Factors affecting access to treatment of early breast cancer: Case studies from Brazil, Canada, Italy, Spain and UK

Implications for future research, policy and practice

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Preface

This document presents the findings from one element of a body of work sponsored by F. Hoffmann-La Roche on the topic of early breast cancer. This qualitative study uses desk research and key informant interviews to explore the factors affecting access to and delivery of treatment for early breast cancer in order to identify what works around the current access to and delivery of treatment for early breast cancer and what can be improved. It focuses on Brazil, Canada, Italy, Spain and the United Kingdom, and also presents insights at a supranational level – for example it looks at policy and practice in the European Union – and makes broader comments on factors affecting low and middle-income countries.

This document is complemented by a mapping review exploring the focus of research on early breast cancer and particularly the types of outcomes examined in literature (Ghiga et al. 2019), and a systematic review on the non-clinical impacts of progression of early breast cancer treatment on individuals, their support network and wider society (Elmore et al. 2019).

This report is of interest to policymakers, healthcare professionals, patient advocates and others within the healthcare system. It aims to look not only at the current policy and evidence but also the opportunities for the future.

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Executive summary

Breast cancer is the most frequently occurring cancer in women. Early diagnosis of breast cancer results in earlier treatment of breast cancer, which has been associated with better survival prospects and improved quality of life. The risk of disease progression from early breast cancer is higher without treatment than if treatment is begun. However, the risk of disease progression after treatment of early breast cancer is still relatively high and some challenges do exist. There is still a need for innovation in treatment for early breast cancer. To make the case for investment in new technologies that will improve diagnosis and treatment of early breast cancer, more comprehensive evidence is required on the impacts of early breast cancer and disease progression on society, as well as on the factors affecting access to and delivery of treatment for early breast cancer.

In order to identify what works around the current access to and delivery of treatment for early breast cancer and what can be improved, we performed a study comprising desk research and qualitative interviews on five selected countries (Brazil, Canada, Italy, Spain and the United Kingdom), using a PESTLE framework to explore the factors. A PESTLE framework is used to explore the political, economic, social, technological, legal and environmental context for a given situation. Our research found that differences within countries are often related to regional discrepancies that arise from a decentralised structure of the healthcare system that has an impact on the financing, implementation, and/or delivery of care. We found that cultural and socioeconomic factors, such as a person’s education or income, also affect equal access to treatment within an individual country.

In all countries considered, breast cancer is a disease that benefits from strong patient advocacy, which has played an important role in raising the profile of breast cancer with patients, policymakers and the public, both at a national and international level. However, there is still little awareness of the impact of disease progression on society, although there was consensus among interviewees in different countries that the cost to society of disease progression was greater than the cost of early breast cancer. This cost was usually related to non-clinical outcomes associated with breast cancer, such as loss of productivity, as well as the increased cost of treatment available for metastatic disease. Therefore, there is a need for evidence on the impact of disease progression to society, as seen in the other elements of this study (the mapping and the systematic reviews), which could be used as evidence to help raise awareness on the benefits to society of investing in and treating early breast cancer.

Evidence of the impact to society of disease progression could also contribute to broadening the value of treatment beyond the standard cost-benefit analysis used in most countries to inform decisions around investment in new treatment, for example, factors such as patient satisfaction from new therapies, the broader benefits and potential cost saving from early treatment (e.g. loss of productivity and return to
work), and prevention of disease progression to metastatic disease. Broadening the value of treatment beyond economics and survival could encourage those developing newer treatments for early breast cancer and those investing at national level in new drugs to introduce new options in a market that considers there are sufficient successful treatments available.
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<th>Full Form</th>
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<tr>
<td>AEMPS</td>
<td>Agencia Española de Medicamentos y Productos Sanitarios</td>
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<tr>
<td>ASL</td>
<td>Aziende Sanitarie Locale</td>
</tr>
<tr>
<td>CADTH</td>
<td>Canadian Agency for Drug and Technologies in Health</td>
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<td>CCG</td>
<td>Clinical Commissioning Group</td>
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<td>CONITEC</td>
<td>Comissão Nacional de Incorporação de Tecnologias no Sistema Único de Saúde</td>
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<td>ECIBC</td>
<td>European Commission Initiative on Breast Cancer</td>
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<tr>
<td>EMA</td>
<td>European Medicines Agency</td>
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<td>EU</td>
<td>European Union</td>
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<tr>
<td>FAST</td>
<td>Faster Radiotherapy for Breast Cancer Patients</td>
</tr>
<tr>
<td>FDA</td>
<td>Federal and Drug Administration</td>
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<tr>
<td>GDP</td>
<td>Gross Domestic Product</td>
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<tr>
<td>GP</td>
<td>General Practitioner</td>
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<tr>
<td>HTA</td>
<td>Health Technology Assessment</td>
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<tr>
<td>INT</td>
<td>Interview number</td>
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<tr>
<td>LMICs</td>
<td>Low- and Middle-Income Countries</td>
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<td>MoU</td>
<td>Memorandum of Understanding</td>
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<tr>
<td>NHS</td>
<td>National Health System</td>
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<tr>
<td>NICE</td>
<td>National Institute for Health and Care Excellence</td>
</tr>
<tr>
<td>PESTLE</td>
<td>Political, Economic, Social, Technological, Legal, Environmental</td>
</tr>
<tr>
<td>SEOM</td>
<td>Sociedad Española de Oncología Médica</td>
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<tr>
<td>SSN</td>
<td>Servizio Sanitario Nazionale</td>
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<tr>
<td>SUS</td>
<td>Sistema Único de Saúde</td>
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<td>UK</td>
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Acknowledgements

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1. Introduction

1.1. Background and context

Breast cancer is the most common form of cancer, accounting for 25% of all cancer diagnoses worldwide; it is the leading cause of cancer-related mortality in women (Ferlay et al. 2015; World Health Organization 2018). Most women with breast cancer are diagnosed with early stage breast cancer (when disease is confined to the breast with or without regional lymph node involvement) rather than regionally advanced or metastatic cancer, and that has not metastasised (Union for International Cancer Control 2014).

Treatment of breast cancer, diagnosed at an early stage, is associated with reduced risks of progression, reduced rate of recurrence and better survival prospects (McPhail et al. 2015; NHS 2015; Walters et al. 2013). Early stage breast cancer is potentially curable with local and systemic therapy (Anampa, Makower and Sparano 2015), whereas survival rates for metastatic disease remain poor (García Rodríguez et al. 2010; Union for International Cancer Control 2014). Approximately 5–10% of breast cancers in women are metastatic at diagnosis; of these, approximately only one-fifth of women survive five years¹ (Cardoso et al. 2012). Therefore, continued efforts in earlier diagnosis are needed.

There are substantial differences in survival rates among early stage breast cancer patients, both between European countries and worldwide (Walters et al. 2013). This variation is explained by several factors, including accuracy of staging assessments, and access to or the effectiveness of stage-specific treatment (Walters et al. 2013). Challenges may also stem from a poor understanding of cancer subtypes likely to benefit from specific treatment (Di Leo et al. 2015). Therefore, improved treatment options could help to improve survival outcomes for early stage breast cancer patients.

When women are diagnosed with breast cancer it can have a significant impact on them, their families and wider society. It can affect the emotional, physical, psychological and social well-being of patients and their families, and their long-term quality of life (Glück, Mamounas and Klem 2010). It can result in substantial lifestyle changes during treatment and can reduce household income (e.g. through the personal costs of receiving treatment and restricting the ability to work). Breast cancer impacts on society directly through health systems costs (e.g. expenses associated with treatment) and indirectly (e.g. through loss of labour productivity). A recent report calculated that in a given year cancer deaths result in a loss of £585

¹ Further insights on comparative survival rates for those with non-metastatic cancers would help with comparative assessments of survival.
million to the United Kingdom (UK) economy (Creighton, Beach and Bamford 2015). In 2010 it was
estimated that the overall cost of breast cancer care to the UK health system was £542 million in hospital
care, with metastatic breast cancer associated with markedly higher costs than early stage disease
(Laudicella et al. 2016). Therefore, a better understanding of the societal impacts of early breast cancer
could contribute to the development and approval of new and effective treatment options.

1.2. Aims and objectives of the study

This study was conducted between September 2017 and December 2018 and aimed to understand the
environment influencing policy about access to treatment of breast cancer with an interest in early stage
treatment in a subset of countries. It used a PESTLE\(^4\) framework as a guiding structure and sought to
address the following research questions:

1. How do political, economic, social, scientific and technological, infrastructure-related and
regulatory and legal factors influence policy about and access to treatment of (early) breast cancer
in selected countries? We considered how national strategies in selected countries and European
Union (EU)-level guidance relate to each other.

2. Are limitations with current treatment options an influence on treatment strategies in the
countries we studied?

3. What innovation in treatments and the health system more widely are needed for early treatment
strategies to change?

\(^4\) Political, economic, social, technological, legal and environmental
Our study focused on five countries (Brazil, Canada, Italy, Spain and the United Kingdom), and a supranational perspective. These were selected to cover a variety of health systems and geographies across Europe and beyond, and were selected based on research activities in the field of breast cancer in these countries, and on insights into the level of activity of national patient groups, given that these were one of the stakeholders whose perspectives we wanted to gain.

Initially, the study team conducted a review of grey literature for each country, focusing on policy reports, guidelines and relevant literature from diverse stakeholder groups. Our scoping research during this stage was guided by the PESTLE framework with the study team engaged in targeted searching for relevant documents under each of the key framework areas, rather than by a pre-set search string as in a systematic review. The goal of this stage was to develop a general understanding of factors influencing treating early breast cancer within the selected countries. We used information from this initial desk research to develop the interview protocol, identify interviewees, and better guide the discussion with country experts. Following stakeholder interviews, we conducted a subsequent round of desk research to complement or verify the information gathered through the interviews, and the study team searched academic and grey literature sources, again guided by the PESTLE framework rather than pre-set search strings.

We conducted 19 expert interviews with diverse stakeholders (e.g. policymakers, payers, medical profession staff, healthcare providers, patient advocacy groups) in the selected countries (Table 2.1).

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2 Originally our sample also included Germany and France, but we could not secure any interviews in these countries. The reasons for this are not entirely clear, possibly because we did not offer reimbursement and potential interviewees were not comfortable speaking in English.

3 Initially we conducted a search was conducted on Google using the search string ‘early breast cancer [country]’. The search was in English for Brazil, Canada, Italy, the United Kingdom and the international context, and in English and Spanish for Spain.

4 One consequence of our search strategy for the grey literature is that unlike with a systematic review there is no list of titles and abstracts that the team reviewed, nor inclusion and exclusion criteria. All of the grey literature sources deemed relevant for inclusion are included in this report.

5 We also conducted scoping interviews with F. Hoffmann-La Roche affiliates to obtain details for Canada, Italy, Spain, the United Kingdom and the international context.
We conducted interviews over the telephone, with a duration of 45–60 minutes, in a semi-structured format, allowing consistent information to be captured, while retaining flexibility to explore issues in more detail as appropriate, reflecting the background and expertise of the respondent. We asked participants to complete a consent form (see Annex A), which had details of their participation in the study and their right to refuse participation. Following consent, we audio recorded interviews for the purposes of accurate note taking. The interview protocol used can be found in Annex B and the interview codes used for analysis and reporting in 0.

We extracted data from the desk research and interviews into a template containing the following fields for the different PESTLE factors:

- **Political**: context, health system governance and regulation, health system infrastructure, health innovation policies, policymaker awareness, breast cancer as a political priority
- **Economic**: treatment cost and pricing, payment of treatment (state, individual, etc.), workforce capacity, skills and capabilities, health system financing, investment in prevention and research
- **Social**: advocacy movements, cultural issues, public awareness, patient compliance, patient education, support programmes, hard to reach populations, stigma
- **Technological**: standard course of treatment, gold standard diagnostic tool, technological advances and breakthroughs, research
- **Legal**: regulatory frameworks, prioritisation, level of adherence to clinical guidelines
- **Environment**: regional differences.

An ‘other’ field was included for information that did not fit into the predetermined fields but was still seen as relevant for the study. For the interviews the following fields were added to the PESTLE:

- **Impact of early breast cancer**: on the patient, the carer, broader society, other
- **What works well**
- **What could be improved**.

Following country-specific analysis summarising the findings from the extraction template, we held an internal workshop to identify cross-cutting themes focusing on the drivers and barriers to accessing treatment in the different countries.
2.1.1. Caveats and limitations

There are some caveats and limitations to this approach to consider. Our desk research was limited mainly to the information available in English, so we could have missed relevant information written in the native country languages. Similarly, we sent interview invitations in English and Spanish for Spain, English and French for France, and English for Brazil, Germany, Italy and the United Kingdom. It is possible that the low response rate from invitees in Brazil and Italy, and the lack of response from invitees in France and Germany, was because invitees were not comfortable conducting an interview in English (although we gave interviewees alternatives when this was the case, including conducting the interview in a language other than English or performing a written interview in their native language).

There was also variability in the ability to secure interviewees from specific stakeholder groups across different countries and in general response rates to requests for interview, which were somewhat lower than we had hoped for. There may be a variety of reasons for this, including the lack of payment provisions for securing an interview in the study and conflicts of interest.

Overall, the number of interviews was lower than planned for all countries except Canada. We sought to recruit five or six interviewees from each country, plus four or five representing the international context, in order to capture a diverse range of stakeholder views. Then information obtained from the interviews could represent an individual’s perspective rather than a broader view on the PESTLE factors in a given country. Moreover, information gathered may reflect the context of breast cancer as a whole rather than early breast cancer, as interviewees did not always refer specifically to early breast cancer in their replies.

A further limitation is that this report focuses on early breast cancer in women. This is not intended to discriminate against or dismiss the very real issue of breast cancer in men. We focus on breast cancer in women because most information and evidence available on breast cancer focuses on women, as did the evidence offered by the interviewees.

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6 We accessed some documents in other languages, especially Spanish, and considered within the linguistic skills in the team and the project resources, but the research mainly considered information presented in English.

7 RAND Europe has an international staff. The study team identified colleagues with the required language skills to conduct the interview in languages other than English. However, no interviewees accepted the offer to carry out the interview in a language other than English.
3. Results

In each section below we describe the findings from the interviews and desk research on the barriers and enablers to access to treatment within and between different nations. We begin by presenting the findings from the PESTLE analysis on factors influencing access to treatment of early breast cancer at the EU level, followed by giving country profiles from three selected EU countries (Italy, Spain and the United Kingdom). We then present the country profile for Canada, where the delivery of care resembles that of a European country. We continue by presenting the findings on the PESTLE factors influencing access to treatment of early breast cancer in low- and middle-income countries (LMICs) at a broader level, followed by the country profile for Brazil as an example of a LMIC. The findings for each section are organised by the different types of factors: political, economic, social, technological, legal and environmental, followed by sections on the challenges and opportunities identified for treatment of early breast cancer in each country.

3.1. Policy and practice at a European level

Across EU-28 countries, there are significant differences in the incidence, prevalence, mortality and survival from breast cancer (European Commission 2017). There are also significant inequalities in availability of and access to quality cancer care (Aapro et al. 2017). The following section provides an overview of some of the factors identified through interviews, enriched by complementary insights from a literature review, which may influence these differences.

3.1.1. Political

Some interviewees were of the opinion that delivering high quality, equitable breast cancer care is not always considered a political priority by policymakers in all countries in the EU (INT17, INT18). Some EU countries in Central and Eastern Europe (e.g. Croatia, Romania and Serbia) do not have national cancer plans or cancer registries (Eniu and Antone 2018; Vrdoljak et al. 2016). This can be due to limited financial resources, poor infrastructure, or a lack of awareness among policymakers of the importance of investing in cancer care (Eniu and Antone 2018). Even in those countries that do have cancer plans, implementation remains a barrier as it can require major reorganisation of healthcare systems (Cardoso et al. 2017), and the EU does not have the mandate to enforce implementation of its health policies. Availability of specialist breast units, which have been shown to raise chances of survival and improve quality of life, varies considerably across countries (Cardoso et al. 2017).
This means that the necessary investments in innovations to improve the care and management of breast cancer patients are not being made consistently across the EU-28 (Aapro et al. 2017). However, interviewees highlighted a number of policy initiatives at EU level in the last 20 years that have aimed to raise political awareness and harmonise the care and treatment of breast cancer patients across Europe (INT17, INT18) (Cardoso et al. 2017). There have been several European Parliament resolutions, including in 2003 and 2006, and written declarations on breast cancer in 2010 and 2015 (Cardoso et al. 2017). More recently, the European Commission Initiative on Breast Cancer programme aims to improve and ensure harmonised breast cancer care at EU level (INT17) (Cardoso et al. 2017).

Strong advocacy from patient groups has helped to stimulate awareness and growing interest among policymakers and the public, particularly on the importance of early diagnosis and treatment (INT17, INT18) (European Commission 2017). Individual patients, organisations and physicians play an important role in advocating for greater access to and fairer prices for cancer drugs (Aggarwal, Ginsburg and Fojo 2014). For example, there has recently been a push by various stakeholders, including clinicians and patient advocates, to encourage policymakers to invest in breast cancer units and specialist breast practitioners (Cardoso et al. 2017).

3.1.2. Economic

In 2009, an economic estimate indicated the cost of cancer in general costs the EU €126 billion, with the cost of healthcare accounting for €51 billion (Luengo-Fernandez et al. 2013). This study looked at the costs associated with productivity loss due to early deaths and lost working days, and found that across the EU the cost of productivity loss as a result of early death due to cancer overall was €42.6 billion and €9.43 billion as a result of lost working days. This study also looked at the cost associated with the different types of cancer and found that the care and management of breast cancer costs the EU €15 billion, of which only half were associated with the price of treatment (Luengo-Fernandez et al. 2013). Another study calculated the cost of breast cancer in the Netherlands (Vondeling et al. 2018). It found that breast cancer in the Netherlands accounts for approximately 26,000 life years lost, 65,000 disability adjusted life years and an economic burden of €1.27 billion (Vondeling et al. 2018). This significant level of cost is challenging when there are financial constraints and shrinking budgets (INT19) (Luengo-Fernandez et al. 2013).

Although a number of early breast cancer treatments are relatively cheap (e.g. generic drugs, chemotherapy) (INT18), the cost of funding new cancer treatments is a challenge and represents a rising proportion of the cancer care budget in many EU countries, which leads to large disparities in access within and between countries (INT18) (Aggarwal, Ginsburg and Fojo 2014; ECL 2018). Some studies show that there are inconsistencies between countries in the use of cost-effectiveness analysis to support decision making, which leads to inequalities in drug access (Pauwels et al. 2014).

One interviewee suggested that investment in prevention, particularly through population-based screening programmes, can help to reduce costs on the healthcare system by reducing the need for expensive maintenance treatment (e.g. chemotherapy) in patients with metastatic breast cancer (INT18). Interviewees perceived investment in prevention to be relatively good at EU level, with most countries (23 out of 28) having established population-based screening programmes (INT17, INT18) (Altobelli et al. 2017).
3.1.3. Social
Across the EU, a number of socioeconomic and cultural factors were found to account for the disparity in access to breast cancer screening and treatment (Deandrea et al. 2016). There is evidence that women of lower socioeconomic status participate less in cancer screening programmes than women of higher socioeconomic status (Deandrea et al. 2016), one interviewee suggesting this might be because of lack of awareness, stigma, cultural factors and language barriers (not understanding the invitation) (INT17).

Most EU countries have established population-based screening programmes (Deandrea et al. 2016). There is some evidence that these ensure more equity in access than opportunistic screening programmes, as they do not rely as much on an individual having information about preventative practices or frequent contact with a doctor, which individuals in a higher socioeconomic position are more likely to have (Palència et al. 2010). Social support is also important in promoting good outcomes and good quality of life following cancer, and interventions to provide or enhance social support could help groups experiencing disparities, particularly in communities that experience stigma around cancer (Ashley and Lawrie 2016). There is evidence that the provision of psychosocial support interventions varies across Europe and often depends on whether stakeholders in a given country and its cancer control programme consider it a priority (Travado et al. 2017).

3.1.4. Technological
In Europe, a number of innovations at various stages of development are becoming available that will transform breast cancer care by enabling earlier detection, providing more targeted therapies and maybe even permanent cures (INT17, INT18, INT20) (Aapro et al. 2017; Albrecht et al. 2016). Notably, advances in genomics and personalised medicine, as well as digitalisation and data analytics, are predicted to have a big impact and could be on the market by 2020 (INT17, INT20) (Albrecht et al. 2016). Interviewees felt the personalisation of treatments will importantly help to reduce the need for unnecessary chemotherapy and associated side-effects (INT17, INT18).

Several advanced innovations, such as gene therapy or biologic cancer drugs, are not covered by all healthcare systems and are not available in many European countries (INT17) (ECL 2018). This leads to significant out-of-pocket costs for patients (Aapro et al. 2017). The faster pace of innovation and some of the more ‘disruptive’ forms of innovation face a number of regulatory barriers (e.g. the use of inappropriate clinical trial models or the existence of uncoordinated regulatory pathways), which slow their entry to market (Albrecht et al. 2016).

Digital technology has the potential to improve access to quality cancer care by reducing fragmentation of information, empowering patients and delivering a patient-centred approach (Clauser et al. 2011). One interviewee thought that the increasing digitalisation of healthcare could potentially help to improve access to healthcare systems. For example, invitations to screening and how people respond will become increasingly digitalised in the future (INT17).

3.1.5. Legal
Part of the perceived inequalities in access to care for patients is due to inconsistencies in regulatory approval and reimbursement mechanisms across EU member states (INT17) (Aapro et al. 2017).
Different regulatory requirements and reimbursement procedures by regulators and health authorities across Europe can lead to delays in market access and reimbursement decisions in some countries (Aapro et al. 2017). There are also country differences regarding best practice around clinical guidelines and level of adherence to them (European Commission 2017). However, recent policy initiatives aim to create EU-level clinical guidelines to attempt to harmonise treating breast cancer across Europe (INT17) (Cardoso et al. 2017).

Different national bodies are often involved in making funding decisions for cancer care using different types of evidence (Aapro et al. 2017). There are also differences in the level of evidence available to judge the value of therapies and diagnostics, and Aapro et al. (2017) suggests that physicians are often inadequately trained to make decisions. Another major concern is the time taken to review new cancer drugs (Van Norman 2016). For example, one study found that the European Medicines Agency (EMA) took longer and approved fewer cancer drugs between 2003 and 2010 than the United States (US) Food and Drug Administration (FDA) (Roberts, Allen and Sigal 2011).

In recent years, the EMA has made efforts to accelerate the approval of potential innovations (Aapro et al. 2017). For example, there are special allowances for orphan drugs, which allow for greater flexibility in the regulatory process and faster access to innovative medicines (Aapro et al. 2017). The EU Clinical Trial Regulation published in 2014 aims to streamline clinical development programmes (European Parliament 2014). The development of EU-level guidelines will help to provide evidence-based guidance and quality assurance to EU policymakers and healthcare professionals regarding the screening and care of breast cancer (European Commission 2017).

3.1.6. Environmental

There are significant regional differences within and between countries in the cost and access to care, and the management of breast cancer (INT17, INT18) (Aggarwal, Ginsburg and Fojo 2014). Central and Eastern European countries often experience limitations in access to screening programmes and cancer care compared with Western European countries. This is particularly an issue for newer, typically more expensive, cancer treatments. The main barrier in these countries is lack of resources (financial, staff, health infrastructure) (Eniu and Antone 2018). Within countries, individuals living in rural areas can experience difficulty accessing specialist centres especially given that they often have to travel long distances (Hubbard et al. 2015).

The provision of mobile mammogram units can give greater access to screening for women living in rural or remote areas, particularly the elderly, those experiencing fatigue or living with disability (Todd and Stuifbergen 2012). Innovations such as single-dose radiotherapy programmes compared with standard radiotherapy programmes that last several weeks can significantly reduce journey times and improve access and uptake (Coombs et al. 2016).

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8 Orphan drugs are pharmaceuticals developed to treat a rare medical condition.
3.2. Italy

3.2.1. Political

Italy’s national healthcare system, the Italian Servizio Sanitario Nazionale (SSN), was established in 1978 and provides universal coverage that is largely free at the point of care, including all breast cancer care. The SSN is administered through Italy’s 20 regional governments and financed mainly through a combination of national and regional taxes, and co-payments for pharmaceuticals and specialist ambulatory services (European Observatory on Health Systems and Policies 2018b; France, Taroni and Donatini 2005). The national government is responsible for setting the core benefits that must be made available to citizens, but regional governments are granted significant autonomy in determining how to deliver those benefits (France, Taroni and Donatini 2005). The national government also has responsibility for allocating and dispersing nationally collected funds to the regions. Regional autonomy in decision making has resulted in substantial variation across regions in the organisation of care (European Observatory on Health Systems and Policies 2018b; France, Taroni and Donatini 2005).

Regional autonomy was a foundational principle of the 2001 constitutional reforms, which devolved most authorities for the development and implementation of health policy to regional governments. Regional administration occurs through an Aziende Sanitarie Locale (ASL). These are public organisations responsible for providing healthcare services to regional populations, and they are financed on a capitation (per population) basis (France, Taroni and Donatini 2005). It is up to each region whether the ASL directly administers and delivers healthcare through publicly run hospitals or if it contracts these responsibilities out to a private hospital or provider (European Observatory on Health Systems and Policies 2018b). Private contracting is more common in the south of Italy than in the north (France, Taroni and Donatini 2005).

The decentralisation within the Italian healthcare system presents challenges for policymakers seeking to implement change, including with efforts to provide better breast cancer care. For example, the Ministry of Health issued the Memorandum of Understanding (MoU) on the Reduction of Cancer Disease Burden for 2010–13, which seeks to improve the integration of cancer care services, promote best practices through professional development programmes, and reduce regional disparities. However, the decentralisation of authority within the system has meant that the MoU has not been fully implemented within all regions and the national government does not have the authority to enforce its implementation (The Economist Intelligence Unit Limited 2017).

Since 2001, a major focus of the government has been on cost control and containment within the SSN as public spending on healthcare was increasing at a faster rate than gross domestic product (GDP) (European Observatory on Health Systems and Policies 2018b). As part of this focus, the Ministry of Economics and Finance now plays a large role within the healthcare system, monitoring healthcare expenditures and overseeing the budgets of regions that have gone into debt. The consequences for regions that overrun their healthcare budgets vary, but can include compulsory financial recovery plans, the appointment of a national-government-appointed commissioner to oversee the system temporarily, or mandated tax increases (European Observatory on Health Systems and Policies 2018b). Among its
impacts, the focus on cost control and containment affects the recruitment and retention of the healthcare workforce, purchasing of new equipment, construction of new hospitals and supply of pharmaceuticals.

Our interviewees report that breast cancer is viewed as a political priority by Italian policymakers, and their high awareness of the importance of prevention and treatment of breast cancer is due in part to patient advocacy groups (INT14, INT16). These groups are considered effective in their work to raise public and policymaker awareness of the disease (INT14, INT16), and as an example one interviewee cited how treatment options for cancer patients were maintained despite the spending constraints imposed on the healthcare system (INT14).

3.2.2. Economic

The SSN is largely financed through public sources with approximately 80% of funds coming from national and regional taxes, and out-of-pocket spending making up the remainder. However, there are substantial regional differences in funding due to the portion of funding that comes from regional taxation (European Observatory on Health Systems and Policies 2018b).

The national healthcare system covers the full direct costs of screening and treatment for early breast cancer, including any co-payments that would normally apply to specialist treatment (INT14, INT15) (Capri and Russo 2017). A 2017 study estimated that the average cost to diagnose breast cancer in Italy per person was €414, with average treatment costing €8,780 and average costs of follow-up care being €10,970 (Capri and Russo 2017). The study authors noted that patient age, tumour stage and employment level of patient were significant predictors of follow-up costs, with older patients being associated with lower costs, and more advanced tumours and higher levels of patient employment being associated with higher follow-up costs. Another study used evidence from the cancer registry in Italy and found that the average overall cost per person to treat non-metastatic breast cancer (including diagnosis, treatment and follow-up) was €10,315.23 compared with €12,825.90 for metastatic breast cancer (Capri and Russo 2017). Furthermore, the authors found that the costs of treatment increased progressively with the stage of the disease (Capri and Russo 2017).

On an individual level, our interviewees reported that most patients do not experience economic hardships due to expenses related to treating early breast cancer (INT14, INT15, INT16). However, given regional differences in the quality and available supply of healthcare, some patients may choose to travel to receive care in a different region and the costs associated with this travel are not covered by the government (INT14) (France, Taroni and Donatini 2005; Nante et al. 2016). Interregional mobility for treatment has risen since the 1990s, with the largest group being patients travelling from southern regions to northern regions for care (France, Taroni and Donatini 2005).

Although the direct costs of treatment are covered, early breast cancer patients can benefit from additional forms of support that are not covered by the healthcare system. These include assistance with travel to their appointments or therapeutic activities such as yoga. Generally, patient advocacy groups within Italy provide these and other forms of support to early breast cancer patients and breast cancer survivors (INT16), as mentioned by one interviewee.

One interviewee perceived funding for breast cancer research as inadequate, though they saw this to be the result of a general lack of funding for scientific and clinical research rather than underinvestment in breast
cancer research specifically (INT14). In general, the Italian government provides a similar level of funding for cancer research as other European governments, in relation to its GDP (Begum et al. 2018). The Italian Ministry of Health was one of the largest individual governmental funders of cancer research in Europe from 2009 to 2013, spending €142 million. This was in conjunction with the Italian National Cancer Institute, Italian Ministry of Research and Universities and Italian National Research Council, which together provided an additional €172 million during the same period (Begum et al. 2018).

3.2.3. Social

As national health care is available to all citizens in Italy, social differences in healthcare are largely manifested in uptake of services rather than access to services. One example is found in breast cancer screening. The breast cancer screening programme in Italy provides free mammogram screening to every woman between the ages of 50 and 69, with guidelines recommending that personal invitations to attend a mammography screening be sent to women in this age group once every two years (Ventura et al. 2015). However, differences in uptake between northern and southern Italy are persistent; for example, for the target population in 2011–2012 in northern Italy the screening rate was 94% and in southern Italy it was less than 40% (Ventura et al. 2015). Ventura et al. (2015) note that there are also differences in uptake within regions, suggesting factors beyond region affect women’s participation in screening programmes. There is evidence that differences in education and occupation affect uptake of breast cancer screening: women with higher education levels and some occupational classes are more likely to undergo screening than others (INT14, INT16) (Damiani et al. 2012).

Differences also exist in the ability of patients to navigate complex healthcare systems. Once a patient receives a diagnosis of breast cancer, the quality of their care can depend in part on their health literacy, including their knowledge of their treatment options and their ability to identify appropriate healthcare providers to treat them. One interviewee highlighted how patients with lower education levels or with less experience with the healthcare system may be less likely to explore different treatment options or to search for the best doctors to provide their care (INT14). Prior research has confirmed that low health literacy, in the form of being able to understand instructions from doctors and adhere to medication regimens, is linked with poorer health outcomes broadly (Berkman et al. 2011), and for members of disadvantaged social groups with chronic illness (Schillinger et al. 2002).

3.2.4. Technological

New medical technologies are incorporated into the Italian health system via a regional health technology assessment (HTA) system, and the decentralised nature of the system has resulted in regional differences in available drugs and treatments. Regional HTAs differ in size of staff and budgets, available skills and knowledge base in their regions regarding HTA processes, and their resulting approach to the economic evaluation of health technologies (Garattini, van de Vooren and Curto 2012). These variations add up to real differences in the ability of staff in regional HTAs to evaluate new health technologies appropriately, with some simply lacking the skills to conduct the necessary assessment. The result is often delays in approvals for new treatments in resource-poor regions. Ultimately this means that northern and more urban regions generally have greater access to advanced medical technologies, partly because of the HTA process (European Observatory on Health Systems and Policies 2018b).
When considering the relevant technologies for treating early breast cancer in Italy, our interviewees suggested that there is a need to focus on the appropriate use of existing technologies through better organisation of care, as well as on managing access to new technologies (INT14, INT16). They highlighted in particular the issue of long wait times as affecting patients’ access to breast cancer treatment that is delivered in accordance with clinical guidelines (INT14, INT15). This is supported by data on long wait times for healthcare in Italy. Citizens perceive the quality of the healthcare system in Italy to be fairly poor, with Italy ranking 20th out of the 27 EU Member States in the 2012 Eurobarometer survey (European Observatory on Health Systems and Policies 2018b). Long wait times for outpatient specialist and diagnostic care in Italy can account for some of this dissatisfaction, and this combined with excessive bureaucratic hurdles can interfere with the ability of physicians to provide appropriate treatment on schedule according to clinical guidelines (European Observatory on Health Systems and Policies 2018b). Long wait times are perceived to be a significant enough issue that the national government passed legislation setting maximum wait times for various procedures (France, Taroni and Donatini 2005).

3.2.5. Legal
In Italy, there is a variety of available clinical guidelines relevant for breast cancer care that are published at international, national and regional levels. Adherence to any of the guidelines is not mandatory and physicians and hospitals are allowed to request different pharmaceuticals or treatments than those listed on the guidelines based on their expert judgement. However, our interviewees reported that although the guidelines do not dictate what is covered and reimbursed by the national healthcare system, it is easier for hospitals to get reimbursement for procedures and pharmaceuticals when they conform to national guidelines (INT14). Studies suggest that adherence to guidelines varies, with underuse of chemotherapy, radiotherapy and hormonal therapy being evident (Aristei et al. 2008; Sacerdote et al. 2013).

3.2.6. Environmental
The SSN is mandated to provide equitable access throughout Italy, yet regional differences in healthcare quality exist. In addition to previously mentioned variations (economic resources, screening uptake), differences in healthcare quality are evident in breast cancer mortality and incidence rates in Italy, which differ between the northern and central regions and the southern regions (Grande et al. 2007). Grande et al. (2007) report that breast cancer mortality rates began to fall approximately a decade later in southern regions, in the late 1990s, than in north and central Italy. Similarly, they report that incidence rates of new breast cancer cases have levelled off in northern and central regions, whereas they continue to climb in the south. The authors explain the regional discrepancy in mortality rates by the differences in breast cancer screening between the two regions.

Our interviewees also highlight the difficult geography of Italy. They note that mountainous regions in the north and seaside areas throughout the country can make travel to local hospitals difficult (INT14). These challenges are most pronounced for people of lower economic status.

3.2.7. Challenges
The national healthcare system is struggling with financial and organisational challenges, as well as regional variation in resource availability and uptake of services. By some accounts, the cost containment
measures implemented by the national government have been effective and the growth in healthcare expenditures has slowed or stalled (European Observatory on Health Systems and Policies 2018b). However, the consequences of the ongoing underinvestment in infrastructure that contributed to successful cost containment are likely contributing to some of the organisational challenges in delivering care underlying long wait times for treatment. Our interviewees highlighted the need to address the healthcare infrastructure in order to treat women with breast cancer on schedule in accordance with clinical guidelines, including by expanding the number of breast cancer units and through reducing wait times during cancer treatment (INT14, INT15).

The regional nature of the healthcare system also presents challenges as it introduces variability in financial resources within the local tax base, differences in the organisation and implementation of care, and differences in the functioning of regional HTA bodies. Regional autonomy has been a core principle of the SSN since the 2001 constitutional reforms, and most recent policy changes have been in the direction of greater regionalisation, not less (European Observatory on Health Systems and Policies 2018b). This suggests that those attempting to reduce regional disparities must do so in a way that respects regional autonomy. However, as the Ministry of Health’s experience with affecting cancer care through its non-binding MoU on the Reduction of Cancer Disease Burden for 2010–13 demonstrates, it can be difficult for the national system to drive changes in delivering care when it does not have the legal authority to compel change.

3.2.8. Opportunities

Regional differences in mortality trends and incidence rates of breast cancer may be related to differences in the uptake of screening (Grande et al. 2007). Furthermore, evidence suggests that differences in uptake of screening may be related to women’s socioeconomic status (INT14, INT16) (Damiani et al. 2012). This could be due to women with lower socioeconomic status having difficulties reaching the hospital to schedule or undergo their screening (INT14), or lower awareness of the benefits of screening among lower socioeconomic status women (INT14, INT16). Patient advocacy groups in Italy already work to educate patients about breast cancer and the benefits of screening (INT14, INT16). Some provide additional services to patients such as transportation to their appointments (INT16). Given the already active role of patient advocacy groups in Italy, patient advocacy groups could provide a valuable resource for addressing regional differences in screening uptake and potentially expand already existing campaigns to focus on these regional differences.

Our interviewees also highlighted potential technological opportunities for the diagnosis and treatment of breast cancer in Italy. The diagnosis of early breast cancer could be improved by the use of more digital mammography tools, which would enhance screening efforts and aid in detecting new malignancies (INT14). Regarding treatment, there is reportedly substantial interest from patients in advanced breast cancer treatments, such as genomics and personalised medicines, with patient advocacy groups reporting that patients are increasingly well informed about these new, advanced options for care (INT16).
3.3. Spain

3.3.1. Political

The political organisation of Spain comprises the central state and 17 regional administrations (termed autonomous communities), each with its respective government and parliament. The Spanish government must guarantee the right to health protection and healthcare for all citizens, as dictated in Article 43 of the Spanish Constitution of 1978 (Constitución Española 1978). It does so through the Ministry of Health and Social Policy, the coordinating authority of the Spanish National Health System, and the regional ministries or departments of health (INT08, INT09, INT10) (Avanzas, Pascual and Moris 2017; Bernal-Delgado et al. 2018; European Observatory on Health Systems and Policies 2018c).

The Ministry of Health and Social Policy is responsible for drafting health policy and the necessary enabling legislation. Specific responsibilities include: general organisation and coordination of health matters, international health and international health relations and agreements, and legislation on pharmaceutical products (Peralta 2006). Each autonomous region has legislative and implementation powers in the fields of public health, community care and most social services (European Observatory on Health Systems and Policies 2018c). The regional ministry or department of health controls the territorial organisation of health services within their jurisdiction, including the design of the healthcare areas and basic health zones, and the degree of decentralisation to the managerial structures in charge of each (European Observatory on Health Systems and Policies 2018c). The regional departments of health are responsible for the centres, services and facilities in its own community (Peralta 2006).

According to interviewees, the establishment of a national health system with 17 regional autonomous health services in Spain has led to differences in the delivery of care in breast cancer across Spain (INT09, INT10). For example, the implementation of the national screening strategy in Spain for early detection of breast cancer is region-dependent (INT08, INT09, INT10). These differences also extend to treatment availability, as drug budgets are regional (INT08, INT09, INT10) (discussed in more detail in Section 3.3.2).

Cancer is one of the top three causes of death in Spain, with breast cancer as the main malignant neoplasm in women. However, the mortality rate of cancer in Spain is almost 11% lower than the EU average. This is partly attributed to the breast-cancer-specific mortality rate, which is the lowest in Europe (23.4 per 100,000 inhabitants in 2018) (Eurostat 2018). This has been achieved through developing a national strategy promoting quality in cancer care (Minister of Health and Social Policy 2006), implementing early detection programmes, and making advances in diagnosis and treatment (INT09, INT10) (Ministry of Health, Social Services and Equality 2009). Additionally, in 2014 the Scientific Coordinator of the National Strategy for Cancer, Josep María Borrás stated that ‘cancer is a political priority in all health services because it is a social priority’ (Valerio 2014).

However, one interviewee commented that the successful reduction of mortality in breast cancer has led to a challenge for new treatment of early breast cancer in Spain (INT09), as breast cancer in Spain is currently perceived as a disease with available treatment and good survival rate, which has led to decreased focus in policymakers for the need of new treatment (INT07).
One interviewee commented that patient advocacy groups have played an important role in increasing awareness of breast cancer among the general population, encouraging patients to be active patients (INT10). For example, the First Impact Programme by the Asociación Española Contra el Cáncer Española Contra el Cáncer (Spanish Association Against Cancer) aims to provide patient and carer education (Tovar 2014). Patient groups have also contributed to the high media visibility of breast cancer, through organised events and campaigns, including Breast Cancer Awareness Day on which breast cancer is featured in almost every newspaper in Spain (Bertran 2017; EFE 2017; Romero 2017; Lucio 2017). However, an interviewee argued that the role of patient advocacy groups has been debated as most patient associations are funded by pharmaceutical companies, which may compromise their objectivity when advocating for better treatment (INT09).

Interviewees suggested there is an opportunity for patient advocacy groups to raise awareness of the impact of early breast cancer to society among policymakers and to make a case beyond survival when advocating for new treatment (INT07, INT10).

### 3.3.2. Economic

Spain has both a public and a private healthcare system (INT08), which account for 70% and 30% of healthcare costs, respectively (TforG Editorial 2016). The public national health system provides free basic healthcare to anyone contributing to the Spanish social security system and their families (Pencille 2008). It is funded through compulsory social security contributions from employees and employers, income taxes and state grants (TforG Editorial 2016).

Before 2012, all Spanish residents had free healthcare coverage at the point of delivery, with the exception of pharmaceuticals prescribed to people aged under 65, which entailed co-payment of 40% of the retail price (INT10) (European Observatory on Health Systems and Policies 2018c; World Health Organization Regional Office for Europe 2018). In 2012 the then Minister of Health, Ana Mato, introduced co-payments9 on a number of medications, including oral chemotherapy and certain adjuvants for cancer (De Vera 2017).

The cost of chemotherapy in Spain for women with breast cancer was estimated to be €428.5 per-patient per-cycle in 2004 (Paladio Duran 2008). This cost was increased when the patient presented with metastatic disease to €640.4 per-cycle. A second study estimated the cost of metastatic breast cancer over a five year period in a 100 patient cohort in Spain to range from €38,511 to €308,869 per-patient, depending on the number of treatment cycles required (Albanell et al. 2016).10 A separate study found the average cost of hospital admission in 2003 increased from €2,374 in patients with early breast cancer to €3,515 in patients with metastatic bone disease (Pockett et al. 2010).

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9 Co-payments now include a 10% co-payment on medicines for pensioners and 40–50% on medicines for non-pensioners (World Health Organization Regional Office for Europe 2018).

10 This study included both direct and indirect costs. Direct costs included medication and healthcare resources costs (visits, tests, hospitalisations, surgery, adverse events management and treatment of specific metastases). Indirect costs were estimated using the human capital approach.
Health expenditure is mainly determined by the regional administrations (INT08, INT09) (European Observatory on Health Systems and Policies 2018c). Each autonomous community covers the cost of treatment, including surgery and in-hospital care (INT08, INT09, INT10). Each regional administration has its own drug budget to invest in treatment available in the different regions. Once a drug is approved by the Spanish Agency of Drugs and Medical Products, each region can decide whether to invest and incorporate the new drug into its regional formulary. In some regions, staff in individual hospitals decide whether to invest in a nationally approved drug (INT09). Interviewees commented that this regional investment in treatment leads to delays in the availability of new treatment options between regions (INT08, INT09, INT10).

There are additional costs associated with breast cancer, such as those mentioned by interviewees: unemployment, paying for psychological support and travel expenses. Patients receiving treatment for early breast cancer are generally unable to work. In Spain, unemployment benefit is paid for either by government or employer, and covers up to 18 months of unemployment (INT09, INT10). One study estimated the annual cost of productivity loss in Spain due to breast cancer to be between €11.6 million12 and €288.7 million13 depending on the approach taken (Oliva et al. 2005). Although the figures are significantly different, both approaches found the main cause of productivity loss was permanent disability as a result of breast cancer.14

Temporary disability may have additional costs beyond income reduction. In many instances patients must be accompanied to the hospital where they receive treatment. In Spain, if a parent must care for a sick child or a person must care for elderly relatives, carers can receive a paid leave of absence (INT10), but it does not extend to other close family members and would not cover caring for partners or sisters (INT10).

Interviewees commented that patients with early breast cancer may require additional support to cope with their diagnosis and treatment (INT09, INT10), but psychological support during breast cancer is not covered by the public health system, but rather provided by patient associations (INT09, INT10). Additionally, the director of the Department of Psycho-oncology of the Spanish Association Against

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11 This study did not focus specifically on early breast cancer.

12 Estimated using the friction cost method, which is based on the idea that workers with a temporary disability can make up for lost work when they return to work, co-workers can replace them in urgent tasks, and non-urgent tasks can be cancelled. In the case of permanent disability or early mortality the worker would be replaced by another person from the unemployment pool, filling the vacant position.

13 Estimated using the human capital method, which assumes that when workers leave the labour market, their labour productivity is lost until they return to work, in the case of temporary disability, or until the end of their working life, in the case of permanent disability.

14 The European Foundation for Improvement of Living and Working Conditions defines disability as a physical or mental condition which makes a person totally or partially incapable of working, whether as an employee or self-employed. Spanish law divides disability into two categories: temporary, where the individual is likely to recover in the short or medium term, and permanent, where the reduction or loss of capacity is likely to be permanent. Permanent disability can be partial, which makes it difficult but not impossible for the individual to pursue their usual occupation; total, which makes individuals unable to pursue their usual occupation; absolute, which prevents individuals from pursuing any occupation; or major, where individuals require a carer.
Cancer highlighted that psychological support is generally sought after treatment has ended (Ximenez 2016).

Travel expenses are another cost patients with early breast cancer incur, when they travel to a hospital to receive treatment (INT10). The cost of travel is generally not reimbursed, though there is an exception. A representative of a patient advocacy group in the Canary Islands (INT10) told us that in the autonomous communities comprising archipelagos, such as the Canary Islands, the best available treatment is usually found in the main islands. Therefore patients from smaller islands must travel to be treated and relocate for a period of time (INT09, INT10). In these particular cases, the regional administration covers the patients’ travel costs (INT10).

3.3.3. Social

Interviewees consulted during this study identified no marginalised groups or stigma that would prevent patients from seeking treatment for early breast cancer (INT08, INT09). However, a study looking at barriers and discourses about breast cancer in Spain found that immigrant women were more reluctant than native women to talk about breast cancer (March et al. 2018), suggesting there is a cultural stigma around the disease. This study also found that language barriers, income and fear due to status as an undocumented immigrant were sometimes barriers to accessing screening. Another study looking at uptake of breast cancer screening programmes in Spain found that being an immigrant was a negative predictor for breast screening uptake (Ricardo-Rodrigues et al. 2015). Therefore, there are cultural barriers that may prevent immigrant women from seeking diagnosis and treatment of early breast cancer.

3.3.4. Technological

Interviewees thought the drug approval process was the main regulatory barrier to accessing treatment in Spain (INT08, INT09). The Agencia Española de Medicamentos y Productos Sanitarios (AEMPS) or Spanish Agency of Drugs and Medical Products, the agency responsible for approving new drugs in Spain, is in charge of ensuring that pharmaceutical products registered in Spain meet the criteria for quality, safety and clinical efficacy. Once the drug has a positive opinion from the EMA’s Committee for Medicinal Products for Human Use, the AEMPS coordinates the production of the Therapeutic Positioning Report. This task complements the work of the General Directorate of Pharmacy and Health Products, which has authority regarding public funding of licensed pharmaceuticals (European Observatory on Health Systems and Policies 2018c).

Once a drug is approved and the price agreed at a national level, the different regions decide whether to cover the cost of new technologies and pharmaceuticals (INT09). Therefore, the availability of new technologies and treatments depends on the autonomous communities, which interviewees believed to result in differences in available treatment because of the economic differences between regions (INT08, INT09).

15 The Therapeutic Positioning Report is a network document written by an expert panel in collaboration with experts designated by the autonomous communities. It assesses the risk-benefit balance of new drugs and indications in order to position them with the rest of available therapeutic alternatives.

16 At the time of this study, 12 autonomous communities have centralised decisions and decisions are made at a hospital level in only five regions.
INT09, INT10). However, one interviewee argued that the differences in drug availability in the different regions was not solely dependent on economic factors, providing Navarra as an example of a rich region with very restrictive access to drugs due to their cost-effectiveness assessment (INT07). These differences are only true for the public system. Once a drug is approved nationally, an autonomous community cannot deny a patient access to the drug (Corbacho et al. 2015) therefore, according to one interviewee, if a patient can fund their treatment personally they can access it through the private health system (INT08).

3.3.5. Legal
Spain does not have national guidelines for treating early breast cancer. In 2015, the Sociedad Española de Oncología Médica (SEOM) or Spanish Society of Medical Oncology conducted an evidence review and developed recommendations to serve as clinical guidelines for early breast cancer (Garcia-Saenz et al. 2015). These guidelines were updated in 2018 (Ayala de la Peña et al. 2019). However, interviewees told us these are seen as recommendations and are not adhered to more than other international guidelines because there is no defined model to follow at country or regional level (INT08, INT09).

3.3.6. Environmental
As explained previously, because of the decentralised healthcare system in Spain, delivery of care for early breast cancer varies in the different regions of Spain (INT08, INT09, INT10). Interviewees commented this is due to not only economic differences but also geographical barriers (e.g. mountain villages or rural populations) (INT09, INT10). For example, the mortality rate for breast cancer between 2009 and 2014 was 23.07 per 100,000 women in Madrid, but 36.32 per 100,000 in Asturias (L.A. 2016). This is mostly due to economic differences between the regions and geography. Madrid is the capital region of Spain, with good access to treatment and clinical trials. It has numerous hospitals, many of which are university hospitals. On the contrary, Asturias is a more rural mountainous region in Spain.

Differences in the incidence of early breast cancer across Spain are also related to differences in the implementation of screening programmes. Spanish public health authorities provide a population-based breast cancer screening programme for all women aged 50–69, offering a biannual screening mammography free of charge (Ministry of Health, Social Services and Equality 2009). However, some regions, such as Navarra, recommend starting screening at the age of 40 (INT09) (Martín-López et al. 2013). One interviewee commented that screening at an earlier age (40) did not increase the rate of early detection of early breast cancer, but rather led to more false positives (INT09).

3.3.7. Challenges
The main challenges in Spain to policymaking and accessing treatment for early breast cancer are the decentralised healthcare system, the process of drug approval and the cost of delivery of care. The decentralised healthcare system results in regional policies in diagnosing and treating early breast cancer. Regional policies and drug budgets lead to variation in delivering care across Spain, as different communities invest in different resources for care and management of early breast cancer. Although interviewees commented that the quality of regional healthcare is not a big issue for current available
treatments for early breast cancer, it is an important factor when new treatment options become available (INT08, INT09).

The second barrier is associated with the cost of delivering care. As mentioned previously, Spain has the lowest mortality rate for breast cancer in Europe, due to its implementation of screening programmes and advances in diagnosis and treatment. However, these advances, together with an ageing population, have contributed to an increased incidence in the diagnosis of breast cancer in Spain (Andrade, Sacristan and Dilla 2017). Interviewees commented that this has led to increased cost to the health system as more women are being diagnosed and receiving treatment (INT08, INT09, INT10). They thought it difficult to make a case now for new drugs to treat early breast cancer because of the costs involved and the perception that early breast cancer does not require investment in new drugs as there is sufficient efficient treatment available (INT07, INT10).

3.3.8. Opportunities

There are good survival rates for women with breast cancer in Spain and treatment is available for them, but there are non-clinical effects of early breast cancer that impact society. Interviewees agreed there is an increased cost to society associated with good survival and available treatment resulting from loss of productivity in an increasing number of patients receiving treatment (INT09, INT10). Therefore, there is an opportunity for new treatment that can improve the quality of life of patients, enabling them to remain active members of society while receiving treatment.

Patient advocacy and awareness campaigns have been very successful at raising awareness of early breast cancer among the general public. One interviewee considered there is an opportunity for patient groups to raise awareness further on issues around quality of life in patients receiving treatment for breast cancer (INT10).

3.4. The United Kingdom

Most information presented for the United Kingdom in this study focuses on practices within England, not Scotland, Northern Ireland or Wales. This reflects the knowledge of the four interviewees, although where possible we complemented and mitigated this limitation with information from the literature. As governance, funding and practice in the four countries of the United Kingdom are very different, we focus on England, pulling information together to extend beyond England to a UK level where relevant.

3.4.1. Political

The United Kingdom is composed of four nations: England, Scotland, Wales and Northern Ireland. In 1948 the United Kingdom established the National Health Service (NHS), which is available to all legal residents and largely free at the point of care (European Observatory on Health Systems and Policies 2018d). Decision making and delivery of healthcare have been devolved to the individual countries such that each country is responsible for its own health policy, though the health budget is set by the UK government (European Observatory on Health Systems and Policies 2018d). A guiding principle of the NHS is that all citizens have equal access to healthcare (Goddard and Smith 2001). This principle influences the structure of the health system such that primary care services are prioritised, with every legal
resident being encouraged to register with a primary care general practitioner (GP), and those GPs in turn serving as gatekeepers to more expensive secondary care (Goddard and Smith 2001).

Within England, recent changes under The Health and Social Care Act 2012 have led to further devolution in decision making along with structural shifts designed to increase market-based competition, while giving GPs a greater say in the commissioning of health services (Ham et al. 2015). The 2012 legislation established local clinical commissioning groups (CCGs) composed of GPs and elected representatives, and gave them responsibility for two-thirds of the total NHS England budget (Ham et al. 2015; NHS 2018). CCGs directly commission health services by issuing contracts to private providers and government agencies to provide services to their local communities through the NHS system. Approximately half of commission services flow through NHS trusts, most commonly foundation trusts, which are not-for-profit public benefit corporations with the primary purpose of providing NHS services to patients (NHS England 2005, 2018).

According to interviewees, breast cancer is considered a political priority in the United Kingdom (INT21, INT22, INT23), and an example of this is the government’s support for initiatives from the UK NHS to encourage early diagnosis (INT22). One such initiative is the National Breast Cancer screening programme, which offers screening to both younger women (aged 47–49) and older women (aged 71–73) in order to assess the effectiveness of expanding the screening programme.17

Patient advocacy is perceived to play an important role in raising awareness of breast cancer among the general public and policymakers (INT21, INT22, INT23, INT24). Patient advocacy can be beneficial to patients when it promotes appropriate treatment or enhances awareness. However, one interviewee expressed concern about the role of patient groups in advocating for treatment with unproven efficacy or potential side-effects (INT23).

3.4.2. Economic

Healthcare is mainly funded through general taxation with a small portion of total health expenditure coming from out-of-pocket payments (9.3%), private medical insurance (2.3%), or other forms of private expenditure (5%) (European Observatory on Health Systems and Policies 2018d). A study estimated the total average cost of care for providing breast cancer treatment to be between £25,966 and £26,304,18 depending on the age of the patient at time of diagnosis (Laudicella et al. 2016). NHS England covers the costs of breast cancer care related to the main treatment pathway, from diagnosis through treatment. However, our interviewees report that additional associated costs such as travel and lost wages are out-of-pocket expenses covered by the patient (INT22, INT24), and that costs such as those associated with travel may act as a barrier to individuals receiving treatment (INT23).

In England, employers must make reasonable accommodations or adjustments for people who have a health condition, including those with breast cancer, and are not allowed to discriminate against them

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17 Current practice in England consists of automatically inviting women aged 50–71 who are registered with a GP for screening every three years. Women over the age of 70 can arrange screening themselves despite not being formally sent an invitation letter to attend screening (NHS 2017b).

18 This estimated cost is based on data from 2010.
during the recruitment or hiring process in line with the Equality Act 2010 (Government Equalities Office n.d.). One common type of accommodation is to request a flexible work schedule or paid time off through statutory sick pay to accommodate treatment schedules (Macmillan Cancer Support 2016). Carers also have the legal right to request flexible work schedules under the Children and Families Act 2014 and to take reasonable time off to handle medical emergencies related to their dependants under the Employment Rights Act 1996. However, employers are not required to provide flexible schedules or make other reasonable accommodations for carers, only to consider their requests (Macmillan Cancer Support 2016). Furthermore, employers are only required to make accommodations for people that are financially and practically feasible (Government Equalities Office n.d.), which in practice can leave patients uncertain of their rights.

Local authorities have faced budget cuts in recent years, with planned cuts averaging 3.9% a year to 2020/21 (BMA 2018). This has contributed to cuts in prevention interventions, such as smoking cessation services, substance misuse services including the prevention of alcohol misuse, and obesity services, all of which are known risk factors for breast cancer (INT23, INT24) (BMA 2018; Cancer Research UK 2015b).

Budget cuts have an impact on preventative measures, and the potential to increase wait time targets by reducing necessary resources to address patient needs in a timely manner (Iacobucci 2017; The King’s Fund 2017). One interviewee noted that institutions that do not meet wait time targets may not get further funding, even though the additional funding could aid them to meet those wait time targets (INT24). Budget cuts may further affect the ability to implement new guidelines of the National Institute for Care Excellence (NICE) (INT23) (Iacobucci 2017) by influencing the decision of CCGs on which medications they choose to fund, and of clinicians on which medications they offer to their patients (The King’s Fund 2016).

Finally, there is a perception that when measuring the cost-effectiveness of prevention and treatment other factors than solely the cost of the medication drug should be considered (INT23, INT24), such as quality of life, the ability to return to employment more rapidly, or a reduction in the cost burden on carers (INT21, INT23, INT24). One interviewee acknowledged that new advances in treatment may not necessarily result in better survival outcomes, but in better delivery of care, or in patients perceiving that they are receiving better care (INT23).

3.4.3. Social
Access to screening and early diagnosis is available to all women aged 50–71, though uptake of screening programmes varies across demographic groups. Differences in screening uptake have been linked with economic deprivation, ethnicity and language, with Bangladeshi and black women having some of the lowest rates, although population differences vary by region (All-Party Parliamentary Group on Breast Cancer 2018). These factors affect screening uptake as some women have limited resources for travel or cannot easily take time off work, they may have cultural taboos around breasts and cancer, and some face

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19 Local authorities are responsible for many of the local needs of the population including promoting health (e.g. by having public health programmes) (NHS n.d.).

Socioeconomic status has also been associated with breast cancer occurrence, and some argue that breast cancer is more likely to occur in higher than lower income individuals (INT22) (Cancer Research UK 2015c). This may be partly because women of lower socioeconomic status are less likely than other women to attend screening programmes (Jack et al. 2014).

There are also ethnic differences in the incidence of breast cancer. Black, Asian and minority ethnic (BAME) populations are often less frequently diagnosed with breast cancer than the white ethnic group (Cancer Research UK 2015a). One reason for this may be that BAME populations are less exposed to risk factors associated with breast cancer (Gathani et al. 2014). However, despite the lower incidence of breast cancer in these ethnic minorities, data show that when diagnosed they are more likely to die from the disease than white ethnic women (Martins and Hamilton 2016). One interviewee argued that the higher mortality rates among BAME women may be because patients did not adhere to the course of treatment (INT22).

3.4.4. Technological

New health technologies and drugs in England are appraised for clinical efficacy and cost-effectiveness by the NICE HTA. NICE is the English regulatory body for approval of new drugs in England, and the body responsible for updating clinical guidelines (NICE 2019a, b). Since 2008, NICE has included the assessment of health-related quality of life in its guidelines for technology appraisal using the EF-5D-3L tool (NICE 2018b). England is one of the countries that includes the valuation of quality of life when approving drugs.

One interviewee mentioned there is often a three-month delay between NICE approving a new drug and the drug being available through the NHS (INT21). As a countermeasure for the effects of this delay on cancer patients, NICE set up the Cancer Drugs Fund in 2016, which aims to enable patients to access certain drugs before the price of the drug has been negotiated, thereby reducing the three-month wait time (INT21) (NICE 2019a).

According to two interviewees, publicity can be a driving force for the uptake of new technology (INT21, INT23). One said that when patients advocate for new technologies, it increases the likelihood of uptake of that technology (INT21), but these new technologies are not always valuable, useful and/or scientifically sound (INT23). For example, the 21-gene test is given to women who are hormone receptor positive (HER+) and used to predict the risk of breast cancer recurrence in these women. Despite its popularity, there is little evidence that it reduces the need for chemotherapy (Ray et al. 2016).

Other technologies gaining popularity across the health sector include increased genomic profiling and personalised medicine (INT22, INT24) (Lancet 2018). One example of genetic profiling is via the Oncotype DX genetic test, which allows better prediction of which individuals will benefit from chemotherapy or other treatment options (INT22) (Breastcancer.org n.d.). However, there is large cost associated with personalised medicines (INT24). One interviewee stressed that cost-effectiveness should take into consideration the cost of the technology, as well as quality of care of women not having to undergo unnecessary treatment (INT22).
The way existing technologies are used can in itself be changed. For example, a UK trial, Faster Radiotherapy for Breast Cancer Patients (FAST), is investigating the effects of having fewer radiotherapy sessions (once a week for five weeks) with a larger treatment dose, compared with conventional therapy (daily for five weeks). Both the initial results published in 2011 and the subsequent results presented at the San Antonio conference in 2018 suggest that there is no difference in patient outcomes for either of the treatment options (ASTRO 2018; The FAST Trialists Group 2011), and the number of hospital visits for patients is greatly reduced with the new course of treatment (INT22) (ASTRO 2018).

3.4.5. Legal

Compliance and adherence to guidelines were found to vary across NHS trusts in the United Kingdom (Ashken et al. 2016; Mylvaganam et al. 2018) and interviewees suggested this might be because of a lack of physical resources (INT22, INT23), but the reasons are more complex than that. In a study of innovation uptake in the NHS, Marjanovic et al. (2018) found a number of additional factors related to skills, leadership, motivations, accountabilities and other drivers, such as what needs to be stopped and decommissioned for a new innovation to be embedded into the system.

One interview noted that if guidelines state that an oral drug should always be paired with another intravenous drug when prescribed, but the hospital has insufficient intravenous equipment to treat the patient in this way, then clinicians may find it necessary to prescribe drugs that are more readily deployable (even if inferior) in order to get patients the care they need in a timely manner (INT22). Additionally, implementation of guidelines is limited by available funding for the cost of treatment (INT23). The same interviewee also commented that lack of adherence to clinical guidelines could be due to lack of regulation of adherence (INT22). NICE guidelines stipulate what services CCGs in England should commission, but following fiscal austerity measures there are insufficient funds to police whether this is happening in reality (INT22).

3.4.6. Environmental

Despite the emphasis placed on there being equality of access within the NHS, a recent report from the All-Party Parliamentary Group on Breast Cancer found significant differences across England in the diagnosis, treatment and care that women receive for breast cancer (All-Party Parliamentary Group on Breast Cancer 2018). Disparities generally occur at the level of the CCG, or between more localised levels such as cities and towns, which the report argues result from population differences and the decentralised nature of service commissioning and the organisation of care. The report found considerable variability across regions in the percentage of breast cancers being detected at stage I or II, with detection rates ranging from 36.3% to 88.0%. It noted that differences between CCGs in the number of radiographers and radiologists available to perform and interpret mammograms contributes to variability in wait times between diagnosis and treatment. CCGs have a strong role in determining which treatments to fund, so patients in different areas can be offered different treatment options, and variable access to preventative

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20 A NHS trust is an organisation within the NHS that serves either a geographical area or a specialised function.
medicines such as tamoxifen and bisphosphonates, depending on the policy of their CCG (All-Party Parliamentary Group on Breast Cancer 2018).

Each of the four nations of the United Kingdom has their own corresponding HTA process. For example, in England NICE decides which new medications to adopt (NICE 2018a), while in Scotland the Patient Access Scheme Assessment Group makes these decisions (Healthcare Improvement Scotland [2017]). Therefore not all guidelines or drugs available in one nation are necessarily available in another. One interviewee suggested that policymakers in Wales and Northern Ireland often adopt NICE recommendations, whereas those in Scotland take a different approach, using a unique patient voice system, Patient and Clinician Engagement (INT22). Therefore there may be differences in access to treatment between Scotland and the other countries of the United Kingdom for women with breast cancer (INT24) (Healthcare Improvement Scotland [2014]). Furthermore, although women with breast cancer should have equitable access to treatment wherever they live in England, one interviewee commented that more deprived areas struggle to offer all services to patients (INT24).

3.4.7. Challenges

Different CCGs in the United Kingdom approve different new cancer drugs for use, leading to different guidelines throughout the country (INT24). Although the HTA process in England is viewed as a comprehensive model, there are limits to its use because of factors beyond traditional cost-effectiveness (Pitini et al. 2018), such as quality of life, patient satisfaction and additional considerations, including time off work.

Although there is in theory universal access to treatment for breast cancer in the United Kingdom, in practice some women face language and cultural barriers to accessing and receiving it (INT22, INT23, INT24) (All-Party Parliamentary Group on Breast Cancer 2018), and some services are limited because of insufficient funding and workforce capacity. There is a lack of appropriately trained professionals, such as radiologists (INT22) (All-Party Parliamentary Group on Breast Cancer 2018). One interviewee suggested that workforce issues could worsen after Brexit (INT22), although other stakeholders might have different views. In preparation, the Independent Cancer Taskforce within the UK NHS has put together a document specifying that some practices may need to change post-Brexit, but the exact nature of the changes remain unclear (NHS 2017a).

Treatment of breast cancer is expensive. Nevertheless, the costs of not treating early breast cancer are known to surpass the upfront cost of treating the disease (INT22, INT23) (Sun et al. 2018; Wolstenholme, Smith and Whynes 1998). One interviewee thought the high cost of disease progression may be because breast cancer tends to act as a chronic disease, increasing the length of treatment and therefore the overall cost of cancer care for patients with metastatic disease (INT23).

3.4.8. Opportunities

There is high awareness of breast cancer in the United Kingdom, partly due to the advocacy activity of patient groups. Although only patients in Scotland are directly involved in deciding which new medications to adopt (through the Patient Access Scheme Assessment Group), patient groups in England, Wales and Northern Ireland can influence whether new drugs are approved for use within the NHS in
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England (INT21, INT22, INT23, INT24), but there is an opportunity to further incorporate the patient voice into HTA processes.

The introduction of additional key worker roles (e.g. clinical nurse specialists) to help patients navigate the service would be beneficial, according to one interviewee (INT22), and has been shown to improve patient health outcomes (NICE 2016). Additionally, the use of artificial intelligence could potentially reduce the burden of current healthcare workers. Artificial intelligence could be used to read mammogram scans, freeing up clinician time if only one rather than two readers is needed to examine mammogram scans (INT22) (Lindemann 2018; Massat 2018).

3.5. Canada

3.5.1. Political

Canada has a decentralised healthcare system, which governs, organises and delivers care (European Observatory on Health Systems and Policies 2018a; Government of Canada 2011). Provincial and territorial administrations are responsible for funding and delivering most healthcare services, and multiple organisations operate closely with provincial governments. These include regional health authorities and private long-term care facilities; physicians may be independent contractors (Axelsson, Marchildon and Repullo-Labrador 2007). Most planning of the health system is conducted at provincial and territorial levels, though some provinces have established regional health authorities that plan and deliver publicly funded services for their defined populations (Allin and Rudoln n.d.; European Observatory on Health Systems and Policies 2018a). Until recently some provincial ministries of health and regional health authorities had provincial quality councils and HTA programmes, which were responsible for assessing new drugs and technologies at regional level (Allin and Rudoln n.d.).

In recent years, there has been a trend towards greater centralisation and harmonisation of care across Canada (INT04, INT05) (European Observatory on Health Systems and Policies 2018a). Although provinces and territories administer and deliver most of Canada’s healthcare services, all provincial and territorial health insurance plans are expected to meet national principles set out under the Canada Health Act, related to public administration, comprehensiveness, universality, accessibility and portability (Government of Canada 2011). The HTA process has been centralised and is the same for all provinces, with the exception of Quebec (INT03, INT04, INT05), which conducts its own provincial HTA through the Institut National d’Excellence en Santé et en Services Sociaux (the National Institution of Excellence in Health and Social Services). Both the Canada Health Act and the centralised HTA attempt to support the harmonised delivery of care for breast cancer across Canada. However, there are still differences in the extent to which treatment is covered (discussed in detail in Section 3.5.2) and the time from approval to access (discussed in detail in Section 3.5.4) in the different provinces (INT03, INT04, INT05, INT25).

Most interviewees agreed that cancer in general is a political priority in Canada (INT03, INT04, INT25). One argued this was partly because policymakers have become increasingly aware of the potential epidemic of age-related diseases associated with an ageing population (INT25), though no individual cancer is prioritised above others (INT03, INT04, INT25). In 2016, the Canadian Partnership Against
Cancer developed the Canadian Strategy for Cancer Control 2017–2022 with the aim of reducing the burden of cancer on the healthcare system and Canadians (Canadian Partnership Against Cancer, n.d.). Although this is a positive aim, one interviewee mentioned there was still little real understanding of the differences between the different types of cancer, lengths of treatment, debilitating effects associated with different types of cancer and so on, which could drive cancer-specific policies (INT25).

Patient organisations play a strong advocacy role in increasing public awareness of breast cancer in Canada and getting it onto the political agenda (INT03, INT04). Patient advocacy initiatives include providing input into the HTA, liaising with provincial and federal decision makers to ensure they address the needs and concerns of patients affected by breast cancer, engaging media to raise awareness around priority issues, connecting patients and partner organisations, and publishing reports calling for action and awareness around priority issues (Canadian Breast Cancer Network n.d.). Patient advocacy groups have contributed to breast cancer being one of the most visible cancers in the country (INT04).

The patient voice has been represented in the HTA process in Canada for the reimbursement evaluation of oncology drugs since 2010 (INT03, INT04) (Jutai and MacKean 2015; Stein 2016). The HTA process in Canada is divided into four quadrants: overall clinical benefit, cost-effectiveness, feasibility of adoption into the public health system, and alignment with patient values (Pan-Canadian Oncology Drug Review 2011) (INT04). Each quadrant has the same weight when decisions are made on reimbursement of new drugs. On behalf of individual patients and their caregivers, representatives from patient organisations provide perspectives on living with breast cancer, the limitations imposed by the disease, patients’ needs and preferences in managing the symptoms and side-effects of treatment, and their experience with the drug under review (Stein 2016). The Pan-Canadian Oncology Drug Review Committee (which sometimes has patient representatives) evaluates new drugs and discusses issues patients raise (INT03, INT04).

3.5.2. Economic

Each province and territory is responsible for administering its own tax-funded and universal hospital and Medicare21 plans (INT03, INT04, INT05, INT25) (European Observatory on Health Systems and Policies 2018a). Provincial and territorial residents are entitled to free medically necessary22 hospital, diagnostic and physician services received at the point of care (Government of Canada 2011). Provincial and territorial governments also subsidise other health services, including prescription drug coverage and long-term and home care. These provincial programmes generally target specific populations based on age or income and generally require contributory user fees (European Observatory on Health Systems and Policies 2018a; Government of Canada 2011). These fees can be paid for out of pocket, or be covered under an employment-based insurance plan or through private insurance (INT04, INT05) (Government of Canada 2011). However, most provincial and territorial laws restrict private insurers from offering

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21 Medicare is the term given to the publicly funded health care system in Canada.
22 Medically necessary services are not defined in the Canada Health Act. Each provincial and territorial health plan determines which services are medically necessary for health insurance purposes.
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coverage that duplicates what is funded through the public system so private funding can only be used to cover supplementary services (Government of Canada 2011).

Overall, in-hospital treatment is provided without charge to patients as part of National Medicare (INT03, INT04, INT05, INT25) (European Observatory on Health Systems and Policies 2018a). The cost of outpatient treatment can be covered in whole or partly through public or private drug plans (INT04, INT05) (European Observatory on Health Systems and Policies 2018a). A study calculating the economic burden of cancer care in Canada found that the costs had risen from Can$2.9 billion in 2005 to Can$7.5 billion in 2012, following an increase in costs of hospital-based care driven mostly by an increase in chemotherapy and radiation therapy expenditures (Oliveira et al. 2018). A study conducted in Ontario between 2005 and 2009 estimated the overall mean cost from a public payer per case of breast cancer in the first two years after diagnosis was $41,686, and that this cost increased over the two-year period by stage from Can$29,938 in stage I breast cancer to Can$66,627 in stage IV breast cancer (Mittmann et al. 2014). The study identified the costs as relating to cancer clinic visits, physician billings and hospitalisations.

Cost of treatment varies according to each province and territory. A study comparing the estimated cost of cancer care in British Columbia and Ontario found that overall the costs for cancer treatment were higher in Ontario, with the main differences being the costs for physician services and diagnostics tests (De Oliveira et al. 2017), mainly due to the extent and depth of coverage in provincial and territorial drug plans (INT03, INT25) (Chafe et al. 2011; Menon, Stafinski and Stuart 2005). For example, in Ontario and Nova Scotia, once the government has decided to cover the cost of a drug, access depends on whether the drug is intravenous or oral (INT03). If the drug is intravenous, no payment is required from the patient. If the drug is oral, it is made available to patients through the government programme: patients can get their prescription filled through the pharmacy but there is a required co-payment (INT03). This system impacts patients decisions on whether to obtain non-intravenous drugs or intravenous ones, depending on what costs they can afford, irrespective of whether it is the most suitable treatment course for them (INT03, INT06). Oncologists struggle to provide optimal cancer care when they have limited access to their preferred treatment options (INT25) (Chan et al. 2012), including drugs for side-effects (INT25).

As mentioned previously, there are provincial and territorial benefits plans that provide additional health services. Patients can access these health services in a different province if they wish, and generally meet the cost of travel and accommodation (INT05). Patients do not usually receive reimbursement for seeking treatment in a different province, with the exception of patients residing in the three Northern Territories. Patients from this region have access to treatment in five cities across five provinces in Southern Canada and are reimbursed (INT05). Some formal agreements allow residents in certain provinces to be compensated for out-of-province healthcare. For example, Prince Edward Island offers out-of-province travel support programmes including agreements with the Maritime Bus Service and

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23 The out-of-pocket expense for oral therapy in this case is less if the patient is employed and has an active health plan or over 65.
Hope Air (Prince Edward Island 2018), though Health Prince Edward Island (the health authority for the Canadian province of Prince Edward Island) must approve patients’ out-of-province medical services. Other services also vary across provinces. For example, drug treatment may be generally covered everywhere in Canada, but access to psychosocial support\(^{24}\) and key healthcare professionals varies by and within province (INT05, INT06). Cancer centres can provide psychosocial support publicly but there is limited access to this benefit (INT05).

Interviewees mentioned unemployment as being an additional cost for patients with breast cancer (INT05, INT06, INT25), which usually affects women of working age who must take time away from work to receive treatment. The national government currently covers 15 weeks of unemployment due to sickness (McGill BC Cancer n.d.), but this is usually less than the length of treatment for breast cancer (INT05). Once the 15 weeks have passed, patients can access their private insurance or, if they have metastatic cancer, use their Canadian pension plan (INT05). A prospective cohort study from 2008 found that wage losses and their effects on a patient’s financial situation constitute an important adverse consequence of breast cancer in Canada (Lauzier et al. 2008). The authors found than on average women with breast cancer lost 27% of their projected usual annual wages and that a higher percentage of lost wages was associated with a lower level of education, living more than 50 km away from the hospital where surgery was performed, and lower social support, among others (Lauzier et al. 2008). In a further study Lauzier et al. (2013) found that although out-of-pocket costs from breast cancer for the year after diagnosis are probably not unmanageable for most women in Canada, some women experience financial burden resulting from these costs. In this second study, the authors found that higher out-of-pocket costs were associated with higher education, working at the time of diagnosis, living more than 50 km from the hospital where surgery was performed, and having two and three different types of adjuvant treatments (Lauzier et al. 2013).

3.5.3. Social
Canada is very multicultural country. Interviewees reported stigma\(^{25}\) around breast cancer in certain communities, such as aboriginal communities (INT05, INT06, INT25) and language barriers to cancer care. Regional authorities and patient advocacy groups provide most information on breast cancer care in English and French so patients who do not speak these languages can find it challenging to access information (INT05).\(^{26}\)

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\(^{24}\) Psychosocial support is generally provided in the form of organised support groups or programmes that allow patients to meet and share experiences. These groups may be offered through the hospital or treatment centre, a doctor’s office and other organisations(Canadian Cancer Society n.d.).

\(^{25}\) Stigma is usually associated with religious beliefs of illness, including breast cancer, as a punishment for your actions. It can lead patients to seek cultural rituals for their ailment rather than hospital diagnosis and treatment.

\(^{26}\) According to a 2011 census, 68.1% of the population in Canada could conduct a conversation only in English, 12.6% could conduct a conversation only in French, 17.5% could conduct a conversation in both English and French, and 1.8% could not conduct a conversation in either English or French.
3.5.4. Technological

Drug reimbursement recommendation in Canada is a lengthy process, taking up to a year solely for the economic evaluation (INT04, INT05). Two interviewees highlighted that new drugs would need to prove more cost-effective to encourage payers to invest, given the availability of existing effective therapies for early breast cancer (INT03, INT04). One way of showing cost-effectiveness is through treatment options focused on personalised medicine, which can reduce the number of cycles of treatment required and result in better outcomes, therefore reducing the overall cost of treatment (INT03, INT04). Knowledge of the genetics of different tumour types could lead to more targeted and personalised treatment options (INT25). There are measures in place to improve access to new therapies and technologies across Canada. Since 2006, the HTA process has been centralised under the responsibility of the Canadian Agency for Drugs and Technologies in Health (CADTH) (INAHTA n.d.), which oversees the process of reimbursement for new medicines and technologies for all provinces and territories with the exception of Quebec (INT03, INT04, INT05) (European Observatory on Health Systems and Policies 2018a). However, the CADTH only makes recommendations. It is representatives from provincial and territorial governments who ultimately decide whether or not to include specific pharmaceuticals in their respective formularies, leading to differences in the treatment available across the country (INT03, INT04, INT05, INT25) (European Observatory on Health Systems and Policies 2018a).

At the time of this study, there are discussions on how to implement a national pharmacare plan in an attempt to improve equitable access to publicly funded drugs and treatment across Canada (INT05). A variety of stakeholders including clinicians, pharmacists, payers and patients are involved in order to decide what the plan will look like and address (INT05). A first research report, Pharmacare 2020, presents a clear and coherent vision of pharmacare for Canada (Morgan et al. 2015). It provides evidence that once established pharmacare will enable patients to have universal access to necessary medicines, which will ensure there is equitable access to drugs for treating early breast cancer.

3.5.5. Legal

Treatment for early breast cancer, like all treatment in Canada, is approved by Health Canada from a health and safety perspective. Interviewees viewed approval by Health Canada to be partly influenced by decisions from the FDA of the United States (INT04, INT25). Following approval, CADTH undertakes HTA review and makes reimbursement recommendations. Once a drug is approved and reimbursement considered it is incorporated into national guidelines. Most regional cancer centres adopt existing guidelines, but some develop their own based on treatment availability (INT25). One interviewee argued this is because there may be a delay of up to two years in some provinces between approving a drug at national level and investing in the drug at regional level (INT25).

3.5.6. Environmental

Interviewees believed the size of Canada and the distribution of the population was an environmental barrier to equitable access to care of early breast cancer across the country (INT04, INT05, INT25). Most of the population lives in the south of Canada; approximately 86% of the population in 2006 lived between Ontario, Quebec, British Columbia and Alberta (Statistics Canada 2008). Residents in these
provinces have overall good access to cancer care, though it is more challenging for residents from more rural areas (INT04, INT05, INT25).

Patients living in more rural or remote areas may have less access to health and knowledge services, and may therefore seek treatment once the disease has progressed (INT06, INT25). As the health system is mainly funded through province-generated resources, the available budget to invest in treatment and infrastructure varies. Bigger and more economically rich provinces have access to new therapies before smaller provinces (INT03, INT05).

3.5.7. Challenges

The main challenge to access to treatment of early breast cancer in Canada is diagnosis and treatment in remote areas. Patients living in these areas are generally required to travel for screening and treatment. These patients often have less access to information on breast cancer than women living in cities and are less aware of the mechanisms by which they can seek testing or treatment, and the benefits of accessing these services. Recently, mobile screening units have been implemented to extend the reach of breast cancer screening services (INT25). A study conducted in Quebec found that regions serviced exclusively by mobile unit had a participation rate of 63.4% compared with 54.7% of the entire study population (Fontenoy et al. 2013).

A second challenge relates to the time between a drug being approved by Health Canada and it being available to patients through the provincial and territorial public drug plan. There is a delay in women having access to new treatment, mainly in smaller provinces, which according to one interviewee can lead to metastasis (INT25). Interviewees argued that the costs of treatment should be a national rather than a provincial issue so there is equitable access to treatment (INT03, INT05).

Interviewees observed that another challenge was for new treatment options to show value for money (INT03, INT04) as there are good treatment options available for breast cancer, so investment in newer therapies is not a priority (INT04). Newer treatment must therefore prove to be more cost-effective than currently available treatment in order to be covered by the public health system (INT04). Those considering the cost-effectiveness of new drugs in the HTA process currently do not consider the societal perspective of treatment, with the exception of the Institut National d’Excellence en Santé et en Services Sociaux in Quebec (INT03, INT05).

3.5.8. Opportunities

At the moment, Quebec is the only province that considers societal perspective when determining whether to invest in new therapies (INT03, INT04, INT05), but interviewees commented that the impact of early breast cancer extends beyond clinical outcomes, considering that new therapies could prove beneficial and indirectly cost-effective (INT05, INT06). Personalised medicine or targeted therapy has the potential to be more cost-effective than conventional medicine by reducing the length of treatment or the side-effects associated with treatment, so patients can remain active at work while receiving treatment (INT05, INT25).

Interviewees thought the implementation of a national HTA process had contributed to harmonisation in drug approval across Canada (INT05). However, each province and territory decides whether to
incorporate a new drug, and such decisions are highly dependent on the available budget. The implementation of national pharmacare could improve women’s access to new treatments across Canada by creating a centralised drug formulary (INT05) (Morgan et al. 2015).

3.6. Low- and middle-income countries

Breast cancer is a significant disease burden and health challenge for people living in LMICs (Prager et al. 2018). Women in LMICs have lower survival rates from breast cancer than women in high income countries (Rivera-Franco and Leon-Rodriguez 2018) because they face numerous barriers to quality and timely breast cancer care, from accessing early detection programmes to receiving timely diagnosis and appropriate treatment, so women are often diagnosed late and at the metastatic stage (Birnbaum et al. 2018). Moreover, it is estimated that the incidence of breast cancer in LMICs will continue to rise as women increasingly adopt Western lifestyles (Rivera-Franco and Leon-Rodriguez 2018), and most breast cancer deaths in the future are predicted to occur in the developing world (Rivera-Franco and Leon-Rodriguez 2018). The following section provides an overview of some of the factors that influence some of the disparity in breast cancer care between the developed and developing world, and some of the opportunities and challenges related to them.

3.6.1. Political

In LMICs, breast cancer has not traditionally been considered a political priority, so interviewees observed that people living in these countries often have a limited healthcare infrastructure to provide adequate care and treatment for breast cancer (INT18, INT19, INT20) (Prager et al. 2018). However, global cancer control is a growing priority among governments globally and in 2017 world governments committed to further invest in cancer control (Prager et al. 2018).

LMICs often lack adequate breast cancer policies, such as national cancer control plans, programmes and strategies (Prager et al. 2018). They typically have other health-related priorities (e.g. controlling infectious diseases) and face competing demands from other issues (e.g. food and water security) (INT20) (El Saghir et al. 2014). Public health policies in high income countries are not easily transferred to LMICs, as these suffer from limited healthcare infrastructure and resources (e.g. technology or trained healthcare professionals) to provide adequate care and treatment of breast cancer (INT20) (Rivera-Franco and Leon-Rodriguez 2018). For example, many LMICs lack breast cancer screening programmes, and therefore Prager et al. suggested that screening should not be prioritised until there is adequate health system capacity to treat diagnosed cases (Prager et al. 2018).

Cancer control, including of breast cancer, is increasingly recognised as a global health priority and receiving growing attention from policymakers and international bodies (Prager et al. 2018). There have been several international cancer control initiatives, including the 2017 World Health Assembly Resolution on Cancer Prevention and Control (WHO 2017). Advocacy groups in particular play an important role in raising awareness in LMICs of the benefits of early intervention for breast cancer, for example through screening programmes for early detection (INT19, INT20) (El Saghir et al. 2014). In India, Narayana Health is developing an early detection screening programme called HOPE (INT20). In
Africa, the Advanced Breast Cancer (ABC) Global Alliance and several African organisations are lobbying to raise awareness about early diagnosis among policymakers (INT20).

3.6.2. Economic
Breast cancer is one of the cancers with the largest economic impact in LMICs and presents a significant financial burden (Ginsburg 2013). Government budgets in LMICs are often limited, with very little allocated to health services (Prager et al. 2018). Often limited resources are spent on competing public health needs (e.g. security). There is also a lack of evidence of the cost-effectiveness of different interventions in LMICs, and prices of many medicines is prohibitive (Prager et al. 2018). Thus, national health systems often do not cover the costs of diagnosis and treatment programmes, so individual patients and households face significant out-of-pocket costs when seeking treatment (INT20) (Prager et al. 2018).

Cost-effective approaches for breast cancer treatment in low resource settings are possible and are being investigated in a number of regions, such as sub-Saharan Africa and Southeast Asia (Ginsburg 2013; Varughese and Richman 2010). For example, a clinical trial using a conventional cancer drug such as trastuzumab (as opposed to newer generation drugs) during a shorter treatment interval demonstrated good outcomes and cost savings (Varughese and Richman 2010). International initiatives, such as the Breast Health Global Initiative, founded in 2002, aim to develop and implement evidence-based and economically feasible guidelines for cancer control in LMICs (Ginsburg 2013).

3.6.3. Social
A number of socioeconomic and cultural factors prevent women in LMICs from accessing breast cancer care (INT18, INT19, INT20). In many LMICs cultural and religious factors and gender discrimination lead to considerable stigma associated with breast cancer, which is often considered taboo (INT18, INT19, INT20) (Shulman et al. 2010). Many women fear being abandoned by their husbands, being ostracised by their communities or losing their job, all of which discourages them from seeking care early on (Shulman et al. 2010). Women are often expected to act as the main provider of care in their traditional family role, leading to significant competing demands on their time and financial resources (INT20) (Ginsburg 2013). Many of these challenges are compounded by poverty (Ginsburg 2013).

Support groups can help to promote awareness of breast cancer in LMICs, which can educate and empower women to overcome stigma and discrimination (Stefan et al. 2013; WHO 2012). For example, organisations such as the Breast Cancer Association of Nigeria or Cáncer de Mama: Tómatelo a Pecho in Mexico provide public education and patient support (WHO 2012). Patient navigation programmes can help facilitate access to care and treatment for women in lower socioeconomic or minority ethnic groups (INT20) when a patient navigator provides transport (or funds its cost), subsidises the cost of childcare or scheduling, and makes appointments (Krok-Schoen, Oliveri and Paskett 2016).

3.6.4. Technological
Many LMICs lack adequate technological capacity to deliver basic cancer services (INT18, INT20) (Varughese and Richman 2010), but some new technologies, including digital technologies, are expected to improve the care and treatment of breast cancer in LMICs (INT20). For example, there is some evidence that mobile technology can help to improve breast cancer care delivery and access to care in
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LMICs, although evidence is mostly from small-scale pilot studies (INT20) (Hall et al. 2014). Mobile technology can help health workers to provide better breast health awareness, encourage treatment adherence, and obtain a more holistic view of the patient by facilitating continuous health monitoring (INT20) (Ginsburg et al. 2014). A pilot study in Bangladesh demonstrated community acceptance of mobile technology, including mobile apps, paving the way for them to be scaled up (INT20) (Ginsburg et al. 2014).

Many LMICs lack basic cancer care services and technologies, with radiotherapy being a particularly limited resource, especially in Africa (Pace and Shulman 2016). For example, in Ethiopia there were a reported two radiotherapy machines for the whole population of over 80 million people and in Morocco just one machine for every 1.1 million people (Abdel-Wahab et al. 2013). In contrast, in Western Europe there are a reported six radiotherapy machines per million people (Abdel-Wahab et al. 2013). In 2013 there were 29 countries in Africa without teletherapy facilities (Abdel-Wahab et al. 2013; Pace and Shulman 2016; Varughese and Richman 2010).

Advanced technologies, such as genomics and personalised medicine, are expected to improve the detection and diagnosis of breast cancer in general (INT17, INT20) (Albrecht et al. 2016), but because of the significant costs associated with these types of technology, and the capacity needed to deliver them, they are not likely to be widely available in LMICs (INT17) (Tekola-Ayele and Rotimi 2015). Moreover, investment in breast cancer genomics research, including genetic and lifestyle risk factors, is understudied globally, and lifestyle risk factors for breast cancer in LMICs in Africa and Asia are less well studied than those in Western countries (INT20) (Tekola-Ayele and Rotimi 2015).

3.6.5. Legal

There are a number of legal and regulatory challenges to breast cancer care in LMICs, which typically have few regulatory measures, including clinical guidelines, possibly because of resource constraints (INT18). Individual doctors often make treatment decisions according to the treatments available at any given time, rather than what is outlined in clinical guidelines (INT18).

International initiatives, such as the Breast Health Global Initiative, aim to develop and implement evidence-based and economically feasible guidelines for cancer control and resource-appropriate guidelines for breast cancer care in LMICs (Ginsburg 2013).

3.6.6. Environmental

There are significant regional differences in access to the care and management of breast cancer, as well as in the cost of medicines, between and within LMICs (INT20) (Prager et al. 2018). Cancer centres and advanced therapies often exist in major cities but are harder to access for those living in rural areas (INT20) (Prager et al. 2018). Women living in rural areas are often unable to afford the cost of travel to the nearest hospital (Ginsburg 2013). Moreover, standards of care often differ between urban and rural areas, with services provided at centralised, urban facilities often having better outcomes than those provided in rural areas (Prager et al. 2018).

Decentralisation of care and establishment of cancer centres in rural areas can be helpful (El Saghir et al. 2014). For example, in Egypt, healthcare workers visited local women in rural areas to increase their
awareness about breast cancer and this led to a decrease in advanced breast cancer cases in those areas, with an increased number of breast cancer cases amenable to conservative surgery (El Saghir et al. 2014; Stefan et al. 2013).

3.7. Brazil

3.7.1. Political

Brazil has a mixed-model health system, with public and private elements. The largest element is the integrated public health system, Sistema Único de Saúde (SUS), which is administered at federal, state and municipal levels and provides universal access to medical care that is free at the point of care for all Brazilian citizens (Kuchenbecker and Polanczyk 2012). The SUS was established within the 1988 Brazilian Constitution, which mandated that the government provide all the necessary mechanisms to deliver healthcare, including free access to medicines. The SUS provides primary, secondary and tertiary healthcare. Primary care is delivered through basic health units, which are responsible for some aspects of breast cancer care, including clinical breast examination, promotion of mammography screening and referral (Berdzuli and Olson 2012).

Approximately half of the population relies exclusively on SUS for healthcare (Berdzuli and Olson 2012), and in 2015 SUS spending accounted for 43% of all health expenditures (World Bank 2018). The remainder of healthcare expenditures are covered by the private health system, which consists of private providers and hospitals that are contracted by the government and private health insurance or out-of-pocket spending (Berdzuli and Olson 2012). Breast cancer screening and basic treatment for breast cancer are covered by SUS, although challenges around access to the latest treatments and receiving timely care exist.

Breast cancer accounts for approximately 15% of all cancer deaths in Brazilian women and incidence rates and age-standardised mortality rates increased between 2004 and 2014, although some of the higher incidence rate may be due to better screening programmes (Figueiredo et al. 2017; Justo et al. 2013). Over the past 30 years, the Brazilian government has adopted several official policies related to breast cancer and breast cancer screening, including a national cancer policy, and the National Policy for Oncological Care in 2005 and updated in 2013, which addresses breast cancer care (The Economist Intelligence Unit 2017). The national government also runs public awareness campaigns to promote breast cancer screening, including Outubro Rosa (Pink October) and Mais Médicos (More Doctors) (Figueiredo et al. 2017).

Despite these efforts, our interviewees viewed the political awareness of Brazilian policymakers regarding breast cancer, and early breast cancer, as generally poor (INT11, INT12). Although they felt that policymakers have begun to recognise the importance of investing in and promoting early breast cancer in recent years (INT11), it was not currently viewed as a political priority (INT12, INT13). Technical staff within government ministries, such as the Ministry of Health, were considered to have some awareness and understanding of the issue, but did not promote new early breast cancer treatments for the public system or meaningful political change (INT12, INT13).
Patient advocacy groups around breast cancer are active in Brazil and our interviewees viewed them as effective in empowering and educating the public, promoting efforts to detect breast cancer early, and bringing pressure on the government to improve access to new technologies and drugs for treating early breast cancer (INT11, INT12, INT13). It is important to note that two of the three interviewees for Brazil have a connection to patient advocacy groups. Public advocacy has made real improvements in cancer policy, notably leading to the passage of legislation mandating that private health insurance companies provide access to oral chemotherapy drugs (Massard da Fonseca, Bastos and Lopes 2016). Before this legislation private health insurance rarely covered these drugs despite their potential benefits to patients who could administer them at home and often experienced fewer side-effects than when treated with traditional chemotherapy (Massard da Fonseca, Bastos and Lopes 2016).

3.7.2. Economic

The public system is constitutionally mandated to provide universal care and all necessary monies to cover that care (Kuchenbecker and Polanczyk 2012). It covers the costs of all stages of breast cancer care, including screening, treatment and palliative care, but often doesn’t cover newer treatments (INT11, INT12, INT13). Three-quarters (75%) of breast cancer patients get their care exclusively from the national health system where average per-patient direct costs for treatment were US$4,757 in 2010, although this cost varied by cancer stage (Justo et al. 2013). Justo et al. (2013) also found that the mean direct medical care costs of cancer treatment in a private clinic in Brazil increased from US$21,659 for stage I breast cancer to US$63,697 for stage IV breast cancer. Indirect costs to society have been estimated to be 70% of total costs of breast cancer treatment, and although this figure comes from a study of breast cancer in Europe, the indirect costs to Brazilian society can be assumed to be significant given the high mortality of relatively young women (INT11, INT12, INT13) (Justo et al. 2013).

The question of who pays for breast cancer treatment is complex, with some costs being covered by the federal government and others covered by state or municipal governments, or the private health insurance system (INT12) (Berdzuli and Olson 2012; Kuchenbecker and Polanczyk 2012; Massard da Fonseca, Bastos and Lopes 2016). For example, the National Policy for Cancer Control and Prevention mandates that cancer care be provided in an integrated fashion (The Economist Intelligence Unit 2017), and cancer treatment, including for early breast cancer, is reimbursed by the government as a bundled payment to cover all treatment rather than on a fee-for-service basis (INT12). Reimbursing medical care in this manner is argued to contain medical costs by improving the coordination of care among providers and encouraging pharmaceutical companies to price their drugs to fit within bundled payment schemes, among other factors (Newcomer 2012).

Coverage for pharmaceuticals varies between the public and private systems. The private health system typically has newer drugs and treatments available than the public health system (INT11, INT12, INT13) with the exception of oral drugs, because private health insurance companies are only required to provide coverage for medicines used while patients are hospitalised; whereas the public system covers all of the costs associated with a patient’s care (INT13) (Massard da Fonseca, Bastos and Lopes 2016). This was a particular concern for the coverage of oral chemotherapy drugs administered for breast cancer until the passage of legislation in 2013 mandating that private insurance plans cover all oral chemotherapy drugs (Massard da Fonseca, Bastos and Lopes 2016).
Both the public and private systems are overburdened and struggling with the high costs of some treatments, and the public system has been chronically underfunded for many years (INT11, INT12) (Kuchenbecker and Polanczyk 2012; Massuda et al. 2018). Even patients with private insurance and access to the private healthcare system find that some treatment options such as newer oncology drugs are not covered by their insurance and are not available because of their high cost (INT12). In instances where a patient has been denied a treatment that their physician prescribes to them, the patient may petition a judge for the right to have the federal government provide access to and financial support for the treatment (Chieffi, De Cassia Barata Barrada and Golbaum 2017; Kuchenbecker and Polanczyk 2012). This has been termed the ‘judicialisation of the right to health’ whereby citizens who have a constitutionally guaranteed right to healthcare within a system that cannot afford to deliver all of that healthcare turn to the courts for redress (Biehl et al. 2009). The right to sue the government for access to medication or other treatments was initially seen as a way to bring greater equality to the system and to address failures of provision, such as delays in care or poor regulations, but scholars have now come to view the lawsuits as disproportionately benefiting wealthier Brazilians and increasing inequality within the healthcare system (Chieffi, De Cassia Barata Barrada and Golbaum 2017; Kuchenbecker and Polanczyk 2012). The infrastructure of the public healthcare system, the healthcare workforce and available treatments are under-resourced, which leads to long wait times (Massuda et al. 2018) for initial biopsies and treatment after they have been diagnosed with breast cancer. This delay interferes with the ability of physicians to provide appropriate treatment on schedule according to clinical guidelines (INT11, INT13). The delays play out within the public system at each new step in the treatment process (e.g. between biopsy and surgery, or surgery and radiation therapy), when patients are sent to the back of the line to wait for the next stage of treatment, leading to further delays, which may result in the progression of the patient’s cancer (INT11).

3.7.3. Social

The public health system in Brazil theoretically provides equal access to early breast cancer screening and treatment for everyone in Brazil, but there are differential access levels arising from income and racial inequalities (INT11, INT12) (Barcelos et al. 2018; Massuda et al. 2018). Issues around differential access to early treatment and diagnosis of breast cancer are fundamentally attached to differences in income and wealth, which manifest themselves in two main ways: directly and indirectly. Those with greater income are more likely to have access to the private healthcare system and newer treatments, and to be better able to bear the associated costs of treatment such as travel or time off work (INT11, INT12, INT13). They are also more likely to be aware of their rights and options within the healthcare system in what can be termed an asymmetry of information (INT12). Poorer people are less likely to seek screening and receive diagnoses in a timely manner, and once diagnosed may also be less likely to receive the most effective and efficient treatment for their cancer. Evidence from breast cancer screening programmes reveals racial disparities in screening uptake, with white women being more likely to have had clinical breast examinations and mammograms than non-white women (Barcelos et al. 2018). There is also less uptake of screening among lower income women. One interviewee suggested that cultural barriers to women returning to work after breast cancer treatment lead some young women to drop out of the labour force.
after completing treatment (INT13). Instead of returning to work, they may seek support from the government to retire.

3.7.4. Technological

When considering the relevant technologies for treating early breast cancer in Brazil, our interviewees suggest that there is a need to focus on the appropriate use of existing technologies through better organisation of care and improving infrastructure, as well as on managing access to new technologies (INT11, INT13). Some of the key challenges in treating early breast cancer in Brazil arise from delays in diagnosis and treatment. Our interviewees suggested that in order to reduce delays, care needs to be better organised, there should be changes in bureaucratic governance, and investment in surgical centres and the healthcare workforce (INT11, INT13). They suggest that overall investments in the infrastructure for breast cancer management, with a particular focus on surgical centres and confirmatory biopsies, are especially needed.

The public health system in Brazil struggles to incorporate and pay for new high-cost medicines, such as genomics-based and personalised medicines for treating breast cancer (INT11, INT12) (Massuda et al. 2018). The public system does not cover these advanced treatments, and even private health insurance may not cover them because of their high cost; however, they may be available to individuals who challenge their right to receive the drug in the court system, in a process described as judicialisation (INT11) (Kuchenbecker and Polanczyk 2012). Targeted treatment for breast cancer has the potential to improve treatment outcomes, but our interviewees felt that they need to be cost-effective to compete with other demands for limited healthcare resources (INT11, INT12).

In order for new oncology drugs to be incorporated into the public health system in Brazil, they must be approved by the Brazilian Health Authority and Brazil’s HTA body (Ades et al. 2014). Brazil’s HTA process has been criticised for offering confusing and vague assessments of new drugs, with some critics charging that it rejects high-cost drugs because of societal pressure over costs to the health system (Ades et al. 2014). In recent years, Brazil has reformed the HTA process to provide more structure with the intent of promoting transparency and accountability by including representatives from relevant stakeholder groups in the decision-making process, and mandatory public consultation (Kuchenbecker and Polanczyk 2012). These reforms had the potential to create a more integrated and equitable healthcare system by bringing together stakeholders from across different governance levels (e.g. federal, state, municipal) to participate in the decision-making process (Kuchenbecker and Polanczyk 2012). The HTA reforms took place over a period of years, beginning in 2000 with the creation of the Department of Science and Technology (Lessa and Ferraz 2017) and culminating in 2011 with the establishment of the Comissão Nacional de Incorporação de Tecnologias no Sistema Único de Saúde (CONITEC) as the new advisory HTA body to work in concert with the Brazilian Ministry of Health in approving new health technologies (Kuchenbecker and Polanczyk 2012). CONITEC is tasked with addressing the efficacy, effectiveness, safety and impact of new technologies, while ensuring that they be integrated within national clinical protocols and guidelines. However, the success of these reforms is questionable; one interviewee reported that it takes about two years for new treatments to be approved through the revised HTA process (INT11).
3.7.5. Legal

Interviewees thought the Brazilian healthcare system is characterised by bureaucratic delays that impede the diagnosis and treatment of early breast cancer (INT11, INT13). A recent legal reform effort designed to address one aspect of this was the passage of the Law of 60 Days (Bukowski et al. 2016), which aims to improve treatment times for cancer patients by mandating that treatment begins within 60 days of a cancer diagnosis. However, adherence to the Law of 60 Days is reportedly low, with patients routinely waiting 60–120 days between initial mammogram and biopsy, and waiting six months or more between diagnosis and treatment (Berdzuli and Olson 2012). Hospitals are even reported to attempt to ‘game the system’ and reset the clock on the mandatory 60 days between diagnosis and treatment by unnecessarily repeating diagnostic tests on some patients (INT13).

The perception of Brazil’s system as overly bureaucratic also limits its desirability as a location for running clinical trials, therefore limiting access to new treatments for early breast cancer patients (Ernani and Barrios 2018). Currently, only about 1% of phase I and 17% of phase III cancer studies are conducted in Latin America, though the proportion has been growing by approximately 13% annually (Barrios, Werutsky and Martinez-Mesa 2015). North American pharmaceutical companies increasingly see Latin American countries as desirable locations to conduct clinical trials because their costs are lower than in the United States, patients are treatment-naïve and have not been exposed to competing trials, and there are generally comparatively high participation rates by patients, which speeds up recruitment and can reduce the overall length of the trial (Barrios, Werutsky and Martinez-Mesa 2015). However, Brazil’s process for evaluating new clinical research studies is relatively lengthy, requiring multiple ethics and regulatory approvals from national and regional bodies in a process that historically takes 12 months or more (Clinical Trials Arena 2016). The Brazilian government has recognised the need to address this barrier and after public consultation began introducing reforms in 2015 to speed up the process. These reforms include creating a priority review process for some clinical trials and allowing the simultaneous review of application materials by various regulatory agencies rather than requiring sequential review (Fagundes, Dresel and Miller 2018).

3.7.6. Environmental

Brazil is the largest country in Latin America. Its geographical size presents challenges to the management of early breast cancer. The multi-tiered funding system with federal, state and municipal sources of funding for healthcare also contribute to regional variations in services. The availability of specialty breast cancer services varies by region (Figueiredo et al. 2017), with some local areas reportedly not offering any oncology services (INT12). The majority of specialised cancer centres that provide complex services or a full range of cancer services are located in urban areas and coastal regions; some of the most highly rated are in São Paulo (INT11, INT13). Brazilians living outside these areas might need to travel for treatment, which our interviewees noted can be expensive and time consuming, potentially leading to delays in treatment, which allows time for their disease to progress (INT11, INT12, INT13) (Figueiredo et al. 2017). Some patients even decide to discontinue treatment because they lack treatment options near their place of residence (Berdzuli and Olson 2012).
Cancer mortality varies by region, with the most developed regions in the south and southeast having higher age-standardised mortality rates than more deprived areas in the north, north east and central regions (Azevedo e Silva et al. 2014; Figueiredo et al. 2017). Breast cancer is associated with increased urbanisation, higher life expectancy and cancer-related behaviours such as diets and sedentary lifestyles associated with higher socioeconomic status, and breast cancer is more common in the urbanised southern regions of Brazil (Cecilio et al. 2015; Kluthcovsky et al. 2014). Screening uptake also varies regionally. According to one study, there is higher screening uptake in southern Brazil than northern Brazil (Barcelos et al. 2018). The study authors suggest that more limited availability of x-ray equipment in the north could explain at least some of this difference in screening.

3.7.7. Challenges

Our PESTLE analysis demonstrates that Brazil’s health system struggles with issues of underfinancing, regionalisation and bureaucratic burden. Long-term struggles with financing have been exacerbated by the 2014 recession and subsequent austerity policies, which reduced funding for the public health budgets (Massuda et al. 2018). In addition, political instability in Brazil led to the introduction of public spending caps, including a 2016 constitutional amendment to limit public health expenditure over the next 20 years, further reducing real-term spending on health (Massuda et al. 2018).

There are substantial issues around regional variation in healthcare provision, because of the fractionalised nature of the health system whereby funding is sourced at the federal, state and municipal level, and geographical barriers, such as distance and undeveloped land, which physically limit access to resources including regional hospitals. In general, people living in the north of Brazil have greater unmet healthcare needs and receive fewer resources than those in other areas of Brazil (Massuda et al. 2018).

The bureaucratic burden is most closely associated with the drug and clinical trials approvals processes, though our interviewees encountered hurdles throughout their cancer care pathways, such as difficulty hiring medical staff and long wait times for treatment. Recent efforts to improve the HTA system and clinical trials approval process demonstrate that the government is aware of the burden that excessive bureaucracy within these areas imposes on the health system.

3.7.8. Opportunities

Our interviewees suggested that there are opportunities for pharmaceutical companies to collaborate with the public and private healthcare systems on creative ways to provide effective, timely and cost-effective early breast cancer treatment. Ideally the collaboration would work to ensure the long-term survivability of the health system by addressing the tensions inherent in a resource-constrained system mandated to provide healthcare to every citizen.

Evidence suggests that differences in breast cancer screening uptake vary by socioeconomic status. There are clear opportunities to eliminate the knowledge gap across socioeconomic groups through public advocacy campaigns, along with efforts to address cultural factors that may encourage women to drop out of the labour force after completing breast cancer treatment. Given the strong support expressed for the work of patient advocacy groups within Brazil, this is an area in which patient advocacy groups could contribute through public awareness campaigns.
This study explored the health system and policy factors in a range of countries, to understand the barriers and opportunities to timely diagnosis and treatment of early breast cancer. Across the countries in our analysis, several factors stood out as either enhancing or limiting access to care for early breast cancer. We discuss them within the context of the limitations of the study, such as the fact that desk research was conducted mostly on literature available in English, we had a low response rate to interview requests, we interviewed a variety of stakeholders, and responses referred to breast cancer as a whole rather than specifically to early breast cancer.

Below we discuss what works and what factors could be improved in order to deliver timely, appropriate and equitable care for the diagnosis and treatment of early breast cancer with the ambition of improving outcomes for patients and broader society.

4.1. What works?

Public health systems cover the direct costs of care and protect early breast cancer patients from economic hardship. All of the countries in our analysis have public health systems that provide free-of-the-point-of-care diagnosis and treatment of early breast cancer. These systems cover the direct costs associated with early breast cancer, thereby relieving individual patients of much of the economic burden associated with cancer care. Interviewees frequently said that breast cancer patients in their countries did not experience economic hardships due to the direct costs of their care (see for example Italy and Spain), though individuals could accrue significant indirect costs.

Public health systems invest in prevention. The public health systems within our study also fund and/or deliver preventative services for breast cancer. Interviewees generally regarded screening programmes as highly successful, even where countries could not meet their aspiration to provide universal screening for women. Effective prevention screening strategies make it possible to detect breast cancer early, leading to timely treatment, therefore reducing the impact of disease progression in breast cancer.

The HTA process for evaluating new health technologies and treatments ensures countries strive to invest in the best available treatment options, by providing evidence of the value of investing in the most cost-effective treatments. The HTA process enables comparison between currently available treatment and newer options, ensuring treatment options provide greater benefit for less cost. In some countries, the assessment process considers the views of patient representatives, as well as medical opinion
and economic considerations. Approval in one country may stimulate or support approval in a second country, broadening the reach of new more effective treatments.

**Patient advocacy groups are effective at raising awareness of breast cancer among patients, the public and policymakers.** Interviewees in all the countries we studied considered patient advocacy groups to be effective at providing education on and raising awareness of breast cancer among patients, the public and policymakers. Policymakers believe that greater public awareness about early detection can increase the number of individuals receiving early diagnosis and treatment, therefore reducing mortality from the disease and incidence of metastatic cases. They can also put pressure on the political system to invest in innovation and improvements to current treatment and systems.

Patient advocates can support the approval of new therapies, and the need to provide specialist services not covered by the national health system, such as psychological support. Therefore, patient advocates could use their influence to encourage more funding into effective treatment options and representation in the HTA process in future.

### 4.2. Areas where access to treatment of early breast cancer can be improvement

**Public health systems and private insurance do not cover the indirect costs of breast cancer.** Although health systems cover the direct costs of diagnosis and treatment associated with early breast cancer, they often do not consider the wider impact of the disease in their considerations of what expenses to cover or reimburse. These costs include unemployment, psychological support and travel expenses. Within the countries in our analysis, unemployment insurance is typically available during at least a portion of the treatment time, but interviewees in all countries considered it insufficient to replace all lost wages, and in some cases it ended before treatment was completed. The public health systems in some countries, such as Brazil and Spain, do not provide psychosocial support to breast cancer patients. Instead, patient advocacy groups offer some of these support services. Given the cost to society associated with disease progression, it could prove beneficial for the health system to cover the additional costs associated with early breast cancer, which may result in productivity gains for the workforce if breast cancer patients are able to work and be productive while not undergoing treatment rather than take sick leave. Additionally, increased investment into research and approval of new treatments that reduce the side-effects associated with cancer treatment, treatments that can be administered at home, and treatment that require fewer sessions could reduce the indirect costs of breast cancer.

**Existing effective treatment options for early breast cancer may lead policymakers and payers to underestimate the need to invest in new drugs.** Early breast cancer is perceived to be a disease with existing effective treatment options. Some of our interviewees in Canada and Spain suggested that this has led policymakers and payers to underestimate the need to invest in new drugs for early breast cancer. Currently decisions around access to treatment are traditionally made using cost-benefit analysis, but the indirect costs to society of early breast cancer are substantial. One study estimated the indirect costs of treatment to be 70% of direct costs of treatment (Lidgren, Wilking and Jönsson 2007). Therefore, there is a need to consider a wide range of factors when assessing the value of therapy, such as patient satisfaction.
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from new therapies, the broader benefits and potential cost saving from early treatment (e.g. loss of productivity and return to work), and prevention of disease progression to metastatic cancer.

Regionalisation within health systems contributes to differences in the care and management of early breast cancer within countries, and contributes to delays between the approval of drugs at the national level and their availability across the country. All countries in our study have an overarching national healthcare system but with elements of regionalisation in the financing, implementation and/or delivery of care. This can lead to differences in the implementation of national screening strategies for breast cancer, out-of-pocket expenses patients incur, and availability of new drugs for treatment of early breast cancer (European Observatory on Health Systems and Policies 2018c; France, Taroni and Donatini 2005). The solution to this issue is not straightforward because regionalisation is often driven by a desire to give local populations greater control over their healthcare decision making and spending (All-Party Parliamentary Group on Breast Cancer 2018), and centralisation of decision making can lead to its own problems including political corruption and systems that are slow to respond to changing contexts (France, Taroni and Donatini 2005). However, the issues of inequities in access caused by regionalisation are too important to disregard. Policymakers in health systems should be aware of the potential issues raised by regionalisation around access to diagnosis and treatment of breast cancer and work to ameliorate them.

Barriers to treatment for early breast cancer include income, language, culture, education and geography. Limited resources for travel or time off work, cultural taboos around breasts and cancer, and language barriers to reading informational or service provision materials act as barriers to women seeking screening and treatment (All-Party Parliamentary Group on Breast Cancer 2018). Geography can also act as a barrier. For example, there is limited cancer treatment available on small islands in Canada and Spain, in mountainous regions in Italy, and in remote areas in any country, so patients must travel to obtain it. In Brazil it is reported that some patients discontinue treatment when there are no treatment options near their place of residence (Berdzuli and Olson 2012). This echoes worldwide data suggesting that the further individuals live from major treatment centres, the worse their health outcome may be (Kelly et al. 2016). Therefore special attention and tailored programmes are needed in these areas to identify and treat these subpopulations. For example, the use of mobile mammogram units for screening could overcome some of the geographic barriers. Outreach programmes aimed at overcoming cultural taboos and language barriers among vulnerable populations are also needed.

4.3. Where do we go from here?

This study found that stakeholders such as practitioners and healthcare providers, patient advocacy groups and interested members of the public can help raise awareness on the impact of disease progression of breast cancer on society by providing evidence of the cost to patients, carers and the system of treating early breast cancer compared with treating metastatic disease, including in non-economic areas, such as social functioning and productivity.

This evidence would help make the case for broadening the value of treatment beyond economic and survival in the HTA process and encourage investment in newer treatments. This is likely to encourage payers to invest in new drugs, and researchers to develop new and effective treatments.
5. References


Aristei, Cynthia, Maurizio Amichetti, Mario Ciocca, Luigia Nardone, Filippo Bertoni, Cristina Vidali, and Italian Society of Radiation Oncology. 2008. “Radiotherapy in Italy after Conservative


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Annex A. Interview consent form

Societal Impacts of Treatment of Early Breast Cancer

Consent

RAND Europe has been commissioned by Roche to undertake an assessment of the societal impacts of treatment of early breast cancer. As part of this study, we are aiming to identify how decisions around early breast cancer treatment are made within the UK, Germany, France, Italy, Spain, Sweden, Canada and Brazil. To carry out this task, we will be conducting interviews with stakeholders and experts on the topic, including patient advocates, medical personnel and policymakers. The interviews will focus on the factors influencing treatment of early breast cancer in the different countries to better understand the landscape for policymaking surrounding treatment of early breast cancer. We will also ask questions on the impact of disease progression on individuals and broader society.

You have been invited to participate in an expert interview for this project due to your involvement in or knowledge of treatment of early breast cancer. The interview will take approximately 40-60 minutes of your time. Your participation in this research is entirely voluntary. It is your choice whether to participate or not and you may choose to change your mind about participating at any time before, during or after the interview. You do not have to give any reasons for withdrawing but we draw your attention to your rights to delete your data at the bottom of this form. During the interview you can also choose not to answer any questions. With your permission we would like to record this interview, but the recordings, any notes and transcripts will be kept strictly confidential and never be made available to any third party, including Roche.

The project will be written up as an independent RAND report and/or academic publication. Any quotes included in the final report will not be explicitly identifying you by name. However, given your role it may be that certain responses may be able to be identified as coming from you based on content and context.

All records will be kept in compliance with the General Data Protection Regulation (GDPR) 2018. This interview will be conducted by RAND Europe researchers so the data will be recorded and stored in accordance with RAND Europe’s procedures. Further information about RAND Europe’s data security practices can be provided upon request.

To provide RAND Europe with authority to use your information for this project we would like to ask you to confirm a few data protection statements:

1. Do you agree that the interview can be digitally recorded by RAND Europe and that these recordings can then be transcribed for the purpose of providing an accurate record of the interviews?
   Yes ☐ No ☐

2. Do you agree that RAND Europe can store this data securely on password-protected computers and folders on its servers for the duration of the project?
   Yes ☐ No ☐
3. Do you agree that RAND Europe can destroy the recordings and all notes and transcripts after the project has been completed?
   Yes □ No □

4. Do you agree that RAND Europe can securely use the data you have provided to identify the decision making process in regards to treatment of early breast cancer in your country and write reports on that process?
   Yes □ No □

5. RAND Europe will not directly attribute any quotes explicitly to you by name. It may be, however, that reader could reasonably attribute some information or quotes to you based on content and context. Do you give us permission to include such information?
   Yes □ No □

Should you change your mind on any of these points please contact us at redpo@rand.org using reference ‘Breast cancer screening and treatment impacts’.

__________________________  
Name

__________________________  
Date and signature
Annex B. Interview protocol

Societal impacts of treatment of early breast cancer: implications for future research, policy and practice

Thank you for agreeing to participate in our study. RAND Europe has been commissioned by Roche to undertake an assessment of the societal impacts of treatment of early breast cancer. For the purpose of this study, early breast cancer refers both to non-invasive and invasive cancer that is confined to the breast, with or without regional lymph node involvement, and that has not metastasised.

As part of this study, we are aiming to identify how decisions around early breast cancer treatment are made within the UK, Germany, France, Italy, Spain, Sweden, Canada and Brazil. To carry out this task, we will be conducting interviews with stakeholders and experts on the topic, including patient advocates, medical personnel and policymakers. The interviews will focus on the political, economic, societal, technological, legal and environmental (PESTLE) aspects of early breast cancer care and management in the different countries to better understand the landscape for policymaking surrounding care and management of early breast cancer. Towards the end we will also ask questions on the impact of disease progression on individuals and broader society.

The project will be written up as an independent RAND report and/or academic publication. In either case it will be subject to an independent peer review process and publicly available on the RAND website. It should be completed by late 2018.

Do you have any questions for us before we begin?

As explained in further detail in the consent form provided by RAND Europe, which you have signed and returned to us prior to this interview, we would like to record the interview for our own internal records. The recording will only be for the use of the project team, and will not be shared with the client or others. We will not quote you directly without asking permission. With your consent, we will now switch on the recording.

[Note to interviewers: the order of the PESTLE factors should be aligned with the expertise of the interviewee and then the impact questions included at the end]

Political

1. What are the political trends in [country name] affecting care and management of early breast cancer?
   
   Interviewer prompts:
   
   E.g.: healthcare system and infrastructure, health innovation policy, access to healthcare, national strategy, etc.
   
   i. Is breast cancer considered a political priority in your country? If not, why not?
   
   ii. In your view, is there enough awareness by policymakers on the impacts of early breast cancer to society?
   
   iii. What is the role of advocacy or patient groups in [country name] for the care and management of early breast cancer?
Economic

2. What are the economic factors affecting the provision of early care and management of early breast cancer in [country name]?  
   *Interviewer prompts:*
   
   i. What costs are covered by the national health system? (treatment, unemployment, psychological support etc.)
   
   ii. Are there measures for co-payment? If so, when were these introduced and what has been the impact?
   
   iii. What level of national investment is there in: (a) prevention activities for early breast cancer and (b) research for treatment of early breast cancer?

Societal

3. What are the social factors affecting early care and management of early breast cancer in [country name]?  
   *Interviewer prompts:*
   
   E.g. culture, inequality (e.g. hard to reach/marginalised groups), stigma, community awareness, ethnicity, etc.
   
   There may be issues around access, care, management and outcomes

Technological

4. What are the technological advances that may affect management and care in of early breast cancer in the future?  
   *Interviewer prompts:*
   
   i. What new technological/medical breakthroughs are on the horizon?
   
   ii. What are the main opportunities and technological breakthroughs needed to have an impact on early breast cancer outcomes?
   
   iii. What are the challenges associated with this? e.g. research infrastructure, acceptability etc.

Legal

5. What are the regulatory factors affecting access to treatment of early breast cancer in [country name]?  
   *Interviewer prompts:*
   
   i. What is the level of adherence to clinical guidelines? We are particularly interested in early treatment

Environmental

6. What role do environmental factors play on access to care and management of early breast cancer in [country name]?  
   *Interviewer prompts:*
   
   Are there regional or sub-regional differences in terms of care and management availability for early breast cancer?

Impact of early breast cancer

7. What in your opinion is the cost of  
   a. early breast cancer to society?  
   b. Disease progression to society?  
   *Interviewer prompts:*
   
   costs/implications to:
Factors affecting access to treatment of early breast cancer

i. the individual: clinical outcomes, psychosocial wellbeing, out of pocket

ii. the carers: Career impacts, monetary costs (out-of-pocket costs, loss of income) psychological impact

iii. broader society: health-resource use such as number of hospitalisations, readmissions, absenteeism from work

8. On what factors are decisions on care and management currently assessed?

Final questions

9. What do you think works well in [country name] in terms of access to early treatment of early breast cancer?

10. What do you think can be done to improve access to early treatment in early breast cancer in [country name]?

11. Is there anything else you think we should consider in our study?

12. Is there anyone else you think we should speak to during these interviews
## Annex C. Interview codes

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