CoRIPS RESEARCH AWARDS OCTOBER 2020

Heather Drury-Smith

CoRIPS Research Grant 193 (Covid)
£8,575.00 Awarded

Title of Project
Barriers and facilitators to engaging with health services for patients with breast cancer symptoms or a breast cancer diagnosis during the COVID-19 pandemic.

Lay summary of the project (250 words maximum)
There are an estimated 600,000 people living in the UK with a diagnosis of breast cancer; 1 in 7 women in the UK will develop breast cancer in their lifetime. There are many different signs and symptoms of breast cancer, so regularly checking the breasts for any changes is important. The earlier breast cancer is diagnosed, the better the chance of successful treatment.

A new acute respiratory syndrome coronavirus, named COVID-19 has rapidly spread around the world. As a direct result of the coronavirus pandemic there has been a 78% drop in UK screening and referrals for people presenting with breast cancer related symptoms. The delay experienced by some patients with cancer-related symptoms may increase the risk that the patient may require more extensive surgery, or in some cases reduce the patient's prognosis in the long term.

We are interested in understanding the experiences of people who have noticed a potential breast cancer symptom during the COVID-19 pandemic, as well as patients diagnosed with breast cancer just before the lockdown in March 2020. We will interview people to identify barriers or challenges in seeking an appointment with a General Practitioner (GP) or accessing cancer services for breast cancer treatment during the COVID-19 pandemic. Understanding the barriers to accessing cancer services will inform appropriate information or toolkits for patients, GPs and cancer service providers. Recommendations to policy makers and cancer service managers will enhance patient access to services should there be a further wave of Covid-19 infections.

a) Review of the literature and identification of current gaps in knowledge

Please note in this review the SARS-CoV-2 coronavirus will also be referred to as Covid-19.

A new acute respiratory syndrome coronavirus, named SARS-CoV-2 by the World Health Organization (WHO), has rapidly spread around the world since its first reported case in late December 2019 from Wuhan, China (Guan et al, 2020). As of October 2020, the virus has affected more than 200 countries and territories; in the UK it has infected more than 500,000 individuals and caused more than 42,000 deaths (Gov.UK, 2020). In the UK cancer affects a significant portion of the population with more than 367,000 people diagnosed each year (Cancer Research UK a, 2015-2017). Breast cancer is the most common cancer in women and accounts for over 55,000 new cases each year in the UK (Cancer Research UK b, 2017).
Individuals affected by cancer are more susceptible to infections in particular if they also have a coexisting chronic disease and those with a compromised immune system caused by both cancer and anticancer treatments (Desai et al, 2020). As a consequence, patients with cancer who are infected by the SARS-CoV-2 coronavirus may experience poorer outcomes than other

populations. There is relatively limited data as to the effects that the SARS-CoV-2 coronavirus has on patients with cancer in a representative population. A recent study reported a higher risk of severe events (composite endpoint defined as the percentage of patients being admitted to the intensive care unit requiring invasive ventilation, or death) in patients with cancer when compared with patients without cancer (Liang et al, 2020); however, the small sample size of SARS-CoV-2 patients with cancer used in the study limited how representative it was of the whole population. There was also the difficulty of comparing clinical characteristics of patients with different types of cancer, as well as anticancer treatments which could have identified further insights (Xia et al, 2020). As part of the UK Coronavirus Cancer Monitoring Project (UKCCMP) Lee et al (2020) using a prospective observational study analysed 800 patients with a diagnosis of cancer and symptomatic COVID-19. The study concluded that mortality from COVID-19 in cancer patients appears to be principally driven by age, gender, and comorbidities. The authors were unable to identify evidence that cancer patients on cytotoxic chemotherapy or other anticancer treatment are at an increased risk of mortality from COVID-19 disease. However, Dai et al (2020) in their multicentre study including 105 patients with cancer and 536 age-matched patients with no cancer with confirmed COVID-19 demonstrated that COVID-19 patients with cancer had higher risks in all severe outcomes. Patients with haematological cancer, lung cancer, or with metastatic cancer (stage IV) had the highest frequency of severe events (defined as death, admission to intensive care units, employing invasive mechanical ventilation, development of critical / severe symptoms). Patients with nonmetastatic cancer experienced similar frequencies of severe conditions to those observed in patients without cancer. Patients who received surgery had higher risks of having severe events, whereas patients who underwent only radiotherapy did not demonstrate significant differences in severe events when compared with patients without cancer. The authors therefore concluded that patients with cancer appear more vulnerable to SARS-CoV-2 outbreak. Due to the hypothesis that cancer patients are more susceptible to COVID-19 this has led to widespread and global changes to the patterns of prescribing anti-cancer treatments (Lancet Oncology, 2020).

It has been stated that delays in diagnosing and treating people with cancer could lead to more years of lost life than with COVID-19 (Sud et al, 2020). Existing Public Health England data has been analysed by scientists from The Institute of Cancer Research, London, on delays to cancer surgery on patients' five-year survival rates to estimate the effect of three-month or six-month delays, respectively. The authors having factored in the risk of hospital-acquired COVID-19 infection in their modelling reported dramatic differences in the impact of delay on cancer survival depending on patients' age, their cancer type and whether it was earlier- or later-stage cancer. A delay of three months across all 94,912 patients who would have had surgery to remove their cancer over the course of a year would lead to an additional 4,755 deaths. Taking into account the length of time that patients are expected to live after their surgery, the delay would amount to 92,214 years of life lost (Sud et al, 2020).

Indeed Cancer research UK (c, 2020) has reported a drop off in screening and referrals which has amounted to approximately 2700 fewer people being diagnosed with cancer each week during the pandemic. Due to the COVID-19 pandemic urgent cancer referrals have seen a 60 per cent drop in numbers (Lai et al, 2020). NHS England statistics (a, 2020) have demonstrated that there were 79,573 urgent cancer referrals made by GPs in England in April 2020, down from 199,217 in April 2019. Breast cancer referrals fell by 78% in this same time period from 16,753 in April 2019 to 3,759 in April 2020 (NHS England b, 2020). Furthermore the number of people in England who had to wait more than two months for a GP referral to their first treatment for cancer dropped by 20 per cent, from 13,519 in April 2019 to 10,792 in April 2020

(NHS England b, 2020). Due to cancer screening being paused during the lockdown follow-up appointments for all breast, bowel and cervical screening programmes are being delayed (Cancer Research UK c, 2020). People are still being urged by the NHS, cancer charities and the government to contact their GP with any worrying symptoms however it has been suggested that fear of COVID-19 is greater than fear of having cancer at the moment (Sullivan, 2020). It is estimated that there could be more than 35,000 cancer patient deaths in a year due to treatment delays caused by COVID-19 (HDRUK, 2020). These estimates are based on people with cancer symptoms not receiving early diagnosis as well as treatment being delayed. Cancer research UK (d, 2020) estimate almost 2.5 million patients have missed out on diagnosis and treatment because of the pandemic with 2.1 million patients currently awaiting screening for breast cancer. Screening is the route with the highest proportion of cases diagnosed at an early stage for breast cancer, so when screening was on hold there is a worry that this will result in many patients potentially having to undergo more extensive surgery. Even if people are referred much of the diagnostic activity is still on hold or delayed (Cancer Research UK d, 2020). Due to services being scaled back to manage the impact of the pandemic there has been a decrease in the amount of elective cancer surgery as well as delays to chemotherapy and radiotherapy; 21,600 patients have had their treatment postponed during the pandemic so far (COVID Surg Collaborative, 2020). There is also the worry that many patients are stuck in a backlog when cancer services are fully opened again particularly as the standard pathway of care for patients diagnosed with breast cancer involves 81% of patients receiving surgery to remove the tumour, 63% of patients receiving radiotherapy and 34% of patients having chemotherapy as part of their primary cancer treatment (Cancer Research UK b, 2020).

In 2015 a YouGov poll for Breast Cancer Care of 409 patients found that almost a fifth of women (17%) who have been diagnosed with breast cancer after spotting a potential symptom wait more than a month before seeing their GP, the equivalent of about 6,000 women every year in the UK and 1 in 20 women wait more than six months (YouGov, 2015). Reasons for waiting included patients believing their symptoms were not a serious issue (one third of participants who waited a month) and one in five were too scared to see the doctor because of their fear it might be breast cancer. Nearly a tenth (8%) of women surveyed said they waited to see their GP because they did not want to be a nuisance. It is a well-known fact that the sooner cancer is diagnosed the more effective a treatment is likely to be; the fact that some patients wait up to six months before reporting a symptom outside of a pandemic is concerning. In the UK approximately 65% of breast cancer cases are identified through symptoms. An early stage diagnosis achieves a survival figure of almost 100% for one year or more, compared with 2 in 3 (66%) people when the disease is diagnosed at the latest stage (Cancer Research UK b, 20). When referring to 5 year survival almost 98% of people diagnosed with breast cancer at the earliest stage will survive, compared with around 1 in 4 (26%) people when the disease is diagnosed at the latest stage (Cancer Research UK b, 2020).
In terms of breast cancer there is no medical definition of a standard interval to diagnosis or treatment, although published studies often used specific thresholds (Mclauglin et al 2012, Shin et al 2012) to investigate when times become detrimental. It is suggested that longer times to treatment probably have a gradual and continuous effect on outcomes, so evaluation of progressive time intervals rather than a specific cut-off may capture the effect on survival more realistically (Bleicher et al, 2016, Polverini et al, 2016). In Bleicher's (2019) review of published data he found that times to surgery, chemotherapy, and radiotherapy have an impact on breast cancer treatment outcomes. Time from diagnosis to surgery (in the non-neoadjuvant setting) of >90 days lowers overall survival by 3.1–4.6%. Furthermore Ho et al (2020) studied

the impact of delayed first treatment on overall survival across different tumour stages in addition to the impact of delayed adjuvant treatments on survival in patients with invasive non-metastatic breast cancer who had surgery ≤90 days post-diagnosis. Over eleven thousand breast cancer patients were analysed in the population based study. Delayed first treatment (>90 vs ≤30 days post-diagnosis) was associated with worse overall survival in patients with invasive non-metastatic (HR: 2.25, 95% CI 1.55-3.28) and metastatic (HR: 2.09, 95% CI 1.66-2.64) breast cancer. Delayed adjuvant treatment (>90 vs 31-60 days post-surgery) was associated with worse survival in patients with invasive non-metastatic breast cancer (HR: 1.50, 95% CI 1.29-1.74). This data highlights the potential impact for patients affected by treatment delays during the pandemic.

As breast cancer is the most prevalent cancer in women worldwide (WHO, ND) survival is related to advances in treatment, detection through screening programmes and a greater awareness of the disease. Five-year survival for breast cancer has been improving in the UK over time. However, despite the relatively high uptake of breast cancer screening when compared to several other Organisation for Economic Co-operation and Development (OECD) countries, the UK continues to fall behind in terms of survival (OECD, 2017). This begs the question as to if the COVID-19 pandemic is impacting upon referrals for breast cancer what further impact will it have on breast cancer outcomes and survivorship. Current projections indicate that COVID-19-related disruption may well last for 18 months, until there is either long-term effective containment in the population or large-scale vaccination (Sud et al, 2020).

In summary, there is data to support a drop in referrals for suspected breast cancer during the COVID-19 pandemic and evidence of a drop in uptake of referrals from GPs by hospitals for diagnostic tests and delays in primary treatment i.e. surgery was suspended. This drop in self-referral to GP services for symptomatic cases is important because delays could mean significant changes in the treatment options that are subsequently available to these women (or men). More aggressive surgery, or adjuvant therapies maybe required if delays are substantial, leading to greater potential side effects and greater impact on patient quality of life. In some cases, substantial delays to making a self-referral to a GP about potential breast cancer signs or symptoms could result in a significant change in future life expectancy. Therefore, it is important to investigate what the barriers, challenges or facilitators to patient self-referral have been in order that appropriate public health messages and health service policies accommodate changes to facilitate increases in self-referral or GP referral during the rest of the period of pandemic lockdown measures. Even after an easing of the current lock-down it is possible a further peak in COVID-19 cases may occur necessitating a further period of lockdown or restrictions. It is important to learn from the current situation in order to avoid repetition of this public health crisis in cancer referrals at a later date.

Methodology

The research to be undertaken and illustrated in this study aims to understand the factors that are and have been preventing women or men with potential breast cancer symptoms seeking appointments with their GP and gaining access to vital treatment during the COVID-19 pandemic.

This lends itself to qualitative research methods, more specifically under the paradigm of interpretivism (Crotty, 1998). As little is known about the personal choices people make about their health during a pandemic the study will use a grounded theory approach namely Kathy Charmaz's 'Constructivist Grounded Theory' (2016) using open interviews to elicit understanding of patients experiences and personal drives in order to generate theory. The aim

is to develop a theory around the barriers and facilitators to active self-referral during a pandemic and the service limitations that prevented timely interventions.

Method

This research will employ the use of telephone or electronic interviews with respondents that are willing to participate to explore the factors that impact upon women or men in seeking advice on a breast cancer symptom with their GP during the COVID-19 pandemic. It also seeks to understand what impact the pandemic plays in self-referral and service experiences in the early stages of breast cancer diagnosis.

Ethical considerations

This study has been approved by the Health Research Institute research ethics panel at Sheffield Hallam University; Sheffield Hallam University will act as sponsor to the study. Approval will be sought from the Breast Cancer Now charity to advertise the study on their patient forums for recruitment purposes. The study will be conducted in accordance with the principles of Good Clinical Practice.

1. References:

Bleicher, R.J., Chang, C., Wang, C.E. et al. Treatment delays from transfers of care and their impact on breast cancer quality measures. Breast Cancer Res Treat 173, 603–617

Bowen, G. A. (2008). Naturalistic inquiry and the saturation concept: a research note. Qualitative Research, 8(1), 137–152

Cancer Research UK a (2015-2017) Cancer Statistics for the UK last accessed 28/06/2020 at https://www.cancerresearchuk.org/health-professional/cancer-statistics-for-the-uk

Cancer Research UK b (2017) Breast Cancer Statistics last accessed 20/06/2020 at https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer#heading-Zero

Cancer Research UK c (2020) 'Urgent cancer referrals being turned down during coronavirus pandemic' last accessed 28/06/2020 at https://www.cancerresearchuk.org/about-us/cancer-news/news-report/2020-07-08-urgent-cancer-referrals-being-turned-down-during-coronavirus-pandemic

Cancer Research UK d (2020) 'Cancer screening and coronavirus (COVID-19)' https://www.cancerresearchuk.org/about-cancer/cancer-in-general/coronavirus/cancer-screening

Charmaz. (2016) Constructing Grounded Theory. A practical guide through Qualitative Analysis. SAGE publication

Creswell, J. W. (2015). Educational research: Planning, conducting, and evaluating quantitative and qualitative research (5th ed.). Boston, MA: Pearson.

COVIDSurg Collaborative (2020) Elective surgery cancellations due to the COVID -19 pandemic: global predictive modelling to inform surgical recovery plans

Crotty (1998) The Foundations of Social Research, SAGE Publication

Dai et al (2020) Patients with cancer appear more vulnerable to SARS-COV-2: a multi-center study during the COVID-19 outbreak. American Association for Cancer Research, April 2020.

Desai et al (2020) COVID-19 and Cancer: Lessons from a Pooled Meta-Analysis. JCO Glob Oncol. April 2020

Egan, T. M. (2002). Grounded Theory Research and Theory Building. Advances in Developing Human Resources, 4(3), 277–295

Elective surgery cancellations due to the Covid-19 pandemic: global predictive modelling to inform surgical recovery plans. British Journal of Surgery. 12 May 2020.

Glaser, B. G. & Strauss, A. L. (1967). The Discovery of Grounded Theory. Strategies for Qualitative Research. Chicago: Aldine.
Gov.UK (2020) Weekly COVID-19 surveillance report last accessed 2/07/2020 at https://www.gov.uk/government/news/weekly-covid-19-surveillance-report-published
Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020; 382:1708–20
Guest, G., Bunce, A., & Johnson, L. (2006). How Many Interviews Are Enough?: An Experiment with Data Saturation and Variability. Field Methods, 18(1), 59–82
HDRUK (2020) COVID-19 last accessed 1/07/2020 at https://www.hdruk.ac.uk/covid-19/
Ho, P.J., Lau, H.S.H., Ho, W.K. et al. (2020) Incidence of breast cancer attributable to breast density, modifiable and non-modifiable breast cancer risk factors in Singapore. Sci Rep 10, 503
Im, E. O., Chee, W. (2006). An online forum as a qualitative research method: Practical issues. Nursing Research, 55, 267–273.
Im EO, Chee W. (2012) Practical guidelines for qualitative research using online forums. Comput Inform Nurs. 2012;30(11):604-611
Kuzel, A. J. (1992). Sampling in qualitative inquiry. In B. F. Crabtree & W. L. Miller (Eds.), Research methods for primary care, Vol. 3. Doing qualitative research (p. 31–44). Sage Publications, Inc.
Lai et al. (2020) Estimating excess mortality in people with cancer and multimorbidity in the COVID-19 emergency. ResearchGate preprint, April 2020.
https://www.researchgate.net/publication/340984562_Estimating_excess_mortality_in_people_with_cancer_and_multimorbidity_in_the_COVID-19_emergency
Lancet Oncology COVID-19: global consequences for oncology. Lancet Oncol. 2020; 21: 467
Lee et al (2020) COVID-19 mortality in patients with Cancer on chemotherapy or other anticancer treatments: a prospective cohort study. The Lancet 395: 1919-1926
Liang W, Guan W, Chen R, Wang W, Li J, Xu K, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. Lancet Oncol 2020; 21:335–37.
Mason. (2010) Sample Size and Saturation in PhD Studies Using Qualitative Interviews. Forum: Qualitative Social Research, Volume 11, No. 3, Art.
McLaughlin JM, Anderson RT, Ferketich AK, Seiber EE, Balkrishnan R, Paskett ED. Effect on survival of longer intervals between confirmed diagnosis and treatment initiation among low-income women with breast cancer. J Clin Oncol. 2012;30(36):4493-4500. doi:10.1200/JCO.2012.39.7695
Morse, J. M. (1994). Designing funded qualitative research. In N. K. Denzin & Y. S. Lincoln (Eds.), Handbook of qualitative research (p. 220–235). Sage Publications, Inc.
NHS England a (2020) 'NHS warning to seek help for cancer symptoms, as half of public report concerns with getting checked' last accessed 30/06/2020 at https://www.england.nhs.uk/2020/04/nhs-warning-seek-help-cancer-symptoms/
NHS England b (2020) ' Cancer Waiting Times' last accessed 28/06/2020 at https://www.england.nhs.uk/statistics/statistical-work-areas/cancer-waiting-times/
Organisation for Economic Co-operation and Development (OECD, 2017) Health Care Quality Indicators - Cancer Care last accessed 10/06/2020 at http://www.oecd.org/els/health-systems/hcqi-cancer-care.htm
Polverini AC, Nelson RA, Marcinkowski E, et al. Time to Treatment: Measuring Quality Breast Cancer Care. Ann Surg Oncol. 2016;23(10):3392-3402. doi:10.1245/s10434-016-5486-7
Sbaraini, A., Carter, S.M., Evans, R.W. et al. (2011) How to do a grounded theory study: a worked example of a study of dental practices. BMC Med Res Methodol 11, 128

Shin, H.J., Baek, H.-M., Ahn, J.-H., Baek, S., Kim, H., Cha, J.H. and Kim, H.H. (2012), Prediction of pathologic response to neoadjuvant chemotherapy in patients with breast cancer using diffusion-weighted imaging and MRS. NMR Biomed., 25: 1349-1359
Sud et al (2020) Collateral Damage: The Impact on Cancer Outcomes of the COVID-19 Pandemic (4/20/2020). Available at SSRN: https://ssrn.com/abstract=3582775 or http://dx.doi.org/10.2139/ssrn.3582775
Thomson, S. B. (2010). Sample Size and Grounded Theory. Journal of Administration and Governance, 5(1), 45-52.
World Health Organisation (ND) Breast cancer: prevention and control last accessed 10/06/2020 at https://www.who.int/cancer/detection/breastcancer/en/index1.html
Xia Y, Jin R, Zhao J, Li W, Shen H. Risk of COVID-19 for cancer patients. Lancet Oncol 2020; 21:e180.
You Gov Poll for Breast Cancer Care (2015) accessed on 10/06/2020 at https://breastcancernow.org/about-us/media/press-releases/one-in-three-women-dont-check-breasts-cancer-symptoms