

# Chapter 7

## Social Disparities in Survival from Breast Cancer in Europe



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### Introduction

Breast cancer is the most common cancer and the main cause of death from cancer among women in Europe and worldwide (Bray et al. 2018).

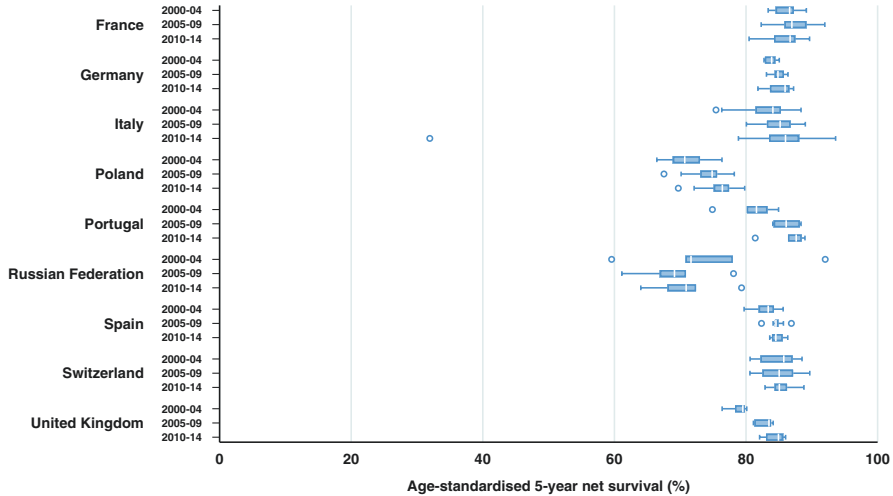
The third cycle of the CONCORD programme (CONCORD-3) updated the global surveillance of cancer survival to include patients diagnosed during the 15-year period from 2000–2014 with one of 18 malignancies, including breast cancer. It included individual data on more than 37.5 million cancer patients from 322 population-based cancer registries in 71 countries and territories worldwide (Allemani et al. 2018). The main outcome measure was five-year net survival: this is the cumulative probability of surviving at least 5 years from diagnosis, after correction for mortality due to other causes of death. Net survival is usually expressed as a percentage for convenience.

The results show that five-year net survival for adult women (aged 15–99 years) diagnosed with breast cancer has varied widely in Europe, both between countries and over time. Age-standardised five-year net survival for women diagnosed during 2000–2004 ranged from 65% (95% confidence interval [CI] 63–66%) in Lithuania to 87% (83–92%) in Iceland. For women diagnosed 10 years later, during 2010–2014, the range was from 71% (69–72%) in the Russian Federation to 89% (85–93%) in Iceland (Allemani et al. 2018).

CONCORD-3 also showed that survival varies widely within countries, although in most countries, these regional differences have narrowed over time (Fig. 7.1). Germany, France, Italy and the United Kingdom are exceptions. In these countries, regional variation in five-year net survival for women diagnosed during 2010–2014

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**Fig. 7.1** Range in age-standardised five-year net survival (%) for adult women (15–99 years) diagnosed with breast cancer during 2000–2014: European countries with regional cancer registration (CONCORD-3)

had changed very little from the variation seen among women diagnosed during 2000–2004.

These data reveal wide disparities in breast cancer outcomes across Europe. Population-based cancer survival is a key indicator of the overall effectiveness of health systems in managing care and treatment for all cancer patients. However, there are significant inequalities in the availability of and access to high-quality cancer care (Aapro et al. 2017). The inequalities in cancer survival arise within societies.

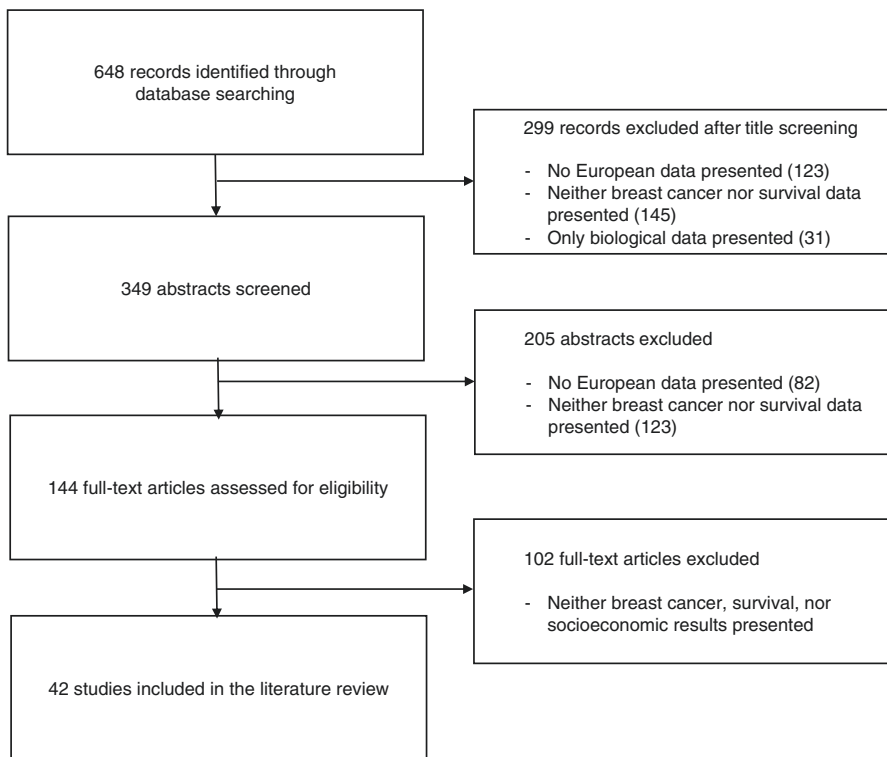
The determinants of population-based cancer survival differences can be divided into two groups. Factors related to the social environment include the availability and organisation of diagnostic facilities, organised mass screening, adequate treatment facilities, and sufficient numbers of doctors and other health personnel. Factors related to the individual cancer patient include socioeconomic status, serious concomitant disease at diagnosis [comorbidity], lifestyle factors such as smoking, alcohol use and physical activity, and race/ethnicity (Sant et al. 2015).

A worldwide review of all cancers in the late 1990s found that patients in lower social classes had consistently lower survival than those in higher social classes (Kogevinas and Porta 1997). A more recent worldwide review found that part of the association between socioeconomic groups and cancer survival is attributable to unfavourable stage distribution at diagnosis and lower access to optimal treatment (Woods et al. 2006). However, the authors underlined that more investigations were needed: (i) on patients characteristics, such as nutrition and comorbidities that may interact with treatment decisions and with the outcome; and (ii) on how socioeconomic differences are associated with access to health services, participation in screening programmes and, ultimately, to differences in cancer survival.

We conducted a PubMed literature search to investigate the current state of the art on this topic. The search terms used were designed to identify references that indexed or mentioned: (i) breast cancer, (ii) survival, (iii) a European country and (iv) socioeconomic or social status, or their synonyms. All European countries were included as search terms. Only articles published in the 10 years up to December 2019 and explicitly showing results on socioeconomic differences in survival were selected.

## Literature Review

We selected 648 articles for abstract review, of which 144 were selected for full-text review (flow chart in Fig. 7.2). Of these, 42 were finally included in our review. The studies varied widely in the calendar period of diagnosis examined, as well as the sample size, statistical methods, definition of socioeconomic status and the co-variables included in the analyses, as well as between the countries included. The main results and key descriptors are summarised in Table 7.1.



**Fig. 7.2** Flow chart of the study selection process

**Table 7.1** Description of the studies included in the literature review, including country involved, data source accessed, study population, statistical methods applied, socioeconomic measures used, and any further information considered in relation to socioeconomic survival estimates, together with main study results

Reference (Country)	Data sources	Study population	Statistical methods	Socioeconomic measure	Further investigated variables <sup>a†</sup>	Main survival results
(Belot et al. 2018) (France)	Calvados and Manche population-based cancer registries	Women diagnosed during 1997–2010	Net survival	Area deprivation [based on the European Deprivation Index based on (country-specific) census variables]	–	1-year net survival varied from 97% in most affluent to 95% in most deprived women; 5-year net survival varied from 87% in most affluent to 85% in most deprived women; 10-year net survival varied from 81% in most affluent to 75% in most deprived women
(Lyrazopoulos et al. 2011) (UK)	Office for National Statistics for residents of England and Wales Hospital Episodes Statistics data	Women diagnosed during 1971–2006	Relative survival	Area deprivation index [based on Carstairs index and the Index of Multiple Deprivation, according to period of diagnosis]	Year of diagnosis	The deprivation gap (i.e. the absolute difference between survival estimated for most deprived and that estimated for most affluent women) in five-year relative survival reduced over time (from around –10% in 1973 to approx. –7% in 2003) ( <i>A negative value means that survival in most deprived women was lower than that estimated for most affluent women</i> )
(Exarchakou et al. 2018) (UK)	National Cancer Registry National Cancer Registration and Analysis Service in Public Health England Office for National Statistics Health and Social Care Information Centre	Women aged 15–99 diagnosed in England during 1996–2013	Net survival	Area deprivation index [based on the Income Domain of the Index of Multiple Deprivation]	Year of diagnosis	Although survival increased from 1996 to 2013 (e.g. survival for most affluent women was 91% in 1996 and 98% in 2013), it remained consistently lower among more deprived than among most affluent patients. The deprivation gap in 1-year net survival remained unchanged in 1996–2013 (–3.2%* over the entire period)

(Dalton et al. 2019) (Denmark)	Income Statistics Register, Danish Cancer Registry, Central Population Registry	Women aged $\geq 20$ years diagnosed during 1987–2009, with available information on income	Relative survival	Individual disposable income	Year of diagnosis	five-year relative survival varied from 67% in most affluent to 55% in most deprived women in 1987 ( <i>data extracted from graphics</i> ) five-year relative survival varied from 78% in most affluent to 71% in most deprived women in 2013 ( <i>data extracted from graphics</i> )
(Sytiopoulou et al. 2017) (UK)	National Cancer Registry	Women diagnosed during 1998–2013	Average loss in life expectancy Percentage of life lost	Area deprivation index [based on the Income Domain of the Index of Multiple Deprivation]	Age at diagnosis	Average loss in expectation of life for each deprivation group ranged from 5 to 6 years from least to most deprived women. Results varied with age at diagnosis, being slightly lower for 70-year olds or older. Proportion of life lost varied from 22% to 27% from least to most deprived women. Results varied with age at diagnosis, being higher for 70-year olds or older.
(Rutherford et al. 2015) (UK)	National Cancer Registry Data	Women aged 30–99 diagnosed in England and Wales during 1999–2009	Life expectancy estimated (by using flexible parametric excess hazard regression models)	Area deprivation index [based on the Income Domain of the Index of Multiple Deprivation]	Age at diagnosis	<i>Age at diagnosis: 60 years</i> The difference in life expectancy with and without cancer was estimated to be 4.7 and 4.9 years for the least and most deprived groups, respectively The proportion of the deprivation gap in number of years remaining that is due to differences in relative (cancer) survival was approx. 28%; thus, over two-thirds of the deprivation gap in differential life expectancy was explained by differences in other-cause survival.

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Table 7.1 (continued)

Reference (Country)	Data sources	Study population	Statistical methods	Socioeconomic measure	Further investigated variables <sup>a</sup>	Main survival results
(Berger et al. 2012) (France)	<i>ONLY abstract</i>	Women diagnosed and treated in the Institut Curie during 1981–2001	Cox proportional hazards regression models for all-cause survival	Socioeconomic status was determined from district of residence, median income for town of residence corrected by the consumption unit and body mass index	Period of diagnosis, age at diagnosis	Hazard ratio [HR] = 0.93* for high-income women compared to low-income women After adjusting for age at diagnosis and period of diagnosis, the risk of cancer death decreased for patients residing in districts with median income greater than 15,770 € (HR = 0.92*)
(Nur et al. 2015) (UK)	England Cancer registry, Office for National Statistics	Women aged 15–99 years diagnosed in England during 2001–2005	Net survival weighted least-squares regression models	Area deprivation index [based on the Income Domain of the Index of Multiple Deprivation]	Age at diagnosis	The deprivation gap in 1-year net survival widened with increasing age at diagnosis (−0.8%* for 15–44-year olds to −4.8%* for 75–99-year olds) This also happened for patients diagnosed up to 74 years for five-year net survival (deprivation gap: −5.2%* for 15–44-year olds to −8.3%* for 65–74-year olds, but −5.1* for 75–99-year olds) and 10-year net survival (deprivation gap: −5.7%* for 15–44-year olds to −8.9%* for 65–74-year olds, but −7.4* for 75–99-year olds).

(Beiki et al. 2012) (Sweden)	Swedish nationwide registers	Women diagnosed during 1961–2007	Cox proportional hazards regression models for cause-specific survival	Education	Period diagnosis, age at diagnosis, immigrant status or immigrants' daughter status	<p>Women with the highest number of years of education had approx. 30% higher risk of dying from breast cancer than women with the lowest number of years of education (<i>data not shown in the paper</i>)</p> <p>Compared to native Swedes, no significant differences were evident in the risk of dying from breast cancer among immigrants (hazard ratios [HRs] range: 0.99–1.03) and immigrants' daughters (HRs range: 0.85 to 0.98), according to years of education after adjusting for age and period of diagnosis</p>
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Table 7.1 (continued)

Reference (Country)	Data sources	Study population	Statistical methods	Socioeconomic measure	Further investigated variables <sup>a</sup>	Main survival results
(Rutherford et al. 2013) (UK)	Eastern Cancer Registration Information Centre	Women diagnosed in the East of England during 2006–2010	Relative survival No. of avoidable deaths (by using flexible parametric excess hazard regression models)	Area deprivation index [based on the Index of Multiple Deprivation]	Stage at diagnosis	5-year stage-specific survival was quite similar across deprivation quintiles 1–4 (e.g. approx. 90% for stage II, approx. 60% for stage III and 18–20% for stage IV), but decreased for most deprived women, i.e. deprivation quintile 5 (e.g. approx. 85% for stage II, approx. 50% for stage III and approx. 10% for stage IV). No differences in five-year survival were evident for stage I tumours across deprivation quintiles 1–5.  Socioeconomic differences in stage explained nearly all of the deprivation differences in relative survival found between women in deprivation quintiles 3 or 4 and those in deprivation quintile 1 (most affluent).  Eliminating stage differences only removed about half of the survival inequalities found for most deprived women with respect to most affluent women  Equalising stage at diagnosis for women in deprivation quintiles 2–5 to that observed for women in deprivation quintile 1, no. of avoidable deaths were approx. 80 for women in deprivation quintiles 2 and 3, 120 in deprivation quintile 4, and 170 in deprivation quintile 5



<p>(Bower et al. 2019) (Sweden)</p>	<p>Breast Cancer Data Base Sweden (including Breast Cancer Quality Registers from the Stockholm/ Gotland, Uppsala/ Orebro and North healthcare regions)</p>	<p>Women diagnosed during 1992–2012</p>	<p>Loss in expectation of life (by using flexible parametric excess hazard regression models)</p>	<p>Education</p>	<p>Age at diagnosis Stage at diagnosis</p>	<p>Life years lost in low, middle and high education groups vary from 9.90, 9.69, 9.11 for 45-year olds to 2.28, 1.89, 2.11 for 75-year olds, respectively. Considering the cohort of 3843 women diagnosed in a typical calendar year with breast cancer, removing differences in stage distribution would result in postponing 25 deaths beyond 5 years from diagnosis, compared to a postponement of 26 deaths when removing differences in stage-specific survival. Considering the whole life span of women with breast cancer, 573 life years could be gained if differences in stage at diagnosis were eliminated, in comparison to 692 life years when removing stage-specific survival.</p>
<p>(Aarts et al. 2013) (Netherlands)</p>	<p>Eindhoven Cancer Registry</p>	<p>Women diagnosed in Eindhoven during 1991–2008</p>	<p>Cox proportional hazards regression models for all-cause survival</p>	<p>Education</p>	<p>Period of diagnosis, age at diagnosis, stage at diagnosis</p>	<p>HR = 1.5 for women with low education level compared to those with high education level, after adjusting for year of diagnosis, age and stage at diagnosis</p>

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Table 7.1 (continued)

Reference (Country)	Data sources	Study population	Statistical methods	Socioeconomic measure	Further investigated variables <sup>a</sup>	Main survival results
(Baker et al. 2010) (UK)	Ninewells Hospital Medical School database	Resected Caucasian patients diagnosed in 1997–2001, with frozen tissue stored in the regional tissue bank	Kaplan Meier estimates and Cox proportional hazards regression models for cancer-specific survival and disease-free survival	Area deprivation index [based on Carstairs index, grouped as 1st–9th deciles and 10th decile]	p53 mutation tumour grade, stage at diagnosis (tumour size, lymph nodal status) oestrogen receptor status, HER2, triple negative tumour	Women in deprivation decile 10 were more likely to have a relapse (HR = 3.7*) or die (HR = 6.1*) compared to those in deciles 1–9, after adjusting for all the considered variables. Within the p53-mutant patients, those in deprivation decile 10 were more likely to have a relapse (five-year survival: 24% vs 72%) or die (five-year survival: 20% vs 55%) compared to those in deciles 1–9, after adjusting for all the considered variables (excluding p53 mutation)
(Morris et al. 2017) (UK)	West Midlands Breast Screening Quality Assurance Reference Centre, Hospital Episode Statistics, General Practice Research Database	Women aged 50–70 diagnosed during 1989–2006 in the West Midlands region of England	Net survival	Area deprivation [based on the Income Domain of the Index of Multiple Deprivation]	Age at diagnosis, comorbidity lifestyle (alcohol habits, smoking habits, body mass index [BMI])	5-year net survival ranged from 94% in most affluent women to 83% in most deprived women ( <i>data extracted from graphics</i> ) 10-year net survival ranged from 88% in most affluent women to 72% in most deprived women ( <i>data extracted from graphics</i> ) This disadvantage in prognosis for most deprived women was present irrespective of the woman's obesity, alcohol, smoking or comorbidity status

(Morris et al. 2016) (UK)	West Midlands Breast Screening Quality Assurance Reference Centre Hospital Episode Statistics National Breast Screening Service records	Women aged 50–70 years diagnosed during 01/04/1989–31/03/2011 who were continuously eligible for screening from the age of 50 up to either 65 or 70 years and who would have received their first invitation letter from their 50th birthday onwards	Flexible parametric excess hazards regression models to estimate the excess hazard rate ratio (EHR)	Area deprivation index [based on the Income Domain of the Index of Multiple Deprivation]	Age at diagnosis, stage at diagnosis (tumour size, nodal involvement, presence of metastases), year of diagnosis (as a proxy of screening history) tumour characteristics (histology) treatment (surgery and time to surgery) comorbidity	<p><i>Women with non-screen detected cancer</i> The excess hazard of death from breast cancer, within 5 years of diagnosis, was 64% higher in most deprived women compared to most affluent women (EHR = 1.64*, adjusted for age and year of diagnosis)</p> <p><i>Women with screen-detected cancer</i> The excess hazard of death from breast cancer, within 5 years of diagnosis, was more than double among screen-detected women (EHR = 2.12*, adjusted for age and year of diagnosis).</p> <p>These hazard rate ratios reduced by approx. 10% for non-screen-detected women and by approx. 25% for screen-detected women, after adjustment for stage of disease.</p> <p>Tumour characteristics and treatment did not have any notable impact.</p> <p>The inclusion of comorbidity reduced the excess hazard rate ratios slightly in both screen-detected (EHR = 1.39*) and non-screen detected (EHR = 1.54*) women.</p>
(Ward et al. 2018) (UK)	UK cancer registry regions (West Midlands, Northern and Yorkshire), Office for National Statistics database Hospital Episode Statistics database	Women aged ≥70 years diagnosed during 2002–2010	Cox proportional hazards regression models and Royston-Parnar restricted cubic splines models for cause-specific survival	Deprivation index (no further information)	Stage at diagnosis (tumour size, lymph nodal status), treatment (surgery, endocrine therapy) comorbidity	<p>HR = 1.26* for most deprived women compared to most affluent women, after adjusting for comorbidity, stage and treatment</p>

(continued)

Table 7.1 (continued)

Reference (Country)	Data sources	Study population	Statistical methods	Socioeconomic measure	Further investigated variables <sup>a</sup>	Main survival results
(Redaniel et al. 2012) (UK)	UK General Practice Research Database (GPRD)	Women who were registered in the GPRD during 1987–2007	Cox proportional hazards regression models for all-cause survival	Area deprivation [based on the Index of Multiple Deprivation]	Year of diagnosis, age at diagnosis, region of residence, lifestyle (BMI, smoking and alcohol habits), oestrogen use	HR = 1.05 for most deprived women compared to most affluent women in the unadjusted model HR = 0.97 for most deprived women compared to most affluent women, after adjusting for all listed variables
(Walsh et al. 2014) (Ireland)	Cancer Registry database Hospital Inpatient Enquiry System	Women aged 15–99 years diagnosed during 1994–2008 in Ireland	Kaplan Meier estimates for cause-specific survival Cox proportional hazards regression models for cause-specific survival	Area deprivation index [based on the SAHRU index based on the 3409 electoral divisions in the Republic of Ireland]	Year of diagnosis, age at diagnosis, stage at diagnosis, method of presentation ( <i>screening history</i> ) grade, tumour morphology, hormonal status, comorbidity, lifestyle (smoking habits), region of residence	<i>15–49-year olds</i> 5-year cause-specific survival ranged from 90% in most affluent women to 83% in most deprived women <i>65–99-year olds</i> 5-year cause-specific survival ranged from 75% in most affluent women to 70% in most deprived women HR = 1.33* for most deprived women compared to most affluent women, after adjusting for age at diagnosis HR = 1.18 for most deprived women compared to most affluent women, after adjusting for all variables listed

<p>(Larsen et al. 2015) (Denmark)</p>	<p>Danish Breast Cancer Database Danish Diet, Cancer and Health Study Danish registries</p>	<p>Postmenopausal women included in the Danish Diet, Cancer and Health Study (i.e. women aged 50–64 years between December 1993 and May 1997, born in Denmark, and living in the Copenhagen or Aarhus area and replying positively to the invitation to the study) diagnosed during 1993–2008</p>	<p>Cox proportional hazards regression models for all-cause survival</p>	<p>Education income</p>	<p>Stage at diagnosis (tumour size, lymph node status, no. of positive lymph nodes, malignancy) grade hormone receptor status comorbidity lifestyle at baseline (BMI, waist circumference, diabetes, smoking and alcohol habits) lifestyle at diagnosis (BMI, diabetes, smoking and alcohol habits)</p>	<p>HRs for women with low education level compared to those with high education level ranged from 1.40*, after adjusting for age at diagnosis, to 1.24 also adjusting for stage at diagnosis, receptor status, BMI, comorbidity, diabetes, and smoking and alcohol habits. HRs for women with low income compared to those with high income ranged from 0.96, after adjusting for age at diagnosis, to 0.93 also adjusting for stage at diagnosis, receptor status, BMI, comorbidity, diabetes, and smoking and alcohol habits</p>
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Table 7.1 (continued)

Reference (Country)	Data sources	Study population	Statistical methods	Socioeconomic measure	Further investigated variables <sup>a</sup>	Main survival results
(Morris et al. 2015) (UK)	West Midlands Breast Screening Quality Assurance Reference Centre, Hospital Episode Statistics National Breast Screening Service records, the National Mortality Database	Women aged 50–70 years, diagnosed during 1989–2011 and invited for screening	Net survival	Area deprivation index [based on the Townsend score and the Income Domain of the Index of Multiple Deprivation, according to the period of diagnosis]	Screening history	<p>five-year net survival ranged from 90% in most affluent women to 87% in middle/most deprived women.</p> <p><i>Women with screen-detected cancer.</i></p> <p>five-year net survival ranged from 94% in most affluent women to 89% in middle/most deprived women</p> <p><i>Women whose last screening attendance had resulted in a negative screen and had not yet been invited to a subsequent screening:</i></p> <p>five-year net survival ranged from 86% in most affluent women to 81% in middle/most deprived women</p> <p><i>Women whose cancer was diagnosed after having previously had a negative screen, but who had not attended their most recent screening appointment:</i></p> <p>five-year net survival ranged from 81% in most affluent women to 77% in middle/most deprived women</p> <p><i>Women who had never presented for screening:</i></p> <p>five-year net survival ranged from 73% in most affluent women to 62% in middle/most deprived women</p>

(Woods et al. 2016) (UK)	West Midlands Breast Screening Quality Assurance Reference Centre Hospital Episode Statistics National Breast Screening Service records	Women aged 50–65 years in 1997–2006 and ≤51 years in 1997	Net survival	Quintiles of the regional distribution of the percentage of unemployment in their small area of residence	Stage at diagnosis screening history	five-year net survival in most affluent women (quintiles 1–2): 93% (99% screen-detected cancer, 88% non-screen detected cancer) five-year net survival in most deprived women (quintiles 3–5): 89% (96% screen-detected cancer, 84% non-screen detected cancer) Most deprived women in both screening groups experienced lower survival than that experienced by most affluent women. In particular, most deprived women diagnosed with regional non-screen detected diseases had the lowest net survival (approx. 80%)
(Davies et al. 2013) (UK)	Thames Cancer Registry London Cancer Screening Quality Assurance Reference Centre (QARC) NHS Cancer Screening Programme NHS Central Register via the Office for National Statistics	Women aged 50–64 diagnosed during 1998–2005 in London	Net survival	Area deprivation [based on the Index of Multiple Deprivation]	Screening history	five-year net survival ranged from 90% in most affluent women to 82% in most deprived women. <i>Women with screen-detected cancer:</i> five-year net survival ranged from 98% in most affluent women to 94% in most deprived women <i>Women who had never presented for screening:</i> five-year net survival ranged from 85% in most affluent women to 73% in most deprived women (data extracted from graphics)

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Table 7.1 (continued)

Reference (Country)	Data sources	Study population	Statistical methods	Socioeconomic measure	Further investigated variables <sup>a</sup>	Main survival results
(Aarts et al. 2011) (Netherlands)	Population-based screening program database (BoBZ) Eindhoven Cancer Registry (IKZ)	Women eligible for screening diagnosed during the overlapping regions of the BoBZ and IKZ in 1998–2006 with invasive breast cancer or DCIS	Cox proportional hazards regression models for all-cause survival	Socioeconomic status [based on individual fiscal data on the economic value of the home and household income]	Age at diagnosis stage at diagnosis treatment (surgery, radiotherapy, systemic therapy) comorbidity	<p><i>Women with screen-detected cancer:</i>            five-year survival ranged from 90% in most deprived women to 92% in most affluent women (HR for most deprived compared to most affluent women = 1.32* after adjusting for age and stage; 1.23 also adjusting for comorbidity and treatment)</p> <p><i>women with interval cancer:</i>            five-year survival ranged from 78% in most deprived women to 90% in most affluent women (HR for most deprived compared to most affluent women = 1.47* after adjusting for age and stage; 1.45 also adjusting for comorbidity and treatment)</p> <p><i>women with non-screen detected cancer:</i>            five-year survival ranged from 73% in most deprived women to 80% in most affluent women (HR for most deprived compared to most affluent women = 1.22 after adjusting for age and stage; 1.17 also adjusting for comorbidity and treatment)</p>



(Puliti et al. 2012) (Italy)	Tuscan Cancer Registry	Women aged 15–69 years diagnosed during 1985–2000	Cox proportional hazards regression models for all-cause survival	Area deprivation index [based on national census data]	Period of diagnosis ( <i>as a proxy of screening history</i> ), age at diagnosis, stage at diagnosis (pathological T and N stages)	<p>The deprivation gap in 10-year survival between most deprived and most affluent women aged &lt;50 years at diagnosis decreased from 12% in 1985–1986 to 10% in 1996–2000</p> <p>The deprivation gap in 10-year survival between most deprived and most affluent women aged 50–69 years at diagnosis decreased from 12% in 1985–1986 to –1% in 1996–2000</p> <p>In the first two calendar periods (1985–1986, 1991–1996), the differences in the risk of death between most deprived and most affluent women disappeared (HRs around 1) after adjusting for stage at diagnosis, both in &lt;50-year olds and 50–69-year olds.</p> <p>As regards the last period (1996–2000), the same was for 50–69-year olds, but the risk doubled in most deprived compared to most affluent &lt;50-year-old women</p>
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Table 7.1 (continued)

Reference (Country)	Data sources	Study population	Statistical methods	Socioeconomic measure	Further investigated variables <sup>a</sup>	Main survival results
(Pacelli et al. 2014) (Italy)	Regional breast cancer registry census individual database hospital discharge records	Women aged 30–69 years diagnosed during 1997–2003 in Emilia-Romagna region	Cox proportional hazards regression models for all-cause survival	Socioeconomic indicators [based on education level]	Period diagnosis (as a proxy of screening history), age at diagnosis, stage at diagnosis	<p>Transitional period (1997–2000) five-year survival ranged from 87% in most deprived to 94% in most affluent 30–49-year-old women (HR for most affluent compared to most deprived women = 0.75, after adjusting for stage and age at diagnosis)</p> <p>five-year survival ranged from 87% in most deprived to 91% in most affluent 50–69-year-old women (HR for most affluent compared to most deprived women = 0.64, after adjusting for stage and age at diagnosis)</p> <p>Consolidation period (i.e. after the full implementation of the screening programme; 2001–2003)</p> <p>The above-mentioned differences decreased in both 30–49-year olds (range: 89–93%; HR = 0.63, after adjusting for stage and age) and 50–69-screening target population (range 95%–93%; HR = 1.23, after adjusting for stage and age), thus disappearing completely among women in the age-group invited to screening</p>

<p>(Feller et al. 2017) (Switzerland)</p>	<p>Swiss National Cohort National Institute for Cancer Epidemiology and Registration cancer registry data; Federal Statistical Office</p>	<p>Women diagnosed with invasive or in situ breast cancer in December 2000–December 2008</p>	<p>Subhazard ratio (by using competing risk regression models based on Fine and Gray's proportional hazard regression models)</p>	<p>Education Urbanity (urban/rural area)</p>	<p>Age at diagnosis, stage at diagnosis, place of residence (<i>canton with organised and non-organised screening</i>) nationality (Swiss, non-Swiss) civil status</p>	<p>Differences in survival among least and more deprived women were still evident (subhazard ratios = 1.22*) after adjusting for age at diagnosis, civil status, nationality, stage at diagnosis, urbanity, and screening availability.</p>
<p>(Rachet et al. 2010) (UK)</p>	<p>National Cancer Registry</p>	<p>Women diagnosed during 1996–2006 in England and Wales</p>	<p>Relative survival variance-weighted linear regression</p>	<p>Area deprivation index [based on the Index of Multiple Deprivation]</p>	<p>Period of diagnosis (<i>as a proxy of screening history</i>)</p>	<p>The deprivation gap in 1-year relative survival between most deprived and most affluent women was -4%* in 1996 and -3%* in 2006 The deprivation gap in 3-year relative survival ranged from -6.7%* in 1996–2000 to -4.7%* in 2004–2006 Mean absolute change (%) in the deprivation gap in 1-year relative survival within the three periods (pre-cancer plan [1996–2000], implementation [2001–2003], implementation [2004–2006]) was stable and not negative, meaning that the deprivation gap has not widened. Similar results were found for the deprivation gap in 3-year relative survival</p>

(continued)

Table 7.1 (continued)

Reference (Country)	Data sources	Study population	Statistical methods	Socioeconomic measure	Further investigated variables <sup>a</sup>	Main survival results
(Li et al. 2016) (UK)	Northern and Yorkshire Cancer Registry Hospital episode statistics	Women diagnosed during 2000–2007	Net survival G-computation procedures to estimate the proportion of the effect of deprivation on survival mediated by stage, and on survival mediated by treatment	Area deprivation index [based on the Index of Multiple Deprivation]	Stage at diagnosis, treatment (surgery)	1-year net survival ranged from 97% in most affluent women to 94% in most deprived women five-year net survival ranged from 86% in most affluent women to 76% in most deprived women Stage-specific survival estimates were consistently lower in most deprived patients. Large deprivation gap existed for the 1-year net survival in stage IV, and for the five-year net survival in stages II–III Most deprived women were almost three times more likely to die within 6 months after diagnosis than the most affluent women (odds ratio = 2.77*) Stage accounted for about one-third of the total effect of deprivation at 6 months and 1 year (proportion mediated: 35% and 30%, respectively). This proportion decreased to just over a tenth at 3 and 5 years since diagnosis (12% and 14%, respectively). The main mediation analysis found no evidence for the effect of deprivation on mortality mediated through differential treatment
(Downing et al. 2007) (UK)	Northern and Yorkshire Cancer Registry; Information Service database	Women diagnosed during 1998–2000 in Northern and Yorkshire regions of England	Cox proportional hazards regression models for all-cause survival	Area deprivation index [based on the Townsend score]	Age at diagnosis stage at diagnosis treatment (surgery, type of surgery)	Living in most deprived areas was associated with an increased risk of death for all women overall (HR = 1.08* per quartile increase in Townsend score, after adjusting for age and stage at diagnosis) and for those undergoing a breast-conserving surgery (HR = 1.13*), but not for those undergoing mastectomy (HR = 1.04) or not resected (HR = 1.03)

<p>(Eaker et al. 2009) (Sweden)</p>	<p>Regional Breast Cancer Register of the Uppsala social database the Multi-Generation Register the Cause of Death Register</p>	<p>Women aged 20–79 diagnosed during 1993–2003</p>	<p>Kaplan Meier estimates for cause-specific survival (CSS) Cox proportional hazards regression models for cause-specific survival Relative survival (RS)</p>	<p>Education, socioeconomic index (based on occupational group), employment status, income, home ownership, and welfare</p>	<p>Period of diagnosis, Age at diagnosis, stage at diagnosis (number of lymph nodes examined, tumour size, lymph node involvement, distant metastases) proliferation status, oestrogen and progesterone receptor status, detection mode, treatment (surgery, radiotherapy, chemotherapy, hormonal therapy), type of clinic</p>	<p>five-year CCS (RS) ranged from 86% (85%) in women with low level of education to 91% (92%) in women with high level of education (HR for women with high level compared to low level of education = 0.65*, after adjusting for age, stage at diagnosis, and period of diagnosis; HR = 0.68* adjusting also for diagnostic intensity, tumour characteristics, and treatment) HRs for 20–49, 50–65 and 66–79 years old women with high level of education were 0.51*, 0.64* and 0.76, respectively Five-year CCS (RS) ranged from 87% (88%) in women with low socioeconomic index to 91% (92%) in women with high socioeconomic index (HR for women with high socioeconomic index compared to women with low socioeconomic index = 0.61*, after adjusting for age, stage at diagnosis, and period of diagnosis) Five-year CCS (RS) ranged from 86% (86%) in women with low income to 90% (90%) in women with high income (HR for women with high income compared to women with low income = 0.76*, after adjusting for age, stage at diagnosis, and period of diagnosis)</p>
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(continued)

Table 7.1 (continued)

Reference (Country)	Data sources	Study population	Statistical methods	Socioeconomic measure	Further investigated variables <sup>a</sup>	Main survival results
						<p>Five-year CCS (RS) ranged from 86% (85%) in women who did not own their own home to 89% (89%) in women who owned their own home (HR for women who did compared to women who did not own their own home = 0.82*, after adjusting for age, stage at diagnosis, and period of diagnosis)</p> <p>Five-year CCS (RS) ranged from 88% (88%) in women without welfare status to 83% (83%) in women with welfare status (HR for women with welfare status compared to women without welfare status = 1.40*, after adjusting for age, stage at diagnosis and period of diagnosis)</p> <p>The social gradient in the risk of death for women with high level of education compared to women with low level of education did not vary markedly across the diagnostic intensity variables investigated (HRs around 0.60*);</p> <p>was somewhat small among women with high proliferation (HR = 0.82) and large (HR = 0.80) tumours, but great among women with low proliferation (HR = 0.53*), hormone sensitive tumours (HR = 0.54*) and small tumours (HR = 0.50*);</p> <p>was present for all treatment variables (HRs ranged 0.60*-0.70*), except for breast-conserving surgery associated with (HR = 0.83) or not associated with (HR = 0.80) radiotherapy</p>

(Redaniel et al. 2013) (UK)	West Midlands Cancer Intelligence Unit inpatient Hospital Episode Statistics the Office of the National Statistics	Women, aged 15 years or older, diagnosed during 1996–2009 with localised stage undergoing surgical resection	Relative survival Generalised linear regression models to estimate the Relative Excess Risks of death (RER)	Area deprivation index [based on the Income Domain of the Index of Multiple Deprivation]	Age at diagnosis, period of the waiting time targets ( <i>as a proxy of screening history</i> ); stage at diagnosis, grade, histology, treatment (waiting time from diagnosis to first curative surgery) region of residence, ethnicity	High risk of death for most deprived women compared to most affluent women (HR = 1.28*, after adjusting for age, ethnicity, place of residence, waiting time from diagnosis to first curative surgery, stage, grade, histology and period)
(Jack et al. 2009) (UK)	Thames Cancer Registry, Hospital Episode Statistics, National Health Service Central Register through the Office for National Statistics	Women diagnosed during 1998–2003 in South East England	Cox proportional hazards regression models for all-cause and cause-specific survival	Area deprivation index [based on the Index of Multiple Deprivation]	Age at diagnosis, stage at diagnosis, treatment (surgery, radiotherapy, chemotherapy, hormone therapy) ethnicity	Living in most deprived areas was associated with an increased risk of death compared to living in most affluent areas (HR = 1.36*, after adjusting for age and ethnicity; HR = 1.25*, adjusting also for stage and treatment).

(continued)

Table 7.1 (continued)

Reference (Country)	Data sources	Study population	Statistical methods	Socioeconomic measure	Further investigated variables <sup>a</sup>	Main survival results
(Bastiaannet et al. 2011) (Netherlands)	Netherlands Cancer Registry Netherlands Institute for Social Research	Women diagnosed with invasive and/or in situ breast cancer in 1995–2005	Cox proportional hazards regression models for all-cause survival Relative survival Generalised linear regression models to estimate the Relative Excess Risks of death (RER) No. of avoidable deaths for each socioeconomic group relative to the highest socioeconomic group	Area socioeconomic status score [based on income, employment and education]	Year of diagnosis, age at diagnosis stage at diagnosis (T-stage, N-stage, M-stage, tumour size) histology, tumour grade, treatment (surgery, adjuvant treatment)	Low socioeconomic status was associated with worse survival, even stratified for tumour size or stage of disease. 10-year observed survival ranged from 65% in most affluent women to 58% in most deprived women (HR for most deprived women compared to most affluent women = 1.10*, after adjusting for all listed variables) 10-year relative survival ranged from 79% in most affluent women to 74% in most deprived women (RER for most deprived women compared to most affluent women = 1.19*, after adjusting for all listed variables) For the lowest socioeconomic group, 777 deaths out of 3748 excess deaths due to cancer within 5 years could be avoided if the survival was equally high as in the highest socioeconomic group
(Davies et al. 2010) (UK)	Thames Cancer Registry local screening programme Hospital Episode Statistics	Women diagnosed during 2001–2005 in London	Cox proportional hazards regression models for cause-specific survival	Area deprivation index [based on the Income Domain of the Index of Multiple Deprivation]	Age at diagnosis, stage at diagnosis, treatment (surgery, chemotherapy, radiotherapy, hormone therapy), ethnicity place of residence	HR = 1.45* for most deprived women compared to most affluent women, after adjusting for age, stage, ethnicity, treatment, and place of residence



(Davies et al. 2016) (UK)	Inpatient Hospital Episode Statistics NHS, Princess Grace Hospital Breast Services	Women diagnosed during 2005–2011	Cox proportional hazards regression models for all-cause survival	Area deprivation index [based on the Income Domain of the Index of Multiple Deprivation]	Year of diagnosis, age at diagnosis, stage at diagnosis, place of treatment (private providers only, private and public providers only), treatment (surgery, radiotherapy, chemotherapy, hormonal therapy)	HR = 1.37* for most deprived women compared to most affluent women, after adjusting for age at diagnosis and place of treatment HR = 1.22 for most deprived women compared to most affluent women, after adjusting for age at diagnosis, stage, year of diagnosis, treatment and place of treatment
(Skyrud et al. 2016) (Norway)	Cancer Registry of Norway Norwegian Patient Register	Women diagnosed during 2002–2011	Generalised linear regression models to estimate the Relative Excess Risks of death (RER)	Highest education level achieved within 1 year of diagnosis, household income 1 year prior to diagnosis	Age at diagnosis stage at diagnosis, place of residence (as a proxy of health services regions) treatment (surgery, radiotherapy) comorbidity	RER = 0.60* for women with high level of education compared to women with low level of education, after adjusting for sex, age, tumour stage, household income, surgery, radiotherapy and health services region RER = 0.68* for women with high income compared to women with low income, after adjusting for sex, age, tumour stage, education, surgery, radiotherapy and health services region After adjusting for comorbidity and all variables mentioned before, there was only one regional variation that remained unexplained, which could result from inequalities in the quality of cancer care delivered by the relevant health services regions

(continued)

Table 7.1 (continued)

Reference (Country)	Data sources	Study population	Statistical methods	Socioeconomic measure	Further investigated variables <sup>a</sup>	Main survival results
(Quaglia et al. 2011) (Italy)	Liguria Region CR	Women diagnosed during 1996–2000	Cox proportional hazards regression models for all-cause survival Generalised linear regression models to estimate the Relative Excess Risks of death (RER)	Regional Deprivation Index	Period of diagnosis age at diagnosis stage at diagnosis (tumour size, lymph nodal status), oestrogen receptor status, treatment (surgery, chemotherapy, radiotherapy, hormonal treatment, lymphadenectomy)	Most deprived women experienced a poorer prognosis (five-year relative survival = 77%) than women with higher socioeconomic status (five-year relative survival = 89%). RER = 2.34* for most deprived women compared to most affluent women, with no adjustments. RER decreased to 1.82, after adjusting for age, incidence period, tumour size, lymph nodes, oestrogen receptor status and treatment
(Redaniel et al. 2015) (UK)	Merged Cancer Registry, Office for National Statistics database Hospital Episode Statistics database	Women aged ≥15 years diagnosed during 1998–2009	Relative survival	Area deprivation index [based on the Index of Multiple Deprivation]	Age at diagnosis, calendar period ( <i>as proxy for screening history</i> ), histology, tumour differentiation, -no. consultations, treatment, comorbidity, diagnostic interval, region of residence, ethnicity	HR = 1.20 for more deprived women compared to most affluent women, after adjusting for all listed variables

<p>(Lillini et al. 2011) (21 European countries)</p>	<p>EUROCARE 3 Study OECD database WHO-HFA database EUROSTAT database</p>	<p>Women diagnosed during 1990–1994</p>	<p>Relative survival Linear regression models considering relative survival as dependent variable and socioeconomic and health care-related (SEH) indicators as independent variables</p>	<p>SEH factors belonging to macro-economy</p>	<p>health technologies and medical resources labour market</p>	<p>Survival was strongly associated with the availability of clinical facilities (Computed Tomography Scanners [coefficient = -0.009*]), to the organisation of the healthcare systems (% of labour force in Services [coefficient = -0.023*]), and to factors describing the sociodemographic environment where the patient lives (Total Public Expenditure [coefficient = -0.013*]) The linear regression model explained a large part (R<sup>2</sup> = 70%) of the geographic variability in survival among European countries</p>
<p>(Dialla et al. 2015) (France)</p>	<p>Côte d’Or breast and gynaecological Cancer Registry</p>	<p>Women diagnosed during 1998–2009 and residing in Côte d’Or</p>	<p>Relative survival</p>	<p>Area deprivation index [based on the French European Deprivation Index (FEDI)], Urbanity (urban/rural area) distance from the place of residence to the nearest cancer radiology centre</p>		<p>five-year survival ranged from 88% in most deprived women to 93% in most affluent women five-year survival was 91% in women living in an urban area and 90% for women living in a rural area five-year survival ranged from 89% in women living ≥9 km from the nearest cancer radiology centre to 93% in women living &lt;2 km from the nearest cancer radiology centre</p>

(continued)

**Table 7.1** (continued)

Reference (Country)	Data sources	Study population	Statistical methods	Socioeconomic measure	Further investigated variables <sup>a</sup>	Main survival results
(Verkooijen et al. 2009) (Switzerland)	Geneva Cancer Registry, Cantonal Population Office	Women diagnosed during 1990–2005	Cox proportional hazards regression models for cancer-specific survival	Socioeconomic indicator based on the woman's last occupation or, for the unemployed, that of the spouse	Age at diagnosis, stage at diagnosis, method of detection ( <i>screening history</i> ), grade, oestrogen receptor status, treatment (surgery, radiotherapy, chemotherapy, hormonal therapy), family history	After adjusting for all listed variables, there was still a trend towards lower mortality risk among women with a positive family history compared to women with a negative family history (HR = 0.84, overall; HRs ranged from 0.58 to 0.92 according to socioeconomic status), in particular among women with high socioeconomic status (HR = 0.58)
(Brooke et al. 2017) (Sweden)	Swedish Cancer Register Longitudinal Integration Database for Health Insurance and Labour Market Studies	Women, aged 65–79 years, with a child aged ≥30 years diagnosed during 2001–2010	Relative survival Flexible parametric regression models to estimate the excess hazard rate ratio (EHR)	Offspring's education Offspring's disposable income	Year of diagnosis, country of birth, mothers' education level, mothers' income, partners' education level, number of children, sex of child, age of child in year prior to mother's diagnosis, –proximity of residence between mother and child, marital status	10-year overall survival (relative survival) ranged from 69% (89% in women with offspring's education >14 years to 58% (79% in women with offspring's education <12 years (EHR = 1.69* for women with offspring's education <12 years compared to women with offspring's education >14 years, after adjusting for all listed variables and offspring's disposable income) 10-year relative survival ranged from 65% (87% in women with offspring with high income to 66% (85% in women with offspring with low income (EHR for women with offspring with low income compared to women with offspring with high income = 1.06, after adjusting for all listed variables and offspring's education level)

<sup>a</sup>Any further information considered in relation to socioeconomic survival estimates

Thirty-three studies (79%) were conducted in Northern Europe (Denmark, Ireland, Norway, Sweden, the Netherlands, UK), five (12%) in Central Europe (France, Switzerland) and three (7%) in Southern Europe (Italy). One study involved 21 countries.

Most studies used population-based cancer registry data, together with information from national statistics databases. Only one study used information from hospital databases (Baker et al. 2010).

Crude survival estimates (e.g. survival from cancer or all causes of death combined) or hazard ratios were provided by 20 studies. Twenty-two studies presented either net or relative survival estimates, or the relative excess risk of death (sometimes called excess hazard rate ratios). Five studies only provided the number of avoidable deaths or the average loss in life expectancy, estimated with regression survival models.

Survival was examined in relation to various indices of socioeconomic status. Ten studies used education level, home ownership or household income. Three studies considered occupational group or type of employment, but most studies considered tertiles, quintiles or deciles of a socioeconomic status score, usually based on summaries of individual fiscal data for residents in a given area and assigned to each patient living in that area, using her postcode of residence at diagnosis. The scores of socioeconomic status were derived with different variables in each country, typically income and occupation, but sometimes educational level, home rental or ownership status, the economic value of the home, the social class or the civil status (single, married, divorced, etc.).

Differences between the studies were also evident in the additional variables investigated to assess socioeconomic differences in survival. Some studies only reported results on socioeconomic differences in survival, overall or over time. Others considered the age of the women at diagnosis, the tumour stage at diagnosis, tumour characteristics (e.g. histology or hormonal status), and modality of cancer detection (screen-detected vs. non-screen detected). Comorbidities were analysed with or without lifestyle factors. Other studies also investigated treatments or the familial and social environment.

In line with the results for all cancers combined, survival from breast cancer was higher for less deprived (more affluent) women than more deprived women at 1, 5 and 10 years after diagnosis (Belot et al. 2018). However, although survival has generally increased over time, the absolute change in the deprivation gap (i.e. the difference between the five-year survival estimate for the most affluent and the most deprived women) was stable or only slightly smaller for women diagnosed more recently (Lyrtatzopoulos et al. 2011; Exarchakou et al. 2018; Dalton et al. 2019; Rachet et al. 2010). In other words, over 20 years since these differences in survival were first identified, more deprived women with breast cancer continue to have lower survival and shorter life expectancy than more affluent women with the same disease (Syriopoulou et al. 2017; Rutherford et al. 2015).

Potential explanations for socioeconomic differences in survival can be separated into three main groups: those related to characteristics of the patient and the tumour, to the healthcare system and to the wider social environment.

## Patient and Tumour Characteristics

### *Place of Birth and Age at Diagnosis*

Breast cancer is generally more common among more affluent women (Nur et al. 2015). However, more deprived women are generally older at diagnosis: less often aged under 50 years and more often aged 65 years or over (Nur et al. 2015; Walsh et al. 2014).

It has been observed that the deprivation gap in short-term (one-year) breast cancer survival tends to be wider among older women (Nur et al. 2015), but socio-economic inequalities in survival remain evident up to 10 years after diagnosis in all age groups (Berger et al. 2012; Nur et al. 2015).

A slightly different result has been reported from Sweden, where social gradients in breast cancer survival were of similar magnitude for women aged 20–49 and 50–65 years, and no statistically significant socioeconomic differences in survival were evident among women aged 66–79 years (Eaker et al. 2009).

Lower survival among cancer patients with lower social position may in part be attributed to differences in nationality and/or ethnicity. However, one Swedish study found no significant differences in the risk of dying from breast cancer between native Swedes and immigrant women or their daughters at each level of education (Beiki et al. 2012). Further possible explanations include more advanced stage or higher levels of comorbidity at diagnosis among more deprived women (Dalton et al. 2019), or socioeconomic disparities in participation in screening programmes and in the management of the primary tumour or any recurrence, especially among the elderly (Nur et al. 2015).

### *Disease Stage at Diagnosis*

The stage or extent of disease at diagnosis is a crucial contributory factor to the duration of survival. Notable socioeconomic differences in the distribution of stage at diagnosis have been reported, with more affluent women generally being diagnosed with less advanced tumours (Eaker et al. 2009; Quaglia et al. 2011; Berger et al. 2012; Bower et al. 2019), irrespective of age at diagnosis (Rutherford et al. 2013).

Five-year relative survival estimates at each stage at diagnosis were comparable among the deprivation quintiles 1–4 but were approximately 10% lower in the fifth, or most deprived, quintile (Rutherford et al. 2013). This suggests that a substantial reduction in the number of premature deaths among women with breast cancer could be achieved if inequalities in stage at diagnosis could be eliminated (Rutherford et al. 2013; Bower et al. 2019; Aarts et al. 2013). Although differences in stage at diagnosis explained most of the survival differences between women in deprivation quintiles 3, 4 and 5, eliminating differences in the distribution of stage would only

be expected to remove about half of the inequalities in survival between women in the most deprived and most affluent groups (Rutherford et al. 2013; Li et al. 2016).

### ***Cell Proliferation Rate and Molecular Markers***

Since the beginning of the twenty-first century, many clinical trials and hospital-based studies have shown that breast cancer is a heterogeneous disease, with gene expression patterns or immunohistochemical determination of oestrogen (ER) and progesterone (PgR) receptor expression, human epidermal growth factor receptor 2 (HER2) over-expression, and cell proliferation status identifying distinct subtypes that are also characterised by different outcomes. Differences in cancer survival between these groups have been confirmed at the population level. Women with hormone-positive (ER+ or PgR+), HER2-negative (HER2-) tumours, or tumours with low cell proliferation rate, experience better survival than women diagnosed with hormone-negative (ER- and PgR-), HER2+, or tumours with a high cell proliferation rate (Minicozzi et al. 2013).

Less-educated women seem to be diagnosed more often with tumours that have a high proliferation rate (Eaker et al. 2009) and less often with hormone-positive tumours than women with higher levels of education (Walsh et al. 2014). More deprived women with breast cancer are also less likely to be HER2-negative.

It has also been found that even after adjusting for age, period of diagnosis and stage at diagnosis, the same socioeconomic differences in survival were still present among women with hormone-positive tumours or tumours with a low cell proliferation rate (Eaker et al. 2009).

It has been suggested that the p53 mutation, which may have aberrant responses to inflammatory stress, with therapeutic consequences, may partly account for the worse prognosis in more deprived women (Baker et al. 2010). Among women with the p53 mutation, those in the most deprived group (the tenth decile) were more likely to relapse, or to die, than those in deciles 1–9.

### ***Lifestyle and Comorbidity***

Women diagnosed with breast cancer in more deprived groups are more likely to be current smokers or ex-smokers and to have a higher body mass index (BMI) but are less likely to be current drinkers (Morris et al. 2017; Larsen et al. 2015). While some authors have observed that women living in more deprived areas have higher levels of comorbidity when diagnosed with breast cancer (Dialla et al. 2015), such as diabetes (Redaniel et al. 2012), others have not found any association between deprivation and comorbidity (Morris et al. 2017).

However, the deprivation gap in survival for women with breast cancer was present irrespective of obesity, alcohol consumption, smoking habit or comorbidity

(Morris et al. 2017). Adjustment for characteristics of the woman, her tumour and any comorbidity had little influence on socioeconomic differences in survival (Morris et al. 2016; Ward et al. 2018), but adjustment for lifestyle, represented by metabolic indicators, smoking and alcohol habits, does reduce the deprivation gap to some extent (Larsen et al. 2015; Redaniel et al. 2012; Walsh et al. 2014).

These findings suggest that improvements in lifestyle might improve survival among women with lower socioeconomic position (Larsen et al. 2015).

## Factors Related to the Healthcare System

### Screening

Inequalities in the use of breast cancer screening services between socioeconomic groups defined by education level have been described in several European countries (Palencia et al. 2010). These inequalities are more marked in countries that do not have organised cancer screening programmes.

However, adherence to breast cancer screening recommendations is variable. Women living in deprived or rural areas, and those who live far from screening centres, are less compliant with screening recommendations (Ouedraogo et al. 2014), as well as women who are obese or diabetic (Constantinou et al. 2016).

In the Netherlands, *in situ* tumours (mostly screen-detected) were more commonly seen among more affluent women, suggesting higher attendance at the screening programme (Bastiaannet et al. 2011). By contrast, in one region of England, the proportion of regional and advanced tumours was particularly high in the most deprived women with screen-detected tumours (Morris et al. 2016). These women also had larger tumours than those diagnosed in more affluent women with screen-detected tumours. The authors suggested that deprived women may use screening as an entry point to the healthcare system, after they are already symptomatic, more often than women in more affluent categories.

Studies in London and Ireland (Davies et al. 2013; Walsh et al. 2014) have shown that more deprived women were less likely to have presented via screening. Similar results have been seen in France, where for women diagnosed during 1998–2009, residence in a deprived area was linked to advanced stage at diagnosis only among those aged 50–74 years (Dialla et al. 2015). This suggests socioeconomic disparities in participation in organised breast cancer screening programmes. In England, women in the most deprived group also appeared to wait longer for a hospital appointment after the general practitioner's referral (Downing et al. 2007) and to experience somewhat longer delays between the last breast-related consultation and diagnosis, although the difference was not significant (Morris et al. 2017).

The deprivation gap in breast cancer survival has been reported by many authors, whether the tumour is screen-detected or not (Morris et al. 2015, 2016; Davies et al. 2013; Woods et al. 2016; Aarts et al. 2011). However, among screen-detected women, the deprivation gap in survival was either similar to (Morris et al. 2015;



Woods et al. 2016) or somewhat smaller than (Morris et al. 2016; Aarts et al. 2011; Davies et al. 2013) the deprivation gap in survival among women whose tumour was diagnosed clinically, even after correction for lead-time bias and potential over-diagnosis (Morris et al. 2015).

Two studies in Italy, in Tuscany and Emilia Romagna, have shown that, after adjustment for stage, the risk of death from breast cancer becomes similar across the socioeconomic spectrum 10 years after the introduction of a screening programme for women. These changes were seen among women in the age range invited to screening (50–69 years), but not among women diagnosed under the age of 50 years (Puliti et al. 2012; Pacelli et al. 2014). These studies suggest that the screening programmes successfully reduced socioeconomic inequalities in early detection, shortened the time to diagnosis and improved the quality of treatment in more deprived groups, thus producing greater equity in breast cancer survival.

However, since socioeconomic differences in survival remain evident after participation in a screening programme has been taken into account (Rachet et al. 2010; Feller et al. 2017), they could be related to the lack of timely screening, which could lead to delayed diagnosis and a larger tumour burden at diagnosis (Siddharth and Sharma 2018). Some authors have concluded that the type and quality of treatment provided could also play a role, although a few studies have found no effect of treatment on socioeconomic survival differences (Morris et al. 2016; Li et al. 2016).

Further investigations are required of the timeliness and appropriateness of treatment, adherence to treatment and the quality of clinical follow-up between women with breast cancer in the different social groups, together with the influence of these variables on cancer care.

### *Treatment and Access to Care*

Substantial differences in access to treatment exist both between and within European countries, and they contribute to differences in cancer survival (Siddharth and Sharma 2018).

For example, in England, the most deprived women appeared to have to wait a longer time from diagnosis to surgery than the most affluent women (Downing et al. 2007; Morris et al. 2016, 2017), although those findings were not confirmed after selecting women with localised stage disease who only underwent surgical treatment (Redaniel et al. 2013). Furthermore, women receiving some or all of their care within private provider(s) were often living in the most affluent area, as well as being younger, non-screen detected and less often diagnosed at an early stage, than women who were treated in public hospitals (Davies et al. 2016).

One Italian study found that women with a very low socioeconomic status who were diagnosed with invasive breast cancer during 1996–2000 in Liguria were less likely to be treated with curative intent or according to current guidelines (Quaglia et al. 2011). In particular, more deprived women in the Northern and Yorkshire

region of England who were diagnosed during 1998–2000 were less likely to receive surgery, and when they did receive it, were less likely to have breast-conserving surgery (Downing et al. 2007), or to receive radiotherapy or chemotherapy, according to a Swedish study of women who were diagnosed during 1993–2003 in the Uppsala/Örebro region (Eaker et al. 2009).

By contrast, another Italian study found that socioeconomic indicators (education, occupational status and housing characteristics) showed only a marginal independent effect on indicators of the pathway of care relative to timeliness, for 50- to 69-year-old women diagnosed in Piedmont during 1995–2008 (Zengarini et al. 2016).

After taking into account age and stage at diagnosis, the association between socioeconomic status and survival was stronger among women who underwent breast-conserving surgery as part of treatment with curative intent than those who underwent mastectomy (Downing et al. 2007). It is striking that socioeconomic differences in survival have been shown to persist even after a wide range of factors have been taken into account, including the waiting time from diagnosis to surgery (Redaniel et al. 2013), chemotherapy, radiotherapy and hormonal treatment (Eaker et al. 2009; Jack et al. 2009; Davies et al. 2010; Bastiaannet et al. 2011), place of treatment (private vs. public hospital) (Davies et al. 2016), and health service region (Skyrud et al. 2016), although these adjustments do all contribute to reducing socioeconomic inequalities (Jack et al. 2009; Eaker et al. 2009; Quaglia et al. 2011; Davies et al. 2016; Aarts et al. 2011). However, they seem to disappear after considering the diagnostic interval, that is, the time from primary care presentation to definitive diagnosis (Redaniel et al. 2015), thus suggesting that differences in access to medical services do play a role. Examples include the availability of clinical facilities (e.g. computed tomography scanners), the organisation of the healthcare system (e.g. percentage of the labour force working in health services) and factors describing the sociodemographic environment where the patient lives (e.g. total public expenditure), all of which are associated with survival (Lillini et al. 2011), as well as differences in access to specialist centres, especially given that women often have to travel long distances (Dialla et al. 2015; Gentil et al. 2012), ease of travel to appointments, flexibility of work, other commitments and the level of social support (Morris et al. 2016).

## **Factors Related to the Social Environment**

### ***Familial Environment***

According to one study using data from the Irish National Cancer Registry (Walsh et al. 2014), no more than half of the socioeconomic gap in breast cancer survival can be explained by the available information on patients and tumour

characteristics, and treatment, that is, age, stage, comorbidities at diagnosis, hormonal status and all treatments administered. This suggests that other factors or mechanisms may be involved.

When women are diagnosed with breast cancer, it can affect the emotional, physical, psychological and social well-being of their families, as well as the women themselves (Gluck and Mamounas 2010). This may be reflected in lifestyle changes during treatment or reduction of household income (e.g. through the personal costs of receiving treatment, or restriction of the woman's ability to work).

Breast cancer impacts society both directly (e.g. through health system costs: expenses associated with treatment) and indirectly (e.g. through the loss of labour productivity). All these aspects may contribute to socioeconomic differences in survival among women with breast cancer. However, cultural factors within the family may also play a role.

It has been noted that the presence of a positive family history of breast cancer eliminated socioeconomic differences in access to screening and optimal treatment, but this did not translate into a reduction in socioeconomic differences in breast cancer survival (Verkooijen et al. 2009). In fact, among more deprived women, the presence of a family history increased the probability of being detected at an earlier stage compared with deprived women who did not have a family history. However, most deprived women were those with the lowest positive effect of having a family history on the risk of death from their breast cancer. The authors argued that a possible explanation includes socioeconomic differences in lifestyle, as mentioned above. Thus, the positive effect of improved access to screening and optimal treatment associated with a positive family history may be offset by the higher prevalence of unfavourable lifestyles among the most deprived women.

It has also been found that lower education level among adult children of mothers with a breast cancer diagnosis is associated with poorer survival, independently of the mother's education level or income (Brooke et al. 2017). This association was stronger among women diagnosed at an earlier clinical stage. These results suggest that health awareness or the ability to interpret information, rather than material resources, may be particularly important in improving outcome.

### ***Social Relationships***

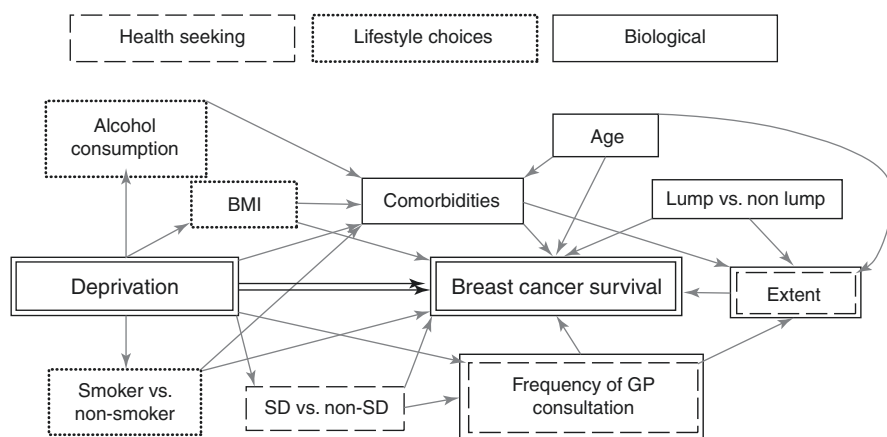
Favourable associations have also been observed between positive developments in romantic relationships and hobbies and death from breast cancer. Similarly, higher breast cancer mortality has been reported in relation to negative life events, even after adjusting for characteristics of the patient and the tumour, lifestyle and socioeconomic status (Heikkinen et al. 2017). It would seem that social interaction with and support from friends and family are particularly important in times of illness, and they may contribute to disparities in cancer outcomes.

## Comment

The relation between breast cancer survival and the characteristics of the woman and her tumour, including biological, lifestyle, social and health-seeking factors, is complex (Fig. 7.3). Thus, differences in women's baseline characteristics, primary care consultation patterns, symptom presentation, and the time intervals between the first report of symptoms and the eventual diagnosis, and then between diagnosis and the start of treatment, all contribute to socioeconomic differences in breast cancer survival. Factors related to the behavioural norms or education of the woman's children (Torssander 2014) or causes of death other than breast cancer (Rutherford et al. 2015) are plausibly correlated with these differences.

It is insufficient to concentrate attention on one small area within a complex whole. Rudolf Virchow (1848), the founder of cellular pathology, pointed out a long time ago: Medicine is a social science, and politics is nothing else but medicine on a large scale. "Medicine, as a social science, as the science of human beings, has the obligation to point out problems and to attempt their theoretical solution: the politician, the practical anthropologist, must find the means for their actual solution" (Munro 2014). Thus, the ultimate goal of research is not only to improve our understanding of a problem but also to show how research findings can be translated into clinical benefits, in particular into interventions that deliver benefits to more socioeconomically deprived patients through earlier diagnosis and better treatment, follow-up and rehabilitation, in order to improve cancer outcomes overall, as well as to reduce the socioeconomic gap in survival (Dalton et al. 2019).

Virtually all the studies we have reviewed suggest that socioeconomic inequalities in breast cancer survival remain even after controlling for stage at diagnosis,



**Fig. 7.3** Potential links between deprivation and breast cancer survival and the woman's biological, lifestyle and health-seeking characteristics. SD screen-detected, non-SD non-screen-detected. (Reprinted from Morris et al. (2017), Fig. 1, licensed under the terms of the Creative Commons Attribution License [<https://creativecommons.org/licenses/by/4.0/>])

treatment, hormonal receptors, the woman's lifestyle, comorbidities at diagnosis and screening attendance. Deeper insight into the complex inter-relation between these factors and breast cancer survival is required. Studies must include all these factors, together with the social environment, as well as socioeconomic status. Studies of this type could contribute to a better understanding of socioeconomic inequalities in breast cancer survival, and they would be expected to offer more useful information for public health interventions.

## Recommendations

Demographic factors, socioeconomic conditions and clinical aspects should be considered together in research, policy and clinical or public health interventions aimed at reducing socioeconomic inequalities in breast cancer survival.

Clinicians should address the broader environment and social context of patient care, at the same time as integrating the increasing molecular understanding of cancer. They also need to be aware of the educational context of their patients with breast cancer and to pay particular attention to women who require extra support. Further improvements are needed in the quality of care in healthcare facilities that are not reference or tertiary centres, and to the distribution of these specialised centres in European countries, to avoid aggravating socioeconomic differences in outcome. Screening programmes should be more closely adapted to the personal and social characteristics of the women they serve. Better research will be required to pinpoint the causes that underlie socioeconomic differences in survival, especially in those European countries where this important issue has never been considered.

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