Gender Disparities in Concerns of Cancer Research Participation During COVID-19 Climate

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Abstract

The unprecedented threat of COVID-19 has taken its toll on the field of cancer research, with trial accrual rates seeing a sharp decline since the beginning of the pandemic. Recent evidence has suggested that decreased participation appears to be more pronounced in women than men, which raises concerns about an exacerbation of gender bias in research. The following manuscript is a commentary article to the recent study by Fox et al, who aimed at investigating the concerns of patients with regard to participating to cancer research, as well as examining potential gender disparities within their sample population. We provide a brief critique of their work, especially focusing on important limitations concerning sample size and underrepresentation of ethnic minority groups, before discussing their findings in light of current literature on gender differences in anxiety and risk perception, how this might be interpreted in the context of the current pandemic, and its impact on participation in cancer research. We present multiple lines of evidence which support the idea that women might experience greater anxiety during the COVID-19 pandemic which could have a significant impact on cancer research participation and consequently the external validity of studies in the field. The first attempts to tackle these challenges have shown promise, but further research is required to perfect this process and target those groups who are at greatest need of intervention.

Keywords

cancer, COVID-19, gender, research, coronavirus

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The current coronavirus disease (COVID-19) pandemic has had a detrimental impact on various infrastructures worldwide, from economy, daily living to healthcare.^{1,2} While the vaccine provides hope, and COVID-19 has understandably become the focus of present research, the collateral damage to other healthcare specialties is prominent, in particular oncology and its research.³ Recently, Fox et al conducted a cross-sectional online survey providing an insight into the potential concerns and reasons behind the decreased participation rates in cancer research during the COVID-19 pandemic.⁴ Their preliminary data may cue future studies to explore the specific nature of such concerns, which could prove critical in the development of strategies to encourage participation in research. Considering results of a cohort study conducted by Unger et al⁵ showing evidence of difference

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between the decrease in trial accrual rates in women compared to men, Fox et al also explored potential gender disparities in their own research. Their findings revealed that, in women, anxiety scores predicted concerns about participation in cancer research, while the same did not follow in men.⁴ In our article, we first provide a brief critique of Fox et al's manuscript, focusing on its limitations regarding underrepresentation of ethnic minority groups as well as older patients; the subsequent paragraphs will draw on current literature in order to build on Fox et al's discussion about gender differences in anxiety and risk perception, how this may be interpreted during the present pandemic and how it may affect cancer research participation.

We commend Fox et al on their work as they draw upon the unseen impacts of COVID-19 on the field of cancer research.⁴ However, clear limitations exist concerning participation bias and sample size, posing issues with regard to the generalizability of their findings. Indeed, the lack of representation of ethnic minority groups is the epitome of this study's main weakness. A conspicuous body of evidence has established that ethnic minority groups have been disproportionately affected by the COVID-19 pandemic,⁶ as portrayed by the dramatic ethnic differences in hospital death rates from COVID-19,⁷ prompting calls to the government to go further in terms of its economic response to protect vulnerable groups.⁸ Therefore, with regard to Fox et al's work, this research appears to suggest that it is likely that patients from ethnic minority groups are likely to experience specific anxieties and concerns about the pandemic and participating in cancer research. It can thus be argued that their scarce inclusion in the study denotes a major shortcoming, especially in light of articles expressing concern about underrepresentation of BAME patients in COVID-19 studies.⁹

Furthermore, the use of an online questionnaire may be a double-edged sword: while it allowed to obtain data through a COVID-19 friendly means, it was likely to have excluded from the study a significant portion of older patients, a group where rates of adoption of technology remains low.¹⁰ Elderly people have been characterized as vulnerable to COVID-19,¹¹ so Fox et al exclude a number of valuable opinions due to their methodology of collating results via the internet.

Psychological and Social Factors Affecting Participation

Fox et al propose that the rationale behind the more pronounced decline in trial accrual rates in women versus men could partly stem from gender disparities in anxiety levels as a result of COVID-19, affecting willingness to participate in cancer research.⁴ Several lines of evidence appear to be consistent with this hypothesis. Epidemiological data document that during the pandemic women reported more psychological consequences than men, including anxiety and post-traumatic stress disorder (PTSD).¹² Additionally, research on the etiological factors of anxiety further corroborates these observations. The seminal work of emotion theorist David H. Barlow, describes a model which integrates heritable and psychological diatheses

as the root of the development of anxiety and its related disorders.¹³ In this respect, McLean and Anderson argue that genetic factors in the development of anxiety disorders have a greater influence in women than in men.¹⁴ Furthermore, women might be more likely than men to overestimate the probability of danger and expectation of harm. The authors offer insight regarding this evidence by interpreting it from an evolutionary perspective, in a context akin to the huntergatherer theory where vigilance to danger in women serves the adaptive purpose of preserving the self as well as the offspring.^{14,15} Some evidence seems to support this theory, with imaging studies revealing gender differences in patterns of neural activation in structures mediating attention to threat.^{14,16} An additional contributing factor could lie in the theory of gender role socialization, whereby individuals are driven to develop socially prescribed behaviors and traits consistently with sociocultural norms.¹⁷ Applying these concepts to current times, it seems plausible to infer that COVID-19 may be more strongly perceived as a threat by women than men. This evidence appears to be consistent with Fox et al's findings, albeit the extent to which gender differences in anxiety and risk perception may play a role on participation in cancer research remains unclear. Nonetheless, not addressing the gendered impact of COVID-19 in the context of health research would risk further diminishing female participation in research. Clearly, this would have significant repercussions on the external validity and overall value of studies. Current literature highlights how, historically, women have been largely excluded from health research, with a consequent lack of integration of gender-specific data into evidence-based medicine.¹⁸ A review by Bartlett et al in 2005 investigated the exclusions of sociodemographic groups, including women, focusing on 2 drug exemplars, namely statins and nonsteroidal anti-inflammatory drugs (NSAIDs).¹⁹ Their assessment led them to recognize the neglect of the UK research community toward representation issues for women, as well as older patients and ethnic minorities, resulting in bias in the absolute effect estimates in drug trials. In the same manuscript, the authors concluded that further research should focus on identifying and addressing barriers to facilitate involvement of women and different population groups in research.

Conversely, one must consider the reluctancy of men to voice or acknowledge psychological suffering compared to women.²⁰ Since COVID-19 is more likely to lead to poorer prognosis in men, the anxiety and reluctance in putting oneself at risk could be greater, therefore decreasing participation in research.²¹ Males are less resistant to infections, which may be mediated by physiological factors and environmental factors. Physiological factors include sex hormones and increased expression of "coronavirus receptors" are supporting an environment for the pathogenesis of COVID-19. Lifestyle factors include increased rates of smoking and drinking comparative to women which impact the overall health and immunocompetence of the individual.²² These findings make the male sex a risk factor toward poor prognosis of COVID-19.

Social factors are likely to be of primary importance in the discussion regarding concerns about cancer research participation during COVID-19, and a comprehensive analysis of the gender disparities in this area must take those into consideration. Goodman et al in 2019 showed that women were more likely than men to endorse a family benefit as a key motivator to take part in cancer research.²³ This critical finding is one of the first to provide convincing evidence that gender differences in motivations to participate in cancer research exist. During the COVID-19 pandemic, it could be speculated that the family benefit aspect of participation in research may likely be undermined as participating could expose the individual and thus their family to serious risk of infection. The absence of this important motivator could thus contribute to greater reluctancy in women to take part in research. Nonetheless, this concern is certainly relevant for men too, and it is possible that the conclusions of Goodman and colleagues may not be entirely applicable to the present situation due to the unprecedented threat of COVID-19.

Implementations Made to Sustain Participation in Oncology Research

Whilst disparities might exist between genders, addressing them and finding solutions are the next steps. Fontana and Arkenau state that oncology research trials have adapted to the COVID-19 pandemic by decreasing the number of in person procedures, increasing the amount of telemedicine consultations and also providing "oral investigational medications" to patients remotely.²⁴ Leung and colleagues also commend the use of telemedicine in improving patient care as the infection risk in an immunocompromised cancer patient participating in face to face research proves to be high.²⁵ Therefore, COVID-19 might have highlighted ways to accelerate "clinical trial simplification" and the need to leverage telemedicine in the current climate. The aim is not to stop challenging people's anxiety, as otherwise fears will remain for any "in person" research. Effective communication can be used to offer an appropriate amount of reassurance to the public. For example, expressing concern, providing facts and repeating information where necessary could decrease the concerns about the "catastrophic potential" and the "trust in authorities" aspects that people worry about respectively.²⁶

In summary, Fox et al's conclusions shine light on crucial challenges that the field of cancer research must overcome in order to increase trial accrual rates during the COVID-19 pandemic, especially among women. Current literature on the etiological factors of anxiety and risk perception seems to be generally consistent with Fox et al's results. However, the study has major limitations regarding representation and sample size, most noticeably affecting the BAME community, which severely undermine the reliability and generalizability of their findings. The field of cancer research has already started to adapt to respond to the new challenges. Further research exploring in detail the specific nature of patients' concerns will prove essential to expedite and perfect this transition.

Authors' Note

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