The *Lancet* Breast Cancer Commission

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Executive summary

The *Lancet* Breast Cancer Commission—a diverse, multidisciplinary international group—are unanimous in our determination to improve the lives of all people who live with or are at risk of breast cancer. We came together in July, 2021, and are committed to raising the standard of breast cancer care to close the equity gap that exists between and within countries. Over a 2-year period, we brainstormed ideas, scoped the literature, obtained funding for dedicated pilot research that provided new data, and produced this Commission report to reduce the effects that breast cancer has on society.

We highlight that, despite tremendous advances in breast cancer research and treatment over the past three decades—leading to a more than 40% reduction in breast cancer mortality in some high-income countries—there remain inequities, with many groups being systematically left behind, ignored, and even forgotten. Our findings suggest that this is a mistake, as people with breast cancer are indispensable to our socioeconomic fabric and culture. We show that the number of people living with metastatic breast cancer is unknown because many cancer registries do not record relapses. Many patients with metastatic breast cancer feel abandoned, isolated, alone, and might not receive appropriate care in both high-income and lower-middle-income countries: this should, and can, be tackled. With adequate evidence-based resources and a shift away from negative societal attitudes towards metastatic breast cancer, it might be possible to cure some patients, treat most, alleviate the suffering of all, and forget or abandon none. We have identified that the hidden costs of breast cancer and associated suffering are considerable, varied, and have far-reaching effects. Costs and suffering can be financial, physical, psychological, emotional, and social, they affect children, families, local communities, and wider society, can occur at all stages of breast cancer, and are evident even within health-care services that are free at the point of delivery. Exposing and reducing costs and suffering provides incentives for policy makers to invest in prevention, early detection, cost-effective therapies, and optimal management of breast cancer. We show that improving patient communication and decision making in breast cancer care improves quality of life, body image, and adherence to therapy, which can affect survival outcomes. Breast cancer is a disease that many patients describe as robbing them of power, but through good communication and facilitating patient autonomy, there could be opportunities for them to regain power and emerge stronger to exercise empowerment in other areas of their lives.

We acknowledge that early detection of breast cancer is fundamentally important and should be available to all individuals, wherever they live. We encourage broadening breast cancer early detection efforts in low-income and middle-income countries (LMICs) from a narrow focus on mammographic screening—which can be unaffordable or unachievable in resource-constrained settings—to include breast cancer early diagnosis as recommended by WHO. Every country that successfully reduced national breast cancer mortality rates between 1990 and 2020 has, as of 2023, the ability to diagnose at least 60% of invasive breast cancers at stages I or II. Evidence from the past 5 years shows that awareness and education focused on finding and treating symptomatic (palpable) breast cancers when they are first discoverable promotes stage-shifting towards reaching—or even surpassing—the stage I or II at diagnosis threshold of 60%. This finding is especially relevant for women younger than the typical screening age of around 50–70 years and older women living in regions where limited access to health care prevents widespread implementation of early detection efforts. We have developed an inclusive evidence-based roadmap of six themes to address these urgent breast cancer challenges.

Prevent: globally, breast cancer is the most common cancer and by 2040, the incidence of new breast cancers is predicted to be more than 3 million per year, rising most rapidly in LMICs. The mindset that this upward trajectory is inevitable and therefore acceptable should be changed; action now can prevent many of these future breast cancers. We emphasise that breast cancer risk factor education is vital, but should be combined with policy change to support sustained behavioural changes and decrease health inequalities. For example, policy makers should reject commercial marketing for products that increase the risk of breast cancer, such as alcohol. We propose that developing coordinated approaches to systematically identify individuals with increased risk of breast cancer and offer them evidence-based prevention interventions relevant to their risk is an aspirational goal to be developed through ongoing research.

Personalise: scientific and clinical research can facilitate equitable and prompt access to the right breast cancer treatment at the right time for individuals, while respecting personal needs and preferences. Better

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targeting of existing treatments through development of validated biomarkers is needed to identify the people who benefit the most and to reduce treatment burden for those more likely to have higher toxicity than gain. We identify the need to develop and facilitate novel, efficient, patient-centred translational clinical trials and enable a research culture and infrastructure to ensure these can be undertaken globally. Digital health technologies might facilitate personalised breast cancer care and alleviate inequalities through integration of multimodal complex datasets, promoting flexible, coordinated care—particularly for vulnerable patients—democratising access to research, and decentralising trial participation. However, these must be implemented in an equitable way to avoid increasing inequity, as seen with some health technologies.

Include: we urge for the inclusion of patients with metastatic breast cancer in optimal breast cancer care and clinical research. We justify why optimal metastatic breast cancer management is valuable to individuals, families, and society. We show the results of the Commission's international health-care professionals survey, which suggests that there is a growing belief that patients with some subtypes of metastatic breast cancer can be treated for many years as having chronic illnesses, and some patients might even be cured. In addition to collecting data on cancer incidence and stage at presentation, we call for high-quality data on cancer relapses worldwide to include not just those with metastatic breast cancer, but also those with other metastatic cancers. We recommend that stigma around metastatic breast cancer be addressed through raising awareness and educating stakeholders (eg, patients, families, health-care practitioners, and policy makers) and wider society.

Collaboration: we must collaborate (between the previously mentioned stakeholders and wider society) to close the equity gap in breast cancer care and outcomes through global early detection, treatment frameworks, and innovative technologies that are equitably implemented. People with low incomes and those from minoritised populations in all countries often have their breast cancer diagnosed at a late stage with a high risk of dying from their cancer. The early diagnosis inequity gap will widen without intervention. Equitable access to early diagnosis and treatment is a fundamental need for all individuals to improve their breast cancer survival and quality of life. In collaboration with the WHO Global Breast Cancer Initiative, we call for action to deliver stage-shifting, as a sustained decline in breast cancer mortality rates is achieved by diagnosing at least 60% of invasive cancers at stages I–II. Population-based mammographic screening programmes can be established, when feasible, to operate sustainably, but early detection approaches should be adapted to local contexts and resources. We suggest that technological innovations could aid the speed, efficacy, and inclusivity of early breast cancer diagnosis and treatment implementation globally, and these should be combined with an integrated health-care system policy as well as education and advocacy.

Identify: the hidden costs and serious health-related suffering of breast cancer go unmeasured in global health metrics, so its alleviation is not prioritised by policy makers. We call for new, validated tools to record the myriad of costs and suffering sustained by patients, caregivers, and families of those with breast cancer. We also indicate the urgency of developing metrics to measure the full benefits that patients and society place on alleviating suffering related to breast cancer. These novel tools could influence policy makers to set new priorities for breast and other cancers to guarantee that supportive and palliative care is available to all at every stage of the breast cancer pathway, alongside financial protection to prevent catastrophic and impoverishing health expenditure from direct and indirect health-care costs and lost family income.

Communicate: being female is the greatest risk factor for breast cancer and women constitute a group whose fundamental human rights have historically been accorded lesser respect than men in all settings. As such, our final theme focuses on communication and empowerment related to breast cancer. We suggest that prioritising patient autonomy regarding medical treatment is paramount to close the gender equity gap and will have broader impacts for the physical, social, and financial wellbeing of women globally.

We propose a framework to improve communication and aid decision making for those with breast cancer. Placing patients at the centre of clinical communication and empowering them to exercise their voices, become fully informed, and choose their degree of involvement in decisions about their care, is an achievable and necessary global goal. Health communication training should be person-centred and include eliciting patients' core values and preferences for information, explaining goals of care, risk–benefit communication, skills to help estimate and explain prognosis, share serious news, and empathetically and honestly respond to questions, and considerations of local cultural traits and individual differences.

Our inclusive roadmap for change is evidence-based, including new data. It is designed for everyone with a connection to breast cancer but is particularly aimed at policy makers. We suggest detailed measurable indicators of progress with targets and suggested responsible groups. These indicators are designed to be actionable, auditable, and to facilitate lobbying for change. Our work with the *Lancet* Breast Cancer Commission has catalysed lasting partnerships between co-authors and with other Commissions, key international organisations, and patient groups. As a result, we have ongoing collaborative research and will continue to strive to raise the bar and close the equity gap for breast cancer (panel 1).

Panel 1: **Summary of the *Lancet* Breast Cancer Commission key messages**

The *Lancet* Breast Cancer Commission report shows inequities in prevention, detection, treatment, and supportive care, with many groups of people with breast cancer being systematically left behind and forgotten. This is a global error as people with breast cancer are indispensable to our culture and socioeconomic system.

New findings

- The number of people living with metastatic breast cancer is unknown and many do not receive appropriate care. With adequate resources and a shift in attitudes, it might be possible to cure some people, treat most, alleviate the suffering of all, and abandon no one.
- Hidden breast cancer costs and suffering can be financial, physical, psychological, emotional, and social, affecting children, families, communities, and wider society. Exposing and reducing costs and suffering provides incentives for policy makers to invest in prevention, early detection, cost-effective therapies, and optimal management of breast cancer.
- Improving patient communication in breast cancer improves not only quality of life and body image, but also adherence to therapy, which can affect survival outcomes. Breast cancer can be seen as robbing many patients of power, but through good communication and facilitating patient autonomy, there could be an opportunity to regain power and exercise empowerment in other areas of their lives.

Roadmap for change

Our inclusive roadmap addresses urgent breast cancer challenges through six themes:

- Society should prevent as many as possible of the 3 million new diagnoses of breast cancers that are predicted to occur per year by 2040, through global national policy changes to minimise modifiable risk factors and coordinated, systematic personalised risk prevention programmes.
- Health-care systems and clinicians should personalise the right treatment at the right time for individuals while respecting their personal needs and preferences.
- We call for high-quality cancer registry data on cancer relapses to be collected worldwide and include not just those with metastatic breast cancer, but also with other metastatic cancers.
- Collaboration is key to close the equity gap through global early diagnosis, treatment frameworks, and innovative technologies.
- We should identify the value that society places on relief of the hidden costs and suffering related to breast cancer and measure the benefits of addressing these costs.
- Placing patients at the centre of clinical communication and empowering them to exercise their voices about their breast cancer care is an achievable and necessary global goal.

Introduction

Scientific advances that have dramatically improved what is possible for breast cancer prevention and treatment contrast with the failure to deliver good care to most patients with breast cancer around the world. The *Lancet* Breast Cancer Commission calls for raised awareness and change to ensure the translation of evidence into policy and practice for breast cancer care and prevention.

In 2020, more than 2·3 million women were diagnosed with breast cancer and breast cancer caused 685 000 deaths globally.[1] In addition, around 1% of the total incidence of breast cancer occurs in men. It is now the world's most prevalent cancer; at the end of 2020, 7·8 million women with breast cancer had been diagnosed in the previous 5 years, with an unknown number of people living with metastatic breast cancer.[1]

Breast cancer affects people in every country, but large geographical variations exist around the world. For example, annual incidence rates from 2020 range from fewer than 40 per 100 000 females in some regions such as south-central Asia and central, middle, and eastern Africa, to more than 80 per 100 000 females in Australia, New Zealand, Australia, New Zealand, USA, Canada, and western and northern Europe.[2] Low-income and middle-income countries (LMICs) have a disproportionate number of deaths due to breast cancer. The burden of breast cancer is predicted to increase to more than 3 million new diagnoses per year (an increase of 40% from 2020) and more than 1 million deaths per year (an increase of 50% from 2020) by 2040. In countries with a low human development index (HDI), the numbers of new diagnoses and deaths are anticipated to double by 2040,[1] and in countries with a medium HDI, incidence and mortality rates are predicted to increase by 70% and 60%, respectively.

In 2020, 4·4 million women died from cancer worldwide, leaving behind 1·04 million maternally orphaned children, 25% of whom lost their parent to breast cancer.[3] There is a strong inverse relationship between the HDI of a country and the number of new maternal orphans per 100 deaths due to cancer.[4] The chronic social disruption and financial harms of breast cancer will continue to disproportionately affect LMICs for future generations; families are left impoverished after expenditure on cancer care and orphaned children are less likely to complete education, so they are more likely to be affected by poverty and the cycle continues. In addition, deep gender, ethnic, and socioeconomic divides exist both within and between countries.[5] Racial and ethnic inequities in the outcomes and lived experiences of patients with breast cancer have been documented in numerous rigorous studies.[6] However, biomedical advances have dramatically improved breast cancer outcomes over the past 30 years, contributing to falling

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mortality rates, although these gains have been largest in higher income countries, because more people can afford access to treatment, including new expensive therapies with incremental survival benefits. Globally, a pivotal point for breast cancer has been reached in which either inequities between and within countries widen irreparably, or society unites to ensure equitable access to evidence-based breast cancer prevention and care as a fundamental right for all.

The *Lancet* Breast Cancer Commission structure and aim

It is against this background that the *Lancet* Breast Cancer Commission convened in July, 2021. Its aim was to provide a new perspective and identify key areas for change to influence global policy and ultimately improve the lives of those affected by breast cancer.[7] The Commission is multidisciplinary and diverse in terms of geographical distribution (members are from high-income, middle-income, and low-income countries), gender, ethnicity, professional role, and career level, including patient advocate commissioners with lived experience of early and metastatic breast cancer (appendix pp 11–14). The first Commission meeting identified five workstreams—each with two co-chairs—to coordinate scoping and evidence synthesis, with assistance from early-career researchers, relating to 12 key questions identified by the group.[7] Main meetings were held quarterly over 2 years. Most meetings were virtual, with one 2-day meeting in Cambridge, UK, in the summer of 2022. Workstream meetings were held and work consisted of literature reviews, an international health-care professionals survey, and new research projects, some of which were funded specifically to produce new data to inform the Commission report. The *Lancet* Breast Cancer Commission is collaborating with other key groups, including the *Lancet* Commission on Cancer and Health Systems,[8] the *Lancet* Commission on Global Access to Palliative Care and Pain Relief,[9] the WHO Global Breast Cancer Initiative (GBCI), and the ABC Global Alliance.

Each section in this report starts with a summary and ends with suggested measurable indicators for change. Any forward-looking document runs the risk of only addressing surface issues rather than their causes. The commissioners therefore felt it important that their work led to real change for the sake of people with breast cancer, past, present, and future, worldwide. We decided to include a set of indicators to reflect specific changes that we feel are needed to empower real change. These indicators were drafted by the leads of the six final themes, focused not only on what the indicator could be, but also who or what should be responsible for ensuring their delivery. The indicators were based on the appraisal of evidence accumulated during the 2 years and were then shared with the whole commissioning group for comments and revisions. The specific numerical targets were drafted in the same way and were chosen as being probable to engineer real change for patients while acknowledging that there are always challenges in changing systems.

Individuals with breast cancer or those who are at risk of breast cancer are referred to variously as individuals, patients, and sometimes women throughout the report, but the Commission acknowledges that gender definitions are much broader, for example including men and transgender people who can have experience of considerable stigma and inequity (appendix pp 15–17). We also use the terms women and breastfeeding throughout for brevity and because most people who breastfeed identify as women; we recognise that not all people who breastfeed or chestfeed identify as women. A glossary of terms used in the report is available in the appendix (pp 2–10). The Commission report is not a review of the biomedical management of breast cancer but, in response to the inadequacies and inequities in global breast cancer care, is a call to action on specific global challenges, each coupled with opportunities for positive change. We propose this evidence-based narrative to initiate change for all those affected by breast cancer, now and in the future.

***Panel 2:* Summary for breast cancer prevention**

- Action now could prevent many of the 3 million new diagnoses of breast cancer that are predicted to be diagnosed per year by 2040
- Breast cancer risk factor education is vital but should be combined with policy change to support sustained behavioural changes and decrease health disparities
- Governments and policy makers should have the will, courage, and integrity to reject lobbying from groups with vested interests that profit from exposing populations to breast cancer risk factors
- Approaches to systematically identify individuals at increased risk of breast cancer and to offer evidence-based prevention interventions on the basis of their risk level should be implemented and refined through ongoing research

Theme 1: breast cancer prevention

On average, in 2020, women globally had a 1 in 12 risk of being diagnosed with breast cancer by age 75 years, and this incidence is rising.[2,10] With this trajectory, by 2040, an estimated 3 million individuals will be diagnosed annually;[10] this is neither acceptable nor inevitable as action now can prevent many of these future cancers. Prevention potentially offers the most cost-effective strategy for breast cancer control and would reduce the effects of breast cancer on individuals and all aspects of society (panel 2).[11,12]

There are two complementary approaches to primary prevention. The first is population prevention, done by minimising risk factor exposure for all individuals,

regardless of their personal breast cancer risk. Understanding the extent to which each risk factor contributes to the number of individuals with breast cancer in a population can inform the focus of education programmes in partnership with policy change to drive population-wide prevention. The second approach is personalised prevention through targeted delivery of intensified interventions. Prevention involves identifying the 20–30%[13,14] of women with a substantially higher than average risk of breast cancer by use of existing tools, and refining and implementing these tools through ongoing research and development. Interventions proven to substantially reduce breast cancer risk, such as inexpensive medications or, for those at very high risk, preventive surgery, should be offered on the basis of individual risk (figure 1).

Breast cancer risk factors

The most important risk factor for breast cancer is being a woman and risk generally increases with increasing age. At least 5% of breast cancers are attributable to rare inherited pathogenic variants in major breast cancer predisposition genes, of which half are due to *BRCA1* and *BRCA2*.[15,16] Women with pathogenic variants in these genes have a substantially increased risk for breast cancer and can be identified by genetic testing. There are other more common genetic variants that individually increase breast cancer risk very little, but clustering of several variants in one individual can lead to higher risk.[17] The polygenic risk score summarises a person's risk of breast cancer, attributable to their individual profile of these common variants.[17] Other established risk factors include a family history of breast cancer, a history of radiation exposure (involving the breasts), non-invasive breast conditions, such as atypical hyperplasia and lobular carcinoma in situ, a tall height, reproductive history (such as nulliparity and older age at first birth), and modifiable risk factors, such as alcohol consumption, having an elevated BMI, physical inactivity, little or no breastfeeding in parous people,

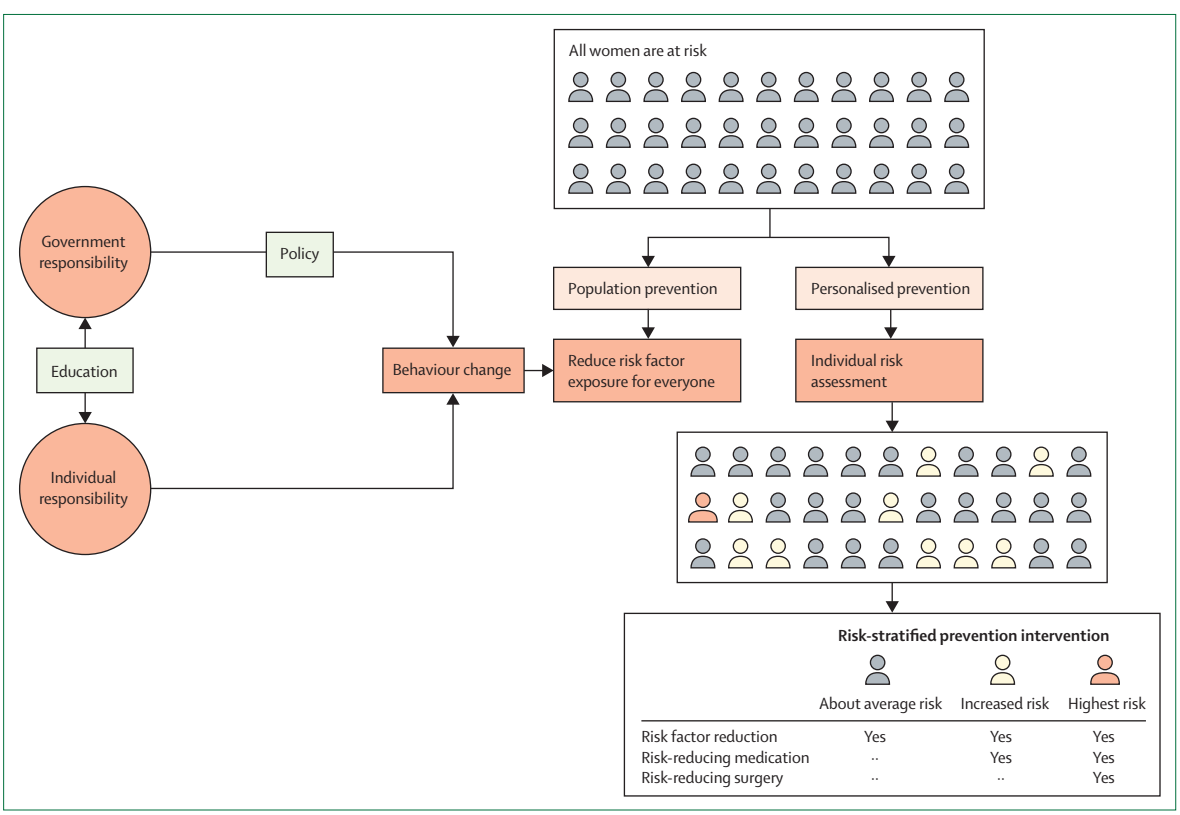

Figure 1: **Approaches to breast cancer prevention**

Prevention of breast cancer requires a dual approach. First, population prevention minimises exposure to risk factors for everyone, regardless of their personal risk of breast cancer. Minimisation can be achieved with policies that reduce exposure to harmful risk factors, such as alcohol and obesity, and policies that increase exposure to protective factors, such as physical activity and breastfeeding or chestfeeding. Educating the population on these risk factors can help governments to legislate what could otherwise be unpopular policies. Education can also lead to risk factor optimisation by individuals, but sustained behavioural changes are difficult to achieve with education alone. Second, personalised prevention is decided on the basis of an individual's risk of breast cancer. This approach requires identification of those at increased risk, preferably through proactive, systematic risk assessment of all individuals, not just those that sign up for it. Identification should be followed by risk-stratified prevention interventions on the basis of individual risk. More than 20% of women in most populations probably have an increased risk of breast cancer and should consider use of risk-reducing medications (eg, tamoxifen, raloxifene, anastrozole, or exemestane). Those with the highest risk of breast cancer (eg, those with germline pathogenic variants that greatly increase risk) can consider risk-reducing surgery (bilateral mastectomy).

Panel 3: Major potentially modifiable breast cancer risk factors

Post-menopausal overweight and obesity

- Associated with post-menopausal breast cancer, especially in tumours positive for oestrogen receptors and progesterone receptors.[18–22]
- Worldwide, 110 000 instances of breast cancer were attributable to obesity in 2012,[19] mostly in the USA and Canada, western and eastern Europe, and Latin America.[19]
- The percentage of breast cancers attributable to obesity is around 8–13% in some high-income countries, such as the UK,[18,23] and is up to 28% in post-menopausal Black women in the USA.[24]

Alcohol

- Alcohol is a well established carcinogen.[25,26]
- There is no so-called safe consumption threshold; 13% of all cancers attributable to alcohol in Europe in 2017 were due to light to moderate consumption (20 g or 2 units per day), of which 50% were breast cancers.[27]
- Compared with non-drinkers, the relative risk of breast cancer is 9%, 13–23%, and 60% higher in women who consume up to 15 g (2 units), 12·5–50 g (1·5–6 units), or more than 50 g (equal to or more than 6 units) of alcohol per day, respectively.[28,29]
- In 2020, 98 300 instances of breast cancer (ie, 4% of all breast cancers globally) and 8–16% of breast cancers in some high-income countries, such as the UK and USA, were attributable to alcohol consumption.[18,30]
- Cessation of or a sustained reduction in alcohol consumption reduces the incidence of alcohol-related cancers and other cancers.[31]

Breastfeeding

- The percentage of breast cancers attributable to not breastfeeding after giving birth in the UK is 4·7%,[18] but is not well defined in LMICs.[32]
- The relative risk of breast cancer decreases by 4·3% for every 12 months of breastfeeding.[33]
- It reduces the risk of triple-negative breast cancer, an aggressive subtype that is more common in younger women and those with African ancestry.[34–36]

Physical inactivity

- Associated with an increased risk of breast cancer, independent of BMI.[37]
- Between 2% and 10% of breast cancers are attributable to physical inactivity in high-income countries.[23]
- Breast cancer disability-adjusted life years attributable to low physical activity are highest in high-income countries, but low-income countries have the fastest increase in low physical activity-associated disability-adjusted life years between 1990 and 2019, with an estimated annual percentage change of 1·02%; 95% CI 0·94–1·10.[38]

Exogenous hormone use

- Combined oestrogen–progestogen hormone replacement therapy increases the risk of breast cancer and this risk increases with longer durations of use. For people who have currently been on combined hormone therapy for 1–4 years, the relative risk is 1·60.[11,39] This excess risk is not for oestrogen-only hormone replacement therapy,[39] but unopposed oestrogen should not be used by people with a uterus because of the increased risk of uterine cancer.[11]
- The relative risk of having breast cancer in people who are using combined oral contraceptives is 1·24.[40] This risk declines after cessation with no excess risk 10 years later.[40] Risk is similar with other forms of hormonal contraception.[41]
- The percentages of breast cancer attributable to hormone replacement therapy and hormonal contraceptives in the UK is 2·1% and 0·8%, respectively.[24]

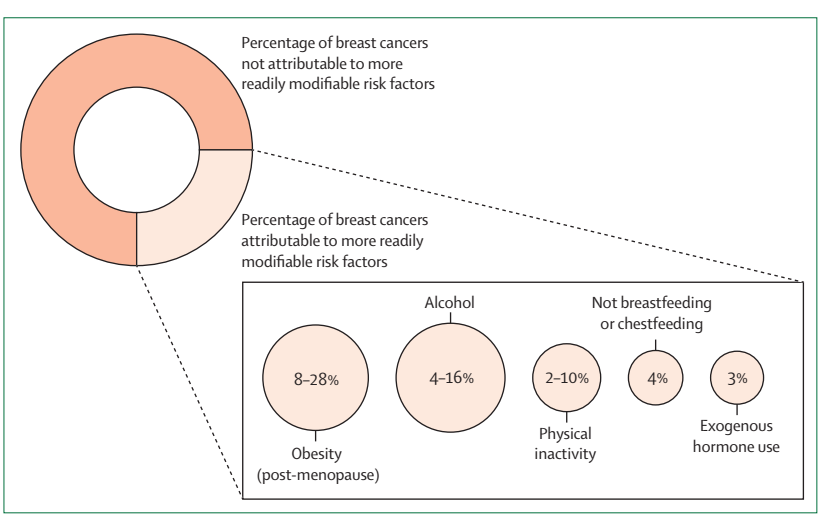

Figure 2: **Approximate population-attributable risks in high-income countries of more readily modifiable breast cancer risk factors**

exogenous female hormone use, and increased breast density (modifiable with the use of medications; panel 3).[18–53]

Population breast cancer prevention

Up to 25% of breast cancers in high-income countries could be prevented by modifying risk factors (figure 2).[18,19,30,43,48,49] The proportion of breast cancers attributable to each risk factor varies by world region and sociodemographic index (SDI).[54,55] Deriving these attributable risk factor estimates in the global population is difficult due to scarce epidemiological studies in LMICs.[32] However, it is estimated that 21% of global deaths due to breast cancer could be attributed to alcohol, post-menopausal overweight and obesity, and physical inactivity.[23] Population-wide approaches to breast cancer prevention have mainly focused on education to motivate individual responsibility in reducing exposure to risk factors. There is low community awareness about

Panel 4: **Public health policy case study comparing and contrasting approaches to tobacco and alcohol**

WHO recommendations

Tobacco

MPOWER tobacco control strategies[72]

- Monitor tobacco use and prevention policies
- Protect people from tobacco smoke
- Offer help to quit smoking
- Warn about the dangers of tobacco
- Enforce bans on tobacco advertising, promotion, and sponsorship
- Raise taxes on tobacco

Alcohol

WHO-recommended policies[76–79]

- Make alcohol less affordable
- Ban or restrict alcohol marketing
- Raise public awareness of the risks of alcohol and cancer—the WHO 5 facts about alcohol and cancer factsheet,[80] including the message that cancers due to alcohol consumption are preventable
- Enforce drink driving laws
- Provide interventions for hazardous drinking

Barriers to reduction in risk factor exposure

Tobacco

Tobacco use is reducing in countries that implement most of the MPOWER measures, but more than 80% of the 1·3 billion people who use tobacco globally live in low-income and middle-income countries (LMICs).[72] In addition, 41 of the 49 countries that have not adopted a single MPOWER measure are LMICs.[72] Insufficient policy adoption facilitates tobacco market expansion through aggressive marketing, low prices, third party advocacy influencing policy makers, and branding tobacco industry activities as corporate social responsibility initiatives.[70]

Barriers to alcohol control as a health priority

- Influence of alcohol industry in policy making
- Little political will and investment
- Low capacity to develop and implement control interventions
- Scarce robust studies and data collection

Alcohol regulation barriers

- Industry self-regulation
- Insufficient international regulation
- Differences in cultural norms and contexts between countries
- Informally or illegally produced products challenge regulations
- Digital marketing more challenging to regulate than physical marketing
- Inappropriately branding alcohol industry activities as corporate social responsibility initiatives[77–79]

Public health policy implementation of packaging

Tobacco

Health warnings on cigarettes have led to decreased smoking commencement and increased cessation rates of smoking.[81] Plain paper packaging of cigarettes in high-income countries have reduced the appeal of tobacco products, decreased uptake, and increased cessation rates of cigarette smoking.[82,83] Evidence suggests the same behavioural effects are possible in LMICs.[84]

Alcohol

Health warnings on alcoholic beverages are generally subject to voluntary action by the industry and have not been associated with a consistent change in alcohol consumption.[85–90] Learning from tobacco control, policy makers should consider regulation of alcohol packaging that is independent of industry influence.

Public health policy implementation of taxation and price regulation

Tobacco

Increased taxation has consistently been shown to reduce cigarette consumption.[72,74,88,89]

Alcohol

A 10% increase in alcohol price is associated with an average decrease of 5% in consumption studies conducted predominantly in high-income countries.[91] In Canada, in 2010, a 10% increase in minimum alcohol price was associated with an 8% reduction in consumption within 2 years[92] and reduced alcohol-related deaths by 32%, hospital admissions by 9%, traffic violations by 19%, and crime by 9%. Introduction of minimum unit pricing for alcohol in Scotland in 2018 was associated with reduced deaths and hospital admissions, especially in the lowest socioeconomic groups.[69]

modifiable risk factors for breast cancer in most countries.[56–62] Although educational interventions can increase knowledge about risk factors,[63] knowledge alone is not generally sufficient for sustained behavioural change.

There is evidence that some breast cancer prevention strategies work for some people. For example, women who followed the American Cancer Society guidelines on weight control, physical activity, alcohol intake, and diet[64] had a 22–31% lower risk of breast cancer compared with women who were less adherent.[65,66] Reliance on individual responsibility, although empowering for some, can be perceived as blame culture by others. Changing health behaviours to reduce the risk of breast cancer can also be more challenging for people struggling with other health and social problems. For example, a small proportion of people who have given birth are unable to breastfeed and must have access to formula milk. Another example is the positive dose–response relationship between obesity-related cancer mortality in the USA and food deserts (ie, few healthy food resources) and food swamps (ie, high access to fast food). One population-based study in California found that patients with breast or colorectal cancer who lived in

a food desert had worse five-year survival rates than patients with breast or colorectal cancer who did not live in a food desert.[67] Another US study that included 3038 counties showed higher rates of poverty and non-Hispanic Black residents in regions with high obesity-related cancer mortality, showing the complex intersection between cancer, ethnicity, and poverty.[68]

By contrast, policy and legislative changes have the potential to reach an entire population and in some cases (such as taxation on products) can have the greatest effects in disadvantaged groups, reducing deprivation-based inequalities in harms attributable to risk factors.[69–73] Increased tobacco tax has consistently resulted in immediate and sustained reductions in the prevalence of smoking in both high-income countries and low-income countries[72–74] when coupled with other policies that increase the financial and social costs of smoking. In addition, the introduction of plain paper packaging of tobacco products in Australia was associated with a 25% reduction in the number of people who smoked cigarettes over the next 3 years.[75] Many of the alcohol and food industry strategies to increase consumption resemble those of the tobacco industry, so successful tobacco policies can be used to inform harm reduction policy agendas (panel 4), as seen in the *Lancet's* Commercial Determinants of Health Series. As with tobacco policies, prioritisation of sustainable, highly effective, and cost-effective alcohol and food policies are needed, supported by legislation addressing affordability and availability. Restrictions on advertising and sponsorship and penalties for false advertising should be enforced. Warning labels and public education campaigns should be independent of industry influence.

For the ***Lancet's* Commerical determinants of health Series** see https://www.thelancet.com/series/commercial-determinants-health

A key aspiration of this Commission is to help policy makers recognise that the predicted upward trajectory of breast cancer incidence can be modulated by policies that reduce exposure to risk factors at the population level. The development and delivery of such policies will require governments to show strong political will and integrity in resisting lobbying by industries that might be adversely affected by the policy changes. Implementation of education strategies around alcohol consumption, obesity, physical inactivity, and low levels of breastfeeding will be needed to support and enhance policy changes (figure 1).

Public health policies

There are existing WHO-endorsed recommendations to reduce harmful alcohol use,[76] increase breastfeeding,[93] decrease overweight and obesity,[94] and decrease physical inactivity.[95] WHO provides policy makers with a list of recommended cost-effective interventions to address these risk factors.[96] Examples focus on taxation, marketing regulations, and restrictions on the availability of alcohol and specific foods, such as reduced hours of sale of alcohol.[76,94,96] However, the rates and success of policy implementation are variable[97,98] and tracking how effectively policies have been implemented is hampered in some regions by inadequate data collection on the prevalence of some breast cancer risk factors, such as breastfeeding.[99] For improved policy implementation, there must be adequate data collection to understand the effectiveness of proposed interventions in different local contexts.[100]

Common barriers to public health policy implementation include insufficient prioritisation, a perceived insufficient evidence base, the power and influence of industry over governments, variations in complex political and policy systems, and scarce resources.[101,102] Obesity, alcohol consumption, and breastfeeding are all influenced by the food (including baby milk formula) and alcohol industries. Policies and legislation that limit the influence of these industries and reduce exposure of the population to risk factors are therefore essential, as are policies that promote protective behaviours, such as breastfeeding or expressing at work. Regarding physical inactivity, governments should prioritise urban planning that promotes physical activity, such as providing adequate walking paths and open spaces.

Role of education in facilitating successful policy implementation

Education at a community level is important so that policies have social validity and acceptability.[103] Policies that are not well understood are often unpopular and difficult to implement, as seen during the COVID-19 pandemic in which differences between public communications could explain some of the observed differences in adherence to government-recommended interventions across different countries.[104] Therefore, multisector and multistakeholder actions and partnerships are needed[102,103] from politicians, celebrities (such as sporting heroes), civil organisations, and health-care providers, to encourage successful policy change at a population level.

Existing recommendations call for breast cancer awareness campaigns to target everyone.[105] The US Education and Awareness Requires Learning Young Act aims to develop age-appropriate education initiatives for young women and their health-care professionals to increase knowledge regarding breast cancer.[106] Introducing teaching on breast cancer in the US high school health education curriculum might increase awareness and knowledge about breast cancer risk factors[107,108] through intergenerational transmission of knowledge.[108] Other educational methods are required, particularly where access to high school education is lacking, and could include cooperation with local authorities, faith leaders, and traditional healers, as well as the use of social media and engaging celebrities as ambassadors to convey the importance of breast cancer awareness.

Systematic risk assessment and personalised prevention

To date, practice in high-income countries involves selective risk assessment and genetic testing of women who typically have already developed breast cancer and

have specific additional criteria, such as young age, family history, Ashkenazi Jewish heritage, or the triple-negative breast cancer subtype. Germline pathogenic variants resulting in the highest risk of breast cancer (eg, *BRCA* pathogenic variants) are present in a small percentage of women. However, a much larger group of women have a moderately increased risk of breast cancer due to other modifiable and non-modifiable risk factors and they typically receive no personalised risk assessment, nor are they offered tailored prevention strategies unless they seek out information or testing. Effective medical and surgical interventions can reduce risk in women who have a substantially greater risk of developing breast cancer than the general population. Medications (eg, tamoxifen, including a low-dose option,[109,110] raloxifene, or aromatase inhibitors) taken once a day for 3–5 years reduce the relative risk of breast cancer by 30–60%[109–117] and should be considered for women identified to be at increased risk of breast cancer. Although these medications only reduce the risk of hormone receptor-positive breast cancer, this is the most common breast cancer phenotype and is also the phenotype that is increasing in incidence. Tamoxifen is an affordable option in low-income countries. Medical prevention of hormone receptor-negative breast cancers remains an area of unmet need. Prevention trials using the RANK ligand inhibitor denosumab are currently underway.[118,119] RANK and RANK ligand have been shown to be key regulators in the development of hormone-receptor negative BRCA1-associated breast cancers.[118,119] Bilateral mastectomy is associated with a more than 90% decreased risk of breast cancer in observational studies[120] and surgery should be accessible for people at very high risk of breast cancer, such as those with high penetrance pathogenic variants in breast cancer predisposition genes.[120] However, it is important that these women are supported to feel empowered to make their own informed decision, considering the potential benefits and risks of surgery.

If an individual is unaware that their risk of breast cancer is substantially elevated above that of the general population, they miss the opportunity to access proven prevention strategies. Therefore, the first step in personalised breast cancer prevention is high-quality risk assessment. Proactive, systematic breast cancer risk assessment for all women (rather than just for those who request it or who are diagnosed with cancer), followed by personalised advice about effective, evidence-based preventive interventions for those at increased risk, should become an integral part of high-quality care. Health-care systems and policy makers should start moving towards this goal by using the existing assessment tools available locally. These tools can range from basic to more sophisticated methods, depending on local infrastructure and resources, that can be developed and refined over time. Engagement of health services researchers and implementation scientists will be required to elucidate the most appropriate implementation pathways for each health-care setting, considering the health-care system's structure, resources, and sociocultural setting. Considerations for systematic high-quality risk assessment are outlined below.

Achieving systematic risk assessment

Risk assessment would need to commence at a young age (eg, aged 25–30 years) to facilitate identification of, and preventive interventions for, those who are at high risk of early-onset breast cancer (eg, carriers of *BRCA1* pathogenic variants). Comprehensive risk assessment of all genetic and non-genetic risk factors might not be necessary until later in life; systematic population-based assessment of highly penetrant genetic factors alone might be an appropriate first risk assessment step. This population-based assessment could consist of offering testing to all women aged 25 years and older for major breast cancer predisposition genes. Studies are already examining the feasibility and acceptability of this type of genetic risk assessment in young people.[121] Women with a pathogenic *BRCA1* or *BRCA2* variant and a family history of breast cancer are at higher risk than those without a family history of breast cancer.[122] Therefore, in resource-constrained settings in which population genetic testing is not feasible, initial assessment of family cancer history to triage those for genetic testing could be another approach. However, not everyone has a family structure that can provide information (eg, due to adoption, loss of family due to genocide, young maternal death from non-cancer causes, and underdiagnosis of cancers in some contexts), so reliance on family history could lead to inequities.

At subsequent timepoints in an individual's life trajectory, more comprehensive risk assessments considering other genetic and non-genetic risk factors will be needed, particularly to identify those at moderate risk of breast cancer, which is a much larger group than those at very high risk. A potential timepoint for more comprehensive risk assessment could be at age 40 years, or when an individual has decided that they do not want any or more children, in which case risk-reducing medication such as tamoxifen could be considered. Targeted prevention interventions, such as risk-reducing medications, for those with moderate risk could potentially reduce the incidence of breast cancer in the population. Risk assessment would need to occur at regular intervals (eg, every 10 years) to account for changing risk factors and advances in medical knowledge that might inform the risk assessment. Systematic risk assessment by use of algorithms validated in the relevant populations could be embedded in broader routine health care, specifically in primary care, cancer screening programmes (eg, cervical screening), and early cancer-detection programmes. Countries that already have population-wide mammographic screening programmes could consider incorporating routine risk assessment,

linked to prevention interventions and advice.[123–125] This linkage would be opportune because mammographic density is an important risk factor for breast cancer.[126]

For the **iPrevent tool** see https://www.petermac.org/iprevent

There are several tools based on mathematical algorithms that are available to estimate breast cancer risk according to risk factor profiles. No single algorithm or tool is the best in all circumstances.[127] Algorithms, such as the Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm model[128] and the Breast Cancer Intervention Study model,[129] which integrate genetic and non-genetic risk factors, tend to perform the best in most settings.[130]

It is recommended to only use validated algorithms that have been proven to provide accurate risk assessment. The optimal validated algorithm for systematic breast cancer risk assessment will vary between settings, depending on the ethnicity and age characteristics of the population being assessed and the availability of risk factor information (eg, mammographic density) in each setting. It should be easy to use and affordable. Most risk assessment tools to date were developed and validated using data from people with European ancestry. However, validated risk assessment tools can be adapted and calibrated for local contexts. For example, the Breast Cancer Risk Assessment Tool has been validated for use in White, Black, African American, Hispanic, Asian, and Pacific Islander women in the USA.[131–133] Attempts at using genetic ancestral composition to expand polygenic risk assessment to women of diverse ancestries are a step towards improving equity in breast cancer risk assessments.[134] In women undergoing age-based population mammographic screening, risk estimation tools that incorporate mammographic density are valuable, although probably only feasible if automated measures of mammographic density are available.[135] There is also increasing research regarding the use of artificial intelligence-based risk models that incorporate mammographic data.[136–139] Tools that provide tailored risk management advice on the basis of local guidelines, an individual's absolute risk, and other factors that affect risk management decisions, are also desirable, such as the iPrevent tool from the Peter MacCallum Cancer Centre.[140]

Research needed to support systematic risk assessment and personalised risk management

To successfully implement proactive and systematic breast cancer risk assessments to drive delivery of targeted preventive interventions, stakeholders and funders must understand their potential benefits and invest in ongoing research. Implementation of evidence-based access to genetic testing for breast cancer risk will be important. In addition, there should be high quality evidence that systematic breast cancer risk assessment is clinically effective in preventing or downstaging breast cancer and results in behavioural changes and risk-appropriate uptake of preventives in women identified to be at increased risk of breast cancer. To date, there is little prescribing of preventive medications,[141] despite evidence from multiple randomised controlled trials showing major reductions in breast cancer events,[109–115] and unanimous guidelines recommending their consideration for women at increased risk of breast cancer;[116,117,142] workforce education is a major barrier. Clinician capability and knowledge has been identified as a major barrier to the discussion of, and prescribing of, risk-reducing medications.[143,144] This barrier must be addressed and resources must be prioritised for successful widespread implementation of preventive medications that can bridge the large evidence–implementation gap. Research will also need to show that systematic risk assessment does not substantially increase health-care anxiety in recipients and can be implemented in a variety of health-care systems.

	Definition	Rationale	Data sources	Responsible entity	Target	Comments
Alcohol and baby milk formula	Effectively control alcohol and commercial milk formula advertising and sponsorship	Use of alcohol and little or no breastfeeding are important modifiable causes of breast cancer globally	Legislation	Ministry of Health in collaboration with Ministry of Commerce	95% of countries fully legislating the UNICEF Code[93] for advertising and promoting baby milk formula products and adhering to the WHO best buys[151] for alcohol advertising	Close loopholes in advertising
Parental leave and supportive work environment for breastfeeding and expressing	Ensure adequate publicly funded parental leave and provision of paid breaks and nursing facilities on return to work	Parents who work should be supported to breastfeed if they choose; supporting breastfeeding reduces risk of breast cancer and provides other important health benefits to parents and children	Legislation	Ministry of Health	Statutory access to at least 18 weeks and preferably 26 weeks of parental leave at 100% pay; mandatory provision of paid breaks and nursing expressing facilities on return to work[152]	NA
Non-alcoholic sugar-sweetened beverages	Limit consumption of sugar-sweetened beverage	Sugar-sweetened beverages contribute to weight gain and obesity, which increase risk for non-communicable diseases	Measure change in the total volume of sugar sold in sugar-sweetened beverages	Ministry of Health	Tax sugar-sweetened beverages to raise their retail price by at least 20%[153]	Tax according to sugar content might encourage reformulation and shift to lower sugar content drinks

NA=not applicable.

Table 1: **Proposed measurable indicators of change for breast cancer prevention**

A measure of progress is the proportion of women who undergo personalised risk assessment, have access to genetic testing for major breast cancer predisposition genes, and start risk-appropriate prevention interventions. In countries with high-quality collections of administrative data, these measures could be assessed through data linkage. Monitoring the change in the prevalence of key modifiable risk factors, such as alcohol, obesity, and breastfeeding, with existing tools, such as the Global Cancer Observatory, the Global Health Observatory, and the Global Breastfeeding Collective Scorecards, could be another marker of progress, emphasising the need for countries to adequately collect these data.[55,145,146] Moreover, reductions in the sales of alcohol and baby milk formula would also indicate progress.

Future work and potential wider effects

As an immediate action, equitable access to effective resources and interventions, such as germline genetic testing and preventive surgeries and medications is vital for successful breast cancer prevention globally. Research into novel prevention strategies should be prioritised, including medications that target molecular pro-survival signals,[109,147] medications that mimic the breast cancer protection mechanisms from pregnancy and lactation,[148,149] and vaccines that boost the immune system.[150]

Many breast cancer risk factors, such as alcohol, postmenopausal obesity or overweight, physical inactivity, and low levels of breastfeeding also predispose people to other non-communicable diseases. For example, breastfeeding is well recognised to be beneficial to both maternal and child health.[34,66] Modification of the prevalence of these risk factors could therefore have wider reaching benefits for other health conditions. Successful implementation of personalised prevention approaches in breast cancer could also pave the way for similar approaches to other cancers, such as colorectal cancer (table 1).

Theme 2: personalising breast cancer treatment

There have been extraordinary advances in breast cancer discovery, biology, and translational and clinical research in the past decade. However, without action now, the cost of treatment and research will become unaffordable to all but the privileged few and will increase the equity gap. This Commission has an aspirational goal for everyone with breast cancer to be able to access personalised treatment (panel 5). We want to foster greater patient diversity in clinical trials, which would go some way to improve the information available to minority groups to inform personalised treatments. This may also enable the development of therapeutics tailored appropriately for specific genetic variants prevalent in specific populations. For this aspiration to become reality, there must be a substantial shift in how breast cancer treatment and research is undertaken globally. For example, future clinical trials should be risk-adapted and fit for purpose or breast cancer clinical trials will not be feasible or affordable, aside from those motivated and conducted by

Panel 5: Summary of personalising breast cancer treatment

Breast cancer research and digital health can facilitate equitable and prompt access to the most appropriate breast cancer treatment at the right time for each individual, while respecting personal needs and preferences.

- Better targeting of existing treatments through development of validated accessible biomarkers and equitable global access to existing biomarkers is needed to identify the people who benefit the most and reduce treatment burden for those more likely to have more toxicity than benefits
- Development and facilitation of novel, efficient, patient-centred translational clinical trials are required to enable a research culture and infrastructure across the globe
- Digital health can facilitate innovation through integration of multimodal complex datasets; promote flexible, coordinated care, particularly for patients who are socially vulnerable; democratise access to research; and decentralise trial participation
- If used optimally, digital health technology can alleviate inequalities in breast cancer rather than drive them
- Development of artificial intelligence and machine learning software that deliver automated pathology scoring or image-related risk triaging could also reduce workforce-related issues

Panel 6: Approaches required for personalised breast cancer treatments

1. Precision—determining and exploiting the molecular characteristics of each breast cancer and tumour microenvironment by identifying validated accessible biomarkers, and adapting treatment to response or resistance is necessary for early interventions.
2. Optimisation—establishing the best cancer-related outcomes with the least toxicity and minimal treatment burden for everyone. Optimisation considers patient comorbidities, needs, and personal preferences, seeks to reduce the number of deaths due to breast cancer, and seeks to allow the safe reduction of treatment burden for people with breast cancer with a good prognosis who might be overtreated.
3. Innovation—ensuring equity of access with the best use of resources for treatments and clinical trials. Innovation is accelerated through interactions with disciplines outside medicine.
4. Interpretation—understanding the roles of the prognostic biomarkers that establish the risk of disease recurrence and predictive biomarkers that inform an individual's probable sensitivity to treatment.

pharmaceutical companies, which must be recognised by funding agencies and regulators. This Commission proposes that the framework underpinning this goal can be applied to other cancers and a wider range of health conditions (panel 6).

To date, despite considerable global efforts, true predictive biomarkers—such as ER and HER2—are rare, with benefits for treatment largely determined by absolute risk dictated by the many individual and composite factors affecting prognosis. Modelling tumour biology at an individual level will enable mechanisms of cancer progression and drug resistance to be deciphered and permit identification of specific therapeutic targets. Proof of concept has been done with genomics, including the identification of *BRCA1, BRCA2, HER2* (also known as *ERBB2*), and *PIK3CA* alterations. However, this approach is limited[154] because we have not yet fully explored the role of epigenetics, tumour microenvironment, spatial biology, including spatial measurements of gene and protein expression, and single cell analysis, all of which may provide additional information in all types of risk prediction. These advances will enhance prediction of responses to treatments and early indications of metastatic dissemination potential, allowing more precise and potentially earlier treatment of micrometastatic disease. However, improved model systems are required to predict which patients will benefit from specific treatments, including newer targeted agents—such as antibody–drug conjugates—and to identify those who are either less likely to benefit or more likely to have serious side-effects from treatment. Living diagnostic tools, including ex-vivo models, such as organoids, spheroids, and patient-derived xenografts, allow definition of the proteins involved in the progression of cancer and therefore the refinement of treatment.[155] These diagnostic tools are being assessed by drug exposure ex vivo and ongoing efforts are testing whether gene editing of living models could model cancer biology in individuals.[156] Once refined, we should consider the optimal way of integrating the information gained from these models into health-care systems to support the care of individual patients.

Given the rare nature of many molecular aberrant changes in cancers, many might not appear targetable, or they are so rare that a clinical trial to test the efficacy of an intervention is not possible. There is a need to rethink both drug development and clinical trial design in the era of molecular medicine, while also acknowledging the global inequalities in access to research. The use of pan-cancer trials could help us to understand the similarities and differences of molecular markers within and across tumour types. These trials must integrate both genomics (germline and somatic) and other omics if relevant. Biological differences in diverse ethnic populations and the tumour microenvironment of different subtypes at different stages of breast cancer must be considered in clinical trial design to enable tailored treatments.

Optimisation of breast cancer treatment

The Early Breast Cancer Trialists Collaborative Group have done meta-analyses of global evidence from randomised clinical trials for 40 years and have enabled precise estimation of breast cancer treatment effects beyond the time of trial primary endpoint analysis. These seminal analyses have enabled evaluation of treatment effects within subgroups across follow-up periods. With the exceptions of ER-positive breast cancer and HER2-positive breast cancer, consistent benefits of treatments have been shown across different clinical and prognostic patient groups. This leads to an understanding that it will be the absolute gain (informed by prognosis) that most influences both optimised treatment decisions and the concept of precision approaches to treatment choice for patients. Precision approaches have great potential value in the early disease setting. In this setting, many patients are overtreated, which results in a substantial burden of therapy—particularly toxicity and time-toxicity—which is also costly. Optimisation of treatment aims to maintain excellent outcomes while reducing financial, physical, and psychological costs. Treatment deimplementation can be achieved by use of prognostic biomarkers at the start of the therapeutic pathway to identify patients more likely to have very good outcomes due to an intrinsically non-aggressive cancer. In the past decade, biomarkers have been used to assess dynamic responses to initial therapy and inform decisions to safely reduce treatment components. One model of this approach is the pre-operative window study, in which short duration treatments can be used to identify responsive tumours and improve prediction of outcomes.[157] Another model is neoadjuvant systemic therapy with the pathological response to that treatment assessed at the time of surgery. Patients without a pathological complete response have been shown to benefit from escalation of further therapies (eg, antibody–drug conjugates or a different chemotherapy agent) and those with an excellent response might require less adjuvant therapy to maintain the same excellent oncological results. The neoadjuvant systemic therapy approach is being tested for HER2-positive breast cancer in ongoing clinical trials, such as HER2-RADiCAL (UK)[158] and OPTIMICE (USA; NCT05812807).

Despite the rapid advances in treatment approaches, most patients with breast cancer continue to be treated with a standardised approach: primary surgery followed by adjuvant systemic therapies and radiotherapy. This approach does not consider breast cancer as a highly heterogeneous disease with a broad spectrum of risk ranging from early, low-risk screen-detected disease with favourable biology, through to highly aggressive, life-threatening tumours. Furthermore, such a conventional approach does not use all the available information, such as more refined measures of risk or evidence of response to a particular therapy, and can lead to suboptimal treatment choices at all points in this risk continuum.

This approach underscores the need for diagnostic precision and optimisation of treatment. However, the Early Breast Cancer Trialists Collaborative Group analyses (appendix p 17) show that widespread global use of a 5-year course of the endocrine therapy (eg, tamoxifen) or several months of anthracycline chemotherapy (eg, doxorubicin) alone substantially reduces breast cancer recurrence and ultimate survival at a modest treatment cost and substantial personal and societal gain.

In many patients with early-stage disease and favourable biology, it is probable that locoregional therapy alone is curative.[159] Although it is believed that more breast cancer therapy results in improved outcomes, evidence suggests that in many instances, less therapy can be enough.[159,160] An example is the similar oncological outcomes of breast-conserving surgery plus radiotherapy to those of more extensive mastectomy surgeries,[159,160] with the former approach providing improved aesthetic outcomes, better quality of life, and increased cost-effectiveness.[161–163] The use of breast-conserving approaches, however, is dependent on timely and equitable access to adjuvant radiotherapy, which is not available to all across the world, and those without access are also denied the potential proven overall survival advantages associated with radiotherapy.[164] Hypofractionation (ie, giving larger radiotherapy doses in fewer treatments) is another form of optimisation because it decreases the treatment burden for patients while maintaining efficacy with similar or reduced side-effects both in terms of number and grade of severity; hypofractionation is also more cost-effective than breast radiotherapy with more treatments (appendix pp 20–21). Allowing all patients informed choices and equitable access to optimal locoregional treatments is dependent on improved and integrated health-care infrastructure. Optimisation of systemic treatments in early breast cancer could include immunotherapy in triple-negative breast cancer (appendix pp 21–23) and reduced duration adjuvant trastuzumab in HER2-positive breast cancer.[165]

Implementation of stage-shifting strategies (theme 4) will probably increase the number of patients for whom locoregional therapy will be curative, but this will take several years. Subsequent improved precision approaches will allow the identification of patients whose treatment could be further de-escalated or optimised. Examples include the omission of radiotherapy for very low-risk breast cancer[166] or de-escalation of surgery by either omission of surgical axillary staging or minimally invasive treatment of the primary tumour.[167–169] Thus, optimisation of treatment is dependent on access to a full range of both diagnostic and therapeutic modalities.

Despite efforts to increase rates of early diagnosis, there will remain individuals with high-risk tumours for whom treatment optimisation will require escalation of therapy. In this context, neoadjuvant systemic therapy is increasingly used as a standard of care that provides opportunities to test reducing therapies in those with a complete pathological response. However, it also enables treatment escalation or alternative treatment strategies in patients with substantial residual disease. Furthermore, this approach could allow tailoring of locoregional treatments of the breast and axilla.[170]

To ensure optimised treatments, a multidisciplinary approach from diagnosis is essential. Information regarding tumour molecular characteristics is needed to establish an individual's risk and therefore their optimal treatment sequence. This information will allow the patient to see the right specialists at the right point in their treatment pathway. All patients with breast cancer need access to multidisciplinary teams and tumour boards at the point of diagnosis to facilitate optimal treatment planning, and later, to choose subsequent therapies on the basis of their initial response or management of recurrence.

It is essential that this multidisciplinary approach of optimal care is applied to all individuals with breast cancer without discriminating against subpopulations, such as with the management of older patients with breast cancer. More than 35% of women diagnosed with invasive breast cancer in the UK are aged 65 years or older,[171] this proportion is increasing globally due to population demographics, and the management of older patients presents several additional factors to consider.[172] Older patients have the highest rates of breast cancer mortality—when adjusted for tumour characteristics and stage—than any other age group, have greater variation in care, and are not eligible for systematic breast screening because of their exclusion from formative trials.[171,173] Unfortunately, the mistaken notion that older patients have indolent disease is still prevalent. Simple and reliable assessments of comorbidity and fitness are now routinely available and could allow more consistent care and facilitate ongoing national audits, which should remain a priority for this large and growing patient group.

Optimisation of treatment with value-based health care

Value-based approaches[174] aim to deliver the best possible outcomes at lower costs.[175,176] Value in breast cancer care can be defined as the sum of quality, outcome, cost, and patient preference. Porter[177] and Teisberg and colleagues[178] introduced the concept of value-based health care as a strategy to reduce health-care expenditure while maintaining or even improving outcomes. The value-based health-care framework consists of understanding the health needs of the patient, designing solutions to improve outcomes, integrating learning teams, measuring outcomes, and expanding partnerships between patients and all groups involved in health-care delivery. Value-based health care is particularly important in breast cancer management worldwide. The health economy of breast cancer has seen enormous funds invested in discovery science, translational and clinical research by academia, public and charitable funding, and

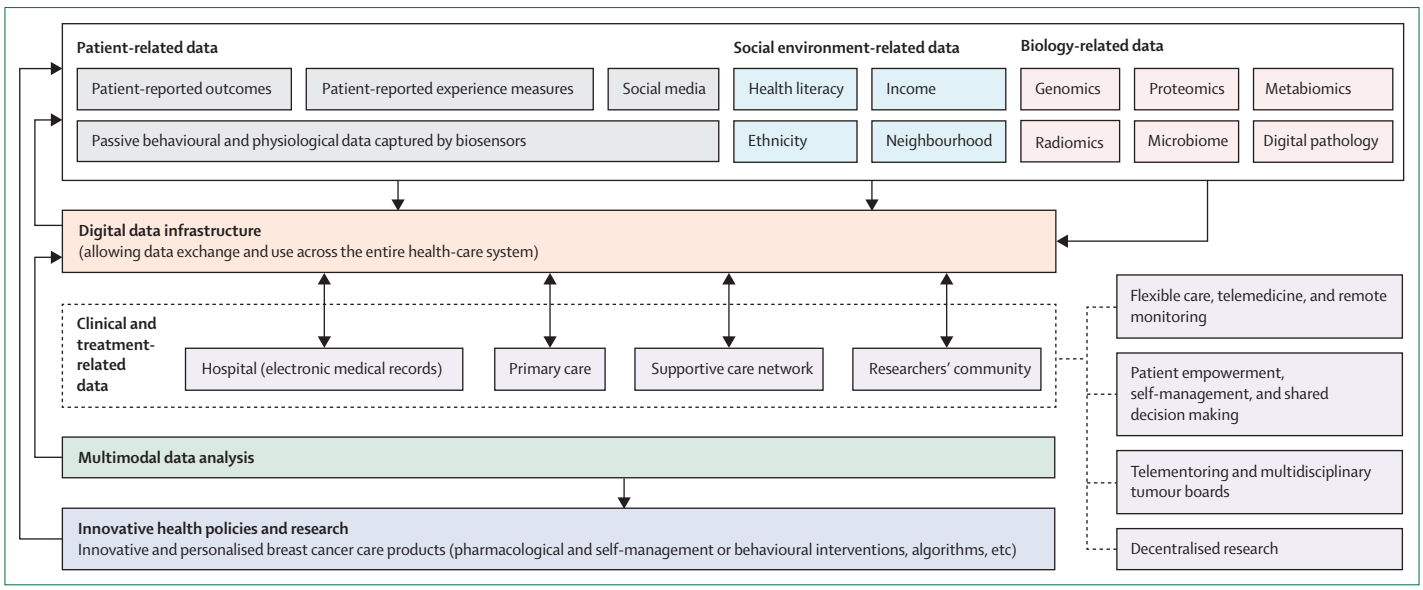

Figure 3: **Vision for technology-enabled breast cancer treatment and research**

***Panel 7:* Digital health general terms and applications:**

- Telemedicine: medical care by health-care professionals delivered by telecommunication
- Remote monitoring: real-time monitoring of symptoms or vital signs by use of technological devices
- Electronic medical records: digital patient charts allowing data storage, access, and sharing within information governance frameworks
- mHealth: technology for health on mobile devices
- Biosensors: sensors capturing physiological and behavioural data for patient and medical purposes
- Digital therapeutics: evidence-based software interventions to prevent, manage, or treat a condition or disease
- Advanced analytical techniques: evaluating datasets with artificial intelligence to predict medical events (eg, response, relapse, and toxicity)

pharmaceutical companies. This has resulted in substantial improvements in breast cancer care and outcomes for patients in high-income countries, which has meant that breast cancer has led innovations within the cancer field. This success has contributed to a more is better approach, which has led to the adoption of expensive new treatments. Expensive treatments that add little to improvement in outcomes can be associated with substantial toxicity—including time-toxicity—and out-of-pocket and hidden costs (see theme 5). In LMICs, the adoption of a value-based health-care system would particularly benefit patients diagnosed with breast cancer, since this would encourage policy makers to choose therapies with the best value from the many available breast cancer treatments. However, in many countries, the business model of health-care systems (eg, in the USA) continues to be followed, contributing to inequities within and between countries. To date, people with breast cancer in high-income countries are often overtreated, but people with breast cancer in LMICs can get less than optimal care, and people in the countries with the lowest incomes might not even receive a diagnosis. Adopting value-based health care for breast cancer has the potential to optimise care in high-income countries by rejecting treatments that are expensive and represent little added value, give guidance to LMICs to improve outcomes without bankruptcy, and help those countries with minimal provisions to initiate breast cancer care. Sharing technologies and making the outcomes of research freely available will help to establish and maintain value-based breast cancer care, as will the acceleration of technological change. It is to be hoped that the breast cancer community can provide further examples of excellence in care that can be followed by other specialties within oncology.

Technology-enabled breast cancer management

Technology can facilitate the integration of multimodal data inputs from complex and large datasets to set up personalised treatment and follow-up. Figure 3 depicts a vision for technology-enabled breast cancer treatment and research. In this vision, data are collected digitally from multiple sources: patient-generated data, the social environment—including the social determinants of health inequities—biological tumour omics, and classic, clinical, pathological, and treatment data, all of which are integrated into a multimodal data model[179–188] with real-time interpretation and large-scale interoperability. This model should allow data exchange between all stakeholders of the oncology health-care system (patients, providers, and researchers at hospitals,

primary care facilities, and the supportive care network) to inform personalised risk-stratified pathways of care that could reduce treatment toxicity, improve survival and quality of life, potentially reduce health-care costs and burden, and inform innovative health policies.[189,190] Several specific digital health applications could facilitate the implementation of this framework and affect clinical care and research in several aspects (panel 7).

Improving the organisation, quality of care, and efficiency of health-care systems through digital health involves telemedicine and teleradiology. Telemedicine was rapidly implemented in breast cancer care[191–195] during the COVID-19 pandemic and enabled prioritisation of inpatient critical care and allowed for decentralised care to reduce in-person hospital visits for patients.[193,196,197] Patient satisfaction was high[191,192,198] and positive experiences of care[199] were reported among patients across the breast cancer continuum[191,200] in high health-care resource settings,[201] resource-constrained settings,[202,203] and remote rural areas.[192] Telemedicine has been used in some multidisciplinary teams for years,[204] and telephone-led consultations for follow-up breast cancer care have also been used in some settings for decades. A randomised study[205] showed that telemedicine was well perceived with no detrimental effect on anxiety or the ability to detect relapses in the context of breast cancer. Telemedicine is seen as a valuable tool to enhance breast cancer care by oncologists[206] and teleradiology can provide timely diagnostic assessments and efficient breast cancer screenings in areas with scarce local radiology support.[207,208]

Remote monitoring

A breast cancer cluster randomised trial among 20 Canadian centres with 2158 patients receiving chemotherapy showed that nurse-led telephone-based management was associated with lower rates of grade 3 toxicity, although there were no statistically significant effects on hospital admission rates or patient-reported outcomes (PROs).[209] Several randomised clinical trials have confirmed the benefit of PROs with validated patient assessment questionnaires to assess both global and cancer-specific quality of life and function, as early warning monitoring to avoid or reduce severe treatment-related toxicity and increase quality of life for patients with early and metastatic cancers receiving systemic therapy, including patients with breast cancer.[210–215] Although remote monitoring is already recommended in oncology[216] and deployed in some health-care systems,[217] global real-world implementation is still slow. Efforts regarding awareness, training, integration with electronic medical records, policy, and reimbursement are needed for reorganisation of care to allow real-time responses to patients' electronic PROs (ePROs) in routine practice.

Rehabilitation and self-symptom management

Delivering comprehensive breast cancer survivorship care, including management of long-term physical and psychosocial consequences of cancer and its treatments, is complex, costly, and insufficiently implemented (themes 3, 5, and 6).[218] Digital health offers an opportunity to facilitate comprehensive survivorship care and self-management support. Randomised clinical studies have shown that digital support increases quality of life and self-management for patients with breast cancer during the post-treatment follow-up phase.[219,220] Examples include use of digital cognitive behavioural therapy for fatigue,[221] insomnia,[222] fear of recurrence,[223] and emotional distress.[224] Cognitive rehabilitation with digital health solutions after chemotherapy has also proved promising[225] and health promotion, such as physical activity and weight management programmes, can be successfully delivered with digital health solutions.[226–229] Advances in data interoperability and standardisation are needed to ensure full integration of self-management support and PROs with electronic medical records.[230] Several studies of breast cancer care suggest that the efficacy of digital health tools is related to persistent engagement with the use of digital health tools and more efforts are needed to understand who will benefit most from digital health solutions and what is required to maximise adoption and engagement.[231,232]

Facilitating communication within health-care systems

Use of electronic health records improves patient safety, operational efficiency, and quality of care.[233] For example, electronic health records integrated with tumour board applications save preparation time and reduce errors.[233–235] Electronic health records might also increase patient engagement through automated mammographic screening scheduling, screening reminders, establishing eligibility for genetic testing and counselling, identifying patients who would benefit from weight management, and establishing clinical trial eligibility.[236] Technology can create virtual mapping and linking of the patient's address with community mobile health-care professionals and comprehensive cancer centres, which enable more flexible care (eg, anti-HER2 subcutaneous therapies).[237]

Telementoring

Telementoring can enhance training to increase the number of health-care practitioners, especially in underserved areas (such as the Project Extension for Community Health-Care Outcomes).[238] It can support virtual multidisciplinary team meetings[189,239] and enable resource sharing between comprehensive cancer centres and local community hospitals.[240] Multidisciplinary telemedicine resources could also be developed between high-income countries and LMICs.[241,242] The COVID-19 pandemic has increased implementation of effective virtual multidisciplinary meetings in oncology centres[243] and this should be expanded globally to increase patient access to multidisciplinary cancer care.

Digital health as a care equaliser

Effort and careful planning are needed to expand access to technologies and ensure that the digital divide does not exacerbate breast cancer care disparities.[244] Technology can be transformative in care and research if digital health tools are co-designed with patients and providers, considering different levels of patient electronic health literacy.[230] In oncology, randomised clinical trials have shown that using low complexity digital health devices for weekly symptom monitoring was feasible among patients with lower educational levels and low electronic health literacy. This finding led to fewer emergency visits and improvements in quality of life.[212,213] In the cluster randomised clinical trial PRO-TECT,[213] weekly symptom monitoring with ePROs was implemented in 52 community-based oncology practices in the USA. Around 20% of patients in the trial had never used email before and 30% had financial difficulties. The option to assess symptoms through an automated telephone rather than the internet was chosen by 36% of patients and was associated with older age and lower education. Another example is the Accountability for Cancer Care through Undoing Racism and Equity Pragmatic Quality Improvement Trial, which led to the elimination of Black–White treatment gaps for patients with early-stage breast and lung cancer in the USA.[245] This was a multifaceted digital health intervention in which an automated warning system from patients' electronic health records automatically sent alerts to the care team when a key milestone of treatment (eg, appointments or examinations) was missed. Second, a proactive nurse navigator trained in health equity monitored the warning system and addressed care barriers, including medical mistrust, lack of self-efficacy, poor communication and beliefs that negatively influenced care, and implicit bias from health-care providers.

With respect to diagnosis, machine learning algorithms could be used to decrease breast cancer care disparities, especially in low-income settings. Promising results have been reported for analysing breast cancer mammograms to automate or improve the sensitivity of breast cancer screenings[246–248] and in digital pathology slides to provide timely breast cancer diagnoses. Further work uses AI-algorithms applied in digital pathology to expand the access and implementation of biomarkers to guide treatment decisions, including the automated evaluation of tumour-infiltrating lymphocytes and their statistical correlation with outcomes,[249] and the evaluation of molecular profiles and risk of relapse.[181] Datasets used to train artificial intelligence algorithms must be representative of the real-world population with breast cancer, or these models might not be applicable in clinical practice or could increase inequalities for groups of patients that are usually excluded from research and face difficulties in accessing care.

Panel 8: Summary of digital health and breast cancer

- Digital health has been used in breast cancer care to a low extent over the past two decades, but its use expanded and accelerated during the COVID-19 pandemic
- Digital health has the potential to improve efficiency of health-care systems, reduce breast cancer care delivery barriers and costs, and promote patient empowerment and self-management
- The use of electronic patient-reported outcomes in routine clinical care improves symptom management and quality of life and offers patients an opportunity to participate in their care
- Digital technology could enable multimodal data integration to inform personalised treatment and follow-up plans
- Digitally-enabled clinical trials simplify and accelerate research workflows and can increase community engagement and reach
- Digital health can promote care equity, especially if technology innovations are co-designed with patients and navigation is provided
- Digital literacy and social determinants of health, contextual patient factors, confidentiality and information governance, and health-care organisations all need to be considered when implementing digital health measures
- Policies are required to increase broadband access and promote large-scale digital navigation for populations frequently excluded from health-care innovations

Digital health as a tool to enhance research

Digital technology can improve participant access and engagement, trial-related measurements, and the delivery of interventions. It can enable the allocation of concealed randomised interventions, improve the speed and collection of patient-generated and clinical data, and has the potential to transform clinical trials and lower their costs.[250] The need for efficient and generalisable research calls for all patient groups to be involved throughout the process.[251] Nevertheless, groups often facing disparities and difficulties in health-care are particularly under-represented in oncology research.[252–254] Barriers include low understanding of research, unconscious bias from researchers, out-of-pocket costs, and accessibility issues (appendix pp 24–26). There are many strategies to reduce inequities in access to cancer research, including digital education programmes to improve cultural competence, promote self-assessment, and reduce unconscious bias;[255–257] automated clinical trial eligibility screening[251,258,259] and matching algorithms; decentralised tools for patient consent, inclusion, study conduct, ePROs, and digital capturing of study endpoints;[250] activating community engagement and fostering co-design and participatory research;[260] incorporation of ePROs co-developed with patients that

	Definition	Rationale	Data sources	Responsible entity	Target	Comments
Breast cancer diagnosis	Ensure high-quality breast cancer receptor testing at diagnosis	Ensuring all patients with breast cancer have access to accurate tumour subtyping to enable appropriate treatment sequencing and selection of therapies (eg, endocrine, targeted, and chemotherapies)	Facility records; national audits; national and international certification procedures for breast units	Facility and Ministry of Health	>80% (aiming for 95%) of patients have access to accurate tumour subtyping	Must ensure global collection of these data
Multidisciplinary meeting review at diagnosis	Ensure the review is multidisciplinary, linking with expert team members virtually if appropriate	All new diagnoses of breast cancer should be discussed by a multidisciplinary team to allow optimal treatment planning	Facility records; national and international certification procedures for breast units	Facility and Ministry of Health	>80% (aiming for 95%) of patients with new diagnosis to be discussed at a multidisciplinary meeting	NA
Range of treatments	Appropriate access to appropriate range of surgical, radiotherapy, and systemic treatments	All patients with breast cancer should have access to a full range of treatment modalities to allow equitable treatment choices globally and ensure optimal outcomes	Facility records; national and international certification procedures for breast units	Ministry of Health	100% of patients with breast cancer to have access to full range of treatment modalities	Integrated cancer health-care system with regional infrastructures based on burden of disease in each country
Clinical trials	Increase global leadership and participation with clinical breast cancer research	Ensure that patients participating in clinical trials are representative of the global population of people with breast cancer and research leadership includes high-income countries and LMICs	Clinical trial registries; PubMed; global patient ID	Policy makers, research funders, and higher education institutes	At least 10% (aiming for >25%) of participants of international breast cancer trials from LMICs; at least 10% (aiming for >25%) of all breast cancer trials are led or co-led by researchers from LMICs	Ensure clinical trials are representative and generalisable globally; to build research capacity, infrastructure, and expertise globally

LMICs=low-income and middle-income countries. NA=not applicable.

Table 2: **Personalising breast cancer proposed measurable indicators of change**

can optimally capture patient lived experience and outcomes;[250] set-up of global clinical trials and equal research collaborations between high-income countries and LMICs through innovative digital networks with fully digital clinical trials;[261] and digital navigation support (panel 8, table 2).[262]

Theme 3: optimal inclusive management of metastatic breast cancer

In many regions of the world, people with metastatic breast cancer are unseen. The global number of people with metastatic breast cancer is unknown[263] and this knowledge gap both prevents adequate allocation of resources and intensifies associated stigma and inequities. These patients often have restricted access to treatments, despite proven overall survival benefits, and have barriers to supportive care.[264–267] As a result, people with metastatic breast cancer can feel abandoned and stigmatised not only by policy makers and society, but also by health-care providers and sometimes even the advocacy community, which is a problem that should be urgently addressed (panel 9).

A diagnosis of metastatic breast cancer should not stop someone's contributions to society as part of a workforce, in unpaid, caring roles, and by contributing to cultural life. Breast cancer predominantly affects women and, globally, women spend up to ten times more of their time on unpaid care work than men.[268] It has been estimated that in 2015, metastatic breast cancer was associated with US$6·6 billion in lost productivity in the USA alone, mostly due to days missed at work and home due to illness and premature mortality.[269] Inadequate or absent treatment not only has a devastating effect on the patient, their families, and local communities, but also creates a global economic disadvantage (panel 10). Even with the best possible treatments,[271] 20–30% of those with early breast cancer relapse, so optimal treatments for people with metastatic breast cancer are valuable to individuals and society.

Panel 9: **Summary of metastatic breast cancer**

Many patients with metastatic breast cancer feel abandoned, isolated, and alone and some do not receive appropriate care—this can and should be tackled.

- The number of people living with metastatic breast cancer is unknown and high-quality cancer registry data must be collected worldwide
- Optimal management of metastatic breast cancer is valuable to individuals and society—stigma and inequities must be addressed
- There is a growing belief that some subtypes of metastatic breast cancer can be treated as chronic diseases for many years
- With adequate resources and a shift in attitudes it might be possible to cure some of these patients, treat most, alleviate the suffering of all, and forget or abandon no one

Panel 10: **Economic modelling study for patients with metastatic breast cancer in Portugal[270]**

The ABC Global Alliance and Centre for Evidence Based Medicine jointly developed a project aiming to show that allowing women with metastatic breast cancer to continue to work would be beneficial not only to the patient and their family, but also to the state and society in general. Breast cancer is the most common malignancy among women in Portugal, with an incidence rate of 156 per 100 000 women. Given that most diagnoses occur in women aged 20–64 years, studying the effects of breast cancer on the female labour market is of major economic and social relevance.

This study quantified the productivity costs (ie, losses) of unemployment due to metastatic breast cancer in Portugal and evaluated potential labour market policies designed to promote employment in this group. The analysis was based on an original cumulative incidence model that allowed estimation of the prevalence of women of working age with metastatic breast cancer in 2019, and on an observational study that characterised their employment status and working conditions. To establish productivity costs, the human capital approach was adopted.

A total of 2151 women of working age were estimated to have metastatic breast cancer in 2019, with productivity costs amounting to €28 676 754 between 2019 and 2021. In addition, unemployment subsidies and disability pensions were estimated to be €3 468 866 with a total cost of over €32 million. The 3-year period was chosen in view of the median overall survival of metastatic breast cancer being 3 years. The researchers modelled the effects of a subsidised, part-time employment scheme designed to encourage women with metastatic breast cancer to continue working. The estimated increased cost of this policy for the government was €11 951 048 over the 3-year period. However, a reduction of €14 338 377 in productivity costs led to a cost saving of nearly €2·5 million over the same 3-year period. The authors call for changes in labour market laws to enable all patients with metastatic cancers the right to choose part-time or flexible working without first acquiring employer permission.

A shift in the attitudes of policy makers and the public must occur to ensure all people with metastatic breast cancer are recognised and receive individualised treatment with an honest but positive approach (theme 6). This shift is necessary so that people with metastatic breast cancer feel empowered and are supported to continue to contribute to local communities and wider society. We have identified four key themes as crucial areas to be addressed.

Area 1: data

To date, we do not know the prevalence of metastatic breast cancer, since most cancer registries record information on initial diagnoses and deaths, but not on recurrences.[263,271] This challenge is made more difficult by an increasingly mobile global population, which makes longitudinal tracking challenging. Data protection regulations and laws, although necessary, render sharing of patient information and cross-checking between databases virtually impossible. In addition, not all cancer registries record cancer stage at diagnosis.

In high-income countries, only about 5–10% of patients with breast cancer are metastatic at initial diagnosis, whereas in LMICs, the proportion of patients with de novo stage III/IV breast cancer can reach 50–60%.[272–274] Distinguishing between stage III (locally advanced) and IV (metastatic) disease in LMICs is difficult because the definitive diagnosis of stage IV requires costly imaging and, in some cases, metastatic biopsy to establish distant disease. These investigations often require out-of-pocket payment by patients. As a result, de novo metastatic disease often goes undetected, which is supported by the unusually rapid decline in and very poor 3-year overall survival seen in the African Breast Cancer-Disparities in Outcomes study.[275]

In high-income countries, some national and regional registries have been developed that are specifically dedicated to metastatic breast cancer (appendix pp 27–28), a development mostly made by patient advocates. However, in LMICs, data for metastatic breast cancer are largely absent and any reports are primarily single-centre analyses.[276] Data collection in LMICs must be made possible by encouraging the establishment of cancer registries funded by government or non-government agencies. For high-income countries, the solution is complex and will require waivers regarding sharing of information between databases and the development of big data analytical processes (theme 2). The International Agency for Research on Cancer and the ABC Global Alliance are defining the essential data to be collected and strategies to overcome data collection difficulties for metastatic breast cancer, which will allow metastatic breast cancer to be a beacon of change for global health-care systems.

Area 2: individualised management of metastatic breast cancer with equitable access to evidence-based therapies

Cancer-directed therapies and overall survival

Outcomes of metastatic breast cancer have improved considerably in the past decade and patients should not be denied access to life-extending therapies. The median overall survival of metastatic breast cancer has remained at around 2–3 years for decades,[277] but within the past 5 years, median overall survival has reached 5 years for two of its three main subtypes (HER2-positive and ER-positive and HER2-negative), which account for approximately 85% of people with metastatic breast cancer.[278–280] Some patients can now live 10 years or longer with metastatic disease and some subgroups are beginning to be considered as having a chronic disease. Metastatic breast cancer is a spectrum of disease, both at a molecular level (theme 2) and in terms of disease burden, including potentially curable oligometastatic disease, long-term remissions or stabilisations, and more rapidly progressive disease (often the triple-negative subtype). Therefore, management of metastatic breast cancer must be individualised, not just on the basis of tumour biology, but also on patient characteristics, preferences, and toxicities of treatments.

The use of validated tools, such as the European Society for Medical Oncology (ESMO) Magnitude of Clinical

Benefit Scale[281] or the American Society of Clinical Oncology (ASCO) Framework of Value,[282] allows for the use of cost-effective prioritisation of existing therapies on the basis of their clinical value. Furthermore, the development and use of biomarkers that could allow the identification of patients who derive the most benefit and those who do not benefit from these therapies is crucial to optimise resources and should be a research priority (theme 2). The advances in treatments for metastatic breast cancer in the past decade have been shown to reduce mortality in the general population by the model-based analysis Cancer and Intervention Surveillance Network[283] and have contributed to 20–24% of the overall reduction in mortality seen (appendix pp 29–33).

Continuum of care

Supportive care and palliative care are crucial parts of the management of metastatic breast cancer and should be incorporated from diagnosis (including supportive care for early breast cancer) throughout the whole breast cancer journey (themes 5 and 6). Early integration of supportive care has been shown to improve quality of life and reduce depression[284] and there must be better education on this topic for clinicians, patients, and the public (themes 5 and 6). Definitions have been extensively discussed and proposed by the *Lancet* Commission on Global Access to Palliative Care and Pain Relief[8] (appendix pp 2–10). The importance of early supportive and palliative care involvement has been highlighted in ASCO guidelines, National Comprehensive Cancer Network (NCCN) Clinical Practice guidelines, and Advanced Breast Cancer International Consensus Guidelines.[285–287] These fundamental aspects of metastatic breast cancer care are often neglected and there must be a transition from traditional siloed care into integrated, patient-centred, holistic management.

In a survey of 240 US oncologists, only 17% said that they refer patients to palliative care upon diagnosis of metastatic disease, despite two-thirds of respondents agreeing that earlier introduction of palliative care leads to better outcomes.[288] In addition, 14% of oncologists reported that they only refer patients to palliative care once all standard-of-care treatment options are exhausted.[288] Resistance from patients and their families is also a problem, often due to stigma and the perception that palliative care only means end-of-life care. Almost 40% of the survey respondents reported that this stigma and perception is the main barrier to patients receiving appropriate and timely palliative care.[288] There are insufficient palliative care resources, especially in LMICs but also in high-income countries, and oncologists and primary care physicians must focus on symptom control as well as cancer treatments (themes 5 and 6).

Quality of life measurement

The balance between efficacy and toxicity of treatments, and between the focus on survival, quality of life, and relief of serious health-related suffering (theme 5) is delicate and very personal for each individual in the metastatic setting. An additional hurdle is that quality of life measurement tools have all been developed for the early cancer setting and do not accurately capture the most important aspects of the metastatic setting for patients, such as living with an uncurable disease and uncertainties regarding life expectancy and disease evolution. To overcome these challenges, the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Group has partnered with the ABC Global Alliance to develop a new quality of life tool dedicated to metastatic breast cancer that will be incorporated into clinical trials and clinical practice after validation. In addition, the EU-funded multinational Innovative Medicines Initiative Health Outcomes Observatory Consortium published core outcome sets[289] for assessing health-related quality of life in patients with metastatic breast cancer in 2023, which aligns with the EORTC–ABC Global Alliance work. These initiatives will make the evaluation of quality of life for people with metastatic breast cancer more accurate in the future.

Communication

Communicating well with patients throughout their disease journey and giving realistic hopes and expectations is also important (theme 6). Maggie Jencks, a patient with metastatic breast cancer who was fundamental in setting up Maggie's centres in the UK, wrote "however bad the prognosis, it will still help the patient to know that the median may not be the message".[290] Suggestions on how to improve patient–health-care professional communication are given in theme 6.

Equitable access to treatments for metastatic breast cancer

It is crucial to address the global inequities between and within countries in accessing all therapies (including medicines), supportive care, and clinical trials for metastatic breast cancer. An example of inequity in access to treatment is trastuzumab for HER2-positive metastatic breast cancer. Despite the development of highly successful anti-HER2 therapies, and trastuzumab being included in WHO's list of essential medicines, it is often not funded in the metastatic setting. In Brazil, an analysis done in 2016 projected that an additional 600 patients with metastatic breast cancer would be alive 2 years after diagnosis of metastases if trastuzumab was available to them, and this number increased to 768 patients with the addition of pertuzumab.[265] Inequitable access is not an issue restricted to low-income countries; there are often discrepancies in funding in middle-income and high-income countries. An observational study of people with HER2-positive breast cancer in China in 2017 reported that 27% of those with metastatic disease did not receive trastuzumab at all, regardless of the availability of local resources.[266] Observational studies between 2000 and 2015 in people

with HER2-positive metastatic breast cancer have shown that 27–54% of those in Europe, 12% of those in the USA, and 27–49% of those in China did not receive trastuzumab or other anti-HER2 therapies as either first-line or subsequent-line treatments.[267] A fundamental barrier to accessing trastuzumab is cost and the availability of effective and safe biosimilars should allow greater use of anti-HER2 therapies.[267] Unfortunately, to date, price reductions have not been enough to make trastuzumab more available in LMICs (panels 11, 12).

Area 3: multidisciplinary management and the use of evidence-based guidelines

Multidisciplinary care

In early breast cancer, multidisciplinary specialised care and management according to high-quality guidelines have contributed greatly to the decrease in mortality, together with screening, early diagnosis, and new therapies. The same oncology principles should be applied to the management and treatment of metastatic breast cancer. Multidisciplinary management improves health outcomes and quality of life in people with metastatic breast cancer, for example by offering specialised locoregional therapies, access to clinical trials, early involvement of palliative care teams, and psychosocial support.[297]

The European Society of Breast Cancer Specialists (EUSOMA) established multidisciplinary care as one of its mandatory high-quality indicators.[298] Through a collaboration between EUSOMA and the ABC Global Alliance, new quality indicators specifically dedicated to metastatic breast cancer have been established and are being progressively incorporated into the certification process.[299] The EUSOMA requirements for a specialist breast centre state that at least 50% of metastatic diagnoses must be discussed at a multidisciplinary meeting, with the aim of discussing every patient with metastatic breast cancer, ideally at each point of progression.[297] These indicators recommend that the core team members for a metastatic multidisciplinary meeting include a medical oncologist, radiation oncologist, radiologist, breast care nurse, nuclear medicine physician, palliative care specialist, and data manager.[297] The ABC International Consensus Guidelines also emphasise that multidisciplinary input is crucial for the management of metastatic breast cancer and should include at least medical, radiation, and surgical oncologists, imaging experts, pathologists, gynaecologists, psycho-oncologists, social workers, specialised oncology nurses, and palliative

Panel 11: Aotearoa New Zealand case study for inequities within high-income countries

In 2018, the first study of incidence, treatment, and survival of metastatic breast cancer in Aotearoa New Zealand was done.[264] Before the study, the New Zealand Ministry of Health only tracked outcomes for patients with curable or de novo metastatic breast cancer and patients with relapsed disease were not counted.[264]

The study revealed that the median survival after a diagnosis of metastatic breast cancer was 16 months, which was considerably worse than countries with a similar socioeconomic index (2–3 years). There was substantial inequity in outcomes within Aotearoa New Zealand, with 5-year survival significantly worse in the Māori population (5%) than the non-Māori population (15%). Despite evidence to show that quality of life and survival improved if more lines of treatment were given, only 15% of patients with metastatic breast cancer received more than three lines of therapy, and 10–30% received no treatments. There was little awareness or adherence to international guidelines for the treatment of metastatic breast cancer, no national metastatic breast cancer guidelines, and the possibility for treating oligometastases with curative intent was underexplored. There was also restricted access to many therapies proven to be effective in metastatic breast cancer. For the HER2-positive breast cancer subtype, only one line of HER2-directed therapy could be given, since trastuzumab use beyond progression was not allowed and there was no access to any other anti-HER2 therapies besides trastuzumab and pertuzumab. These factors led to a 15-month median survival in patients with HER2-positive breast cancer compared with 5 years in other high-income countries.[278] For this subtype, the most important therapeutic approach is to continue to block the HER2 pathway as leaving it unblocked leads to quicker mortality.

Since the study was published, three new treatments—including one additional anti-HER2 therapy—have been funded in Aotearoa New Zealand after extensive petitioning, but many others, including the use of trastuzumab beyond progression, are still not publicly funded.[291] National guidelines for the management of metastatic breast cancer have also been developed.[292] Five areas of focus for change to improve these outcomes were identified: drugs, symptom management, medical care, support, and investing in the future.[264] The progress made in Aotearoa New Zealand is an outstanding example of recognising the deficit of metastatic breast cancer data locally, analysing and reporting outcomes, and using this information to drive change to improve and extend the lives of people with metastatic breast cancer.

Panel 12: Inequity in access to clinical trials

Clinical trials can not only be beneficial for participating and future patients, but can also increase the quality of care within health services.[293] Inequity in access to research studies is a problem for patients with all stages of breast cancer, including metastatic breast cancer. Randomised clinical trials in oncology are conducted predominantly in high-income countries and there is often publication and funding bias against trials done in low-income and middle-income countries.[294] Patient access to oncological clinical trials remains inadequate, particularly for minoritised racial and ethnic populations, and it is well documented that many ethnic groups are under-represented.[295,296] Other patient populations that tend to be under-represented include older people, patients with several comorbidities, those of low socioeconomic status, and those living in rural areas.[295] This under-representation reduces the generalisability of trial findings and creates disparity in access to high-quality care.[295] This disparity stems from interlinked practices and policies and barriers at individual (patients and health-care professionals), interpersonal, and system levels.[295]
To overcome these inequities, multilevel interventions are needed to increase global access to trials and stimulate diverse enrolment, including the use of education, training, and high-quality communication (theme 2).[295]

care specialists.[287] There are no specific recommendations for what a metastatic multidisciplinary meeting should consist of in the ESMO, ASCO, or NCCN breast cancer guidelines. Telemedicine could accelerate widespread implementation of multidisciplinary meetings for metastatic breast cancer (theme 2).

Guidelines

For metastatic breast cancer, there are often variations in adherence to clinical guidelines by health-care professionals in LMICs and high-income countries, despite evidence that adherence is associated with improved outcomes in breast cancer. For example, a systematic review in the EU and a cohort study in Canada both showed that adherence is associated with improved disease-free survival and overall survival.[300,301] These improvements also apply to resource-constrained settings; a study in Malaysia found similar improved outcomes in breast cancer survival when treatment was in line with locally adapted management guidelines.[302] However, most breast cancer management guidelines available are not adapted to the local availability of resources.[303] Therefore, observation of resource-adapted guidelines and support for patients to avoid treatment abandonment—for financial or toxicity reasons—should be a priority in metastatic breast cancer management and will translate to improved outcomes (theme 4). There is evidence that treating people according to high-quality guidelines is cost-effective and would contribute to avoiding unnecessary costs and optimisation of resources in cancer care.[304] Even when guidelines are implemented, treatment abandonment is a problem in LMICs and in marginalised and hard-to-reach populations in high-income countries, sometimes due to toxicities, but frequently due to financial reasons and insufficient social support.[305,306] These factors are another argument for improved treatment access and support for patients (theme 4). Despite the ready availability of many high-quality guidelines in the management of breast cancer, analyses using information from national datasets routinely show marked care variation. Pursuing small incremental improvements from new drugs in clinical trials is of little value if these new drugs cannot be used in clinical practice. The translation of evidence into practice is often difficult, particularly in LMICs, but is a priority.

Area 4: stigma

People with metastatic breast cancer can be stigmatised by society, policy makers, health-care professionals, and some patient advocacy groups. This stigma is isolating and can have huge effects on their physical, social, and emotional functioning, leading to worse outcomes[307] (theme 5). Misconceptions among the general population and health-care providers regarding the nature and expected outcomes of metastatic breast cancer substantially contribute to this stigma. Stigma is responsible for prejudice against these patients within health-care systems, socially, and professionally, which generates isolation, loneliness, and feelings of guilt. Stigma is a major driver of poor health outcomes globally because it can lead to reduced help-seeking and social withdrawal and can be a barrier to therapy adherence.[307] As a result, mortality can occur earlier due to not receiving adequate care. Educating and raising awareness of metastatic breast cancer for stakeholders and the public is paramount: these issues must be highlighted repeatedly until attitudes change.

Characterisation of metastatic breast cancer as a rapidly fatal disease also contributes to social stigma and abandonment. Furthermore, characterising early breast cancer as curable if everything is done well creates misconceptions about those who develop metastatic disease, even though approximately 30% of patients with early disease will develop metastatic breast cancer, despite optimal therapy.[308] Slogans such as early detection saves lives, although important for creating awareness, can promote myths that patients with metastatic breast cancer did not, for example, receive mammographic screening or self-examine. There is a difficult balance between generating breast cancer awareness and avoiding attributing blame to the individual with metastatic breast cancer. Stigma is accentuated within societies that do not typically acknowledge or discuss mortality, and this can create negative experiences for people with metastatic breast cancer.

Quantifying metastatic breast cancer stigma

The Decade Report—an analysis of the status and evolution of metastatic breast cancer between 2005 and 2015—included a general population survey analysing awareness of metastatic breast cancer in 14 315 participants from 14 countries.[272] The results emphasised that public understanding of metastatic breast cancer was inadequate. Across all countries, 14–61% of respondents agreed with the statement that there is no point in treating advanced or metastatic breast cancer.[272] 18–49% of participants indicated that people with advanced or metastatic breast cancer should not talk about it with anyone other than their physician.[272] Two extreme misconceptions exist among the general population regarding metastatic breast cancer; some believe it is equal to early breast cancer and therefore curable, and others believe it is a terminal illness for which there is no hope. These findings illustrate that myths can fuel stigma and isolation for people with metastatic breast cancer. Furthermore, the misconception that it is a rapid terminal illness leads to prejudicial policy decisions in many LMICs and some high-income countries whose health-care resources are usually dedicated to early-detected cancers, hence reducing the survival and increasing the suffering of people with metastatic breast cancer (panel 13).

Panel 13: The *Lancet* Breast Cancer Commission health-care practitioner survey

We conducted a global, bespoke web-based survey for health-care professionals to study their views and perceptions regarding metastatic breast cancer (appendix pp 34–65). We obtained a total of 382 responses; 46% of participants were from Europe, with fewer responses from North America, Africa, and the Middle East. Most of the respondents (70%) were oncologists with more than 10 years of professional activity, and approximately 75% of them had devoted more than 50% of their clinical practice to breast cancer.

When asked how many lines of treatment patients receive on average, patients with hormone receptor-positive and HER2-positive breast cancer were reported to receive more treatment lines than patients with other subtypes (five or more and four or more, respectively). Patients with triple-negative breast cancer received the fewest lines of treatment, with an average of three lines of therapy. These results probably reflect the biology of the disease and the available treatment alternatives within these subtypes.

80% of respondents considered metastatic breast cancer an incurable disease and when asked whether metastatic breast cancer would become curable within the next decade, most were undecided or disagreed. However, 55% agreed that it might become curable for specific subtypes, and 75% agreed that metastatic breast cancer will become considered a chronic disease. More than 70% of health-care professionals reported that they inform patients with metastatic breast cancer that their disease is incurable. These professionals considered they had received adequate communication training and felt confident in communicating difficult issues with patients, such as poor prognosis and death. However, this statement did not reflect what patients reported. For example, a survey of 185 patients with metastatic breast cancer in Mexico revealed that only 52% of patients were aware that their disease was incurable, 31% were not sure, and 17% thought it was curable.[309] These statistics show the inadequate understanding that some patients have regarding their disease, despite most health-care professionals feeling confident in their communication skills. This communication gap needs urgent attention if we aim to improve the overall management and outcomes of metastatic breast cancer (theme 6). When asked to rank objectives for patients with metastatic breast cancer, 72% of the health-care professionals stated quality of life as the most important. Progression-free survival and overall survival were also highly ranked, whereas improving communication was felt to be a lower priority. Only 18% of professionals were very familiar with the ABC Global Alliance 10 Actions for Change, which is an important global initiative to address urgent and actionable gaps in management of patients with metastatic breast cancer.[271]

This survey of health-care professionals reflects the negative views associated with metastatic breast cancer that contribute to stigma. Additionally, a substantial proportion of physicians think that new treatment advances will have a positive effect on outcomes for patients with breast cancer (eg, survival and quality of life). This perception might be a good starting point to begin to change the overall negative perception of the disease and consider that not all patients with metastatic breast cancer are destined to have poor outcomes.

Cross-cutting features of health-related stigma and identifying interventions

For more on the **Male Breast Cancer Global Alliance** see https://mbcglobalalliance.org/

Stigma has been studied in many medical conditions outside of cancer, such as HIV and mental health, but often a siloed, disease-specific measurement and intervention approach is suggested.[310] The concept of health-related stigma could facilitate generic stigma assessment tools and interventions rather than disease-specific ones, which would be a highly beneficial and cost-effective approach from a health-care system perspective.[310,311]

There are multiple theoretical models describing the cross-cutting elements of health-related stigma.[310,312–315] It has been shown that a patient-centred, multicomponent approach directed at many socioecological factors is required if stigma is to be effectively addressed.[316] The ABC Global Alliance has created a toolkit to address unmet needs for hard-to-reach populations that includes examples of community-based initiatives that target stigma.[271] For example, Project PINK BLUE was set up in Nigeria in 2016 to address stigma and misunderstandings around breast cancer. Their aim is to support, empower, and educate people with breast cancer by providing educational materials, financial and telephone support, monthly support groups, and patient navigators. Another example is the Male Breast Cancer Global Alliance, which was created to address stigma and raise awareness for male breast cancer, with initiatives including breast self-examination cards, support calls, and an annual conference.

For more on **Project PINK BLUE** see https://projectpinkblue.org/abc-sg/

Potential effects outside of metastatic breast cancer

By using breast cancer as a model cancer, we hope that our suggestions for reducing discrepancies and stigma and improving metastatic breast cancer care can be applied as a framework for positive change to other cancers. Updating cancer registries is integral to more accurate outcome data collection and better allocation of resources, which is important across all tumour types. We strongly urge a shift in mindset and aims when treating people with metastatic breast cancer, as this will be valuable not only to the individual and their family, but also to society (table 3).

Theme 4: tackling breast cancer gaps and inequities though global collaboration

In the early 1990s, many high-income countries witnessed a change in diagnoses and coordinated multidisciplinary

evidence-based treatments, as exemplified by the initiation of the Early Breast Cancer Trialist Collaborative Group. These changes have shown declines in breast cancer mortality rates of around 2% per year or greater (figure 4), translating to an overall 40% reduction in breast cancer age-standardised mortality rates over 3 decades.[317,318] This 40% improvement has not yet been achieved in most LMICs,[319] where advanced stages at diagnosis and low diagnostic and treatment capacities contribute to poorer breast cancer survival rates.[274,320] 5-year breast cancer survival rates exceed 90% in high-income countries, compared with 66% in India and 40% in South Africa.[321] To address this inequity, applying approaches that have worked well in high-income countries to settings with fewer resource is required, but these approaches must be tailored to local contexts (panel 14).

According to the International Agency for Research on Cancer, there is sufficient evidence to assert that

	Definition	Rationale	Data sources	Responsible entity	Target
Data collection	Improvements in cancer registry data collection: stage at diagnosis, including de novo metastatic disease and breast cancer relapse data	Knowing the number of people living with metastatic breast cancer would allow a better allocation of resources	Cancer registries	Ministry of Health	Minimum of 70% of global cancer registries registering people with metastatic breast cancer, aiming at 100%.
Multidisciplinary meeting review	Patients with metastatic breast cancer discussed at a multidisciplinary meeting	Improve outcomes: survival and quality of life	Facility records; national and international certification procedures for breast units	Ministry of Health	Minimum of 50%, aiming at 95% of patients with metastatic breast cancer discussed at multidisciplinary meetings
Metastatic breast cancer outcomes	Improvements in median overall survival	Improve outcomes	Cancer registries; facility records; national and international certification procedures for breast units	Facility; Ministry of Health	Record the number of people with metastatic breast cancer and double the median overall survival in a decade
End-of-life care	Number of patients with breast cancer dying in pain: morphine use as an indicator of suffering.	Improved quality of life and reduced suffering	Pharmacy registries	Ministry of Health	Aiming for less than 5% of patients at end of life without access to morphine
Essential medicines for metastatic breast cancer are affordable globally	Updates and uptake in WHO essential medicines to promote equal access	Improve outcomes	WHO essential medicines list updates; national regulators data	Ministry of Health	All patients with metastatic breast cancer have access to life-saving cancer medicines

Table 3: **Optimal inclusive management of metastatic breast cancer proposed measurable indicators of change**

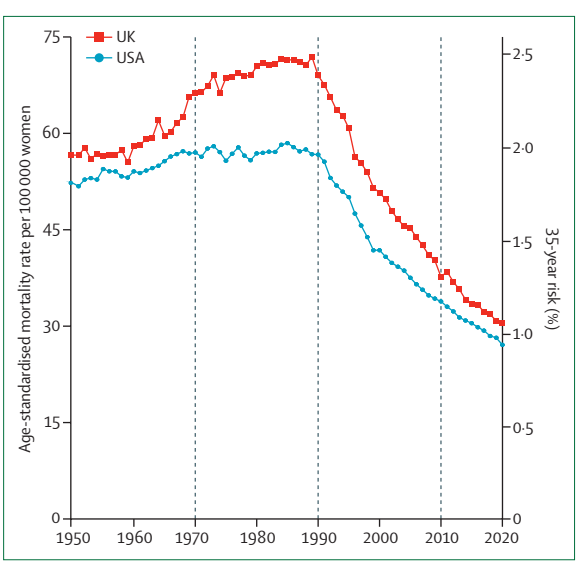

Figure 4: **Fall in breast cancer mortality rates in the UK and USA in people aged 35–69 years (1950–2020)**
The age-standardised mortality rate is a mean of annual rates in the seven component 5-year age groups (ages 35–39 years, 40–44 years, 45–49 years, 50–54 years, 55–59 years, 60–64 years, and 65–69 years). At a death rate of 30 per 100 000 women, there was a large effect on UK and USA breast cancer mortality due to the combination of several moderate effects. At a mortality rate of 15 per 100 000 women, further moderate effects are still necessary and achievable. Data is from the WHO Mortality Database and UN World Population Prospects 2022 revision. Graph reproduced with permission from the Early Breast Cancer Trialists' Collaborative Group.

Panel 14: Summary for tackling breast cancer gaps and inequities though global collaboration

People with lower incomes and those from minoritised populations are more commonly diagnosed with late-stage breast cancer and are at higher risk of mortality. This equity gap will widen without global collaborative intervention.

- Equitable access to early diagnosis and treatment is a fundamental need for all individuals to improve breast cancer survival and quality of life
- In alignment with the WHO Global Breast Cancer Initiative Framework,[322] we call for action to promote stage-shifting towards earlier staged disease at diagnosis, as a sustained decline in breast cancer mortality rates has only been achieved in countries in which at least 60% of invasive cancers are diagnosed at stages I–II[319]
- Approaches and tools to achieve this 60% threshold can be adapted to local contexts and resource availabilities
- Technological innovations can catalyse the speed and efficacy of early diagnosis and treatment implementation globally
- Integrated health-care system policies, education, and advocacy are needed; and pioneering approaches in breast cancer early detection, prompt diagnosis, and multimodality treatment can be used as a model for other cancers

For the **WHO Mortality Database** see https://platform.who.int/mortality

For the **UN World Population Prospects 2022 revision** see https://population.un.org/wpp/

Panel 15: WHO Global Breast Cancer Initiative (GBCI) pillars

A population-based health systems analysis of 148 countries showed two health-care system characteristics were significantly associated with lower age-standardised mortality rates: higher levels of health expenditure as measured by the Universal Health Coverage Index and improved access to care as measured by higher numbers of public cancer centres per 10 000 patients with cancer.[319] In 2021, the GBCI was established with the aim of reducing breast cancer mortality by 2·5% per year and potentially preventing 2·5 million premature deaths over 20 years.[325] To achieve this target, the GBCI suggested three sequential care intervals or pillars for effective management.[322]

Pillar 1: health promotion for early detection (pre-diagnostic interval)

Individuals enter the pre-diagnostic interval either by presenting with breast symptoms, such as a breast lump or thickening, or presenting without breast symptoms to a screening programme if available. Analysis by the GBCI shows that not all countries that achieve a sustained breast cancer mortality reduction have population-based mammographic screening programmes.[319] These findings encourage a focus on early detection programmes that adapt to the needs of individual countries. In the majority of LMICs, stage-shifting is required to increase the proportion of people with invasive breast cancer who are initially diagnosed with early-stage disease. Early detection begins with breast health awareness and the establishment of early diagnosis programmes to identify people with subtle symptoms, signs, or both of possible breast malignancies and then to link them to diagnostic services where definitive malignant or benign diagnoses are determined. Breast cancer screening cannot be effective until the required infrastructure and quality control measures are fully functional, including patient tracking systems to ensure women undergo repeated screening studies every 1–2 years, as indicated in screening guidelines. All health-care systems require the capacity to diagnose symptomatic breast findings in a timely manner, regardless of whether they have mammographic screening programmes or not. Pillar 1 key performance indicator (KPI): at least 60% of invasive cancers are diagnosed at stages I or II.

Pillar 2: timely diagnosis (diagnostic interval)

Correct cancer diagnosis requires that suspicious breast lesions undergo clinical evaluation, breast imaging, and tissue sampling with pathological interpretations (triple assessment). The optimal imaging and sampling methods vary depending on the availability of equipment and trained staff.[326] Treatment delays beyond 90 days lead to lower rates of breast cancer survival.[327] In 2012, Brazil established the 60 days law in which all patients with cancer should start treatment within 60 days of diagnosis.[328] Pillar 2 KPI: the diagnostic process is to take place within 60 days of the patient's first presentation to the health-care system.

Pillar 3: comprehensive breast cancer management (treatment interval)

Effective treatment requires a multidisciplinary approach from radiology, pathology, and surgical, medical, radiation, and supportive oncology. However, these treatment strategies are usually only effective if the entire treatment course is given. Treatment abandonment, in which the patient begins treatment but does not complete it for reasons other than a clinical decision to stop, is a common problem in LMICs. In the African Breast Cancer Disparities in Outcomes study of five countries in sub-Saharan African, less than 50% of patients started and completed their treatment course.[305] Pillar 3 KPI: more than 80% of individuals must complete multimodal treatment without abandonment.

mammographic screening reduces breast cancer mortality in women aged 50–74 years and some evidence to support a similar benefit in women aged 45–49 years.[323] Although the evidence for the net benefits of mammographic screening is well established for women aged 50 years or older, the obstacles to applying these findings to implementable strategies in LMICs are substantial.[324]

To reduce breast cancer mortality, early detection—including early clinical diagnosis and screening programmes (appendix pp 66–67)—and effective multimodality treatments are needed (panel 15).[329] The infrastructure and processes used for breast cancer management are similar for other adult solid tumours, such as colorectal, prostate, and lung cancers. If breast cancer can be managed effectively in a resource-constrained setting, improved management of other malignancies is more likely to follow.

Most high-income countries have low rates of later-stage diagnosis and better outcomes than LMICs; however, there can be differences in breast cancer mortality rates within most high-income countries, with evidence supporting this from the USA (panel 16), Scotland,[332] the Netherlands,[333] and Australia.[334] All countries should focus on reducing diagnostic inequities, but they will not all start from the same place (panel 17, figure 5, table 4). For more on stage-shifting strategies with and without functioning screening programmes and future directions, see the appendix (pp 66–69).

Adapting technologies for early breast cancer diagnosis and treatment to local settings

Diagnostic services coupled with treatment provisions are the foundation for high-quality and effective health-care delivery.[337] By adapting technologies to local settings, there is potential to leapfrog ahead of existing methods and move closer to equity across all contexts, if a framework of smart leapfrogging is adopted. Adapting to local contexts with local knowledge and innovation is also required.

Panel 16: **Case history of breast cancer stage disparities in Miami, USA[330]**

Background

Unmet social needs are direct mediators of health outcomes. We aimed to evaluate whether a county-funded mammographic screening programme (the Florida Breast and Cervical Early Detection Program) was associated with an increase in uptake of mammographic screening, whether unmet social needs were associated with decreased uptake of mammographic screening, and whether unmet social needs were associated with a later-stage (III or IV *vs* I or II) breast cancer diagnosis.

Methods

A prospective cohort study of patients with stage I–IV breast cancer were recruited from 2020 to 2023 at an underserved safety-net hospital and a National Cancer Institute-designated Academic Cancer Centre. Univariable and multivariable logistic regression was done to evaluate the primary outcomes:

- Routine mammographic screening
- American Joint Committee on Cancer (8th edition) clinical stage at presentation

Unmet social needs were measured by the Health Leads Social Needs Screening Toolit, a screening tool that gathers information on the most common social need domains affecting patient health.[331]

Findings

Of the 322 women who completed the Health Leads Social Needs Screening Toolkit questionnaire, 76% of those with access to county-funded mammographic screening completed a mammographic screening study. Patients who presented to the safety-net hospital were more likely to present with late-stage disease compared with early-stage disease (31% *vs* 18%, p=0·04). With multivariable logistic regression, independent predictors of not completing a mammographic screening were having an increasing number of unmet social needs, such as food insecurity, housing instability, utility needs, financial resource strain, transportation challenges, and exposure to violence (odds ratio 0·74 [95% CI 0·55–0·99], p=0·047) and an increasing age at diagnosis (0·92 [0·89–0·96], p=<0·001). Moreover, increasing the number of unmet social needs, specifically the domains of utility needs and childcare accessibility, was an independent predictor of late-stage breast cancer at diagnosis, above and beyond mammographic screening (1·38 [1·01–1·89], p=0·04).

Interpretation

Our prospective cohort study found that access to mammographic screening did not translate to increased screening uptake and increasing numbers of unmet social needs significantly predicted both lower rates of mammographic screening uptake and increased rates of late-stage diagnosis. This effect transcended recruitment site effects (safety-net hospital *vs* Academic Cancer Centre), indicating that patients in any hospital setting might benefit from screening for unmet social needs to overcome access to care barriers associated with late-stage disease at diagnosis.

Leapfrogging technologies are either novel technologies that augment or bypass an existing technology or address a previously unmet need, or an innovation achieved by reorganising or reframing existing practices or resources. An example of the first category are automated systems that measure RNA quantities to establish the status of breast cancer biomarkers. These systems could potentially bypass immunohistochemistry and fluorescence in situ hybridisation in places where these options are absent, unreliable, or only available in tertiary care facilities.[338–340] An example of the second category is the shift to virtual multidisciplinary tumour boards by use of existing teleconferencing software during the COVID-19 pandemic, which increased access to expert multidisciplinary care for non-tertiary care settings and enabled remote patient consultations (theme 2).

The key principles of smart leapfrogging include defining the specific local context by doing a situational analysis to identify gaps that are barriers to equitable access to care and identifying an innovation or technology that could fill the gap and add value to the local context. A limitation in the development and validation of novel technologies is that specific tools can be tested in isolation without considering how they fit into the health-care system.

Panel 17: **Case study of economic evaluation of breast cancer control in Kenya**

In 2020, the Kenyan Ministry of Health partnered with the World Bank to create an investment case for combatting non-communicable diseases. Working in collaboration with WHO and the Global Breast Cancer Initiative, the team developed a health system model to predict breast cancer outcomes and related implementation costs. The resulting Kenya model for early detection proposes a 15-year implementation plan by use of a phased implementation approach.[335] During the first 5 years, health system strengthening focuses on the establishment of diagnostic services to evaluate and diagnose clinically detectable breast changes through organised and accessible early diagnosis services. In years 6–15, Kenya plans to establish screening programmes with a combination of clinical breast examination-led screening and mammogram-led screening by use of the infrastructure and programming established during the first 5 years. Predictions and cost estimates were projected on the basis of the Kenya-specific baseline data and outcomes as measured by stage-shifting projected to 15 years (figure 5A), breast cancer survival rates projected to 40 years (figure 5B), and project-associated costs for each development strategy (table 4).[336]

Technologies or innovations shown to be highly effective in settings with many health-care resources might not have the same characteristics in a resource-constrained setting, and other technologies might be better in these settings.[341–343] For example, the systematic measurement of breast residual cancer burden and stage after neoadjuvant chemotherapy provides prognostic

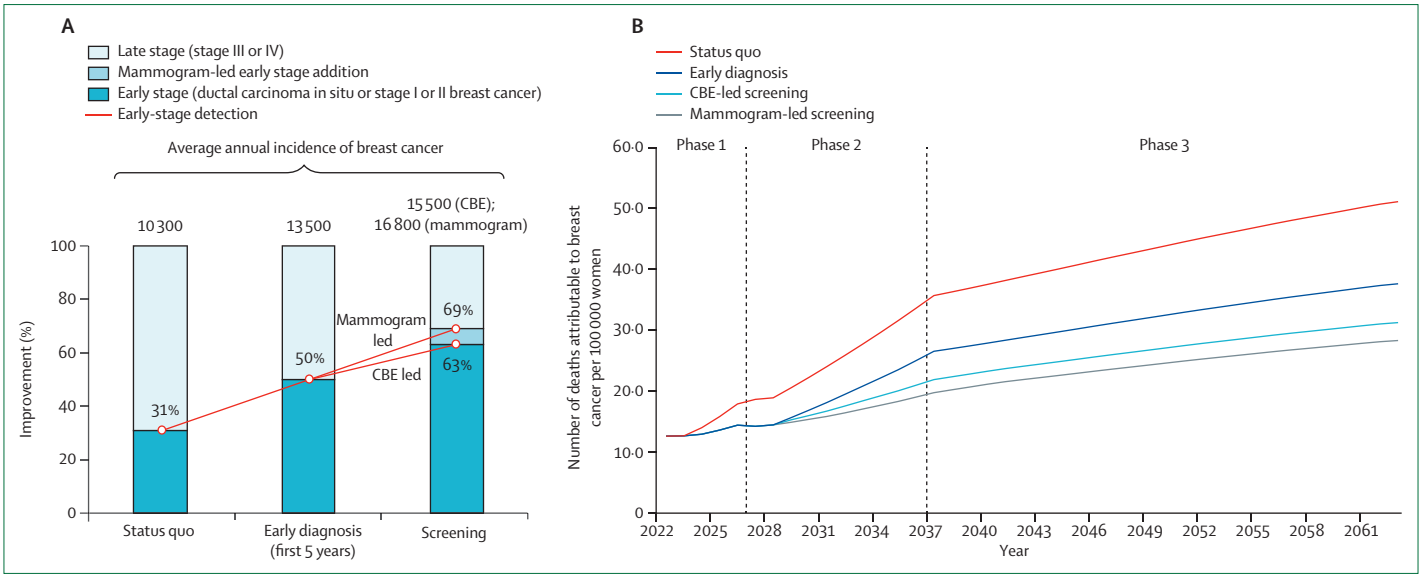

Figure 5: **Improved breast cancer early detection (stage distribution) and treatment outcomes (mortality) in Kenya**
A) Predicted breast cancer stage distribution showing improved early-stage detection (favourable stage-shifting) promoted by strengthened diagnostic services at 5 years (2027) and clinical versus mammographic screening programming at 15 years (2037) in Kenya. B) Predicted breast cancer mortality reductions over 40 years (2022–62) in Kenya. Both reproduced with permission from the Kenyan Ministry of Health. CBE=clinical breast examination.

	Total costs for early diagnosis programmes only in the absence of screening programmes		Total costs over 15 years with CBE-led screening programmes introduced at 5 years		Total costs over 15 years with mammography-led screening programmes introduced at 5 years	
	KES	US$	KES	US$	KES	US$
Health system strengthening	8·54 billion	63·20 million	14·56 billion	107·74 million	15·59 billion	115·37 million
Direct treatment	11·46 billion	84·80 million	16·74 billion	123·88 million	38·04 billion	281·50 million
Screening	..	..	1·67 billion	12·36 million	19·97 billion	147·78 million
Diagnosis	1·46 billion	10·80 million	3·46 billion	25·60 million	5·34 billion	39·52 million
Treatment	7·42 billion	54·91 million	8·77 billion	64·90 million	9·77 billion	72·30 million
Palliative	2·56 billion	18·94 million	2·83 billion	20·94 million	2·96 billion	21·90 million
Total	19·99 billion	147·93 million	31·30 billion	231·62 million	53·63 billion	396·86 million

KES=Kenyan shilling. Data taken from the Kenyan Ministry of Health with permission of the publisher. All USD approximations based on conversion statistics as of March 15, 2024 (KES1=US$0·0074). CBE=clinical breast examination.

Table 4: **Predicted breast cancer programme and service-delivery costs over a 15-year period (2022–37) in Kenya**

information that helps treatment decisions for subsequent adjuvant therapies. There is negligible cost for measuring residual cancer burden because it is an adaptation of usual pathology practice.[344–346] However, a prerequisite for a neoadjuvant systemic therapy approach is a functioning health-care system to coordinate analysis of results and deliver multimodal therapies in a timely and safe manner.

Novel technologies have been proposed as potential methods for screening, monitoring treatment responses, predicting disease progressions or relapses, and guiding therapies, which will have wider implications beyond breast cancer diagnosis. Examples are magnetic markers that can be non-radioactive for the localisation of sentinel lymph nodes and wireless alternatives for the localisation of non-palpable breast lesions.[347] With standard metal clips, image-guided wire localisation is required, but with magnetic markers, the surgeon can find the correct region without assistance from the radiologist. Whole slide imaging and digital pathology can also be used to increase access to expert assessments of responses to neoadjuvant therapies in regions that have few pathology services, allowing for a more personalised and cost-effective therapeutic approach. Moreover, several blood-based technologies (ie, liquid biopsies) that leverage a broad scope of technologies have emerged, ranging from detection of tumour biomarkers with low-cost methods—such as enzyme-linked immunosorbent assays—to high complexity methods, such as sequencing and methylation profiling of circulating tumour DNA (ctDNA) and cell-free DNA (cfDNA).[348,349] For example, the US Food and Drug Administration and the European Medicines Agency have approved the use of alpelisib for patients with metastatic breast cancer with mutations in *PIK3CA*

detected either in ctDNA or tissue.[349,350] These blood-based methods are still under investigation and the clinical role they will play in the future is unclear.

Patient navigation and equitable access to medications

Access to high-quality breast cancer care can be hampered by delays in diagnosis and treatment.[351,352] Prioritising patients scheduled for diagnostic evaluation according to suspicion of malignancy on the basis of image findings or symptoms can reduce health-care system delays. This strategy has been used by navigation programmes in Mexico[353] and Colombia[354] that have been successful at reducing the time to diagnosis of breast cancer. In Mexico, the Alerta Rosa programme introduced a triage system to stratify and prioritise patients for imaging studies and appointments with breast specialists to accelerate access to diagnostic procedures and treatment. In Colombia, the Breast Cancer Early Detection Pilot Program focused on evaluating care barriers and coordinating timely referrals for early breast cancer detection and prompt access to treatment. A similar approach was developed in the UK, with national referral guidelines requiring that every patient with suspicion of breast cancer should receive a specialist consultation within 2 weeks of referral by their general practitioner. Adherence to these guidelines resulted in a significant improvement in adequate patient prioritisation and a reduction in health-care system waiting times.[355] Equitable access to medications is essential across the breast cancer continuum and is discussed in panel 18, the appendix (pp 21–23), and theme 3.

Patient advocacy to improve equity in breast cancer detection and care

Health advocacy has been defined in the medical profession as activities related to ensuring access to care, navigating health-care systems, mobilising resources, addressing health inequities, influencing health policy, and creating system change.[362] Cancer advocacy relates to the application of these strategies to the cancer care continuum and has been largely led by civil society organisations in many countries.[363] Historically, advocacy has been powerful in bringing about global change in disease and health care, but it is not understood by many

Panel 18: **Equitable access to medicines**

Access to medicines is a complex and multidimensional problem, with cost being a major barrier to optimal treatment. Access is a global problem, but underserved populations are commonly and consistently worse affected than non-underserved populations. Potential strategies to address drug access include establishing universal health coverage for essential cancer medicines (for both early and metastatic cancers), fair drug pricing, optimising regulatory demands, and improving global supply.[356] Treating patients according to context-adapted high-quality guidelines is another important strategy to optimise care and avoid the unnecessary use of resources.

Access to medications released to the market over the past 5 years shows discrepancies related to the different cancer outcomes seen in different regions of the world.[357] While the USA, western Europe, and Japan consume approximately 90% of all new medications, the rest of the world's population accounts for the remaining 10%.[357] Too frequently, we are seeing a dissonance between the price of new cancer medicines and the benefits seen in registration clinical trials. Analyses between 2015 and 2020 indicate no association between medicine prices and the magnitude of benefits on endpoints, such as progression-free survival, overall survival, or objective response rate, suggesting that cancer medicines are priced on the basis of what the market can stand, not the clinical benefits they provide.[358] Addressing this inappropriate process in a transparent way is fundamental for the future of breast and other cancer care, as it leads to differential medicine access within high-income countries and the rest of the world.

The recurrent argument that prices should cover not only the few medications that make it to the market, but all failed experiments as well, has been questioned by an analysis indicating that cancer medicines have generated returns far in excess of officially reported research and development costs.[359] This scenario has led to increasing interest in alternative pricing strategies, including different versions of value-based pricing, a discussion that should be encouraged. Affordability of a particular country or region should also be considered. Outcome-based payment is also being explored in specific scenarios[360] and different prices according to the benefits a medicine could have on different indications has been proposed. In addition, US Food and Drug Administration accelerated approvals could be priced lower, to be adjusted after confirmatory evidence is generated.[358] Regulators should be more active in withdrawing approval when benefits are not confirmed by clinical trials or when real-world data fail to show benefits.

Furthermore, payers should not be influenced by pharmaceutical industries and should use an objective assessment tool—such as the European Society for Medical Oncology's Magnitude of Clinical Benefit Scale[281] or the American Society of Clinical Oncology's Framework of Value[361]—to prioritise cancer medicines that should be approved in each country. Medicines that provide the highest benefits should be approved faster than those that provide only marginal benefits. This system is crucial in countries with few health-care resources but, in view of the uncontrolled rise in costs, it is important in high-income countries as well. Improving access to cancer medicines for all populations is a universal and urgent unmet need. Panel 11 highlights inequities within high-income countries, with New Zealand as a breast cancer-specific case study for improving equity of access to HER2-directed therapies.

and does not have a robust evidence base. Even so, it plays a fundamental role in every society and drives the evolution of breast cancer care globally. For example, advocacy efforts could be aligned to the GBCI pillars to facilitate achieving their three major key performance indicators (KPIs).

Self-advocacy or patient activation is an important overarching theme in the literature.[364] Patients should be empowered to feel they have control over their body, health, and decision making, for example regarding breast cancer treatment options (theme 6). With the understanding of the disease process, self-advocacy could help push for supporting timely diagnosis and enhance treatment adherence and completion of care (GBCI pillars 2 and 3).

A structured advocacy approach can address awareness and early detection concerns and treatment and survivorship needs. This organised approach to advocacy can touch on legal, educational, research, and policy aspects of care. A proposal by the African Coalition of

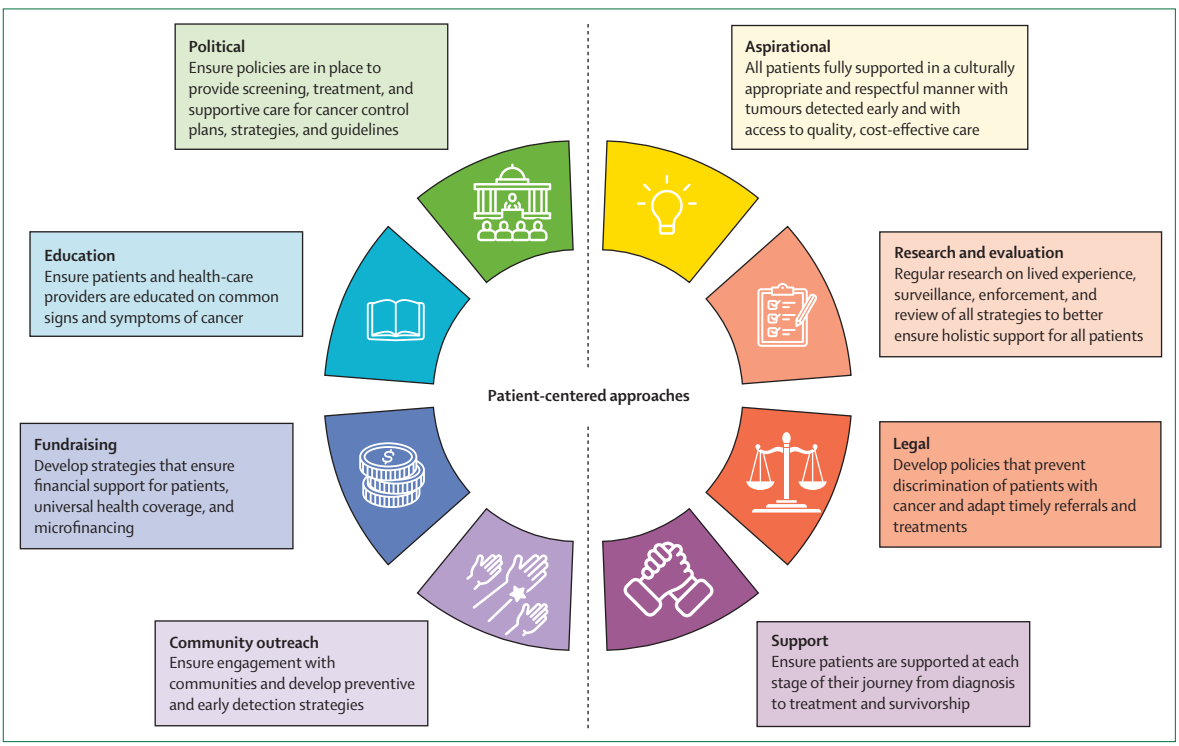

Figure 6: **Aspirational advocacy framework**
Eight patient-centred approaches in different areas that intersect to form the aspirational advocacy framework.

	Definition	Rationale	Data sources	Responsible entity	Target	Comments
Stage-shifting	Ensuring prompt diagnosis of breast cancer	Decrease breast cancer mortality rates and prolong life	Cancer registries	Ministry of Health	60% of all invasive cancers are at stage 1–2 at diagnosis	WHO GBCI pillar 1 KPI
Timely and appropriate treatment	Evaluation, imaging, tissue sampling, and pathology	Improve breast cancer outcomes	Facility records; national audit	Ministry of Health	Evaluation, imaging, tissue sampling, and pathology within 60 days of presentation	WHO GBCI pillar 2 KPI
Treatment abandonment as defined by WHO GBCI	Optimising multimodality treatment without abandonment	Improve breast cancer outcomes	Facility records; national audit; national and international certification procedures for breast units	Ministry of Health	80% of patients undergo multimodality treatment without abandonment	WHO GBCI pillar 3 KPI
Access to medicines	Reduce inequalities in access to medicines between and within countries	Improve breast cancer outcomes	Harmonisation of global clinical trials to decrease time from FDA and EMA approval to global availability for patients	Ministry of Health; national regulatory bodies	Time from FDA and EMA approval to availability to the patient of <6 months for high-priority agents, <1 year for intermediate-priority agents	Use an objective assessment tool to prioritise cancer medicines for approval in each country

GBCI=Global Breast Cancer Initiative. KPI=key performance indicator. FDA=US Food and Drug Administration. EMA=European Medicines Agency.

Table 5: **Tackling breast cancer gaps and inequities through global collaboration-proposed measurable indicators of change**

Cancer Advocates suggests six key areas of prioritisation for comprehensive cancer advocacy: political, education, research, fundraising, support, and community outreach.[365,366] These key tenets must however be contextualised to different settings (appendix p 69). Innovative approaches and strategies need to be considered to enable advocacy to bridge global gaps in care. Advocacy must be contextual, but should also leverage existing networks. Developing a cadre of advocates that will engage all stakeholders—including policy makers—about concerns along the care continuum—whether financial, legal, or supportive—and provide funding for care is important. Advocates should prompt researchers to ask relevant questions for their communities to empower and improve the lived experience of people with cancer and their caregivers. This advocacy could mark the first steps towards achieving equitable care in many settings and the additive effects of the outputs of these advocacy efforts must be assessed, along with the GBCI pillars and targets.

In rethinking approaches to cancer advocacy, we propose an aspirational advocacy framework (figure 6) that builds on previous breast cancer advocacy to form a broader relationship around equity and health. It is important to widen the focus beyond individual needs to target broader platforms in civil society, such as women's rights. Here, aspirational advocacy could contribute more broadly to women's empowerment, health-care system strengthening, and anti-poverty efforts, and address violence against women, with measurable outcomes (table 5). Education of women in LMICs is paramount in general, but specifically education on breast cancer to develop preventive aspects of breast cancer care as early as possible. This need highlights the importance of females remaining in formal education.

Theme 5: identifying the hidden costs of breast cancer

The burden of suffering

Both health-care systems in general and cancer systems must acknowledge serious health-related suffering and therefore the value of alleviating this suffering by better investing in appropriate supportive and palliative care.[9] Yet this alleviation, which is paramount to patients and their families, goes unmeasured in global health metrics and is undervalued (panel 19).

The *Lancet* Commission on Palliative Care and Pain Relief[9] showed that because many key interventions for alleviating suffering are absent in priority settings, they are not considered in either covered health-care packages or in universal health coverage. The Commission estimated that more than 61 million people per year experience serious health-related suffering, 24% of which is due to cancer. Although much of this serious health-related suffering could be relieved with better access to palliative care and pain relief,[9] between 80% and 90% of this global need is unmet due to insufficient available workforces, training, health-care system investment, and access to palliative care medicines.[9,367] Serious health-related suffering can affect patients throughout the breast cancer trajectory and hence the measure is relevant not only for patients in their last 12 months of life, but also at earlier stages (before the year of death). Hence, to accurately count the number of people and the days per year spent with serious health-related suffering, both mortality and prevalence data are required. A decedent is a person who dies in a given year and they have serious health-related suffering in that year and non-decedents are people who do not die in a given year but can also have serious health-related suffering. By 2060, it is projected that 16·3 million people each year will die from cancer and will have serious health-related suffering. Breast cancer is predicted to account for the highest proportion of cancer-decedent serious health-related suffering in low-income and lower-middle-income countries.[361]

All people with breast cancer have suffering at some point in their cancer journey, regardless of their stage of illness. This suffering affects their quality of life, relationships, self-perceptions, and independence.[368–372] Patients can face physical, psychological, spiritual, and existential distress over a long period,[373–384] which begins with the realities of diagnosis and continues with fears associated with prognostic uncertainty and the possibility of mortality. Treatments have collateral physical and psychological effects and this adds to the long-term challenges of survivorship (panel 20), with fear of recurrence and possible debilitating symptoms. Families and caregivers of people with breast cancer might also have extended periods of social and financial hardship,[385–388] including not only out-of-pocket costs for health care, but also loss of income for the person with breast cancer and their caregivers, with the added possibility of orphaned children.

***Panel* 19: Summary of hidden costs of breast cancer**

The costs of breast cancer and its associated suffering are immense; as of writing, society and policy makers see only the surface. The full costs of breast cancer should be exposed and quantified to be reduced.

- Costs include financial, emotional, social, and economic costs that affect children, families, local communities, and wider society
- Even within health services that are free at the point of delivery, those affected by breast cancer face additional costs that can particularly affect those in society with the lowest incomes
- Serious health-related suffering goes unmeasured in global health metrics, so its alleviation is not prioritised by policy makers
- Exposing and reducing costs provides an incentive for policy makers to invest in prevention, early detection, cost-effective therapies, and optimal management of breast cancer
- Initial estimates of the hidden costs of suffering from breast cancer can catalyse new priority-setting tools for breast and other cancers; this research is pivotal and in process as part of the *Lancet* Commission on Cancer and Health Systems

Panel 20: **The Costs and Supportive Care in Breast Cancer (CASCARA) study—participant direct quotes**

CASCARA is a UK pilot study scoping the economic burden, financial toxicity, and supportive care needs of individuals with breast cancer in a high-income country with the National Health Service that is free at the point of use. Participants had the opportunity to write free text related to the different survey domains and some quotes are illustrated here.

Employment

- Extreme fatigue impacts how much work I can do. Brain fog has led to me making numerous little mistakes.
- I lost my job when I started chemotherapy as I could not cope very well.
- Treatment causes too many side-effects to hold down work. Daughter became the main priority as a single parent.
- I am struggling with fatigue and menopause symptoms so needed to reduce my working hours.

Financial situation

- Losing your home and business shatters all future plans.
- I really struggled to pay for all the things I needed such as new bras, clothing (front-fastening shirts and pyjamas), wig, heating when in the house more, etc. I had to scrap any idea of future holidays and also had to get a second job where I could earn a bit more.
- Can't mend a leaking roof. Stopped all nice things such as treats, days out as can't even afford cinema. Cannot afford gym membership, need to pay back family who loaned us money to live during treatment.
- I've had to cut back on making memories as I can't afford it with rising cost of travel for treatment.

Caring

- My husband had to take unpaid leave for multiple months.
- My partner has had to reduce his working hours to cover childcare and that has also impacted on his income.
- My mother now needs care and we are paying for home help to support where I am unable to physical do things.
- My son is often left on his iPad or watching TV while I sleep in the afternoon.

Supportive care needs

- Once you have completed active treatment you are considered well.
- After radiotherapy finished I was left on my own.
- It took me a long time to ask for help with sexual dysfunction.
- Because I'm in my thirties I've had a lot of pushback from people telling me I don't need the help as much as older patients. I've also had problems as I've lived longer than expected with stage IV. Most help dried up after 6 months.

Attitudes to terminology

Cancer survivor

- I'm not a survivor as I still need monitoring. I see myself as have lived through cancer and it's changed my life forever. I'm now a different person with a different perspective and I will live with its consequences forever. It's the gift that keeps on giving!
- I hate the whole battle analogies of cancer. It's a disease not a battle. Also cancer survivor is derogatory to stage IV patients, as the implication is that they have somehow failed.

Palliative care

- I associate this term with end of life, although I now know this not to be correct.
- I find it hard to shake off the end of life meaning. I think a new name should be found, but the services should be available to all patients with breast cancer who need them.

Serious health-related suffering specific to breast cancer

As part of the follow-up work for the *Lancet* Commission on Global Access to Palliative Care and Pain Relief,[9] the measurement of serious health-related suffering is being updated with a disease-specific approach. In collaboration with the *Lancet* Commission on Cancer and Health Systems,[8] a pilot study was undertaken on breast cancer with expert providers and patient advocate groups. The group of 14 experts were invited to participate in a three-part process: an online survey, a focus group, and a structured one-to-one interview. Their collective experience was from Jamaica, Haiti, Rwanda, Mexico, Brazil, India, Lebanon, Portugal, the USA, the UK, Malaysia, and South Africa and their specialities were breast surgery, medical oncology, radiation oncology, physiotherapy, palliative medicine, and the patient and patient advocacy experience.

The findings of this study showed that serious health-related suffering is not restricted to metastatic breast cancer but is also relevant for early-stage disease and survivorship, although these groups had a lower serious health-related suffering burden compared with groups with metastatic disease. Non-decedents include patients with early cancer and patients with metastatic disease, whose life-expectancy—even in LMICs—can be several years, and they might have a high serious health-related suffering burden throughout that time. Non-decedents also include patients in survivorship who will probably not die of breast cancer. Adjuvant systemic therapies (eg, hormonal therapies and the newer CDK4 and CDK6 inhibitors) are used for years into survivorship and can cause toxicity. Patients might also have ongoing sequelae from curative surgery, chemotherapy, or radiotherapy. These patients can have a high prevalence of serious health-related suffering symptoms, such as

pain or fatigue and reproductive health challenges. The expectation that they are symptom-free within a few years post-treatment veils their need for supportive care.

The expert group agreed that patients have approximately 175 days of serious health-related suffering in their last 12 months of life. The typical patient was estimated to need access to approximately 60 mg of opioid morphine equivalent per day in their 12 months of life to sufficiently manage pain and breathlessness. The expected lifespan for people with metastatic or locally advanced breast cancer (non-decedents) was estimated to be about 4 years, with an average of close to 70 serious health-related suffering days per year. The group considered that for those who died of their breast cancer and those living with the disease, approximately two-thirds of serious health-related suffering days each year are probably preventable through improved access to care. However, these estimates refer to a typical patient and mask inequities across and within countries.

The term survivor was challenged by experts and more strongly by patients. In alignment with people-centred language, the term survivorship was preferred to include patients who are disease-free following curative therapy, those still receiving adjuvant therapies, and those with metastatic disease. Survivorship is also a depersonalised term that refers to a health state rather than a nominal patient. This term is aligned with an ongoing change of concept for some types of breast cancer, which is now perceived less as a life-limiting disease and more as a chronic illness[389] (themes 3 and 6).

There was also some reluctance to use the term palliative care for people with early breast cancer. Whereas experts working in resource-constrained settings tended to accept a much broader range of palliative care, experts from high-income countries found it difficult to accept the term for treating people with early breast cancer. A broader terminology of supportive and palliative care was found to be acceptable to all experts.

Breast cancer can cause substantial social stigma (theme 3) and suffering, for example from a feeling of disfigurement, issues with body image, reduced sexual quality of life, and diminished feelings of sexual attraction and femininity.[390–394] Social stigma, secondary or associative stigma experienced by family members, and self-stigma or internalised shame can result from discriminatory sociocultural beliefs and practices that reinforce gender roles. These include ascribing value on the basis of a woman's reproductive capacity or potential marital status and the effect of illness on these factors.[52] Due to the prevalence of pre-menopausal breast cancer in LMICs,[71,395–397] these types of suffering are of particular concern. Women in resource-constrained settings are also less likely to have access to reconstructive surgery and assistance with protecting fertility.[398–400] Men with breast cancer, although a minority, suffer from social stigma related to the diagnosis of what is perceived as a women's disease[401] (theme 2).

The expert panel recommended adding sexual, reproductive, and gynaecological health items to the serious health-related suffering assessment. Patients are often reluctant to raise these problems in their medical consultations, requiring health-care professionals to actively address them sensitively (theme 6). Although these results are based on a small sample of professionals, our exploratory analysis provides a preliminary quantification of suffering that is primarily based on the provider perspective to initiate discussion on the need to assess and treat serious health-related suffering in patients with breast cancer. The effort to strengthen measurement of the disease-specific burden of serious health-related suffering complements ongoing research on the value of suffering alleviation for patients, caregivers, and health-care systems. This research is a component of the linked work with the *Lancet* Commission on Cancer and Health Systems and in follow-up to the *Lancet* Commission on Palliative Care and Pain Relief (panel 21).

Hidden financial costs from breast cancer

A diagnosis of breast cancer can threaten financial wellbeing, even in countries and for populations that have financial protection through public or private health

***Panel 21:* Case study on the dimensions of suffering and the value of alleviating suffering among patients with breast cancer in Mexico**

The research agenda set out in the *Lancet* Commission on Global Access to Palliative Care and Pain Relief report[9] called for in-depth work on the dimensions of suffering as an input to developing more inclusive, effective, and patient-responsive indicators for health system priority settings. A preprint methodological paper was published as part of the exploratory phase of a multicountry study to identify the dimensions of suffering and the need for palliative care[402] and qualitative research was undertaken at the Mexican National Social Security Institute and consisted of in-depth interviews with 14 women with breast cancer who were receiving care at the pain clinic in Mexico City and approaching the end of their lives. The thematic analysis identified two main themes: serious health-related suffering as a multifaceted phenomenon and relief of serious health-related suffering as requiring a joint effort from the patient, family, and health services.

The first theme encompassed intrapersonal serious health-related suffering (physical and emotional suffering increasing over time due to disease progression), interpersonal serious health-related suffering (familial, psychological, and economic suffering due to job loss and health service scarcities, social suffering, and cultural influences on the perception of serious health-related suffering), and differences in serious health-related suffering according to age and socioeconomic status. The second theme encompassed serious health-related suffering relief and included intrapersonal and interpersonal strategies for alleviation and health service responses. The women expressed the importance of serious health-related suffering relief for everyone and acknowledged the need for a joint effort from the person living with the disease, their family, and health services, including more palliative care services, pain clinics, and innovations for alleviation. These findings are consistent with research on serious health-related suffering associated with various cancer types and diabetes, including some patients with breast cancer.[403] Furthermore, these findings are part of ongoing research to understand the meaning of serious health-related suffering and the value of alleviating it in monetary and non-monetary terms across sociocultural, socioeconomic, and health-care system contexts.

and disability insurance.[404–408] More systematic monitoring of family income loss, cost-related non-adherence, treatment withdrawal, and quality of life would allow identification of these hidden costs to calculate the true cost of breast cancer to societies.

With the *Lancet* Commission on Cancer and Health Systems,[8] the *Lancet* Breast Cancer Commission initiated a collaboration with partners in several countries to generate country-level, context-relevant costs and cost burden data to better inform priority setting on a health-care system level for cancer control. Exploratory pilot research in the UK, a country with universal health coverage for cancer care (the National Health Service), was done through the Costs and Supportive Care in Breast Cancer (CASCARA) study (panel 20).

The CASCARA study

CASCARA is a UK pilot study scoping the economic burden, financial toxicity, and supportive care needs of individuals with breast cancer in a high-income country with the National Health Service that is free at the point of use. Online anonymous population-based surveys were designed by researchers from the *Lancet* Breast Cancer Commission and The Institute of Cancer Research Clinical Trials and Statistics Unit in collaboration with volunteers with lived experience of primary and metastatic breast cancer. A patient survey and a survey for carers were designed and opened from Jan 24, 2023, to March 3, 2023. Individuals with lived experience of primary or metastatic breast cancer who were treated in the UK were eligible to complete the CASCARA survey and were asked to provide information relating to their most recent episode of breast cancer disease. The survey respondents included patients and carers, which could include family and friends. Survey participants were recruited via two main routes. The first was from the Breast Cancer Now Patient Forum and the second was through other charity groups, including Macmillan Cancer Support, Cancer Research UK, and Maggie's Centres. Completion and submission of the survey were taken as consent for participation.

The CASCARA patient survey had 606 responses. 470 and 136 participants reported lived experience of primary and metastatic breast cancer, respectively. 24% of participants had their diagnosis within the past year and 25% of participants had their diagnosis more than 5 years ago. 35% of the participants were aged 41–50 years at diagnosis and 33% were aged 51–60 years. 96% of participants described their ethnicity as White. 69% of participants had a postgraduate degree, degree, or professional qualification. The CASCARA carer survey had 30 responses. 70% of participants reported themselves as the partner of a patient, 50% were aged 51–60 years, and 40% self-described as female. 97% described their ethnicity as White and 63% had a postgraduate degree, degree, or professional qualification.

For participants with early breast cancer, 77% were in employment at the time of diagnosis and 61% were still in employment at the time of survey completion. With income presented in bracketed ranges (eg, <£12 500 per annum, £12 500–£25 000 per annum, etc), 25% of participants reported a decrease in income bracket after diagnosis compared with reported income bracket at time of diagnosis. Of those reporting to be in employment at diagnosis, the median working hours per week were 37 h (IQR 28–40), compared with 30 h (IQR 18–37) at the time of survey completion. For those with metastatic breast cancer, 79% were in employment at diagnosis and 40% were still in employment at the time of survey completion. 38% reported a decrease in income bracket after diagnosis. Of those reporting to be in employment at diagnosis, the median working hours per week were 37 h (IQR 29–40) compared with 24 h (IQR 12–37)at the time of survey completion. 47% of carers reported changes in their employment because of their caring role

	Definition	Rationale	Data sources	Responsible entity	Target	Comments
Physical, psychological, social, spiritual, and financial serious health-related suffering in breast cancer care	Screen patients at intervals throughout the breast cancer trajectory for serious health-related suffering	Making the hidden costs of serious health-related suffering visible in individual health-care plans	Facility records; third party and government records; patients self-report and develop specific patient-reported outcome measures	Health-care facilities; Ministry of Health	Screening for serious health-related suffering at diagnosis and key milestones throughout the breast cancer trajectory as a research tool with an aim for widespread implementation after validation	Aim to implement suffering intensity-adjusted life years, a new metric under development for health-care system performance assessment and quality assurance
Breast cancer health-care costs	Identify the proportion of each phase of the breast cancer trajectory covered by insurance and proportion of the population with access to this insurance in countries without universal health coverage	Making the hidden costs of financial toxicity visible and identifying which groups are affected and when	Expansion of national cancer registries	Ministry of Health	Upward trajectory year on year for universal health coverage of breast cancer across the continuum of care—aiming at 100%—to eliminate financial catastrophe and impoverishment for all families with lived experience of breast cancer; at least 20% (aiming at 100%) of patients and families with the lowest incomes receiving public financing and provision of an essential package of supportive and palliative care across the breast cancer pathway	Research needed on out-of-pocket spending on all aspects of breast cancer measured over the breast cancer trajectory

Table 6: **Proposed measurable indicators of change for identifying the hidden costs of breast cancer**

for the person with breast cancer. 23% of carers reported a decrease in income and 27% of carers took compassionate leave or carer's leave.

20% of participants with early breast cancer and 25% of those with metastatic breast cancer reported difficulty in covering costs of travel for treatment. 27% of participants with early breast cancer and 35% of participants with metastatic breast cancer reported having financial problems. A small proportion of participants also reported loss or change of home, not being able to keep up with the mortgage or rent, or attending food banks.

48% of participants reported people were dependent upon them, with 41% of participants having dependent children. For those with early breast cancer, 33% could not fulfil their caring responsibilities at diagnosis and 8% at the time of survey completion. For participants with metastatic breast cancer, 41% could not fulfil their caring responsibilities at diagnosis and 26% at the time of survey completion. 29% of participants with early breast cancer and 32% with metastatic breast cancer had their family and friends fulfilling their caring responsibilities at diagnosis and 6% of participants with early breast cancer and 21% with metastatic breast cancer needed support from family and friends at the time of survey completion. 33% of carers reported having other people dependent upon them, with 27% of carers having dependent children. 20% could not fulfil their other caring responsibilities at the time the patient was diagnosed, 10% of carers had some or all caring responsibilities left, and 10% had received support from family and friends.

Nearly all participants reported physical or wellbeing issues related to breast cancer. For participants with early breast cancer, common issues included fatigue (83%), menopausal symptoms (75%), anxiety (71%), pain (67%), loss of confidence (65%), effects on sexual health (62%), memory problems (61%), and concerns regarding body image (60%). For those with metastatic breast cancer, common issues included fatigue (88%), menopausal symptoms (78%), memory problems (70%), pain (70%), effects on sexual health (68%), anxiety (66%), loss of confidence (66%), reduced mobility (63%), and concerns regarding body image (60%).

51% of participants reporting lived experience of early breast cancer and 67% of those reporting lived experience of metastatic breast cancer disliked the term cancer survivor. 33% of participants reporting lived experience of early breast cancer and 47% of those reporting lived experience of metastatic breast cancer disliked the term palliative care. 79% of participants had never heard the term supportive care. 59% of participants reporting lived experience of early breast cancer and 55% of those reporting lived experience of metastatic breast cancer agreed that supportive care includes all supportive care needs.

CASCARA provides exploratory evidence that is hypothesis-generating for future research. Given the web-based questionnaire dissemination model and short timeframe, the study was limited in its ability to recruit a representative sample of those in the UK affected by breast cancer. Respondents appeared to report higher educational attainment levels and higher financial security than would be expected if the sample was truly representative, yet continued suffering and unmet needs was reported. This suggests that the effects of breast cancer are non-negligible, even in a country such as the UK with health care free at the point of care. Subsequent research will form part of the *Lancet* Commission on Cancer and Health Systems report, with a focus on countries and settings without national health insurance.

Strategies to tackle serious health-related suffering and the hidden costs from breast cancer

Taking the reported statistic that 685 000[409] patients worldwide die each year from breast cancer and applying the expert group average of suffering days in the last year of life gives an estimated serious health-related suffering decedent total of more than 120 million days per year. In addition, the 7·8 million non-decedent patients with breast cancer[409] accumulate more than 520 million additional days per year. Behind these numbers are patients suffering from pain, dyspnoea, fatigue, and other distressing symptoms who might benefit from supportive or palliative care, but in many regions of the world, and especially for those living in poverty, there is no access to this care. Unfortunately, those in society with the lowest incomes have the worst palliative and psychosocial services. Meeting this need requires large-scale, global capacity building in palliative

Panel 22: **Summary for communication and empowerment**

Being female is the greatest risk factor for breast cancer—women constitute a group whose fundamental human rights have historically been accorded less respect than men in all settings.

We propose that a framework to improve communication and decision making for those with breast cancer can be used for women to take control over other aspects of their lives.

- Placing patients at the centre of clinical communication and empowering them to exercise their voices, become fully informed, and choose their own degree of involvement in decisions about their care is an achievable and necessary goal worldwide.
- Improving patient communication and decision making in breast cancer improves not only quality of life and body image, but also adherence to therapy, which can affect survival.
- Health-care professional education should include person-centred and culturally sensitive communication skills training, especially if patient literacy or numeracy is low or other barriers to participation in decision making exist.
- Health communication training should include eliciting patients' core values and preferences for information, explaining goals of care, risk–benefit communication, skills to help estimate and explain prognosis and share serious news, and empathically but honestly responding to questions.
- Breast cancer is a disease that many patients describe as robbing them of power, but through good communication and facilitating patient autonomy, it could be transformed into an opportunity to return power and emerge stronger than before.

care and psychosocial services as a component of comprehensive breast cancer management, and training efforts should begin immediately. Yet the cancer divide—differences in access to effective screening, diagnosis, and treatment options in resource-constrained health-care systems fuelled by poverty and inequity—compounds rather than complements the need for palliative care.[410] A first step is to recognise and quantify the costs and suffering associated with breast cancer and develop validated tools to incorporate them into global health metrics (table 6).

Theme 6: communication and empowerment in breast cancer

Introduction and methodology

We acknowledge that patient empowerment should be defined as being fully informed and supported to confidently participate in decisions about personal health and wellbeing to the desired extent (panel 22). We define patient-centred communication as acknowledging the unique background and need for information of each individual, considering their situation holistically, and working with the patient to define and achieve shared goals in their care. Some commonly held beliefs about the barriers to patient empowerment were initially discussed by the Commission group and a literature search on patient empowerment and communication was conducted to challenge these preconceptions, focused on LMICs to ensure cross-cultural considerations (appendix p 70; panel 23).

Where are we now?

There is wide global variation in the empowerment shown by patients with breast cancer. At one end of the spectrum, involving women in treatment decisions is recognised as crucial, not only to protect individuals' autonomy and dignity, but also because it strengthens the foundation for gender equity beyond the specific context of breast cancer. For example, patient and public involvement and engagement is mandatory for clinical research funding applications in some countries. At the other end of the spectrum, women in many parts of the world have extremely limited body, social, and financial autonomy; free choice is unavailable to them not just in breast cancer treatment decisions, but also in their reproductive rights, family finances, access to education, and myriad other social and political domains.[26] These stark differences in patient empowerment can occur between countries, but also within a single country, as highlighted by the US Supreme Court ruling that led to the overturning of rights to reproductive autonomy in some states. Communication, patient empowerment, and patient choice are all inextricably linked. Potential barriers to patient involvement in decision making and choice of treatment are manifold and can occur at individual and system levels (panel 24).

Many types of interventions to support patient autonomy and choice in breast cancer treatment have been published. Examples include translating and validating symptom scales into local languages (eg, a self-efficacy scale translated into Urdu in Pakistan[431]); hyper-local

Panel 23: **Commonly held beliefs (myths) about patient empowerment and communication in breast cancer compared with the literature search results (facts)**

Myth

Publications on communication and shared decision making are largely from high-income countries and the ideals presented in the literature might only be feasible in high-income countries. Outcome from literature review: false.

Fact

Patient decision making and communication research in low-income and middle-income countries (LMICs) exists, although there is more from high-income countries. Many different interventions for supporting patient choice have been published in LMICs, with the overarching theme of adapting communication methods to socioeconomic and cultural circumstances being key to improving patient–clinician dialogue and empowerment.[411–420]

Myth

The extra health-care professional time invested in inviting patients to share decision making does not meaningfully benefit patients. Outcome from literature review: false.

Fact

Evidence supports that improving patient communication and decision making in breast cancer improves not only quality of life and body image, but also adherence to therapy, which can affect survival.[421–423]

Myth

Little can be done to improve patient involvement in decision making in LMICs. Outcome from literature review: false.

Fact

Individual-level and system-level barriers exist for patients with breast cancer choosing their treatments and patient involvement in decision making.[309,412,413,424–430] Multiple interventions to overcome these barriers have been successfully trialled in LMICs and high-income countries.[415,417–420,431–434]

Myth

Most alternative treatments are detrimental to patient outcomes. Outcome from literature review: false.

Fact

There is evidence that some traditional, complementary, and integrative therapies can be beneficial for symptom management in patients with breast cancer and can be used safely alongside (but not instead of) conventional therapy.[435]

culturally adapted interventions (eg, performance of a traditional folk play aimed at raising breast cancer awareness in Bangladesh); and targeted research into population preferences (eg, discrete choice experiments in Belarus to establish preferences about types of national breast cancer screening programmes[415,432]). Interventions can involve training a small number of trusted community members[420] to support patients, using media and technology to target many people to improve breast cancer awareness,[418] or clinical follow-up—for example using mobile phones to avoid travelling to clinic appointments in Nigeria.[419] The use of decision aids to improve breast cancer decision making has a long history,[433] although adaptation of such tools to the local circumstances and languages is crucial and research thus far into logistics is inadequate. In the past decade, interactive, tailored decision tools have been developed to promote the quality of patient decisions[434] and enhancements to harness insights from psychology about emotional support have been evaluated (SHARES trial [NCT04549571][436]). Improving the quality of online information is also important, given that many people with breast cancer now access the internet to obtain information.[437]

What are our goals for patient communication and empowerment?

We assert that centring clinical communication on patients and empowering them and their chosen advocates to be as involved as they wish in decisions about their care is an achievable and necessary global goal. Patient-centred communication is an important goal; in breast cancer, effective communication from health-care professionals has been shown to improve long-term adherence to therapy[423,438] and poor communication has been shown to have long-lasting negative effects on multiple quality of life domains, including function, symptoms, self-body image, lifestyle, and other worries scores.[439] Feeling involved in decisions can provide lasting positive effects on quality of life,[421] but patient preferences about treatment options and their desired degree of involvement in clinical decision making will vary considerably.[440,441] A central factor in patient satisfaction with the decision-making process is the concordance between patient preferences about involvement and the actual amount of involvement.[442] Empowering patients requires understanding their values and preferences and having adequate accessible information to allow patients to arrive at a decision that is right for them.[443] The opportunity for patients to feel heard and have their questions answered (regardless of perceived relevance of those questions by the clinician) is also key to patient-centred communication.

We acknowledge that informal support people (eg, family, friends, or faith representatives) can often be involved in decision making and that such involvement can be both positive and negative for individuals. Generally, research suggests that having a variety of informal decision support people available to patients from different backgrounds can have positive effects on the treatment deliberation process. The concept of relational autonomy has emerged from feminist philosophy and is garnering growing attention in clinical ethics discussions. Nevertheless, although every individual will be inherently influenced by their unique cultural context and relationships, we advocate that the choice of who to involve in decision making or who should be a decision supporter should remain with the individual.

Recognising inequalities between and within countries and that available choices for patients about their breast cancer care can be extensive in some settings or extremely narrow in others, it is always possible to offer some degree of choice to a patient. It is possible to elicit what matters to a particular patient (their values), provide them with information in an understandable way that describes their options (even if few), and empower them to engage in the treatment planning process. Offering someone the

***Panel 24*: Barriers to patient choice of treatment and patient involvement in decision making**

Individual

- Low literacy and numeracy skills
- Little health education
- Little understanding of prognosis and likelihood of cure
- Social or geographical isolation
- Family or faith community objections to treatment or patient involvement
- Unwillingness to engage with conventional medicine due to preference for traditional healers and remedies
- Inability or difficulty discussing prognosis, advance care planning, and preferences for end-of-life care
- Language and communication barriers (eg, absence of health professional or interpreter speaking same language or dialect, or patients with hearing or visual impairments)
- Undiagnosed or untreated psychological illness or emotional distress (eg, anxiety and depression)
- Fear of disclosure of illness due to cultural norms, becoming a burden to others, and stigma
- Poor health-care professional communication skills (eg, eliciting patient values, goals, and preferences, shared decision making, discussing prognosis, and empathetic communication)
- Health-care professional beliefs that patients are unable to process the information needed to be involved in decision making
- Health-care professional inability or unwillingness to culturally adapt services

System

- Geographical inaccessibility of treatments
- Health-care resource constraints, including infrastructure and health-care professional time and specialty knowledge limitations
- High out-of-pocket costs for patients
- Economic, political, or climate-related crises
- Unequal patient–provider power dynamics
- Insufficient psychosocial services at all levels of care
- Pervasive biomedical models that prevent tailored services and care plans

opportunity to bring their relative or friend into the consultation is an example of a small choice that costs no additional time or money, but improves dignity and autonomy.

Patient-centred communication skills applied by treating health-care professionals have important effects on later quality of life.[413] Helping patients to understand their condition, options, and the availability of these options as well as assessing patient preferences and using active listening are skills that can be applied across national borders and the socioeconomic spectrum. Such skills can also be learnt and taught; we propose that education of health-care providers should include specific examples of risk–benefit communication and evidence-based medical decision making in a context-specific way to facilitate patient empowerment.

How do we start the journey towards better communication and empowerment in breast cancer care?

A global survey of 382 health-care professionals conducted by the *Lancet* Breast Cancer Commission group (panel 13) showed that more than 70% of health-care professionals felt confident they had received adequate communication skills training. Although this is encouraging, it might not align with patient expectations and experiences and a substantial number of professionals did not express confidence in these core skills.[444,445]

The available time that health-care professionals have for each patient is a difficult and global issue. We strongly advocate that senior health-care professionals, researchers, and patient advocates in breast cancer care engage with policy makers to improve investments. High-income countries have substantially better overall survival for breast cancer than LMICs, and a 2021 model suggested that scaling up comprehensive breast cancer care to be available globally would not only improve overall survival, but also lead to substantial longer-term economic returns.[446] Such large-scale investments are long-term strategies because training the appropriate staff, including pathologists, radiologists, oncologists, surgeons, radiographers, and specialist breast cancer nurses takes many years. Additionally, although the ideal for patients and staff would be to have as much consultation time as needed, the realities of high-income countries and LMICs necessitate optimisation of existing resources alongside long-term lobbying for increased investment.

We encourage health-care professionals to take a patient-centred approach to communication—to focus

Panel 25: **Framework to help develop a patient-centred consultation, adapted from Bylund et al[449–453]**

Build rapport and check understanding

- Introduce yourself and listen to the patient's story of their health-care problem (evidence suggests most patients will speak for <2 min if left to spontaneously tell their story).[454]

Example talking points

- I've had a look through your notes, but I'd like to hear from you what your understanding is about what has happened so far and what you are expecting next.

Set and negotiate agenda for consultation

- State the purpose of the consultation. If there is a decision to be made, that should be made clear.
- Specifically ask about the patient's priorities for the consultation and their preferences for information and decision involvement.
- Negotiate a consultation that includes goals of both the clinician and patient.

Example talking points

- I am hoping to talk about your options for treatment today. Is there anything else on your mind that you would like to make sure we discuss?
- (Negotiate agenda on the basis of the patient's response) Why don't I begin by discussing treatment options for your breast cancer and then we can address those specific questions you have about possible side-effects and your ability to work while you are receiving care. Does that sound like a good plan?
- Some people like to have lots of information about their illness and some people just want the basics. How much information would you like me to give you today?

Share information

- Identify and clearly describe all relevant options and associated risks and benefits, including active surveillance, a supportive or palliative (comfort focused) approach when appropriate, and acknowledging what is achievable in that particular health-care setting.
- Share the best, worst, and most likely case scenarios related to treatment outcomes.

Example talking points

- At this stage of illness, we have multiple options to treat your breast cancer. There is a type of chemotherapy that has shown excellent outcomes in women with your type of illness. There are some side-effects to the treatment and we will talk more in detail about these as we go through the consent process. Fatigue, nausea, and low blood counts causing an increased risk of infection are the most common side-effects. We can try to minimise some of the side-effects with additional medications.
- I know you are really struggling with your pain right now and it is keeping you from doing many of the things that are important for you. While we continue with radiation I would like to focus also on symptom control, make sure we are most effectively treating your pain, and provide you with the support you need.

(Continues on next page)

(Panel continued from previous page)

Convey respect for patient with or without family involvement

- Validate their concerns as important and relevant to their decision and explicitly encourage patients to ask questions.
- State that you fully support the patient's right to make the final decision.
- Ask the patient about use of non-prescribed therapies, traditional, complementary, and alternative medicines, lifestyle changes since their diagnosis of breast cancer, and their medical and drug history.
- Ask anyone accompanying the patient if there is anything else important they wish to add or have observed as a caregiver.

Example talking points

- What are your thoughts about what we have discussed so far?
- What questions do you have?
- (To family member or caregiver) I know that you are an important part of (the patient's name) life. Is there anything you think is important that we are missing or that you would like to talk about?

Empathise

- Acknowledge the patient's emotions and experiences.
- Validate their lived experiences.
- Normalise their emotional responses.

Example talking points

- It sounds like this has been a hard time. But it also sounds like you have a lot of support from your loved ones.
- It would be completely reasonable to take some time off from work to focus on your recovery.
- Lots of people talk about feeling overwhelmed during a time like this.

Review and recommend

- Clarify whether the patient has enough information and offer more time for them to decide, if appropriate.
- Consider how much the patient wishes to be involved in decision making and offer a treatment recommendation if there is a best option from a medical perspective, or if the patient has requested the health-care professional's opinion.
- When applicable, review multiple options—including no treatment—and state the rationale for your recommendation. Include key risks and benefits and normalise decisions that differ from recommendations.
- In the absence of a treatment recommendation from the health-care professional, validate and support patient decision making autonomy. In the absence of curative treatment, emphasise continued supportive or palliative care if available, emphasising ongoing supportive aspects of care for patients and their families.

Example talking points

- Today we talked about the treatment options available at this time. Do you have a preference about how you would like to proceed?

Summarise the consultation and agree the next steps

- Summarise the consultation verbally and ideally provide a short, written summary that includes all options, states any recommendations, and describes the key risks and benefits.
- Agree on next steps and appropriate follow-up or further discussion.
- In settings with limited literacy, aim for diagrams or other follow-up mechanisms, such as another appointment or discussion with a community health navigator.

Example talking points

- I will refer you to our chemotherapy unit and they will be in contact with a date for your first treatment. Please have some blood tests done on your way out so we know it's alright to go ahead with the treatment. If you think of any concerns or questions later, please call us.

on assessing what patients need and empowering them to participate in their own care by use of established communication techniques.[447,448] We suggest a framework to help develop a patient-centred consultation, acknowledging that this should serve as an iterative and non-linear guide and be adapted to each consultation. It might not be necessary to include each step or communication skill in every consultation. There are different ways to achieve the same goal and any consultation should be culturally adapted to the unique needs of the person with breast cancer, their family (as appropriate), and the local clinical or community setting. The examples given in panel 25 were developed by native English speakers for use in settings in which English is the native language, so alternative wording might be necessary in other settings.

Communication in specific situations

When discussing breast cancer with patients, we encourage health-care professionals to choose terminology carefully in their own cultural context.[455,456] Many patients dislike the term survivor due to fears that the cancer might still later recur, feelings of wanting to return to normal life rather than being defined as a cancer survivor, or connotations of the term survivor with war or other violent events. Similarly, tumour characteristics, such as oestrogen receptor status or progression status should not be applied to the whole patient—person-centred language is essential. The term survivorship, when used to describe a part of the journey or problems specific to past breast cancer treatment, seems more acceptable to many patients. Although it is important to discuss risks of recurrence and long-term modifiable risk factors with

Panel 26: **Communication examples**

Examples of inappropriate health-care professional language around breast cancer

- The patient has progressed
- The patient is oestrogen receptor-positive
- Breast cancer survivor
- This patient suffers from breast cancer
- We will be withdrawing care
- There is nothing left for us to do

Examples of more appropriate ways to communicate the same message

- The patient has a cancer that has grown and got worse
- The patient has a primary tumour that is oestrogen receptor-positive
- Person who has had breast cancer
- This patient has breast cancer
- We will be with you every step of the way and continue to focus on your comfort
- While I worry that additional anticancer treatments would do more harm than good at this time, we can focus on managing your symptoms and helping you to feel better

patients with breast cancer, some patients might wish to forget their diagnosis and past treatment and not be defined by their previous breast cancer. A diagnosis of metastatic breast cancer has lifelong effects on the patients and as such there are specific areas to consider for patient-centred communication in this setting (panel 26).

1) The concept of metastatic cancer and goals of treatment

Patients and their family members should be told that although metastatic breast cancer is usually incurable, it is treatable and can often be controlled for many years. It is important to explain that treatment aims to slow cancer progression, reduce symptoms, improve quality of life, and prolong survival. Many patients receiving chemotherapy for metastatic cancers might not understand that chemotherapy is unlikely to be curative.[457] Health-care professionals must help patients make the treatment decisions that are best for them, which requires the patient to understand the goals, logistics, and side-effects of treatment and the clinician to understand the patient's individual preferences, values, and life goals (ie, wanting to attend a loved one's wedding, travel, meet a grandchild, or avoid any change in appearance). Understanding how a patient prioritises longevity, comfort, and independence is important. The aims of communicating about treatment goals in the metastatic breast cancer setting could not be stated better than by the founder of Maggie's centres (a UK charity providing cancer support centres near hospitals): "above all what matters is not to lose the joy of living in the fear of dying".

2) Prognosis

Prognostic information is vitally important for people living with metastatic breast cancer for decision making around treatment, finances, work, and for helping patients maximise time with loved ones and prepare for death. Prognostic misunderstandings are common in people with early stage and advanced cancer[458–460] and is associated with more aggressive and futile treatments at the end of life.[458,461,462] Patients who want prognostic information might not always ask for it,[463] so it is recommended that doctors ask explicitly if, when, and how patients want to talk about prognosis.[464] It is best not to confront patients with information they do not want. Up to 20% of patients in studies report not wanting to discuss prognosis[463,465] and decision making does not always require that the patient understand detailed prognostic information.[458,464]

Estimating and explaining expected survival time is difficult and doctors require guidance and communication skills training that is tailored to cultural issues and local resources. Studies of oncologists show many report a reluctance to provide estimates of expected survival time.[466,467] Factors contributing to this include not knowing how to estimate survival time, fear of getting the estimate wrong, fear of upsetting the patient, fear of negatively affecting the patient–doctor relationship, requests from family to withhold prognostic information, and insufficient time during consultations.[467–469] Although prognostic information is upsetting, many patients still find it helpful to know the truth and there is no evidence that increased information about prognosis with sensitive communication is harmful to patients, or that it increases anxiety or distress.[468,470–474] For patients wanting quantitative information on life expectancy, providing ranges for worst-case, typical, and best-case scenarios is helpful and conveys more hope than providing a single point estimate of median survival.[475,476] Most patients with advanced cancer who were surveyed after requesting and receiving their expected survival time formatted as these three scenarios reported that the information made sense, helped them make plans, and improved their understanding of their prognosis.[475] The majority also responded that the information about their prognosis was the same as or better than they expected before discussing it with their oncologist. Providing ranges for scenarios helps convey the inherent uncertainty of survival estimates and is more accurate than providing a single point estimate.[475,477,478] Resources are available to help health-care professionals estimate scenarios for survival time to facilitate conversations about prognosis with their patients.[479,480]

3) End-of-life care and advanced care planning

Discussing prognosis often facilitates conversations about priorities, wishes, advance care planning, palliative care services, and hospice and end-of-life care. Although these conversations can be difficult, they can also be crucial opportunities to identify new goals of care for the

patient and their caregivers beyond disease-directed treatment; these conversations should be part of routine oncological care.[481] Patients with cancer are more likely to receive end-of-life care that is consistent with their preferences when they have had the opportunity to discuss their wishes with a health-care practitioner.[461,481]

Traditional, complementary, alternative, and integrative medicine (TCIM) are terms often used interchangeably by practitioners of conventional medicine (allopathic medicine), although their meanings can be very different (appendix pp 71–74). WHO defines traditional medicine as "the sum total of the knowledge, skill, and practices based on the theories, beliefs, and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health as well as in the prevention, diagnosis, improvement or treatment of physical and mental illness".[482] Complementary medicine refers to non-mainstream practices used together with conventional medicine. Alternative medicine refers to non-mainstream practices used instead of conventional medicine. The Society for Integrative Oncology defines integrative oncology as a field based around a patient-centred, evidence-informed approach to cancer care that uses lifestyle modifications, mind and body therapies, and natural products from different traditions in tandem with conventional cancer treatments.[483]

A 2012 systematic review of TCIM use in the USA, Canada, Europe, Australia, and New Zealand indicated that 40% of people with cancer used some form of TCIM.[484] Women with breast cancer are frequent users of TCIM in both high-income countries and LMICs; up to 80% use TCIM in some populations in the Caribbean.[485] Although many patients with cancer use TCIM, their oncology providers have scarce knowledge or understanding of this area of medicine.[486] Exploring and understanding patient TCIM use is a useful part of building rapport and sharing information in a patient-centred consultation. Example talking points could be: are you currently receiving, or have you previously received care from other healers in the community or other clinicians in the health-care system before this appointment? Another point could be: can you tell me more about these treatments or medicines? Acknowledging that discussions of TCIM should be nuanced due to potential harmful interactions of some TCIM with chemotherapy and radiotherapy, we encourage clinicians and patients to access evidence-based information, such as the ASCO and Society for Integrative Oncology joint recommendations (panel 27) and the Memorial Sloan Kettering Cancer Center guide to herbs, botanicals, and other products.[487]

Panel 27: **Society for Integrative Oncology recommendations for goals, adapted from information from the Memorial Sloan Kettering Cancer Center[487]**

Anxiety or stress reduction
- Music therapy
- Meditation
- Stress management
- Yoga

Improvement of depression or mood disorders
- Meditation
- Relaxation
- Yoga
- Massage
- Music therapy

Quality of life improvement
- Meditation
- Yoga

Reduction of chemotherapy-induced nausea and vomiting
- Acupressure
- Acupuncture

Pain management
- Hypnosis
- Acupuncture
- Music therapy

How do we measure progress in communication and empowerment?

Patient empowerment does not have a universal definition and is more difficult to measure than numeric outcomes, such as survival. Patient satisfaction with breast cancer care could be a useful surrogate and should be measured by the treating health-care professionals, ideally both quantitively and qualitatively. Specifically, measuring the degree of involvement of patients in their decision making could be a surrogate for patient empowerment and adherence to proposed therapy is another useful measure to include in empowerment-focused research. Community-based participatory research methods will be integral to understanding and creating interventions that meet patients in the context of their cultural needs and preferences and assist with dismantling care inequities.[488–491] Progress can be measured by global research into societal discussions of breast cancer asking if we can freely talk about symptoms, diagnosis, and treatment of breast cancer in all global spheres.

Clinician-facilitated discussions of patients' core values in the setting of newly diagnosed cancers have shown promise in enhancing individual autonomy and leveraging interpersonal supports.[492,493] Unfortunately, these discussions are often withheld until the end of life. Integrating these conversations regarding who the patient is and what is most important to them as a person can help ensure person-centred decision making and care planning across the breast cancer continuum, from diagnosis to end of life.

A measurable indicator of change is the inclusion of mandatory communication training for all health-care professionals and this should be measured by both

policy makers (as a measure of quality of professional education) and researchers. Training in understanding one's own cultural beliefs and values, recognising and understanding differences in culture, values, and beliefs in others, and recognising one's own inherent biases (sometimes called cultural competence or cultural humility[494]), is important to enable health-care professionals to communicate effectively with all their patients.

The role of patient advocates is to promote issues that are important to patients and engage with policy makers to ensure empowerment and communication are considered as interventions that improve long-term outcomes more affordably than some expensive drugs. The role of policy makers is to mandate and facilitate patient and public involvement in research design and practice in all spheres.

Potential wider effects

Our vision is that empowering patients with breast cancer to be engaged in decisions about their care in all health-care settings is a step towards wider female empowerment that addresses the insufficient body, social, and financial autonomy for women in some societies worldwide. As a condition that predominantly affects women, breast cancer constitutes not only a challenge to women's health, but an opportunity to identify ways in which provider-level interventions and system-level changes can generally facilitate women's power and voice in society. When women are treated with respect and recognised for their key, often underappreciated, roles in societies in which the division of labour remains gendered, they might begin to identify opportunities in other settings to exercise greater autonomy. Breast cancer is a disease that many patients describe as robbing them of power, but through good communication and facilitating patient autonomy, it could be an opportunity to return power and emerge stronger than before. This concept is especially important for those who have faced marginalisation on the basis of intersecting identity characteristics, such as race, socioeconomic status, and gender (table 7).

Future directions

Breast cancer prevention

Our vision for prevention is to be able to identify those at substantially increased risk of breast cancer in the whole population and offer them precision prevention strategies to reduce that risk, thus reducing breast cancer incidence. To achieve this vision, risk assessment will need to be equitable, proactive, and systematic rather than largely opportunistic, as is the case to date. A coordinated approach to the prescription of risk-reducing medications and the care of those who take them is required. To date, this is not considered to be in the domain of primary care providers or specialists and insufficient clinician knowledge and confidence is a major barrier to uptake.[143] Catalysed by this Commission, an implementation pilot has commenced in Australia aimed at solving the existing workforce capability gap in a way that is potentially scaleable. It will examine whether a nurse practitioner-led telehealth service can increase uptake and continuation of risk-reducing medications, such as by providing assessment and prescriptions before discharging clients back to their primary health-care provider for ongoing prescriptions. A hotline and rapid re-entry into the service if required will be available to support health-care practitioners and patients in managing side-effects during the full treatment course. At the same time, better population prevention is needed. Governments can help by prioritising reduction of population exposure to breast cancer risk factors by adjusting health policies. Implementation of simple preventives (eg, low-dose tamoxifen in women <50 years) will require increased workforces and training of primary and secondary health-care providers. There is much work to be done in the education and training of health-care practitioners so that risks, benefits, and uncertainties are clearer for individuals to inform their personal lifestyle choices. Specifically, governments must recognise that the rising rates of breast cancer are a major and expensive public health problem and there is a need to legislate for changes on the basis of policies that have been effective in other areas of public health to reduce exposure to breast cancer risk factors.

	Definition	Rationale	Data sources	Responsible entity	Target
Communication skills training	Proportion of those in regulated health-care roles receive culturally sensitive person-centred communication skills training	Health-care professional communication is key to empowering patients and developing person-centred care	Facility records; university regulators	Universities; health-care facilities	100% of health-care professionals in every country should receive communication skills training
Patient and public involvement in ethical design of breast cancer research	Proportion of breast cancer clinical trials that have partnered with PPIE	PPIE in research promotes patient empowerment and improves the likelihood of the study being important to patients	Clinical trial databases; research funding body records	Ministry of Health; research funding bodies, including charities; patient advocacy	100% of breast cancer clinical research in every country should partner with PPIE from research concept to reporting and translation into practice

PPIE=patient and public involvement and engagement.

Table 7: **Communication and empowerment in breast cancer proposed measurable indicators of change**

Personalising breast cancer treatment

Breast cancer communities in high-income countries have made breakthroughs in terms of personalising breast cancer treatments; these are perhaps the most applicable in the early disease setting in which there is increasing recognition that many people at present are overtreated, resulting in a substantial burden of treatment that is costly and unnecessary. Emerging technologies will allow the integration of existing clinical data with new molecular data on germline genomics, tumour genomics, pharmacogenomics, and ctDNA. The aim is to provide a personalised approach for each patient, rather than the more common population approach. Optimisation of treatment can preserve the excellent outcomes that have been achieved while reducing rising financial, physical, and psychological costs.

In addition, artificial intelligence and allied technologies can democratise this information, making it available for everyone. Recognising that each nations' health-care system is subtly—or at times radically—different from their neighbours' systems, the leaders for breast cancer (both breast cancer experts and policy makers) would be responsible for interpreting this new information within their own country and for their own citizens.

Once developed, it would be a second challenge to get advanced communications technology to communicate directly with health-care personnel and patients globally. Applying new technology assessments would allow personalised information from patients and their tumours to train algorithms advising best management. For breast cancer, it is probable that these algorithms would reduce the number of treatments for most patients, thus saving money to invest in more targeted treatments for those who need them. This approach will allow LMICs to reap the benefits of advancing technology and communications very quickly.

Optimal inclusive management of metastatic breast cancer

To fully understand and address the global effects of metastatic breast cancer, the first crucial step is to collect high-quality metastatic cancer registry data, including regarding relapses. This data collection will ensure that patients with metastatic breast cancer are seen and should also better guide allocation of resources. There is an urgent need to improve equitable access to evidence-based therapies and clinical trials for people with metastatic breast cancer and we urge that patients are managed with an individualised approach that includes tailoring therapies appropriately to tumour biology, evaluating quality of life regularly, incorporating supportive and palliative care from diagnosis, and always accounting for patients' preferences. People with metastatic breast cancer should be managed with a multidisciplinary approach and according to high-quality context-adapted clinical guidelines, both of which have been shown to improve health outcomes and quality of life. Metastatic breast cancer remains a stigmatised and poorly understood disease for the general population, policy makers, and even for health-care professionals. A change in mentality—moving from a fatalistic to a more optimistic approach—is needed to truly change patient outcomes. We propose measurable indicators of positive change with actionable targets for metastatic breast cancer and hope that this framework can be applied to other metastatic cancers to induce global change.

Tackling breast cancer gaps and inequities though global collaboration

Addressing global inequities cannot be achieved by expecting all countries to play linear catch-up with high-income countries, but must have increasing emphasis on the regionalisation of cancer care provision. This goal requires adoption of approaches for earlier diagnosis and better treatments that are effective in the local context. Developing models that encourage the advancement of regional centres of excellence, regional pooled procurement, and manufacturing of relevant medications and health-related products will ensure greater access at lower cost to all patients. Grassroots advocacy and patient education and empowerment across all regions are needed to ensure that health is acknowledged as a global basic right. While continuing to highlight concerns around health gaps and inequities on a broader global platform, there must also be leverage that works to hold regional policy makers and other local stakeholders to account. Investment in developing location-based and contextualised training of a competent workforce across the care continuum is essential. Maintaining links to and support from broader global networks, alongside developing the skill sets necessary to address local and region-specific challenges, will encourage the expansion and retention of necessary workforces in LMICs. Although innovations and technologies hold promise in mitigating some of these disparities, especially when backed by evidence-driven outcomes, they are not a panacea for dysfunctional health-care systems; deliberate investment in health-care systems and workforces should remain the basis for global innovation. For sustainable global solutions to occur, a multifaceted approach and persistent commitment is needed that harnesses all sectors of society, including finance, education, and industry to address health disparities in breast cancer and other health sectors.

Identifying and responding to the hidden costs of breast cancer

The hidden costs of breast cancer must be exposed and quantified to be reduced. These hidden costs are myriad and have yet to be fully explored, quantified, and incorporated into the framework of serious health-related suffering or developed into an inclusive suffering metric that combines physical, psychological, social, and spiritual components as experienced by patients, caregivers, and their families. Furthermore, many of the

financial costs of breast cancer are overlooked or go unmeasured, including the lost family income of both patients and caregivers. The hidden costs of breast cancer are embedded in and intensified by gender inequity and layer onto poverty and marginalisation. Financial protection and quality service delivery must span the entire breast cancer trajectory, but the design, monitoring, and evaluation of these interventions requires a full costing model to identify the necessary resources to alleviate more of the breast cancer suffering spectrum. Screening for hidden costs and suffering must be designed to influence priority setting and resource allocation around an informed but achievable target of suffering reduction. Strategies must be grounded in and tailored to the specific stages of the breast cancer trajectory. Better understanding and responding to the value that patients, caregivers, and families place on the alleviation of suffering—in addition to the reduction of morbidity and mortality—is core to more efficacious and responsive patient-centred care.

Communication and empowerment in breast cancer

We envisage that reliable and sustainable skills in person-centred communication will be consistently integrated throughout all patient–provider interactions. These skills will become fundamental to the training of health-care professionals in breast cancer care, with emphasis on discussing prognosis and encouraging patient participation in decision making. Communication that prioritises empathy, respect, and inclusion recognises the patient's dignity and ensures the provision of truly person-centred care. When patient engagement in research design, conduct, and evaluation becomes mandatory globally, it will ensure clinical research delivers benefits to patients and meaningful answers to research questions of interest. Policy makers can invest to provide global minimum numbers of treating

Panel 28: **Summary of the *Lancet* Breast Cancer Commission suggested targets for change**

Breast cancer prevention

- 95% of countries should fully legislate the UNICEF Code for Advertising and Promotion of Commercial Milk Formula Products and adhere to WHO's Best Buys with respect to alcohol advertising
- Statutory access to at least 18 weeks, and preferably 26 weeks, of parental leave at 100% pay
- Mandatory provision of paid breaks and nursing expressing facilities on return to work
- Tax sugar-sweetened beverages to raise the retail price by at least 20%

Personalising breast cancer treatment

- More than 80% (aiming for 95%) of patients have access to accurate tumour subtyping
- More than 80% (aiming for 95%) of patients with a new diagnosis to be discussed at multidisciplinary meetings
- 100% of patients with breast cancer to have access to a full range of treatment modalities
- At least 10% (aiming for >25%) of participants of international breast cancer trials should be from low-income and middle-income countries (LMICs)
- At least 10% (aiming for >25%) of all breast cancer trials to be led or co-led by researchers from LMICs

Optimal inclusive management of metastatic breast cancer

- Minimum of 70% (aiming at 100%) of cancer registries to record cancer stage and relapses
- Minimum of 50%, aiming at 95%, of people with newly diagnosed metastatic breast cancer to be discussed at multidisciplinary meetings
- Record the number of people with metastatic breast cancer and aim to double the median overall survival in a decade
- Aiming for less than 5% of patients at the end of their life to not have access to morphine
- 100% of people with metastatic breast cancer to have access to life-saving cancer medicines

Tackling breast cancer gaps and inequities though global collaboration

- 60% of all invasive cancers to be diagnosed at stage I–II
- Evaluation, imaging, tissue sampling, and pathology within 60 days of presentation
- 80% of patients to undergo multimodal treatment without abandonment
- Time from drug approval to availability to the patient of less than 6 months for high-priority agents and less than 1 year for intermediate-priority agents

Identifying the hidden costs of breast cancer

- Upward trajectory year on year for universal health coverage of breast cancer across the continuum of care—aiming at 100%—to eliminate financial catastrophe and impoverishment for all families experiencing breast cancer
- Screening for serious health-related suffering at diagnosis and key milestones throughout the breast cancer pathway as a research tool with an aim for widespread implementation after validation
- Minimum of 20% (aiming at 100%) of the patients and families with the lowest incomes to receive public financing and provision of an essential package of supportive and palliative care across the breast cancer pathway

Communication and empowerment in breast cancer

- 100% of health-care professionals in every country should receive communication skills training
- 100% of breast cancer clinical research in every country should partner with patients from research concept to reporting and translation into practice

health-care staff per capita, which will improve both global survival rates for breast cancer and patient satisfaction with their degree of involvement in treatment decision making. By normalising and honouring patient involvement, a powerful message will exist of women publicly exercising their voices and rights, providing opportunities for wider global empowerment.

Conclusion

The *Lancet* Breast Cancer Commission has produced an evidence-based inclusive roadmap to address urgent global breast cancer challenges. However, we call society to action to scrutinise approaches to breast cancer, challenge the status quo, and expose practices that create inequity in every country of the world or waste scarce resources. We implore all stakeholders in breast cancer care to disseminate, implement, and adapt our roadmap to facilitate changes to practice and outcomes.

We have shown throughout this Commission report that data are powerful promoters for change. Therefore, it is imperative that our breast cancer targets (panel 28) are measured, used to hold policy makers and communities to account, and used to lobby for better, equitable approaches to breast cancer. We anticipate a united, collaborative, and evidence-based approach that empowers patients, families, communities, health-care providers, and policy makers to evolve and improve this roadmap. We believe that this approach will prevent the inevitability of the anticipated 3 million new diagnoses of breast cancer per year, that breast cancer will no longer be the leading cause of cancer death, and will provide better visibility and treatment for everyone affected by breast cancer, regardless of who they are or where they live.

Contributors

All listed authors have substantially contributed to the conception and design of this Commission or the acquisition, analysis, or interpretation of data. All authors drafted the Commission or reviewed it critically for important intellectual content. All authors approved the final version to be published and agree to be accountable for all aspects of the Commission in ensuring that questions related to accuracy or integrity of any part of the work are appropriately investigated and resolved.

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References

1 WHO. Breast cancer. World Health Organisation. 2021. https://www.who.int/news-room/fact-sheets/detail/breast-cancer (accessed April 1, 2023).

2 Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2021; **71:** 209–49.

3 Mailhot Vega RB, Balogun OD, Ishaq OF, Bray F, Ginsburg O, Formenti SC. Estimating child mortality associated with maternal mortality from breast and cervical cancer. *Cancer* 2019; **125:** 109–17.

4 Cavallo J. Maternal deaths from cancer worldwide have led to approximately 1 million new maternal orphans. The ASCO Post, Oct 20, 2022. https://ascopost.com/news/october-2022/maternal-deaths-from-cancer-worldwide-have-led-to-approximately-1-million-new-maternal-orphans/ (accessed April 1, 2023).

5 United Nations Department of Economic and Social Affairs. World Social Report 2020: inequality in a rapidly changing world. United Nations. 2020. https://www.un.org/development/desa/dspd/wp-content/uploads/sites/22/2020/02/World-Social-Report2020-FullReport.pdf (accessed April 1, 2023).

6 Daly B, Olopade OI. A perfect storm: how tumor biology, genomics, and health care delivery patterns collide to create a racial survival disparity in breast cancer and proposed interventions for change. *CA Cancer J Clin* 2015; **65:** 221–38.

7 Coles CE, Anderson BO, Cameron D, et al. The *Lancet* Breast Cancer Commission: tackling a global health, gender, and equity challenge. *Lancet* 2022; **399:** 1101–03.

8 Knaul FM, Garcia PJ, Gospodarowicz M, Essue BM, Lee N, Horton R. The *Lancet* Commission on cancer and health systems: harnessing synergies to achieve solutions. 2021; **398:** 1114–16.

9 Knaul FM, Farmer PE, Krakauer EL, et al. Alleviating the access abyss in palliative care and pain relief–an imperative of universal health coverage: the *Lancet* Commission report. *Lancet* 2018; **391:** 1391–454.

10 Arnold M, Morgan E, Rumgay H, et al. Current and future burden of breast cancer: global statistics for 2020 and 2040. *Breast* 2022; **66:** 15–23.

11 Jayasekera J, Mandelblatt JS. Systematic review of the cost effectiveness of breast cancer prevention, screening, and treatment interventions. *J Clin Oncol* 2020; **38:** 332–50.

12 Bellanger M, Barry K, Rana J, Regnaux JP. Cost-effectiveness of lifestyle-related interventions for the primary prevention of breast cancer: a rapid review. *Front Med* 2020; **6:** 325.

13 Li SX, Milne RL, Nguyen-Dumont T, et al. Prospective evaluation of the addition of polygenic risk scores to breast cancer risk models. *JNCI Cancer Spectr* 2021; **5:** pkab021.

14 Howell A, Anderson AS, Clarke RB, et al. Risk determination and prevention of breast cancer. *Breast Cancer Res* 2014; **16:** 446.

15 Dorling L, Carvalho S, Allen J, et al. Breast cancer risk genes - association analysis in more than 113 000 women. *N Engl J Med* 2021; **384:** 428–39.

16 Hu C, Hart SN, Gnanaolivu R, et al. A population-based study of genes previously implicated in breast cancer. *N Engl J Med* 2021; **384:** 440–51.

17 Mavaddat N, Michailidou K, Dennis J, et al. Polygenic risk scores for prediction of breast cancer and breast cancer subtypes. *Am J Hum Genet* 2019; **104:** 21–34.

18 Brown KF, Rumgay H, Dunlop C, et al. The fraction of cancer attributable to modifiable risk factors in England, Wales, Scotland, Northern Ireland, and the United Kingdom in 2015. *Br J Cancer* 2018; **118:** 1130–41.

19 International Agency for Research on Cancer, WHO. Cancer attributable to obesity. 2022. https://gco.iarc.fr/causes/obesity (accessed Oct 27, 2022).

20 Cheraghi Z, Poorolajal J, Hashem T, Esmailnasab N, Doosti Irani A. Effect of body mass index on breast cancer during premenopausal and postmenopausal periods: a meta-analysis. *PLoS One* 2012; **7:** e51446.

21 Suzuki R, Orsini N, Saji S, Key TJ, Wolk A. Body weight and incidence of breast cancer defined by estrogen and progesterone receptor status—a meta-analysis. *Int J Cancer* 2009; **124:** 698–712.

22 Vrieling A, Buck K, Kaaks R, Chang-Claude J. Adult weight gain in relation to breast cancer risk by estrogen and progesterone receptor status: a meta-analysis. *Breast Cancer Res Treat* 2010; **123:** 641–49.

23 Danaei G, Vander Hoorn S, Lopez AD, Murray CJ, Ezzati M. Causes of cancer in the world: comparative risk assessment of nine behavioural and environmental risk factors. *Lancet* 2005; **366:** 1784–93.

24 Bissell MCS, Kerlikowske K, Sprague BL, et al. Breast cancer population attributable risk proportions associated with body mass index and breast density by race/ethnicity and menopausal status. *Cancer Epidemiol Biomarkers Prev* 2020; **29:** 2048–56.

25 Secretan B, Straif K, Baan R, et al. A review of human carcinogens—part E: tobacco, areca nut, alcohol, coal smoke, and salted fish. *Lancet Oncol* 2009; **10:** 1033–34.

26 Ginsburg O, Vanderpuye V, Beddoe AM, et al. Women, power, and cancer: a *Lancet* Commission. *Lancet* 2023; **402:** 2113–66.

27 Rovira P, Rehm J. Estimation of cancers caused by light to moderate alcohol consumption in the European Union. *Eur J Public Health* 2021; **31:** 591–96.

28 Bagnardi V, Rota M, Botteri E, et al. Alcohol consumption and site-specific cancer risk: a comprehensive dose-response meta-analysis. *Br J Cancer* 2015; **112:** 580–93.

29 Choi Y-J, Myung S-K, Lee J-H. Light alcohol drinking and risk of cancer: a meta-analysis of cohort studies. *Cancer Res Treat* 2018; **50:** 474–87.

30 International Agency for Research on Cancer, WHO. Cancers attributable to alcohol. 2022. https://gco.iarc.fr/causes/alcohol/ (accessed Oct 27, 2022).

31 Yoo JE, Han K, Shin DW, et al. Association between changes in alcohol consumption and cancer risk. *JAMA Netw Open* 2022; **5:** e2228544.

32 Brinton LA, Figueroa JD, Awuah B, et al. Breast cancer in sub-Saharan Africa: opportunities for prevention. *Breast Cancer Res Treat* 2014; **144:** 467–78.

33 Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50 302 women with breast cancer and 96 973 women without the disease. *Lancet* 2002; **360:** 187–95.

34 Rollins NC, Bhandari N, Hajeebhoy N, et al. Why invest, and what it will take to improve breastfeeding practices? *Lancet* 2016; **387:** 491–504.

35 Victora CG, Bahl R, Barros AJ, et al. Breastfeeding in the 21st century: epidemiology, mechanisms, and lifelong effect. *Lancet* 2016; **387:** 475–90.

36 Jung AY, Ahearn TU, Behrens S, et al. Distinct reproductive risk profiles for intrinsic-like breast cancer subtypes: pooled analysis of population-based studies. *J Natl Cancer Inst* 2022; **114:** 1706–19.

37 Shi Y, Li T, Wang Y, et al. Household physical activity and cancer risk: a systematic review and dose-response meta-analysis of epidemiological studies. *Sci Rep* 2015; **5:** 14901.

38 Yin X, Zhang T, Zhang Y, Man J, Yang X, Lu M. The global, regional, and national disease burden of breast cancer attributable to low physical activity from 1990 to 2019: an analysis of the Global Burden of Disease Study 2019. *Int J Behav Nutr Phys Act* 2022; **19:** 42.

39 Chlebowski RT, Rohan TE, Manson JE, et al. Breast cancer after use of estrogen plus progestin and estrogen alone: analyses of data from 2 women's health initiative randomized clinical trials. *JAMA Oncol* 2015; **1:** 296–305.

40 Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormonal contraceptives: collaborative reanalysis of individual data on 53 297 women with breast cancer and 100 239 women without breast cancer from 54 epidemiological studies. *Lancet* 1996; **347:** 1713–27.

41 Mørch LS, Skovlund CW, Hannaford PC, Iversen L, Fielding S, Lidegaard Ø. Contemporary hormonal contraception and the risk of breast cancer. *N Engl J Med* 2017; **377:** 2228–39.

42 Fitzpatrick D, Pirie K, Reeves G, Green J, Beral V. Combined and progestagen-only hormonal contraceptives and breast cancer risk: a UK nested case-control study and meta-analysis. *PLoS Med* 2023; **20:** e1004188.

43 Parkin DM, Boyd L, Walker LC. 16. The fraction of cancer attributable to lifestyle and environmental factors in the UK in 2010. *Br J Cancer* 2011; **105** (suppl 2)**:** S77–81.

44 Madigan MP, Ziegler RG, Benichou J, Byrne C, Hoover RN. Proportion of breast cancer cases in the United States explained by well-established risk factors. *J Natl Cancer Inst* 1995; **87:** 1681–85.

45 Britt KL, Cuzick J, Phillips K-A. Key steps for effective breast cancer prevention. *Nat Rev Cancer* 2020; **20:** 417–36.

46 Zhang B, Shu X-O, Delahanty RJ, et al. Height and breast cancer risk: evidence from prospective studies and Mendelian randomization. *J Natl Cancer Inst* 2015; **107:** djv219.

47 Maas P, Barrdahl M, Joshi AD, et al. Breast cancer risk from modifiable and nonmodifiable risk factors among white women in the United States. *JAMA Oncol* 2016; **2:** 1295–302.

48 Islami F, Goding Sauer A, Miller KD, et al. Proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors in the United States. *CA Cancer J Clin* 2018; **68:** 31–54.

49 Parkin DM. 9. Cancers attributable to inadequate physical exercise in the UK in 2010. *Br J Cancer* 2011; **105** (suppl 2)**:** S38–41.

50 Rumgay H, Shield K, Charvat H, et al. Global burden of cancer in 2020 attributable to alcohol consumption: a population-based study. *Lancet Oncol* 2021; **22:** 1071–80.

51 Guo W, Fensom GK, Reeves GK, Key TJ. Physical activity and breast cancer risk: results from the UK Biobank prospective cohort. *Br J Cancer* 2020; **122:** 726–32.

52 Collaborative Group on Hormonal Factors in Breast Cancer. Type and timing of menopausal hormone therapy and breast cancer risk: individual participant meta-analysis of the worldwide epidemiological evidence. *Lancet* 2019; **394:** 1159–68.

53 Chen J, Pee D, Ayyagari R, et al. Projecting absolute invasive breast cancer risk in White women with a model that includes mammographic density. *J Natl Cancer Inst* 2006; **98:** 1215–26.

54 Tran KB, Lang JJ, Compton K, et al. The global burden of cancer attributable to risk factors, 2010–19: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 2022; **400:** 563–91.

55 WHO, International Agency for Research on Cancer. Global Cancer Observatory: cancers attributable to alcohol. https://gco.iarc.fr/causes/alcohol/tools-bars?mode=1&sex=0&population=900&population_group=4&country=4&continent=0&cancer=20&key=paf&lock_scale=0&nb_results=10&age_group=3&colored=1 (accessed March 12, 2024).

56 Peacey V, Steptoe A, Davídsdóttir S, Baban A, Wardle J. Low levels of breast cancer risk awareness in young women: an international survey. *Eur J Cancer* 2006; **42:** 2585–89.

57 Peltzer K, Pengpid S. Awareness of breast cancer risk among female university students from 24 low, middle income and emerging economy countries. *Asian Pac J Cancer Prev* 2014; **15:** 7875–78.

58 Gupta A, Shridhar K, Dhillon PK. A review of breast cancer awareness among women in India: cancer literate or awareness deficit? *Eur J Cancer* 2015; **51:** 2058–66.

59 Osei-Afriyie S, Addae AK, Oppong S, Amu H, Ampofo E, Osei E. Breast cancer awareness, risk factors and screening practices among future health professionals in Ghana: a cross-sectional study. *PLoS One* 2021; **16:** e0253373.

60 Elshami M, Usrof FD, Alser M, et al. Awareness of Palestinian women about breast cancer risk factors: a national cross-sectional study. *JCO Glob Oncol* 2022; **8:** e2200087.

61 Sinclair J, McCann M, Sheldon E, Gordon I, Brierley-Jones L, Copson E. The acceptability of addressing alcohol consumption as a modifiable risk factor for breast cancer: a mixed method study within breast screening services and symptomatic breast clinics. *BMJ Open* 2019; **9:** e027371.

62 Khushalani JS, Qin J, Ekwueme DU, White A. Awareness of breast cancer risk related to a positive family history and alcohol consumption among women aged 15–44 years in United States. *Prev Med Rep* 2019; **17:** 101029

63 Grigg J, Manning V, Lockie D, et al. A brief intervention for improving alcohol literacy and reducing harmful alcohol use by women attending a breast screening service: a randomised controlled trial. *Med J Aust* 2023; **218:** 511–19.

64 Kushi LH, Byers T, Doyle C, et al. American Cancer Society Guidelines on nutrition and physical activity for cancer prevention: reducing the risk of cancer with healthy food choices and physical activity. *CA Cancer J Clin* 2006; **56:** 254–81.

65 Catsburg C, Miller AB, Rohan TE. Adherence to cancer prevention guidelines and risk of breast cancer. *Int J Cancer* 2014; **135:** 2444–52.

66 Thomson CA, McCullough ML, Wertheim BC, et al. Nutrition and physical activity cancer prevention guidelines, cancer risk, and mortality in the women's health initiative. *Cancer Prev Res* 2014; **7:** 42–53.

67 Fong AJ, Lafaro K, Ituarte PHG, Fong Y. Association of living in urban food deserts with mortality from breast and colorectal cancer. *Ann Surg Oncol* 2021; **28:** 1311–19.

68 Bevel MS, Tsai M-H, Parham A, Andrzejak SE, Jones S, Moore JX. Association of food deserts and food swamps with obesity-related cancer mortality in the US. *JAMA Oncol* 2023; **9:** 909–16.

69 Wyper GMA, Mackay DF, Fraser C, et al. Evaluating the impact of alcohol minimum unit pricing on deaths and hospitalisations in Scotland: a controlled interrupted time series study. *Lancet* 2023; **401:** 1361–70.

70 Gilmore AB, Fooks G, Drope J, Bialous SA, Jackson RR. Exposing and addressing tobacco industry conduct in low-income and middle-income countries. *Lancet* 2015; **385:** 1029–43.

71 Balekouzou A, Yin P, Pamatika CM, et al. Epidemiology of breast cancer: retrospective study in the Central African Republic. *BMC Public Health* 2016; **16:** 1230.

72 WHO. WHO report on the global tobacco epidemic, 2021: addressing new and emerging products. World Health Organization. 2021. https://www.who.int/publications/i/item/9789240032095 (accessed Sept 26, 2023).

73 Saenz-de-Miera B, Wu DC, Essue BM, Maldonado N, Jha P, Reynales-Shigematsu LM. The distributional effects of tobacco tax increases across regions in Mexico: an extended cost-effectiveness analysis. *Int J Equity Health* 2022; **21:** 8.

74 Wilkinson AL, Scollo MM, Wakefield MA, Spittal MJ, Chaloupka FJ, Durkin SJ. Smoking prevalence following tobacco tax increases in Australia between 2001 and 2017: an interrupted time-series analysis. *Lancet Public Health* 2019; **4:** e618–27.

75 Chipty T. Study of the impact of the tobacco plain packaging measure on smoking prevalence in Australia. Australian Government Department of Health and Aged Care. 2016. https://www.health.gov.au/resources/publications/study-of-the-impact-of-the-tobacco-plain-packaging-measure-on-smoking-prevalence-in-australia?language=en (accessed March 12, 2024).

76 WHO. Political declaration of the third high-level meeting of the General Assembly on the prevention and control of non-communicable diseases. World Health Organisation. 2022. https://apps.who.int/gb/ebwha/pdf_files/EB150/B150_7Add1-en.pdf (accessed Sept 22, 2023).

77 WHO. Regional technical consultation with member states on the working document for development of the action plan (2022–2030) to effectively implement the global strategy to reduce the harmful use of alcohol as a public health priority: virtual meeting, 25–26 March 2021: meeting report. World Health Organization. 2021. https://apps.who.int/iris/handle/10665/341837 (accessed March 12, 2024).

78 Mialon M, McCambridge J. Alcohol industry corporate social responsibility initiatives and harmful drinking: a systematic review. *Eur J Public Health* 2018; **28:** 664–73.

79 McCambridge J, Mialon M, Hawkins B. Alcohol industry involvement in policymaking: a systematic review. *Addiction* 2018; **113:** 1571–84.

80 WHO. Factsheet–5 facts about alcohol and cancer. World Health Organization. 2021. https://www.who.int/andorra/publications/m/item/factsheet-5-facts-about-alcohol-and-cancer (accessed March 12, 2024).

81 Hammond D. Health warning messages on tobacco products: a review. *Tob Control* 2011; **20:** 327–37.

82 Moodie C, Hoek J, Hammond D, et al. Plain tobacco packaging: progress, challenges, learning and opportunities. *Tob Control* 2022; **31:** 263–71.

83 Greenhalgh EM, Scollo MM. 11A.9 real-world research on the effects of plain packaging. In: Greenhalgh EM, Scollo MM, Winstanley MH, eds. Tobacco in Australia: facts and issues. Melbourne: Cancer Council Victoria, 2022: https://www.tobaccoinaustralia.org.au/chapter-11-advertising/indepth-11a-packaging-as-promotion/11a-9-real-world-research-on-the-effects-of-plain- (accessed March 12, 2024).

84 Hughes N, Arora M, Grills N. Perceptions and impact of plain packaging of tobacco products in low and middle income countries, middle to upper income countries and low-income settings in high-income countries: a systematic review of the literature. *BMJ Open* 2016; **6:** e010391.

85 Giesbrecht N, Reisdorfer E, Rios I. Alcohol health warning labels: a rapid review with action recommendations. *Int J Environ Res Public Health* 2022; **19:** 11676.

86 Wilkinson C, Room R. Warnings on alcohol containers and advertisements: international experience and evidence on effects. *Drug Alcohol Rev* 2009; **28:** 426–35.

87 Scholes-Balog KE, Heerde JA, Hemphill SA. Alcohol warning labels: unlikely to affect alcohol-related beliefs and behaviours in adolescents. *Aust N Z J Public Health* 2012; **36:** 524–29.

88 Tam TW, Greenfield TK. Do alcohol warning labels influence men's and women's attempts to deter others from driving when intoxicated? *Hum Factors Ergon Manuf* 2010; **20:** 538–46.

89 Coomber K, Martino F, Barbour IR, Mayshak R, Miller PG. Do consumers 'get the facts'? A survey of alcohol warning label recognition in Australia. *BMC Public Health* 2015; **15:** 816.

90 Petticrew M, Douglas N, Knai C, Durand MA, Eastmure E, Mays N. Health information on alcoholic beverage containers: has the alcohol industry's pledge in England to improve labelling been met? *Addiction* 2016; **111:** 51–55.

91 Wagenaar AC, Salois MJ, Komro KA. Effects of beverage alcohol price and tax levels on drinking: a meta-analysis of 1003 estimates from 112 studies. *Addiction* 2009; **104:** 179–90.

92 Stockwell T, Zhao J, Giesbrecht N, Macdonald S, Thomas G, Wettlaufer A. The raising of minimum alcohol prices in Saskatchewan, Canada: impacts on consumption and implications for public health. *Am J Public Health* 2012; **102:** e103–10.

93 WHO, UNICEF. Implementation guidance: protecting, promoting, and supporting breastfeeding in facilities providing maternity and newborn services: the revised Baby-friendly Hospital Initiative 2018. World Health Organization. 2018. https://www.who.int/publications/i/item/9789241513807 (accessed Nov 13, 2022).

94 WHO. WHO discussion paper: draft recommendations for the prevention and management of obesity over the life course, including potential targets. World Health Organization. 2021. https://www.who.int/publications/m/item/who-discussion-paper-draft-recommendations-for-the-prevention-and-management-of-obesity-over-the-life-course-including-potential-targets (accessed Nov 13, 2022).

95 WHO. Global action plan on physical activity 2018–2030: more active people for a healthier world. World Health Organization. 2018. https://apps.who.int/iris/handle/10665/272722 (accessed Nov 13, 2022).

96 WHO. Political declaration of the third high-level meeting of the General Assembly on the prevention and control of non-communicable diseases, and mental health: draft updated menu of policy options and cost-effective interventions for the prevention and control of noncommunicable diseases. World Health Organization. 2023. https://apps.who.int/gb/ebwha/pdf_files/EB152/B152_6-en.pdf (accessed March 12, 2024).

97 WHO. Global information system on alcohol and health. World Health Organization. 2022. https://www.who.int/data/gho/data/themes/global-information-system-on-alcohol-and-health (accessed Nov 13, 2022).

98 WHO. Time to deliver: report of the WHO independent high-level commission on noncommunicable diseases. World Health Organization. 2018. https://apps.who.int/iris/handle/10665/272710. (accessed Nov 13, 2022).

99 UNICEF. Breastfeeding dataset. 2021. https://data.unicef.org/resources/dataset/breastfeeding/ (accessed Nov 22, 2022).

100 Jackson-Morris AM, Mutungi G, Maree E, Waqanivalu T, Marten R, Nugent R. 'Implementability' matters: using implementation research steps to guide and support non-communicable disease national planning in low-income and middle-income countries. *BMJ Glob Health* 2022; **7:** e008275.

101 Brownson RC, Chriqui JF, Stamatakis KA. Understanding evidence-based public health policy. *Am J Public Health* 2009; **99:** 1576–83.

102 Breda J, Wickramasinghe K, Peters DH, et al. One size does not fit all: implementation of interventions for non-communicable diseases. *BMJ* 2019; **367:** l6434.

103 WHO. A guide to implementation research in the prevention and control of noncommunicable diseases. World Health Organization. 2016. https://apps.who.int/iris/bitstream/handle/10665/252626/9789241511803-eng.pdf (accessed Nov 13, 2022).

104 Lee JK, Bullen C, Ben Amor Y, et al. Institutional and behaviour-change interventions to support COVID-19 public health measures: a review by the *Lancet* Commission Task Force on public health measures to suppress the pandemic. *Int Health* 2021; **13:** 399–409.

105 Elghazaly H, Aref AT, Anderson BO, et al. The first BGICC consensus and recommendations for breast cancer awareness, early detection and risk reduction in low- and middle-income countries and the MENA region. *Int J Cancer* 2021; **149:** 505–13.

106 US Department of Health and Human Services. Charter: advisory committee on breast cancer in young women. US Centers for Disease Control and Prevention. 2022. https://www.cdc.gov/faca/committees/pdfs/acbcyw/acbcyw-charter-508.pdf (accessed April 1, 2023).

107 Nsaful J, Dedey F, Nartey E, Labi J, Adu-Aryee NA, Clegg-Lamptey JN. The impact of a breast cancer educational intervention in Ghanaian high schools. *BMC Cancer* 2022; **22:** 893.

108 Soto-Perez-de-Celis E, Smith DD, Rojo-Castillo MP, et al. Implementation of a school-based educational program to increase breast cancer awareness and promote intergenerational transmission of knowledge in a rural Mexican community. *Oncologist* 2017; **22:** 1249–56.

109 Lazzeroni M, Puntoni M, Guerrieri-Gonzaga A, et al. Randomized placebo controlled trial of low-dose tamoxifen to prevent recurrence in breast noninvasive neoplasia: a 10-year follow-up of TAM-01 study. *J Clin Oncol* 2023; **41:** 3116–21.

110 DeCensi A, Puntoni M, Guerrieri-Gonzaga A, et al. Randomized placebo controlled trial of low-dose tamoxifen to prevent local and contralateral recurrence in breast intraepithelial neoplasia. *J Clin Oncol* 2019; **37:** 1629–37.

111 Powles TJ, Ashley S, Tidy A, Smith IE, Dowsett M. Twenty-year follow-up of the Royal Marsden randomized, double-blinded tamoxifen breast cancer prevention trial. *J Natl Cancer Inst* 2007; **99:** 283–90.

112 Cuzick J, Sestak I, Cawthorn S, et al. Tamoxifen for prevention of breast cancer: extended long-term follow-up of the IBIS-I breast cancer prevention trial. *Lancet Oncol* 2015; **16:** 67–75.

113 Cuzick J, Sestak I, Forbes JF, et al. Use of anastrozole for breast cancer prevention (IBIS-II): long-term results of a randomised controlled trial. *Lancet* 2020; **395:** 117–22.

114 Goss PE, Ingle JN, Alés-Martínez JE, et al. Exemestane for breast-cancer prevention in postmenopausal women. *N Engl J Med* 2011; **364:** 2381–91.

115 Fisher B, Costantino JP, Wickerham DL, et al. Tamoxifen for the prevention of breast cancer: current status of the National Surgical Adjuvant Breast and Bowel Project P-1 study. *J Natl Cancer Inst* 2005; **97:** 1652–62.

116 Visvanathan K, Fabian CJ, Bantug E, et al. Use of endocrine therapy for breast cancer risk reduction: ASCO Clinical Practice Guideline update. *J Clin Oncol* 2019; **37:** 3152–65.

117 Paluch-Shimon S, Cardoso F, Sessa C, et al. Prevention and screening in BRCA mutation carriers and other breast/ovarian hereditary cancer syndromes: ESMO Clinical Practice Guidelines for cancer prevention and screening. *Ann Oncol* 2016; **27** (suppl 5)**:** v103–10.

118 Nolan E, Vaillant F, Branstetter D, et al. RANK ligand as a potential target for breast cancer prevention in BRCA1-mutation carriers. *Nat Med* 2016; **22:** 933–39.

119 Bhulani N, Wood M, Tsai J, et al. A phase 3 study to determine the breast cancer risk reducing effect of denosumab in women carrying a germline BRCA1 mutation (BRCA-P Study). *J Clin Oncol* 2022; **40** (suppl 16)**:** TPS10616.

120 Carbine NE, Lostumbo L, Wallace J, Ko H. Risk-reducing mastectomy for the prevention of primary breast cancer. *Cochrane Database Syst Rev* 2018; **4:** CD002748.

121 Lacaze PA, Tiller J, Winship I, For the DNA Screen Investigator Group. Population DNA screening for medically actionable disease risk in adults. *Med J Aust* 2022; **216:** 278–80.

122 Jackson L, Weedon MN, Green HD, et al. Influence of family history on penetrance of hereditary cancers in a population setting. *EClinicalMedicine* 2023; **64:** 102159.

123 Esserman LJ, WISDOM Study and Athena Investigators. The WISDOM study: breaking the deadlock in the breast cancer screening debate. *NPJ Breast Cancer* 2017; **3:** 34.

124 Sergeant JC, Warwick J, Evans DG, et al. Volumetric and area-based breast density measurement in the predicting risk of cancer at screening (PROCAS) study. In: Maidment ADA, Bakic PR, Gavenonis S, eds. Breast Imaging: 11th International Workshop, IWDM 2012, Philadelphia, PA, USA, July 8–11, 2012, Proceedings. New York City, NY: Springer, 2012: 228–35.

125 Renehan AG, Pegington M, Harvie MN, et al. Young adulthood body mass index, adult weight gain and breast cancer risk: the PROCAS Study (UK). *Br J Cancer* 2020; **122:** 1552–61.

126 Brentnall AR, Harkness EF, Astley SM, et al. Mammographic density adds accuracy to both the Tyrer-Cuzick and Gail breast cancer risk models in a prospective UK screening cohort. *Breast Cancer Res* 2015; **17:** 147.

127 Velentzis LS, Freeman V, Campbell D, et al. Breast cancer risk assessment tools for stratifying women into risk groups: a systematic review. *Cancers* 2023; **15:** 1124.

128 Antoniou AC, Pharoah PP, Smith P, Easton DF. The BOADICEA model of genetic susceptibility to breast and ovarian cancer. *Br J Cancer* 2004; **91:** 1580–90.

129 Tyrer J, Duffy SW, Cuzick J. A breast cancer prediction model incorporating familial and personal risk factors. *Stat Med* 2004; **23:** 1111–30.

130 Terry MB, Liao Y, Whittemore AS, et al. 10-year performance of four models of breast cancer risk: a validation study. *Lancet Oncol* 2019; **20:** 504–17.

131 Banegas MP, John EM, Slattery ML, et al. Projecting individualized absolute invasive breast cancer risk in US Hispanic women. *J Natl Cancer Inst* 2017; **109:** djw215.

132 Matsuno RK, Costantino JP, Ziegler RG, et al. Projecting individualized absolute invasive breast cancer risk in Asian and Pacific Islander American women. *J Natl Cancer Inst* 2011; **103:** 951–61.

133 Gail MH, Costantino JP, Pee D, et al. Projecting individualized absolute invasive breast cancer risk in African American women. *J Natl Cancer Inst* 2007; **99:** 1782–92.

134 Hughes E, Wagner S, Pruss D, et al. Development and validation of a breast cancer polygenic risk score on the basis of genetic ancestry composition. *JCO Precis Oncol* 2022; **6:** e2200084.

135 Eriksson M, Czene K, Vachon C, Conant EF, Hall P. Long-term performance of an image-based short-term risk model for breast cancer. *J Clin Oncol* 2023; **41:** 2536–45.

136 Lehman CD, Mercaldo S, Lamb LR, et al. Deep learning vs traditional breast cancer risk models to support risk-based mammography screening. *J Natl Cancer Inst* 2022; **114:** 1355–63.

137 Yala A, Mikhael PG, Strand F, et al. Multi-institutional validation of a mammography-based breast cancer risk model. *J Clin Oncol* 2022; **40:** 1732–40.

138 Omoleye OJ, Woodard AE, Howard FM, et al. External evaluation of a mammography-based deep learning model for predicting breast cancer in an ethnically diverse population. *Radiol Artif Intel* 2023; **5:** e220299

139 Arasu VA, Habel LA, Achacoso NS, et al. Comparison of Mammography artificial intelligence algorithms for 5-year breast cancer risk prediction: an observational study. *Radiology* 2023; **307:** e222733.

140 Phillips KA, Liao Y, Milne RL, et al. Accuracy of risk estimates from the iPrevent breast cancer risk assessment and management tool. *JNCI Cancer Spectr* 2019; **3:** pkz066.

141 Macdonald C, Chamberlain JA, Mazza D, Milne RL, kConFab investigators, Phillips K-A. Underutilisation of breast cancer prevention medication in Australia. *Breast* 2021; **60:** 35–37.

142 National Comprehensive Cancer Network Practice Guidelines in Oncology, Breast Cancer Risk Reduction version 2. 2024. https://www.nccn.org/professionals/physician_gls/pdf/breast_risk.pdf (accessed March 28, 2024).

143 Macdonald C, Saunders CM, Keogh LA, et al. Breast cancer chemoprevention: use and views of Australian women and their clinicians. *Cancer Prev Res* 2021; **14:** 131–44.

144 Bellhouse S, Hawkes RE, Howell SJ, Gorman L, French DP. Breast cancer risk assessment and primary prevention advice in primary care: a systematic review of provider attitudes and routine behaviours. *Cancers* 2021; **13:** 4150.

145 Global Breastfeeding Collective, WHO, UNICEF. Global breastfeeding scorecard. Global Breastfeeding Collective. 2022. https://www.globalbreastfeedingcollective.org/global-breastfeeding-scorecard (accessed Sept 22, 2023).

146 WHO, The Global Health Observatory. Global information system on alcohol and health: levels of consumption. World Health Organization. 2024. https://www.who.int/data/gho/data/themes/topics/topic-details/GHO/levels-of-consumption (accessed March 12, 2024).

147 Young A, Bu W, Jiang W, et al. Targeting the pro-survival protein BCL-2 to prevent breast cancer. *Cancer Prev Res* 2022; **15:** 3–10.

148 Slepicka PF, Cyrill SL, Dos Santos CO. Pregnancy and breast cancer: pathways to understand risk and prevention. *Trends Mol Med* 2019; **25:** 866–81.

149 Santucci-Pereira J, George C, Armiss D, et al. Mimicking pregnancy as a strategy for breast cancer prevention. *Breast Cancer Manag* 2013; **2:** 283–94.

150 Disis ML, Cecil DL. Breast cancer vaccines for treatment and prevention. *Breast Cancer Res Treat* 2022; **191:** 481–89.

151 WHO. "Best buys" and other recommended interventions for the prevention and control of noncommunicable diseases: tackling NCDs. World Health Organization. 2017. https://iris.who.int/bitstream/handle/10665/259232/WHO-NMH-NVI-17.9-eng.pdf?ua=1 (accessed March 28, 2024).

152 International Labour Organization. R191–maternity protection recommendation, 2000 (no 191). International Labour Organization. 2000. https://www.ilo.org/dyn/normlex/en/f?p=NORMLEXPUB:12100:0::NO::P12100_INSTRUMENT_ID:312529 (accessed March 28, 2024).

153 WHO. WHO manual on sugar-sweetened beverage taxation policies to promote healthy diets. World Health Organization. 2022. https://www.who.int/publications/i/item/9789240056299 (accessed March 28, 2024).

154 Andre F, Filleron T, Kamal M, et al. Genomics to select treatment for patients with metastatic breast cancer. *Nature* 2022; **610:** 343–48.

155 Veninga V, Voest EE. Tumor organoids: opportunities and challenges to guide precision medicine. *Cancer Cell* 2021; **39:** 1190–201.

156 Mou H, Kennedy Z, Anderson DG, Yin H, Xue W. Precision cancer mouse models through genome editing with CRISPR-Cas9. *Genome Med* 2015; **7:** 53.

157 Smith I, Robertson J, Kilburn L, et al. Long-term outcome and prognostic value of Ki67 after perioperative endocrine therapy in postmenopausal women with hormone-sensitive early breast cancer (POETIC): an open-label, multicentre, parallel-group, randomised, phase 3 trial. *Lancet Oncol* 2020; **21:** 1443–54.

158 ISRCTN registry. Tailoring treatment for HER2-positive early breast cancer. 2021. https://www.isrctn.com/ISRCTNISRCTN81408940 (accessed May 2, 2023).

159 Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med* 2002; **347:** 1233–41.

160 Veronesi U, Cascinelli N, Mariani L, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *N Engl J Med* 2002; **347:** 1227–32.

161 Al-Ghazal SK, Fallowfield L, Blamey RW. Comparison of psychological aspects and patient satisfaction following breast conserving surgery, simple mastectomy and breast reconstruction. *Eur J Cancer* 2000; **36:** 1938–43.

162 Kouwenberg CAE, de Ligt KM, Kranenburg LW, et al. Long-term health-related quality of life after four common surgical treatment options for breast cancer and the effect of complications: a retrospective patient-reported survey among 1871 Patients. *Plast Reconstr Surg* 2020; **146:** 1–13.

163 Witmer TJK, Kouwenberg CAE, Bargon CA. Comparing costs of standard breast-conserving surgery to oncoplastic breast-conserving surgery and mastectomy with immediate two-stage implant-based breast reconstruction. *J Plast Reconstr Aesthet Surg* 2022; **75:** 2569–76.

164 Abdel-Wahab M, Gondhowiardjo SS, Rosa AA, et al. Global radiotherapy: current status and future directions–white paper. *JCO Glob Oncol* 2021; **7:** 827–42.

165 Earl H, Hiller L, Vallier AL, et al. Six versus 12 months' adjuvant trastuzumab in patients with HER2-positive early breast cancer: the PERSEPHONE non-inferiority RCT. *Health Technol Assess* 2020; **24:** 1–190.

166 Kirwan CC, Coles CE, Bliss J, PRIMTIME Protocol Working Group. It's PRIMETIME. Postoperative avoidance of radiotherapy: biomarker selection of women at very low risk of local recurrence. *Clin Oncol (R Coll Radiol)* 2016; **28:** 594–96.

167 Gentilini O, Veronesi U. Abandoning sentinel lymph node biopsy in early breast cancer? A new trial in progress at the European Institute of Oncology of Milan (SOUND: sentinel node vs observation after axillary ultrasound). *Breast* 2012; **21:** 678–81.

168 Fine RE, Gilmore RC, Dietz JR, et al. Cryoablation without excision for low-risk early-stage breast cancer: 3-year interim analysis of ipsilateral breast tumor recurrence in the ICE3 trial. *Ann Surg Oncol* 2021; **28:** 5525–34.

169 Morgan J, Potter S, Sharma N, et al. The SMALL trial: a big change for small breast cancers. *Clin Oncol (R Coll Radiol)* 2019; **31:** 659–63.

170 Morrow M, Khan AJ. Locoregional management after neoadjuvant chemotherapy. *J Clin Oncol* 2020; **38:** 2281–89.

171 Taylor C, McGale P, Probert J, et al. Breast cancer mortality in 500 000 women with early invasive breast cancer diagnosed in England, 1993–2015: population based observational cohort study. *BMJ* 2023; **381:** e074684.

172 Pilleron S, Sarfati D, Janssen-Heijnen M, et al. Global cancer incidence in older adults, 2012 and 2035: a population-based study. *Int J Cancer* 2019; **144:** 49–58.

173 Marmot MG, Altman DG, Cameron DA, Dewar JA, Thompson SG, Wilcox M. The benefits and harms of breast cancer screening: an independent review. *Br J Cancer* 2013; **108:** 2205–40.

174 Larsson S, Clawson J, Howard R. Value-based health care at an inflection point: a global agenda for the next decade. NEJM Catalyst [in ital] 2023: published online Feb 24. https://catalyst.nejm.org/doi/full/10.1056/CAT.22.0332.

175 Fayanju OM, Mayo TL, Spinks TE, et al. Value-based breast cancer care: a multidisciplinary approach for defining patient-centered outcomes. *Ann Surg Oncol* 2016; **23:** 2385–90.

176 van Egdom LSE, Lagendijk M, van der Kemp MH, et al. Implementation of value based breast cancer care. *Eur J Surg Oncol* 2019; **45:** 1163–70.

177 Porter ME. What is value in health care? *N Engl J Med* 2010; **363:** 2477–81.

178 Teisberg E, Wallace S, O'Hara S. Defining and implementing value-based health care: a strategic framework. *Acad Med* 2020; **95:** 682–85.

179 Beauchamp A, Batterham RW, Dodson S, et al. Systematic development and implementation of interventions to optimise health literacy and access (Ophelia). *BMC Public Health* 2017; **17:** 230.

180 Beauchamp A, Buchbinder R, Dodson S, et al. Distribution of health literacy strengths and weaknesses across socio-demographic groups: a cross-sectional survey using the Health Literacy Questionnaire (HLQ). *BMC Public Health* 2015; **15:** 678.

181 Garberis IJ, Saillard C, Drubay D, et al. 1124O prediction of distant relapse in patients with invasive breast cancer from deep learning models applied to digital pathology slides. *Ann Oncol* 2021; **32** (suppl 5): S921.

182 Torres FS, Akbar S, Raman S, et al. End-to-end non-small-cell lung cancer prognostication using deep learning applied to pretreatment computed tomography. *JCO Clin Cancer Inform* 2021; **5:** 1141–50.

183 Di Meglio A, Havas J, Gbenou AS, et al. Dynamics of long-term patient-reported quality of life and health behaviors after adjuvant breast cancer chemotherapy. *J Clin Oncol* 2022; **40:** 3190–204.

184 Bayoumy K, Gaber M, Elshafeey A, et al. Smart wearable devices in cardiovascular care: where we are and how to move forward. *Nat Rev Cardiol* 2021; **18:** 581–99.

185 Gresham G, Hendifar AE, Spiegel B, et al. Wearable activity monitors to assess performance status and predict clinical outcomes in advanced cancer patients. *NPJ Digit Med* 2018; **1:** 27.

186 Hasnain Z, Nilanon T, Li M, et al. Quantified kinematics to evaluate patient chemotherapy risks in clinic. *JCO Clin Cancer Inform* 2020; **4:** 583–601.

187 Ward WH, Meeker CR, Handorf E, et al. Feasibility of fitness tracker usage to assess activity level and toxicities in patients with colorectal cancer. *JCO Clin Cancer Inform* 2021; **5:** 125–33.

188 Smuck M, Odonkor CA, Wilt JK, Schmidt N, Swiernik MA. The emerging clinical role of wearables: factors for successful implementation in healthcare. *NPJ Digit Med* 2021; **4:** 45.

189 Acosta JN, Falcone GJ, Rajpurkar P, Topol EJ. Multimodal biomedical AI. *Nat Med* 2022; **28:** 1773–84.

190 ISRCTN Registry. ISRCTN81408940: tailoring treatment for HER2-positive early breast cancer. BMC. 2023. https://www.isrctn.com/ISRCTNISRCTN81408940 (accessed April 1, 2023).

191 Bizot A, Karimi M, Rassy E, et al. Multicenter evaluation of breast cancer patients' satisfaction and experience with oncology telemedicine visits during the COVID-19 pandemic. *Br J Cancer* 2021; **125:** 1486–93.

192 Cadili L, DeGirolamo K, Ma CS, et al. The breast cancer patient experience of telemedicine during COVID-19. *Ann Surg Oncol* 2022; **29:** 2244–52.

193 Curigliano G, Banerjee S, Cervantes A, et al. Managing cancer patients during the COVID-19 pandemic: an ESMO multidisciplinary expert consensus. *Ann Oncol* 2020; **31:** 1320–35.

194 Dietz JR, Moran MS, Isakoff SJ, et al. Recommendations for prioritization, treatment, and triage of breast cancer patients during the COVID-19 pandemic. The COVID-19 Pandemic Breast Cancer Consortium. *Breast Cancer Res Treat* 2020; **181:** 487–97.

195 de Azambuja E, Trapani D, Loibl S, et al. ESMO Management and treatment adapted recommendations in the COVID-19 era: breast cancer. *ESMO Open* 2020; **5** (suppl 3)**:** e000793.

196 Mink van der Molen DR, Bargon CA, Batenburg MCT, et al. The impact of the COVID-19 pandemic on perceived access to health care and preferences for health care provision in individuals (being) treated for breast cancer. *Breast Cancer Res Treat* 2022; **191:** 553–64.

197 Pennell NA, Dillmon M, Levit LA, et al. American Society of Clinical Oncology road to recovery report: learning from the COVID-19 experience to improve clinical research and cancer care. *J Clin Oncol* 2021; **39:** 155–69.

198 Johnson BA, Lindgren BR, Blaes AH, et al. The new normal? Patient satisfaction and usability of telemedicine in breast cancer care. *Ann Surg Oncol* 2021; **28:** 5668–76.

199 Meneses AdFP, Pimentel FF, da Cruz JPF, Candido Dos Reis FJ. Experiences of women with breast cancer using telehealth: a qualitative systematic review. *Clin Breast Cancer* 2023; **23:** 101–07.

200 Calip GS, Cohen A, Rohrer R, et al. Telemedicine use among patients with metastatic breast cancer during the COVID-19 pandemic: differences by race, age, and region. *Pharmacoepidemiol Drug Saf* 2023; **32:** 66–72.

201 Uemoto Y, Yamanaka T, Kataoka Y, et al. Efficacy of telemedicine using videoconferencing systems in outpatient care for patients with cancer: a systematic review and meta-analysis. *JCO Clin Cancer Inform* 2022; **6:** e2200084.

202 Miziara RA, Maesaka JY, Matsumoto DRM, et al. Teleoncology orientation of low-income breast cancer patients during the COVID-19 pandemic: feasibility and patient satisfaction. *Rev Bras Ginecol Obstet* 2021; **43:** 840–46.

203 Restrepo JG, Alarcón J, Hernández A, et al. Clinical outcomes in patients with solid tumors living in rural and urban areas followed via telemedicine: experience in a highly complex Latin American hospital. *BMC Cancer* 2023; **23:** 253.

204 Kunkler IH, Prescott RJ, Lee RJ, et al. TELEMAM: a cluster randomised trial to assess the use of telemedicine in multi-disciplinary breast cancer decision making. *Eur J Cancer* 2007; **43:** 2506–14.

205 Beaver K, Tysver-Robinson D, Campbell M, et al. Comparing hospital and telephone follow-up after treatment for breast cancer: randomised equivalence trial. *BMJ* 2009; **338:** a3147.

206 Stavrou E, Qiu J, Zafar A, et al. Breast medical oncologists' perspectives of telemedicine for breast cancer care: a survey study. *JCO Oncol Pract* 2022; **18:** e1447–53.

207 Malek Pascha VA, Sun L, Gilardino R, Legood R. Telemammography for breast cancer screening: a cost-effective approach in Argentina. *BMJ Health Care Inform* 2021; **28:** 100351.

208 Johnston K. "From the technology came the idea": safe implementation and operation of a high quality teleradiology model increasing access to timely breast cancer assessment services for women in rural Australia. *BMC Health Serv Res* 2020; **20:** 1103.

209 Krzyzanowska MK, Julian JA, Gu CS, et al. Remote, proactive, telephone based management of toxicity in outpatients during adjuvant or neoadjuvant chemotherapy for early stage breast cancer: pragmatic, cluster randomised trial. *BMJ* 2021; **375:** e066588.

210 Mir O, Ferrua M, Fourcade A, et al. Intervention combining nurse navigators (NNs) and a mobile application versus standard of care (SOC) in cancer patients (pts) treated with oral anticancer agents (OAA): results of CapRI, a single-center, randomized phase III trial. *J Clin Oncol* 2020; **38:** 2000.

211 Absolom K, Warrington L, Hudson E, et al. Phase III randomized controlled trial of eRAPID: eHealth intervention during chemotherapy. *J Clin Oncol* 2021; **39:** 734–47.

212 Basch E, Deal AM, Kris MG, et al. Symptom monitoring with patient-reported outcomes during routine cancer treatment: a randomized controlled trial. *J Clin Oncol* 2016; **34:** 557–65.

213 Basch E, Schrag D, Henson S, et al. Effect of electronic symptom monitoring on patient-reported outcomes among patients with metastatic cancer: a randomized clinical trial. *JAMA* 2022; **327:** 2413–22.

214 Maguire R, McCann L, Kotronoulas G, et al. Real time remote symptom monitoring during chemotherapy for cancer: European multicentre randomised controlled trial (eSMART). *BMJ* 2021; **374:** n1647.

215 Harbeck N, Fasching PA, Wuerstlein R, et al. Significantly longer time to deterioration of quality of life due to CANKADO PRO-React eHealth support in HR+ HER2- metastatic breast cancer patients receiving palbociclib and endocrine therapy: primary outcome analysis of the multicenter randomized AGO-B WSG PreCycle trial. *Ann Oncol* 2023; **34:** 660–69.

216 Di Maio M, Basch E, Denis F, et al. The role of patient-reported outcome measures in the continuum of cancer clinical care: ESMO Clinical Practice Guideline. *Ann Oncol* 2022; **33:** 878–92.

217 Patt D, Wilfong L, Hudson KE, et al. Implementation of electronic patient-reported outcomes for symptom monitoring in a large multisite community oncology practice: dancing the Texas two-step through a pandemic. *JCO Clin Cancer Inform* 2021; **5:** 615–21.

218 Alfano CM, Oeffinger K, Sanft T, Tortorella B. Engaging TEAM medicine in patient care: redefining cancer survivorship from diagnosis. *Am Soc Clin Oncol Educ Book* 2022; **42:** 1–11.

219 Chan RJ, Crichton M, Crawford-Williams F, et al. The efficacy, challenges, and facilitators of telemedicine in post-treatment cancer survivorship care: an overview of systematic reviews. *Ann Oncol* 2021; **32:** 1552–70.

220 Singleton AC, Raeside R, Hyun KK, et al. Electronic health interventions for patients with breast cancer: systematic review and meta-analyses. *J Clin Oncol* 2022; **40:** 2257–70.

221 Abrahams HJG, Gielissen MFM, Donders RRT, et al. The efficacy of internet-based cognitive behavioral therapy for severely fatigued survivors of breast cancer compared with care as usual: a randomized controlled trial. *Cancer* 2017; **123:** 3825–34.

222 Zachariae R, Amidi A, Damholdt MF, et al. Internet-delivered cognitive-behavioral therapy for insomnia in breast cancer survivors: a randomized controlled trial. *J Natl Cancer Inst* 2018; **110:** 880–87.

223 Akechi T, Yamaguchi T, Uchida M, et al. Smartphone psychotherapy reduces fear of cancer recurrence among breast cancer survivors: a fully decentralized randomized controlled clinical trial (J-SUPPORT 1703 study). *J Clin Oncol* 2023; **41:** 1069–78.

224 Compen F, Bisseling E, Schellekens M, et al. Face-to-face and internet-based mindfulness-based cognitive therapy compared with treatment as usual in reducing psychological distress in patients with cancer: a multicenter randomized controlled trial. *J Clin Oncol* 2018; **36:** 2413–21.

225 Bray VJ, Dhillon HM, Bell ML, et al. Evaluation of a web-based cognitive rehabilitation program in cancer survivors reporting cognitive symptoms after chemotherapy. *J Clin Oncol* 2017; **35:** 217–25.

226 Goodwin PJ, Segal RJ, Vallis M, et al. The LISA randomized trial of a weight loss intervention in postmenopausal breast cancer. *NPJ Breast Cancer* 2020; **6:** 6.

227 Santa-Maria CA, Coughlin JW, Sharma D, et al. The effects of a remote-based weight loss program on adipocytokines, metabolic markers, and telomere length in breast cancer survivors: the POWER-Remote trial. *Clin Cancer Res* 2020; **26:** 3024–34.

228 Webb J, Fife-Schaw C, Ogden J. A randomised control trial and cost-consequence analysis to examine the effects of a print-based intervention supported by internet tools on the physical activity of UK cancer survivors. *Public Health* 2019; **171:** 106–15.

229 Lozano-Lozano M, Martín-Martín L, Galiano-Castillo N, et al. Mobile health and supervised rehabilitation versus mobile health alone in breast cancer survivors: randomized controlled trial. *Ann Phys Rehabil Med* 2020; **63:** 316–24.

230 Abernethy A, Adams A, Barrett M, et al. The promise of digital health: then, now, and the future. *NAM Perspect* 2022; **2022:** 10.31478/202206e.

231 Leach CR, Hudson SV, Diefenbach MA, et al. Cancer health self-efficacy improvement in a randomized controlled trial. *Cancer* 2022; **128:** 597–605.

232 Cheikh-Moussa K, Mira JJ, Orozco-Beltran D. Improving engagement among patients with chronic cardiometabolic conditions using mHealth: critical review of reviews. *JMIR Mhealth Uhealth* 2020; **8:** e15446.

233 Atasoy H, Greenwood BN, McCullough JS. The digitization of patient care: a review of the effects of electronic health records on health care quality and utilization. *Annu Rev Public Health* 2019; **40:** 487–500.

234 Hammer RD, Fowler D, Sheets LR, Siadimas A, Guo C, Prime MS. Digital tumor board solutions have significant impact on case preparation. *JCO Clin Cancer Inform* 2020; **4:** 757–68.

235 Nobori A, Jumniensuk C, Chen X, et al. Electronic health record-integrated tumor board application to save preparation time and reduce errors. *JCO Clin Cancer Inform* 2022; **6:** e2100142.

236 Bayard S, Fasano G, Tamimi RM, Oh PS. Leveraging electronic health records to address breast cancer disparities. *Curr Breast Cancer Rep* 2022; **14:** 199–204.

237 Wardley A, Canon JL, Elsten L, et al. Flexible care in breast cancer. *ESMO Open* 2021; **6:** 100007.

238 Arora S, Ryals C, Rodriguez JA, Byers E, Clewett E. Leveraging digital technology to reduce cancer care inequities. *Am Soc Clin Oncol Educ Book* 2022; **42:** 1–8.

239 Irwin KE, Ko N, Walsh EP, et al. Developing a virtual equity hub: adapting the tumor board model for equity in cancer care. *Oncologist* 2022; **27:** 518–24.

240 Struminger BB, Arora S. Leveraging telehealth to improve health care access in rural america: it takes more than bandwidth. *Ann Intern Med* 2019; **171:** 376–77.

241 Esteso F, Tissera NS, O'Connor JM, et al. Implementation of a virtual multicenter gastrointestinal tumor board to reduce cancer disparities in Argentina. *World J Clin Oncol* 2022; **13:** 423–28.

242 Fokom Domgue J, Pande M, Yu R, et al. Development, implementation, and evaluation of a distance learning and telementoring program for cervical cancer prevention in Cameroon. *JAMA Netw Open* 2022; **5:** e2240801.

243 Paterson C, Bacon R, Dwyer R, et al. The role of telehealth during the COVID-19 pandemic across the interdisciplinary cancer team: implications for practice. *Semin Oncol Nurs* 2020; **36:** 151090.

244 Kickbusch I, Piselli D, Agrawal A, et al. The *Lancet* and *Financial Times* Commission on governing health futures 2030: growing up in a digital world. *Lancet* 2021; 398: 1727–76.

245 Cykert S, Eng E, Manning MA, et al. A multi-faceted intervention aimed at Black–White disparities in the treatment of early stage cancers: the ACCURE Pragmatic Quality Improvement trial. *J Natl Med Assoc* 2020; **112:** 468–77.

246 Gerbasi A, Clementi G, Corsi F, et al. DeepMiCa: automatic segmentation and classification of breast microcalcifications from mammograms. *Comput Methods Programs Biomed* 2023; **235:** 107483.

247 Zhou W, Zhang X, Ding J, Deng L, Cheng G, Wang X. Improved breast lesion detection in mammogram images using a deep neural network. *Diagn Interv Radiol* 2023; **29:** 588–95.

248 Koch HW, Larsen M, Bartsch H, Kurz KD, Hofvind S. Artificial intelligence in BreastScreen Norway: a retrospective analysis of a cancer-enriched sample including 1254 breast cancer cases. *Eur Radiol* 2023; **33:** 3735–43.

249 Albusayli R, Graham JD, Pathmanathan N, et al. Artificial intelligence-based digital scores of stromal tumour-infiltrating lymphocytes and tumour-associated stroma predict disease-specific survival in triple-negative breast cancer. *J Pathol* 2023; **260:** 32–42.

250 Inan OT, Tenaerts P, Prindiville SA, et al. Digitizing clinical trials. *NPJ Digit Med* 2020; **3:** 101.

251 Guerra CE, Fleury ME, Byatt LP, Lian T, Pierce L. Strategies to advance equity in cancer clinical trials. *Am Soc Clin Oncol Educ Book* 2022; **42:** 1–11.

252 Presti D, Havas J, Soldato D, et al. Factors associated with enrolment in clinical trials among women with early-stage breast cancer. *ESMO Open* 2022; **7:** 100513.

253 Frérot M, Jooste V, Binquet C, Fournel I, Bedenne L, Bouvier AM. Factors influencing inclusion in digestive cancer clinical trials: a population-based study. *Dig Liver Dis* 2015; **47:** 891–96.

254 Ousseine YM, Bouhnik A-D, Mancini J. Health literacy and clinical trial participation in French cancer patients: a national survey. *Curr Oncol* 2022; **29:** 3118–29.

255 Horvat L, Horey D, Romios P, Kis-Rigo J. Cultural competence education for health professionals. *Cochrane Database Syst Rev* 2014; **2014:** CD009405.

256 Barrett NJ, Boehmer L, Schrag J, et al. An assessment of the feasibility and utility of an ACCC-ASCO implicit bias training program to enhance racial and ethnic diversity in cancer clinical trials. *JCO Oncol Pract* 2023; **19:** e570–80.

257 Guerra C, Pressman A, Hurley P, et al. Increasing racial and ethnic equity, diversity, and inclusion in cancer treatment trials: evaluation of an ASCO-association of community cancer centers site self-assessment. *JCO Oncol Pract* 2023; **19:** e581–88.

258 Beck JT, Rammage M, Jackson GP, et al. Artificial intelligence tool for optimizing eligibility screening for clinical trials in a large community cancer center. *JCO Clin Cancer Inform* 2020; **4:** 50–59.

259 Delorme J, Charvet V, Wartelle M, et al. Natural language processing for patient selection in phase I or II oncology clinical trials. *JCO Clin Cancer Inform* 2021; **5:** 709–18.

260 Tan RKJ. Digital approaches to enhancing community engagement in clinical trials. *NPJ Digit Med* 2022; **5:** 37.

261 Perez MV, Mahaffey KW, Hedlin H, et al. Large-scale assessment of a smartwatch to identify atrial fibrillation. *N Engl J Med* 2019; **381:** 1909–17.

262 Offodile AC 2nd, Seitz AJ, Peterson SK. Digital health navigation: an enabling infrastructure for optimizing and integrating virtual care into oncology practice. *JCO Clin Cancer Inform* 2021; **5:** 1151–54.

263 Lord SJ, Bahlmann K, O'Connell DL, et al. De novo and recurrent metastatic breast cancer - a systematic review of population-level changes in survival since 1995. *EClinicalMedicine* 2022; **44:** 101282.

264 Breast Cancer Foundation New Zealand. I'm still here. Insights into living – and dying – with advanced breast cancer in New Zealand: executive summary. 2018. https://www.breastcancerfoundation.org.nz/images/assets/21894/1/bcfnz-abc-report-2018-executive-summary.pdf (accessed Nov 1, 2022).

265 Debiasi M, Reinert T, Kaliks R, et al. Estimation of premature deaths from lack of access to anti-HER2 therapy for advanced breast cancer in the Brazilian public health system. *J Glob Oncol* 2016; **3:** 201–07.

266 Li J, Wang S, Wang Y, et al. Disparities of trastuzumab use in resource-limited or resource-abundant regions and its survival benefit on HER2 positive breast cancer: a real-world study from China. *Oncologist* 2017; **22:** 1333–38.

267 Blackwell K, Gligorov J, Jacobs I, Twelves C. The global need for a trastuzumab biosimilar for patients with HER2-positive breast cancer. *Clin Breast Cancer* 2018; **18:** 95–113.

268 Ferrant G, Pesando LM, Nowacka K. Unpaid care work: the missing link in the analysis of gender gaps in labour outcomes. Organisation for Economic Cooperation and Development. 2014. https://www.oecd.org/dev/development-gender/Unpaid_care_work.pdf (accessed Jan 8, 2023).

268 Trogdon JG, Liu X, Reeder-Hayes KE, Rotter J, Ekwueme DU, Wheeler SB. Productivity costs associated with metastatic breast cancer in younger, midlife, and older women. *Cancer* 2020; **126:** 4118–25.

270 Matos L, Borges M, Oliveira AT, et al. The impact on productivity costs of reducing unemployment in patients with advanced breast cancer: a model estimation based on a Portuguese nationwide observational study. *Breast* 2023; **71** (suppl 1)**:** S28 (abstr OR46).

271 ABC Global Alliance. Advanced breast cancer (ABC) Global Charter. ABC Global Alliance. 2022. https://assets-global.website-files.com/636aa6281af0a10862074bc1/6385dcbb2a42a33d6558ee0b_ABC%20Global%20Charter%20Booklet%20A5%202022%20web%20version.pdf (accessed Jan 8, 2023).

272 Cardoso F, Spence D, Mertz S, et al. Global analysis of advanced/metastatic breast cancer: decade report (2005-2015). *Breast* 2018; **39:** 131–38.

273 McKenzie F, Zietsman A, Galukande M, et al. Drivers of advanced stage at breast cancer diagnosis in the multicountry African breast cancer - disparities in outcomes (ABC-DO) study. *Int J Cancer* 2018; **142:** 1568–79.

274 Benitez Fuentes JD, Morgan E, de Luna Aguilar A, et al. Global stage distribution of breast cancer at diagnosis: a systematic review and meta-analysis. *JAMA Oncol* 2024; **10:** 71–78.

275 McCormack V, McKenzie F, Foerster M, et al. Breast cancer survival and survival gap apportionment in sub-Saharan Africa (ABC-DO): a prospective cohort study. *Lancet Glob Health* 2020; **8:** e1203–12.

276 Gogia A, Deo SVS, Sharma D, et al. Clinicopathologic characteristics and treatment outcomes of patients with up-front metastatic breast cancer: single-center experience in India. *J Glob Oncol* 2019; **5:** 1–9.

277 Deluche E, Antoine A, Bachelot T, et al. Contemporary outcomes of metastatic breast cancer among 22 000 women from the multicentre ESME cohort 2008–2016. *Eur J Cancer* 2020; **129:** 60–70.

278 Swain SM, Miles D, Kim SB, et al. Pertuzumab, trastuzumab, and docetaxel for HER2-positive metastatic breast cancer (CLEOPATRA): end-of-study results from a double-blind, randomised, placebo-controlled, phase 3 study. *Lancet Oncol* 2020; **21:** 519–30.

279 Hortobagyi GN, Stemmer SM, Burris HA, et al. Overall survival with ribociclib plus letrozole in advanced breast cancer. *N Engl J Med* 2022; **386:** 942–50.

280 Slamon DJ, Neven P, Chia S, et al. Ribociclib plus fulvestrant for postmenopausal women with hormone receptor-positive, human epidermal growth factor receptor 2-negative advanced breast cancer in the phase III randomized MONALEESA-3 trial: updated overall survival. *Ann Oncol* 2021; **32:** 1015–24.

281 Cherny NI, Dafni U, Bogaerts J, et al. ESMO-Magnitude of Clinical Benefit Scale version 1.1. *Ann Oncol* 2017; **28:** 2340–66.

282 Schnipper LE, Davidson NE, Wollins DS, et al. American Society of Clinical Oncology Statement: a conceptual framework to assess the value of cancer treatment options. *J Clin Oncol* 2015; **33:** 2563–77.

283 Caswell-Jin JL, Sun L, Munoz D, et al. Contributions of screening, early-stage treatment, and metastatic treatment to breast cancer mortality reduction by molecular subtype in U.S. women, 2000–2017. *J Clin Oncol* 2022; **40** (supp 16): 1008.

284 Temel JS, Greer JA, El-Jawahri A, et al. Effects of early integrated palliative care in patients with lung and GI cancer: a randomized clinical trial. *J Clin Oncol* 2017; **35:** 834–41.

285 Ferrell BR, Temel JS, Temin S, et al. Integration of palliative care into standard oncology care: American Society of Clinical Oncology Clinical Practice Guideline update. *J Clin Oncol* 2017; **35:** 96–112.

286 Dans M, Kutner JS, Agarwal R, et al. NCCN Guidelines Insights: palliative care, version 2.2021. *J Natl Compr Canc Netw* 2021; **19:** 780–88.

287 Cardoso F, Paluch-Shimon S, Senkus E, et al. 5th ESO–ESMO international consensus guidelines for advanced breast cancer (ABC 5). *Ann Oncol* 2020; **31:** 1623–49.

288 Cavallo J. Understanding oncologists' perceptions about palliative care and the barriers preventing its use. The ASCO Post, May 25, 2022. https://ascopost.com/issues/may-25-2022/understanding-oncologists-perceptions-about-palliative-care-and-the-barriers-preventing-its-use/ (accessed Jan 8, 2023).

289 de Ligt KM, de Rooij BH, Hedayati E, et al. International development of a patient-centered core outcome set for assessing health-related quality of life in metastatic breast cancer patients. *JAMA Oncol* 2023; **198:** 265–81.

290 Jencks MK. A view from the front line. London: Maggie's Cancer Caring Centre, 1995.

291 Breast Cancer Aotearoa Coalition. Striving for better care. 2022. https://www.breastcancer.org.nz/content/striving-better-care (accessed Jan 8, 2023).

292 Kuper-Hommel MJJ, Little Z, Gautier A. New Zealand experience with implementation of the ESO–ESMO consensus guidelines for advanced breast cancer–report of achievements and lessons learned. *Breast* 2022; **63:** 108–12.

293 Jonker L, Fisher SJ. The correlation between National Health Service trusts' clinical trial activity and both mortality rates and care quality commission ratings: a retrospective cross-sectional study. *Public Health* 2018; **157:** 1–6.

294 Wells JC, Sharma S, Del Paggio JC, et al. An analysis of contemporary oncology randomized clinical trials from low/middle-income vs high-income countries. *JAMA Oncol* 2021; **7:** 379–85.

295 Hamel LM, Penner LA, Albrecht TL, Heath E, Gwede CK, Eggly S. Barriers to clinical trial enrollment in racial and ethnic minority patients with cancer. *Cancer Control* 2016; **23:** 327–37.

296 Kwiatkowski K, Coe K, Bailar JC, Swanson GM. Inclusion of minorities and women in cancer clinical trials, a decade later: have we improved? *Cancer* 2013; **119:** 2956–63.

297 Biganzoli L, Cardoso F, Beishon M, et al. The requirements of a specialist breast centre. *Breast* 2020; **51:** 65–84.

298 Biganzoli L, Marotti L, Hart CD, et al. Quality indicators in breast cancer care: an update from the EUSOMA working group. *Eur J Cancer* 2017; **86:** 59–81.

299 Cardoso F, McCartney A, Ponti A, et al. European Society of Breast Cancer/Advanced Breast Cancer Global Alliance quality indicators for metastatic breast cancer care. *Eur J Cancer* 2023; **187:** 105–13.

300 Ricci-Cabello I, Vásquez-Mejía A, Canelo-Aybar C, et al. Adherence to breast cancer guidelines is associated with better survival outcomes: a systematic review and meta-analysis of observational studies in EU countries. *BMC Health Serv Res* 2020; **20:** 920.

301 Hébert-Croteau N, Brisson J, Latreille J, Rivard M, Abdelaziz N, Martin G. Compliance with consensus recommendations for systemic therapy is associated with improved survival of women with node-negative breast cancer. *J Clin Oncol* 2004; **22:** 3685–93.

302 Song CV, Yip CH, Mohd Taib NA, et al. Association between adherence to clinical practice guidelines for adjuvant therapy for breast cancer and survival in a resource-limited setting. *JCO Glob Oncol* 2022; **8:** e2100314.

303 Trapani D, Douillard JY, Winer EP, et al. The global landscape of treatment standards for breast cancer. *J Natl Cancer Inst* 2021; **113:** 1143–55.

304 Hébert-Croteau N, Brisson J, Latreille J, Rivard M, Abdelaziz N, Martin G. Compliance with consensus recommendations for systemic therapy is associated with improved survival of women with node-negative breast cancer. *J Clin Oncol* 2004; **22:** 3685–93.

305 Foerster M, McCormack V, Anderson BO, et al. Treatment guideline concordance, initiation, and abandonment in patients with non-metastatic breast cancer from the African Breast Cancer-Disparities in Outcomes (ABC-DO) cohort in sub-Saharan Africa: a prospective cohort study. *Lancet Oncol* 2022; **23:** 729–38.

306 Bestvina CM, Zullig LL, Yousuf Zafar S. The implications of out-of-pocket cost of cancer treatment in the USA: a critical appraisal of the literature. *Future Oncol* 2014; **10:** 2189–99.

307 Nyblade L, Stockton M, Travasso S, Krishnan S. A qualitative exploration of cervical and breast cancer stigma in Karnataka, India. *BMC Womens Health* 2017; **17:** 58.

308 O'Shaughnessy J. Extending survival with chemotherapy in metastatic breast cancer. *Oncologist* 2005; **10** (suppl 3)**:** 20–29.

309 Villarreal-Garza C, Mesa-Chavez F, Lopez-Martinez EA, et al. Gaps in knowledge and understanding of patients with metastatic breast cancer in Mexico. *Cancer Control* 2020; **27:** 1073274820920637.

310 van Brakel WH, Cataldo J, Grover S, et al. Out of the silos: identifying cross-cutting features of health-related stigma to advance measurement and intervention. *BMC Med* 2019; **17:** 13.

311 Weiss MG, Ramakrishna J, Somma D. Health-related stigma: rethinking concepts and interventions. *Psychol Health Med* 2006; **11:** 277–87.

312 Scambler G. Stigma and disease: changing paradigms. *Lancet* 1998; **352:** 1054–55.

313 Link BG, Phelan JC. Conceptualizing stigma. *Annu Rev Sociol* 2001; **27:** 363–85.

314 Pescosolido BA, Martin JK, Lang A, Olafsdottir S. Rethinking theoretical approaches to stigma: a framework integrating normative influences on stigma (FINIS). *Soc Sci Med* 2008; **67:** 431–40.

315 Weiss MG. Stigma and the social burden of neglected tropical diseases. *PLoS Negl Trop Dis* 2008; **2:** e237.

316 Heijnders M, Van Der Meij S. The fight against stigma: an overview of stigma-reduction strategies and interventions. *Psychol Health Med* 2006; **11:** 353–63.

317 Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. *CA Cancer J Clin* 2020; **70:** 7–30.

318 Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2018; **68:** 394–424.

319 Duggan C, Trapani D, Ilbawi AM, et al. National health system characteristics, breast cancer stage at diagnosis, and breast cancer mortality: a population-based analysis. *Lancet Oncol* 2021; **22:** 1632–42.

320 Anderson BO, Cazap E, El Saghir NS, et al. Optimisation of breast cancer management in low-resource and middle-resource countries: executive summary of the Breast Health Global Initiative consensus, 2010. *Lancet Oncol* 2011; **12:** 387–98.

321 Allemani C, Matsuda T, Di Carlo V, et al. Global surveillance of trends in cancer survival 2000-14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. *Lancet* 2018; **391:** 1023–75.

322 WHO. Global breast cancer initiative implementation framework: assessing, strengthening and scaling up of services for the early detection and management of breast cancer. World Health Organization. 2023. https://www.who.int/initiatives/global-breast-cancer-initiative (accessed April 4, 2024).

323 Lauby-Secretan B, Scoccianti C, Loomis D, et al. Breast-cancer screening—viewpoint of the IARC Working Group. *N Engl J Med* 2015; **372:** 2353–58.

324 Harford J, Azavedo E, Fischietto M. Guideline implementation for breast healthcare in low- and middle-income countries: breast healthcare program resource allocation. *Cancer* 2008; **113** (suppl 8)**:** 2282–96.

325 Anderson BO, Ilbawi AM, Fidarova E, et al. The Global Breast Cancer Initiative: a strategic collaboration to strengthen health care for non-communicable diseases. *Lancet Oncol* 2021; **22:** 578–81.

326 Shyyan R, Sener SF, Anderson BO, et al. Guideline implementation for breast healthcare in low- and middle-income countries: diagnosis resource allocation. *Cancer* 2008; **113** (suppl 8): 2257–68.

327 Richards MA, Westcombe AM, Love SB, Littlejohns P, Ramirez AJ. Influence of delay on survival in patients with breast cancer: a systematic review. *Lancet* 1999; **353:** 1119–26.

328 Bukowski A, Gioia S, Chavarri-Guerra Y, et al. Patient navigation to improve access to breast cancer care in Brazil. *J Glob Oncol* 2016; **3:** 433–37.

329 Berry DA, Cronin KA, Plevritis SK, et al. Effect of screening and adjuvant therapy on mortality from breast cancer. *N Engl J Med* 2005; **353:** 1784–92.

330 Goel N, Lubarsky M, Hernandez A, et al. Unmet social needs on breast cancer screening utilization and stage at presentation. *JAMA Netw Open* 2024; **7:** e2355301.

331 Health Leads. The Health Leads Screening Toolkit. Health Leads. 2019. https://healthleadsusa.org/news-resources/the-health-leads-screening-toolkit/ (accessed Oct 22, 2023).

332 Gray E, Figueroa JD, Oikonomidou O, et al. Variation in chemotherapy prescribing rates and mortality in early breast cancer over two decades: a national data linkage study. *ESMO Open* 2021; **6:** 100331.

333 van Maaren MC, Rachet B, Sonke GS, et al. Socioeconomic status and its relation with breast cancer recurrence and survival in young women in the Netherlands. *Cancer Epidemiol* 2022; **77:** 102118.

334 Dasgupta P, Baade PD, Youlden DR, et al. Variations in outcomes by residential location for women with breast cancer: a systematic review. *BMJ Open* 2018; **8:** e019050.

335 Duggan C, Dvaladze A, Rositch AF, et al. The Breast Health Global Initiative 2018 Global Summit on Improving Breast Healthcare Through Resource—stratified phased implementation: methods and overview. *Cancer* 2020; **126** (suppl 10)**:** 2339–52.

336 The World Bank. Tackling non-communicable diseases in Kenya: economic evaluation of breast and cervical cancer control interventions in Kenya. Washington, DC: The World Bank, 2022. https://documents1.worldbank.org/curated/en/458921500385921881/pdf/IL-AISPID-CP-P164301-07-18-2017-1500385913011.pdf (accessed April 1, 2023).

337 Wilson ML, Fleming KA, Kuti MA, Looi LM, Lago N, Ru K. Access to pathology and laboratory medicine services: a crucial gap. *Lancet* 2018; **391:** 1927–38.

338 Mugabe M, Andrici J, Ho K. Comparing the Gene Xpert breast cancer RUO mRNA assay with ER and HER2 immunohistochemistry (IHC) for rapid biomarker analysis. *Mod Pathol* 2017; **30:** 60A (abstr 232).

339 Wu NC, Wong W, Ho KE, et al. Comparison of central laboratory assessments of ER, PR, HER2, and Ki67 by IHC/FISH and the corresponding mRNAs (ESR1, PGR, ERBB2, and MKi67) by RT-qPCR on an automated, broadly deployed diagnostic platform. *Breast Cancer Res Treat* 2018; **172:** 327–38.

340 Kimambo A, Ng D. Validation of the GeneXpert breast cancer STRAT4 assay for rapid analysis of breast cancer biomarker status from fine-needle aspiration biopsies in Tanzania (GX-BCB): preliminary results. *Am J Clin Pathol* 2018; **150** (suppl 1)**:** S138.

341 Denny L, de Sanjose S, Mutebi M, et al. Interventions to close the divide for women with breast and cervical cancer between low-income and middle-income countries and high-income countries. *Lancet* 2017; **389:** 861–70.

341 Black E, Richmond R. Improving early detection of breast cancer in sub-Saharan Africa: why mammography may not be the way forward. *Global Health* 2019; **15:** 3.

343 Catarino R, Petignat P, Dongui G, Vassilakos P. Cervical cancer screening in developing countries at a crossroad: emerging technologies and policy choices. *World J Clin Oncol* 2015; **6:** 281–90.

344 Symmans WF, Peintinger F, Hatzis C, et al. Measurement of residual breast cancer burden to predict survival after neoadjuvant chemotherapy. *J Clin Oncol* 2007; **25:** 4414–22.

345 Symmans WF, Yau C, Chen YY, et al. Assessment of residual cancer burden and event-free survival in neoadjuvant treatment for high-risk breast cancer: an analysis of data from the I-SPY2 randomized clinical trial. *JAMA Oncol* 2021; **7:** 1654–63.

346 Yau C, Osdoit M, van der Noordaa M, et al. Residual cancer burden after neoadjuvant chemotherapy and long-term survival outcomes in breast cancer: a multicentre pooled analysis of 5161 patients. *Lancet Oncol* 2022; **23:** 149–60.

347 Miller ME, Patil N, Li P, et al. Hospital system adoption of magnetic seeds for wireless breast and lymph node localization. *Ann Surg Oncol* 2021; **28:** 3223–29.

348 Serventi F, Musyoka A, Saunders J, et al. NOHA: a promising biomarker for determining estrogen receptor status among patients with breast cancer in resource-constrained settings. *JCO Glob Oncol* 2022; **8:** e2200192.

349 Banys-Paluchowski M, Fehm TN, Grimm-Glang D, Rody A, Krawczyk N. Liquid biopsy in metastatic breast cancer: current role of circulating tumor cells and circulating tumor DNA. *Oncol Res Treat* 2022; **45:** 4–11.

350 André F, Ciruelos E, Rubovszky G, et al. Alpelisib for *PIK3CA*-mutated, hormone receptor-positive advanced breast cancer. *N Engl J Med* 2019; **380:** 1929–40.

351 Autier P, Héry C, Haukka J, Boniol M, Byrnes G. Advanced breast cancer and breast cancer mortality in randomized controlled trials on mammography screening. *J Clin Oncol* 2009; **27:** 5919–23.

352 Chávarri-Guerra Y, Villarreal-Garza C, Liedke PE, et al. Breast cancer in Mexico: a growing challenge to health and the health system. *Lancet Oncol* 2012; **13:** e335–43.

353 Tamez-Salazar J, Mireles-Aguilar T, de la Garza-Ramos C, et al. Prioritization of patients with abnormal breast findings in the Alerta Rosa Navigation Program to reduce diagnostic delays. *Oncologist* 2020; **25:** 1047–54.

354 Perez-Bustos AH, Orozco-Urdaneta M, Erazo R, et al. A patient navigation initiative to improve access to breast cancer care in Cali, Colombia. *Cancer Rep* 2022; **5:** e1564.

355 Imkampe A, Bendall S, Chianakwalam C. Two-week rule: has prioritisation of breast referrals by general practitioners improved? *Breast* 2006; **15:** 654–58.

356 Cortes J, Perez-García JM, Llombart-Cussac A, et al. Enhancing global access to cancer medicines. *CA Cancer J Clin* 2020; **70:** 105–24.

357 IQVIA, MIDAS. Geographical breakdown (by main markets) of sales of new medicines launched during the period 2016–2021. European Federation of Pharmaceutical Industries and Associations. 2022. https://www.efpia.eu/publications/data-center/the-pharma-industry-in-figures-economy/geographical-breakdown-of-sales-of-new-medicines (accessed Dec 13, 2023).

358 Miljkovic MD, Tuia JE, Olivier T, Haslam A, Prasad V. Association between US drug price and measures of efficacy for oncology drugs approved by the US Food and Drug Administration from 2015 to 2020. *JAMA Intern Med* 2022; **182:** 1319–20.

359 Tay-Teo K, Ilbawi A, Hill SR. Comparison of sales income and research and development costs for FDA-approved cancer drugs sold by originator drug companies. *JAMA Netw Open* 2019; **2:** e186875.

360 Cancer Research UK. Outcome-based payment for cancer drugs. 2023. https://www.cancerresearchuk.org/about-us/we-develop-policy/our-policy-on-access-to-cancer-treatments/outcome-based-payment-for-cancer-drugs (accessed Dec 13, 2023).

361 Sleeman KE, Gomes B, de Brito M, Shamieh O, Harding R. The burden of serious health-related suffering among cancer decedents: global projections study to 2060. *Palliat Med* 2021; **35:** 231–35.

362 Hubinette M, Dobson S, Scott I, Sherbino J. Health advocacy. *Med Teach* 2017; **39:** 128–35.

363 Maxwell GL. The state of advocacy in cancer. *Gynecol Oncol* 2015; **139:** 573–79.

364 Janamian T, Greco M, Cosgriff D, Baker L, Dawda P. Activating people to partner in health and self-care: use of the Patient Activation Measure. *Med J Aust* 2022; **216** (suppl 10): S5–8.

365 Morhason-Bello IO, Odedina F, Rebbeck TR, et al. Challenges and opportunities in cancer control in Africa: a perspective from the African Organisation for Research and Training in Cancer. *Lancet Oncol* 2013; **14:** e142–51.

366 Odedina FT, Asante-Shongwe K, Kandusi EJ, et al. The African cancer advocacy consortium: shaping the path for advocacy in Africa. *Infect Agent Cancer* 2013; **8** (suppl 1): S8.

367 Connor SR. Global atlas of palliative care, 2nd edn. Worldwide Hospice Palliative Care Alliance, World Health Organisation. 2021. http://www.thewhpca.org/resources/global-atlas-on-end-of-life-care (accessed Jan 3, 2023).

368 Sun H, Lv H, Zeng H, Niu L, Yan M. Distress thermometer in breast cancer: systematic review and meta-analysis. *BMJ Support Palliat Care* 2022; **12:** 245–52.

369 Chen X, Wu C, Bai D, et al. Health-related quality of life in breast cancer patients in Asia: a meta-analysis and systematic review. *Front Oncol* 2022; **12:** 954179.

370 Gonzalez L, Bardach A, Palacios A, et al. Health-related quality of life in patients with breast cancer in Latin America and the Caribbean: a systematic review and meta-analysis. *Oncologist* 2021; **26:** e794–806.

371 Rezagholi P, Abdi K, Barzanji A, et al. Prevelence of depression in Iranian women with breast cancer: a systematic review and meta-analysis. *Przegl Epidemiol* 2022; **76:** 29–36.

372 Leysen L, Lahousse A, Nijs J, et al. Prevalence and risk factors of sleep disturbances in breast cancersurvivors: systematic review and meta-analyses. *Support Care Cancer* 2019; **27:** 4401–33.

373 Liu L, Wu Y, Cong W, Hu M, Li X, Zhou C. Experience of women with breast cancer undergoing chemotherapy: a systematic review of qualitative research. *Qual Life Res* 2021; **30:** 1249–65.

374 Roberts F, Andrewes T. Exploring the psychological impacts of a gestational cancer diagnosis on women: a literature review. *Br J Nurs* 2022; **31:** S26–33.

375 Fortin J, Leblanc M, Elgbeili G, Cordova MJ, Marin MF, Brunet A. The mental health impacts of receiving a breast cancer diagnosis: a meta-analysis. *Br J Cancer* 2021; **125:** 1582–92.

376 Durosini I, Triberti S, Savioni L, Sebri V, Pravettoni G. The role of emotion-related abilities in the quality of life of breast cancer survivors: a systematic review. *Int J Environ Res Public Health* 2022; **19:** 12704.

377 Maheu C, Singh M, Tock WL, et al. Fear of cancer recurrence, health anxiety, worry, and uncertainty: a scoping review about their conceptualization and measurement within breast cancer survivorship research. *Front Psychol* 2021; **12:** 644932.

378 Lim E, Humphris G. The relationship between fears of cancer recurrence and patient age: a systematic review and meta-analysis. *Cancer Rep* 2020; **3:** e1235.

379 Samuel CA, Mbah OM, Elkins W, et al. Calidad de vida: a systematic review of quality of life in Latino cancer survivors in the USA. *Qual Life Res* 2020; **29:** 2615–30.

380 Zomkowski K, Cruz de Souza B, Pinheiro da Silva F, Moreira GM, de Souza Cunha N, Sperandio FF. Physical symptoms and working performance in female breast cancer survivors: a systematic review. *Disabil Rehabil* 2018; **40:** 1485–93.

381 Wang K, Yee C, Tam S, et al. Prevalence of pain in patients with breast cancer post-treatment: a systematic review. *Breast* 2018; **42:** 113–27.

382 Adler SR, Coulter YZ, Stone K, Glaser J, Duerr M, Enochty S. End-of-life concerns and experiences of living with advanced breast cancer among medically underserved women. *J Pain Symptom Manage* 2019; **58:** 959–67.

383 Matsuoka J, Kunitomi T, Nishizaki M, Iwamoto T, Katayama H. Advance care planning in metastatic breast cancer. *Chin Clin Oncol* 2018; **7:** 33.

384 Accordino MK, Wright JD, Vasan S, et al. Association between survival time with metastatic breast cancer and aggressive end-of-life care. *Breast Cancer Res Treat* 2017; **166:** 549–58.

385 Roberson PNE, Cortez G, Freeman T, Lloyd J, Tasman J, Woods SB. Relationship quality and psychophysiological distress for underserved breast cancer patients and their caregiver before treatment. *Psychooncology* 2022; **31:** 1904–12.

386 Overcash J, Johnston M, Sinnott LT, Williams N. Influence of patient functional status and depression on strain in caregivers. *Clin J Oncol Nurs* 2022; **26:** 406–12.

387 Dumitra S, Jones V, Rodriguez J, et al. Disparities in managing emotions when facing a diagnosis of breast cancer: results of screening program of couples distress. *Surgery* 2018; **164:** 86–90.

388 Selamat Din SH, Nik Jaafar NR, Zakaria H, Mohamed Saini S, Ahmad SN, Midin M. Anxiety disorders in family caregivers of breast cancer patients receiving oncologic treatment in Malaysia. *Asian Pac J Cancer Prev* 2017; **18:** 465–71.

389 Elfgen C, Montagna G, Schmid SM, Bierbauer W, Güth U. Metastatic breast cancer as a chronic disease: evidence-based data on a theoretical concept. *Breast Care* 2020; **15:** 281–88.

390 Tang WZ, Yusuf A, Jia K, et al. Correlates of stigma for patients with breast cancer: a systematic review and meta-analysis. *Support Care Cancer* 2022; **31:** 55.

391 Trusson D, Pilnick A. The role of hair loss in cancer identity: perceptions of chemotherapy-induced alopecia among women treated for early-stage breast cancer or ductal carcinoma in situ. *Cancer Nurs* 2017; **40:** E9–16.

392 Melhem SJ, Nabhani-Gebara S, Kayyali R. Latency of breast cancer stigma during survivorship and its influencing factors: a qualitative study. *Front Oncol* 2023; **13:** 1075298.

393 Lee MC, Bhati RS, von Rottenthaler EE, et al. Therapy choices and quality of life in young breast cancer survivors: a short-term follow-up. *Am J Surg* 2013; **206:** 625–31.

394 Silvestris E, Dellino M, Cafforio P, Paradiso AV, Cormio G, D'Oronzo S. Breast cancer: an update on treatment-related infertility. *J Cancer Res Clin Oncol* 2020; **146:** 647–57.

395 Mungrue K, Ramdath J, Ali S, et al. Challenges to the control of breast cancer in a small developing country. *Breast Cancer* 2014; **8:** 7–13.

396 Pace LE, Dusengimana JM, Hategekimana V, et al. Benign and malignant breast disease at Rwanda's first Public Cancer Referral Center. *Oncologist* 2016; **21:** 571–75.

397 Pace LE, Mpunga T, Hategekimana V, et al. Delays in breast cancer presentation and diagnosis at two rural cancer referral centers in Rwanda. *Oncologist* 2015; **20:** 780–88.

398 Tieman JT, Nourian MM, Agbenorku P, et al. Developing a breast reconstruction program in a resource-constrained Ghanaian teaching hospital: needs assessment and implementation. *Ann Plast Surg* 2021; **86:** 129–31.

399 Ortega CCF, Veiga DF, Camargo K, Juliano Y, Sabino Neto M, Ferreira LM. Breast reconstruction may improve work ability and productivity after breast cancer surgery. *Ann Plast Surg* 2018; **81:** 398–401.

400 Roy N, Villavisanis DF, Taub PJ. Mitigating financial toxicity in breast cancer from diagnosis to treatment and reconstruction. *Clin Breast Cancer* 2023; **23:** e32–36.

401 Quincey K, Williamson I, Winstanley S. 'Marginalised malignancies': a qualitative synthesis of men's accounts of living with breast cancer. *Soc Sci Med* 2016; **149:** 17–25.

402 Bhadelia A, Greaves N, Doubova S, Knaul F. Understanding the value of alleviating health-related suffering and palliative care centered in lived experience: the SAVE toolkit. *Research Square* 2023; published online Dec 6. https://www.researchsquare.com/article/rs-3716807/v1 (preprint).

403 Doubova SV, Bhadelia A, Pérez-Moran D, Martinez-Vega IP, García-Cervantes N, Knaul F. Dimensions of suffering and the need for palliative care: experiences and expectations of patients living with cancer and diabetes and their caregivers in Mexico - a qualitative study. *BMJ Open* 2023; **13:** e075691.

404 Essue BM, Oliveira C, Bushnik T, et al. The burden of health-related out-of-pocket cancer costs in Canada: a case-control study using linked data. *Curr Oncol* 2022; **29:** 4541–57.

405 Iragorri N, de Oliveira C, Fitzgerald N, Essue B. The out-of-pocket cost burden of cancer care–a systematic literature review. *Curr Oncol* 2021; **28:** 1216–48.

406 Iragorri N, de Oliveira C, Fitzgerald N, Essue B. The indirect cost burden of cancer care in Canada: a systematic literature review. *Appl Health Econ Health Policy* 2021; **19:** 325–41.

407 Essue BM, Laba T-L, Knaul F, et al. Economic burden of chronic ill health and injuries for households in low- and middle-income countries. In: Jamison DT, Gelband H, Horton S, et al, eds. Disease control priorities: improving health and reducing poverty, 3rd edn. Washington, DC: The World Bank, 2017: 121–43.

408 Jan S, Kimman M, Peters SA, Woodward M. Financial catastrophe, treatment discontinuation and death associated with surgically operable cancer in south-east Asia: results from the ACTION study. *Surgery* 2015; **157:** 971–82.

409 WHO. Fact sheet: breast cancer. World Health Organisation. 2021. https://www.who.int/news-room/fact-sheets/detail/breast-cancer (accessed Jan 3, 2023).

410 Knaul FM, Gralow JR, Atun R, Bhadelia A, eds. Closing the cancer divide: an equity imperative. Cambridge MA: Harvard Global Equity Initiative, 2012.

411 Tawfik B, Jaffe SA, Mohler L, et al. Developing a survivorship care plan (SCP) delivery process for patients and primary care providers serving poor, rural, and minority patients with cancer. *Support Care Cancer* 2021; **29:** 5021–28.

412 Yeoh Z-Y, Jaganathan M, Rajaram N, et al. Feasibility of patient navigation to improve breast cancer care in Malaysia. *J Glob Oncol* 2018; **4:** 1–13.

413 Ghaffari F, Ghahramanian A, Zamanzadeh V, et al. Patient-centred communication for women with breast cancer: relation to body image perception. *J Clin Nurs* 2020; **29:** 4674–84.

414 Gakunga R, Kinyanjui A, Ali Z, et al. Identifying barriers and facilitators to breast cancer early detection and subsequent treatment engagement in Kenya: a qualitative approach. *Oncologist* 2019; **24:** 1549–56.

415 Kathrikolly TR, Nair S, Poobalan AS, Shetty RS, Tripathee S, Mac Lennan SJ. Increasing engagement for breast cancer screening and treatment: the "ICANTREAT" community of expertise initiative. *Asian Pac J Cancer Prev* 2020; **21:** 3655–59.

416 Guerra RL, Castaneda L, de Albuquerque RCR, et al. Patient preferences for breast cancer treatment interventions: a systematic review of discrete choice experiments. *Patient* 2019; **12:** 559–69.

417 Raisa A, Roberto AJ, Love RR, Steiness HLS, Salim R, Krieger JL. Pot song as a novel cancer communication intervention: lessons learned from developing, implementing, and evaluating a culturally grounded intervention for breast cancer education in rural Bangladesh. *J Cancer Edu* 2023; **38:** 260–73.

418 Schliemann D, Htay MNN, Dahlui M, et al. Impact of a mass media campaign on breast cancer symptoms awareness and screening uptake in Malaysia: findings from a quasi-experimental study. *BMJ Open* 2020; **10:** e036503.

419 Odigie VI, Yusufu LMD, Dawotola DA, et al. The mobile phone as a tool in improving cancer care in Nigeria. *Psychooncology* 2012; **21:** 332–35.

420 Gutnik L, Moses A, Stanley C, Tembo T, Lee C, Gopal S. From community laywomen to breast health workers: a pilot training model to implement clinical breast exam screening in Malawi. *PLoS One* 2016; **11:** e0151389.

421 Zhou Q, Shen J-C, Liu Y-Z, Lin G-Z, Dong H, Li K. Effects of doctor–patient communication on quality of life among breast cancer patients in southern China. *Asian Pac J Cancer Prev* 2014; **15:** 5639–44.

422 Noyan MA, Sertoz OO, Elbi H, Kayar R, Yilmaz R. Variables affecting patient satisfaction in breast surgery: a cross-sectional sample of Turkish women with breast cancer. *Int J Psychiatry Med* 2006; **36:** 299–313.

423 Wako Z, Mengistu D, Dinegde NG, Asefa T, Wassie M. Adherence to adjuvant hormonal therapy and associated factors among women with breast cancer attending the Tikur Anbessa Specialized Hospital, Addis Ababa Ethiopia, 2019: a cross-sectional study. *Breast Cancer (Dove Med Press)* 2021; **13:** 383–92.

424 Yap ML, Zubizarreta E, Bray F, Ferlay J, Barton M. Global access to radiotherapy services: have we made progress during the past decade? *J Glob Oncol* 2016; **2:** 207–15.

425 Agyemang LS, Foster C, McLean C, Fenlon D, Wagland R. The cultural and structural influences that 'hide' information from women diagnosed with breast cancer in Ghana: an ethnography. *BMC Womens Health* 2021; **21:** 364.

426 Geng C, Lu G-J, Zhu J, Li Y-Y. Patients' awareness about their own breast cancer characteristics. *World J Clin Cases* 2021; **9:** 7043–52.

427 Daniel S, Venkateswaran C, Singh C, Hutchinson A, Johnson MJ. "So, when a woman becomes ill, the total structure of the family is affected, they can't do anything…" voices from the community on women with breast cancer in India: a qualitative focus group study. *Support Care Cancer* 2022; **30:** 951–63.

428 Scheel JR, Parker S, Hippe DS, et al. Role of family obligation stress on Ugandan women's participation in preventive breast health. *Oncologist* 2019; **24:** 624–31.

429 Lambert M, Mendenhall E, Kim AW, Cubasch H, Joffe M, Norris SA. Health system experiences of breast cancer survivors in urban South Africa. *Womens Health* 2020; **16:** 1745506520949419.

430 Brinton L, Figueroa J, Adjei E, et al. Factors contributing to delays in diagnosis of breast cancers in Ghana, West Africa. *Breast Cancer Res Treat* 2017; **162:** 105–14.

431 Sajjad S, Gul R, Gowani A, Ali A, Chagani S. Developing the reliability and validity of an Urdu Version-Self-Efficacy Scale for breast cancer patients in Pakistan. *J Nurs Meas* 2021; **29:** 239–53.

432 Mandrik O, Yaumenenka A, Herrero R, Jonker MF. Population preferences for breast cancer screening policies: discrete choice experiment in Belarus. *PLoS One* 2019; **14:** e0224667.

433 Whelan T, Levine M, Willan A, et al. Effect of a decision aid on knowledge and treatment decision making for breast cancer surgery: a randomized trial. *JAMA* 2004; **292:** 435–41.

434 Hawley ST, Li Y, An LC, et al. Improving breast cancer surgical treatment decision making: the iCanDecide randomized clinical trial. *J Clin Oncol* 2018; **36:** 659–66.

435 Lyman GH, Greenlee H, Bohlke K, et al. Integrative therapies during and after breast cancer treatment: ASCO endorsement of the SIO Clinical Practice Guideline. *J Clin Oncol* 2018; **36:** 2647–55.

436 Hawley ST, Kidwell K, Zahrieh D, et al. Improving patient-centered communication in breast cancer: a study protocol for a multilevel intervention of a shared treatment deliberation system (SharES) within the NCI community oncology research program (NCORP) (Alliance A231901CD). *Trials* 2023; **24:** 16.

437 Wallner LP, Martinez KA, Li Y, et al. Use of online communication by patients with newly diagnosed breast cancer during the treatment decision process. *JAMA Oncol* 2016; **2:** 1654–56.

438 Liu Y, Malin JL, Diamant AL, Thind A, Maly RC. Adherence to adjuvant hormone therapy in low-income women with breast cancer: the role of provider-patient communication. *Breast Cancer Res Treat* 2013; **137:** 829–36.

439 Kerr J, Engel J, Schlesinger-Raab A, Sauer H, Hölzel D. Communication, quality of life and age: results of a 5-year prospective study in breast cancer patients. *Ann Oncol* 2003; **14:** 421–27.

440 Seror V, Cortaredona S, Bouhnik AD, et al. Young breast cancer patients' involvement in treatment decisions: the major role played by decision-making about surgery. *Psychooncology* 2013; **22:** 2546–56.

441 Mott N, Wang T, Miller J, et al. Medical maximizing–minimizing preferences in relation to low-value services for older women with hormone receptor-positive breast cancer: a qualitative study. *Ann Surg Oncol* 2021; **28:** 941–49.

442 Lantz PM, Janz NK, Fagerlin A, et al. Satisfaction with surgery outcomes and the decision process in a population-based sample of women with breast cancer. *Health Serv Res* 2005; **40:** 745–68.

443 Martinez KA, Kurian AW, Hawley ST, Jagsi R. How can we best respect patient autonomy in breast cancer treatment decisions? *Breast Cancer Manag* 2015; **4:** 53–64.

444 Khoshnazar TAK, Rassouli M, Akbari ME, et al. Communication needs of patients with breast cancer: a qualitative study. *Indian J Palliat Care* 2016; **22:** 402–09.

445 Shim EJ, Park JE, Yi M, Jung D, Lee KM, Hahm BJ. Tailoring communications to the evolving needs of patients throughout the cancer care trajectory: a qualitative exploration with breast cancer patients. *BMC Womens Health* 2016; **16:** 65.

446 Ward ZJ, Scott AM, Hricak H, Atun R. Global costs, health benefits, and economic benefits of scaling up treatment and imaging modalities for survival of 11 cancers: a simulation-based analysis. *Lancet Oncol* 2021; **22:** 341–50.

447 Caverly TJ, Hayward RA. Dealing with the lack of time for detailed shared decision-making in primary care: everyday shared decision-making. *J Gen Intern Med* 2020; **35:** 3045–49.

448 Street RL Jr, Mazor KM, Arora NK. Assessing patient-centered communication in cancer care: measures for surveillance of communication outcomes. *J Oncol Pract* 2016; **12:** 1198–202.

449 Banerjee SC, Manna R, Coyle N, et al. The implementation and evaluation of a communication skills training program for oncology nurses. *Transl Behav Med* 2017; **7:** 615–23.

450 Bylund CL, Banerjee SC, Bialer PA, et al. A rigorous evaluation of an institutionally-based communication skills program for post-graduate oncology trainees. *Patient Educ Couns* 2018; **101:** 1924–33.

451 Kissane DW, Bylund CL, Banerjee SC, et al. Communication skills training for oncology professionals. *J Clin Oncol* 2012; **30:** 1242–47.

452 Bylund CL, Brown RF, Bialer PA, Levin TT, Lubrano di Ciccone B, Kissane DW. Developing and implementing an advanced communication training program in oncology at a comprehensive cancer center. *J Cancer Educ* 2011; **26:** 604–11.

453 Bylund CL, Brown R, Gueguen JA, Diamond C, Bianculli J, Kissane DW. The implementation and assessment of a comprehensive communication skills training curriculum for oncologists. *Psychooncology* 2010; **19:** 583–93.

454 Langewitz W, Denz M, Keller A, Kiss A, Rütimann S, Wössmer B. Spontaneous talking time at start of consultation in outpatient clinic: cohort study. *BMJ* 2002; **325:** 682–83.

455 Decise D, Gheran MP, Kimhi E, et al. Putting words into practice. *Breast* 2020; **49:** 171–73.

456 Fallowfield L, Boyle FM, Travado L, et al. Gaps in care and support for patients with advanced breast cancer: a report from the Advanced Breast Cancer Global Alliance. *JCO Glob Oncol* 2021; **7:** 976–84.

457 Weeks JC, Catalano PJ, Cronin A, et al. Patients' expectations about effects of chemotherapy for advanced cancer. *N Engl J Med* 2012; **367:** 1616–25.

458 Weeks JC, Cook EF, O'Day SJ, et al. Relationship between cancer patients' predictions of prognosis and their treatment preferences. *JAMA* 1998; **379:** 1709–14.

459 Smith-Uffen MES, Johnson SB, Martin AJ, et al. Estimating survival in advanced cancer: a comparison of estimates made by oncologists and patients. *Support Care Cancer* 2020; **28:** 3399–407.

460 Chen CH, Kuo SC, Tang ST. Current status of accurate prognostic awareness in advanced/terminally ill cancer patients: systematic review and meta-regression analysis. *Palliat Med* 2017; **31:** 406–18.

461 Wright AA, Zhang B, Ray A, et al. Associations between end-of-life discussions, patient mental health, medical care near death, and caregiver bereavement adjustment. *JAMA* 2008; **300:** 1665–73.

462 Mack JW, Cronin A, Keating NL, et al. Associations between end-of-life discussion characteristics and care received near death: a prospective cohort study. *J Clin Oncol* 2012; 30: 4387–95.

463 Kaplowitz SA, Campo S, Chiu WT. Cancer patients' desires for communication of prognosis information. *Health Commun* 2002; **14:** 221–41.

464 Back AL, Arnold RM. Discussing prognosis: "how much do you want to know?" talking to patients who are prepared for explicit information. *J Clin Oncol* 2006; **24:** 4209–13.

465 Jenkins V, Fallowfield L, Saul J. Information needs of patients with cancer: results from a large study in UK cancer centres. *Br J Cancer* 2001; **84:** 48–51.

466 Lamont EB, Christakis NA. Prognostic disclosure to patients with cancer near the end of life. *Ann Intern Med* 2001; **134:** 1096.

467 Baile WF, Lenzi R, Parker PA, Buckman R, Cohen L. Oncologists' attitudes toward and practices in giving bad news: an exploratory study. *J Clin Oncol* 2002; **20:** 2189–96.

468 Fenton JJ, Duberstein PR, Kravitz RL, et al. Impact of prognostic discussions on the patient–physician relationship: prospective cohort study. *J Clin Oncol* 2018; **36:** 225–30.

469 Vasista A, Stockler MR, Martin A, Lawrence NJ, Kiely BE. Communicating prognostic information: what do oncologists think patients with incurable cancer should be told? *Intern Med J* 2020; **50:** 1492–99.

470 Fallowfield LJ, Jenkins VA, Beveridge HA. Truth may hurt but deceit hurts more: communication in palliative care. *Palliat Med* 2002; **16:** 297–303.

471 Barnett MM. Does it hurt to know the worst?—Psychological morbidity, information preferences and understanding of prognosis in patients with advanced cancer. *Psychooncology* 2006; **15:** 44–55.

472 Enzinger AC, Zhang B, Schrag D, Prigerson HG. Outcomes of prognostic disclosure: associations with prognostic understanding, distress, and relationship with physician among patients with advanced cancer. *J Clin Oncol* 2015; **33:** 3809–16.

473 Hagerty RG, Butow PN, Ellis PM, et al. Communicating with realism and hope: incurable cancer patients' views on the disclosure of prognosis. *J Clin Oncol* 2005; **23:** 1278–88.

474 Gattellari M, Voigt KJ, Butow PN, Tattersall MHN. When the treatment goal is not cure: are cancer patients equipped to make informed decisions? *J Clin Oncol* 2002; **20:** 503–13.

475 Nahm SH, Stockler MR, Martin AJ, et al. Using three scenarios to explain life expectancy in advanced cancer: attitudes of patients, family members, and other healthcare professionals. *Support Care Cancer* 2022; **30:** 7763–72.

476 Kiely BE, McCaughan G, Christodoulou S, et al. Using scenarios to explain life expectancy in advanced cancer: attitudes of people with a cancer experience. *Support Care Cancer* 2013; **21:** 369–76.

477 Kiely BE, Martin AJ, Tattersall MHN, et al. The median informs the message: accuracy of individualized scenarios for survival time based on oncologists' estimates. *J Clin Oncol* 2013; **31:** 3565–71.

478 Stockler MR, Tattersall MHN, Boyer MJ, Clarke SJ, Beale PJ, Simes RJ. Disarming the guarded prognosis: predicting survival in newly referred patients with incurable cancer. *Br J Cancer* 2006; **94:** 208–12.

479 NHMRC Clinical Trials Centre. 3 scenarios for survival. 2019. https://ctc.usyd.edu.au/3scenarios/ (accessed Aug 30, 2023).

480 CancerSurvivalRates. 2022. https://cancersurvivalrates.com/ (accessed Aug 30, 2023).

481 Mack JW, Weeks JC, Wright AA, Block SD, Prigerson HG. End-of-life discussions, goal attainment, and distress at the end of life: predictors and outcomes of receipt of care consistent with preferences. *J Clin Oncol* 2010; **28:** 1203–08.

482 WHO. WHO traditional medicine strategy: 2014–2023. World Health Organization. 2013. https://web.archive.org/web/20230430163013/https://www.who.int/publications/i/item/9789241506096 (accessed April 30, 2023).

483 Witt CM, Balneaves LG, Cardoso MJ, et al. A comprehensive definition for integrative oncology. *J Natl Cancer Inst Monogr* 2017; **2017**: lgx012.

484 Horneber M, Bueschel G, Dennert G, Less D, Ritter E, Zwahlen M. How many cancer patients use complementary and alternative medicine: a systematic review and metaanalysis. *Integr Cancer Ther* 2012; **11:** 187–203.

485 Spence D, Brown K, Smith S, Grant D, Picking D. Jamaican cultural and spiritual guidance in caring for cancer patients, Jamaica. In: Silbermann M, Berger A, eds. Global perspectives in cancer care: religion, spirituality, and cultural diversity in health and healing. Oxford: Oxford University Press, 2022: 454–C45.P152

486 Abrams D, Weil A. Integrative Oncology. Oxford: Oxford University Press, 2014.

487 Memorial Sloan Kettering Cancer Center. About herbs, botanicals & other products. 2023. https://www.mskcc.org/cancer-care/diagnosis-treatment/symptom-management/integrative-medicine/herbs (accessed May 1, 2023).

488 Yonas MA, Jones N, Eng E, et al. The art and science of integrating undoing racism with CBPR: challenges of pursuing NIH funding to investigate cancer care and racial equity. *J Urban Health* 2006; **83:** 1004–12.

489 Baker SL, Black KZ, Dixon CE, et al. Expanding the reach of an evidence-based, system-level, racial equity intervention: translating ACCURE to the maternal healthcare and education systems. *Front Public Health* 2021; **9:** 664709.

490 Enard KR, Nicks SE, Campbell BA, McClure SM. In pursuit of equity: partnering to improve breast and prostate cancer outcomes among African Americans. *Cancer Causes Control* 2021; **32:** 473–82.

491 Rodriguez NM, Casanova F, Pages G, et al. Community-based participatory design of a community health worker breast cancer training intervention for South Florida Latinx farmworkers. *PLoS One* 2020; **15:** e0240827.

492 Lynch KA, Bernal C, Romano DR, et al. Navigating a newly diagnosed cancer through clinician-facilitated discussions of health-related patient values: a qualitative analysis. *BMC Palliat Care* 2022; **21:** 29.

493 Desai AV, Michael CL, Kuperman GJ, et al. A novel patient values tab for the electronic health record: a user-centered design approach. *J Med Internet Res* 2021; **23:** e21615.

494 Kamen CS, Reichelt M, Dadgostar P, et al. Sexual and gender minority cultural humility training for oncology settings: an example of iterative adaptation and implementation. *Front Health Serv* 2022; **2:** 958274.