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## A systematic review of the impact of the COVID-19 pandemic on breast cancer screening and diagnosis

Tong Li<sup>a,b,\*</sup>, Brooke Nickel<sup>b</sup>, Preston Ngo<sup>a</sup>, Kathleen McFadden<sup>a</sup>, Meagan Brennan<sup>c</sup>, M Luke Marinovich<sup>a,b,1</sup>, Nehmat Houssami<sup>a,b,1</sup>

<sup>a</sup> The Daffodil Centre, The University of Sydney, a Joint Venture with Cancer Council NSW, Sydney, Australia

<sup>b</sup> School of Public Health, Faculty of Medicine and Health, The University of Sydney, Sydney, New South Wales, Australia

<sup>c</sup> Westmead Breast Cancer Institute, Westmead Hospital, Sydney, Australia

ARTICLE INFO	A B S T R A C T				
Keywords: Breast cancer Screening Diagnosis Mammography COVID-19 Pandemic	Background: Breast cancer care has been affected by the COVID-19 pandemic. This systematic review aims to describe the observed pandemic-related changes in clinical and health services outcomes for breast screening and diagnosis. Methods: Seven databases (January 2020–March 2021) were searched to identify studies of breast cancer screening or diagnosis that reported observed outcomes before and related to the pandemic. Findings were presented using a descriptive and narrative approach. Results: Seventy-four studies were included in this systematic review; all compared periods before and after (or fluctuations during) the pandemic. None were assessed as being at low risk of bias. A reduction in screening volumes during the pandemic was found with over half of studies reporting reductions of ≥49%. A majority (66%) of studies reported reductions of ≥25% in the number of breast cancer diagnoses, and there was a higher proportion of symptomatic than screen-detected cancers. The distribution of cancer stage at diagnosis during the pandemic showed lower proportions of early-stage (stage 0–1/I-II, or Tis and T1) and higher proportions of relatively more advanced cases than that in the pre-pandemic period, however population rates were generally not reported. <i>Conclusions:</i> Evidence of substantial reductions in screening volume and number of diagnosed breast cancers, and higher proportions of advanced stage cancer at diagnosis were found during the pandemic. However, these findings reflect short term outcomes, and higher-quality research examining the long-term impact of the pandemic is needed.				

#### 1. Introduction

On March 11, 2020, the World Health Organization declared coronavirus disease 2019 (COVID-19) a pandemic [1]. A shutdown or suspension of many non-essential medical services was imposed for COVID-19 management globally. Concerns about the impact of the pandemic on utilisation of health services have been raised since then [2,3]. Delays and disruptions to cancer screening and treatment have been reported in recently published systematic reviews [3–5]. However, there is no published systematic review specifically focused on breast cancer screening and diagnosis. across the world [6]. A recent narrative review of modelling studies in seven countries by the COVID-19 and Cancer Global Modelling Consortium highlighted the potential for COVID-19-related disruptions to affect screening participation [7]. The possible consequences of screening and diagnostic delays include significant increases in breast cancer morbidity and mortality. To understand the actual impact of the pandemic on breast cancer, this systematic review aims to describe the change in clinical and health services outcomes related to breast screening and diagnosis using real-world data.

Breast cancer is the most commonly diagnosed neoplasm in women

E-mail address: t.li@sydney.edu.au (T. Li).

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<sup>\*</sup> Corresponding author. Edward Ford Building, Fisher Road, The University of Sydney, Camperdown, NSW, 2006, Australia.

<sup>&</sup>lt;sup>1</sup> These authors contributed equally to this work as senior authors.

#### 2. Materials and methods

#### 2.1. Research question

How has the COVID-19 pandemic affected breast cancer screening and diagnosis?

#### 2.2. Information sources and search strategy

We performed a literature search from January 1, 2020 to March 19, 2022 in seven electronic databases: Embase, Evidence-Based Medicine Reviews (EBMR), Global Health, Medline, Pre-Medline, CINAHL Complete and Scopus via three interfaces (Ovid, EBSCOHost and Scopus). The search strategy was reviewed by the search team prior to execution using the PRESS Checklist [8]. We selected medical subject heading terms and free-text keywords across four broad concepts (including breast cancer, screening, diagnosis, and COVID-19) using Boolean operators 'and' and 'or' to develop search strategy in each database, and iteratively tested it to ensure a sensitive search. Subject heading terms and keywords differed slightly across databases. The full search strategy is detailed in Appendix A.

#### 2.3. Study eligibility criteria

Studies were eligible for inclusion if they: included asymptomatic women who attended breast cancer screening programs or services, or women with symptoms, suspicious lesions or newly-diagnosed breast cancer; investigated the COVID-19 pandemic as an exposure; reported comparisons to evaluate a potential change associated with the pandemic; reported outcomes of breast cancer screening (e.g. number of screens) or cancer diagnosis (e.g. stage at diagnosis); and reported *observed* outcomes. Only studies reported in English were considered. Studies were excluded if they did not report observed changes attributed to the pandemic on screening and/or diagnosis (e.g. hypothetical studies of impact of COVID-19, estimated or projected outcomes). Detailed inclusion and exclusion criteria are available in Appendix B.

#### 2.4. Study selection process

Titles and abstracts were screened by one author (TL) to determine whether studies met the eligibility criteria for full text assessment, and a sample of 12% was screened independently by another author (BN) to ensure consistent application of eligibility criteria. Any disagreement



Fig. 1. PRISMA flow diagram.

was resolved by discussion and consensus. Full text assessment was conducted by one author (TL) and verified by another author (BN). Discordant results were resolved by discussion/consensus or arbitration by a third reviewer (NH or MLM) if required. The PRISMA flowchart (Fig. 1) shows the study identification, screening and inclusion process.

#### 2.5. Data extraction

Data extraction was performed by one author (TL), with another independent extraction by one of three other authors (PN, BN and KM). Disagreements were resolved by discussion and consensus or with arbitration by a third author (MLM) when needed.

The following data were extracted into an Excel spreadsheet using predefined cells: first author, publication year, country or region, publication type, study setting, study design, timeframe of COVID-19 pandemic and comparator periods, comparison type (pre-to-post, or fluctuation over multiple time points, or both), and outcomes related to three domains (i.e. screening, diagnosis and breast imaging). Details of data extraction are available in Appendix C.

#### 2.6. Study appraisal and risk of bias assessment

Risk of bias and methodological quality assessment of eligible studies was performed by one author (TL), and a random sample of 12% was independently assessed by another author (MLM) with disagreements resolved by discussion and consensus. We used appraisal criteria adapted from both the NIH quality assessment tool [9] (items 1–6 and 9–11) and Cochrane EPOC risk of bias tool [10] (items 7–8 and 12) (Appendix D). Each question was answered as 'yes', 'no' or 'not reported', corresponding to 'low', 'high' or 'unclear' risk of bias. We rated the overall risk of bias for each individual study as high-risk if one or more of the questions were rated as high; and low if all questions were classified as low. Studies without a high-risk rating but one or more questions with unclear ratings were classified as unclear for overall risk of bias.

#### 2.7. Data synthesis

Results were presented using a descriptive and narrative approach because the heterogeneity of study outcomes did not support pooling of results.

We created summary tables comprising methodological characteristics and reported outcomes within each domain for individual studies. We summarised study characteristics, including publication type, study region, study design, comparison type, duration of reported pandemic periods, and whether the pandemic period included 2021 as proportions of the total studies.

To synthesise the results for the domains of screening, and diagnosis and breast imaging, we created a table of outcomes that were reported by  $\geq 20\%$  of the total number of studies included in each domain.

#### 2.8. Registration

This systematic review was prospectively registered in PROSPERO (International Prospective Register of Systematic Reviews) with registration number of CRD42021279436.

#### 3. Results

#### 3.1. Study selection

An initial 2451 citations were identified for title and abstract screening, of which 77 were eligible for inclusion (Fig. 1) [11–87]. For 3 studies with multiple publications reporting different or complementary outcomes, we selected the most recently published for inclusion [34,57, 59], and extracted relevant data (where available) from the other

superseded publications [85–87] but did not include them as separate papers. Therefore, a total of 74 studies were included in this review [11–84].

#### 3.2. Study characteristics

AppxFigure E.1 (in Appendix E) summarises study characteristics of all included studies, and AppxTable F.1 (in Appendix F) displays studyspecific characteristics. There were 38 [11–48], 41 [14,15,20,21,29,30, 32–34,37,40,42,44,49–76] and 12 [20,21,42,65,77–84] studies that reported breast screening, diagnosis, and breast imaging related outcomes, respectively. Any study could report outcomes in more than one domain, so 13 studies reported outcomes for both screening and diagnosis [14,15,20,21,29,30,32–34,37,40,42,44], of which 3 reported outcomes in all three domains [20,21,42].

#### 3.2.1. Publication type and study setting

The majority (74%) of the included studies were original research articles, and 26% (19/74) were other types of publications (e.g. letter or brief report) (AppxFigure E.1a). Of all 74 studies: 41% (30/74) were conducted in North America; 35% (26/74) were Europe-based; 15% (11/74) were Asia-based; 7% (5/74) were conducted in South America, and other studies (3%) came from Africa (1/74) and Oceania (1/74) (AppxFigure E.1b).

There was heterogeneity in the reported study design, and there were no prospective studies (AppxFigure E.1c). For study setting (AppxFigure E.1d), 24% of studies were based on breast cancer (or cancer) screening programs (13/74), and cancer or imaging registries (5/74); 34% (25/ 74) were a single institutional (or department-based) study; 42% (31/ 74) used a healthcare or community-based system or network, including 2 studies using health insurance claims.

# 3.2.2. Comparison types and timeline of before and after COVID-19 pandemic

All studies were natural experiments comparing periods before and after the pandemic [88]. Pre-to-post pandemic (86%, 64/74 studies) was the predominant comparison type, and comparison of fluctuations over multiple time points was reported in 7% (5/74) of studies; the remaining 5 studies (7%) had both comparison types (AppxFigure E.1e). Comparison of dichotomous pre-to-post time periods included pre vs during, pre vs peak/shutdown, and pre vs after-peak/reopening, and comparison of fluctuation included changes over multiple time points before and during the pandemic period, such as pre vs shutdown vs reopening.

AppxFigure E.2 displays the timeline of before and after pandemic periods for each individual study. A majority of the studies included the period from March to September 2020 as the main pandemic period, with a minimum duration of 1 month and a maximum of 18 months. Even though the starting timepoint of the reported pandemic period varied across all studies, over half (51%, 38/74) of studies reported the duration of pandemic of  $\leq 6$  months and 43% (32/74) of studies reported the duration period between 6 and 12 months; 4 studies (5%) reported a duration of over 1 year (AppxFigure E.1f). Some months in 2021 were included as part of the pandemic period in 8 (11%) studies (AppxFigure E.1g).

#### 3.3. Risk of bias

AppxTable F.2 (in Appendix F) displays the risk of bias assessment results. The majority of studies were deemed to be at high risk of bias (92%, 68/74) with the remainder having an unclear risk of bias (8%, 6/74). No study was assessed as being at low risk of bias. The main reasons for high and unclear risk bias were study participants not being representative of population of interest (32%, 24/74); absence of formal tests of statistical significance for before-after changes (53%, 39/74); lack of multiple outcome measures (28%, 21/74), and limited consideration of whether the COVID-19 pandemic occurred independently of other

changes (confounding factors) in the time-periods being compared (27%, 20/74 as high-risk; and 62%, 46/74 as unclear-risk).

#### 3.4. Screening-related results

Screening-related outcomes were reported in 38 studies representing most world regions [11–48]. Main outcomes from the individual studies are summarised narratively below, and detailed in Table 1 and AppxT-able F.3-F.5 (Appendix F).

#### 3.4.1. Screening volume

As shown in Table 1, a relative reduction in screening volumes ranged from 2.7% to 100% during the pandemic period [17,25]; over half (54%, 19/35) of studies reported screening volume reductions of  $\geq$ 49% [11,13,14,17,19–24,27,31,33,34,37,43,44,47,48]. Screening uptake reduced by 35%–100% during the pandemic peak in March–May 2020 [14,17,19,21,24,27,29,31,33,34,37,39,43,44,48]; many studies reported suspension of screening programs, or non-essential services shutdown or regional lockdown during this period [17,19,21,27,31,34, 43,44]. However, screening volumes gradually recovered from May-September [14,17,19,24,28,29,31,33,34,37,39]. Due to this fluctuation, studies with relatively long study periods (10–12 months) reported smaller reductions (9.8%–62%) for cumulative screening [15,16, 22,30,35,36,40,46,47] or even an increase (14%–64%) at mid-late stage of the pandemic, possibly indicating signs of recovery [33,34].

#### 3.4.2. Positive screens

Studies based on organised screening programs generally reported a modest absolute increase (0.6%–2.3%) in the proportion of positive screens or recall rate [23,39,45,47], while other studies reported an absolute decrease (0.2%–2.2%) [14,20] (AppxTable F.3). In a similar pattern to screening volume, the number of abnormal ('positive') screening mammograms showed a relative decrease of 32%–49% during the pandemic peak [15,19].

#### 3.4.3. Screening by age

There was heterogeneity in screening data by age and no consistent age-related patterns were found (AppxTable F.4). Compared to the prepandemic period, some studies found reductions in screening across all age groups during the pandemic [28,46]; some studies showed increased proportions of screening participants at younger age and decreased proportions in older age [20,36,45,47]; and one study reported the reverse [13].

### 3.4.4. Screening by ethnicity or race

All studies that reported screening by ethnicity or race were USbased, and most reported a reduction in screening volume or growth in cancellation rate across all ethnicity or race groups (AppxTable F.5). Compared to White or Non-Hispanic, non-White (including Black/ African-American) or Hispanic groups experienced greater declines in screening participation [12,24,33,36,48], particularly at the pandemic peak [38], and slower recovery to the pre-pandemic level [46].

#### 3.5. Diagnosis and breast imaging results

A subtotal of 41 [14,15,20,21,29,30,32–34,37,40,42,44,49–76] and 12 [20,21,42,65,77–84] studies reported diagnosis, and breast imaging outcomes, respectively. Key results from the individual studies are summarised narratively below, and presented in more details in Table 2 and AppxTable F.6-F.8 (Appendix F).

#### 3.5.1. Number of breast cancer diagnoses

There was a reduction in the number (or percentage) of women diagnosed with breast cancer (Table 2). Relative reductions in breast cancer diagnoses ranged from 1% [32,67,76] to 70% [54], with 66% (21/32) of studies reporting reductions of  $\geq$ 25% [14,30,33,34,44,51,52,

54–58,62–64,66,69,70,72,74,75]. The greatest decrease (20%–70%) was witnessed in the pandemic peak [14,29,33,34,54,56,61–63,72], and a gradual recovery [14,29,33,54,56,62] or slight to moderate increases [33,63,64] were reported after the peak. Two studies (which used different measures) showed absolute reduction of 2% in percentage of women diagnosed with breast cancer [49], and increased breast cancer rates per 1000 patients who had mammograms [73].

#### 3.5.2. Diagnosis by detection mode

During the pandemic, both the number of cancers diagnosed via screening and the number of symptomatic diagnoses were reduced, but the reduction in numbers was more evident for screen-detected compared to symptomatic cancers (AppxTable F.6) [44,52,54,57,60, 65]. The general pattern across studies was a higher proportion of symptomatic diagnoses than the proportion diagnosed via screening [44,51,52,54].

#### 3.5.3. Stage at diagnosis

Overall, the distribution of cancer stage at diagnosis in the pandemic period showed lower proportions of early-stage (including less stage 0–1, or I-II, or Tis and T1) and higher proportions of relatively more advanced cases than that in the pre-pandemic period [29,51-54,57,60, 63,64,66,69,70], and this pattern was more obvious in the after-peak (versus the peak) period [29,54,64] (AppxTable F.7). Compared to the pre-pandemic, lower proportions of carcinoma in situ [44,57,63,74], and higher proportions of cancers with axillary node metastases or distant metastases [44,52,61,64] were found in the pandemic period (although noting small numbers and incomplete reporting for distant metastases at diagnosis). Two studies showed decreased proportions of T2-T4, because one study used all T-stages together with N+ and M1 stages as the denominator [61] and the other study reported an increased proportion of Tx stage [74].

#### 3.5.4. Mammography volume

In medical imaging studies or studies with a mixed screening and symptomatic population (AppxTable F.8a), the number of mammography examinations during the pandemic [20,77–84] generally showed a relative reduction of between 8.9% [84] and 92.7% [81], with 67% (6/9) of studies reporting cumulative (or average) reductions of 9%– 37% [20,77–79,82,83]. In an additional 6 studies of symptomatic populations (AppxTable F.8b) [20,21,29,37,42,73], a similar reduction was found for the number of diagnostic mammography (range: 4.7%–83.8%) with 50% (3/6) of studies observing reductions between 4% and 21% [20,29,42].

#### 4. Discussion

This is the first systematic evidence review of the global impact attributed to the COVID-19 pandemic on breast cancer screening and diagnosis. Although we report heterogeneity in study outcomes, there were some key patterns in findings that are relevant to informing the recovery phase and identifying emerging priorities for breast cancer detection. Our study found consistent evidence of substantial reductions in screening volume, and similarly reductions in the number of diagnosed breast cancers and diagnostic mammography volume during the pandemic, particularly at the peak stage. These three observed patterns of changes attributed to the COVID-19 pandemic were generally consistent across countries (or regions) and across study settings, highlighting that screening participation, referral in symptomatic cancer diagnosis and other cancer diagnostic pathways have all been affected by the pandemic.

The above findings partially reflect the effect of the pandemic on populations as well as the global health system's response to the pandemic, such as suspension of screening programs, shutdown of nonurgent healthcare services, and enforced regional lockdowns, that accounted for some of the immediate reductions. Even though the 82

Study, Country/Region	Health	Pre-pandemic	Pandemic		Number of screening mammograms or number of women having screening	
	service setting	Time period	Time period	Services suspension/ lockdown	Pre-pandemic vs Pandemic (data are frequency (N) unless specified)	Relative change in outcome (unless specified)
Al-Kuwari 2021, Qatar [11]	HCS	01/01/2019 to 31/07/ 2019	01/01/2020 to 31/07/2020	11/03/2020-31/07/2020	4854 vs 2156	↓55.58%
Amran 2021, US [13]	HCS	01/04/2019 to 31/12/ 2019	01/04/2020 to 31/12/2020	NR	55,678 vs 27,522	↓49%
Bakouny 2021, US [14]	HCS	Same months 2019: 02/ 03/2019 to 02/06/2019; Pre-peak: 01/12/2019 to 02/03/2020.	Peak: 02/03/2020 to 02/06/ 2020; After-peak: 03/06/2020 to 03/09/2020.	NR	Same months 2019 vs Peak: 24,660 vs 5305; Pre-peak vs Peak: 29,158 vs 5305; After-peak vs Peak: 24,788 vs 5305.	Same months 2019 vs Peak: ↓77.67%; Pre-peak vs Peak: ↓81.49%; After-peak vs Peak: ↓78.06%.
Bentley 2021, Canada [15]	BCSP	01/01/2019 to 31/12/ 2019	01/01/2020 to 31/12/2020	18/03/2020-30/05/2020	265,479 vs 185,154	↓30.2%
Bessa 2021, Brazil [16]	BCSP	01/01/2019 to 31/12/ 2019	01/01/2020 to 31/12/2020	17/03/2020-NR	1,948,471 vs 1,126,688	↓42.18%
Brugel 2021, France [17]	HCS	01/01/2019 to 31/05/ 2019	01/01/2020 to 31/05/2020	17/03/2020–11/05/2020	Jan: 2541 vs 2607; Feb: 2128 vs 2203; Mar: 2316 vs 965; Apr: 2288 vs 0; May: 2089 vs 636.	Jan: ↑2%; Feb: ↑3%; Mar: ↓58%; Apr: ↓100%; May: ↓70%.
Chiarelli 2021 <sup>a</sup> , Canada [19]	BCSP	01/01/2019 to 29/02/ 2020	Suspension: 01/03/2020 to 31/05/2020; Resumption: 01/06/2020 to 31/03/2021.	23/03/2020-26/05/2020	Pre vs Suspension vs Resumption: 822,862 vs 32,408 vs 394,559	Pre vs Suspension: 196.1%; Pre vs Resumption: 152.1%; Suspension vs Resumption: †1117.5%.
Chou 2020, Taiwan [20]	ASI	Week 1, 2019 to Week 22, 2019	Week 1, 2020 to Week 22, 2020	NR	NR	$\downarrow$ 51%, p $<$ 0.001
Collado-Mesa 2020, US [21]	HCS	1/04/2018–2019 to 30/ 04/2018–2019	01/04/2020 to 30/04/2020	20/03/2020-Mid May to early June 2020	2722 vs 105	↓96%
Dabkeviciene 2021, Lithuania [22]	ASI	01/02/2019 to 31/12/ 2019	01/02/2020 to 31/12/2020	18/03/2020–17/06/2020; 04/11/2020–31/12/2020.	9704 vs 3653	↓62%
de Degani 2021, Argentina [23]	BCSP	19/03/2019 to 19/09/ 2019	19/03/2020 to 19/09/2020	19/03/2020-19/09/2020	9918 vs 2098	↓78.85% (95% CI: 78.03–79.65%), p < 0.0001
DeGroff 2021, US [24]	BCSP	01/01/2015–2019 to 30/ 06/2015–2019	01/01/2020 to 30/06/2020	NR	Total: 1,112,126 vs 71,704. Apr: 19,366 vs 2607; Jun: 17,385 vs 10,626.	<i>Total:</i> ↓94%. Apr: ↓97%, p < 0.001; Jun: ↓39%, p < 0.001.
Fedewa 2021, Italy [25]	HCS	01/07/2019 to 31/07/ 2019	01/07/2020 to 31/07/2020	NR	76,430 vs 74,340	↓2.7%
Gorin 2021, US [27]	ASI	19/03/2019 to 09/05/ 2019	19/03/2020 to 09/05/2020	19/03/2020-09/05/2020	3339 vs 6	↓ <b>99.8%</b>
Kang 2021 <sup>b</sup> , Korea [29]	HCS	01/02/2019 to 31/07/ 2019	01/02/2020 to 31/07/2020	NR	Total: 20,923 vs 11,982. Peak (Feb–Apr): 8837 vs 3697; After-peak (May–Jul): 12,086 vs 8285.	Total: ↓42.7%. Peak (Feb-Apr): ↓58.2%; After-peak (May-Jul): ↓31.4%.
Kidwai 2022, US [30]	ASI	01/01/2019 to 31/12/ 2019	01/01/2020 to 31/12/2020	NR	435 vs 382	↓12%
Labaki 2021, US [33]	HCS	Pre-peak: 01/12/2019 to 02/03/2020	1st peak: 02/03/2020 to 02/ 06/2020; Period between two peaks: 03/06/2020 to 03/09/2020; 2nd peak: 04/09/2020 to 05/12/2020.	NR	Pre-peak vs 1st peak: 29,305 vs 5379; Pre-peak vs Period between two peaks: 29,305 vs 24,876; Pre-peak vs 2nd peak: 29,305 vs 33,282.	Pre-peak vs 1st peak: ↓82%; Pre-peak vs Period between two peaks: ↓15%; Pre-peak vs 2nd peak: ↑14%.
London 2022, US [34]	HCS	01/01/2019 to 30/04/ 2020	01/01/2020 to 30/04/2021	01/03/2020-30/04/2020	NR	Apr 1–15, 2020 (lowest): ↓89%; Jun 30- Jul 14, 2020 (recovery): ↑21%; Mar 2–16, 2021 (highest): ↑64%.
Losurdo 2022, Italy [35]	BCSP	01/01/2019 to 31/12/ 2019	01/01/2020 to 31/12/2020	09/03/2020-NR	NR	↓37.6%
Miller 2021, US [36]	ASI	Week 1, 2019 to Week 47, 2019	Week 1, 2020 to Week 47, 2020	Weeks 11–17	15,339 vs 13,841	↓9.8%

(continued on next page)

Study, Country/Region	Health	Pre-pandemic	Pandemic		Number of screening mammograms or number of women having screening	
	service setting	Time period	Time period	Services suspension/ lockdown	Pre-pandemic vs Pandemic (data are frequency (N) unless specified)	Relative change in outcome (unless specified)
Norbash 2020, US [37]	HCS	Week 1, 2019 to Week 21, 2019	Week 1, 2020 to Week 21, 2020	NR	Nadir: in weeks 15–16: 12,027 vs 152	Weekly change range: Weeks 1–10: ↑3%–16%; Weeks 11–13: ↓10%–96%; Weeks 14–20: ↓95%–99% (Nadir: ↓99% in weeks 15–16); Week 21: ↓73%.
Peng 2020, Taiwan [39]	BCSP	01/01/2019 to 31/05/ 2019	01/01/2020 to 31/05/2020	No suspension	Total: 496,207 vs 358,771	<i>Total:</i> ↓27.70%. Mar: ↓35% (p < 0.0001); Apr: ↓60% (p < 0.0001); May: ↓49% (p < 0.0001).
Ribeiro 2022, Brazil [40]	HCS	01/01/2019 to 31/12/ 2019	01/01/2020 to 31/12/2020	No lockdown	Total: 3,810,427 vs 218,371. Percentage of screening mammography performed in women aged 50–69 years: 64.8% vs 64.4%.	Total: \$42.62%. Percentage of screening mammography performed women aged 50–69 years: \$0.4%.
Shen 2022, Taiwan [41]	BCSP	01/01/2019 to 30/04/ 2019	01/01/2020 to 30/04/2020	No suspension	Inreach (hospital): 150,903 vs 94,796; Outreach (mobile): 242,482 vs 211,730.	Average monthly percentage change: Inreach (hospital): ↓41.43%; Outreach (mobile): 123 99%
Sprague 2021, US [42]	CIR	01/01/2019 to 31/07/ 2019	01/01/2020 to 31/07/2020	NR	190,454 vs 126,040	↓33.8% (95% CI: 27.4–39.7%)
Sutherland 2020, Australia [43]	BCSP	01/03/2019 to 30/06/	01/03/2020 to 30/06/2020	24/03/2020-18/05/2020	NR vs 58,478	↓51.5%
Tang 2022, US [44]	HCS	17/03/2019 to 17/05/	17/03/2020 to 17/05/2020	17/03/2020-17/05/2020	180,724 vs 1681	↓ <b>99.1%</b>
Tsai 2020, Taiwan [45]	BCSP	01/01/2019 to 30/04/	01/01/2020 to 30/04/2020	No suspension	396,371 vs 308,463	$\downarrow$ 22.2%, p < 0.001
Velazquez 2021, US [46]	ASI	01/01/2019 to 31/12/ 2019	01/01/2020 to 31/12/2020	16/03/2020-16/05/2020	5662 vs 3385	↓40%
Walker 2021 <sup>a</sup> , Canada [47]	BCSP	01/03/2019 to 31/12/ 2019	01/03/2020 to 31/12/2020	Mid 03/2020-End 05/2020	605,889 vs 284,242	\$ <i>53.1%</i>
Study, Country/Region	Health	Pre-pandemic	Pand	emic	Screening rate or use rate of mammograms	
	setting	Time period	Time period	Services suspension/ lockdown	Pre-pandemic vs Pandemic (data are in proportion (%) unless specified)	Relative change in outcome (unless specified)
Chen 2021, US [18]	HIC	01/01/2019 to 31/07/ 2019	01/01/2020 to 31/07/2020	NR	4133 vs 2971 screens per 100,000 enrolees	↓28.1%
Fedewa 2021, US [25]	HCS	01/07/2019 to 31/07/ 2019	01/07/2020 to 31/07/2020	NR	53.9% vs 49.6%	Rate ratio: 0.92 (95% CI: 0.92–0.93)
Jidkova 2022, Belgium [28]	BCSP	01/01/2019 to 31/12/ 2019	01/01/2020 to 31/12/2020	23/03/2020-28/06/2020	NR	Absolute change: Entire year: ↓1.0% (95% CI: 0.8%–1.3%); Before shutdown (01/01–21/03): ↓1.4% (95% CI: 1.0%–1.9%); Reopen (05/07–31/12): ↓1.0% (95% CI: 1.3%–2.0%).
Kim 2022, US [31]	HCS	01/01/2020 to 03/03/ 2020	Stat-at-home: 04/03/2020 to 08/05/2020; Reopen: 09/05/2020 to 08/ 07/2020.	04/03/2020-08/05/2020	Odds Ratio (95% CI) <sup>d</sup> : Stay-at-home vs Pre: 0.34 (0.31–0.37); Reopen vs Pre: 0.49 (0.45–0.53); Reopen vs Stat-at-home: 1.44 (1.31–1.58).	Stay-at-home vs Pre: ↓66%, p < 0.001; Reopen vs Pre: ↓51%, p < 0.001; Reopen vs Stat-at-home: ↑44%, p < 0.001.
Koczkodaj 2021, Poland [32]	BCSP	01/01/2019 to 30/09/ 2019	01/01/2020 to 30/09/2020	NR	38.15% vs 35.92%	Absolute change: $\downarrow 2.2\%$
Whaley 2020, US [48]	HIC	01/03/2019 to 30/04/ 2019	01/03/2020 to 30/04/2020.	NR	Mar: 358.4 per 10,000 women vs NR; Apr: 378.5 per 10,000 women vs NR.	Mar: ↓41.6% <sup>c</sup> ; Apr: ↓90.4% <sup>c</sup> .

BCSP= Breast cancer (or cancer) screening program, HCS=Healthcare (or community-based) system/network/database, ASI = A single institution or department, CIR=Cancer or imaging registry, HIC=Health insurance claims, NR=Not reported, CI=Confidence interval.

Italics: computed data (see Appendix C).

<sup>a</sup> Screening modality includes both mammography and magnetic resonance imaging.

<sup>b</sup> Screening modality includes both mammography and ultrasound.

<sup>c</sup> Controls for the age categories, state, year, and month.

<sup>d</sup> Adjusted for age, race/ethnicity, enrolment in the patient portal (MyChart), COVID-19 risk score, and provider specialty.

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Table 2

Summary of breast cancer diagnoses (number of breast cancer cases or percentage of women diagnosed with breast cancer, n = 32).

Study, Health Country/ service		Pre-pandemic	Pandemic		Number of breast cancer cases or number of women diagnosed with breast cancer		
Region	setting	Time period	Time period	Services suspension/ lockdown	Pre-pandemic vs Pandemic (data are frequency (N) unless specified)	Relative change in outcome (unless specified)	
Bakouny 2021, US [14]	HCS	Same months 2019: 02/03/2019 to 02/ 06/2019;	Peak: 02/03/2020 to 02/06/2020;	NR	NR	Same months 2019 vs Peak: ↓61.29%; Pre-peak vs Peak: ↓62.44%;	
		Pre-peak: 01/12/ 2019 to 02/03/ 2020.	After-peak: 03/06/ 2020 to 03/09/2020.			After-peak vs Peak: ↓52.87%.	
Blay 2021, France [50]	HCS	01/03/2019 to 31/ 07/2019	01/03/2020 to 31/07/ 2020	04/2020-NR	10,525 vs 8428	↓20%	
Bonadio 2021, Brazil [51]	ASI	01/09/2019 to 31/ 01/2020	01/09/2020 to 31/01/ 2021	NR	457 vs 268	↓41.4%	
Borsky 2022, UK [52]	ASI	01/05/2019 to 31/ 10/2019	01/05/2020 to 31/10/ 2020	01/05/2020–31/ 07/2020	276 vs 163	↓ <b>40.9%</b>	
Chou 2021 <sup>a</sup> , Taiwan [53]	ASI	21/01/2019 to 31/ 07/2019	21/01/2020 to 31/07/ 2020	NR	128 vs 115	$\downarrow 10\%, p = 0.52$	
Citgez 2021, Turkey [54]	ASI	Pre-peak: 01/12/ 2019 to 29/02/2020	Peak: 01/03/2020 to 31/05/2020; After-peak: 01/06/ 2020 to 31/08/2020.	NR	Pre-peak vs Peak: 72 vs 22 (daily average: 0.8 vs 0.24); Pre-peak vs After-peak: 72 vs 46 (daily average: 0.8 vs 0.51); Peak vs After-peak: 22 vs 46 (daily average: 0.24 vs 0.51).	Pre-peak vs Peak: 169.4% (daily average: 170.0%); Pre-peak vs After-peak: 136.1% (daily average: 136.3%); Peak vs After-peak: 1109.1% (daily average: 1112.5%)	
De Vincentiis 2021, Italy	ASI	Week 11, 2018–2019 to Week 20, 2018–2019	Week 11, 2020 to Week 20, 2020	Weeks 11-20	47 vs 35	↓26%	
Drescher 2022,	HCS	04/03/2019 to 03/	04/03/2020 to 03/03/	NR	6135 vs 5257	↓14.3%	
Eijkelboom	CIR	Week 2, 2018–2019	Week 2, 2020 to Week	Weeks 12-29	Total: 7302 vs 5306.	<i>Total:</i> ↓27% (weeks 9–35: ↓37%)	
Netherlands [57]		2018–2019	00,2020		Average weekly incidence in each period of the pandemic year (per 100,000 women): 8.3 vs 7.6 vs 5.0 (screening suspension started) vs 2.1 (referrals ended) vs 3.7 vs 4.6 (screening restarted) vs 6.3	<i>40170</i>	
Ferrara 2021, Italy [58]	HCS	Week 11, 2018–2019 to Week 20, 2018–2019	Week 11, 2020 to Week 20, 2020	Weeks 11-20	620 vs 383	↓38.2%	
Kaltofen 2021 <sup>a</sup> , Germany [61]	ASI	01/01/2019 to 30/ 06/2019	01/01/2020 to 30/06/ 2020	22/03/2020–05/ 05/2020	Total: 170 vs 150. Lockdown (22/03–05/05): 30 vs 24.	Total: ↓12%. Lockdown (22/03–05/05): ↓20%	
Kang 2021 <sup>a</sup> , Korea [29]	HCS	01/02/2019 to 31/ 07/2019	01/02/2020 to 31/07/ 2020	NR	Total: 1669 vs 1369. Peak (Feb–Apr): 798 vs 638; After-peak (May–Jul): 871 vs 731.	Total: \18.0%. Peak (Feb-Apr): \20.1%; After-peak (May-Jul): \16.1%.	
Kempf 2021 <sup>a</sup> , France [62]	HCS	Comparison 1: 01/03/2018–2019 to 31/05/ 2018–2019; Comparison 2: 01/06/2018–2019 to 30/09/ 2018–2019	Comparison 1 (lockdown): 01/03/ 2020 to 31/05/2020; Comparison 2 (after- lockdown): 01/06/ 2020 to 30/09/2020	17/03/2020–11/ 05/2020	Comparison 1 (lockdown): 715 vs 507; Comparison 2 (after-lockdown): 870 vs 752.	Comparison 1 (lockdown): ↓29%; Comparison 2 (after- lockdown): ↓14%.	
Kidwai 2022, US [30]	ASI	01/01/2019 to 31/ 12/2019	01/01/2020 to 31/12/ 2020	NR	4 vs 3	↓25%	
Knoll 2021 <sup>a</sup> , Austria [63]	ASI	Comparison 1: 16/03/2019 to 30/ 04/2019, and 03/ 11/2019 to 31/12/ 2019. Comparison 2: 01/05/2019 to 02/ 11/2019;	Comparison 1 (two lockdowns): 16/03/ 2020 to 30/04/2020, and 03/11/2020 to 31/ 12/2020. Comparison 2 (periods between 2 lockdowns): 01/05/2020 to 02/11/ 2020.	16/03/2020-30/ 04/2020, and 03/ 11/2020-31/12/ 2020.	Comparison 1 (two lockdowns): 115 vs 55; Comparison 2 (periods between two lockdowns): 148 vs 157.	Comparison 1 (two lockdowns): ↓52%; Comparison 2 (periods between two lockdowns): ↑6%.	
Koczkodaj 2021ª, Poland [32]	BCSP	01/01/2019 to 31/ 08/2019	01/01/2020 to 31/08/ 2020	NR	31,762 vs 31,414	↓1.1%	
Labaki 2021 <sup>a</sup> , US [33]	HCS	Pre-peak: 01/12/ 2019 to 02/03/2020	1st peak: 02/03/2020 to 02/06/2020;	NR	Pre-peak vs 1st peak: 587 vs 219; Pre-peak vs Period between two	Pre vs 1st peak: ↓63%; Pre vs Period between two	

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Study, Heal Country/ servi Region settin	Health service	Pre-pandemic	Pander	mic	Number of breast cancer cases or number of women diagnosed with breast cancer	
	setting	Time period	Time period	Services suspension/ lockdown	Pre-pandemic vs Pandemic (data are frequency (N) unless specified)	Relative change in outcome (unless specified
			Period between two		peaks: 587 vs 466;	peaks: ↓21%;
			peaks: 03/06/2020 to 03/09/2020;		Pre-peak vs 2nd peak: 587 vs 593.	Pre vs 2nd peak: ↑1%.
			2nd peak: 04/09/2020 to 05/12/2020.			
France [64]	ASI	Reference: average 36 working days between 28/01/	2020 to 16/03/2020;	17/03/2020–11/ 05/2020	Reference vs Lockdown: 40 vs 32; Reference vs After-lockdown: 40 vs 59;	Reference vs Lockdown: ↓20%;
		2019 and 03/07/ 2019.	Lockdown: 17/03/ 2020 to 05/05/2020;		Pre-lockdown vs Lockdown: 43 vs 32; Pre-lockdown vs After-lockdown: 43 vs 59.	Reference vs After- lockdown: ↑48%;
			After-lockdown: 11/ 05/2020 to 01/07/ 2020.			Pre-lockdown vs Lockdown ↓26%;
						Pre-lockdown vs After-
London 2022 <sup>a</sup> ,	HCS	01/01/2019 to 31/	01/01/2020 to 31/12/	01/03/2020-30/	NR	Jan: †26.2%;
US [34]		12/2019	2020	04/2020		Feb: ↑8.5%; Mar: ↓13.7%;
Lowry 2021 <sup>a</sup> , US	CIR	01/03/2019 to 30/	01/03/2020 to 30/09/	NR	2171 vs 1650	↓24% (95% CI: 17–31%), p
[65] Morais 2022,	ASI	09/2019 02/03/2019 to 01/	2020 02/03/2020 to 01/07/	18/03/2020-02/	370 vs 227	< 0.001 ↓38.6% (95%CI: 27.6%–
Portugal [66]	ACT	07/2019	2020	05/2020	107 105	48.0%)
Ireland [67]	ASI	07/2019 10 31/	2020	05/2020	197 VS 195	11%
Peacock 2021, Belgium [68]	HCS	01/01/2019 to 31/	01/01/2020 to 31/12/	16/03/2020-30/ 06/2020	NR	Total: ↓6% (Nadir in April:
Purushotham 2021, UK [69]	HCS	01/01/2019 to 30/ 09/2019	01/01/2020 to 30/09/ 2020	20/03/2020-NR	973 vs 686	↓29.5%
Ruiz-Medina 2021, Spain [70]	HCS	13/03/2019 to 13/ 03/2020	13/03/2020 to 13/03/ 2021	NR	746 vs 551	↓26.1%
Skovlund 2021, Denmark [72]	CIR	01/02/2015–2019 to 31/05/ 2015–2019	01/02/2020 to 31/05/ 2020	11/03/2020–05/ 2020	NR	Mar–May: ↓30% (95% CI: 18%–40%).
		2010 2017				Feb: ↓17% (95% CI: 10%– 23%);
						Mar: ↓21% (95% CI: -44% to 11%);
						Apr: ↓29% (95% CI: 18%–
						May: ↓39% (95% CI: 32%–
Tang 2022, US	HCS	17/03/2019 to 17/	17/03/2020 to 17/05/	17/03/2020-17/	703 vs 247	45%). ↓65%
[44] Teibulah 2020	1100	05/2019	2020	05/2020	251 201	1420/
Austria [74]	HCS	05/2019 to 31/	2020	16/03/2020–31/ 05/2020	351 V\$ 201	↓4 <i>3</i> %
van Wyk 2021, South Africa	ASI	01/04/2019 to 30/ 06/2019	01/04/2020 to 30/06/ 2020	26/03/2020-NR	By histopathology: 152 vs 102; By cytopathology: 95 vs 37.	By histopathology: ↓32.9%; By cytopathology: ↓61.1%.
Vrdoljak 2021, Croatia [76]	CIR	01/01/2019 to 31/ 12/2019	01/01/2020 to 31/12/ 2020	15/03/2020-Mid 05/2020;	2875 vs 2848	Total: ↓1% (Apr–Jun: ↓24%
				26/10/2020-Mid 12/2020		
Study, Country/	Health service	Pre-pandemic	Pandemic		Diagnosis rate (i.e. percentage of women diagnosed with breas cancer)	
Region	setting –	Time period	Time period	Services suspension/ lockdown	Pre-pandemic vs Pandemic (data are in proportion (%) unless specified)	Absolute change in outcome (unless specified
Bansal 2021, UK	ASI	01/04/2019 to 30/	01/04/2020 to 30/04/	NR	7% vs 5%	Absolute change: $\downarrow 2\%$
Drescher 2022,	HCS	01/01/2019 to 03/	Early: 04/03/2020 to	NR	NR	Incidence rate ratio (95%
03 [30]		03/2020	Middle: 01/04/2020 to			Pre: 1.00;

Middle: 0.57 (0.53–0.62), p

Early: 0.81 (0.73–0.89), p <

0.001;

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09/06/2020; Late: 10/06/2020 to 31/05/2021.

Study, H Country/ so Region so	Health service	ealth Pre-pandemic rrvice Time period	Pandemic		Number of breast cancer cases or number of women diagnosed with breast cancer	
	setting		Time period	Services suspension/ lockdown	Pre-pandemic vs Pandemic (data are frequency (N) unless specified)	Relative change in outcome (unless specified)
Tachibana 2021, Brazil [73]	ASI	24/03/2019 to 31/ 12/2019	24/03/2020 to 31/12/ 2020	26/03/2020–21/ 06/2020	Total: 8.5 (134/15,816) vs 12.4 (128/ 10,321) breast cancer per 1000 patients submitted to mammograms. During social isolation (24/03–21/ 06)): 6.4 (36/5661) vs 19.4 (18/927) breast cancer per 1000 patients submitted to mammograms; After social isolation (22/06–31/12): 9.7 (98/10,155) vs 11.7 (110/9394) per 1000 patients submitted to mammograms.	< 0.001; Late: 0.95 (0.91–0.98), p = 0.002. Total: †3.9 breast cancer per 1000 patients submitted to mammograms, p = 0.002. During social isolation (24/ 03–21/06)): †13.0 breast cancer per 1000 patients submitted to mammograms, p < 0.001; After social isolation (22/ 06–31/12): †2.0 breast cancer per 1000 patients submitted to mammograms, p = 0.165.

BCSP= Breast cancer (or cancer) screening program, HCS=Healthcare (or community-based) system/network/database, ASI = A single institution or department, CIR=Cancer or imaging registry, HIC=Health insurance claims, NR=Not reported, CI=Confidence interval.

Italics: computed data (see Appendix C).

<sup>a</sup> Study sample also contains in situ tumour, and/or benign tumour cases.

<sup>b</sup> Adjusted for the number of weeks for each study period.

above-noted response measures released health system capacity for better COVID-19 containment and mitigation, these measures to some extent compromised the delivery of health care services, including cancer prevention and control strategies, to general populations. Beyond the health system's response, other factors that may have contributed to the reductions were COVID-19 related anxiety and fear of COVID-19 infection [89], and decreased or difficult access to healthcare providers imposed by COVID-19 safety protocols [35].

In keeping with the reduction in screening volume, there was a decrease in the proportion of screen-detected cancers and a relative increase in cases diagnosed clinically through symptomatic presentations. This aligns with our review findings on stage at diagnosis of breast cancer. Lower proportions of early-stage and higher proportions of relatively more advanced cases were reported in the pandemic compared to the pre-pandemic period. Concomitantly, greater proportions of cancers with nodal and distant metastases were found. Even though the stage distributions might raise concerns about potentially worse long-term outcomes, these results should be interpreted with the caveat that these are the percentage of cases from the diagnosed breast cancers, and do not reflect population rates. Moreover, the association between diagnosis delay and prognosis has not been well-established [90]. While a delay of 3-6 months has been found to be associated with worse long-term prognosis and shorter survival [91], a shorter delay of 6-12 weeks may not affect the overall outcome [92]. It is also possible that diagnosis of the more advanced cancers was less affected by the pandemic as these are more likely to present with symptoms rather than through screening.

The reductions in breast screening volume and number of diagnosed breast cancers found in our study were also noted in other systematic reviews of the impact of COVID-19 pandemic related to cancer health-care. One review identified significant declines in cancer screening or tests and cancer diagnosis rate, and found an increase in advanced cancers, but this study only included 17 publications [4]. One meta-analysis with relatively smaller number of papers (13 publications) reported incidence rate ratios of 0.10–0.63 for cancer screening services [5]. Another review also identified a remarkable frequency (up to 79%) of delays and disruptions in all cancer care attributed to the pandemic [3].

We not only found a large reduction in breast screening volumes and breast cancer diagnoses during the pandemic peak, but also found a

slight to moderate rebound in these outcomes after the peak, which highlighted a possible recovery of cancer screening and diagnostic services. We further noted a slow persistent recovery or increase in both screening volume and cancer diagnosis where data were available (i.e. studies with longer time period after the onset of the pandemic) [33,34, 63,64]. This reduction-rebound trend was also identified in a recent meta-analysis, which also reported decreases in the number of screening examinations of 45%–52% for cancer screening services [93]. Moreover, compared to studies which covered short duration of the pandemic, the reduction of screening volume was relatively less substantial in those that covered longer periods [15,16,22,30,35,36,40,46,47]. This might provide an insight that the impact of the pandemic on breast cancer screening and diagnosis may not be as sustained as expected. However, this cannot be determined without evidence of long-term outcome such as breast cancer mortality, survival and quality of life. It is therefore essential that ongoing research examines the longer-term impact of the pandemic.

This review also found that in studies from the US, non-White women were less likely to have breast cancer screening (than White women) during the pandemic in the context of reduction in screening volume more generally. This is consistent with other research that has shown a disproportionate effect of the pandemic on the health of minority groups [94,95]. These groups could be a focus for 'catch-up screening' during the pandemic recovery to manage any incremental effect from the pandemic on existing disparities.

This review has some limitations. Firstly, most of the included studies reported short-term impact and lacked data on long-term health outcomes. It is therefore unknown whether the pandemic will lead to worse longer-term outcomes, such as increased breast cancer mortality rates. Also, we did not extract (secular) trend from the included studies because the majority (94%) of studies reported the pandemic period of 1 year or less. Secondly, we used a narrative description without a meta-analysis due to considerable heterogeneity of reported outcomes. We provided the range of relative percentage change for screening volume and number of diagnoses, but we did not provide summary estimates (e. g. medians) due to the variability in reporting of these two outcomes in the included studies. Thirdly, as our review includes studies from all over the world, there is a possibility there may be studies with overlapping populations because many studies used aggregated data. However we ruled out superseded publications from same study at data

synthesis to minimise the influence.

In addition, the studies in our review were generally at high risk of bias, reflecting both the observational nature of the comparisons and the urgency of reporting data to inform timely responses to a global pandemic. Although many studies accounted for seasonal variation by comparing the same calendar months across pandemic periods, other potential confounding of pre-versus-during pandemic comparisons was not commonly considered in the analyses or interpretation of results. Interrupted time series analysis, where temporal trends are assessed through multiple measurements over time, was used relatively infrequently. Although the impact of COVID-19 pandemic is likely to be dominant in the included studies, an interrupted time series approach would provide stronger evidence of the magnitude of changes in breast cancer screening and diagnostic outcomes [96].

#### 5. Conclusions

This systematic review identified considerable reductions in breast screening volume and number of diagnosed breast cancers during the pandemic peak, and a relatively smaller reduction was noted after the peak. Changes in proportions of detection mode and stage at diagnosis were found, with higher proportions of cases diagnosed through symptomatic presentations and greater proportions of relatively more advanced stage at diagnosis during the pandemic. As our review includes studies reporting outcomes for early-mid-phase of the pandemic, high-quality studies examining the long-term impact are needed.

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#### Declaration of competing interest

The authors declared no conflict of interest.

#### Ethics

Ethical approval was not required.

#### Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.breast.2023.01.001.

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