



## Diagnosis and treatment of breast cancer in Denmark during the COVID-19 pandemic: a nationwide population-based study

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### ABSTRACT

**Background:** The COVID-19 pandemic was a global health crisis with population-wide behavioural restrictions imposed worldwide to reduce transmission of infection and to limit the potential burden on the healthcare systems. We examined whether there was any change in the diagnosis or treatment of breast cancer during the pandemic as compared to previous years.

**Material and Methods:** The study population comprised all women aged  $\geq 18$  years diagnosed with breast cancer in 2015–2021 with data obtained from the clinical quality registry of the Danish Breast Cancer Cooperative Group (DBCG). Data on socioeconomic factors were retrieved from Statistics Denmark. Prevalence ratios (PR) with 95% confidence intervals (CI) were estimated from a generalised linear model (GLM) with a log link for the Poisson family with robust standard errors (SE) of each outcome, using the COVID-19 pandemic period in Denmark as the exposure of interest.

**Results:** In total, 30,598 breast cancers were diagnosed during the study period. There was a small decrease (4.5%) in the total number of breast cancer cases in 2020 compared with previous years. During the pandemic, a lower proportion of the patients diagnosed with breast cancer had a short educational level (28.5 vs. 26.9%; PR = 0.91; 95% CI: 0.88–0.95), a low income (20.5 vs. 19.0%; PR = 0.90; 0.85–0.95) and fewer than expected in the age group 60–69 years (27.8 vs. 25.3; PR = 0.90; 0.86–0.94) were diagnosed, as compared with the pre-pandemic period. No difference in type of surgery or tumour size was observed. A higher proportion of patients received neo-adjuvant chemotherapy (49.0 vs 55.0%; PR = 1.15; 1.06–1.24), whereas a lower proportion received adjuvant chemotherapy (93.5 vs 85.6%; PR = 0.92; 0.90–0.93) during the pandemic, compared with the pre-pandemic period.

**Conclusions:** During the pandemic, a small decrease in the number of breast cancer diagnoses was observed particularly among socially disadvantaged groups. Overall, the quality of breast cancer treatment was maintained.

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## Background

The COVID-19 pandemic was a global health crisis, causing extensive disruptions to societies and huge strains on healthcare systems across the world. Population-wide restrictions (“lockdowns”) were imposed worldwide to reduce the transmission of SARS-CoV-2 virus and hereby to limit the potential burden on the healthcare systems. In Denmark prioritisations and re-organisations aimed to ensure sufficient capacity to take care of patients in need of hospitalization due to COVID-19, while still managing patients in acute need of medical care; e.g. patients with cancer.

Early detection of cancer as well as cancer treatment pathways were maintained in Denmark throughout the pandemic as were the mammography screening programmes; nonetheless, the sudden disruptions to the healthcare system may have influenced the diagnosis and treatment of cancer.

Psychological effects of lockdown and fear of the infection might have caused a change in health-seeking behaviour and thereby possibly a delay in the diagnosis of breast cancer for some patients. In an early study from Denmark, it was found that fewer breast cancers were diagnosed in the spring of 2020 [1], and later we showed that also participation in mammography screening was lower at the start of the pandemic than before the COVID-19 outbreak [2]. Patient delay and lower screening participation could result in findings of cancers with more advanced disease stages that might require more extensive treatment. Congruently, studies from the Netherlands found a reduction in screen-detected breast cancers and early-stage tumours at the start of the pandemic [3–5].

Social inequity in the stage of disease and survival after breast cancer has earlier been reported [6,7]. The pandemic lockdown may have had a differential effect on the population causing more disadvantaged groups to further delay healthcare

seeking, miss out on or experience delay in important treatments, thus increasing the social inequity in diagnosis and treatment. Social differences in mammography screening were found to be exacerbated during the pandemic [2] however it is unknown whether social factors influenced the total number of breast cancer diagnoses.

In this large nationwide, population-based study, we examined the diagnosis and treatment of breast cancer in Denmark during the COVID-19 pandemic. Specifically, we investigated whether there was a change in diagnoses, type of treatment (surgery and adjuvant treatment) or the distribution of tumour size during the pandemic, compared with pre-pandemic period. Moreover, we examined whether breast cancer cases differed across socioeconomic and demographic population groups during the pandemic as compared with before.

## Material and methods

### Setting

Denmark has a population of 5.8 million inhabitants [8], and a tax-funded healthcare system where all residents have access to free-of-charge healthcare to most healthcare services. The general practitioner acts as a gatekeeper to the specialized healthcare system. In Denmark, well-defined standardized cancer patient pathways encompassing guidelines and maximum timelines for more than 30 cancer diagnoses have been in place since 2008 [9]. Denmark holds extensive population-based administrative and health registries which can be linked using the unique personal identifier assigned to all residents in Denmark at birth or immigration [10,11].

### The COVID-19 pandemic in Denmark

Three main waves of the COVID-19 pandemic occurred in Denmark that is, in the spring of 2020, in the winter of 2020/2021, and in the winter of 2021/2022 [12].

The pandemic response in Denmark comprised societal lockdown, COVID-19 testing and vaccination against COVID-19. The first lockdown was introduced in Denmark on 11 March 2020, where large parts of the society were closed down (i.e. schools and some public workplaces and with the advice to work from home if possible). Within the healthcare system, elective procedures were cancelled or postponed with the aim of releasing resources to take care of acute patients with COVID-19, if needed. COVID-19 testing began in Denmark in May 2020 providing COVID-19 tests free-of-charge to the whole population [13]. A COVID-19 vaccination program was implemented in December 2020 [14]. There was high vaccination coverage in Denmark and by March 2022, approximately 81% of the population had received two doses or more [15].

### Study population

The study population comprised all women aged  $\geq 18$  years old diagnosed with a first-time diagnosis of breast cancer (C50) between 1 January 2015 and 30 June 2021, as

registered in the clinical quality registry of the Danish Breast Cancer Cooperative Group (DBCG) [16]. The registry contains information on all women diagnosed with breast cancer in Denmark since 1977 with data collected for quality-of-care purposes. Clinical data are reported directly to DBCG registry by the clinicians and supplemented by data from the Danish National Patient Register regarding follow-up and treatment [17], and from the Danish Pathology Register securing completeness of cases [18]. The estimated national coverage of total breast cancer cases in the DBCG registry is above 95%.

We excluded women who emigrated within 1 year from diagnosis and women with an unknown postal address (29 patients (0.1%)) as they did not have sufficient treatment follow-up or central data reported.

### Exposure of interest

We considered the COVID-19 pandemic period in Denmark as the main explanatory variable. The pandemic phases were defined, in accordance with the governmental responses to the COVID-19 pandemic in Denmark, as follows:

*Pre-lockdown period:* 1st February to 10 March 2020. *1st lockdown:* 11 March to 15 April 2020. *1st re-opening:* 16 April to 15 December 2020. *2nd lockdown:* 16 December 2020 to 27 February 2021. *2nd re-opening:* 28 February 2021 to 30 June 2021 (end of inclusion period).

We defined two overall periods of interest for the main analyses: *The pre-pandemic period* (1 January 2015 to 31 January 2020) and *the pandemic period* (1 February 2020 to 30 June 2021). For neoadjuvant chemotherapy the pre-pandemic period began 1 January 2017 from when treatment guidelines were adjusted and registration of this treatment was mandatory to the DBCG registry. The follow-up regarding treatment outcomes ended 31 December 2021.

### Outcomes of interest

The main outcomes of interest were total number of breast cancer cases, primary surgery, tumour size, neoadjuvant chemotherapy (NACT), adjuvant systemic treatments, and radiation therapy. Treatment outcomes were categorized in accordance with the national clinical quality indicators measuring good clinical practise [19], defined by the DBCG steering group on the basis of the national clinical guidelines for breast cancer treatment. These treatment outcomes included patients who were eligible for the treatment and we investigated whether they received the treatment according to DBCG guidelines. For primary surgery the patient group was categorized into lumpectomy, mastectomy and other. For adjuvant systemic treatments, patients were included if they were diagnosed with high-risk breast cancer and the outcome was categorized into receiving either chemotherapy or endocrine therapy or not. For NACT, the group included were patients with double negative or HER2 (human epidermal growth factor receptor 2) positive cancer and at the same time tumour size  $> 2$  centimeters or lymph node-positive. The outcome was categorized into receiving NACT or not. For radiation therapy, patients were included if they

had either lumpectomy or mastectomy with an indication for radiation therapy. The outcome was categorized into receiving postoperative radiation therapy or not.

### Explanatory variables

The following covariates were included in the analyses of a total number of breast cancer cases: age, cohabitation status, educational level, disposable income, and healthcare region. Age was defined at the date of diagnosis, as registered in the DBCG registry [16]. From Statistics Denmark [8], we obtained information on cohabitation status, educational level, and disposable income. Cohabiting status was categorized as living alone or co-habiting/co-living/married (i.e. married or registered partnership) in accordance with Statistics Denmark [8]. In accordance with the International Standard Classification of Education (ISCED) of the United Nations Education, Scientific and Cultural Organization (UNESCO) educational level was categorized into lower level (ISCED level 1-2: Primary education to Lower secondary education), medium level (ISCED level 3-5: Upper secondary education and Vocational education), and higher level (ISCED level 6-8: Bachelors programmes to PhD programmes [8]. Income was defined as official disposable income depreciated to 2015 level and categorised into quintiles. The healthcare region was obtained from the DBCG registry.

### Statistical analyses

We described the characteristics of women diagnosed with breast cancer during the study period. With the use of a generalised linear model (GLM) with log link for the Poisson family with robust standard errors (SE), we estimated prevalence ratios (PR) and 95% confidence intervals (CI) of each outcome of interest during the phases of the pandemic overall and stratifying by the explanatory variables. The analyses were adjusted for age at diagnosis (to take into account the effect of age on the other variables) and month of diagnosis (to account for seasonal variation and to account for any underlying trend in the diagnosis of breast cancer). All analyses were conducted using STATA version 17.0.

### Ethical considerations

The study was registered at the Central Denmark Region's register of research projects (journal number 1-16-02-381-20). Patient consent is not required by Danish law for register-based studies.

### Results

In total, 30,598 women diagnosed with breast cancer (median age at diagnosis 64 years; IQI = 53-74) were included in the study. Altogether, 28.2% of the patients had a short educational level, 39.5% lived alone, and 28.6% had any severe comorbid condition (either a low, medium or high comorbidity index score). Regarding primary surgery, 26.9% had a mastectomy performed and 61.3% a breast-

conserving surgery (BCS). 37.7% of the patients had a tumour size above 20 mm. For neo-adjuvant chemotherapy, 50.6% of eligible patients received this treatment. Of patients eligible for adjuvant oncological treatment, 92.0% received chemotherapy, 90.4% received endocrine therapy, and 92.9% and 86.6 received radiation therapy respectively in the BCS and mastectomy group following clinical guidelines (Table 1).

The number of breast cancer cases decreased by 4.5% in 2020 compared with before the pandemic; the decrease was more pronounced during 1<sup>st</sup> lockdown (Figure 1). The average of diagnosed cancers in 2021 resembled the numbers before the pandemic. During the pandemic period, there was a lower proportion of patients diagnosed with breast cancer with short educational level (28.5 vs 26.9%; PR = 0.91; 95% CI: 0.88-0.95) and in the lowest or second lowest income quintile (20.5 vs 19.0%; PR = 0.90; 95% CI: 0.85-0.95) than in the pre-pandemic period. Also, a lower proportion than expected was in the age group 60-69 years old (27.8 vs. 25.3; PR = 0.90 95% CI: 0.86-0.94), had no underlying comorbidity (72.0 vs 69.3%; PR = 0.97; 95% CI: 0.96-0.99), and fewer breast cancers were screen-detected (30.8 vs 27.8% PR = 0.91; 95% CI: 0.87-0.95) compared with the pre-pandemic period. No differences were found across health care regions (Table 1).

There was no difference in the type of primary surgery, and no difference in tumour size in patients diagnosed in the pandemic compared with the pre-pandemic period (Table 1). Of patients who were recommended specific adjuvant treatments following clinical guidelines, a larger proportion received neoadjuvant chemotherapy (49.0 vs 55.0%; PR = 1.15; 95% CI: 1.06-1.24), whilst a smaller proportion received adjuvant chemotherapy (93.5 vs 85.6%; PR = 0.92; 95% CI: 0.90; 0.93) during the pandemic versus before the pandemic. Fewer patients received adjuvant radiation therapy after mastectomy in the pandemic period as compared with the pre-pandemic period (88.6 vs. 80.2; PR = 0.91; 95% CI: 0.87-0.96) (Table 1). As the mastectomy group was small, the absolute number of patients not treated with radiation therapy was very low. Figure 2 shows the numbers and proportion of cases according to clinical factors and treatment across the time periods of interest. Figure 2(c-e) gives the proportions treated out of the total patients who were recommended the treatment of interest following national clinical guidelines.

In Supplemental Table 1 the results for all pandemic sub-periods are presented showing the same trends across sub-periods as the total pandemic period from our main analysis.

### Discussion

#### Main findings

The total number of diagnosed breast cancer cases was slightly lower during the pandemic, whereas no change in tumour size was observed. During the pandemic, the proportion of breast cancer patients with a low social position was lower, fewer patients than expected were in the middle aged group 60-69 years, and fewer breast cancers were screen-detected compared with the pre-pandemic period. Small changes in adjuvant treatment were present, but the quality

**Table 1.** Number of breast cancer cases in total, before and during the COVID-19 pandemic and Prevalence Ratios (PR) for selected socio-demographic and clinical factors.

	Pre-pandemic period (1 Jan 2015 – 31 Jan 2020)		Pandemic period (1 Feb 2020 – 30 June 2021)		Pre-pandemic (ref.)	Prevalence ratio (PR) (95 %CI) pandemic vs. pre-pandemic period (adjusted for age and month)	
	Total Numbers (%)	Numbers (%)	Missing %	Numbers (%)		Missing %	
<b>Total</b>	30,598 (100.0)	23,923 (78.2)		6675 (21.8)			
<i>Socio-demographic factors</i>							
Age groups, n (%)			0		0		
18–39 years	1249 (4.1)	984 (4.1)		265 (4.0)		1	1.11 [1.00; 1.25]
40–49 years	3728 (12.2)	2939 (12.3)		789 (11.8)		1	1.03 [0.95; 1.11]
50–59 years	6687 (21.9)	5265 (22.0)		1422 (21.3)		1	1.00 [0.95; 1.05]
60–69 years	8326 (27.2)	6640 (27.8)		1686 (25.3)		1	0.90 [0.86; 0.94]
70–75 years	4082 (13.3)	3118 (13.0)		964 (14.4)		1	1.05 [0.98; 1.12]
76 or more	6526 (21.3)	4977 (20.8)		1549 (23.2)		1	1.01 [0.97; 1.06]
Cohabitation status, n (%)			0.2		0.5		
Living alone	12064 (39.5)	9455 (39.6)		2609 (39.3)		1	0.97 [0.94; 1.00]
Married/Cohabiting	18463 (60.5)	14432 (60.4)		4031 (60.7)		1	1.02 [1.00; 1.04]
Educational level (ISCED), n (%)*			1.6		1.6		
ISCED15 level 1–2	8484 (28.2)	6714 (28.5)		1770 (26.9)		1	0.91 [0.88; 0.95]
ISCED15 level 3–5	12861 (42.7)	10068 (42.8)		2793 (42.5)		1	1.00 [0.96; 1.03]
ISCED15 level 6–8	8757 (29.1)	6752 (28.7)		2005 (30.5)		1	1.09 [1.04; 1.13]
Disposable income (quintiles), n (%)			0.2		0.5		
Lowest quintile	6165 (20.2)	4904 (20.5)		1261 (19.0)		1	0.90 [0.85; 0.95]
Second quintile	6143 (20.1)	4916 (20.6)		1227 (18.5)		1	0.87 [0.82; 0.92]
Third quintile	6099 (20.0)	4780 (20.0)		1319 (19.9)		1	1.00 [0.94; 1.05]
Fourth quintile	6113 (20.0)	4823 (20.2)		1290 (19.4)		1	0.98 [0.92; 1.03]
Highest quintile	6001 (19.7)	4459 (18.7)		1542 (23.2)		1	1.28 [1.22; 1.35]
Healthcare region, n (%)			0.2		0.5		
Capital Region of Denmark	9350 (30.6)	7366 (30.8)		1984 (29.9)		1	0.97 [0.93; 1.01]
Region Zealand	5079 (16.6)	3995 (16.7)		1084 (16.3)		1	0.97 [0.91; 1.03]
Region of Southern Denmark	6780 (22.2)	5309 (22.2)		1471 (22.2)		1	0.99 [0.94; 1.04]
Central Denmark Region	6371 (20.9)	4943 (20.7)		1428 (21.5)		1	1.05 [0.99; 1.11]
Northern Denmark Region	2947 (9.7)	2274 (9.5)		673 (10.1)		1	1.07 [0.98; 1.16]
<i>Clinical factors</i>							
Comorbidity, n (%)**			0		0		
None	21,840 (71.4)	17,216 (72.0)		4624 (69.3)		1	0.97 [0.96; 0.99]
Low	4076 (13.3)	3147 (13.2)		929 (13.9)		1	1.04 [0.97; 1.11]
Moderate	2766 (9.0)	2116 (8.8)		650 (9.7)		1	1.06 [0.97; 1.15]
High	1916 (6.3)	1444 (6.0)		472 (7.1)		1	1.12 [1.01; 1.23]
Screen-detected, n (%)	8848 (30.1)	7038 (30.8)	4.6	1810 (27.8)	2.3	1	0.91 [0.87; 0.95]
Surgery - primary, n (%)			2.2		1.6		
Mastectomy	8217 (26.9)	6392 (26.7)		1825 (27.3)		1	1.04 [1.00; 1.09]
Lumpectomy	18,761 (61.3)	14,739 (61.6)		4022 (60.3)		1	0.98 [0.96; 1.00]
Other	3620 (11.8)	2792 (11.7)		828 (12.4)		1	1.01 [0.94; 1.08]
Tumour size, n (%)			7.3		6.0		
0–10mm	6449 (22.7)	5063 (22.8)		1386 (22.1)		1	0.97 [0.92; 1.02]
11–20mm	11281 (39.7)	8804 (39.7)		2477 (39.5)		1	0.99 [0.96; 1.03]
21–50mm	9500 (33.4)	7341 (33.1)		2159 (34.4)		1	1.04 [1.00; 1.09]
>50mm	1211 (4.3)	959 (4.3)		252 (4.0)		1	0.92 [0.80; 1.06]
Neo-adjuvant chemotherapy (NACT), n (%)***	1251 (50.6)	875 (49.0)	0	376 (55.0)	0	1	1.15 [1.06; 1.24]
Adjuvant chemotherapy, n (%)	9440 (92.0)	7726 (93.5)	0.4	1714 (85.6)	0.6	1	0.92 [0.90; 0.93]
Adjuvant endocrine therapy, n (%)	15,536 (90.4)	12,410 (90.2)	0.9	3126 (91.1)	1.8	1	1.01 [1.00; 1.02]
Adjuvant radiation therapy - lumpectomy, n (%)	13058 (92.9)	10704 (92.9)	4.3	2354 (92.9)	10.3	1	1.00 [0.99; 1.02]
Adjuvant radiation therapy - mastectomy, n (%)	1810 (86.6)	1418 (88.6)		392 (80.2)		1	0.91 [0.87; 0.96]

\*ISCED: International Standard Classification of Education. Short (ISCED level 1–2: primary education to upper lower secondary education), medium (ISCED level 3–5: Upper secondary education and Vocational education) and long (ISCED level 6–8: bachelors programmes to PhD programmes).

\*\*CCI: Charlson Comorbidity Index score. Low: 1, moderate: 2, high: 3+ comorbid conditions treated at hospital.

\*\*\*Pre-pandemic period for neoadjuvant treatment: 1 Jan 2017 to 31 January 2020.

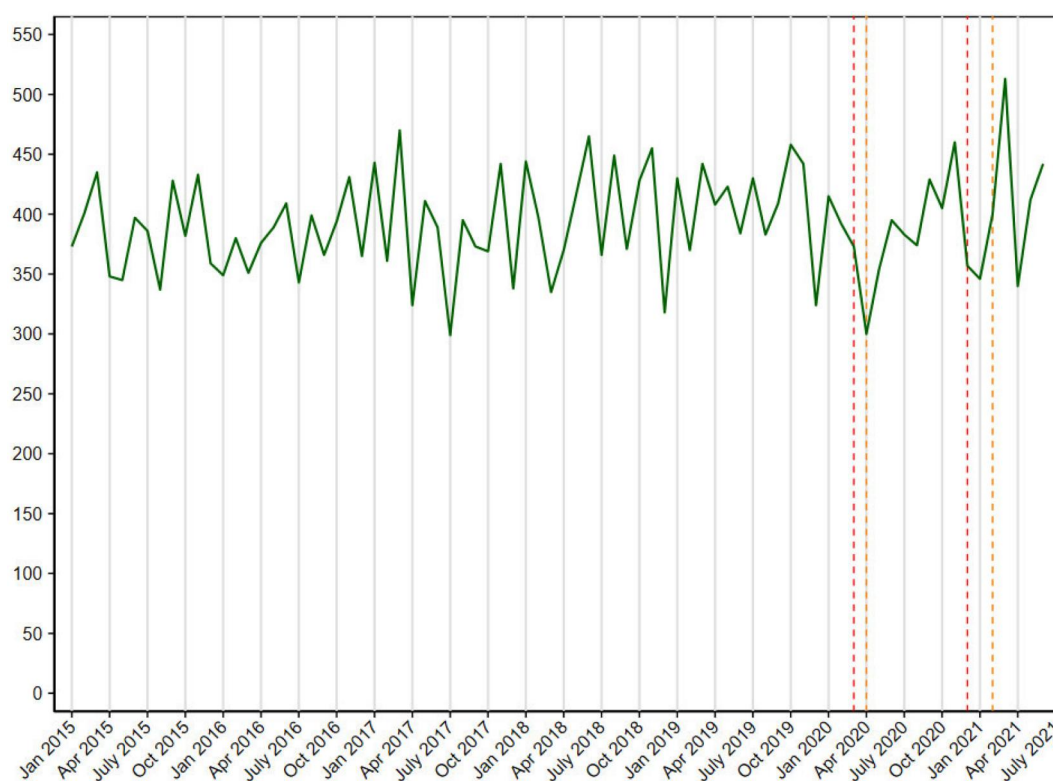
of breast cancer care was overall maintained during the pandemic as compared with earlier.

### Discussion of findings and comparison with previous studies

The existing knowledge from reviews and population-based studies supports our findings of a decrease in incident cases of breast cancer during the COVID-19 pandemic

compared with earlier periods. A meta-analysis including studies from 18 countries showed a decline in breast cancer screening and diagnosis rates from 2019 to 2020. The decrease in diagnoses was 18–29% covering 4 registry-based and 10 single or multi-institutional studies, and a decrease in mammography screening of 41–53% across 23 studies was found [20].

In Denmark, national cancer patient pathways were implemented more than a decade ago [9], which means that very



**Figure 1.** Number of breast cancer cases by month from January 2015 to June 2021. Vertical dashed lines indicate the month of implementation of social lockdowns (red dash) and lifting of lockdowns (orange dash).

well-defined treatment trajectory models exist going from first visit in primary care to examinations in highly specialized cancer care. This might, together with the fact that the screening programme continued as usual, be some of the explanation as to why the decrease in breast cancer diagnoses during the pandemic in Denmark was relatively small as compared to what was found in other countries. However, we observed social differences in diagnosis and across social groups, there may be different responses to national guidelines regarding social behaviour during the pandemic. Women with lower social positions may be more reluctant to contact the healthcare system under pandemic circumstances and have more practical or emotional barriers to health-seeking. Thus, a delay in healthcare seeking may explain why a lower proportion of breast cancers was diagnosed among socially disadvantaged groups.

In a previous study, we found that fewer women underwent mammography screening during the pandemic in Denmark [2], and this corresponds with our current finding of fewer screen-detected breast cancer cases. In the present study, we also found fewer breast cancer diagnoses than expected among women aged 60–69 years during the pandemic period. This age group is the oldest group covered by the breast cancer screening programme, and some may have skipped or chosen to postpone their screening appointment in order to avoid exposure and risk of infection in themselves, their partner or relatives who may be elderly or have chronic diseases. A nationwide study from the United Kingdom based on national cancer electronic health records and admission data found a decreased incidence of female breast cancer in 2020 compared with 2019, the declines were observed across

all income groups; however, more pronounced among the least deprived groups. The largest decrease was found among the 50–69-year-old women (which is the target age group for mammography screening) and in screen-detected breast cancers [21]. Similarly, in the population-based study from the Netherlands, the decrease in breast cancer incidence was largest in the age group 50–74 years [5].

A study from the USA on nationwide private health insurance claims data showed that the incidence of breast cancer declined by about 40% during the first two months of the pandemic in 2020, but afterwards, the incidence returned to the pre-pandemic level with a trend towards higher incidence in the second period of the pandemic. There were no geographical, social, or ethnic differences in the observed incidence [22]. The population did not include uninsured patients and thus may be missing out on some of the most deprived patients. Moreover, in the studies from UK and USA, the social or income deprivation information was based on area-level data [21,22], and therefore may not have captured the individual socioeconomic position as in our data.

No difference was found in primary surgery during the pandemic compared with before the pandemic in our study, and we observed no difference in tumour size during the pandemic compared with before. The population-based study from the Netherlands reported fewer patients diagnosed with stage I cancer [5], which was also found in the UK study, however with a simultaneous increase in unknown stages [21]. Even though our study does not point to changes in tumour size distribution during the pandemic, we speculate whether some of the cases, that were not diagnosed during the early



**Figure 2.** Overview of selected clinical quality outcomes by month: (a) average tumour size, (b) number of cases by type of primary operation, (c) proportion treated with adjuvant or neoadjuvant chemotherapy, (d) proportion treated with endocrine therapy, (e) proportion treated with adjuvant radiation therapy by primary operation. (Proportions were calculated as patients treated divided by the number of patients recommended the treatment following national clinical guidelines). Vertical dashed lines indicate the month of implementation of social lockdowns (red dash) and lifting of lockdowns (orange dash).

stages of the pandemic in Denmark, will show up at a later point in time with more advanced cancer.

We found an increase in the proportion of patients receiving neoadjuvant chemotherapy and a decrease in adjuvant chemotherapy. It is in line with the current clinical recommendations to change to neoadjuvant therapy for some patients. However, the group who are recommended neoadjuvant treatment is smaller than the patient group eligible for post-operative treatment, so even though a higher proportion received neoadjuvant treatment there seems to be a small decrease in patients receiving adjuvant chemotherapy under the pandemic, which we cannot explain. We also found that a lower proportion of women who underwent mastectomy received adjuvant

radiation therapy; however, this finding is based on very small numbers and should be interpreted with caution due to more missing data on radiation therapy in the pandemic period. Some patients might have chosen to postpone their adjuvant treatment during the pandemic and therefore we observe a decrease in the pandemic period. A general trend towards the use of shared decision-making may also have had an impact on the small changes in adjuvant treatments.

A systematic review and meta-analysis of outcomes in various types of cancer reported, in line with our results, no change in the number of performed surgical procedures for breast cancer on the basis of five studies [23]. The population-based study from the Netherlands; however, found that

fewer patients underwent breast-conserving surgery or mastectomy with immediate breast reconstruction, but more received hormonal therapy in the outbreak period in 2020 compared with 2018–2019, whereas treatment with chemotherapy was lower in the beginning of the pandemic but higher later on [5]. A population-based study from Ontario, Canada found that neoadjuvant systemic treatment was more commonly used in the pandemic months in 2020 compared with the six months prior to the pandemic. The findings varied by patient age and geography. There was no reduction in receiving surgery following neoadjuvant treatment [24]. The nationwide insurance study from USA likewise found higher uptake of pre-operative systemic therapy (chemotherapy and in particular endocrine therapy) during the first phase of the pandemic in 2020 and there was a trend of higher levels also in the following year [22].

A review of 10 studies in Northern America (including the USA, Canada and Mexico) investigated waiting times and time to initiation of breast cancer treatment, and overall found no major changes during the pandemic as compared with pre-pandemic; in some studies, time to treatment was even shorter. However, for studies that investigated the patient perspective, it was highlighted that navigating the disease in a time period where interacting with people was difficult, caused some extra concern in breast cancer patients [25].

Overall, from these studies, the treatment quality seemed to have been maintained. However, local changes in treatment and diverse communication strategies in different countries might have resulted in minor changes in care for breast cancer during the pandemic.

### Strengths and limitations

The strengths of the study include the national population-based cohort of Danish breast cancer patients with data obtained from dedicated registration and administrative registers. This means there is a very high completeness of cases from the whole country and selection bias are minimized. Another strength is that data from DBCG are validated each year as a part of monitoring the quality of care on a national, regional and department level in Denmark, which ensures a high validity and completeness of most data. A further strength is that we were able to merge data with sociodemographic information at an individual level which enabled us to investigate possible differential social effects of the pandemic period.

Limitations include some missing data on the outcomes of interest. The data in the DBCG quality registry are reported manually as a part of patients' care, and even though the register holds a high completeness of data there are some missings in adjuvant outcomes, however, only on the radiation outcome there seem to be a higher percentage of missing data during the pandemic than before. The data quality of biological treatments in the registry was not adequate and therefore not included in this study. Also, information on the dose of chemotherapy and radiation treatments was unknown in the DBCG quality registry, and therefore, we did not assess whether doses

of adjuvant treatment were reduced, i.e. in order to prevent immunosuppression.

Information on the clinical cancer stage did not exist in the DBCG quality registry and was therefore not included in our analyses, which is also a limitation.

Further, the pre-defined time intervals of pandemic and non-pandemic periods might not thoroughly have captured the true picture of change in behaviour among patients or doctors as a change in behaviour might occur before or after the time points of the actual lockdown.

Lastly, we did not have data on the status of COVID-19 infection or vaccination among breast cancer patients. However, cancer patients with decreased immune response were prioritized for early vaccinations together with other risk groups. These factors could have affected patients' healthcare-seeking behaviour, treatment options or delay in treatment and may also be differently distributed according to sociodemographic factors.

The severity of the pandemic, its political impact, and the societal consequences were different in different countries. In Denmark, the focus was on keeping the number of hospitalisations due to COVID-19 infections as low as possible. The generalizability of our results regarding breast cancer should be seen in light of this approach to societal intervention. The breast cancer screening program remained open and there were no recommended changes to the clinical course for breast cancer.

### Conclusion

During the COVID-19 pandemic, the total number of breast cancer diagnoses decreased slightly in 2020, and fewer patients with low social positions were diagnosed compared with the pre-pandemic period. Overall, the quality of breast cancer care was maintained during the pandemic as compared with earlier time periods, however with small changes observed in the adjuvant treatment.

It is an important finding that the social differences in diagnosis seem to have increased during the pandemic period. Targeted intervention aimed at socially disadvantaged groups in order to secure early diagnosis and screening participation is therefore recommended in future perturbation to the health care system.

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### Author contribution

EHI, HJ, BO, MBH, HM, PC and TBO designed the study. EHI, TBO and HJ acquired the data; HJ analysed the data. All authors contributed to the interpretation of the data. EHI and TBO drafted the article. All authors revised the article critically for important intellectual content and approved the final version of the article to be published. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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## Data availability statement

In order to comply with the Danish regulations on data privacy, the datasets generated and analysed during this project are not publicly available as the data are stored and maintained electronically at Statistics Denmark's research platform, where it only can be accessed by pre-approved researchers. Data can be accessed for research purposes through application to the Danish Clinical Quality Program - National Clinical Registries (RKKP) and Statistics Denmark.

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