

The Impact of the COVID-19 Pandemic on Breast and Cervical Cancer Screening: A Systematic Review

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Abstract. *Background/Aim:* COVID-19 has dramatically impacted non-pandemic-related care, including preventive medicine. Our objective was to quantify the alterations in the volume of screening tests for breast and cervical cancer during the COVID-19 era compared to pre-pandemic levels. *Secondarily,* we discussed the causes responsible for this change, presented suggestions for screening optimization and conducted a targeted search of the relevant literature for worsening of future mortality due to screening setback. *Materials and Methods:* We systematically searched Pubmed, Google Scholar and Epistemonikos for articles in English or Greek, published from March 11th, 2020, until September 14th, 2022, that illustrated quantitative variations of mammograms or Pap/HPV tests. Preprint articles, editorials and speeches were excluded. *Quality of included studies* was assessed via the JBI critical appraisal checklist for studies reporting prevalence data. *The evidence was narratively synthesized. Results:* A total of 56 articles were included, being either observational studies or reports from cancer registries. Large reductions were universally identified, peaked during the first wave but partially persisted after easing of the restrictions. *Conclusion:* Our

systematic review provides an updated record of the variations in screening volume and approaches screening neglect from a multidimensional perspective answering why it happened and how we could achieve recovery. A strong awareness campaign is proposed, in conjunction with triaging citizens more likely to benefit from screening. Cervical self-sampling is emphasized in the literature. Various studies displayed a potential increase in cancer mortality in the future based on predictive statistical models.

Since March 2020, when the Coronavirus disease 2019 (COVID-19) was officially declared a pandemic by the World Health Organization (WHO) (1), healthcare systems have been pushed to drastic adjustments in service provision and public health has been affected both directly and indirectly. By October 2022, more than 625 million people were infected, and total registered deaths had risen to over 6.5 million. Furthermore, major victims of this unprecedented health crisis have been non-emergency care and preventive medicine (2-4).

Malignant neoplasms are a major cause of morbidity and mortality with a global footprint, being the second leading cause of death worldwide with low- and middle-income countries already affected, partially due to the adoption of the western lifestyle (5).

Cancer screening is a method of secondary prevention and aims at detecting cancerous or precancerous lesions before they cause clinical symptoms. It is well established that screening of appropriate population groups can reduce the mortality of certain types of cancer, as early treatment can be more effective (6). The cancer types, in which screening has a proven benefit, include breast and cervical cancer. For breast cancer screening, mammography is mainly used, while regarding cervical cancer, Pap tests (cytological examination of cervical smear), possibly combined with HPV test, are the golden standard (6, 7).

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By 2030, breast cancer diagnoses are expected to exceed 2.4 million annually, demonstrating the enormous burden of the disease and its impact on global health. The screening of asymptomatic populations allows the detection of non-palpable tumors smaller than 15 millimeters. The method considered most sensitive and broadly used is screening mammography combined with clinical examination (8). The guidelines regarding at what age screening should start, at what age it should stop, and how often it should be repeated, are not unanimous (9, 10). In many studies, it becomes clear that women who undergo regular screening have 10-25% lower chance of dying from breast cancer and thus demonstrate a net benefit in adopting screening guidelines (11).

Cervical cancer on the other hand is the most common malignancy of the female genital tract worldwide. A total of 85% of cases affect women in developing countries due to the lack of organized screening and vaccination programs for the HPV virus. Screening for the disease is carried out with a Pap test and/or an HPV test. (12). Thanks to the widespread acceptance of screening, the risk for a woman in the US of being diagnosed with cervical cancer in her lifetime is only 0.6% (13). According to the meta-analysis by Peirson *et al.*, women who have had regular screening based on guidelines are 65 percent less likely to have developed cervical cancer (14).

As Primary Health Care was focusing on controlling the COVID-19 pandemic, cancer screening programs along with outpatient care for chronic disease suffered from defunding and restrictions imposed by the governments on a global scale (15). Our study aimed to quantify screening variations for breast and cervical cancer both during and after lockdown restrictions compared to the pre pandemic period.

Materials and Methods

Our systematic review was conducted in accordance with the PRISMA statement (Preferred Reporting Items for Systematic Reviews and Meta-analyses) of 2020. The review protocol is registered in PROSPERO and has been available online since January 17th, 2023 (CRD42023390559).

Search strategy and selection criteria. Our search strategy was generated by consensus among all researchers. Two authors independently identified records that reported on the change of the volume of screening tests performed during the COVID-19 pandemic, via systematically searching PubMed, Google Scholar and Epistemonikos databases for entries published from March 11th, 2020 (onset of the pandemic) until September 14th, 2022. Snowball sampling by searching reference lists and citation tracking was performed in each retrieved article. The following search terms were used: ("cancer screening" OR "mammography" OR "breast cancer screening" OR "Pap testing" OR "cervical cancer screening") AND ("SARS-COV-2" OR "COVID-19" OR "pandemic").

Criteria for inclusion followed the PICOT format. The population (P) of our study refers to female adults who meet the criteria of screening for breast or cervical cancer. Interventions (I) studied

were mammography for breast cancer and Pap test or HPV test for cervical cancer, compared (C) with the same screening programs during the prepandemic period. The outcomes (O) were changes in number (or percentage variation) of screening tests performed and the type (T) of studies included were observational studies and data from cancer screening registries.

Only studies published in English or Greek were included. Articles referring to changes in test volume that did not distinguish pre-symptomatic from post-symptomatic control were excluded. Moreover, preprint articles published on Medrxiv and SSRN servers were excluded, as well as editorial type entries, commentaries, case reports, summaries of conference speeches, oral presentations, and posters.

Data collection, quality assessment and analysis. Rayyan software was used to identify and remove duplicate entries among the three databases. Duplicate articles that could not be identified by the software were manually removed afterwards. Two authors independently reviewed the unique entries initially with title and abstract screening against eligibility criteria, followed by full-text reading of all potentially relevant publications. Further irrelevant articles were excluded at this second stage, and reasons for exclusion were recorded. The exact course of the procedure is presented in the flow chart on the 2020 PRISMA guidelines (Figure 1).

The following data were extracted from the included studies by two independent investigators: name of the first author, date of publication, country, design of the study, type of cancer, type of screening test and the changes in number of screening tests performed. The accuracy of the aforementioned data was confirmed by comparing the collection forms of the involved investigators.

The quality of included studies was assessed using the JBI critical appraisal checklist for studies reporting prevalence data, a tool consisting of 9 criteria (Figure 2). Studies meeting a small proportion of these criteria are considered to be at high risk of bias and their results should be interpreted with caution (16). No article was excluded because of a low-quality score. Due to the high level of heterogeneity among the studies, a narrative synthesis of the evidence was conducted. Disagreements were resolved by discussion among all authors until a consensus was achieved.

Results

Our search in PubMed, Google Scholar and Epistemonikos databases produced 1,094 articles after the deletion of 251 duplicate records. After reviewing the title and the abstract, 119 articles remained. Finally, 52 articles were selected after full text reading and further 4 articles were selected from the references of the included articles. The total number of the reviewed articles was 56 (17-72).

The 56 articles that were selected came from the following countries in descending order of frequency: USA (25 articles), Canada (6 articles), Taiwan (4 articles), Brazil (4 articles), Australia (2 articles), UK (2 articles), South Korea (2 articles), Bangladesh (1 article), France (1 article), Belgium (1 article), Puerto Rico (1 article), Cameroon (1 article), Mexico (1 article), Turkey (1 article), Slovenia (1 article), Spain (1 article), Italy (1 article), Hungary (1 article) and Japan (1 article).

During the COVID-19 pandemic, everyday life changed violently and non-emergency care, including cancer

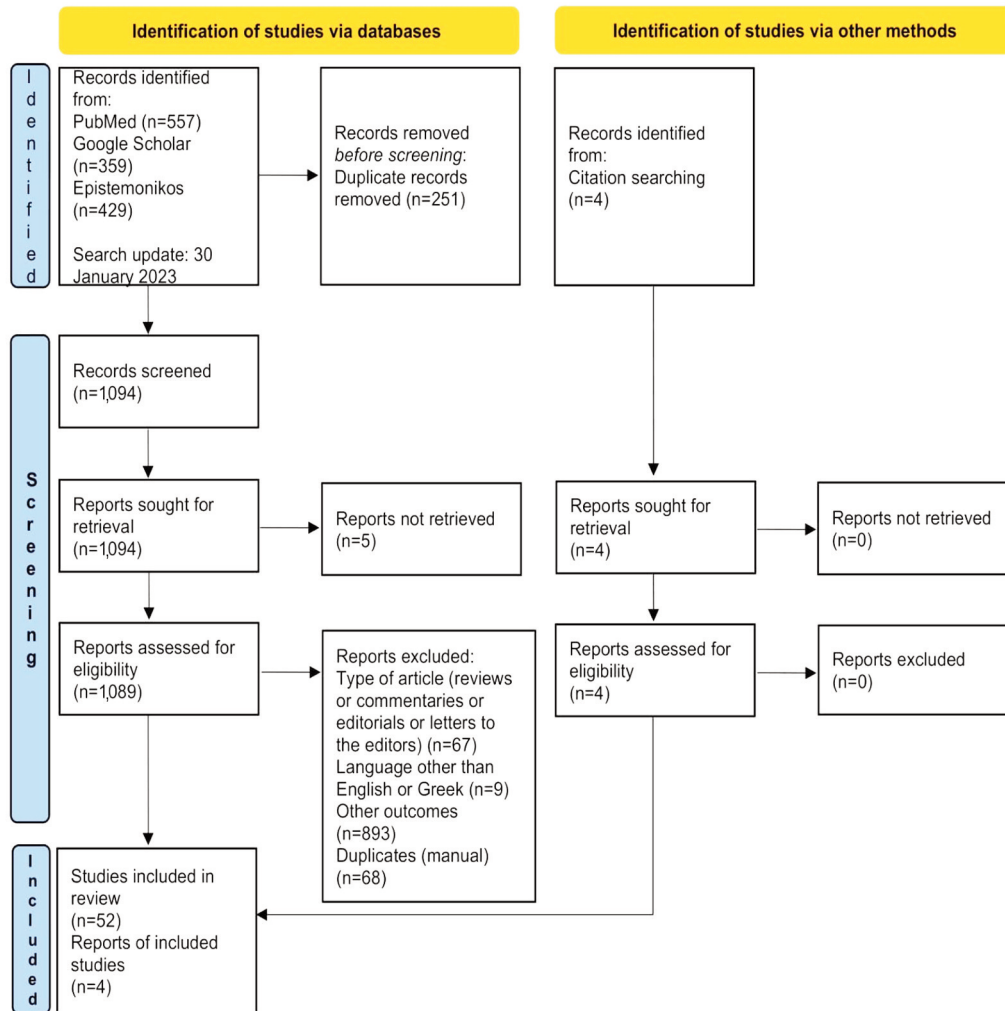


Figure 1. Flow diagram demonstrating the selection process of appropriate records based to PRISMA 2020 guidelines.

screening, was significantly disrupted. The review of the literature highlighted, in an overwhelming way, a decisive reduction in the number of screening tests performed for breast and cervical cancer, especially during the first months of the pandemic, when the fear of the unknown virus was evident, and the restrictive measures were notably strict on a global scale in order to flatten the transmission curve. Since the summer of 2020 there has been a recovery in numbers of screening tests performed, however not to a satisfactory extent that could make up lost ground (Table I).

Discussion

The present systematic review investigated the association of the COVID-19 pandemic with cancer screening and found evidence of a significant decline in the volume of screening tests performed for both breast and cervical cancer,

especially during the early phase of the pandemic. The easing of restrictions coincided with a recovery in the number of screening tests, which, although in some studies it approached the pre-pandemic levels, in almost no case exceeded them, therefore the deficit of tests that had accumulated from the previous months did not shrink (19, 22, 55, 67, 69). These findings are in accordance with other relevant systematic reviews (2, 73, 74).

This decline appears to be attributed to a number of causes. Initially, during the first phase of the pandemic health policies around the globe focused on combating the COVID-19; resource allocation was drastically redesigned and material as well as human resources were shifted from non-COVID-19 services directly to the COVID-19 front, in order to reduce the extent of the unprecedented health crisis and to minimize its morbidity and mortality (18-20, 22, 30, 33, 37, 38, 54, 56, 60, 61, 75). As a result, many non-emergency

No.	Authors, year of publication (Ref)	1	2	3	4	5	6	7	8	9
1	Bakouny <i>et al.</i> (2021) (17)	N	Y	Y	Y	Y	Y	Y	Y	N/A
2	Gorin <i>et al.</i> (2020) (18)	N	Y	N	Y	Y	Y	Y	Y	N/A
3	Chen <i>et al.</i> (2021) (19)	Y	Y	Y	Y	Y	Y	Y	Y	N/A
4	Peng <i>et al.</i> (2020) (20)	UN	Y	Y	N	Y	Y	Y	Y	N/A
5	Walker <i>et al.</i> (2021) (21)	Y	Y	Y	Y	Y	Y	Y	Y	N/A
6	Miller <i>et al.</i> (2021) (22)	N	Y	Y	Y	Y	Y	Y	Y	N/A
7	DeGroff <i>et al.</i> (2021) (23)	N	Y	Y	Y	Y	Y	Y	Y	N/A
8	Amran <i>et al.</i> (2021) (24)	Y	Y	Y	Y	Y	Y	Y	Y	N/A
9	Ortiz <i>et al.</i> (2021) (25)	N	UN	Y	Y	Y	Y	Y	Y	N/A
10	Cairns <i>et al.</i> (2022) (26)	Y	Y	Y	Y	Y	Y	Y	Y	N/A
11	Duarte <i>et al.</i> (2022) (27)	Y	UN	Y	Y	Y	Y	Y	UN	N/A
12	Martellucci <i>et al.</i> (2021) (28)	UN	Y	UN	Y	Y	Y	Y	Y	N/A
13	Tsai <i>et al.</i> (2020) (29)	Y	Y	Y	Y	Y	Y	Y	Y	N/A
14	Song <i>et al.</i> (2021) (30)	N	Y	UN	Y	Y	Y	Y	Y	N/A
15	Becker <i>et al.</i> (2021) (31)	Y	Y	Y	Y	Y	Y	Y	Y	N/A
16	Fedewa <i>et al.</i> (2021) (32)	N	Y	Y	Y	Y	Y	Y	Y	N/A
17	Nyante <i>et al.</i> (2021) (33)	N	Y	UN	Y	Y	Y	Y	Y	N/A
18	Velazquez <i>et al.</i> (2021) (34)	N	Y	N	Y	Y	Y	Y	Y	N/A
19	Lou <i>et al.</i> (2022) (35)	Y	Y	Y	Y	Y	Y	Y	Y	N/A
20	McBain <i>et al.</i> (2021) (36)	N	Y	Y	Y	Y	Y	Y	Y	N/A
21	Chiarelli <i>et al.</i> (2021) (37)	Y	Y	Y	Y	Y	Y	Y	Y	N/A
22	Miller <i>et al.</i> (2021) (38)	N	Y	UN	Y	Y	Y	Y	Y	N/A
23	Chou <i>et al.</i> (2021) (39)	N	Y	UN	UN	Y	Y	Y	Y	N/A
24	Sormani <i>et al.</i> (2021) (40)	N	UN	UN	N	UN	Y	UN	N	N/A
25	Sprague <i>et al.</i> (2021) (41)	Y	Y	Y	Y	Y	Y	Y	Y	N/A
26	Decker <i>et al.</i> (2022) (42)	N	Y	Y	Y	Y	Y	Y	Y	N/A

Figure 2. Continued

27	Moterani Junior <i>et al.</i> (2022) (43)	Y	Y	Y	Y	Y	Y	Y	Y	N/A
28	Lee <i>et al.</i> (2022) (44)	Y	Y	Y	Y	Y	Y	Y	Y	N/A
29	Castanon <i>et al.</i> (2022) (45)	Y	Y	Y	Y	Y	Y	Y	Y	N/A
30	Grimm <i>et al.</i> (2022) (46)	Y	Y	Y	Y	Y	Y	Y	Y	N/A
31	Amram <i>et al.</i> (2022) (47)	Y	Y	Y	Y	Y	Y	Y	Y	N/A
32	Ribeiro <i>et al.</i> (2021) (48)	Y	Y	Y	Y	Y	Y	Y	Y	N/A
33	Trinh <i>et al.</i> (2022) (49)	Y	Y	Y	Y	Y	Y	Y	Y	N/A
34	Battisti <i>et al.</i> (2022) (50)	UN	Y	UN	Y	Y	Y	Y	Y	N/A
35	Bosch <i>et al.</i> (2022) (51)	Y	Y	Y	Y	Y	Y	Y	Y	N/A
36	Nogami <i>et al.</i> (2022) (52)	Y	Y	Y	Y	Y	Y	Y	Y	N/A
37	Elek <i>et al.</i> (2022) (53)	UN	Y	UN	Y	Y	Y	Y	Y	N/A
38	Kidwai (2022) (54)	N	Y	N	Y	Y	Y	Y	Y	N/A
39	Labaki <i>et al.</i> (2021) (55)	UN	Y	Y	N	Y	Y	Y	Y	N/A
40	de Pelsemaeker <i>et al.</i> (2021) (56)	N	Y	N	N	Y	Y	Y	UN	N/A
41	Doubova <i>et al.</i> (2021) (57)	Y	Y	Y	Y	Y	Y	Y	Y	N/A
42	Laing and Johnston (2021) (58)	N	Y	Y	N	Y	Y	Y	Y	N/A
43	London <i>et al.</i> (2020) (59)	Y	Y	Y	Y	Y	Y	Y	Y	N/A
44	Patt <i>et al.</i> (2020) (60)	UN	Y	Y	Y	Y	Y	Y	Y	N/A
45	Meggetto <i>et al.</i> (2021) (61)	UN	Y	Y	Y	Y	Y	Y	Y	N/A
46	Sutherland <i>et al.</i> (2020) (62)	Y	Y	Y	Y	Y	Y	Y	Y	N/A
47	Brugel <i>et al.</i> (2021) (63)	N	Y	UN	N	Y	Y	Y	UN	N/A
48	Shen <i>et al.</i> (2022) (64)	Y	Y	Y	Y	Y	Y	Y	Y	N/A
49	Ivanus <i>et al.</i> (2021) (65)	Y	Y	Y	N	Y	Y	Y	Y	N/A
50	Dennis <i>et al.</i> (2021) (66)	Y	Y	Y	Y	Y	Y	Y	Y	N/A
51	Bentley <i>et al.</i> (2021) (67)	UN	Y	Y	N	Y	Y	Y	Y	N/A

Figure 2. *Continued*

52	Ozsari (2022) (68)	N	Y	Y	N	N	Y	Y	Y	N/A
53	Imai <i>et al.</i> (2021) (69)	Y	Y	Y	Y	Y	Y	Y	Y	N/A
54	Solla Negro <i>et al.</i> (2022) (70)	Y	UN	Y	Y	Y	Y	Y	Y	N/A
55	Joung <i>et al.</i> (2022) (71)	Y	Y	Y	Y	Y	Y	Y	Y	N/A
56	Collado-Mesa <i>et al.</i> (2022) (72)	Y	Y	Y	Y	Y	Y	Y	Y	N/A

Figure 2. Quality assessment of included articles using JBI checklist for prevalence studies. Y: Yes; N: no; UN: unclear; N/A: not applicable.

chronic care services including cancer preventive programs had been marginalized (76, 77).

Stay-at-home orders issued by almost every government globally, as well as recommendations by prestigious scientific organizations played a significant role in the screening setback; the Center for Disease Control and Prevention (CDC) and the Center for Medicare and Medicaid Services (CMS) but also many medical scientific societies such as the American College of Radiology, the Society of Breast Imaging and the American Cancer Society published guidelines urging the general public to comply with the government guidelines and suggested a temporary shutdown of non-emergency medical practices (33, 78), not to mention people’s fear of the infection (79), reluctance to seek medical help and limited access to in-person medical examinations (18, 20-22, 62). Finally, another factor that disrupted the continuity of screening programs, especially in low-income countries, was the disruption of supply chains resulting in the unavailability of materials required for obtaining and processing cervical smears (40).

The most concerning potential adverse effect of cancer screening decline would be an increase in future cancer morbidity and mortality. The disruption of cancer screening programs could delay diagnosis of tumors, causing a shift to more advanced stages at diagnosis and fewer treatment options (*e.g.*, surgical removal) resulting in a worse prognosis (19, 30, 32, 59, 60). Furthermore, this could potentially increase preventable deaths from cancer as well as healthcare spending (4, 59, 60, 74).

The WHO, as early as 2019, had demonstrated the need to increase spending on PHC by at least 1% of GDP, a goal considered financially sustainable even for low-income countries (80). This need becomes even more urgent during pandemic times, when additional financial resources are required to cover the lost ground. Health facilities should increase the number of tests they process daily and temporarily achieve volumes higher than the pre-pandemic

levels. This could be attainable by extending the operating hours and by upgrading the service capabilities of each unit, *e.g.*, by hiring extra staff, creating new spaces, and meeting other needs (81, 82).

Triaging eligible citizens seems of particular value, especially during times of limited resources, when maximal efficiency is desirable. The aim would be to prioritize those who are most likely to develop cancer and therefore screen positive. Examples of such could be women with a personal or family history of breast cancer, women with HIV infection, citizens with many years since their last check-up, or socially and economically marginalized individuals who face high barriers to healthcare access and are therefore less likely to self-seek participation (82-84).

Masson *et al.* stated that known and documented barriers to participation in screening related to insufficient information such as the fear that the procedure will be painful or the fear that the result may lead to the finding of cancer and the belief that the screening refers to specific categories of women, may have swelled during the pandemic (85). It is of paramount importance, awareness raising measures about the benefits of screening and the risks posed by neglecting it, to be massively promoted, in combination with building trust regarding the safety and hygiene measures that are taken in health facilities where the screening examinations are held, in order to limit patients’ fear of SARS-CoV-2 transmission and to increase the motivation of participating. The awareness campaign can use mass media, social media, but also personalized email messages or mobile phone messages. The existence of special support and information telephone lines as well as the creation of informative websites are considered necessary steps, while the opinion of expert scientists may play a decisive role, if it is communicated in a coordinated but at the same time comprehensible way (81, 84).

Another possibility would be the transition from the classical cytological cervical smear (Pap test) to the HPV DNA test. The greatest difference lies in the fact that Pap

Table I. Screening volume alterations during COVID-19: studies characteristics and main findings.

No.	Authors, year of publication (Ref)	Country of origin	Study design	Type of screening test	Results	Comments-Conclusions
1	Bakouny <i>et al.</i> (2021) (17)	USA	Cohort study	Mammography Pap test	This study comprised four 3-month periods. The period from March 2 to June 2, 2020, (first peak of the pandemic) was compared to 3 control periods (December 1, 2019, to March 2, 2020; March 2 to June 2, 2019; and the 3 months after the main study period from June 3 to September 3, 2020). The percentage decreases in screening were pronounced across all screening tests, compared with all 3 control periods, and ranged from -60% to -82%.	The decrease in screening tests was accompanied by decreases in ensuing diagnoses.
2	Gorin <i>et al.</i> (2020) (18)	USA	Observational study	Mammography Pap test	Screening tests for breast, cervical, and colorectal cancer were compared year to year for the periods between March 19 and May 9 in 2017, 2018, 2019, and 2020 and during the clinic reopenings between May 10 and June 7, 2020, by comparison with the respective time periods in 2017, 2018, and 2019. Unique patient visits for cancer screening decreased markedly (4,990 to 444 overall) with mammograms for breast cancer (3,339 to 6) and Pap test for cervical cancer screening being considerably fewer during the shelter-in-place orders.	After the clinic reopenings breast and cervical cancer screenings increased slightly.
3	Chen <i>et al.</i> (2021) (19)	USA	Retrospective cohort study	Mammography	Screening for breast cancer declined sharply during the period of March-May of 2020 compared to the respective period of 2019, with the sharpest decline recorded in April (-90.8%). The absolute deficit of mammographies across the USA population associated with the COVID-19 pandemic was estimated to be 3.9 million tests.	Near complete recovery of monthly screening rates for breast cancer by July 2020.
4	Peng <i>et al.</i> (2020) (20)	Taiwan	Observational study	Mammography	The researchers attempted to evaluate the impact of COVID-19 on breast cancer screening by comparing the number of tests between January and May in the year of the COVID-19 pandemic (2020) to the previous three years (2017-2019). The number of participating women in March, April, and May 2020 decreased by 35%, 60%, and 49%, compared with their respective counterparts in the past 3 years ($p < 0.0001$).	
5	Walker <i>et al.</i> (2021) (21)	Canada	Population-based retrospective observational study	Mammography Pap test	Screening mammograms and Pap tests decreased considerably by up to 99.8% and 92.3% respectively during the early pandemic period (April 2020 compared to April 2019).	
6	Miller <i>et al.</i> (2021) (22)	USA	Observational study	Pap test HPV test	Compared with the 2019 baseline, cervical cancer screening rates declined substantially during the stay-at-home order. Among women 21-29 years old, cervical cytology screening rates per 100 person-months declined by 78%. Among women aged 30-65 years, HPV test screening rates per 100 person-months were decreased by 82%. After the stay-at-home order was lifted, screening rates nearly returned to baseline.	As the pandemic continues, groups at higher risk for developing cervical cancer should be evaluated first.

Table I. Continued

Table I. *Continued*

No.	Authors, year of publication (Ref)	Country of origin	Study design	Type of screening test	Results	Comments-Conclusions
7	DeGroff <i>et al.</i> (2021) (23)	USA	Observational study	Mammography Pap test	The investigators evaluated the COVID-19 impact on National Breast and Cervical Cancer Early Detection Program (NBCCEDP) screening services during January-June 2020. The total number of NBCCEDP-funded breast and cervical cancer screening tests declined by 87% and 84%, respectively, during April 2020 compared with the previous 5-year averages for that month.	Test volume began to recover in May and, by June 2020, NBCCEDP breast and cervical cancer screening test volume was 39% and 40% below the 5-year average for that month, respectively.
8	Amran <i>et al.</i> (2021) (24)	USA	Cohort study	Mammography	There was a 49% decrease in screening mammograms in 2020 compared with the same period of 2019 (55,678 in 2019 vs. 27,522 in 2020).	Larger decline in screening was observed among women from underserved racial/ethnic groups and lower socio-economic status.
9	Ortiz <i>et al.</i> (2021) (25)	Puerto Rico	Observational study	Pap test HPV test	The authors described time trends (from January 1, 2016, to July 28, 2020) in cervical cancer screening among eligible women. A substantial decrease occurred in screening utilization comparing January 2016 (2.81 per 100 person-months) to July 2020 (0.72 per 100 person-months). Screening rates were particularly low after the hurricanes (September 2017: 1.02 per 100 person-months) and after the COVID-19–related lockdown (April 2020: 0.37 per 100 person-months)	Public health efforts should focus on improving infrastructure and resilience of healthcare, including setting goals and objectives for cancer care (prevention and treatment) during and after disasters.
10	Cairns <i>et al.</i> (2022) (26)	USA	Retrospective observational study	Mammography	Mammography rates were calculated using county level census data for eligible women (Z-test). Data revealed a relative decline in breast cancer screening by 44% (1558 fewer tests) during 2020 compared to 2019 ($p < 0.00001$).	Screening mammography was impacted by the COVID-19 pandemic, however, more data needs to be collected to evaluate future morbidity and mortality related to delay in breast cancer care due to COVID-19.

Table I. *Continued*

Table I. *Continued*

No.	Authors, year of publication (Ref)	Country of origin	Study design	Type of screening test	Results	Comments-Conclusions
11	Duarte <i>et al.</i> (2022) (27)	Brazil	Observational study	Mammography Pap test	The authors estimated that 1,149,727 pap tests, 2,693 conizations and 713,616 mammograms, were missed or delayed during the COVID-19 pandemic (from April 2020 to November 2021), in comparison with the years immediately before the COVID-19 stay-at-home restrictions.	An acute decrease of tests and procedures was observed after the COVID-19 stay-at-home restrictions, with a trend to recovery in the long term.
12	Martellucci <i>et al.</i> (2021) (28)	Italy	Observational study	Pap test	The researchers recorded the work hours and number of Pap tests performed during 2019 and 2020, overall and by semester, and calculated the hourly rate of tests and the percentage changes from 2019 to 2020. The number of tests conducted per hour decreased from 4.1 (July–December 2019) to 3.6 (July–December 2020).	
13	Tsai <i>et al.</i> (2020) (29)	Taiwan	Observational study	Mammography	Nationwide data showed that the total number of screening mammograms decreased by 22.2% during January to April 2020 compared with the same period of 2019. This variation was more pronounced for in-hospital examinations (–37.2%), rather than outreach screening (–12.9%).	
14	Song <i>et al.</i> (2021) (30)	USA	Observational study	Mammography	Over a period of 20 weeks following March 11, 2020, the volume of screening mammograms declined by 58% on average compared to expected levels. The lowest volumes were observed in week 15 (April 8 to 14), when screening mammograms were 99% fewer than expected.	Test volumes began to rebound in week 19 (May), with screening mammograms remaining 14% below expectations.
15	Becker <i>et al.</i> (2021) (31)	USA (Michigan)	Cross-sectional study	Mammography, Pap test	Among women aged 18 to 74 years enrolled in a commercial health maintenance organization in Michigan, for services requiring an in-person visit (breast cancer screening, cervical cancer screening), utilization declined by 60% to 90% during the spring of 2020, with a nadir recorded in April 2020, after which utilization of all services. recovered to almost 2019 levels by July 2020. The Adjusted Odds Ratios of a woman using a given preventive service in 2020 compared with 2019 were significantly lower for breast cancer screening (AOR, 0.80; 95% CI=0.79-0.80) and cervical cancer screening (AOR, 0.80; 95% CI=0.80-0.81).	Further research into disparities in access to care and the health outcomes of decreased use of these key health services is warranted.
16	Fedewa <i>et al.</i> (2021) (32)	USA	Observational study	Mammography	Breast cancer screening rates declined by 8% between 2019 and 2020 (from 53.9% of eligible women to 49.6%; SRR, 0.92; 95% CI=0.92-0.93), signaling 47,517 fewer mammograms and 242 potentially missed breast cancer diagnoses in this population.	

Table I. *Continued*

Table I. Continued

No.	Authors, year of publication (Ref)	Country of origin	Study design	Type of screening test	Results	Comments-Conclusions
17	Nyante <i>et al.</i> (2021) (33)	USA	Observational study	Mammography	Fewer examinations than expected were performed after the onset of COVID-19. The greatest reductions were recorded in March 2020 for screening mammography (-85.1%; 95% CI=-100.0% to -70.0%). The deficit shrunk gradually, with no significant difference between observed and expected numbers by August 2020.	Several months after the pandemic onset, women had higher predicted breast cancer risk (screening mammography, $p < 0.001$) compared with the pre-pandemic population. In contrast to reports demonstrating recovery of screening volumes, this study highlights persistently low breast cancer screening volumes and an absolute decrease in the proportion of completed mammograms among Latino and Black women.
18	Velazquez <i>et al.</i> (2021) (34)	USA	Cross-sectional study	Mammography	During the first stay-at-home order (February 1, 2020, to May 31, 2020), the absolute number of screening mammograms decreased to 194 in March (41% of baseline -mean of 472 mammograms per month during 2019) and to 0 in April. The number of missed appointments increased during 2020, with 127 of 321 (40%) missed in March, compared with 585 of 2764 (21%) from September 2019 to January 2020 (pre-COVID-19). During the reopening phase (June 1, 2020, to November 30, 2020), the number of screening mammograms increased but remained below baseline, except October, when 496 mammograms were performed. The number of screening mammograms declined during the second stay-at-home order.	In 2020, there was no statistical difference in screening studies for lung and breast cancer (compared to 2016-2019) but a decrease in new diagnoses was recorded.
19	Lou <i>et al.</i> (2022) (35)	USA	Retrospective analysis of a single-center registry	Mammography	48,093 screening mammograms were performed from 2017 to 2020, with no significant change in the mean volume during the pandemic year compared to pre pandemic levels (2016-2019) [1,017.0 (SEM 171.8) vs. 809.4 (SEM 56.41), $p=0.177$]. In Q1, there was no difference in 2020 [932.0 (SEM 183.5) vs. 894.6 (SEM 28.76), $p=0.736$]. There was a decrease in Q2 of 2020 [465.0 (SEM 344.5) vs. 982.7 (SEM 16.95), $p=0.017$] followed by an increase in Q3 compared with the prepandemic years [1,243.0 (SEM 11.27) vs. 1,019.7 (SEM 39.07), $p=0.010$]. There was no statistical difference in the number of mammograms during the pandemic in Q4 [1,343.0 (SEM 65.26) vs. 1,081.2 (SEM 59.60), $p=0.052$].	In 2020, there was no statistical difference in screening studies for lung and breast cancer (compared to 2016-2019) but a decrease in new diagnoses was recorded.
20	McBain <i>et al.</i> (2021) (36)	USA	Observational study	Mammography	Prior to the national emergency declaration on March 13, 2020, the median weekly rate of screening mammography was 87.8 women per 10,000 beneficiaries, which declined to 6.9 in April – a 96% decline. By the end of July, this figure had rebounded to 88.2 screenings per 10,000 beneficiaries.	

Table I. Continued

Table I. *Continued*

No.	Authors, year of publication (Ref)	Country of origin	Study design	Type of screening test	Results	Comments-Conclusions
21	Chiarelli <i>et al.</i> (2021) (37)	Canada	Observational study	Mammography	The volume of screening mammograms demonstrated the greatest decline in April and May 2020 (>99% decrease) and achieved pre pandemic levels once again in March 2021, with an accumulated backlog of 340,876 examinations. As of March 2021, prioritization had reduced the backlog volumes of screens for participants at high risk for breast cancer by 96.5% (186 vs. 5,469 expected) and annual rescreens for participants at average risk for breast cancer by 13.5% (62,432 vs. 72,202 expected); there was a minimal decline for initial screens.	More than half (59.4%) of mammographic examinations with abnormal results belonged to participants of high-risk groups. Prioritizing screening for those at higher risk for breast cancer may increase diagnostic yield and redirect resources to minimizing potential long-term harms caused by the pandemic. This further supports the clinical utility of risk-stratified cancer screening.
22	Miller <i>et al.</i> (2021) (38)	USA	Observational study	Mammography	Weekly total screening mammograms performed throughout 2019 (baseline year) and 2020 (COVID-19-impacted year) were compared. The year-over-year cumulative difference in screening mammogram volumes peaked in week 21, with 2962 fewer exams in the COVID-19-impacted year. By week 47, this deficit had shrunk (by 49.4%) to 1498 tests.	
23	Chou <i>et al.</i> (2021) (39)	Taiwan	Retrospective observational study	Mammography	Screening mammograms in 2020 (week 1 – week 22), were decreased by 51% compared to the respective pre-COVID-19 period.	
24	Sormani <i>et al.</i> (2021) (40)	Cameroon	Observational study	Pap test HPV test	The number of women screened in 2020 dropped by almost 80% compared with the same period of 2019.	The authors suggested the introduction of home based cervical self-sampling

Table I. *Continued*

Table I. Continued

No.	Authors, year of publication (Ref)	Country of origin	Study design	Type of screening test	Results	Comments-Conclusions
25	Sprague <i>et al.</i> (2021) (41)	USA	Observational study	Mammography	Screening mammograms performed in April 2020 dropped to just 1.1% (95% confidence interval=0.5% to 2.4%) of the April 2019 pre pandemic volumes demonstrating a 98.9% decline. By July 2020 they had rebounded to 89.7% (95% confidence interval=79.6% to 101.1%) of the July 2019 levels.	to reduce the risk of exposure to COVID-19 at the hospital or during transportation to the screening facilities. Screening mammography rebound was similar across age groups and not affected by family history of breast cancer status.
26	Decker <i>et al.</i> (2022) (42)	Canada	Observational study	Mammography Pap test	In June 2020 (breast screening was suspended during April and May 2020), there was a 54% decrease between the predicted (<i>i.e.</i> , observed data produced from regression models) and expected (<i>i.e.</i> , counterfactual values produced for the COVID-19 period by assuming COVID-19 did not occur) number of screening mammograms (ratio=0.46, 95% confidence interval=0.28-0.64). In April 2020, there was an 83% decrease in the number of Pap tests (ratio=0.17, 95% confidence interval=0.04-0.30) compared to expected levels. In May 2020, Pap tests performed were 49% fewer than expected. By January 2021, there was no significant difference between predicted and expected number of Pap tests (ratio=0.93, 95% confidence interval=0.81-1.06).	
27	Moterani Junior <i>et al.</i> (2022) (43)	Brazil	Retrospective observational study	Mammography	The mean monthly screening mammograms were decreased from 14.8/1,000 in 2019 to 9.25/1,000 in 2020, with the lowest rates being recorded in May 2020 (3.1/1,000). The mean monthly high-risk mammograms decreased from 12.8/100,000 in 2019 to 9.1/100,000 in 2020, with the lowest rates recorded in April 2020 (4.3/100,000).	The COVID-19 pandemic led to significant reductions in mammography screening, signaling a warning for early-stage breast cancer diagnosis and higher advanced stage diagnoses and mortality in the future.

Table I. Continued

Table I. *Continued*

No.	Authors, year of publication (Ref)	Country of origin	Study design	Type of screening test	Results	Comments- Conclusions
28	Lee <i>et al.</i> (2022) (44)	South Korea	Annual cross-sectional study (2018-2020) from the Korean National Cancer Screening Survey	Mammography Pap test	Between 2019 and 2020, screening rates declined significantly by 12%, for breast cancer (SRR 0.88; 95% confidence interval=0.82-0.93), and by 8% for cervical cancer (SRR 0.92; 95% confidence interval=0.87-0.97).	
29	Castanon <i>et al.</i> (2022) (45)	UK (England)	Observational study	Pap test HPV test	The number of samples received was 91% lower than expected during April 2020, 85% lower during May 2020 and 43% lower during June 2020 compared to the respective months of 2018. Although on average, laboratories received 12.6% more samples between August 2020 and April 2021 than over the same period of 2018, by April 2021 there was a short fall of 200,949 samples (6.4% fewer than in 2018).	
30	Grimm <i>et al.</i> (2022) (46)	USA	Observational study (ACR National Mammography Database)	Mammography	In total, 5,633,783 screening mammograms were analyzed. Peak COVID-19 metrics were less than pre-COVID-19 volumes: 36.3% of pre-COVID-19 for screening mammography. There was some rebound during COVID-19 recovery as a percentage of pre-COVID-19 volumes: 85.3% of pre-COVID-19 for screening mammography.	COVID-19 had a great impact on screening mammography volumes, which have not returned to pre-COVID-19 levels.
31	Amram <i>et al.</i> (2022) (47)	USA	Retrospective observational study	Pap test	In the pre-COVID-19 period, 22,395 (10.7%) women were administered Pap tests compared to 20,455 (9.6%) women during the pandemic, signaling a 7.4% reduction. During the pre-COVID-19 period 1780 women were referred to colposcopy, compared to only 1680 patients during the pandemic (4.3% reduction).	
32	Ribeiro <i>et al.</i> (2021) (48)	Brazil	Observational study	Mammography Pap test	In 2020, cytopathology tests declined by 3,767,686 (-44.6%) and screening mammograms by 1,624,056 (-42.6%), compared to 2019.	
33	Trinh <i>et al.</i> (2022) (49)	South Korea	Observational study (annual cross-sectional survey based on Korean National Cancer Screening Survey)	Mammography Pap test	The survey was conducted among cancer-free men aged 40-74 years and women aged 20-74 years. The 1-year screening rates for both types of cancer decreased during the pandemic (breast cancer: -2.5%, cervical cancer: -1.5%)	Since the COVID-19 pandemic, the cancer screening rate has decreased significantly, especially in large cities. Public health efforts are required to improve cancer screening rates.

Table I. *Continued*

Table I. *Continued*

No.	Authors, year of publication (Ref)	Country of origin	Study design	Type of screening test	Results	Comments-Conclusions
34	Battisti <i>et al.</i> (2022) (50)	Italy	Observational study	Mammography Pap test HPV test	In 2020, screening tests for breast and cervical cancer decreased by 37.6% and 43.4% respectively in comparison with 2019	
35	Bosch <i>et al.</i> (2022) (51)	Spain	Observational study	Mammography	During the COVID-19 period, the odds of participation were lower for first-time invitees [AOR=0.90 (95% confidence interval=0.84-0.96)] and for those who had previously participated either regularly or semiregularly [AOR=0.63 (95% confidence interval=0.59-0.67) and AOR=0.95 (95% confidence interval=0.86-1.05), respectively]. Participation showed a modest increase in women not attending any of the previous rounds (2012-2019) [AOR=1.10 (95% confidence interval=1.01-1.20)].	The COVID-19 pandemic negatively affected screening attendance, especially for previous participants and newcomers. There is a need for further evaluations of interval cancers and potential diagnostic delays.
36	Nogami <i>et al.</i> (2022) (52)	Japan	Observational study	N/A	The number of cancer screening tests from March to August 2020, was less than 50% of that in the previous year with May being the month demonstrating the greatest decline. However, after August, the number recovered to baseline expected levels, despite the second wave of the pandemic occurring nationwide.	
37	Elek <i>et al.</i> (2022) (53)	Hungary	Observational study	Mammography	After adjusting for trend and seasonality, the number of mammography examinations decreased by 68% in 2020q2, was around its usual level in 2020q3 and was reduced by 20-35% throughout 2020q4-2021q2. The reduction was caused by a combination of supply-side (temporary suspensions of screening) and demand-side (lower screening participation during the pandemic waves) factors.	
38	Kidwai (2022) (54)	USA	Observational study	Mammography	In 2019 and 2020, 435 and 382 mammograms were performed respectively. These numbers translate to a percentage reduction of 12%.	
39	Labaki <i>et al.</i> (2021) (55)	USA	Observational study	Mammography Pap test	Cancer screening tests were assessed during seven 3-month periods: period 1 (March 2–June 2, 2019), period 2 (June 3–September 2, 2019), period 3 (September 3–November 30, 2019), period 4 (December 1, 2019–March 2, 2020), period 5 (first pandemic peak: March 2–June 2, 2020), period 6 (June 3–September 3, 2020), and period 7 (second pandemic peak: September 4–December 5, 2020) Following a substantial decrease in screening examinations from March to June 2020 (n=15,453, compared	Following a dramatic decline during the first pandemic peak, we demonstrate a substantial increase in screening procedures during more recent time

Table I. *Continued*

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No.	Authors, year of publication (Ref)	Country of origin	Study design	Type of screening test	Results	Comments- Conclusions
					to 60,344 and 57,502 in periods 1 and 2, respectively), the highest numbers of tests were recorded during period 7 (September–December 2020; n=72,156), surpassing those seen during the pre-pandemic period (December 2019–March 2020; n=64,269). Compared to pre-pandemic times (December 2019–March 2020), an increase in tests performed during period 7 (September–December 2020) was identified across all screening types	periods (September–December 2020), with numbers exceeding those seen before the pandemic. Of note, four pre-pandemic periods were included in order to ascertain that increases in screening numbers were due to a rebound rather than to random or seasonal variation occurring in pre-pandemic months. Although this increase will help identify “missed” cancer diagnoses, only modest numbers have been recovered.
40	de Pelsemaeker <i>et al.</i> (2021) (56)	Belgium	Observational study	Pap test	Cervical cytology rates dramatically collapsed during the first trimester of 2020 (decline up to 80%) compared to the same 4-month-periods for the years 2017 till 2020.	Health care actions during the deconfinement period should focus on restarting cancer screening programs. Health care professionals should assure that patient contacts related to cancer screening are postponed instead of cancelled.

Table I. *Continued*

Table I. Continued

No.	Authors, year of publication (Ref)	Country of origin	Study design	Type of screening test	Results	Comments-Conclusions
41	Dobova <i>et al.</i> (2021) (57)	Mexico	Observational study	Mammography Pap test	A decline of breast and cervical cancer screening exams (79% and 68%, respectively) was recorded from January 2019 to August 2021 compared to the pre-pandemic period. By August 2021, most services were still below pre-pandemic levels.	
42	Laing and Johnston (2021) (58)	Canada	Observational cohort study	Pap test	From March to November 2020, the mean percentage of eligible patients screened for cervical cancer decreased by 7.5% (95% confidence interval=-0.3% to -14.7%) (estimated) using 2016 census data.	COVID-19 decreased the delivery of preventive care services, which may cause delayed diagnoses, increased mortality, and increased health care costs. Virtual care and reopening measures have not restored the provision of preventive care services
43	London <i>et al.</i> (2020) (59)	USA/UK	Observational study	Mammography	Breast cancer screening declined by -5.0% and -9.1% in January and February 2020 compared to the respective months of 2019. The number of patients with family history of breast cancer who underwent screening in March 2020 was shown to decline by -43.8%. April displayed the greatest drop in screenings. Patients with family history of breast cancer who underwent screening were 89.2% fewer, when comparing 2020 with 2019.	
44	Patt <i>et al.</i> (2020) (60)	USA	Observational study	Mammography	During the period of March-July 2020, compared to the baseline of March-July 2019, there is a substantial decrease in cancer screening. At the peak of the pandemic in April, screening tests for breast cancer declined by 85%.	
45	Meggetto <i>et al.</i> (2021) (61)	Canada	Population-based retrospective observational study	Pap test	During the first 6 months of the COVID-19 pandemic, the monthly average number of cervical screening cytology tests decreased by 63.8% (range=-92.3 to -41.0%), when compared with the corresponding months of 2019.	
46	Sutherland <i>et al.</i> (2020) (62)	Australia	Observational study	Mammography	In March to June 2020, compared with the same period of 2019, breast screening activity was reduced by 51.5%.	
47	Brugel <i>et al.</i> (2021) (63)	France	Observational study	Mammography	Compared with the same trimester in 2019, oncological activity decreased dramatically on all essential oncological care pathway steps during January 2019 and May 2020. COVID-19 had a dramatic impact in terms of breast cancer screening (up to -100%).	

Table I. Continued

Table I. *Continued*

No.	Authors, year of publication (Ref)	Country of origin	Study design	Type of screening test	Results	Comments- Conclusions
48	Shen <i>et al.</i> (2022) (64)	Taiwan	Observational study	Mammography Pap test	The percentage changes in screening participants at inreach and outreach services were calculated and compared between January to April 2020 (COVID-19 pandemic) and January to April 2019. Percentage change of -62.7% and -62.8% for cervical and breast cancer screening respectively were observed.	
49	Ivanus <i>et al.</i> (2021) (65)	Slovenia	Observational study	Pap test HPV test	A two-month screening lock-down between March 12 th and May 8 th , 2020, resulted in a reduction of screening (-92%), follow-up (-70%), and HPV DNA tests (-68%).	
50	Dennis <i>et al.</i> (2021) (66)	USA	Observational study	Mammography Pap test	Reported mammograms had a 5.3% reduction in April–December 2020 compared to the respective months of 2014-2019 for women aged over 50, with similar reductions of 7.2% for women 40-49 years. An 8.6% reduction in reported pap tests was recorded.	
51	Bentley <i>et al.</i> (2021) (67)	Canada	Observational study	Mammography	A 30.2% decline in breast screening volume was observed in 2020 compared to 2019.	
52	Ozsari (2022) (68)	Turkey	Observational study	Mammography Pap test HPV test	In 2020 cervical smear/HPV cancer screenings decreased by 51.2%; while mammography scans decreased by 56.5% compared to the average of cancer screening in the last 3 years (2017-2019) before the pandemic. The number of mammograms performed in primary care facilities decreased by 71.4%.	
53	Imai <i>et al.</i> (2021) (69)	Australia	Observational study	Mammography Pap test HPV test	Both general practice data and the AIHW report identified large declines in mammograms and cervical cancer tests during the months of COVID-19 flare ups. Mammograms ordered in general practice from January to September in 2020 (<i>vs.</i> 2019) showed a 11.9% decrease in NSW and a 32.2% decrease in Victoria.	After the initial decline during the first wave of the COVID-19 pandemic, the number of mammograms began to recover, and in September 2020 reached the same baseline level as in September 2019. However, the total volume of performed mammograms in 2020 was below that of 2019.

Table I. *Continued*

Table I. Continued

No.	Authors, year of publication (Ref)	Country of origin	Study design	Type of screening test	Results	Comments-Conclusions
54	Solla Negroa <i>et al.</i> (2022) (70)	Brazil	Observational study	Mammography	Two periods were analyzed. During the pre-COVID period (2019), 19,914 screening mammograms were performed. During the pandemic period (2020), 8,478 screening mammograms were performed: (a reduction of 57.4%).	
55	Joung <i>et al.</i> (2022) (71)	USA	Observational study	Mammography Pap test HPV test	Local prepandemic and pandemic monthly screening test volumes (MTVs) were used to calculate the relative percent change in MTV to describe the monthly screening gap from April through June 2021. The majority of facilities reported monthly screening deficits [cervical cancer, 69.0% (n=20/29); breast cancer, 55.3% (n=241/436)]. Overall, the median relative percent change in monthly screening test volumes ranged from -6.8% for cervical cancer (IQR=-29.4% to 1.7%) to -1.6% for breast cancer (IQR=-9.6% to 7.0%).	Cancer screening is still in need of urgent attention, and the screening resources made available online may help facilities to fill critical gaps and address screenings missed in 2020.
56	Collado-Mesa <i>et al.</i> (2022) (72)	USA	Observational study	Mammography	There was a marked decrease in the number of screening mammograms (n=2,722, average during April 2018 and 2019 vs. n=53 during April 2020). The percent decrease in the number of breast cancer screening examinations during April 2020 as compared to April 2018-2019 was -98.1% in facilities under COVID-19 rescheduling measures vs. -75.4% in control facilities not under such measures.	

tests are performed every three years while HPV DNA tests can be performed every five years, reducing the burden on health facilities. Despite the higher costs, their economic viability has been studied and proven even for low-income countries, while an additional advantage is the fact that the performance of the result is objective and does not depend on the skills of the performer (86).

The successful example of the fecal immunohistochemical (FIT) test could be cited as an alternative to screening colonoscopy, in which citizens collect a stool sample themselves and send it to the relevant laboratories. Cervical self-sampling could function similarly and constitutes an option suggested by several literature sources, as a solution that could reduce the risk of SARS-COV-2 transmission, while at the same time could diminish reluctance of many women to be examined in the genital area by a healthcare provider (81, 83, 86-88).

Strengths and limitations. A clear methodology was faithfully followed, described in detail previously. Our research being a systematic review, offers evidence ranked highly by the evidence hierarchy pyramid (89). We searched thoroughly three different databases (Pubmed, Google scholar and Epistemonikos) and the studies included in our review underwent quality assessment following the criteria of a widely recognized assessment checklist. However, the utility of our study could be partially limited by the fact that no meta-analysis was conducted to better quantify variations; studies included come from a small number of different countries, as most of them didn't publish screening data for the time period we examined. Therefore, the conclusions we reached might not apply to each and every geographical region globally. Finally, most studies included did not offer screening data after the massive vaccinations for Covid-19 and the possibly milder course the pandemic started to follow.

Conclusion

The impact of the COVID-19 pandemic on breast and cervical cancer screening has been particularly significant. The unanimous conclusion from the entire literature of the large reduction in the number of tests performed combined with the statistical model predictions for an increase of avoidable advanced cancers and cancer-related deaths in the future, make it imperative to implement measures to reestablish cancer screening as the cornerstone of preventive medicine. As future pandemics caused by viral or other outbreaks are an unfortunate possibility, primary health care needs to ensure adequate coverage of the populations even in times of crisis by adopting the necessary steps towards that direction.

Conflicts of Interest

The Authors declare that there are no conflicts of interest.

Authors' Contributions

Conceptualization: S.E., E.S.; literature search and data collection: S.E., P.S.; data analysis: S.E., P.S., A.-B. H., A.M., E.S.; writing original draft: S.E., P.S.; all authors critically revised the work; all authors have read and agreed to the published version of the manuscript.

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