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An audit of provider delay in newly diagreferral hospital in Johannesburg,South Africa

Ross, Douglas Graham

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AN AUDIT OF PROVIDER DELAY IN NEWLY DIAGNOSED BREAST CANCER IN A CENTRAL REFERRAL HOSPITAL IN JOHANNESBURG, SOUTH AFRICA



Douglas Graham Ross

A research report submitted to the Faculty of Health Sciences. University of the Witwatersrand, in partial fulfilment of the requirements for the degree of Master of Medicine (Surgery)

Johannesburg, May 2019

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Declaration

I, Douglas Graham Ross declare that this Research Report is my own, unaided work. It is being submitted for the Degree of Master of Medicine (Surgery) at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University



_____

12th June
_____ day of _____ 2019

Dedicated to my loving wife

Dr Inge Kriel

Presentations arising from this study

The findings of this study were presented at the 45th meeting of the Surgical Research Society, Johannesburg, 2017

Abstract

Introduction

Breast cancer is one of the most common cancers in women worldwide and accounts for an increasing burden of disease. One of the factors identified in improving outcome newly diagnosed breast cancer is decreased time from recognition of a symptom to initiation of primary therapy. This study aims to quantify provider delay and identify potential reasons for the delay.

Methods:

251 patients diagnosed with breast cancer from 1 January 2014 to 31 December 2014 were included. Patient records were examined and date intervals for each patient was recorded, from presentation to primary therapy. The results were compared to a standard of 90% of patients reaching primary therapy within 60 days.

Results:

Median delay (interquartile range) to primary therapy was 49 days (d) (33-80d). The primary chemotherapy group had a median delay of 48d (30-71d), the primary endocrine therapy group had a 28d (22-41d) delay, and the primary surgery group had a delay of 75d (39.8-113.5d). The addition of sentinel lymph node biopsy to the treatment plan added 37d to the chemotherapy group and 38d to the surgery group. 99 patients (39.4%) had a delay greater than 60 days.

Conclusions:

The centre did not achieve the standard of 90% of patients reaching primary therapy within 60 days. Sentinel lymph node biopsy added a significant delay to patients reaching primary therapy, and the recommendation is that that these procedures be done at the time of primary surgery. Factors affecting delay to primary surgery include logistical issues within the unit as well as the health system.

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Introduction

Breast cancer is one of the most common cancers affecting women worldwide, with an estimated 1.67 million new cases diagnosed annually. Breast-cancer related mortalities amount to an estimated 500 000 cases per year [1]. In South Africa, breast cancer accounts for significant burden of disease as the fourth leading cause of death from all malignancies in women [2]. There is therefore a need to assess the systems within which these patients are treated and to understand where breast cancer related services can be improved.

Delay can be defined as the time from recognition of a breast symptom to initiation of therapy, and this can be further divided into patient delay and provider delay [3]. Patient delay is the time from symptom recognition to presentation to a healthcare provider, while provider delay is the time from presentation to initiation of treatment. It is widely accepted in the literature that increased treatment delay can be associated with worse outcomes and increased cost of care. [5-7]

Educational level, marital status, increased age, strong cultural beliefs around surgery, and fear of mastectomy are risk factors associated with patient delay identified in various settings worldwide [8-11]. Initial symptoms other than a palpable mass also increase time to presentation [8-11]. Many of these studies originate in populations in low and middle-income countries, sharing many of the social and socioeconomic characteristics as our patient population, and as such, our patients may share many of these risk factors for delay in treatment. Patient delay is challenging to address as it is a complex problem which necessitates interventions at various levels of administration within the healthcare system. A recent study of patient delay within an urban setting noted a marked delay from recognition of a breast symptom and presentation to a health provider, with factors such as difficulty with transportation, poor education levels and poor job security being cited as important causes of delay [12]. While this illustrates that patient delay is an important aspect of total delay, we cannot ignore the impact of provider delay in our patient population, even in those patients that present at an early stage.

The impact of provider delay in the outcomes of breast cancer patients have been widely reviewed and the current consensus is that delays of more than 3 months from presentation to primary therapy is associated with worse clinical outcomes.[7] In addition to oncological end points, it has been shown that increased time for workup

and diagnosis leads to increased patient anxiety and worse psychological outcomes [13,14]. Decrease in delay is therefore an important goal in increasing quality of care offered to patients. Furthermore, the provider delay has been measured in developing countries and found to be far in excess of that recommended by guidelines, and that provider delay of up to 8 months has been recorded in some low-income countries.

The aim of this audit is to assess provider delay and identify specific areas of delay which could then assist in reducing total treatment delay. In this study a review of patient records within a specialist breast referral centre was performed to determine the aspects of provision of care in which delays is most common.

Methods

This study was designed as a retrospective audit of records of patients with a histological diagnosis of invasive breast carcinoma between 1 January 2014 and 31 December 2014. Data collected included date of presentation, mammogram, core biopsy, histology result, sentinel lymph node biopsy (if applicable) and primary therapy. Patient demographics including age and gender were recorded, as was the disease stage at presentation, classified according to AJCC staging (7th edition).

Patients were identified from the biopsy records of the mammography department, which represent the most reliable documentation of newly diagnosed patients within the centre. Records were verified and supplemented with patient files and theatre records. The dates of first dose of chemotherapy for patients in the primary chemotherapy group were recorded from the breast oncology navigation system, which is a record of all breast cancer patients being treated in the centre, and records date and location of referral and first treatment of neoadjuvant therapies.

Patients diagnosed with loco-regional recurrence, ductal carcinoma in situ without an invasive component and patients for whom the data sets were incomplete or lost to follow up were excluded from the study. Other tumours such as lymphoma or phyllodes tumours were excluded from this study

Study site

The centre is an open access unit. Patients may walk in for investigation and treatment without referral and are not limited by geographical draining district. Care is from point of presentation, through diagnostic work up, up to and including surgical care. Surgical and primary endocrine therapy is provided on-site, while neo/adjuvant chemotherapy or radiation are provided at a nearby quaternary hospital via an academic multi-disciplinary team meeting. Approximately 3000 new patients are seen each year, and 300-350 breast cancers are diagnosed and treated.

Standard management

New patients are triaged, and urgency of triple assessment determined according to published protocol. This is prioritised as urgent (10 days), semi-urgent (4-6 weeks) or routine screening cases (2-3 months). Multi-modality radiology is provided within the centre and lesions requiring biopsy undergo image guided core biopsy, usually on the same day. In a separate visit, once pathology results are available,

therapeutic options are discussed with the patient and family, and a treatment plan is finalized.

At the time of this study, most patients diagnosed with invasive breast cancer with a locally advanced breast cancer, or radiologically positive axillae were referred for neo-adjuvant chemotherapy. Patients with Stage 1 or node negative stage 2A disease would be offered either definitive breast surgery with sentinel lymph node biopsy, or a separate sentinel lymph node biopsy without breast surgery if neo-adjuvant chemotherapy was considered prior to definitive breast surgery. Selected patients with oestrogen-receptor positive tumours and either severe comorbidities or judged to be poor operative risk, were offered primary endocrine therapy in the form of a selective oestrogen-receptor blocker or aromatase inhibitor. Patients referred for neo-adjuvant chemotherapy are referred to the quaternary hospital. On acceptance of the referral, a date is given for first treatment.

Data analysis

Data were captured using Research electronic database (REDCap) hosted by the University of the Witwatersrand [15] and analysed in Excel (Microsoft Corp, USA Version 2010). Date ranges were expressed as median values (with interquartile range) for the given intervals, as measured in days. The entire study population was analysed, and a subgroup analysis was done for each treatment modality. Patients undergoing sentinel lymph node biopsy were also analysed as a separate group. Median values were used, as opposed to mean values, as the study group showed a distribution skewed to the left. Delay between groups was compared using Fisher's exact test of proportions, a p-value <0.05 was considered statistically significant. As an audit, the actual delays were compared to a standard of 90% of patients reaching primary therapy within 60 days from presentation. This standard is in keeping with the South African national breast cancer policy and from established international guidelines as well as review of average delay within other low and middle-income countries. [16]. Ethics was approved by the University of the Witwatersrand Human Research Ethics Committee (study number M160786).

Results

A total of 303 core biopsies with a diagnosis of either invasive malignancy or phyllodes tumour was identified for the period under review. A total of 45 patients were excluded from the audit: 15 of these patients had loco-regional recurrence, 6 patients were diagnosed with phyllodes tumours, 6 patients had incomplete data sets, and 24 patients did not return to the unit after the core biopsy was performed. These patients all underwent core biopsy but did not return for results or treatment. The number of mortalities attributable to this group is unknown. A flow diagram indicating the patients identified, as well as those excluded is shown in Figure 2

Mean age at presentation was 55.6 (SD 14.5), with considerable variation amongst the different groups. The characteristics of the total study population as well as those for each modality of primary therapy are presented in Table 1. A total of 171 (68.1%) patients underwent primary chemotherapy, 54 (21.5%) underwent primary surgery and 26 (10.4%) patients received primary endocrine therapy. When considered as a proportion of the first treatment groups, delay greater than 60 days was experienced by 61.1% of patients in the primary surgery group, 36.8% of patients in the primary chemotherapy group and 11.5% of patients in the primary endocrine therapy group. The steps of care provision with measured intervals are illustrated in Figure 1.

The median delay (IQR) from primary presentation to first therapy was 49 days (33-80 days). A total of 99 (39.4%) patients had a delay of more than the standard of 60 days. Of the 99 patients with extended delay, 63 (63.6%) had primary chemotherapy, 33 (33.3%) had primary surgery, and 3 (3.0%) had primary endocrine therapy. The delay of each group as well as the time intervals for each step are shown in Table 2

Delay within each group was equal throughout the initial stages of diagnosis and workup until initial histology results were obtained and a plan for therapy discussed. Endocrine therapy usually started on the same visit, while the time for chemotherapy and surgery were increased. The median delay for the patients in the primary surgery group of 75 days (IQR: 39.75-113.5) was significantly higher than with primary chemotherapy (48 days IQR: 30-71 days) (p-value < 0.001). 18 (33.3%) patients in the primary surgery group and 16 (9.4%) patients in the primary chemotherapy group had sentinel lymph node biopsy before definitive therapy was undertaken. When sentinel lymph node biopsy was excluded, delay reduced in the primary surgery

group to 58 days (IQR:36.3-84.8 days) but not in the primary chemotherapy group (48 days IQR: 30.0-71.0 days).

Delay was measured by stage of presentation, with early stage being patients that presented as T1 or T2 lesions, and late stage being T3 and T4 lesions. Data is presented in Table 2.

Discussion

In this study of newly diagnosed patients with breast cancer, 60.6% of patients reached primary treatment within 60 days of diagnosis. The target of 90% of patients reaching primary therapy within 60 days in the breast care centre was not attained during the period under review. Nearly two thirds of the patients with delay to first treatment were delayed to chemotherapy (62.3%), and one third (34.7%) were awaiting surgery. However, when considered as a proportion of the treatment groups just over 60% of patients awaiting primary surgery experienced delay with 36.8% of patients in the primary chemotherapy group experiencing delay greater than 60 days.

Delay was most common in the primary surgery treatment group, with a median time to surgery of 75 days (39.8-113.5d) which was 25% longer than the target time of 60 days. This delay to surgery was decreased slightly when the delay to sentinel lymph node biopsy was excluded; however, this decrease was not observed in the primary chemotherapy group. The addition of sentinel lymph node biopsy to the treatment algorithm added a median of 25 – 27 days, with an additional delay of 11-12 days for subsequent histology results.

Of the 251 patients included in this study, 151 patients (60%) were classified as locally advanced disease, in keeping with the trend found in patients from other low and middle-income countries. The reason for delayed presentation is documented within a South African setting [12,17], and is similar to trends seen in other developing countries. Factors for late presentation that have been identified include poor socio-economic circumstances, poor education around cancer symptoms and risk, as well as patient specific concerns around surgery and other invasive treatment modalities [8-11]

Newer studies have been published regarding the impact of provider delay on long term outcome. While older data showed little effect on outcomes in early stage disease with delays of up to 60 days [18], more recent studies revealed a significant decrease in overall survival (OS) and disease specific survival (DSS) with delay. This effect is more pronounced in patients with stage I and stage II disease, with a

less pronounced effect observed in later stage disease. OS and DSS decreased with increasing time to surgery and was approximately 10% for every 30-day interval from presentation [19]. Of concern is that the patients in this population undergoing primary surgery and therefore at risk for the longest delay, are patients with stage I and II disease. Of note is that none of these studies reviewed morbidity or the effect on breast salvage rates in patients with significant delay.

Formal guidelines are varied, with no set standard in acceptable provider delay intervals. European guidelines published in 2008 advise an acceptable delay from diagnosis to primary treatment of 25 working days, with a desirable delay of 23 working days [20]. Only 73 (28.40%) of all patients met this standard. The South African national guideline recommends a provider delay within a specialist breast unit of 60 days [16].

Optimal time to treatment in newly diagnosed breast cancer remains a controversial topic, with conflicting reports and a lack of standardised criteria for delay within individual studies. A clear picture of the effects of delay on morbidity and mortality remain unclear. A retrospective review of patients in 1999 revealed that there was a significant increase in disease specific mortality in patients who underwent primary treatment more than 90 days after a breast symptom first occurred, whereas mortality remain unchanged in those patients who were treated before the 3-month mark. Patients with a delay in treatment of more than 60 days had a worse outcome, with the effect being more pronounced in patients with late stage disease [3]. Provider delay is an important component in the overall delay, and therefore for patient outcomes. It has been shown from various studies within our setting that increased delay leads to later disease stage at presentation, and this is linked to overall survival. Factors contributing to total delay include poor levels of education, issues with reliable transportation, cost of travel and fear of loss of employment [12]. While the impact of this delay is noted, it does not shape policy within a breast care unit as it is largely outside the control of that unit. With late stage at presentation being common in our setting, with more than half of patients presenting with Stage 3 disease at presentation [17] in some centres, further delay needs to be minimised if we are to offer improved outcomes to our patients. The target of 60 days to treatment was set with these factors in mind, as well as being in keeping with the national breast cancer policy [16].

The unit standard is based on national policy, as well as extrapolated from data around delay in low and middle-income countries and from those formal guidelines that exist for high income countries. The difficulty in assessing this data is that reporting is not standardised, with a wide range of delay intervals being reported [21]. Recent data published in a secondary hospital in South Africa showed a median delay of 70 days between presentation and referral to a multi-disciplinary treatment centre, with the time to definitive treatment after referral unknown [22]. This is far higher than the recommend provider delay of 60 days, and likely represents a resource poor environment and fragmented care within our country, with delays far greater than accepted within each step of the diagnostic process.

Every effort is made to decrease provider delay by having an open access centre and an on-site mammography unit with dedicated radiologists, where core biopsies are usually performed on the day of imaging. Time to pathology result was consistent across all groups, nearly in keeping with European recommendations of 5 days. Despite this, time to treatment is still not optimal. If it is considered that patients undergo chemotherapy at a referral centre and that the delay is therefore not controlled by our centre, the conclusion is that the main modifiable cause of delay within this group is the wait to surgery.

One area not assessed by this study was whether the addition of sentinel lymph node biopsy changed overall management of patients, and if so, to what extent. If sentinel lymph node biopsy was to be offered at the time of primary surgery, delay would be decreased by almost three and a half weeks. Many patients who underwent primary surgery did not have sentinel lymph node biopsy beforehand. This may represent an opinion by some of the managing breast care surgeons that this step is not essential to management and can therefore be safely done at the time of primary surgery. This would need to be assessed before determining future policy within the unit.

Delay to surgical intervention is the biggest component of delay within this unit, and therefore the area at which interventions should be aimed. Data from the WHO suggest that around 234 million surgical interventions are performed worldwide per year, the majority of which are performed in developed countries [23]. Poor access to surgical facilities within low-income countries places an increased burden on these facilities. It has been found that all facilities from primary to tertiary settings have a larger load of urgent surgeries, and as such funding and equipment is directed

toward emergency surgery. As expertise and access improves, a wider range of procedures can be offered [24]. The system in which this unit operates faces the challenge that within the specific province, almost all surgical procedure others than obstetric surgery are performed at tertiary level hospitals. Where breast units in more developed settings are able to deal more exclusively with malignancies or complex cases, this unit deals with all breast pathology within the referral area.

A combination of wide range of benign disease being treated and limited theatre time available to the unit result in longer wait times to theatre, even in patients with malignant disease. Added to this is that patients making use of the same theatre resource but not included in this study are patients undergoing surgery after neo-adjuvant chemotherapy. This places a further burden on a limited resource. A final factor to take into consideration is the logistics of booking theatre cases and lists. Due to large burden and limited access, patients are booked dependent on the next available slot, with little stratification of patients. It is possible that the delay in primary surgery for patients that have largely early stage disease may be due to perceived lessened risk compared to patients with advanced disease or prior treatment.

Conclusion

The breast care centre did not achieve the desired standard that was set after consideration of the relevant literature and available guidelines. While it is accepted that our health system is burdened and that there are constraints in resources and personnel, it remains our imperative as clinicians to improve service delivery where possible, in order to improve the standard of care to our patients. With this in mind it is recommended that as far as possible, sentinel lymph node biopsy be performed at the time of primary surgery for clinically and radiologically negative axillae. This has the potential to decrease delay by up to almost 40 days. Specific reasons for the increased time to surgery are unclear as these were not documented, but every effort should be made to improve the waiting time to surgery. Suggestions for improved care would include better utilisation of secondary hospitals for less complex surgery, therefore improving wait times. Streamlining of booking process and periodic review of bookings at a consultant level may also decrease wait times in at-risk patients. It is furthermore recommended that a repeat study be performed once these measures have been implemented, to review the effect on delay.

Tables and figures

Treatment Modality	Number	Age +-SD (years)	Delay >60 days	Delay <60 days
Total study population	251	55.9 (14.3)	99 (39.4%)	152 (60.5%)
Primary Chemotherapy	171	50.9 (12.0)	63 (36.9%)	108 (63.1%)
Primary Surgery	54	62.9 (11.7)	33 (61.1%)	21 (38.9%)
Primary Endocrine Therapy	26	74.8 (11.0)	3 (11.5%)	23 (88.5%)

Table 1: Characteristics of included patients

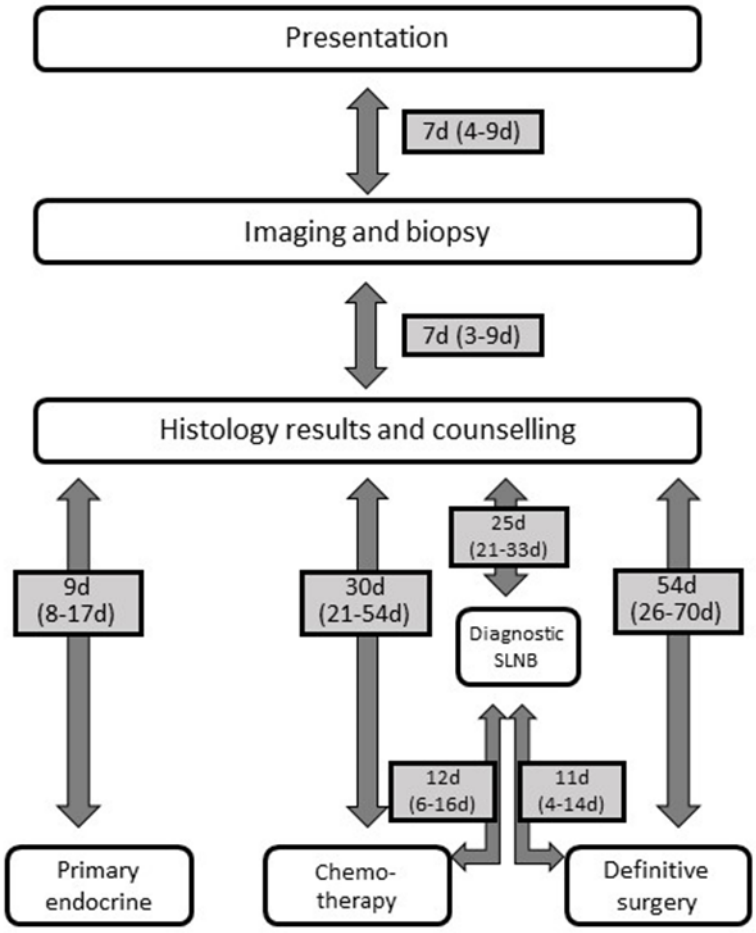


Figure 1: Therapeutic algorithm for newly diagnosed patients

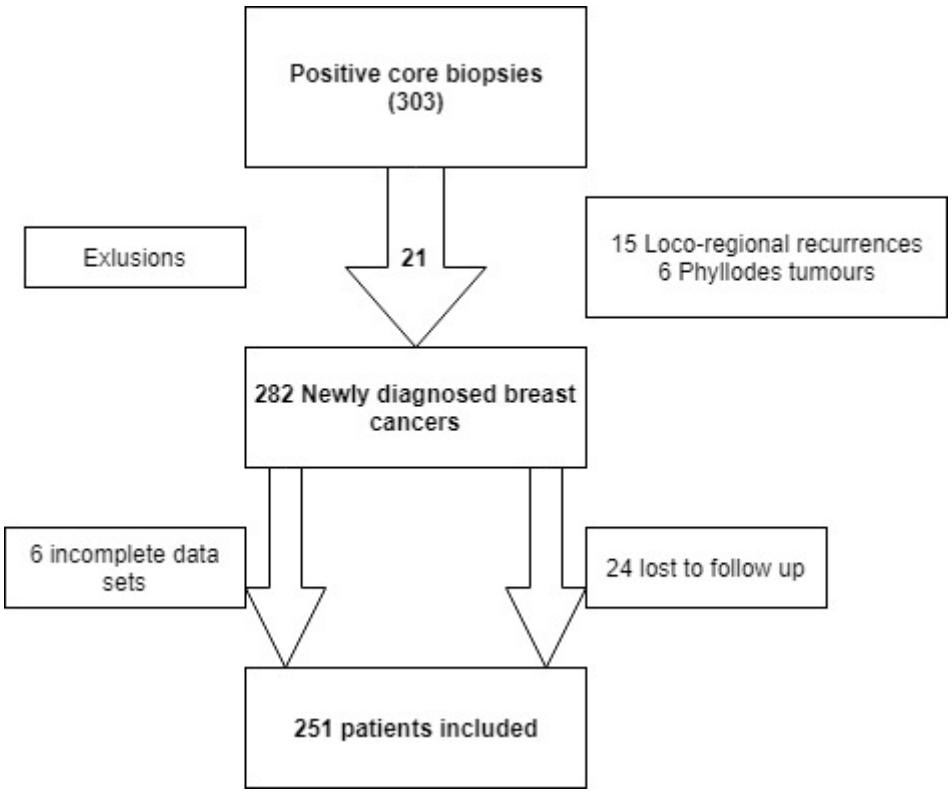
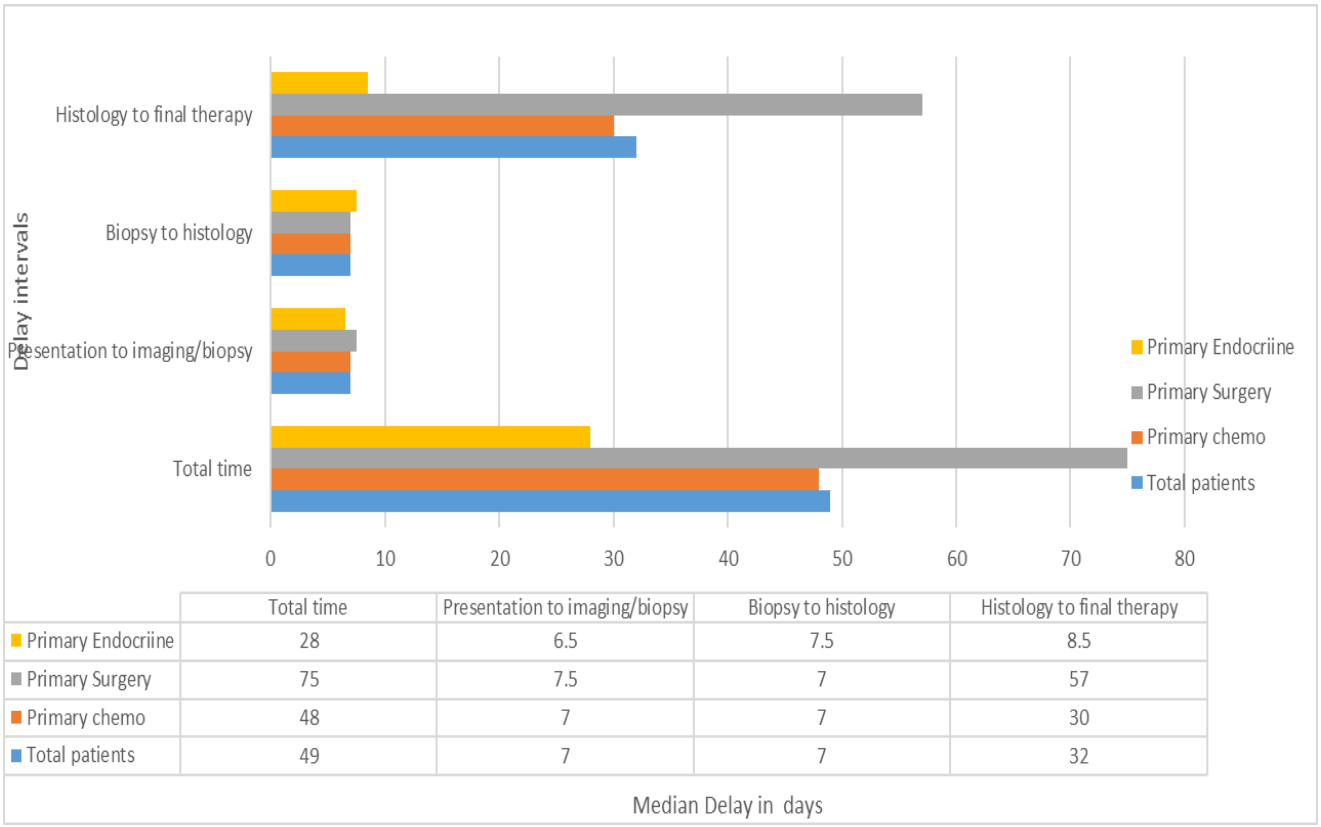


Figure 2: Included patients



	Total time	Presentation to imaging/biopsy	Biopsy to histology	Histology to final therapy
Primary Endocriine	28	6.5	7.5	8.5
Primary Surgery	75	7.5	7	57
Primary chemo	48	7	7	30
Total patients	49	7	7	32

Figure 3: Bar chart of time intervals by modality of therapy

Clinical stage	Number	Total delay	Presentation to imaging/biopsy	Biopsy to histology	Histology to final therapy
Advanced	151	44 (44-46)	7 (2.5-9)	7 (3-9)	28 (18-45)
Early	100	62.5 (36.8-98.5)	7 (5-12)	7 (6-12)	42.5 (22-70)

Table 2: Delay according to clinical stage at presentation

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Appendix 1: Expanded literature review and protocol

Title: An audit of provider delay in newly diagnosed breast cancer patients at a central referral hospital in Johannesburg, South Africa

Introduction and Literature Review

Breast cancer is one of the most common cancers affecting women worldwide, with 1.67 million new cases diagnosed every year and approximately 500000 deaths annually worldwide [1]. Various studies have been undertaken to assess the factors that have an influence on the outcome of patients affected by this disease.

One of the factors that has been assessed in terms of patient outcome is delay in presentation, diagnosis and primary treatment of breast cancer. Delay has been defined in terms of patient delay and provider delay [2]. Patient delay is defined as the time taken for a patient to present to a health care practitioner from initial recognition of a breast symptom. Multiple studies have shown that patient delay of more than three months is associated with a more advanced stage of disease at diagnosis and a consequent increase in morbidity and mortality [3,4]. Furthermore, more aggressive surgical and non-surgical modalities are needed to treat advanced disease, resulting in an increase in morbidity secondary to the treatment modality[5].

It is less clear whether provider delay in breast cancer has any adverse impact on patient outcomes [6,7,8]. Provider delay is defined as the time taken from first presentation to a health care practitioner to receiving the primary treatment, be that

surgical or non-surgical (primary chemotherapy, radiation therapy or hormonal treatment). Some studies have assessed whether a delay of one week, one month or even two months from confirmation of disease via tissue biopsy to primary treatment has any effect on mortality.

A meta-analysis by Richards *et al* found that there was no correlation between provider delay of up to two months and mortality [3]. The one drawback of the studies used in this analysis is that no subset analysis of patients was done with stratification according to stage of disease at presentation, nor tumor biology. McLaughlin *et al* assessed a group of low-income patients in North Carolina in 2012 and found that there was no difference in outcome if the group was assessed, but in those patients presenting with advanced disease, a delay of more than 60 days from tissue diagnosis to primary treatment resulted in a statistically significant adverse impact on mortality. This suggests that there should be some form of prioritisation of patients with advanced disease when it comes to initiating treatment in late stage disease [9].

In sub-Saharan Africa we are potentially faced with a population at risk for poor healthcare delivery and suboptimal care. The factors that place this population at risk include poor socio-economic circumstances, strong cultural beliefs which may impact patients' health seeking behavior, and in some studies, a distancing from if not outright distrust of western medicine, and generally poor educational background [10]. Patient-specific concerns, including fear of mastectomy and other invasive treatment modalities, may result in patients defaulting treatment despite early diagnosis [11]. These factors play a pivotal role when dealing with referrals from our more outlying hospitals. We do however also serve a large number of patients from within our metropolitan area that may have access to better education, internet resources and relatively easy access to the healthcare system and in this setting

these factors play a less prominent role. Most of the South African data around health seeking behaviour and adherence focus on more rural areas such as KwaZulu Natal or the Eastern Cape [12] and as such, the factors specific to patients presenting to our centre are poorly understood. While we acknowledge that there is a paucity of literature in our patient population, a delay in breast cancer treatment is well documented in other parts of the world where patients come from a similar background [13,14]. Factors such as very young patients, very old patients, poor educational level and poor socio-economic status negatively affect health seeking behavior and increase the risk of patients presenting at a late stage of disease [15]. A study of these factors has been undertaken in our unit and the preliminary results are under analysis. This study is conceptualised as complimentary to our current work.

Studies performed in largely developing parts of the world, especially Sub-Saharan Africa, have shown widely varying delays between primary level clinics and specialist referral centres. Factors which contribute to this delay include poor staff attitudes toward breast cancer (possibly from previous experience with poor outcomes), poor healthcare worker knowledge of disease and possible treatments, and ailing health systems with poor availability of transport or poor access to specialist care for patients from outlying regions. It has been shown that the further a patient lives from a referral centre, the higher their risk of developing advanced disease and therefore the greater their risk of poor outcomes[16]. These delays need to be accounted for as it has been reported that some patients are only referred to specialist centres after periods as long as three months.

While some of these risks are not applicable to our metropolitan population, we may find some of the patients from peripheral areas that experience these delays. This has a potential effect on stage at presentation.

As health care providers we try to influence cultural preference, education levels and patient knowledge of disease through patient education and awareness, but we remain unable to change the health system at a political level. We are able to use data and research to influence system within which we work. This enables streamlining of the process once patients enter our system and attempt to provide them with the appropriate care as soon as possible, so as to decrease total delay in these patients.

It would seem prudent to evaluate the delay within our own system at a referral hospital to see if we are able to determine if any delay exists, and if so, where in the system it occurs. Once determined, we could then go about changing that specific step in the therapeutic process with the aim of improving the outcome in our patients.

Provider delay varies widely between high income vs low and middle-income countries. It becomes challenging to define an acceptable standard against which to compare our data as there is marked heterogeneity within the various studies performed around provider delay, with different definitions used in different studies and various time periods examined within the studies. What is very noticeable when comparing high versus low/middle income countries is that there is a marked increase in delay in low and middle-income countries.

Establishing a standard

There is marked heterogeneity in our population group regarding patient and provider delay. Some patients have delays comparable to high income countries, presumably because of socio-economic advantage and access to private health care, while other

patients making use of state healthcare have delays on par with the rest of the developing world [17]. When considering a standard to which we compare our unit, it would be ideal to aim for the same delay intervals as high-income countries within our academic referral units. There are system limitations within our hospitals, and to compare our delay interval to those of first world systems would be unfair. At the same time, if we use the average interval reported by other low/middle income countries (2.5 – 4 months) as our standard, we would be accepting a waiting time that may put patients at risk of adverse outcomes and possibly worse survival, especially those patients presenting with late stage disease. We feel that an acceptable standard in our setting would be an average provider delay of 2 months (60 days) from first presentation at our specialist breast centre to treatment initiation for 90% of our patients.

The interval we will assess is the time from first contact at our specialist unit to initiation of primary treatment. This would include the time from first outpatient visit to radiological investigation and tissue diagnosis, and the time from tissue diagnosis to initiation of primary therapy, including any time taken for staging/sentinel lymph node biopsy.

Study Objectives

Primary objective

To assess provider delay in newly diagnosed breast cancer patients at a specialist breast referral unit

Secondary Objectives

To determine what causes the delay within the specific unit, and during which stage of the therapeutic process it occurs

Research Design and Methods

Design

A retrospective audit of newly diagnosed breast cancer cases from 1 January 2014 to 31 December 2014, from first presentation at a specialist centre to diagnosis and initiation of definitive treatment (defined as primary curative surgery, primary chemotherapy or primary hormonal treatment)

Audit Standard

90% initiation of treatment within 60 days of presentation to out centre

Site of Study

Helen Joseph Breast Care Clinic

Study Population

Both female and male patients who are diagnosed with breast malignancy on core biopsy performed at Helen Joseph Hospital during the year 2014

Sampling

We estimate a study size of 300 patients

Recruitment - all core biopsy positive patients for the designated period (1 January 2014 – 31 December 2014) will be recruited to the study

Inclusion criteria - Inclusion criteria for the study would be all patients with a positive core biopsy performed at Helen Joseph Hospital for the year 2014.

Patients with diagnoses other than primary breast carcinoma would also be included (e.g. Phyllodes tumour or lymphoma of the breast), as they undergo most of the same steps in workup with the same potential for delay in imaging, histopathology and theatre booking.

Exclusion criteria – Those patients who present to the Breast Clinic with the diagnosis of malignancy already having been made on tissue biopsy would be excluded. Patients who have an element of diagnostic uncertainty and require multiple investigations and surgical procedures to reach a diagnosis of malignancy would also be excluded, as we feel that these constitute the minority of cases and the excessive delay would skew our data and not be representative of the average patient being treated in the unit.

Measuring tool - Data would be entered into an Excel spreadsheet with each patient record assessed for delays at various stages:

- Time from first presentation at the unit to radiological examination (mammogram or ultrasound)
- Time from radiological investigation to tissue biopsy
- Time from tissue biopsy to result being released by anatomical pathology
- Time from release of pathology results to sharing these results with the patient
- Time from diagnosis to diagnostic operative procedure (e.g. sentinel lymph node biopsy), if any
- Time from diagnosis or diagnostic operative procedure to primary treatment

The triage level of each patient would also be recorded.

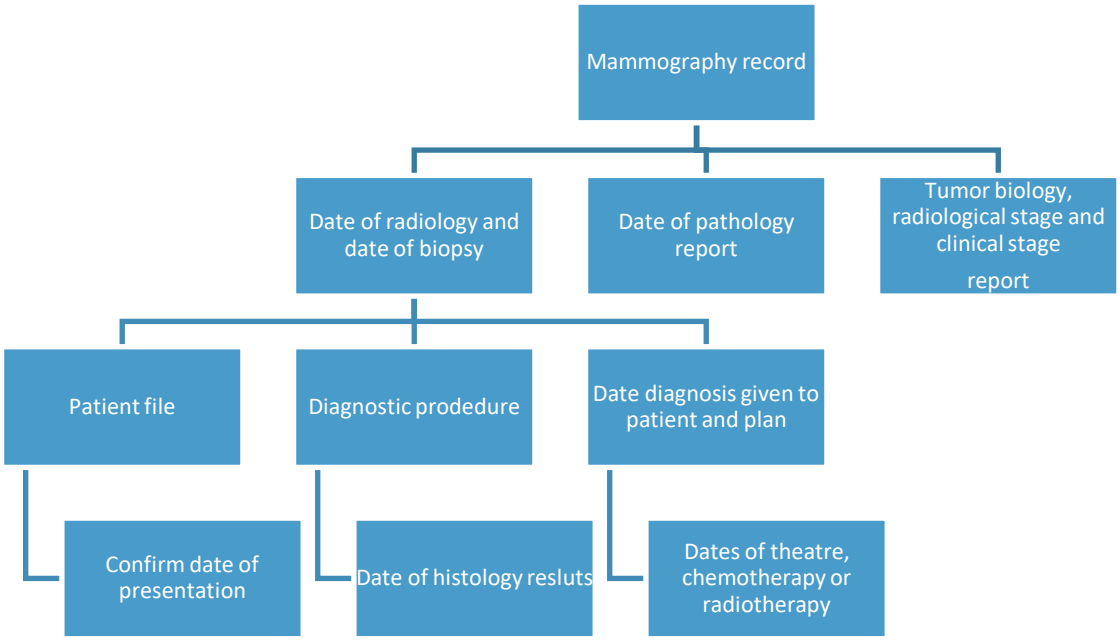
The radiological stage and clinical stage, tumor type and receptor status of each patient would also be documented.

Data collection: Patients would be identified from mammography records at Helen Joseph Hospital. These records show the date of first consult, date of mammogram or ultrasound, date of core biopsy and also contain a copy of the pathology report. The date that the result was signed out by the pathologist is also recorded on the report. The patient files would then be traced using the hospital number and would be checked for the date that the patient was given the diagnosis and what the plan for each specific patient was. The electronic system (BRON) used to capture each new patient would also be checked to make sure that the date radiology was requested was the same as the date the patient first presented to clinic. Dates for theatre, whether diagnostic or therapeutic, would be checked in the theatre booking book and confirmed in the theatre register. Theatre dates would also be checked against the electronic operation log. Delay due to theatre constraints or patient factors such as poor operative risk would also be recorded. The date that the patient was booked for first consultation at medical oncology as well as the date planned for first treatment would be captured from the Navigator book in Breast Clinic. Any delays after referral from our unit for either chemotherapy

or radiotherapy would also be recorded.

Patient number	Clinical stage	Radiological Stage	Tumour Biology	1st consult	MMG/US	Path Report	Diagnosis to pt	Sentinel lymph node biopsy	Histology	Primary Treatmen

(Example of headings from data collection sheet)



(Flow diagram of data collection process)

Statistical Analysis

Data will be captured onto the Epi Info program and analysed by means of percentages, tables, and by determination of the means for each interval. Further statistical analysis will be performed to determine significance stage and age, stage and biology, delay to initiation and stage. We will be making use of the student T-test and the Fischer exact equation of small numbers. We will consider a p value of <0.05 as significant

Ethical Considerations

All patient data obtained from past records would be assigned a number and patients would remain anonymous throughout.

There would be no risk or bias to the included patients, and patients would receive no benefits for participating in the study. There will be no compensation for participation in the study.

Limitations

The limitations that we recognise within our study are incomplete or missing patient records. Percentage of missing data will be recorded in the study as it has potential to increase patient delay.

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Appendix 2: Ethics clearance certificate

R14/49 Dr Douglas Graham Ross

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. Ml 60786

NAME: (Principal Investigator)	Dr Douglas Graham Ross
DEPARTMENT:	Surgery Helen Joseph Hospital
PROJECT TITLE:	An Audit of Provider Delay in Newly Diagnosed Breast Cancer at a Central Referral Hospital in Johannesburg, South Africa
DATE CONSIDERED:	29/07/2016
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr Sarah Rayne

Professor P. Cleaton-Jones,Chai person, HREC (Medical)

DATE OF APPROVAL: 01/03/2017

APPROVED BY:

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 Research Office Secretary in Room 10004, 10th floor, Senate House/2nd floor, Phillip Tobias Building, Parktown, University of the Witwatersrand. l/We fully understand the the conditions under which I am/we are authorised to carry out the above-mentioned research and l/we undertake to ensure compliance with these conditions. Should any departure be contemplated,from the research protocol as approved, l/we undertake to resubmit to the Committee. I agree to submit a yearly progress report. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. in this case, the study was initially review in and will therefore be due in the month of Jul; each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix 3: Guidelines for submission to the 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 40 years of age'. The same applies to ± and º, i.e. '35±6' and '19ºC'.

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]

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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.

CHANGES OF ADDRESS Please notify the Editorial Department of any contact detail changes, including email, to facilitate communication.

CPD POINTS Authors can earn up to 15 CPD CEUs for published articles. Certificates may be requested after publication of the article.

CHARGES There is no charge for the publication of manuscripts.