

Lombardy Region: seven years of breast cancers screening before, during and after the SARS-CoV-2 pandemic

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Abstract

Background. Breast cancer represents the most common form of neoplasm in women, with an estimated 685,000 deaths annually. In this regard, screening programmes represent one of the most effective intervention tools in the field of cancer prevention. The aim of this study is to analyse and describe the key performance indicators of the screening programmes in Lombardy from 2016 to 2022.

Study design. Descriptive temporal analysis study.

Methods. The data pertaining to the screening campaign were subjected to analysis, with the results broken down according to the following criteria: individual province, age group eligible for screening, and campaign year. For each campaign, the data pertaining to the population subjected to screening, as well as the data concerning the rate of cancers identified during the campaign, were subjected to analysis.

Results. For the three age groups, a substantial overlap in call and campaign adherence rates can be observed, with stable values between 2016 and 2019, followed by a significant decline in the 2020 campaign associated with the impact of the pandemic on prevention activities, including cancer screening campaigns. The data for 2021 and 2022 indicate a reversal of the decline in adherence and call rates, particularly in the 45-49 age group, which exhibited an increase of approximately 300% in the call rate between 2021 and 2020. Moreover, the categorization of the provinces into urban, mountainous and rural provinces demonstrates an overlap in the admission rates between the three areas in the different years.

Conclusions. Despite the existence of mammography screening campaigns for more than 20 years, adherence rates in the Lombardy region remain below the targets set out in Europe's Beating Cancer Plan. In this regard, the observed variations, particularly during the period of the pandemic and in the subsequent post-pandemic period, provide an opportunity to rethink the organization of screening campaigns in order to increase adherence and effectiveness.

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Introduction

Breast cancer is the most common type of cancer among women, causing 685,000 deaths globally (1,2). In Italy, it is liable for 12,500 deaths in 2021, with 55,700 recorded new cases in 2022 and 834,200 women living with the disease (3). Due to its prevalence, breast cancer is considered as one of the main public health and preventive medicine issues.

Screening programs are one of the most suitable and cost-effective intervention in public health and specifically in cancer prevention. Screening importance is underlined by several studies that found a decrease in mortality in countries that implemented organized population-based screening programs for early detection of the disease (4-12). Building on this and according to current evidence, the European Commission Initiative on Breast Cancer recommends the implementation of organized screening programs for women aged 45 to 49 (conditional recommendation, moderate certainty of the evidence), 50 to 69 (strong recommendation, moderate certainty of the evidence) and 70 to 74 (conditional recommendation, moderate certainty of the evidence), through digital mammography or tomosynthesis (13).

In 2020, European Union (EU), in order to cut down breast cancer mortality rate, placed a focus on the objectives of cancer screening programs through the Europe's Beating Cancer Plan. The objectives were to reach at least 90% coverage of the eligible population. Despite this ambitious objective and several implementation policies, such as the introduction of population-based breast cancer screening programs in 25 out of the 27 EU member state, coverage levels were still below the goal, ranging from 6% to 90% (14). The importance of screening and of a preventive approach to breast cancer is further highlighted by a study published in 2020 that estimated the decreasing of 12,434 breast cancer deaths in Europe by reaching a screening coverage rate of 100% (9).

In Italy each region is in charge for the implementation of screening programs according to national guidelines, guaranteeing a mammography every two years for women aged 50-69, with the possibility for each region to further extend the target population (15). In particular, Lombardy region has been implementing breast cancer screening since the early 2000s. In 2017 the target population has been extended to women aged 45-49 with annual mammography and to women aged 70-74 with a mammography every two years (16). The whole screening procedure is voluntary and has no cost for

the citizens, aiming to provide equal access to care for all women

Screening programs can only function within a well-organized healthcare system, due to their considerable logistic costs and longtime results. This is one of the reasons why in specific situations, such as pandemic, the goal to guarantee primary care service could lead to a temporary screening service outage. Notably, Lombardy region has been one of the first European areas to be invested by the COVID-19 pandemic in early 2020, resulting in a national lockdown which has severely impacted prevention and screening, with an important decrease in the number of invitations to mammography in 2020 (17,18).

The aim of this paper is to describe key performance indicators (KPIs) of the Lombardy regional breast cancer screening program from 2016 to 2022, a period which also includes the program delay due to the pandemic and eventually the resumption in 2022.

Materials and methods

Lombardy breast-cancer screening program setting

The national healthcare service operates in the territory of Lombardy region through eight local Health Protection Agencies (ATS) led by the Directorate-General Welfare. Each ATS is responsible for the management of the breast-cancer screening program in its area. Within the target population, individuals eligible to participate in the screening program are identified by excluding those who had a recent mammography (temporary suspension) or with diagnosis of breast cancer (permanent suspension). Eligible women receive a letter of invitation containing general information about the screening program and an appointment to perform the exam, which consists of a mammogram in two projections, independently reviewed by two radiologists. In the case of suspicious or positive results, the woman is referred for further diagnostic examinations. In the case of a negative result instead, the women re-enter the program and will be contacted again after two years (women aged 50-74) or one year (women aged 45-49).

Source of data and analysis

The Directorate-General Welfare yearly collects and analyzes data from each ATS through the form to be delivered to the Health Ministry through the National Screening Observatory. One ATS could not deliver complete cancer data for 2022 due to a hacker attack to the screening registry. The hacker attack

seriously corrupted the screening database, for year 2022 and before. Data about screening tests performed was almost rescued, whilst data about lesions detected was poorly restored. Data from 2016 to 2022 were collected in a datasheet on SAS Analytics Software 9.4. A preliminary analysis was performed to assess the viability of the survey's answers, searching for missing data or errors. Descriptive analysis were conducted analyzing categorical data as absolute frequencies and percentages. No inferential analysis was conducted.

Key performance indicators

The following KPIs were analyzed for women aged 45-49, 50-69 and 70-74, for the years 2016-2022:

- adjusted invitation coverage: percentage of individuals invited to screening during the analysed period, compared to the target population, excluding undelivered invitations and individuals with specific exclusion criteria;
- examination coverage: percentage of individuals who underwent the examination compared to the target population, excluding individuals with specific exclusion criteria;
- recall rate (RR): the number of individuals recalled for further assessments as a proportion of all individuals who underwent a screening examination;
- detection rate (DR): the number of all malignant cancers detected every 1,000 screened individuals;

- positive predictive value (PPV): the ratio of lesions that are diagnosed as truly positive to those that test positive at the screening exam

The ATS were eventually clustered according to population and healthcare network difference. The three main ATS of Lombardy, Milano, Bergamo and Brescia were considered as city area, while the north area, corresponding to Varese and Sondrio, was considered as mountain area. The remaining ATSs were merged into countryside area.

Results

Table 1 presents data for the 50-69 age cohorts evaluated between 2016 and 2022. Adjusted invitation coverage was constantly around 100%, with the exception of the pandemic biennium when it dropped to 57.5 % (2020) and 84.3% (2021). Regarding the examination coverage, around half of the target population was covered by screening test in the organized program before the pandemic, whilst in 2020 only one out of three women was covered with the mammography. In terms of RR, the average is 10.4% for initial examinations and 4.4% for subsequent examinations. The PPV is approximately 4.4% for initial examinations and 9.4% for subsequent examinations. DR is between 3.9% and 4.9% for first examinations and between 4.0% and 4.5% for subsequent examinations; the DR below 4.0%

Table 1 - Key performance indicators of Lombardy region breast-cancer screening program, 2016-2022, age group 50-69 years old.

	2016	2017	2018	2019	2020	2021	2022
Target population (n)	700,096	688,828	691,561	695,907	705,152	711,143	720,873
N. of invited subjects	624,502	611,981	652,557	649,903	375,884	563,653	696,303
Adjusted invitation coverage (%)	98.9	99.7	106.0	100.5	57.7	84.3	101.0
Examination coverage (%)	50.4	52.9	52.9	53.4	29.0	53.0	48.3
N. of screened women	352,566	364,139	365,684	371,357	204,750	376,926	347,879
Adjusted participation rate (%)	64.6	67.2	63.7	67.0	62.1	70.8	54.8
Recall rate (%)							
First screening	11.4	10.7	10.3	10.7	9.5	10.5	9.9
Subsequent	4.7	4.2	4.3	4.3	4.5	4.6	4.4
N. of screen-detected cancers	1,469	1,588	1,682	1,535	830	1,688	1,156
Detection rate (%)							
First screening	4.9	4.9	5.0	4.8	3.9	4.2	3.5
Subsequent	4.0	4.3	4.5	4.0	4.1	4.5	3.3
Positive predictive value (%)							
First screening	4.5	4.7	5.0	4.6	4.2	4.4	3.7
Subsequent	8.8	10.2	10.6	9.6	9.2	9.9	7.5

observed in 2022 is probably due to the missing cancer cases registration in one ATS. Moreover, despite the impact of the SARS-CoV-2 pandemic, as evidenced by the reduced invitation rates, an analysis of clinical outcomes as detection rates revealed no substantial differences between the years preceding and those during the pandemic.

Table 2 presents data for the 70-74 cohorts evaluated from 2016 to 2022. Due to the gradual implementation of screening of screening extension for these cohorts by the Lombardy region, for 2016 and 2017 data are not available for all the ATS. The invitation coverage displays an increase followed by a drop, which can be attributed to the Sars-CoV-2 pandemic, and then a new increase. The examination coverage reaches 50% in 2018 and then is hampered as well by the pandemic. RR is similar to the one observed in the 50-69 age range; whilst DR and PPV are markedly higher in this age group: DR is higher than 8% in 2017-2018 and PPV is higher than 15% from 2017 on. In this regards, Table 2 illustrates that the 70-74 age group has been significantly affected by the impact of the SARS-CoV-2 pandemic on screening programmes. Indeed, the adjusted invitation coverage in 2020 is approximately half that observed in 2019, and the first screening detection rate in 2020 and 2021 is, respectively, approximately half and two-thirds of the 2019 rate.

Table 3 presents data for the 45-49 age cohorts evaluated from 2016 to 2022. As a consequence of the gradual implementation of screening extension

for these cohorts by the Lombardy Region, data are not available for all ATSs for the years 2016, 2017, and 2018. The data demonstrate a notable variation in invitation coverage over time, with a consistent upward trajectory following the onset of the SARS-CoV-2 pandemic. Notably, the survey coverage has never exceeded 16% until 2021. The RR is comparable to that observed in both the 50-69 and 70-74 age groups, while the DR and PPV align with the values observed in the 50-69 cohorts.

In Figure 1 a breast screening participation rate is described according to the geographical area. Despite fluctuations we can note a substantial overlap among three areas with an increasing of response rate during 2021, with an average rise of 24.9%. In the same assessment we have also note an increasing of response rate since 2020 during which the response rate between countryside and mountains was 8.6%, while the rage increase to 11.8% during 2021.

Discussion

Screening programs are among the most cost-effective strategies in medicine and they represent a cornerstone in prevention (19). Since its introduction, breast cancer screening has provided a fundamental preventive tool resulting in a decrease of mortality linked to this neoplasia (20). Italian National Healthcare Service (SSN) develops it through several

Table 2 - Key performance indicators of Lombardy region breast-cancer screening program, 2016-2022, age group 70-74 years old.

	2016*	2017**	2018	2019	2020	2021	2022
Target population (n)	35,770	85,565	135,827	140,895	144,787	149,080	146,434
N. of invited subjects	17,456	48,169	133,120	115,964	64,326	110,130	130,835
Adjusted invitation coverage (%)	53.2	59.3	109.2	92.0	47.8	81.5	95.4
Examination coverage (%)	34.1	33.0	53.0	49.3	24.4	49.3	48.5
N. of screened women	12,183	28,216	71,981	69,517	35,304	73,563	71,089
Adjusted participation rate (%)	81.0	68.1	61.4	69.9	62.5	70.2	58.4
Recall rate (%)							
First screening	9.2	10.9	10.1	11.1	7.6	11.6	8.8
Subsequent	5.2	5.0	4.6	4.6	4.1	4.5	4.5
N. of screen-detected cancers	58	240	649	517	244	583	707
Detection rate (%)							
First screening	4.8	13.0	14.9	16.8	8.6	11.5	20.0
Subsequent	4.9	8.4	8.8	7.1	6.9	7.8	9.5
Positive predictive value (%)							
First screening	5.3	12.0	14.8	15.2	11.3	10.0	21.3
Subsequent	9.4	16.6	18.8	15.4	16.7	17.3	21.5

*For 2016, data is available only for two ATS, ** For 2017, data is available only for 6 ATS

Table 3 - Key performance indicators of Lombardy region breast-cancer screening program, 2016-2022, age group 45-49 years old

	2016*	2017**	2018***	2019	2020	2021	2022
Target population (n)	35,570	15,383	57,026	190,912	214,885	201,998	197,941
N. of invited subjects	7,073	971	1,201	57,852	50,731	72,956	177,646
Adjusted invitation coverage (%)	19.64	6.59	2.17	32.04	24.06	36.81	90.09
Examination coverage (%)	9.52	5.60	1.90	15.82	11.66	20.25	47.81
N. of screened women	3,385	861	1,082	30,199	25,060	40,896	94631
Adjusted participation rate (%)	59.6	91.1	92.9	62.5	56.3	61.6	58.7
Recall rate (%)							
First screening	3.3	12.3	10.3	11.4	11.3	11.8	11.3
Subsequent	9.5	7.5	4.9	7.5	7.5	6.8	6.4
N. of screen-detected cancers	13	3	5	106	68	122	274
Detection rate (%)							
First screening	3.5	4.2	4.3	3.6	2.7	3.2	3.2
Subsequent	8.2	0	7.0	3.0	2.7	2.6	1.8
Positive predictive value (%)							
First screening	10.4	3.4	4.1	3.2	2.4	2.7	2.9
Subsequent	8.7	0	14.3	4.0	3.6	3.8	2.8

*For 2016, data are available only for two ATS, ** For 2017, data are available only for 6 ATS, *** For 2018, data are available only for 4 ATS

Regional Healthcare Services (SSR) involved in decision policies making such as screening age range. Our analysis has been performed on the experience of Lombardy SSR between 2016 and 2022 (21). Lombardy is the most populated Italian region with close to 10 million inhabitants and with the sixth lowest average age close to 46 years (22).

To assess the overall effectiveness of breast cancer

screening programmes we focused on organizational and clinical results, such as the ratio of invited women, adherence and cancer diagnosis by stage. Firstly, we analyzed the invited patient ratio and their adherence to the screening program.

The analysis considered three population cohorts: 45-49, 50-69 and 70-74 years. The adjusted coverage showed a significant difference between the cohorts,

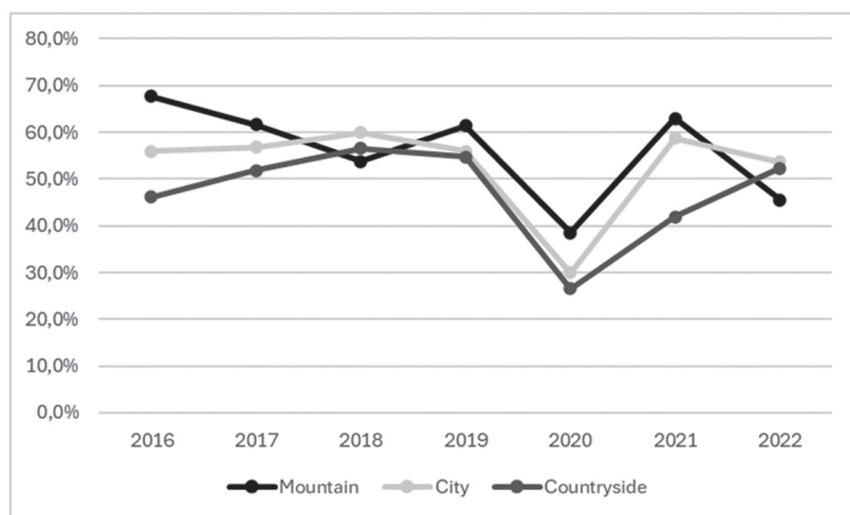


Figure 1 - Clusterized breast screening response rate in Lombardy region 2016-2022 (50-69 y.o. cohort)

which can be partly explained by the different timing of the screening programme introduction and partly by the age difference. Indeed, age is reported as a factor influencing adherence to cancer screening campaigns in the literature, with increased adherence in younger age groups.

At the same time, the mean responder rate of close to 56% emphasizes a sore point, the screening test refusal or hesitancy. Indeed, despite the importance of screening programs to cut down the breast cancer mortality rate, different studies all around the world show a lower adherence to mammography screening (5,23-26). It's interesting to note that adherence increasing in 2021 overcoming the pre-pandemic level, as a response to COVID-19 and the disclosure about the importance of prevention.

In this context, the potential psychological impact of COVID-19 pandemic on public attention to preventive health measures may be a crucial factor in the observed increase in adherence to such measures. Indeed, some studies suggest that the pandemic has influenced the uptake of preventive health interventions (27-29). This evidence lends support to the hypothesis that the observed increase in adherence rates since 2021, which has resulted in even higher rates than during the pandemic period, may be attributable to a shift in perception towards viewing screening interventions as a crucial tool for protecting health.

In addition, the time-frame analysis has highlighted another interesting point; the COVID-19 pandemic has affected the screening program probably through the temporal disruption of the healthcare system schedule, but the adherence remained about the same, close to 55%, and below the average of the European high-income nations, even though screening age targets are different (30). Indeed, despite a dizzying fall of invitation ratio dropping from 90% to 53% which shows the consequence of the pandemic with the interruption of emergency and non-urgent paths of care, especially during the first month of the pandemic, data on temporary trend confirm a lower attention towards these preventive campaigns.

At the same time, in order to assess the influence of healthcare network and spreading among region, our team has performed a partition of Lombardy ATSs by reclassifying them into three areas based on population and healthcare network features.

This study is one of the first in the literature to identify the influence of the territory or the organization of a healthcare system on patient adherence to a screening campaign, rather than socio-economic factors. Notably, a greater range

was observed in the years 2016, 2020, and 2021. The observed differences in adherence rates between the three areas, particularly in 2016 and 2021, could be attributed to the transition of the regional healthcare system in 2015. This involved the reorganization of territorial prevention networks and the resumption of cancer screening activities following the end of the COVID-19 pandemic. Regarding the resumption, the faster rise in rates in certain territorial areas may be due to the presence of large centres that performed most screening tests before the pandemic, compared to areas with a dense network of providers. Many patients may have delayed joining the campaign due to difficulties or complexities in reaching the test site. This is because screening services have been diverted to large hubs to ensure the provision of basic services in territorial networks.

Considering the diagnostic elements, the analysis has highlighted two elements. The first one is, as for the invitation, the effect of the COVID-19 pandemic on cancer detection rates. The comparison between invitation decreases (40.98%) and cancer detection decreases (46.38%) shows a difference close to 5%. Due to our experience and several studies performed on different cancer screening, such as cervical cancer, we can assume that one potential explanation for this phenomenon is that women who adhere to a healthier lifestyle are also more careful about preventive health activities, including participation in cancer screening programmes (31,32). Moreover, the disruption of healthcare systems caused by the COVID-19 pandemic could have exacerbated this trend.

At the same time, the loss of data from the aforementioned ATS, although confined to one ATS and therefore not involving the entire Lombardy region, could offer an additional partial explanation for the diminished detection rate that was observed during the course of 2022. It is important to note that, despite the potential repercussions of the data loss, the reliability of the study's findings appears to remain unaffected. This observation is particularly salient in the context of the outcomes derived from regional screening initiatives. The only result of the study in which this issue has the potential to compromise the reliability pertains to the comparison between the countryside, the city and the mountains. This is due to the fact that the ATS damaged by the attack is predominantly present in one of these areas.

The second one is the decreased trend in benign neoplasms surgery, which could be partially explained by the advancement in diagnostic techniques and a change in the approach towards benign lesions (33).

This approach has changed radically the view of breast cancer interventions and increased the necessity of early diagnosis, underlining the importance of breast cancer screening. Indeed, despite a higher identification rate increasing the incidence of breast cancer, implementing organized population-based screening programs could lead to early detection of malignancy in its first stage, therefore, decreasing mortality as described in several studies (34-40).

Limitations

Cancer screening is one of the most important instruments in preventive medicine and its importance is underlined by the malignancy detection rate that supports early operations to avoid cancer evolution and mortality. Despite more than 20 years of breast cancer screening programs, the adherence in Lombardy region remains low, under 60%. On this regard a study that tried to provide a comprehensive analysis on screening program data and potential explanation for its variation represents a cornerstone. The main limitation of this study is the absence of literature to support this reading framework about the psychological influence of COVID-19 on adhesion. The second one is the short-term follow-up based only on 2021 data that may not reflect a real mindset change but only a specific timeframe due for instance to the 2020 examination skipping. So, this original article could be considered as a first step to a more extensive analysis that could be considered a post-pandemic long-term follow-up to assess the change in breast screening program organization and adherence.

Conclusions

Despite the effects of the COVID-19 pandemic on the healthcare system and the temporary disruption of screening programs, screening program empowerment is essential to provide a widespread organization. The pandemic affects not only the organization and the functions of the healthcare systems, but also the adhesion: in other words, it can begin to show an increase compared to the pre-pandemic percentage.

The rise of post-pandemic adherence calls attention to the fact that during the pandemic the avoidance or delay in accepting the screening practices is probably caused by fear or discomfort; the following reaction to such sentiments could be used to increase screening programs participation and, in a longer run, to radically rethink the organization.

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Riassunto

Regione Lombardia: sette anni di screening del seno prima, durante e dopo la pandemia di SARS-CoV-2

Background. Il tumore mammario rappresenta la tipologia di neoplasia più frequente nel genere femminile responsabile di 685.000 morti ogni anno. I programmi di screening rappresentano a tal proposito uno degli strumenti di intervento più efficaci in ambito di prevenzione neoplastica. Scopo dello studio è quindi quello di analizzare e descrivere i key performance indicators (KPIs) dei programmi di screening lombardi dal 2016 al 2022.

Disegno dello studio. Studio descrittivo di analisi temporale.

Metodi. Sono stati analizzati i dati relativi alle campagne di screening suddivisi per singola provincia, per fascia di età convocata per lo screening e per anno di campagna. Per ogni campagna sono stati analizzati dati relativi alla popolazione soggetta a screening e dati relativi al tasso di cancri identificati nel corso della campagna.

Risultati. Per le tre fasce di età si può osservare una sostanziale sovrapposizione di tasi di chiamata e di adesione alle campagne, con valori stabili tra il 2016 e il 2019, seguiti da un'importante diminuzione nella campagna 2020 associabile all'impatto che il covid ha avuto sulle attività di prevenzione come campagne di screening oncologico. I dati del 2021 e 2022 mostrano una ripresa di adesione e di chiamata, in particolare nella fascia di età 45-49 anni, che mostra un incremento di circa il 300% del tasso di chiamata tra il 2021 e il 2020. Inoltre, la classificazione delle provincie in province urbane, montuose e rurali mostra una sovrapposizione dei tassi di adesione tra le tre aree nei vari anni.

Conclusioni. Nonostante l'esistenza di campagne di screening mammografico da oltre 20 anni i tassi di adesione in regione Lombardia rimangono al di sotto degli obiettivi dello Europe's Beating Cancer Plan. A tal proposito, le variazioni osservati in particolare in occasione della pandemia da Covid-19 e nel periodo post pandemico rappresentano un elemento da cui partire, ripensando l'organizzazione delle campagne di screening, per aumentare l'adesione ed efficacia.

References

1. World Health Organization (WHO). Breast Cancer [Internet]. 2021. Available from: <https://www.who.int/news-room/>

fact-sheets/detail/breast-cancer [Last accessed: 2024 Nov 14].

2. Wilkinson L, Gathani T. Understanding breast cancer as a global health concern. *Br J Radiol.* 2022 Feb 1; **95**(1130):20211033. doi: 10.1259/bjr.20211033. Epub 2021 Dec 14. PMID: 34905391; PMCID: PMC8822551.
3. Associazione Italiana di Oncologia Medica (AIOM), Associazione Italiana Registri Tumori (AIRT), Fondazione AIOM, Osservatorio Nazionale Screening (ONS), PASSI (Progressi delle Aziende Sanitarie per la Salute in Italia), et al. *I numeri del cancro in Italia.* 2022.
4. Lauby-Secretan B, Scoccianti C, Loomis D, Benbrahim-Tallaa L, Bouvard V, Bianchini F, et al. Breast-Cancer Screening-Viewpoint of the IARC Working Group. *N Engl J Med.* 2015 Jun 11; **24**(372):2353-8. doi: 10.1056/NEJMsr1504363. Epub 2015 Jun 3. PMID: 26039523.
5. Coldman A, Phillips N, Wilson C, Decker K, Chiarelli AM, Brisson J, et al. Pan-Canadian study of mammography screening and mortality from breast cancer. *J Natl Cancer Inst.* 2014 Oct 1; **106**(11):261. doi: 10.1093/jnci/dju261. PMID: 25274578.
6. Australian Institute of Health and Welfare. *BreastScreen Australia monitoring report 2008-2009.* Canberra: Australian Institute of Health and Welfare; 2011.
7. Youlden DR, Cramb SM, Dunn NA, Muller JM, Pyke CM, Baade PD. The descriptive epidemiology of female breast cancer: an international comparison of screening, incidence, survival and mortality. *Cancer Epidemiol.* 2012 Jun; **36**(3):237-48. doi: 10.1016/j.canep.2012.02.007. Epub 2012 Mar 27. PMID: 22459198.
8. Njor S, Nyström L, Moss S, Paci E, Broeders M, Segnan N, et al. Breast cancer mortality in mammographic screening in Europe: A review of incidence-based mortality studies. *J Med Screen.* 2012 Sep; **19**(Suppl 1):33-41. doi: 10.1258/jms.2012.012080. PMID: 22972809.
9. Zielonke N, Kregting LM, Heijnsdijk EAM, Veerus P, Heinävaara S, McKee M, de Kok IMCM, et al. The potential of breast cancer screening in Europe. *Int J Cancer.* 2021 Jan 15; **148**(2):406-18. doi: 10.1002/ijc.33204. Epub 2020 Jul 30. PMID: 32683673; PMCID: PMC7754503.
10. Marmot MG, Altman DG, Cameron DA, Dewar JA, Thompson SG, Wilcox M. The benefits and harms of breast cancer screening: an independent review. *Br J Cancer.* 2013 Jun 11; **108**(11):2205-40. doi: 10.1038/bjc.2013.177. Epub 2013 Jun 6. PMID: 23744281; PMCID: PMC3693450.
11. National Healthcare System (NHS). NHS population screening: access and order leaflets [Internet]. 2018. Available from: <https://www.gov.uk/guidance/how-to-order-population-screening-leaflets> [Last accessed: 2024 Nov 14].
12. National Healthcare System (NHS). Breast screening: programme overview [Internet]. 2015. Available from: <https://www.gov.uk/guidance/breast-screening-programme-overview> [Last accessed: 2024 Nov 14].
13. European Commission. Screening ages and frequencies [Internet]. 2023. Available from: https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Cancer_screening_statistics [Last accessed: 2024 Nov 14].
14. Group of Chief Scientific Advisors, European Commission, Directorate-General for Research and Innovation. *Cancer screening in the European Union Independent Expert Report* [Internet]. Brussels; 2022.
15. Repubblica Italiana. Decreto del Presidente del Consiglio dei Ministri 12 gennaio 2017. Definizione e aggiornamento dei livelli essenziali di assistenza, di cui all'articolo 1, comma 7, del decreto legislativo 30 dicembre 1992, n. 502. GU Serie Generale n. 65 del 18 marzo 2017 (Suppl Ord n. 15). Available from: https://www.gazzettaufficiale.it/atto/serie_generale/caricaDettaglioAtto/originario?atto.dataPubblicazioneGazzetta=2017-03-18&atto.codiceRedazione=17A02015&elenco30giorni=false [Last accessed: 2024 Nov 14].
16. Regione Lombardia. Decreto della Direzione Generale Welfare 3 aprile 2017, n. 3711. Aggiornamento fasce eta' target dei programmi di screening oncologici per la prevenzione del tumore della mammella e del colon retto. Available from: <https://www.regione.lombardia.it/wps/portal/istituzionale/HP/DettaglioServizio/servizi-e-informazioni/enti-e-operatori/sistema-welfare/promozione-della-salute/screening-prevenzione-tumori/ddg2017-3711-aggiornamento-fasce-eta-screening> [Last accessed: 2024 Nov 14].
17. Battisti F, Falini P, Gorini G, Sassoli de Bianchi P, Armaroli P, Giubilato P, et al. Cancer screening programmes in Italy during the COVID-19 pandemic: an update of a nationwide survey on activity volumes and delayed diagnoses. *Ann Ist Super Sanita.* 2022 Jan-Mar; **58**(1):16-24. doi: 10.4415/ANN_22_01_03. PMID: 35324470.
18. Battisti F, Mantellini P, Falini P, Ventura L, Giordano L, Saguatti G, et al. Key performance indicators of breast cancer screening programmes in Italy, 2011-2019. *Ann Ist Super Sanita.* 2022 Oct-Dec; **58**(4):244-253. doi: 10.4415/ANN_22_04_04. PMID: 36511195.
19. Iragorri N, Spackman E. Assessing the value of screening tools: reviewing the challenges and opportunities of cost-effectiveness analysis. *Public Health Rev.* 2018 Jul 13; **39**:17. doi: 10.1186/s40985-018-0093-8. PMID: 30009081; PMCID: PMC6043991.
20. Ministero della Salute. *Screening per il cancro del seno* [Internet]. 2023. Available from: <https://www.salute.gov.it/portale/tumori/detttaglioContenutiTumori.jsp?lingua=italiano&id=5542&area=tumori&menu=screening> [Last accessed: 2024 Nov 14].
21. Regione Lombardia. Legge Regionale 30 dicembre 2009, n. 33. Testo unico delle leggi regionali in materia di sanità. BURL n. 52 del 31 dicembre 2009 (3° Suppl Ord). Available from: <https://normelombardia.consiglio.regione.lombardia.it/normelombardia/Accessibile/main.aspx?idoc=lr002009123000033&view=showdoc> [Last accessed: 2024 Nov 14].
22. Istituto Nazionale di Statistica (ISTAT). 2023. Indicatori Demografici. Available from: http://dati.istat.it/Index.aspx?DataSetCode=DCIS_INDDEMOG1# [Last accessed: 2024 Nov 14].
23. Australian Institute of Health and Welfare. *Breast Screen Australia monitoring report 2006-2007 and 2007-2008*

(full publication; 21/7/2010 edition); 2006. Available from: <https://www.aihw.gov.au/getmedia/3a4594c3-1a9b-4fcb-9d1b-5be1eeaa9011/11751.pdf?v=20230605165037&inline=true> [Last accessed: 2024 Nov 14].

- 24. Loewen OK, Sandila N, Shen-Tu G, Vena JE, Yang H, Patterson K, et al. Patterns and predictors of adherence to breast cancer screening recommendations in Alberta's Tomorrow Project. *Prev Med Rep.* 2022 Nov 15; **30**:102056. doi: 10.1016/j.pmedr.2022.102056. PMID: 36531110; PMCID: PMC9747638.
- 25. Israel Cancer Association (ICA). Breast Cancer [Internet]. 2021. Available from: https://en.cancer.org.il/template_e/default.aspx?PageId=7749 [Last accessed: 2024 Nov 14].
- 26. Genovese C, Squeri R, Alessi V, Conti A, D'Amato S, Mazzitelli F, et al. Adherence to the three Italian screening in a sample of women (and men) in the Southern Italy. *Clin Ter.* 2021 Jan 1; **172**(1):e75-e79. doi: 10.7417/CT.2021.2287. PMID: 33346333.
- 27. Sarkar S, Kaur T, Ranjan P, Sahu A, Kumari A. Tools for the evaluation of the psychological impact of COVID-19: A practical guide for Family physicians and Primary Care Practitioners. *J Family Med Prim Care.* 2021 Apr; **10**(4):1503-1507. doi: 10.4103/jfmpc.jfmpc_2107_20. Epub 2021 Apr 29. PMID: 34123881; PMCID: PMC8144778.
- 28. Agorastos A, Tsamakis K, Solmi M, Correll CU, Bozikas VP. The need for holistic, longitudinal and comparable, real-time assessment of the emotional, behavioral and societal impact of the COVID-19 pandemic across nations. *Psychiatriki.* 2021 Apr 19; **32**(1):15-18. English, Greek, Modern. doi: 10.22365/jpsych.2021.010. Epub 2021 Mar 8. PMID: 33759804.
- 29. Perrone PM, Biganzoli G, Lecce M, Campagnoli EM, Castrofino A, Cinnirella A, et al. Influenza Vaccination Campaign during the COVID-19 Pandemic: The Experience of a Research and Teaching Hospital in Milan. *Int J Environ Res Public Health.* 2021 May 30; **18**(11):5874. doi: 10.3390/ijerph18115874. PMID: 34070763; PMCID: PMC8198860.
- 30. Altobelli E, Rapacchietta L, Angeletti PM, Barbante L, Profeta FV, Fagnano R. Breast cancer screening programmes across the WHO European region: Differences among countries based on national income level. *Int J Environ Res Public Health.* 2017 Apr 23; **14**(4):452. doi: 10.3390/ijerph14040452. PMID: 28441745; PMCID: PMC5409652.
- 31. Petkeviciene J, Ivanauskienė R, Klumbienė J. Sociodemographic and lifestyle determinants of non-attendance for cervical cancer screening in Lithuania, 2006–2014. *Public Health.* 2018 Mar; **156**:79-86. doi: 10.1016/j.puhe.2017.12.014. Epub 2018 Feb 3. PMID: 29408192.
- 32. Richard A, Rohrmann S, Schmid SM, Tirri BF, Huang DJ, Güth U, et al. Lifestyle and health-related predictors of cervical cancer screening attendance in a Swiss population-based study. *Cancer Epidemiol.* 2015 Dec 1; **39**(6):870-6. doi: 10.1016/j.canep.2015.09.009. Epub 2015 Nov 9. PMID: 26651449.
- 33. Kumar P, Kumar S, Baruah CC. Breast cancer management. *Biomed Pharmacother.* 2013 Oct; **67**(8):685-6. doi: 10.1016/j.bioph.2013.06.010. Epub 2013 Jul 10. PMID: 23906758.
- 34. Welch HG, Prorok PC, O'Malley AJ, Kramer BS. Breast-Cancer Tumor Size, Overdiagnosis, and Mammography Screening Effectiveness. *N Engl J Med.* 2016 Oct 13; **375**(15):1438-1447. doi: 10.1056/NEJMoa1600249. PMID: 27732805.
- 35. Møller MH, Lousdal ML, Kristiansen IS, Størvring H. Effect of organized mammography screening on breast cancer mortality: A population-based cohort study in Norway. *Int J Cancer.* 2019 Feb 15; **144**(4):697-706. doi: 10.1002/ijc.31832. Epub 2018 Oct 22. PMID: 30144028.
- 36. Niell BL, Freer PE, Weinfurtner RJ, Arleo EK, Drukteinis JS. Screening for Breast Cancer. *Radiol Clin North Am.* 2017 Nov; **55**(6):1145-1162. doi: 10.1016/j.rcl.2017.06.004. PMID: 28991557.
- 37. Monticciolo DL, Newell MS, Moy L, Niell B, Monsees B, Sickles EA. Breast Cancer Screening in Women at Higher-Than-Average Risk: Recommendations From the ACR. *J Am Coll Radiol.* 2018 Mar; **15**(3 Pt A):408-414. doi: 10.1016/j.jacr.2017.11.034. Epub 2018 Jan 19. PMID: 29371086.
- 38. Cooper K, Siefert A, Weinreb J. Skills Beyond the Reading Room: Training in Innovation and Collaboration at a Radiology Hackathon. *J Am Coll Radiol.* 2018 Mar; **15**(3 Pt A):466-468. doi: 10.1016/j.jacr.2017.11.034. Epub 2018 Jan 19. PMID: 29371086.
- 39. Guiberteau MJ, Oates ME. Counterpoint: Nuclear Medicine's Decline: Radiology Is the Solution, Not the Problem. *J Am Coll Radiol.* 2018 Mar; **15**(3 Pt A):387-389. doi: 10.1016/j.jacr.2017.11.029. PMID: 29502650.
- 40. Kovacs MD, Sheafor DH, Thacker PG, Hardie AD, Costello P. Metrix Matrix: A Cloud-Based System for Tracking Non-Relative Value Unit Value-Added Work Metrics. *J Am Coll Radiol.* 2018 Mar; **15**(3 Pt A):415-421. doi: 10.1016/j.jacr.2017.10.028. Epub 2017 Dec 24. PMID: 29279292.