The Breast 37 (2018) 148–153

Contents lists available at ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

Original article

Psychosocial issues of a population approach to high genetic risk identification: Behavioural, emotional and informed choice issues

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ARTICLE INFO

Article history:
Received 24 October 2017
Accepted 9 November 2017
Available online 21 November 2017

Keywords:
Genetic
Risk communication
Breast cancer
Screening
Psychological impact

ABSTRACT

To allow women at high genetic risk of breast cancer to benefit from prevention or early prevention strategies, a screening programme is required to identify them. The present review considers the likelihood of key outcomes that would arise from such a programme, in relation to behavioural, emotional and informed choice outcomes. The likelihood of outcomes in each category is considered in relation to the limited direct evidence and relevant indirect evidence, given the dearth of studies that have directly studied the effects of communication of personal genetic risk of breast cancer. Overall, there is promise that such a programme would have several behavioural benefits, such as good uptake of increased screening in women at high risk but little effect on screening in women at low risk. The available evidence suggests that major adverse effects on emotional outcomes are unlikely. There is very limited evidence in this developing area on the extent to which decisions of women offered breast cancer risk estimation will be fully informed choices. Recommendations are made for increasing benefits and reducing harms of population-wide breast cancer risk estimation in light of current evidence. Key research gaps are identified.

There is an extensive literature on communicating information on genetic markers of risk in women who have been identified due to family history of breast cancer. This literature has produced clear conclusions. For instance, women with such a family history but who find out that they are not BRCA1/2 mutation carriers generally experience a reduction in distress following testing [1]. By contrast, women who do carry these mutations experience a short-lived increase in distress but do not experience any emotional effects over the longer term [1]. Despite this, there are still some apparent problems with understanding the information provided. For instance, women carrying BRCA1/2 mutations who underwent risk-reducing surgery showing no apparent reduction in worry compared to women with the same mutations who did not undergo risk-reducing surgery [2]. Further, in one study over a third of women who did not carry these mutations did not attend routine breast cancer screening despite the genetic test indicating that they were at population risk [3].

Many women at high genetic risk of breast cancer are not aware of this risk. Despite BRCA 1/2 mutation testing, many women at high genetic risk of breast cancer are not aware of this risk, as they have not attended family history clinics or have negative BRCA1/2 mutation test results. To allow these women to benefit from prevention or early prevention strategies, a screening programme is required to identify them [4]. In common with other screening programmes, there are potential harms and benefits of screening [5]. The present review describes the likely harms and benefits of estimating personal risk identified by population screening that is based at least partly upon information from genetic sources.

When considering the likely harms and benefits of providing women with their personal genetic risk estimates, it is helpful to consider the three main aims of risk communication [6]. That is,

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https://doi.org/10.1016/j.breast.2017.11.008
0960-9776/

people communicating risk estimates have at least one, and often more than one of the following aims: (a) to change behaviour of the person receiving the risk estimates, (b) to reduce unnecessary anxiety in the person receiving the risk estimates, and (c) to increase informed choices, through increasing knowledge or understanding of the risk estimates. In line with these aims, the present review will structure what is known about the effects of communicating estimates of breast cancer risk based at least partly on genetic information.

It is important to note that in this rapidly moving area, much of the evidence on the likely harms and benefits will be indirect, as there is a dearth of studies that have directly studied the effects of communication of personal genetic risk of breast cancer. Despite this absence of direct evidence, there is a large literature on the effects of risk communication that allows predictions to be made with a good degree of confidence. The present review will describe this evidence, including the limitations of this evidence base when applied to identifying women at high genetic risk of breast cancer. In the light of this evidence, the review will make recommendations on management of individuals with high genetic risk. It will conclude with recommendations for future research, identifying gaps in evidence that future research should address.

1. Communicating risk estimates to change behaviour

1.1. How many women will take up the offer of breast cancer risk estimation?

Before it is possible to examine the effects of receiving breast cancer risk estimates, it is first essential for the offer of such information to be accepted. There are several studies that have asked women about their interest in receipt of breast cancer risk estimates, e.g. 94% of women in a recent survey of attendees at a breast screening appointment indicated that they would be interested in personal risk assessment [7]. However, this was based on a hypothetical offer. The best information on uptake of breast cancer risk estimates comes from our Predicting Risk of Cancer at Screening (PROCAS) study in Greater Manchester, England [4]. The majority of the women in the PROCAS study had their breast cancer risk estimated based on a two-page self-completed questionnaire assessing risk factors including family history, supplemented by breast density assessed during mammography. A sub-sample of 9200 women had this estimate supplemented by Single Nucleotide Polymorphisms (SNPs) collected via saliva. In this study, 187, 466 women were invited for breast cancer screening, of whom 131,373 women attended screening and were invited to participate in the PROCAS study, via an invitation letter alongside their invitation to attend routine breast screening. This resulted in 53,596 women consenting to the study, of whom 51,011 (95.2%) wanted to know their breast cancer risk in due course. Thus, our best estimate of women who wished to know their breast cancer risk estimates in a sample of the general public identified via screening records is around 27% of women eligible for breast cancer screening, or 39% of attendees. In the same study, when women who had previously indicated wanting to know their risk estimates were offered a telephone or face-to-face appointment to discuss actual risk results around 74% of women at high and moderate risk took up this offer although this uptake was lower (55%) in those with no family history [8], It should be noted that these figures were derived from a research study, with participants required to provide informed consent having read an information sheet, so it may be expected that the proportion of women who would opt to receive risk estimates if offered as part of a routine service would be substantially higher. Irrespective of this, it is apparent that a major challenge to the development of a service that routinely provides breast cancer risk estimates is the number of women who would take up such a service in the first instance.

1.2. What are the types of effects on behaviour?

There are a number of behaviours that could be affected by receipt of personalised risk information that has genetic components. First, there are the behaviours that are the main intended consequences of risk stratified screening programmes for women identified at high risk: uptake of chemoprevention drugs and increased mammography and other screening modalities for women at high risk. Secondary intended consequences of women at high risk are changes in health-related behaviours related to breast cancer incidence. Other consequences include attendance at future rounds of breast cancer screening, which may vary in line with estimated breast cancer risk, and which may be an intended or unintended consequence of giving risk information. Finally, there may also be unintended behavioural effects of receiving personalised risk information, especially on women at lower personal risk. There is considerable variation in the current state of knowledge on these various behavioural consequences, and these will be considered in turn.

1.3. Main intended consequences of receiving breast cancer risk information

A major justification for the implementation of risk adapted screening for breast cancer is that there are large numbers of women who would benefit from interventions that have been shown to be cost-effective, but these women do not receive such interventions as they are unaware of their breast cancer risk [9]. In the UK, the major benefits for women at high risk are increased frequency of mammography for women to detect breast cancer at an earlier stage, and uptake of chemoprevention to reduce incidence of breast cancer. In the PROCAS study, there was high uptake of additional screening at 12–18 monthly intervals, instead of the usual 36 monthly interval: of 383 eligible women, 40 were already receiving screening through the Family History Clinic. Of the remainder, 298 took up the offer, with only four declining [8].

With regard to uptake of chemoprevention, another study in Manchester found that of 1279 women who were eligible for tamoxifen as part of routine care, 136 (10.6%) took up the offer, which is a similar proportion to that found in the IBIS tamoxifen prevention study [10,11]. It may be that uptake of other agents such as raloxifene and anastrozole may be higher, due to some women holding negative associations of tamoxifen as a drug used to treat cancer [10]. However, given the low rate of uptake of chemoprevention that has been seen to date, it seems that a major reduction in the incidence of breast cancer is unlikely to be brought about by this route.

1.4. Secondary intended consequence: changing behaviours related to breast cancer incidence

An alternative route by which communication of high breast cancer risk could reduce breast cancer incidence is by motivating changes in health-related behaviours, specifically those to do with energy balance (physical activity and diet), as well as smoking and drinking alcohol. There is a large body of experimental evidence on the effects of communicating risk information on many health-related behaviours across many populations, which suggests that, in general, inducing increases in risk appraisals are likely to produce effects on health related behaviours that are small in size ($d = +0.23$) [12]. It is also notable that the effects of changing risk appraisals on behaviour were much larger ($d = +0.45$) when