Fig. 1. 'Title...'

All illustrations/figures/graphs must be of **high resolution/quality**: 300 dpi or more is preferable but images must not be resized to increase resolution. Unformatted and uncompressed images must be attached as '**supplementary files**' upon submission (not embedded in the accompanying manuscript). TIFF and PNG formats are preferable; JPEG and PDF formats are accepted, but authors must be wary of image compression. Illustrations and graphs prepared in Microsoft Powerpoint or Excel must be accompanied by the original workbook.

REFERENCES

Authors must verify references from the original sources. *Only complete, correctly formatted reference lists will be accepted.* Reference lists must be generated manually and **not** with the use of reference manager software.

Citations should be inserted in the text as superscript numbers between square brackets, e.g. These regulations are endorsed by the World Health Organization,^[2] and others.^[3,4-6]

All references should be listed at the end of the article in numerical order of appearance in the **Vancouver style** (not alphabetical order). Approved abbreviations of journal titles must be used; see the List of Journals in Index Medicus.

Names and initials of all authors should be given; if there are more than six authors, the first three names should be given followed by et al. First and last page, volume and issue numbers should be given.

Wherever possible, references must be accompanied by a digital object identifier (DOI) link and PubMed ID (PMID)/PubMed Central ID (PMCID).

Authors are encouraged to use the DOI lookup service offered by CrossRef.

Journal references: Price NC, Jacobs NN, Roberts DA, et al. Importance of asking about glaucoma. *Stat Med* 1998;289(1):350-355.

[<http://dx.doi.org/10.1000/hgjr.182>] [PMID: 2764753]

Book references: Jeffcoate N. *Principles of Gynaecology*. 4th ed. London: Butterworth, 1975:96-101.

Chapter/section in a book: Weinstein L, Swartz MN. Pathogenic Properties of Invading Microorganisms. In: Sodeman WA jun, Sodeman WA, eds. *Pathologic Physiology: Mechanisms of Disease*. Philadelphia: WB Saunders, 1974:457-472.

Internet references: World Health Organization. *The World Health Report 2002 - Reducing Risks, Promoting Healthy Life*. Geneva: World Health Organization, 2002. <http://www.who.int/whr/2002> (accessed 16 January 2010).

Other references (e.g. reports) should follow the same format: Author(s). Title. Publisher place: publisher name, year; pages. Cited manuscripts that have been accepted but not yet published can be included as references followed by '(in press)'.

Unpublished observations and personal communications in the text must not

appear in the reference list. The full name of the source person must be provided for personal communications e.g. '(Prof. Michael Jones, personal communication)'

PROOFS

A PDF proof of an article may be sent to the corresponding author before publication to resolve remaining queries. At that stage, **only** typographical changes are permitted; the corresponding author is required, having conferred with his/her co-authors, to reply within 2 working days in order for the article to be published in the issue for which it has been scheduled.

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As part of the submission process, authors are required to check off their submission's compliance with all of the following items, and submissions may be returned to authors that do not adhere to these guidelines.

1. Named authors consent to publication and meet the requirements of authorship as set out by the journal.
2. The submission has not been previously published, nor is it before another journal for consideration.
3. The text complies with the stylistic and bibliographic requirements in **Author Guidelines**.

4. The manuscript is in Microsoft Word or RTF document format. The text is single-spaced, in 12-point Times New Roman font, and contains no unnecessary formatting.
5. Illustrations/figures are high resolution/quality (not compressed) and in an acceptable format (preferably TIFF or PNG). These must be submitted as 'supplementary files' (not in the manuscript).
6. For illustrations/figures or tables that have been published elsewhere, the author has obtained written consent to republication from the copyright holder.
7. Where possible, references are accompanied by a digital object identifier (DOI) and PubMed ID (PMID)/PubMed Central ID (PMCID).
8. An abstract has been included where applicable.
9. The research was approved by a Research Ethics Committee (if applicable)
10. Any conflict of interest (or competing interests) is indicated by the author(s).

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Part D

Ethics Approval

Appendix C

UNIVERSITY OF CAPE TOWN



Faculty of Health Sciences
Faculty of Health Sciences Human Research Ethics Committee
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Telephone [021] 406 6338 • Facsimile [021] 406 6411
e-mail: sumayah.ariefdien@uct.ac.za
www.health.uct.ac.za/research/humanethics/forms

21 February 2013

HREC REF: 117/2013

Dr EK Dalwai
Department of Surgery
J-47
OMB

Dear Dr Dalwai

PROJECT TITLE: SYSTEMS DELAY IN THE MANAGEMENT OF MALIGNANT BREAST DISEASE AT A REGIONAL HOSPITAL ON KWALULU-NATAL, SOUTH AFRICA

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee for review.

It is a pleasure to inform you that the HREC has **formally approved** the above mentioned study.

Approval is granted for one year till the 28 February 2014.

Please submit a progress form, using the standardised Annual Report Form, if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the REC. REF in all your correspondence.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, HSF HUMAN ETHICS

Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

sAriefdien



UNIVERSITY OF
KWAZULU-NATAL[™]
 INYUVESI
YAKWAZULU-NATALI
 21 January 2013

Dr E.K Dalwai
 PO Box 19485
 Dormerton
 4015
 e-mail: edalwai@gmail.com

Dear Dr Dalwai

PROTOCOL: System delays in the management of malignant breast disease at a regional hospital in KwaZulu- Natal. REF: BE122/09.

EXPEDITED APPLICATION

A sub-committee of the Biomedical Research Ethics Committee has considered and noted your application received on 11 June 2009.

The study was provisionally approved pending appropriate responses to queries raised. Your responses received 17 January 2013 to queries raised on 20 August 2009 have been noted by a sub-committee of the Biomedical Research Ethics Committee. The conditions have now been met and the study is given full ethics approval and may begin as from 21 January 2013.

This approval is valid for one year from **21 January 2013**. To ensure uninterrupted approval of this study beyond the approval expiry date, an application for recertification must be submitted to BREC on the appropriate BREC form 2-3 months before the expiry date.

Any amendments to this study, unless urgently required to ensure safety of participants, must be approved by BREC prior to implementation.

Your acceptance of this approval denotes your compliance with South African National Research Ethics Guidelines (2004), South African National Good Clinical Practice Guidelines (2006) (if applicable) and with UKZN BREC ethics requirements as contained in the UKZN BREC Terms of Reference and Standard Operating Procedures, all available at <http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx>.

BREC is registered with the South African National Health Research Ethics Council (REC-290408-009). BREC has US Office for Human Research Protections (OHRP) Federal-wide Assurance (FWA 678).

The sub-committee's decision will be **RATIFIED** by a full Committee at its next meeting taking place on **12 February 2013**.

We wish you well with this study. We would appreciate receiving copies of all publications arising out of this study.

Yours sincerely

Professor D.R Wassenaar
 Chair: Biomedical Research Ethics Committee

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Website: <http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx>

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