

BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open

Understanding Linkage to Biopsy and Treatment for Breast Cancer after a High-risk Tele-Mammography Result in Peru: A Mixed-Methods Study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-050457
Article Type:	Original research
Date Submitted by the Author:	04-Mar-2021
Complete List of Authors:	Errea, Renato; Harvard Medical School, Department of Global Health and Social Medicine Garcia, Patricia; Universidad Peruana Cayetano Heredia, School of Public Health Pace, Lydia; Brigham and Women's Hospital Department of Medicine, Division of Women's Health Galea, Jerome; University of South Florida, School of Social Work and College of Public Health Franke, Molly F.; Harvard Medical School, Department of Global Health and Social Medicine
Keywords:	Breast tumours < ONCOLOGY, Breast imaging < RADIOLOGY & IMAGING, Telemedicine < BIOTECHNOLOGY & BIOINFORMATICS

SCHOLARONE™
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

1
2
3 **Understanding Linkage to Biopsy and Treatment for Breast Cancer after a High-risk Tele-**
4
5 **Mammography Result in Peru: A Mixed-Methods Study**
6
7

8 *Renato A. Errea, Patricia J. García, Lydia E. Pace, Jerome T. Galea, Molly F. Franke*
9

10
11
12
13
14 *Renato A. Errea**. Department of Global Health and Social Medicine, Harvard Medical School,
15
16 Boston, United States of America
17

18
19
20 *Patricia J. Garcia*. School of Public Health, Universidad Peruana Cayetano Heredia, Lima, Peru.
21

22
23 *Lydia E. Pace***, Division of Women's Health, Department of Medicine, Brigham and Women's
24
25 Hospital, Boston, United States of America
26

27
28 *Jerome T. Galea***. School of Social Work & College of Public Health. University of South
29
30 Florida, Tampa, United States of America
31

32
33 *Molly F. Franke*. Department of Global Health and Social Medicine, Harvard Medical School,
34
35 Boston, United States of America
36

37
38 *corresponding author: renato.errea@gmail.com; 641 Huntington Avenue, Boston, MA, 02115,
39
40 USA.
41

42
43 **contributed equally to this paper
44

45
46 **Word count:** 4310 (including the 'article summary')
47
48
49
50
51
52
53
54
55

ABSTRACT

Objectives: This mixed-method study aimed to understand the effectiveness of linkage to biopsy and treatment in women with a high-risk mammography result (BI-RADS 4-5) in the national tele-mammography program and to explore women's experiences during this process.

Setting: Quantitative component: we collected and linked health data from the tele-mammography reading center, the national public insurance, the national center for disease control and the national referral cancer center. Qualitative component: we interviewed participants from 4 different provinces of the country representing diverse social and geographical backgrounds.

Participants: Quantitative: data from all women who underwent tele-mammography between July 2017 and September 2018 and had high-risk results (BI-RADS 4-5) were collected. Qualitative: in-depth interviews with women with a high-risk tele-mammography result, healthcare providers and administrators.

Outcomes measures: Quantitative: we determined biopsy and treatment linkage rates and delays. Qualitative: we explored factors explaining non-linkage and delays.

Results: Of 126 women with high-risk results, 48.4% had documentation of biopsy, and 37.5% experienced a >45-day delay in obtaining it. Of 51 women with breast cancer diagnosis, 86.4% had evidence of treatment initiation, but 69.2% initiated treatment >45 days after biopsy. Travelling to major cities for care, breast cancer misconceptions, and administrative factors impeded timely, continuous care for breast cancer

1
2
3 **Conclusions:** Strengthened breast cancer care capacity outside the capital city, improved
4 dissemination of guidelines among providers, enhanced patient education, standardized referral
5 pathways and ensured financial support for travel expenses are required to secure linkage to the
6 breast cancer care continuum. Robust tracking and information systems are needed to evaluate
7 the program's performance.
8
9
10
11
12
13

14
15
16
17
18 **Key words:** breast cancer; mammography; linkage to care; delays; Peru
19
20

21 **Article summary**

22 ***Main findings***

- 23 • This study evaluated the linkage to biopsy and treatment in the Ministry of
24 Health Tele-mammography Program.
- 25 • Delays in biopsy or treatment initiation and non-linkage to breast cancer care
26 were explained by centralization of services in the capital city, policy and
27 program implementation gaps, and insufficient patient education about breast
28 cancer.
29
30
31
32

33 ***Strengths and the study***

- 34 • This study is among the first to evaluate linkage to biopsy and treatment for
35 breast cancer after high-risk mammography results in a middle-income country.
- 36 • This study is an exhaustive evaluation that used both quantitative and qualitative
37 research methods to comprehend the program's situation in different
38 geographical settings in Peru.
39
40
41
42

43 ***Limitations of the study***

- 44 • The lack of integration of the health information systems of the different
45 Ministry of Health components related to the Tele-mammography Program
46 challenged data collection and may have caused underestimation of the
47 percentage of women who obtained care.
48
49
50
51
52
53

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

INTRODUCTION

Breast cancer is the most commonly diagnosed cancer among women and the leading cause of cancer-related deaths worldwide.[1] To date, mammography screening is the only early detection method that has been proven to reduce mortality due to breast cancer.[2] Pooled results from randomized trials in the U.S, Canada, and Europe, show a 19% reduction in breast cancer mortality associated with mammography screening.[3] Currently, the World Health Organization (WHO) supports organized, population-based mammography screening as an essential tool for the control of breast cancer.[2]

For mammography screening to reduce breast cancer mortality, timely diagnosis and effective treatment must follow.[4] Cancer care is complex and requires coordination across multiple medical specialists, as well as adequate healthcare facilities and equipment.[5] Thus, patients in low- and middle-income countries (LMIC), where less than 5% of the necessary resources for cancer diagnosis and treatment are available,[6] may face the greatest difficulties securing care. Suboptimal diagnosis and treatment rates and delays could undermine the effectiveness of a screening program in reducing breast cancer mortality.

In 2017, the Peru Ministry of Health (MOH) launched a free telemedicine-based mammography program targeting women living outside of the major metropolitan area of Lima and receiving government-subsidized health insurance. The program aimed to circumvent the lack of radiologists in the provinces by digitally transferring mammography images to Lima, the nation's capital, for review. We examined rates of and time to biopsy and breast cancer treatment initiation after a high-risk tele-mammography result among women participating in

1
2
3 this national program and sought to understand women's experiences seeking diagnostic and
4
5 treatment services.
6
7
8
9

10 11 **METHODS**

12 13 **Study setting**

14
15
16 In Peru, individuals living in poverty receive government-subsidized insurance, known as the
17 Comprehensive Health Insurance (SIS). In 2012, breast cancer care (diagnosis, treatment, and
18 palliative services) was added to the SIS health package;[7] however, most services remain
19 centralized in Lima, where they are provided by the National Institute of Neoplastic Diseases
20 (INEN).[8] Outside Lima, two regional cancer institutes and some general hospitals offer cancer
21 services on a varied and limited basis. When services are not available at one of the general
22 hospitals, patients are referred to the regional cancer institute or to INEN.
23
24
25
26
27
28
29
30
31

32
33 Peru's MOH tele-mammography program is the primary mammography provider among SIS
34 recipients and as of September 2018, 14 hospitals in 11 regions participated in the program. At
35 these hospitals, the cancer program staff conduct mammography testing, result reporting, follow-
36 up, and referrals. Asymptomatic women aged 50 to 69 years old are invited for screening
37 through routine clinical visits or community outreach activities. Symptomatic women may be
38 referred for a diagnostic mammogram. Digital images are transferred securely via the internet to
39 a reading center in Lima, where trained radiologists provide a result within a few days.
40
41
42
43
44
45
46
47
48

49 Following international guidelines, individuals with a Breast Imaging Reporting and Data
50 System (BI-RADS) result of 4 or 5 are supposed to be referred for biopsy.[9] If cancer is
51 diagnosed, treatment is planned, including referrals, as needed.
52
53
54
55

Study design

We conducted a mixed-methods study with a concurrent design.[10] We described the frequency and time required for biopsy and treatment initiation, and qualitatively explored the factors impeding and facilitating care.

Study population

Quantitative component

We conducted a retrospective review of data collected from all women aged ≥ 18 years with SIS insurance, who underwent a tele-mammography through the MOH program between July 2017 and September 2018 and obtained a high-risk result.

Qualitative component

We used purposeful sampling to identify and interview 32 key stakeholders comprised of women with a high-risk tele-mammography result, healthcare providers (cancer program nurses and midwives, and physicians from the hospital oncology services), hospital program coordinators supervising the program, and current or former staff of the MOH directly involved in health policy and supervision of cancer activities, nationally. We included women known to have experienced barriers to obtaining care (as identified by the cancer program staff) and women who obtained care more easily. Informants came from eight cities, including Lima, and represented the country's three geographical regions: (coast, highlands, and rainforest).

Key procedures

Quantitative component

Data sources: Tele-mammography results and basic demographic information were obtained from the tele-mammography reading center in Lima (Villa El Salvador Hospital). Because there was no national database for tracking patients along the breast cancer continuum of care, person-data on biopsy and treatment were extracted from three independent data sources using the national identification number of each subject: SIS electronic databases, the National Cancer Surveillance registry of Peru's Center for Control of Diseases (CDC), and INEN medical electronic and paper records. Access to these data sources was requested to the corresponding institutions. These data sources include diagnostic procedures, biopsy results and treatments. Data from SIS, CDC, and INEN were available through December 31st, 2018; November 1st, 2019; and January 15th, 2020; respectively. Thus, each woman was followed for a minimum of 90 days and a maximum of 470 days following mammography. (Figure 1)

Outcomes: A high-risk tele-mammography result was defined as a BI-RADS result of 4 or 5.[11] The biopsy rate was defined as the proportion of women with a high-risk tele-mammography result who had evidence of a breast biopsy documented in the available data sources. The treatment initiation rate was defined as the proportion of women with confirmed breast cancer who had evidence of initiating chemotherapy, surgery, radiation, or hormonal therapy.

We calculated the time to biopsy and treatment initiation among those who secured these services. Adapting definitions from a consensus statement,[12] we defined the diagnosis interval as the time from tele-mammography result to biopsy result, the treatment interval as the time from biopsy result to treatment initiation, and the health system interval as time from tele-

1
2
3 mammography result to treatment initiation. For each interval, we calculated the proportion of
4
5 women who experienced delays. Because delays >90 days from breast cancer symptom
6
7 discovery to treatment initiation correlate with advanced stage at diagnosis and worse
8
9 survival,[13, 14] we defined a health system delay as a health system interval >90 days, and
10
11 diagnosis and treatment delays as >45 days. We calculated the frequency of women with
12
13 suboptimal care, defined as the presence of biopsy or treatment delay or the absence of biopsy or
14
15 treatment in spite of indication.
16
17
18
19
20
21
22

23 Qualitative component

24
25
26 *Data collection:* We conducted individual, in-depth interviews using semi-structured interview
27
28 guides to explore the barriers and facilitators to biopsy or treatment initiation. For women with a
29
30 high-risk tele-mammography, topics included the experience of pursuing and following referral
31
32 for care; strategies for overcoming difficulties in seeking care; and recommendations for
33
34 improvement. Interviews with healthcare providers and administrators covered how breast
35
36 cancer care is administered and delivered; program strengths and weaknesses; and
37
38 recommendations for improvement. The first author (RE) conducted face-to-face interviews in
39
40 Spanish (local language and RE's native language). Interviews lasted approximately 50 minutes
41
42 and were audio-recorded and transcribed verbatim.
43
44
45
46
47
48
49

50 Data analysis

51 52 53 Quantitative component

1
2
3 Data was cleaned thoroughly by RAE using Stata v14 and supervised by MFF. We reported
4
5 descriptive statistics and analyzed data using Stata v14. We examined time intervals to biopsy
6
7 and treatment both as continuous variables and also as binary variables to identify the proportion
8
9 of women experiencing delays in care.
10
11
12
13
14
15

16 Qualitative component

17
18 We conducted content analysis on the transcripts uploaded to Dedoose.[15] A subset of
19
20 interviews was open coded using short descriptive labels from which the first codebook draft was
21
22 constructed. The draft codebook was piloted in a separate subset of interviews; codes were
23
24 added, eliminated, or merged to create the final version used to code the dataset. The coded data
25
26 were inductively analyzed to identify key themes related to the barriers and facilitators for
27
28 obtaining a biopsy or initiating treatment. Using an iterative approach, the draft themes were
29
30 revised, resulting in a set of final themes. Illustrative quotes for each theme were extracted and
31
32 translated into English.
33
34
35
36
37
38
39
40

41 Patient and public involvement

42
43 Patients were not involved in the development of the research question or in the design,
44
45 recruitment or conduction of the study. Personnel from the Ministry of Health were involved in
46
47 study design and recruitment. Results will be disseminated among the Ministry of Health staff.
48
49
50
51
52
53
54
55

Ethical considerations

The study protocol and instruments were approved by Institutional Review Boards from Harvard Medical School, Cayetano Heredia Peruvian University, INEN, and Villa El Salvador Hospital. For the quantitative component, the informed consent requirement was waived. Participants in qualitative interviews provided written consent. Women with high-risk mammography results participating in the interviews received 6 USD for time and transportation compensation.

Role of the funding sources

The funding sources did not play any role in the study design; in the collection, analysis, and interpretation of the data; in writing of the report; nor in the decision to submit the paper for publication. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

RESULTS

Quantitative findings

Biopsy and treatment initiation rates and delays

From July 1st, 2017 to September 30th, 2018, 6899 tele-mammography tests were conducted through the MOH services. Of these, 147 women had a high-risk mammography result. After the exclusion of 21 individuals with data discrepancies or who did not meet the inclusion criteria

(Figure 2), 126 women were included for analysis. Their mean age was 53.3 years (standard deviation: 11.3).

We found evidence of biopsy in 62/126 (48.4%) women (Figure 2). Of these, biopsy result dates were available in 48, of whom 18 (37.5%) experienced a diagnosis delay (median diagnosis interval = 39.5 days [IQR= 5.5-65; range= 7-263]) (Table 1). Among the 62 women with evidence of biopsy, 49 had data on where the procedure was performed, and in 32 (65.3%) it took place in a different region from where they lived.

Table 1. Time intervals and delays between mammography, biopsy and treatment initiation among 126 women with a high-risk tele-mammography result who obtained this care

Time interval	Median days (IQR; range)	Delay n (%)
From tele-mammography result to biopsy result (n=48, N=62)	39.5 (25.5-65; 7-263)	18 (37.5)
From biopsy result to treatment initiation (n=39, N=44)	65.3 (32-118; 8-416)	27 (69.2)
From tele-mammography result to treatment initiation (n=44, N=44)	109.5 (69.5-168; 10-442)	29 (65.9)

N= total number of women who completed the corresponding step
n= number of women with dates available

Of the 62 women who had a biopsy, 51 were diagnosed with breast cancer, four had a benign condition, and seven did not have a result in her medical record. Of those diagnosed, we found evidence that 44/51 (86.3%) initiated treatment. Of these, the dates of the biopsy results and treatment initiation were available in 39, of whom 27 (69.2%) experienced a treatment delay (median treatment interval = 65.3 days [IQR= 32-118; range= 8-416]) (Table 1). Among the 44 women with evidence of treatment, data about the treatment hospital was missing for one

1
2
3 individual; of the 43 remaining, 35 (81.4%) initiated treatment in a different region than where
4 she lived. Health system delays were observed in 29/44 (65.9%) women (median health system
5 interval = 109.5 days [IQR= 69.5-168; range= 10-442]) (Table 1). Excluding 14 individuals with
6 missing dates, 104/112 (92.4%) women appeared to have received suboptimal care: 35 with a
7 biopsy or treatment delay and 69 with no evidence of biopsy or treatment initiation.
8
9
10
11
12
13
14
15
16
17

18 **Qualitative findings**

19 **Study population**

20
21 We interviewed 32 people: 13 women with a high-risk tele-mammography result, 13 healthcare
22 providers, three hospital program coordinators, and three policymakers. Participants represented
23 the different geographic areas of the country (the coast, the Andean highlands, and the
24 Amazonian rainforest).
25
26
27
28
29
30
31
32
33
34
35
36

37 **Findings**

38
39 Undergoing biopsy and initiating breast cancer treatment was impeded by several factors
40 clustering around three primary themes: A) the toll of getting care in major cities following
41 referrals, B) patients' misconceptions and access to information, and C) administrative and
42 operational barriers. Some of these factors primarily affected the diagnosis interval, others
43 influenced mainly the treatment interval, while others impacted both intervals. This relationship is
44 illustrated in Figure 3. Although scarce, a few facilitators were identified and are detailed in a
45 fourth theme, D) facilitators.
46
47
48
49
50
51
52
53
54
55

1
2
3
4
5
6 *Theme A: The toll of getting care in major cities following referrals*
7

8
9 Insufficient financial resources and support for transportation, accommodation, and food
10

11 Referral to a hospital in a major city at some point during follow-up was inevitable for almost all
12 patients living outside of Lima. Informants agreed that most women could not afford the
13 transportation, housing, and food expenses associated with residence outside of their hometowns.
14 Patients mentioned that they did not receive any subsidy from SIS for these expenses. Providers
15 and administrators perceived these constraints as preventing patients from receiving care. (Table
16 2, quote #1)
17
18
19
20
21
22
23
24
25

26 Interviewees highlighted the need to find external sources of financial support. Sometimes
27 families organized fundraising activities. Other times, non-profit organizations, churches, or
28 local municipalities provided financial support for transportation or living expenses; however,
29 interviewees agreed that these resources were limited due to restricted budgets and prioritization
30 of other vulnerable populations such as pediatric patients. (Table 2, quote #2). The economic
31 burden of these expenses forced families to take out loans and/or sell assets (Table 2, quote #3).
32
33
34
35
36
37
38
39
40
41
42
43
44

45 Being away from family and friends' emotional support
46

47 Close relatives and friends were a vital source of motivation and emotional support as patients
48 sought breast cancer care. Patients noted that the presence of loved ones transmitted confidence.
49 Interviewees acknowledged that this accompaniment was essential, especially around the time of
50 diagnosis. (Table 2, quote #4)
51
52
53
54
55

When patients left their hometowns to reside in the cities, this support was frequently diminished. Patients described how the cost of travel and competing responsibilities prevented loved ones from accompanying them. Providers and administrators referred that the weakened support network put patients at risk of withdrawing from care. (Table 2, quote #5)

Table 2. Barriers and facilitators for obtaining a biopsy and initiating treatment after a high-risk tele-mammography result

Theme	Subtheme	Excerpts
A. The toll of getting care in major cities following referrals	Insufficient financial resources and support for transportation, accommodation, and food	Quote #1: <i>They have to assume the expenses; they have to. So, often, because of the little money that they have, they don't go [to the city].</i> [midwife, highlands]
		Quote #2: <i>There are some shelters here where patients can stay, but they have limited access for a group of patients; first the pediatric patients and then the rest.</i> [physician, Lima]
		Quote #3: <i>We sold some animals. On the farm, we had sheep, cattle, and we sold everything, even the land we had to sell, to save her. If we hadn't made those efforts, my wife wouldn't be alive now. We did it to save her.</i> [patient's husband, highlands]
	Being away from family and friends' emotional support	Quote #4 <i>Interviewer: How important do you think family support is during this time [before having the biopsy]? Interviewee: Well, you are desperate, you feel like dying, but they talk to you, they talk with you. They give you support, psychological support. It's as if they were saying, "Mom, you are not alone; you are with me".</i> [patient, highlands]
		Quote #5 <i>Interviewee: If they come from the provinces, they come alone. They can't come with all their family. Or they come to the first consult with a relative, and then they say things like "well, he is my husband, but he has to go back to my town to take care of my children." And they leave. That's the reality of the people who come from the provinces outside of Lima. Interviewer: How does it affect care? Interviewee: It affects care because the patient must think twice before continuing care. Either she abandons it or comes irregularly.</i> [physician, Lima]
	Challenges adjusting to and navigating the city	Quote #6 <i>The cultural shock [of going to the city] is very strong. They feel overwhelmed; sometimes so overwhelmed that they prefer to leave care and go back to their towns.</i> [physician, highlands]
B. Patients' misconceptions and access to information	Misconceptions about breast cancer manifestations and progression	Quote #7 <i>I did not give it too much importance because I did not have any pain. I thought that maybe they were wrong. I didn't give it importance, so I didn't do anything.</i> [patient, highlands]
		Quote #8 <i>Patients say that [having a biopsy] is worse, because when they prick you or take a piece of your breast that's when the cancer awakens. And that's why they don't want to have the biopsy.</i> [nurse, highlands]
	Misconceptions about the treatment	Quote #9 <i>When you tell someone she has breast cancer, the first thing they think of is that it is daño [a sort of witchcraft], so they go first to the shamans and later, if they continue feeling sick, they come back.</i> [program coordinator, rainforest]
	Misconceptions about the prognosis	Quote #10

		<i>Many times, I've heard that when you have cancer you have it until the end. You just have to wait for your death. Once you have it there is no cure. [patient, highlands]</i>
	Limited information provided about the disease	Quote #11 <i>I would have liked for them to explain it to me more thoroughly, perhaps that way I would have gone, it would have encouraged me. Because sometimes, when they explained to you well, you are conscientious and go. But if they give you a test result that only says get another test because the first test wasn't normal, you don't give it adequate importance. [...] They didn't say anything more than giving you a number, where I should go, and all of that. [patient, highlands].</i>
C. Administrative and operational barriers	Delays for obtaining appointments and tests	Quote #12 <i>Interviewer: What happened the day that you went to the hospital? How did it go?</i> <i>Interviewee: I went very early, very early, but the line was already long, and as I needed to work, I got fatigued and didn't go back. So, I haven't done the test. Nothing. I left it there. [patient, highlands]</i>
		Quote #13 <i>For these tests, they have to come one day and for these others another day. And that's how the time passes by. [...] So sometimes when they are told to do one more test they say "Miss, I've been there, three months have passed, and I haven't started treatment yet". [nurse, highlands]</i>
	Low awareness of the program or of its guidelines among providers	Quote #14 <i>We had a patient with BI-RADS 4 who needed a biopsy, but the closest hospital didn't have biopsy services. So, we coordinated to refer her to a regional cancer center. After a lot of insistence, they could transfer her to the regional cancer center, and it happens that when she arrives at the facility they ordered a repeat mammography. [policymaker, Lima]</i>
	Lack of standardized referral pathways	Quote #15 <i>Interviewer: Did they ask you if you wanted to go to [region X] instead of Lima?</i> <i>Interviewee: No, they didn't say anything. If I had known that in [region X] they had chemotherapy, I wouldn't have gone to Lima, because I didn't have enough money or someone to help me. If I knew they had it here, I would have stayed. [patient, coast]</i>
	Inconsistent tracking of patients	Quote #16 <i>Interviewer: What type of follow-up do you do here?</i> <i>Interviewee: Once they have a biopsy in the [local] hospital, and it comes back positive, they call the patient or her primary care center to inform her of the result. They talk with the patient to see what's best: to send her to [the regional hospital] or Lima [...]</i> <i>Interviewer: And what happens once they are referred?</i> <i>Interviewee: We don't do further follow-up. I'd be lying if I say we do. We don't do more follow-up. [program coordinator, coast]</i>
		Quote #17 <i>The systems are divorced; they are not integrated. So, you are taking mammography tests but there is not a structure that integrates the screening with the treatment or with the diagnosis. [policymaker, Lima]</i>
D. Facilitators	Having family or a friend living in the city	Quote #18 <i>They say: "I don't worry much about the stay, Miss, I have family there." The majority that wants to go to [a major city] is because they have family there. [midwife, coast]</i>
	Collaborative and family-inclusive explanation	Quote #19 <i>The psychologist has helped me a lot [...] The psychologist is part of your disease, [the psychologist] cheers you up. It is not only the doctor who helps, the psychologist too. [The psychologist] talks with you in a particular way and makes you understand. [patient, highlands]</i>
		Quote #20 <i>Interviewer: How do you convince them [to obtain a biopsy]?</i> <i>Interviewee: Taking your time and explaining kindly. Sometimes the patient accepts [undergoing biopsy], but the relative doesn't, so you need to explain it all to the family, too. [...] You need to explain to every one of them because in their way of living, all the family influences, and then they accept. [physician, highlands]</i>
Facilitated appointments	Quote #21 <i>Interviewer: How do patients from other regions get care here?</i> <i>Interviewee: They just come and get an appointment. Here in the oncology department, we have a system that we called 'unlimited appointments.' We give an appointment to everyone who arrives before 9:00 a.m.</i> <i>Interviewer: What day is the appointment?</i> <i>Interviewee: For the same day. So, they don't have to come back another day. [physician, highlands]</i>	

Challenges adjusting to and navigating the city

For some patients, residence in a metropolitan area represented a major cultural change and logistical challenges. Informants described how many patients pursuing care in the cities were accustomed to country life. Living in and navigating a new city, at times in a different language, was perceived by providers and program coordinators as a “cultural shock” for patients which interfered in their care. (Table 2, quote #6)

Theme B: Patients' misconceptions and access to information

Misconceptions about breast cancer manifestations and progression

Some misconceptions about how breast cancer manifests and progresses contributed to delays in pursuing a biopsy. For example, a high-risk mammography result was recognized as serious by some patients but denied by others in the absence of symptoms, preventing them from seeking further care. (Table 2, quote #7) Other patients felt that touching or manipulating the breast "awakens" the disease, preferring to "let it rest" instead of obtaining a biopsy. (Table 2, quote #8)

Misconceptions about treatment

Providers reported that women looked for therapies with herbs and shamans as their first treatment option. They felt that this caused disengagement from facility-based health care with women returning only when no improvement was seen with this traditional treatment, at which point symptoms had often worsened. (Table 2, quote #9)

Misconceptions about the prognosis

Prior experiences with breast cancer led some women to perceive the disease as a non-curable condition. Whether because they had heard about others' negative experiences with breast cancer or had personal experiences, many women expressed feeling that the ultimate outcome of breast cancer was certain death (Table 2, quote #10). This fatal conception of breast cancer made some women question the utility of treatment, creating delays for accepting care.

Limited information provided about breast cancer

Many patients noted the limited information about mammography findings, breast cancer treatment and prognosis communicated to them by the clinical team. Instead, they felt that communication was focused on conveying information about the next administrative steps. As some referred, a better explanation would have led to making good choices earlier. (Table 2, quote #11)

Theme C: Administrative and operational barriers

Delays in obtaining appointments and tests

Informants relayed difficulties in obtaining appointments. For example, in 'first come, first served' medical services, many had to arrive at the facility very early in the morning and wait in

1
2
3 long lines without the guarantee of an appointment that day. Some women expressed frustration
4
5 with this process, noting that it led them to discontinue seeking care. (Table 2, quote #12)
6
7

8 When appointments could be booked in advance, they were often scheduled for several weeks
9
10 later, with test results delayed up to a month or more. One nurse described a patient's onerous
11
12 experience trying to complete the tests requested (Table 2, quote #13).
13
14
15

16 17 18 19 Limited awareness of the program among providers 20

21
22 Not all physicians reported awareness of the MOH tele-mammography program. Those
23
24 unfamiliar with the program doubted the validity of mammography results (thinking that they
25
26 were reported by untrained radiologists) and usually ordered a second mammography at their
27
28 hospital. (Table 2, quote #14) In other cases, the cancer program's nurses and midwives wanted
29
30 to “double check” each abnormal tele-mammography result so they would order a breast
31
32 ultrasound before referring for biopsy, contrary to national guidelines. These extra procedures
33
34 contributed to delays and the administrative burdens on the patient.
35
36
37
38
39
40
41

42 Lack of standardized referral pathways 43

44
45 There is no formal standardized referral pathway for high-risk tele-mammography results. The
46
47 providers' choice of referral hospital, particularly for treatment, was usually based on his/her
48
49 perceptions of available services or quality of care. As noted by most informants, INEN was
50
51 often the hospital of choice. Policymakers agreed that this approach did not take advantage of the
52
53
54
55

resources available at closer regional hospitals. One woman's comment illustrated how this system failed to account for patients' convenience. (Table 2, quote #15)

Inconsistent tracking of patients

The follow-up of women did not occur uniformly along the continuum of care. While the cancer program staff closely followed patients who received care in the local hospital, program coordinators agreed that tracking patients in upper-level hospitals was less rigorous. (Table 2, quote #16)

The programmatic follow-up tool, created by the MOH to strengthen tracking activities, was not used consistently and scarcely monitored by the MOH officials. In addition, policymakers reported that tracking of patients through health information systems would not be possible due to a "divorce" between the MOH's and hospitals' digital data systems (Table 2, quote #17).

Theme D: Facilitators

Having family or a friend living in the city

Interviewees expressed that having a relative or a close friend living in the city where patients were referred facilitated access to care. When patients could stay with friends or family, it alleviated much of the financial hardship. (Table 2, quote #18) Also, patients felt secure in knowing that someone could help them navigate the city or take care of them once treatments started.

Collaborative and family-inclusive approaches to care

Addressing patients' concerns about breast cancer through a multidisciplinary approach was seen by providers as useful for improving the patient's understanding of the disease and for making prompt medical decisions. Collaborative work among clinicians, psychologists, and social workers facilitated communication around diagnosis and expectations for future care. Patients highlighted the benefit of receiving psychological support upon diagnosis (Table 2, quote #19), Providers emphasized that involving the family was necessary given its determinant role in health decision making. (Table 2, quote #20)

Facilitated appointments

Some hospitals and providers expedited appointments for their patients. In two hospitals, the medical appointments were scheduled within one day for patients coming from remote areas. In another, all patients arriving early were guaranteed to be seen that day. In other cases, providers coordinated appointments to reduce the administrative burden on the patients or leveraged their influence to secure a spot. These approaches, although not perfect, helped reduce appointment delays. (Table 2, quote #21)

DISCUSSION

We evaluated linkages to breast cancer diagnostic and treatment services in the largest national tele-mammography program in Peru. To our knowledge this is the first such study from a

1
2
3 middle-income country. In women with a high-risk tele-mammography result among whom
4
5 biopsy is indicated, we found evidence that biopsy was performed among fewer than half.
6
7 Among women with breast cancer, we found evidence of treatment initiation in 86□3%. Delays
8
9 in obtaining these services were common. Overall, the vast majority (92□4%) of women
10
11 experienced suboptimal care (delayed care or no evidence of linkage to care). Our quantitative
12
13 findings are complemented by qualitative evidence of substantial barriers to care. Through a
14
15 mixed-methods design, we elucidated the ways in which diagnosis and treatment services for
16
17 breast cancer were not easily accessible for women living in poverty throughout the country.
18
19 These included travel barriers, administrative obstacles and patients' misconceptions about breast
20
21 cancer.
22
23
24
25
26

27 In our study, many women with breast cancer did not have evidence of biopsy or treatment, and
28
29 centralization of cancer services in Lima and a few other major cities likely contributes to delays
30
31 and interruptions in care. Living outside Lima and/or in rural areas of the country has been
32
33 shown to place individuals with cancer at higher risk of discontinuing care.[16, 17]
34
35

36 Centralization of cancer care facilities has also been found to disproportionately affect
37
38 socioeconomically vulnerable populations and may contribute to persistent care disparities for
39
40 breast cancer care in LMIC.[18-20] In our study, although cancer services were offered free-of-
41
42 charge, patients lacked the means for traveling to obtain those services. According to the
43
44 National Cancer Control Plan, SIS should subsidy the costs for transportation and for staying at
45
46 the cities; however, this economic support was not received by any of the patients interviewed. A
47
48 recent study on cervical cancer in Peru highlighted the same policy-implementation gap in
49
50 women with cervical cancer.[21] Given that five in ten women in Peru live in poverty (<150
51
52 USD per month),[22] our finding that insufficient economic resources for the expenses
53
54
55
56
57
58
59
60

1
2
3 associated with centralized care in cities (e.g., transportation, accommodation, and food)
4
5 challenged care is not unexpected. Reducing inequalities for breast cancer care access in middle-
6
7 income countries must incorporate the existing free diagnostic and treatments services with
8
9 decentralization of these resources to bring them closer to those that need them.
10
11

12
13 Among women for whom we could confirm care, delays were common. Our finding that 65% of
14
15 women experienced a health system delay is consistent with reports from other LMIC, where
16
17 over 70% of patients start treatment three or more months after the first abnormal finding (a
18
19 high-risk screening mammography or symptoms discovery).[13] Long health system delays
20
21 leads to advanced disease stage, a known risk factor for death from breast cancer.[23] Efforts to
22
23 decrease delays would be expected to increase breast cancer survival rates.
24
25

26
27 Our results raise several opportunities to improve the outcomes of the tele-mammography
28
29 program by facilitating follow-up care for those with a positive mammography. For instance,
30
31 unorganized referrals and patient tracking could be improved by a monitoring and evaluation
32
33 plan along the entire care continuum.[24] Also, a unified health information system across the
34
35 different MOH hospitals could allow a more accurate, and even real-time patient follow-up.[25]
36
37
38 Low compliance to guidelines among the MOH's providers could be remedied by nationwide
39
40 campaigns to build awareness of the program, its processes and goals. Appointment systems
41
42 could be reconsidered to prioritize a patient-centered approach. Finally, multidisciplinary and
43
44 culturally-tailored patient education, incorporating family members or supporters as appropriate,
45
46 may correct misconceptions about breast cancer that contributed to delays. Overall, a real
47
48 comprehensive tele-mammography program should not be seen as a separate breast cancer
49
50 service but as part of the whole breast cancer continuum of care.
51
52
53
54

1
2
3
4
5
6 Evaluating breast cancer care using routinely collected data was challenging due to a lack of
7
8 integration of health information systems of the different MOH components that managed and
9
10 provided healthcare to the population subsidized by SIS. Although we used multiple national
11
12 data sources to capture care access through different pathways, due to varying levels of follow-
13
14 up and data completeness, we may have underestimated the proportion of women who obtained
15
16 care. Thus, the quantitative results presented here were our best intent to disentangle the current
17
18 health information puzzle existing in the public healthcare sector. Nonetheless, this study is a
19
20 comprehensive evaluation that used both quantitative and qualitative research techniques to
21
22 understand the situation in diverse geographical settings in Peru. Thus, this
23
24 study provides a close perspective of challenges in Peru, which may be broadly applicable to
25
26 other middle-income countries with similar resource levels and health systems.
27
28
29
30

31
32 The benefit of mammography screening can only be realized if women with abnormal findings
33
34 are successfully linked to high-quality and timely diagnostic and treatment services. Our study
35
36 underscores the need for strengthening the breast cancer diagnostic and treatment capacity of
37
38 regional hospitals outside Lima to remove barriers and facilitate access to timely comprehensive
39
40 breast cancer care. It also highlights the need for a strong patient education strategy and better
41
42 dissemination of the information about the program among providers nationwide. Finally, a
43
44 unified health information system is needed to allow better tracking of patients after the
45
46 mammography and along the breast cancer continuum of care. Ensuring timely linkage to
47
48 diagnosis and treatment for women with an abnormal result in the tele-mammography program
49
50
51 will be critical to securing the screening program's success.
52
53
54
55

Contributorship statement

RAE, PJG and MFF conceptualized the study. RAE collected the data and wrote the first draft of the article. MFF, PJG, LEP, JTG, helped to synthesize evidence, interpret results, and critically revise the manuscript. RAE secured funding for the study. All authors approved the final draft.

Competing interests

All authors declare no competing interests.

Data sharing statement

No additional data is available

Funding

This work was funded by Harvard Medical School's Master of Medical Sciences in Global Health Delivery of the Department of Global Health and Social Medicine, Rockefeller Center for Latin American Studies of Harvard, and Peru's National Program of Scholarships and Academic Credits (RJ-117-2017-MINEDU-VMGI-PRONABEC-OBPOST).

Acknowledgments

We are grateful to doctors Jose Cotrina, Willy Ramos, Mercedes Egues, Diego Venegas, Isabel Cotrina, Alcedo Jorges and Victor Palacios for their central role in data collection. We truly appreciate the contribution of all participants of the qualitative interviews.

REFERENCES

REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*2018;68(6):394–424.
2. World Health Organization. WHO position paper on mammography screening. https://www.who.int/cancer/publications/mammography_screening/en/ (accessed 06 Feb 2021)
3. Pace LE, Keating NL. A systematic assessment of benefits and risks to guide breast cancer screening decisions. *JAMA*2014;311(13):1327–35.
4. Berry DA, Cronin KA, Plevritis SK, et al. Effect of screening and adjuvant therapy on mortality from breast cancer. *N Engl J Med*2005;353:1784–92.
5. Harford J, Azavedo E, Fischietto M. Breast Health Global Initiative Healthcare Systems Panel. Guideline implementation for breast healthcare in low- and middle-income countries: breast healthcare program resource allocation. *Cancer*2008;113(Suppl 8):2282–96.
6. Jones L, Chilton JA, Hajek RA, et al. Between and within: international perspectives on cancer health disparities. *J Clin Oncol*2006;24:2204–08.

- 1
2
3 7. Supreme Decree: Declaran de interés nacional la atención integral del cáncer y
4 mejoramiento del acceso a los servicios oncológicos en el Perú y dictan otras medidas,
5 Government of Peru (2012)
6
7
- 8
9
10 8. Vidaurre T, Santos C, Gómez H, et al. Cancer in Peru 3: the implementation of the Plan
11 Esperanza and response to the imPACT Review. *Lancet Oncol*2017;18:e595–e606.
12
- 13
14 9. American Cancer Society. Breast Cancer Early Detection and Diagnosis.
15 <https://www.cancer.org/content/dam/CRC/PDF/Public/8579.00.pdf> (accessed 20 Jan
16 2020).
17
18
- 19
20
21 10. Creswell JW, Plano Clark VL. Designing and conducting mixed methods research. 3rd
22 ed. Thousand Oaks, CA: SAGE Publications 2017
23
- 24
25
26 11. D'Orsi CJ, Sickles EA, Mendelson EB, et al. ACR BI-RADS® Atlas, Breast Imaging
27 Reporting and Data System. 5th ed. Reston, VA, American College of Radiology 2013.
28
- 29
30
31 12. Weller D, Vedsted P, Rubin G, et al. The Aarhus Statement: improving design and
32 reporting of studies on early cancer diagnosis. *Br J Cancer*2012;106:1262–7
33
- 34
35
36 13. Unger-Saldaña K. Challenges to the early diagnosis and treatment of breast cancer in
37 developing countries. *World J Clin Oncol*2014;5(3):465–77.
38
- 39
40
41 14. Richards MA, Westcombe AM, Love SB, et al. Influence of delay on survival in patients
42 with breast cancer: a systematic review. *Lancet*1999;352(9159):1119–26.
43
- 44
45
46 15. Hsieh HF, Shannon SE. Three approaches to qualitative content analysis. *Qual Health
47 Res*2005;15:1277
48
- 49
50
51 16. Paz-Soldán VA, Bayer AM, Nussbaum L, et al. Structural barriers to screening for and
52 treatment of cervical cancer in Peru. *Reprod Health Matters*2012;20(40):49–58.
53
54
55

- 1
2
3 17. Vasquez L, Diaz R, Chavez S, et al. Factors associated with abandonment of therapy by
4
5 children diagnosed with solid tumors in Peru. *Pediatr Blood Cancer*2018;65:e27007
6
- 7
8 18. Stitzenberg KB, Meropol NJ. Trends in centralization of cancer surgery. *Ann Surg*
9
10 *Oncol*2010;17(11):2824–31
11
- 12
13 19. Lieberman-Cribbin W, Liu B, Leoncini E, et al. Temporal trends in centralization and
14
15 racial disparities in utilization of high-volumen hospitals for lung cancer surgery.
16
17 *Medicine (Baltimore)*2017;96(16):e6573.
18
- 19
20 20. Pinto JA, Pinillos L, Villareal-Garza C, et al. Barriers in Latin America for the
21
22 management of locally advanced breast cancer. *Ecancermedicalscience*2019 Jan;13:897.
23
24 <https://doi.org/10.3332/ecancer.2019.897> (accessed 6 Feb 2021)
25
- 26
27 21. Nevin PE, Garcia PJ, Blas MM, et al. Inequities in cervical cancer care in indigenous
28
29 Peruvian women. *Lancet Glob Health*2019;7(5):e556–e557
30
- 31
32 22. Instituto Peruano de Economía. La pobreza extrema en el Perú aumentó en el 2019.
33
34 <https://www.ipe.org.pe/portal/la-pobreza-extrema-en-el-peru-aumento-en-el-2019/>
35
36 (accessed 20 Nov 2020).
37
- 38
39 23. Unger-Saldaña K, Miranda A, Zarco-Espinosa G, et al. Health system delay and its effect
40
41 on clinical stage of breast cancer: Multicenter Study. *Cancer*2015;121:2198–206.
42
- 43
44 24. Anttila A, Lönnberg S, Ponti A, et al. Towards better implementation of cancer screening
45
46 in Europe through improved monitoring and evaluation and greater engagement of cancer
47
48 registries. *Eur J Cancer*2015;51(2):241-251
49
- 50
51 25. Anand V, Sheley ME, Xu S, et al. Real time alert system: a disease management system
52
53 leveraging health information exchange. *Online J Public Health Inform*2012 Dec;4(3).
54
55 <https://doi.org/10/5210/ojphi.v4i3.4303> (accessed 6 Feb 2021)
56
57

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Figures' legends

Figure 1.

— Data available for SIS, CDC and INEN

- - - Data available for CDC and INEN

..... Data available for INEN

SIS, Comprehensive Health Insurance (government-based insurance); CDC, Center for Epidemiology and Control of Disease- National Cancer Surveillance registry; INEN, National Institute of Neoplastic Diseases

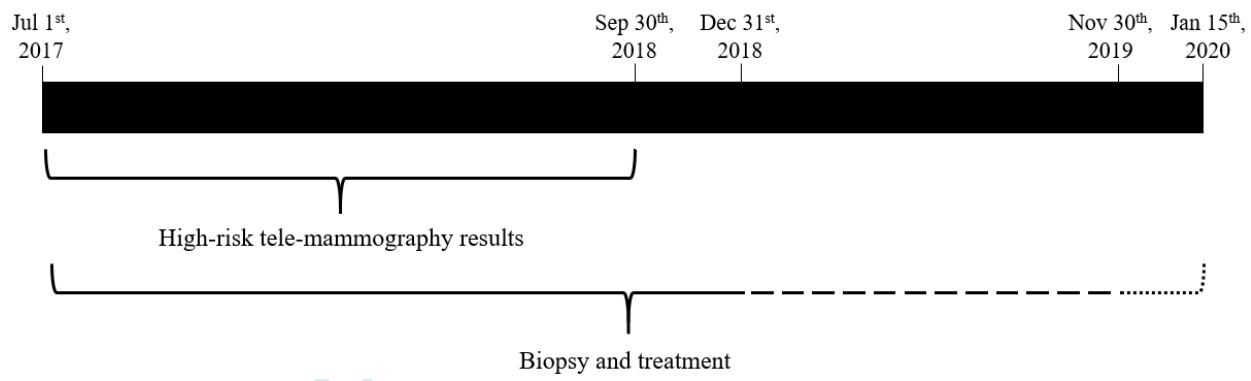
Figure 2.

ID, National Identification Number; SIS, Comprehensive Health Insurance (the government-subsidized insurance)

[I was requested to include a legend for Figure 3, but it does not have a legend, just a title which is already included in the Fig3 document]

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Figure 1. Availability of biopsy and treatment information from the three study data sources



or peer review only

Fig 2. Flowchart of biopsy and treatment initiation rates among women with a high-risk tele-mammography result

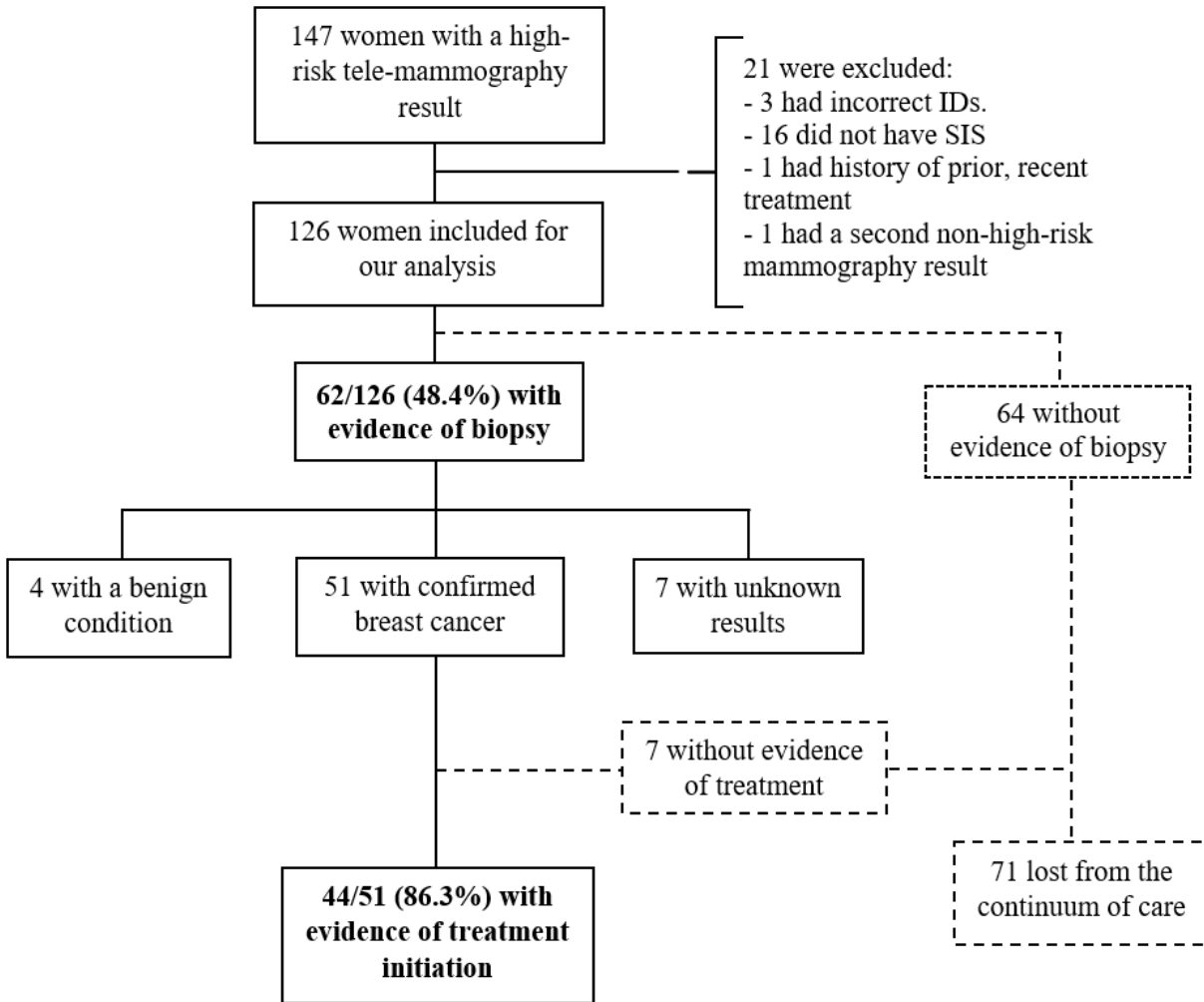
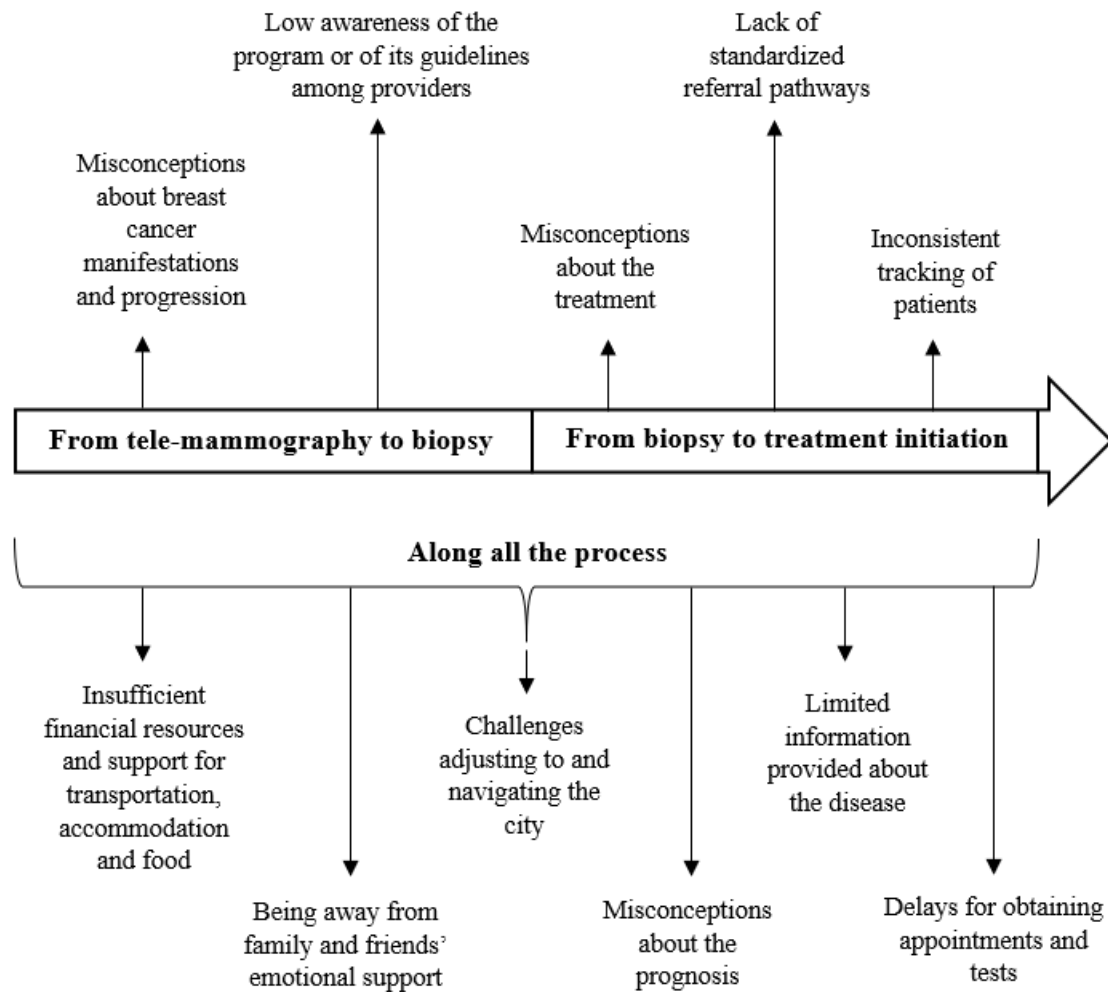


Fig 3. Barriers for obtaining a biopsy and initiating treatment and related affected intervals after obtaining a high-risk tele-mammography result



The RECORD statement – checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found		RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	1.1 Abstract, 'setting' section (page 2) 1.2 Abstract, 'Participants' section (page 2) 1.3 Abstract, 'Setting' section (page 2)
Introduction					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported			
Objectives	3	State specific objectives, including any prespecified hypotheses			
Methods					
Study Design	4	Present key elements of study design early in the paper			
Setting	5	Describe the setting, locations, and relevant dates, including			

		<p>periods of recruitment, exposure, follow-up, and data collection</p>			
<p>Participants</p>	<p>6</p>	<p><i>(a) Cohort study</i> - Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> - Give the eligibility criteria, and the sources and methods of selection of participants <i>(b) Cohort study</i> - For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> - For matched studies, give matching criteria and the number of controls per case</p>		<p>RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided.</p> <p>RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided.</p> <p>RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.</p>	<p>6.1. “Data sources” section (page 7)</p> <p>6.2. No validation studies were conducted.</p> <p>6.3. A graphic representation of the databases merge is included in Figure 1.</p>
<p>Variables</p>	<p>7</p>	<p>Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.</p>		<p>RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.</p>	<p>7.1. No confounders or effect modifiers were included. Exposures and outcomes are explained in the “outcomes” section (page 7)</p>
<p>Data sources/ measurement</p>	<p>8</p>	<p>For each variable of interest, give sources of data and details</p>			

		of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group			
Bias	9	Describe any efforts to address potential sources of bias			
Study size	10	Explain how the study size was arrived at			
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why			
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) <i>Cohort study</i> - If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> - If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> - If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses			
Data access and cleaning methods		..		RECORD 12.1: Authors should describe the extent to which the investigators had access to the database	12.1 'Data sources' section. (page 7)

				population used to create the study population. RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	12.2 “Data analysis’ section (quantitative component) (page 7)
Linkage		..		RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	12.3 “Data analysis’ section (quantitative component) (page 7)
Results					
Participants	13	(a) Report the numbers of individuals at each stage of the study (<i>e.g.</i> , numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram		RECORD 13.1: Describe in detail the selection of the persons included in the study (<i>i.e.</i> , study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	‘Biopsy and treatment initiation rates and delays’ section (page 10)
Descriptive data	14	(a) Give characteristics of study participants (<i>e.g.</i> , demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) <i>Cohort study</i> - summarise follow-up time (<i>e.g.</i> , average and total amount)			

1 2 3 4 5 6 7 8 9 10 11	Outcome data	15	<p><i>Cohort study</i> - Report numbers of outcome events or summary measures over time</p> <p><i>Case-control study</i> - Report numbers in each exposure category, or summary measures of exposure</p> <p><i>Cross-sectional study</i> - Report numbers of outcome events or summary measures</p>			
12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27	Main results	16	<p>(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included</p> <p>(b) Report category boundaries when continuous variables were categorized</p> <p>(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period</p>			
28 29 30 31 32	Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses			
33	Discussion					
34 35	Key results	18	Summarise key results with reference to study objectives			
36 37 38 39 40 41 42 43 44	Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias		RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over	‘Discussion’ section (5 th paragraph).

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

				time, as they pertain to the study being reported.	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence			
Generalisability	21	Discuss the generalisability (external validity) of the study results			
Other Information					
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based			
Accessibility of protocol, raw data, and programming code		..		RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	See 'Data sharing statement' (page 24)

*Reference: Benchimol EI, Smeeth L, Guttman A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.

*Checklist is protected under Creative Commons Attribution ([CC BY](https://creativecommons.org/licenses/by/4.0/)) license.

BMJ Open

Understanding Linkage to Biopsy and Treatment for Breast Cancer after a High-risk Tele-Mammography Result in Peru: A Mixed-Methods Study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-050457.R1
Article Type:	Original research
Date Submitted by the Author:	03-Nov-2021
Complete List of Authors:	Errea, Renato; Harvard Medical School, Department of Global Health and Social Medicine Garcia, Patricia; Universidad Peruana Cayetano Heredia, School of Public Health Pace, Lydia; Brigham and Women's Hospital Department of Medicine, Division of Women's Health Galea, Jerome; University of South Florida, School of Social Work and College of Public Health; Harvard Medical School, Department of Global Health and Social Medicine Franke, Molly F.; Harvard Medical School, Department of Global Health and Social Medicine
Primary Subject Heading:	Global health
Secondary Subject Heading:	Oncology
Keywords:	Breast tumours < ONCOLOGY, Breast imaging < RADIOLOGY & IMAGING, Gynaecological oncology < ONCOLOGY

SCHOLARONE™
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

1
2
3 1 **Understanding Linkage to Biopsy and Treatment for Breast Cancer after a High-risk Tele-**
4
5 2 **Mammography Result in Peru: A Mixed-Methods Study**
6
7

8 3 *Renato A. Errea, Patricia J. García, Lydia E. Pace, Jerome T. Galea, Molly F. Franke*
9

10
11 4
12
13
14 5 *Renato A. Errea**. Department of Global Health and Social Medicine, Harvard Medical School,
15
16 6 Boston, United States of America
17
18

19
20 7 *Patricia J. Garcia*. School of Public Health, Universidad Peruana Cayetano Heredia, Lima, Peru.
21

22
23 8 *Lydia E. Pace***, Division of Women's Health, Department of Medicine, Brigham and Women's
24
25 9 Hospital, Boston, United States of America
26
27

28 10 *Jerome T. Galea***. School of Social Work & College of Public Health. University of South
29
30 11 Florida, Tampa, United States of America; Department of Global Health and Social Medicine,
31
32 12 Harvard Medical School, Boston, United States of America
33
34

35 13 *Molly F. Franke*. Department of Global Health and Social Medicine, Harvard Medical School,
36
37 14 Boston, United States of America
38
39

40
41 15 *corresponding author: renato.errea@gmail.com; 641 Huntington Avenue, Boston, MA, 02115,
42
43 16 USA.
44
45

46 17 **contributed equally to this paper
47
48

49 18 **Word count: 5024**
50
51

52 19
53
54
55 20

1
2
3 **21 ABSTRACT**
4
5

6 **22 Objectives:** This mixed-method study aimed to understand the effectiveness of linkage to biopsy
7
8 **23** and treatment in women with a high-risk mammography result (BI-RADS 4 and5) in the national
9
10 **24** tele-mammography program and to explore women's experiences during this process.

11
12
13 **25 Setting:** Quantitative component: we collected and linked health data from the tele-
14
15 **26** mammography reading center, the national public insurance, the national center for disease
16
17 **27** control, and the national referral cancer center. Qualitative component: we interviewed
18
19 **28** participants from different provinces of the country representing diverse social and geographical
20
21 **29** backgrounds.

22
23
24
25 **30 Participants:** Quantitative: women who underwent tele-mammography between July 2017 and
26
27 **31** September 2018 and had high-risk results (BI-RADS 4-5) were collected. Qualitative: women
28
29 **32** with a high-risk tele-mammography result, healthcare providers, and administrators.

30
31
32
33 **33 Outcomes measures:** Quantitative: we determined biopsy and treatment linkage rates and
34
35 **34** delays. Qualitative: we explored barriers and facilitators for obtaining a biopsy and initiating
36
37 **35** treatment.

38
39
40
41 **36 Results:** Of 126 women with high-risk results, 48.4% had documentation of biopsy, and 37.5%
42
43 **37** experienced a >45-day interval prior to biopsy. Of 51 women diagnosed with breast cancer,
44
45 **38** 86.4% had evidence of treatment initiation, but 69.2% initiated treatment >45 days after biopsy.
46
47 **39** Travelling to major cities for care, administrative factors, and breast cancer misconceptions,
48
49 **40** among other factors, impeded timely, continuous care for breast cancer. A multidisciplinary and
50
51 **41** culturally tailored patient education facilitated understanding of the disease and prompt decision
52
53 **42** making about subsequent medical care.
54
55

1
2
3 43 **Conclusions:** Strengthened breast cancer care capacity outside the capital city, standardized
4
5 44 referral pathways, ensured financial support for travel expenses, and enhanced patient education
6
7 45 are required to secure linkage to the breast cancer care continuum. Robust information systems
8
9 46 are needed to track patients and to evaluate the program's performance.
10
11
12

13 47 **Key words:** breast cancer; mammography; linkage to care; delays; Peru
14
15
16 48

Article summary

Strengths of the study

- This is among the very limited studies evaluating linkages to care after high-risk mammography results in a middle-income country.
- This study is an exhaustive evaluation that used both quantitative and qualitative research methods.
- This study collected user's the perspectives from different geographical settings in Peru

Limitations of the study

- The lack of integration of the health information systems in the Ministry of Health may have caused underestimation of the percentage of women who obtained care.
- The follow-up time for women who obtained a high-risk tele-mammography result was heterogenous

1
2
3 53
4
5 54
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

55 INTRODUCTION

56 Breast cancer is the most commonly diagnosed cancer among women and the leading cause of
57 cancer-related deaths worldwide.[1] To date, mammography screening is the only early detection
58 method that has been proven to reduce breast cancer mortality.[2] Pooled results from
59 randomized trials in the U.S, Canada, and Europe, show a 19% reduction in breast cancer
60 mortality associated with mammography screening.[3] Currently, the World Health Organization
61 (WHO) supports organized, population-based mammography screening as an essential tool for
62 the control of breast cancer.[2]

63 For mammography screening to reduce breast cancer mortality, timely diagnosis and effective
64 treatment must follow.[4] Cancer diagnosis and treatment are complex and requires coordination
65 across multiple medical specialists, as well as adequate healthcare facilities and equipment.[5]
66 Thus, patients in low- and middle-income countries (LMIC), where less than 5% of the necessary
67 resources for cancer diagnosis and treatment are available,[6] may face great difficulties securing
68 care. Suboptimal diagnosis and treatment rates and delays could undermine the effectiveness of a
69 screening program in reducing breast cancer mortality.

70 In 2017, the Peru Ministry of Health (MOH) launched a free telemedicine-based mammography
71 program targeting women living outside of the major metropolitan area of Lima and receiving
72 government-subsidized health insurance. The program aimed to circumvent the lack of
73 radiologists in the provinces by digitally transferring mammography images to Lima, the
74 nation's capital, for review. We examined rates of and time to biopsy and breast cancer
75 treatment initiation after a high-risk tele-mammography result among women participating in

1
2
3 76 this national program and sought to understand women's experiences seeking diagnostic and
4
5 77 treatment services.
6
7

8 78
9

11 79 **METHODS**

13 80 **Study setting**

16 81 In Peru, individuals living in poverty receive government-subsidized insurance, known as the
17
18 82 Comprehensive Health Insurance (SIS). In 2012, breast cancer care (diagnosis, treatment, and
19
20
21 83 palliative services) was added to the SIS health package;[7] however, most services remain
22
23 84 centralized in Lima, where they are provided by the National Institute of Neoplastic Diseases
24
25 85 (INEN).[8] Outside Lima, two regional cancer institutes and some general hospitals offer cancer
26
27
28 86 services on a varied and limited basis. When services are not available at one of the general
29
30 87 hospitals, patients are referred to the regional cancer institute or to INEN.
31
32

33 88 Peru's MOH tele-mammography program is the primary mammography provider among SIS
34
35 89 recipients and as of September 2018, 14 hospitals in 11 regions participated in the program. At
36
37
38 90 these hospitals, the cancer program staff conduct mammography testing, result reporting, follow-
39
40 91 up, and referrals. Asymptomatic women aged 50 to 69 years old are invited for screening
41
42 92 through routine clinical visits or community outreach activities. Symptomatic women may be
43
44 93 referred for a diagnostic mammogram. Digital images are transferred securely via the internet to
45
46
47 94 a reading center in Lima, where trained radiologists provide a result within a few days.
48
49 95 Following international guidelines, individuals with a Breast Imaging Reporting and Data
50
51 96 System (BI-RADS) result of 4 or 5 are supposed to be referred for biopsy.[9] If cancer is
52
53
54 97 diagnosed, treatment is planned, including referrals, as needed.
55

1
2
3 **98 Study design**
4
5

6 **99** We conducted a mixed-methods study with a concurrent design.[10] We described the frequency
7
8 **100** and time required for biopsy and treatment initiation, and qualitatively explored the factors
9
10
11 **101** impeding and facilitating care.
12

13
14 **102**

15
16 **103 Study population**
17

18
19 **104** Quantitative component
20

21
22 **105** We conducted a retrospective review of data collected from all women aged ≥ 18 years with SIS
23
24 **106** insurance, who had a tele-mammography through the MOH program between July 2017 and
25
26 **107** September 2018 and obtained a high-risk result.
27
28

29
30 **108**

31
32 **109** Qualitative component
33

34
35
36 **110** We used purposeful sampling to identify and interview 32 key stakeholders comprised of women
37
38 **111** with a high-risk tele-mammography result, healthcare providers (cancer program nurses and
39
40 **112** midwives, and physicians from the hospital oncology services), hospital program coordinators
41
42 **113** supervising the program, and current or former staff of the MOH directly involved in health
43
44 **114** policy and supervision of cancer activities, nationally. We included women known to have
45
46 **115** experienced barriers to obtaining care and women who obtained care more easily; all of them
47
48 **116** had undergone a mammography through the tele-mammography program. Potential participants
49
50 **117** were first identified by the tele-mammography program staff and provided a brief explanation of
51
52 **118** the research. After a first verbal acceptance, the research team visited them at their homes to
53
54
55

1
2
3 119 formally invite them to participate. To ensure we had perspectives from different part of the
4
5 120 country, informants from diverse geographical areas of the country were selected.
6
7

8 121
9

10 11 122 **Key procedures** 12

13 14 123 Quantitative component 15

16
17 124 *Data sources:* Tele-mammography results and basic demographic information were obtained
18
19 125 from the tele-mammography reading center in Lima (Villa El Salvador Hospital). Because there
20
21 126 was no national database for tracking patients along the breast cancer continuum of care, person-
22
23 127 data on biopsy and treatment were extracted from three independent data sources using the
24
25 128 national identification number of each subject: SIS electronic databases, the National Cancer
26
27 129 Surveillance registry of Peru's Center for Control of Diseases (CDC), and INEN medical
28
29 130 electronic and paper records. Access to these data sources was requested to the corresponding
30
31 131 institutions. These data sources include diagnostic procedures, biopsy results and treatments.
32
33 132 Data from SIS, CDC, and INEN were available through December 31st, 2018; November 1st,
34
35 133 2019; and January 15th, 2020; respectively. Thus, each woman was followed for a minimum of
36
37 134 90 days and a maximum of 470 days following mammography. (Figure 1)
38
39
40
41
42

43 135 *Outcomes:* A high-risk tele-mammography result was defined as a BI-RADS result of 4 or 5.[11]
44
45 136 The biopsy rate was defined as the proportion of women with a high-risk tele-mammography
46
47 137 result who had evidence of a breast biopsy documented in the available data sources. The
48
49 138 treatment initiation rate was defined as the proportion of women with confirmed breast cancer
50
51 139 who had evidence of initiating chemotherapy, surgery, radiation, or hormonal therapy.
52
53
54
55

1
2
3 140 We calculated the time to biopsy and treatment initiation among those who secured these
4
5 141 services. Adapting definitions from a consensus statement,[12] we defined the diagnosis interval
6
7 142 as the time from tele-mammography result to biopsy result, the treatment interval as the time
8
9 143 from biopsy result to treatment initiation, and the health system interval as time from tele-
10
11 144 mammography result to treatment initiation. For each interval, we calculated the proportion of
12
13 145 women that experienced delays. Because delays >90 days from breast cancer symptom discovery
14
15 146 to treatment initiation correlate with advanced stage at diagnosis and worse survival,[13, 14] we
16
17 147 defined a health system delay as a health system interval >90 days, and diagnosis and treatment
18
19 148 delays as >45 days. We calculated the frequency of women with suboptimal care, defined as the
20
21 149 presence of biopsy or treatment delay or the absence of biopsy or treatment despite the
22
23 150 indication.
24
25
26
27
28
29
30
31

32 152 Qualitative component

33
34
35 153 *Data collection:* We conducted individual, in-depth interviews using semi-structured interview
36
37 154 guides to explore the barriers and facilitators to biopsy or treatment initiation. For women with a
38
39 155 high-risk tele-mammography, topics included the experience of pursuing and following referral
40
41 156 for care; strategies for overcoming difficulties in seeking care; and recommendations for
42
43 157 improvement. Interviews with healthcare providers and administrators explored how breast
44
45 158 cancer care is administered and delivered; program strengths and weaknesses; and
46
47 159 recommendations for improvement. The first author (RE) conducted face-to-face interviews in
48
49 160 Spanish (local language and RE's native language). Interviews lasted approximately 50 minutes
50
51 161 and were audio-recorded and transcribed verbatim.
52
53
54
55

1
2
3 162
4
56 163 **Data analysis**
7
89 164 Quantitative component
10
11

12 165 Data was cleaned thoroughly by RAE using Stata v14 and supervised by MFF. We reported
13
14 166 descriptive statistics and analyzed data using Stata v14. We examined time intervals to biopsy
15
16 167 and treatment both as continuous variables and also as binary variables to identify the proportion
17
18 168 of women experiencing delays in care.
19
20
21

22 169

23
24
25 170 Qualitative component
26
27

28 171 We conducted content analysis on the transcripts uploaded to Dedoose.[15] A subset of
29
30 172 interviews was open coded using short descriptive labels from which the first codebook draft was
31
32 173 constructed. The draft codebook was piloted in a separate subset of interviews; codes were
33
34 174 added, eliminated, or merged to create the final version used to code the dataset. The coded data
35
36 175 were inductively analyzed to identify key themes related to the barriers and facilitators for
37
38 176 obtaining a biopsy or initiating treatment. Using an iterative approach, the draft themes were
39
40 177 revised, resulting in a set of final themes. Illustrative quotes for each theme were extracted and
41
42 178 translated into English.
43
44
45
46

47 179

48
49
50 180 **Patient and public involvement**
51
52
53
54
55

1
2
3 181 Patients were not involved in the development of the research question or in the design,
4
5 182 recruitment or conduction of the study. Personnel from the Ministry of Health were involved in
6
7 183 study design and recruitment. Results will be disseminated among the Ministry of Health staff.
8
9
10

11 184

14 185 **Ethical considerations**

16 186 The study protocol and instruments were approved by Institutional Review Boards from Harvard
17
18 187 Medical School (IRB19-0589), Cayetano Heredia Peruvian University (#104252), INEN (INEN
19
20 188 20-02), and Villa El Salvador Hospital (#01744-2019). For the quantitative component, the
21
22 189 informed consent requirement was waived. Participants in qualitative interviews provided
23
24 190 written consent. Women with high-risk mammography results participating in the interviews
25
26 191 received 6 USD for time and transportation compensation.
27
28
29
30

31 192

34 193 **Role of the funding sources**

36
37 194 The funding sources did not play any role in the study design; in the collection, analysis, and
38
39 195 interpretation of the data; in writing of the report; nor in the decision to submit the paper for
40
41 196 publication. The corresponding author had full access to all the data in the study and had final
42
43 197 responsibility for the decision to submit for publication.
44
45
46

47 198

50 199 **RESULTS**

53 200 **Quantitative findings**

201 Biopsy and treatment initiation rates and delays

202 From July 1st, 2017 to September 30th, 2018, 6899 tele-mammography tests were conducted
 203 through the MOH services. Of these, 147 (2.1%) women had a high-risk mammography result
 204 (72.8% with BI-RADS 4 and 27.2 with BI-RADS 5). After the exclusion of 21 individuals with
 205 data discrepancies or who did not meet the inclusion criteria (Figure 2), 126 women were
 206 included for analysis (71.4% with BI-RADS 4 and 28.6% with BI-RADS 5). Their mean age was
 207 53.3 years (standard deviation: 11.3).

208
 209 We found evidence of biopsy in 62/126 (48.4%) women (Figure 2). Of these, biopsy result dates
 210 were available in 48, of whom 18 (37.5%) experienced a diagnosis delay (median diagnosis
 211 interval = 39.5 days) (Table 1). Among the 62 women with evidence of biopsy, 49 had data on
 212 where the procedure was performed, and in 32 (65.3%) it took place in a different region from
 213 where they lived.

214
 215 **Table 1. Time intervals and delays between mammography, biopsy and treatment initiation among 126 women**
 216 **with a high-risk tele-mammography result who obtained this care**

Time interval	Median days (IQR; range)	Delay n (%)
From tele-mammography result to biopsy result (n=48, N=62)	39.5 (25.5-65; 7-263)	18 (37.5)
From biopsy result to treatment initiation (n=39, N=44)	65.3 (32-118; 8-416)	27 (69.2)
From tele-mammography result to treatment initiation (n=44, N=44)	109.5 (69.5-168; 10-442)	29 (65.9)

217 N= total number of women who completed the corresponding step

218 n= number of women with dates available

219

1
2
3 220 Of the 62 women who had a biopsy (67.7% with BI-RADS, 51 were diagnosed with breast
4
5 221 cancer, four had a benign condition, and seven did not have a result in their medical record. Of
6
7 222 the 35 women who had BI-RADS 4 mammography results and had a known biopsy result, 85%
8
9 223 were found to have breast cancer, while among the 20 women with BI-RADS 5 mammography
10
11 224 results and documented biopsy, 100% had breast cancer. Of those diagnosed with breast cancer,
12
13 225 we found evidence that 44/51 (86.3%) initiated treatment. Of these, the dates of the biopsy
14
15 226 results and treatment initiation were available in 39, of whom 27 (69.2%) experienced a
16
17 227 treatment delay (median treatment interval = 65.3 days) (Table 1). Among the 44 women with
18
19 228 evidence of treatment, data about the treatment hospital was missing for one individual; of the 43
20
21 229 remaining, 35 (81.4%) initiated treatment in a different region than where she lived. Health
22
23 230 system delays were observed in 29/44 (65.9%) women (median health system interval = 109.5
24
25 231 days) (Table 1). Excluding 14 individuals with missing dates, 104/112 (92.4%) women appeared
26
27 232 to have received suboptimal care.
28
29
30
31
32
33
34 233
35 234
36 235
37 236

236 **Qualitative findings**

237 **Study population**

238 We interviewed 32 people: 13 women with a high-risk tele-mammography result, 13 healthcare
239 providers, three hospital program coordinators, and three policymakers. See table 2 for details on
240 the geographic areas where informants belonged to.
241

242 **Table 2. Characteristics of the 32 in-depth interview participants**

243

	Patients	Providers	Program coordinators	Policymakers
Provenance				
<i>Lima (capital)</i>	-	4	-	3
<i>Coast (North)</i>	3	1	1	-
<i>Highlands (Center)</i>	3	2	1	-
<i>Highlands (South)</i>	4	4	-	-
<i>Rainforest (East)</i>	3	2	1	-

244

245

246

247

248 Findings

249 Undergoing biopsy and initiating breast cancer treatment was impeded by several factors
 250 clustering around three primary themes: A) the toll of getting care in major cities following
 251 referrals, B) patients' misconceptions and access to information, and C) administrative and
 252 operational barriers. Some of these factors primarily affected the diagnosis interval, others
 253 influenced mainly the treatment interval, while others impacted both intervals. This relationship is
 254 illustrated in Figure 3. Although scarce, a few facilitators were identified and are detailed in a
 255 fourth theme, D) facilitators.

256

257 *Theme A: The toll of getting care in major cities following referrals*

258 Insufficient financial resources and support for transportation, accommodation, and food

259 Referral to a hospital in a major city at some point during follow-up was inevitable for almost all
 260 patients living outside of Lima. Informants agreed that most women could not afford the
 261 transportation, housing, and food expenses associated with residence outside of their hometowns.
 262 Patients mentioned that they did not receive any subsidy from SIS for these expenses. Providers

263 and administrators perceived these constraints as preventing patients from receiving care. (Table
 264 3, quote #1)

265 Interviewees highlighted the need to find external sources of financial support. Sometimes
 266 families organized fundraising activities. Other times, non-profit organizations, churches, or
 267 local municipalities provided financial support for transportation or living expenses; however,
 268 interviewees agreed that these resources were limited due to restricted budgets and prioritization
 269 of other vulnerable populations such as pediatric patients. (Table 3, quote #2). The economic
 270 burden of these expenses forced families to take out loans and/or sell assets (Table 3, quote #3).

271

272 Being away from family and friends' emotional support

273 Close relatives and friends were a vital source of motivation and emotional support as patients
 274 sought breast cancer care. Patients noted that the presence of loved ones transmitted confidence.

275 Interviewees acknowledged that this accompaniment was essential, especially around the time of
 276 diagnosis. (Table 3, quote #4)

277 When patients left their hometowns to reside in the cities, this support was frequently
 278 diminished. Patients described how the cost of travel and competing responsibilities prevented
 279 loved ones from accompanying them. Providers and administrators referred that the weakened
 280 support network put patients at risk of withdrawing from care. (Table 3, quote #5)

281

282 **Table 3. Barriers and facilitators for obtaining a biopsy and initiating treatment after a high-risk tele-**
 283 **mammography result**

Theme	Subtheme	Excerpts
-------	----------	----------

A. The toll of getting care in major cities following referrals	Insufficient financial resources and support for transportation, accommodation, and food	<p>Quote #1: <i>They have to assume the expenses; they have to. So, often, because of the little money that they have, they don't go [to the city]. [midwife, highlands]</i></p> <p>Quote #2: <i>There are some shelters here where patients can stay, but they have limited access for a group of patients; first the pediatric patients and then the rest. [physician, Lima]</i></p> <p>Quote #3: <i>We sold some animals. On the farm, we had sheep, cattle, and we sold everything, even the land we had to sell, to save her. If we hadn't made those efforts, my wife wouldn't be alive now. We did it to save her. [patient's husband, highlands]</i></p>
	Being away from family and friends' emotional support	<p>Quote #4 <i>Interviewer: How important do you think family support is during this time [before having the biopsy]?</i> <i>Interviewee: Well, you are desperate, you feel like dying, but they talk to you, they talk with you. They give you support, psychological support. It's as if they were saying, "Mom, you are not alone; you are with me". [patient, highlands]</i></p> <p>Quote #5 <i>Interviewee: If they come from the provinces, they come alone. They can't come with all their family. Or they come to the first consult with a relative, and then they say things like "well, he is my husband, but he has to go back to my town to take care of my children." And they leave. That's the reality of the people who come from the provinces outside of Lima.</i> <i>Interviewer: How does it affect care?</i> <i>Interviewee: It affects care because the patient must think twice before continuing care. Either she abandons it or comes irregularly. [physician, Lima]</i></p>
	Challenges adjusting to and navigating the city	<p>Quote #6 <i>The cultural shock [of going to the city] is very strong. They feel overwhelmed; sometimes so overwhelmed that they prefer to leave care and go back to their towns. [physician, highlands]</i></p>
B. Patients' misconceptions and access to information	Misconceptions about breast cancer manifestations and progression	<p>Quote #7 <i>I did not give it too much importance because I did not have any pain. I thought that maybe they were wrong. I didn't give it importance, so I didn't do anything. [patient, highlands]</i></p> <p>Quote #8 <i>Patients say that [having a biopsy] is worse, because when they prick you or take a piece of your breast that's when the cancer awakens. And that's why they don't want to have the biopsy. [nurse, highlands]</i></p>
	Misconceptions about the treatment	<p>Quote #9 <i>When you tell someone she has breast cancer, the first thing they think of is that it is <i>daño</i> (a sort of witchcraft), so they go first to the shamans and later, if they continue feeling sick, they come back. [program coordinator, rainforest]</i></p>
	Misconceptions about the prognosis	<p>Quote #10 <i>Many times, I've heard that when you have cancer you have it until the end. You just have to wait for your death. Once you have it there is no cure. [patient, highlands]</i></p>
	Limited information provided about the disease	<p>Quote #11 <i>I would have liked for them to explain it to me more thoroughly, perhaps that way I would have gone, it would have encouraged me. Because sometimes, when they explained to you well, you are conscientious and go. But if they give you a test result that only says get another test because the first test wasn't normal, you don't give it adequate importance. [...] They didn't say anything more than giving you a number, where I should go, and all of that. [patient, highlands].</i></p>
	Delays for obtaining appointments and tests	<p>Quote #12 <i>Interviewer: What happened the day that you went to the hospital? How did it go?</i> <i>Interviewee: I went very early, very early, but the line was already long, and as I needed to work, I got fatigued and didn't go back. So, I haven't done the test. Nothing. I left it there. [patient, highlands]</i></p> <p>Quote #13 <i>For these tests, they have to come one day and for these others another day. And that's how the time passes by. [...]. So sometimes when they are told to do one more test they say "Miss, I've been there, three months have passed, and I haven't started treatment yet". [nurse, highlands]</i></p>

C. Administrative and operational barriers	Low awareness of the program or of its guidelines among providers	Quote #14 <i>We had a patient with BI-RADS 4 who needed a biopsy, but the closest hospital didn't have biopsy services. So, we coordinated to refer her to a regional cancer center. After a lot of insistence, they could transfer her to the regional cancer center, and it happens that when she arrives at the facility, they ordered a repeat mammography. [policymaker, Lima]</i>
	Lack of standardized referral pathways	Quote #15 <i>Interviewer: Did they ask you if you wanted to go to [region X] instead of Lima? Interviewee: No, they didn't say anything. If I had known that in [region X] they had chemotherapy, I wouldn't have gone to Lima, because I didn't have enough money or someone to help me. If I knew they had it here, I would have stayed. [patient, coast]</i>
	Inconsistent tracking of patients	Quote #16 <i>Interviewer: What type of follow-up do you do here? Interviewee: Once they have a biopsy in the [local] hospital, and it comes back positive, they call the patient or her primary care center to inform her of the result. They talk with the patient to see what's best: to send her to [the regional hospital] or Lima [...] Interviewer: And what happens once they are referred? Interviewee: We don't do further follow-up. I'd be lying if I say we do. We don't do more follow-up. [program coordinator, coast]</i>
		Quote #17 <i>The systems are divorced; they are not integrated. So, you are taking mammography tests but there is not a structure that integrates the screening with the treatment or with the diagnosis. [policymaker, Lima]</i>
D. Facilitators	Having family or a friend living in the city	Quote #18 <i>They say: "I don't worry much about the stay, Miss, I have family there." The majority that wants to go to [a major city] is because they have family there. [midwife, coast]</i>
	Collaborative and family-inclusive explanation	Quote #19 <i>The psychologist has helped me a lot [...] The psychologist is part of your disease, [the psychologist] cheers you up. It is not only the doctor who helps, the psychologist too. [The psychologist] talks with you in a particular way and makes you understand. [patient, highlands]</i>
		Quote #20 <i>Interviewer: How do you convince them [to obtain a biopsy]? Interviewee: Taking your time and explaining kindly. Sometimes the patient accepts [undergoing biopsy], but the relative doesn't, so you need to explain it all to the family, too. [...] You need to explain to every one of them because in their way of living, all the family influences, and then they accept. [physician, highlands]</i>
Facilitated appointments	Quote #21 <i>Interviewer: How do patients from other regions get care here? Interviewee: They just come and get an appointment. Here in the oncology department, we have a system that we called 'unlimited appointments.' We give an appointment to everyone who arrives before 9:00 a.m. Interviewer: What day is the appointment? Interviewee: For the same day. So, they don't have to come back another day. [physician, highlands]</i>	

284

285

286 Challenges adjusting to and navigating the city

287 For some patients, residence in a metropolitan area represented a major cultural change and
 288 logistical challenges. Informants described how many patients pursuing care in the cities were
 289 accustomed to country life. Living in and navigating a new city, at times in a different language,

1
2
3 290 was perceived by providers and program coordinators as a “cultural shock” for patients which
4
5 291 interfered in their care. (Table 3, quote #6)
6
7
8
9

10
11 292

12 293 *Theme B: Patients' misconceptions and access to information*

13
14 294 Misconceptions about breast cancer manifestations and progression

15
16
17 295 Some misconceptions about how breast cancer manifests and progresses contributed to delays in
18
19 296 pursuing a biopsy. For example, a high-risk mammography result was recognized as serious by
20
21 297 some patients but denied by others in the absence of symptoms, preventing them from seeking
22
23 298 further care. (Table 3, quote #7) Other patients felt that touching or manipulating the breast
24
25 299 "awakens" the disease, preferring to "let it rest" instead of obtaining a biopsy. (Table 3, quote #8)
26
27
28
29

30
31 300

32 301 Misconceptions about treatment

33
34
35 302 Providers reported that women looked for therapies with herbs and shamans as their first
36
37 303 treatment option. They felt that this caused disengagement from facility-based health care with
38
39 304 women returning only when no improvement was seen with this traditional treatment, at which
40
41 305 point symptoms had often worsened. (Table 3, quote #9)
42
43
44

45 306

46
47
48 307 Misconceptions about the prognosis

49
50
51 308 Prior experiences with breast cancer led some women to perceive the disease as a non-curable
52
53 309 condition. Whether because they had heard or seen others' fatal experiences with breast cancer,
54
55

1
2
3 310 many women expressed feeling that the ultimate outcome of breast cancer was certain death
4
5 311 (Table 3, quote #10). This conception of breast cancer made some women question the utility of
6
7 312 treatment, creating delays for accepting care.
8
9

10
11 313

12
13
14 314 Limited information provided about breast cancer

15
16 315 Many patients noted the limited information about mammography findings, breast cancer
17
18 316 treatment and prognosis communicated to them by the clinical team. Instead, they felt that
19
20 317 communication was focused on conveying information about the next administrative steps. As
21
22 318 some referred, a better explanation would have led to making good choices earlier. (Table 3,
23
24 319 quote #11)
25
26
27
28

29 320

30
31 321 *Theme C: Administrative and operational barriers*

32
33 322 Delays in obtaining appointments and tests

34
35 323 Informants relayed difficulties in obtaining appointments. For example, in “first come, first
36
37 324 served” medical services, many had to arrive at the facility very early in the morning and wait in
38
39 325 long lines without the guarantee of an appointment that day. Some women expressed frustration
40
41 326 with this process, noting that it led them to discontinue seeking care. (Table 3, quote #12)
42
43
44 327 When appointments could be booked in advance, they were often scheduled for several weeks
45
46 328 later, with test results delayed up to a month or more. One nurse described a patient’s onerous
47
48 329 experience trying to complete the tests requested (Table 3, quote #13).
49
50
51
52
53
54
55

1
2
3 330
4
56 331 Limited awareness of the program among providers
7
8

9 332 Not all physicians reported awareness of the MOH tele-mammography program. Those
10
11 333 unfamiliar with the program doubted the validity of mammography results (thinking that they
12
13 334 were reported by untrained radiologists) and usually ordered a second mammography at their
14
15 335 hospital. (Table 3, quote #14) In other cases, the cancer program's nurses and midwives wanted
16
17 336 to “double check” each abnormal tele-mammography result so they would order a breast
18
19 337 ultrasound before referring for biopsy, contrary to national guidelines. These extra procedures
20
21 338 contributed to delays and the administrative burdens on the patient.
22
23
24
25

26 339
27
2829 340 Lack of standardized referral pathways
30
31

32 341 There is no formal standardized referral pathway for high-risk tele-mammography results. The
33
34 342 providers' choice of referral hospital, particularly for treatment, was usually based on his/her
35
36 343 perceptions of available services or quality of care. As noted by most informants, INEN was
37
38 344 often the hospital of choice. Policymakers agreed that this approach did not take advantage of the
39
40 345 resources available at closer regional hospitals. One woman's comment illustrated how this
41
42 346 system failed to account for patients' convenience. (Table 3, quote #15)
43
44
45

46 347
47
4849 348 Inconsistent tracking of patients
50
51

52 349 The follow-up of women did not occur uniformly along the continuum of care. While the cancer
53
54 350 program staff closely followed patients who received care in the local hospital, program

1
2
3 351 coordinators agreed that tracking patients in upper-level hospitals was less rigorous. (Table 3,
4
5 352 quote #16)
6
7

8 353 The programmatic follow-up tool, created by the MOH to strengthen tracking activities, was not
9
10 354 used consistently and scarcely monitored by the MOH officials. In addition, policymakers
11
12 355 reported that tracking of patients through health information systems would not be possible due
13
14 356 to a “divorce” between the MOH’s and hospitals’ digital data systems (Table 3, quote #17).
15
16
17

18 357

19
20
21 358 *Theme D: Facilitators*
22

23
24 359 Having family or a friend living in the city
25
26

27 360 Interviewees expressed that having a relative or a close friend living in the city where patients
28
29 361 were referred facilitated access to care. When patients could stay with friends or family, it
30
31 362 alleviated much of the financial hardship. (Table 3, quote #18) Also, patients felt secure in
32
33 363 knowing that someone could help them navigate the city or take care of them once treatments
34
35 364 started.
36
37
38

39 365

40
41
42 366 Collaborative and family-inclusive approaches to care
43
44

45 367 Addressing patients' concerns about breast cancer through a multidisciplinary approach was seen
46
47 368 by providers as useful for improving the patient's understanding of the disease and for making
48
49 369 prompt medical decisions. Collaborative work among clinicians, psychologists, and social
50
51 370 workers facilitated communication around diagnosis and expectations for future care. Patients
52
53 371 highlighted the benefit of receiving psychological support upon diagnosis (Table 3, quote #19),
54
55

1
2
3 372 Providers emphasized that involving the family was necessary given its determinant role in
4
5 373 health decision making. (Table 3, quote #20)
6
7

8 374
9

10
11 375 Facilitated appointments
12

13
14 376 Some hospitals and providers expedited appointments for their patients. In two hospitals, the
15
16 377 medical appointments were scheduled within one day for patients coming from remote areas. In
17
18 378 another, all patients arriving early were guaranteed to be seen that day. In other cases, providers
19
20 379 coordinated appointments to reduce the administrative burden on the patients or leveraged their
21
22 380 influence to secure a spot. These approaches, although not perfect, helped reduce appointment
23
24 381 delays. (Table 3, quote #21)
25
26
27

28 382
29
30

31
32 383 **DISCUSSION**
33

34
35 384 We evaluated linkages to breast cancer diagnostic and treatment services in the largest national
36
37 385 tele-mammography program in Peru. This adds to the very limited body of literature examining
38
39 386 linkages to care among women undergoing breast cancer screening in a middle-income country.
40
41 387 Identifying health system requirements for rapid breast cancer diagnosis is a priority for the
42
43 388 World Health Organization's new Global Breast Cancer Initiative,[16] and our findings
44
45 389 contribute to understanding of important barriers and facilitators of timely diagnosis in Peru and
46
47 390 similar settings. In women with a high-risk tele-mammography result among whom biopsy is
48
49 391 indicated, we found evidence that biopsy was performed among fewer than half. Among women
50
51 392 with breast cancer, we found evidence of treatment initiation in 86.3%. Delays in obtaining these
52
53
54
55

1
2
3 393 services were common. Overall, the vast majority (92.4%) of women experienced suboptimal
4
5 394 care (delayed care or no evidence of linkage to care). Our quantitative findings are
6
7
8 395 complemented by qualitative evidence of substantial barriers to care. Through a mixed-methods
9
10 396 design, we elucidated the ways in which diagnosis and treatment services for breast cancer were
11
12 397 not easily accessible for women living in poverty throughout the country. These included travel
13
14
15 398 barriers, administrative obstacles, and patients' misconceptions about breast cancer.

16
17
18 399 In our study, many women with breast cancer did not have evidence of biopsy or treatment, and
19
20 400 centralization of cancer services in Lima and a few other major cities likely contributes to delays
21
22 401 and interruptions in care. Living outside Lima and/or in rural areas of the country has been
23
24
25 402 shown to place individuals with cancer at higher risk of discontinuing care.[17, 18]

26
27 403 Centralization of cancer care facilities has also been found to disproportionately affect
28
29 404 socioeconomically vulnerable populations and may contribute to persistent care disparities for
30
31 405 breast cancer care in LMIC.[19-21] In our study, although cancer services were offered free-of-
32
33
34 406 charge, patients lacked the means for traveling to obtain those services. According to the
35
36 407 National Cancer Control Plan, SIS should subsidize the costs for transportation and for staying in
37
38 408 the cities; however, this economic support was not received by any of the patients interviewed. A
39
40
41 409 recent study on cervical cancer in Peru highlighted the same policy-implementation gap in
42
43 410 women with cervical cancer.[22] Given that five in ten women in Peru live in poverty (<150
44
45 411 USD per month),[23] our finding that insufficient economic resources for the expenses
46
47
48 412 associated with centralized care in cities (e.g., transportation, accommodation, and food)
49
50 413 challenged care is not unexpected. Reducing inequalities for breast cancer care access in Peru
51
52 414 must incorporate the existing free diagnostic and treatments services with decentralization of
53
54
55 415 these resources to bring them closer to those that need them.

1
2
3 416 Among women for whom we could confirm care, delays were common. Our finding that 65% of
4
5 417 women experienced a health system delay is consistent with reports from other LMIC, where
6
7 418 over 70% of patients start treatment three or more months after the first abnormal finding (a
8
9 419 high-risk screening mammography or symptoms discovery).[13] This finding is also supported
10
11 420 by one local study reporting even longer health system delays (around 8 months), albeit under
12
13 421 different circumstances and using different definitions.[24] Long health system delays leads to
14
15 422 advanced disease stage, a known risk factor for death from breast cancer.[25] Efforts to decrease
16
17 423 delays would be expected to increase breast cancer survival rates.
18
19
20
21

22 424 The observed 2% prevalence of BI-RADS 4 and 5 results found in our study is comparable to
23
24 425 what would be expected for mammography screening.[26-28] And, while the percentage of BI-
25
26 426 RADS 4 vs. BI-RADS 5 tends to be variable,[26, 28, 29] our finding that 73% percent and 27%
27
28 427 of women had BI-RADS 4 and 5, respectively, was very similar to another Latin American study
29
30 428 conducted in Brazil.[29] In contrast, among women with biopsy results, the positivity rate found
31
32 429 for women with BI-RADS 4 (89%), was higher than the expected. While at least 95% of biopsies
33
34 430 of BI-RADS 5 results are typically positive, this statistic is much lower, around 20-30%, for BI-
35
36 431 RADS 4.[30, 31] While we cannot be certain, we do not believe this observation of our study is
37
38 432 attributable to inadequate training, as radiologists from the tele-mammography program were
39
40 433 employed by the MOH and read de mammographs in compliance with MOH guidelines and
41
42 434 standards. Likewise, most biopsies of our study were taken at INEN, a national referral center for
43
44 435 cancer, staffed with appropriately trained cancer pathologists. This is also unlikely an artefact of
45
46 436 selection bias induced by missing data: the percentage of BI-RADS 4 vs BI-RADS 5 results were
47
48 437 comparable between women with and without evidence of biopsy. Nonetheless, this high
49
50 438 positivity rate for malignancy for BI-RADS 4 results merits further research. This is especially
51
52
53
54
55

1
2
3 439 true given that many women with BI-RADS 4 did not have record of biopsy and therefore may
4
5 440 remained undiagnosed and untreated, supporting the need for a robust tracking information
6
7
8 441 system.

9
10 442 Our results raise several opportunities to improve the outcomes of the tele-mammography
11
12 443 program by facilitating follow-up care and decreasing delays for those with a positive
13
14 444 mammography. Patient tracking could be improved by implementing a unified health
15
16 445 information system that tracks patients across the different public hospitals, allowing an
17
18 446 accurate, full, and even real-time patient follow-up.[32, 33] Specifically for this breast cancer
19
20 447 program, the tracking system should be a digital platform that enables data entry at the care steps
21
22 448 (mammography, result, and patient reporting; biopsy referral, biopsy, result, and patient
23
24 449 reporting; treatment referral, initiation, and completion), at the different public healthcare
25
26 450 facilities and even at private hospitals, enabling also the calculation of the time elapsed between
27
28 451 steps. Appointment systems could be reconsidered to prioritize a patient-centered approach. Low
29
30 452 compliance to guidelines among the MOH's providers could be remedied by nationwide
31
32 453 campaigns to build awareness of the program, its processes and goals. Finally, our data suggest
33
34 454 some misconceptions about breast cancer treatment and prognosis. The source of these
35
36 455 misconceptions is likely multifactorial and includes an unawareness of the success of breast
37
38 456 cancer treatment when diagnosed and treated promptly. Thus, multidisciplinary and culturally
39
40 457 tailored patient education, incorporating family members or supporters as appropriate, and
41
42 458 continued work to ensure access to effective diagnosis and treatment, may correct
43
44 459 misconceptions about breast cancer that contributed to delays and discontinuation seeking care.
45
46 460 Overall, a real comprehensive tele-mammography program should not be seen as a separate
47
48 461 breast cancer service but as part of the whole breast cancer continuum of care.

1
2
3 462 Evaluating breast cancer care using routinely collected data was challenging due to a lack of
4
5 463 integration of health information systems of the different MOH components that managed and
6
7 464 provided healthcare to the population subsidized by SIS. Although we used multiple national
8
9 465 data sources to capture care access through different pathways, due to varying levels of follow-
10
11 466 up and data completeness, we may have underestimated the proportion of women who obtained
12
13 467 care. Thus, the quantitative results presented here were our best intent to disentangle the current
14
15 468 health information puzzle existing in the public healthcare sector. Nonetheless, this study is a
16
17 469 comprehensive evaluation that used both quantitative and qualitative research techniques to
18
19 470 understand the situation in diverse geographical settings in Peru. Although particular challenges
20
21 471 of very hard to reach women living in more remote areas may have not been explored, this
22
23 472 study provides a close perspective of challenges in Peru, which may be broadly applicable to
24
25 473 other middle-income countries with similar resource levels and health systems.

26
27 474 The benefit of mammography screening can only be realized if women with abnormal findings
28
29 475 are successfully linked to high-quality and timely diagnostic and treatment services. Our study
30
31 476 underscores the need for strengthening the breast cancer diagnostic and treatment capacity of
32
33 477 regional hospitals outside Lima to remove barriers and facilitate access to timely comprehensive
34
35 478 breast cancer care. It also highlights the need for a strong patient education strategy and better
36
37 479 dissemination of the information about the program among providers nationwide. A unified
38
39 480 health information system is needed to allow better tracking of patients after the mammography
40
41 481 and along the breast cancer continuum of care. This information system should be part of an
42
43 482 overall breast cancer data management system that facilitates program monitoring, evaluation,
44
45 483 and research to guide appropriate and timely public health decisions and locally tailored policy
46
47 484 development. All in all, ensuring timely linkage to diagnosis and treatment for women with an

1
2
3 485 abnormal result in the tele-mammography program will be critical to securing the screening
4
5 486 program's success.
6
7

8
9 487

10
11 488 **Contributorship statement**
12
13

14 489 RAE, PJG and MFF conceptualized the study. RAE collected the data and wrote the first draft of
15
16 490 the article. MFF, PJG, LEP, JTG, helped to synthesize evidence, interpret results, and critically
17
18 491 revise the manuscript. RAE secured funding for the study. All authors approved the final draft.
19
20
21

22 492

23
24
25 493 **Competing interests**
26
27

28 494 All authors declare no competing interests.
29
30

31 495

32
33
34 496 **Data sharing statement**
35
36

37 497 No additional data is available
38
39

40 498

41
42
43 499 **Funding**
44
45

46 500 This work was funded by Harvard Medical School's Master of Medical Sciences in Global Health
47
48 501 Delivery of the Department of Global Health and Social Medicine, Rockefeller Center for Latin
49
50 502 American Studies of Harvard, and Peru's National Program of Scholarships and Academic Credits
51
52 503 (RJ-117-2017-MINEDU-VMGI-PRONABEC-OBPOST).
53
54
55

1
2
3 504
4
56 505 **Acknowledgments**
7

8
9 506 We are grateful to doctors Jose Cotrina, Willy Ramos, Mercedes Egues, Diego Venegas, Isabel
10
11 507 Cotrina, Alcedo Jorges and Victor Palacios for their central role in data collection. We truly
12
13
14 508 appreciate the contribution of all participants of the qualitative interviews.
15

16
17 509
1819 510 **REFERENCES**
20

- 21
22
23 511 1. Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN
24
25 512 estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA*
26
27 513 *Cancer J Clin*2018;68(6):394–424.
28
29 514 2. World Health Organization. WHO position paper on mammography screening.
30
31
32 515 https://www.who.int/cancer/publications/mammography_screening/en/ (accessed 06 Feb
33
34 516 2021)
35
36
37 517 3. Pace LE, Keating NL. A systematic assessment of benefits and risks to guide breast
38
39 518 cancer screening decisions. *JAMA*2014;311(13):1327–35.
40
41
42 519 4. Berry DA, Cronin KA, Plevritis SK, et al. Effect of screening and adjuvant therapy on
43
44 520 mortality from breast cancer. *N Engl J Med*2005;353:1784–92.
45
46 521 5. Harford J, Azavedo E, Fischietto M. Breast Health Global Initiative Healthcare Systems
47
48 522 Panel. Guideline implementation for breast healthcare in low- and middle-
49
50
51 523 income countries: breast healthcare program resource allocation. *Cancer*2008;113(Suppl
52
53 524 8):2282–96.
54
55

- 1
2
3 525 6. Jones L, Chilton JA, Hajek RA, et al. Between and within: international perspectives on
4
5 526 cancer health disparities. *J Clin Oncol*2006;24:2204–08.
6
7
8 527 7. Supreme Decree: Declaran de interés nacional la atención integral del cáncer y
9
10 528 mejoramiento del acceso a los servicios oncológicos en el Perú y dictan otras medidas,
11
12 529 Government of Peru (2012).
13
14
15 530 8. Vidaurre T, Santos C, Gómez H, et al. Cancer in Peru 3: the implementation of the Plan
16
17 531 Esperanza and response to the impACT Review. *Lancet Oncol*2017;18:e595–e606.
18
19 532 9. American Cancer Society. Breast Cancer Early Detection and Diagnosis.
20
21 533 <https://www.cancer.org/content/dam/CRC/PDF/Public/8579.00.pdf> (accessed 20 Jan
22
23 534 2020).
24
25
26 535 10. Creswell JW, Plano Clark VL. Designing and conducting mixed methods research. 3rd
27
28 536 ed. Thousand Oaks, CA: SAGE Publications 2017.
29
30
31 537 11. D'Orsi CJ, Sickles EA, Mendelson EB, et al. ACR BI-RADS® Atlas, Breast Imaging
32
33 538 Reporting and Data System. 5th ed. Reston, VA, American College of Radiology 2013.
34
35 539 12. Weller D, Vedsted P, Rubin G, et al. The Aarhus Statement: improving design and
36
37 540 reporting of studies on early cancer diagnosis. *Br J Cancer*2012;106:1262–7.
38
39
40 541 13. Unger-Saldaña K. Challenges to the early diagnosis and treatment of breast cancer in
41
42 542 developing countries. *World J Clin Oncol*2014;5(3):465–77.
43
44
45 543 14. Richards MA, Westcombe AM, Love SB, et al. Influence of delay on survival in patients
46
47 544 with breast cancer: a systematic review. *Lancet*1999;352(9159):1119–26.
48
49 545 15. Hsieh HF, Shannon SE. Three approaches to qualitative content analysis. *Qual Health*
50
51 546 *Res*2005;15:1277.
52
53
54
55
56
57
58
59
60

- 1
2
3 547 16. Anderson BO, Ilbawi AM, Fidarova E, et al. The Global Breast Cancer Initiative: a
4
5 548 strategic collaboration to strengthen health care for non-communicable diseases. *Lancet*
6
7 549 *Oncol*2021;22(5):578–81.
- 8
9
10 550 17. Paz-Soldán VA, Bayer AM, Nussbaum L, et al. Structural barriers to screening for and
11
12 551 treatment of cervical cancer in Peru. *Reprod Health Matters*2012;20(40):49–58.
- 13
14 552 18. Vasquez L, Diaz R, Chavez S, et al. Factors associated with abandonment of therapy by
15
16 553 children diagnosed with solid tumors in Peru. *Pediatr Blood Cancer*2018;65:e27007.
- 17
18
19 554 19. Stitzenberg KB, Meropol NJ. Trends in centralization of cancer surgery. *Ann Surg*
20
21 555 *Oncol*2010;17(11):2824–31.
- 22
23 556 20. Lieberman-Cribbin W, Liu B, Leoncini E, et al. Temporal trends in centralization and
24
25 557 racial disparities in utilization of high-volumen hospitals for lung cancer surgery.
26
27 558 *Medicine (Baltimore)*2017;96(16):e6573.
- 28
29 559 21. Pinto JA, Pinillos L, Villareal-Garza C, et al. Barriers in Latin America for the
30
31 560 management of locally advanced breast cancer. *Ecancermedicalscience*2019 Jan;13:897.
32
33 561 <https://doi.org/10.3332/ecancer.2019.897> (accessed 6 Feb 2021).
- 34
35 562 22. Nevin PE, Garcia PJ, Blas MM, et al. Inequities in cervical cancer care in indigenous
36
37 563 Peruvian women. *Lancet Glob Health*2019;7(5):e556–e557.
- 38
39 564 23. Instituto Peruano de Economía. La pobreza extrema en el Perú aumentó en el 2019.
40
41 565 <https://www.ipe.org.pe/portal/la-pobreza-extrema-en-el-peru-aumento-en-el-2019/>
42
43 566 (accessed 20 Nov 2020).
- 44
45 567 24. Romanoff A, Hayes Constant T, Johnson KM, et al. Association of previous clinical breast
46
47 568 examination with reduced delays and earlier-stage breast cancer diagnosis among women
48
49 569 in Peru. *JAMA Oncol*2017;3(11):1563–67.

- 1
2
3 570 25. Unger-Saldaña K, Miranda A, Zarco-Espinosa G, et al. Health system delay and its effect
4
5 571 on clinical stage of breast cancer: Multicenter Study. *Cancer*2015;121:2198–206.
6
7
8 572 26. Poplack SP, Tosteson AN, Grove MR, et al. Mammography in 53,803 women from New
9
10 573 Hampshire Mammography Network. *Radiology*2000;217:832–40.
11
12 574 27. Eberl MM, Fox CH, Edge SB, et al. BI-RADS classification for management of abnormal
13
14 575 mammograms. *J Am Board Fam Med*2006;19(2):161–4.
15
16
17 576 28. Sirous M, Shahnani PS, Sirous A. Investigation of frequency distribution of Breast Imaging
18
19 577 Reporting and Data System (BIRADS) classification and epidemiological factors related
20
21 578 to breast cancer in Iran: a 7-year study (2010-2016). *Adv Biomed Res*2018;7:56.
22
23
24 579 29. Milani V, Menasce Goldman S, Fingerman F, et al. Presumed prevalence analysis on
25
26 580 suspected and highly suspected breast cancer lesions in São Paulo using BIRADS criteria.
27
28 581 *Sao Paulo Med J*2007;125(4):210–4.
29
30
31 582 30. Elezaby M, Li G, Bhargavan-Chatfield M, et al. ACR BI-RADS assessment category 4
32
33 583 subdivisions in diagnostic mammography: utilization and outcomes in the National
34
35 584 Mammography Database. *Radiology*2018;287(2):416–22.
36
37
38 585 31. Orel SG, Kay N, Reynolds C, et al. BI-RADS categorization as a predictor of malignancy.
39
40 586 *Radiology*1999;211(3):845–50.
41
42 587 32. Anttila A, Lönnberg S, Ponti A, et al. Towards better implementation of cancer screening
43
44 588 in Europe through improved monitoring and evaluation and greater engagement of cancer
45
46 589 registries. *Eur J Cancer*2015;51(2):241-251.
47
48
49 590 33. Anand V, Sheley ME, Xu S, et al. Real time alert system: a disease management system
50
51 591 leveraging health information exchange. *Online J Public Health Inform*2012 Dec;4(3).
52
53 592 <https://doi.org/10/5210/ojphi.v4i3.4303> (accessed 6 Feb 2021).
54
55

1
2
3 593
4
5

6 594 Figures' legends
7

8
9 595 Figure 1.
10

11
12 596 — Data available for SIS, CDC and INEN

13
14 597 - - - Data available for CDC and INEN

15 598 Data available for INEN
16

17 599 SIS, Comprehensive Health Insurance (government-based insurance); CDC, Center for Epidemiology and Control
18 600 of Disease- National Cancer Surveillance registry; INEN, National Institute of Neoplastic Diseases
19

20 601
21

22
23 602 Figure 2.
24

25
26 603 ID, National Identification Number; SIS, Comprehensive Health Insurance (the government-subsidized insurance)
27

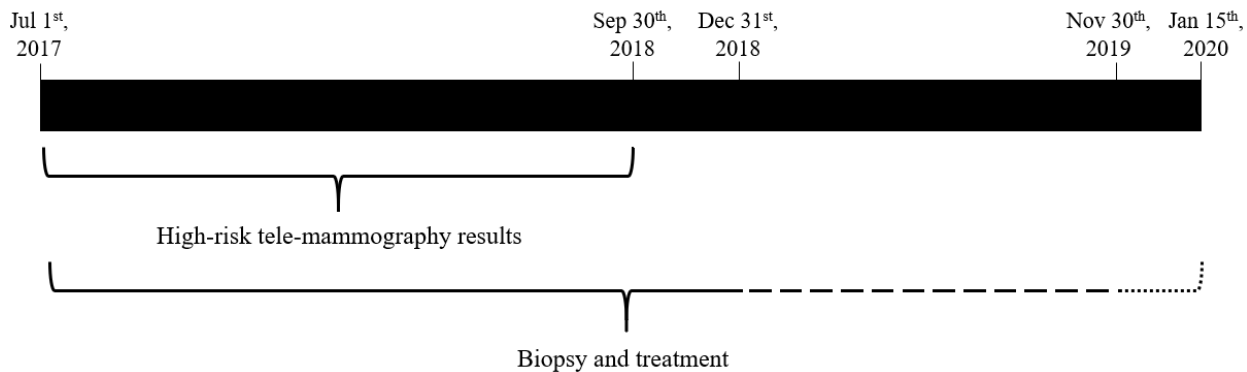
28 604
29
30

31 605 [I was requested to include a legend for Figure 3, but it does not have a legend, just a title which
32

33 606 is already included in the Fig3 document]
34
35

36 607
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55

Figure 1. Availability of biopsy and treatment information from the three study data sources



For peer review only

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Fig 2. Flowchart of biopsy and treatment initiation rates among women with a high-risk tele-mammography result

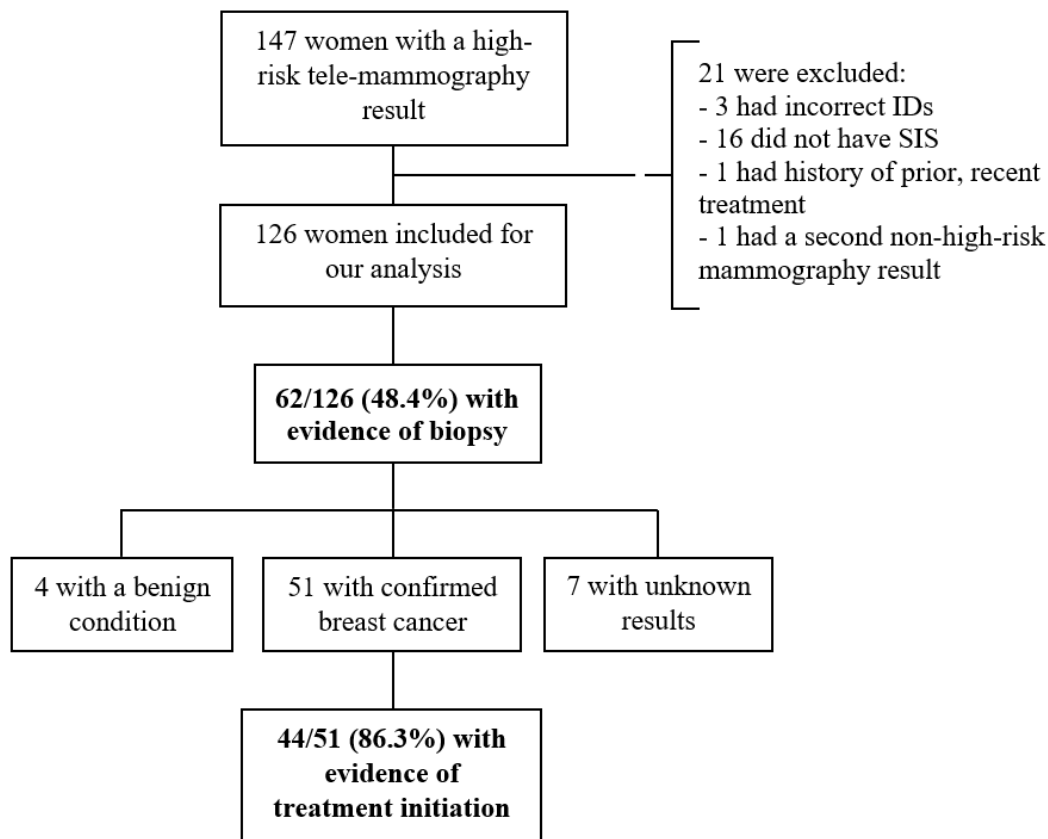
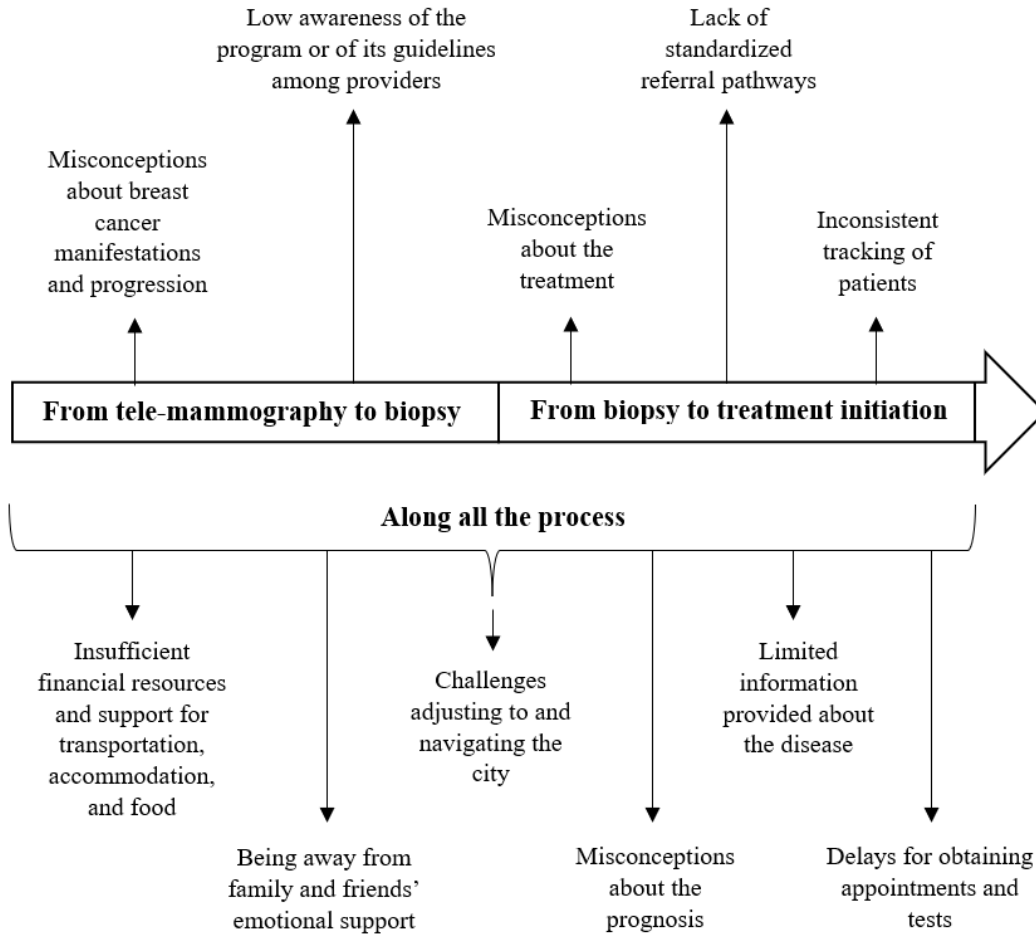


Fig 3. Barriers for obtaining a biopsy and initiating treatment and related affected intervals after obtaining a high-risk tele-mammography result



The RECORD statement – checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found		RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	1.1 Abstract, 'setting' section (page 2) 1.2 Abstract, 'Participants' section (page 2) 1.3 Abstract, 'Setting' section (page 2)
Introduction					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported			
Objectives	3	State specific objectives, including any prespecified hypotheses			
Methods					
Study Design	4	Present key elements of study design early in the paper			
Setting	5	Describe the setting, locations, and relevant dates, including			

1		periods of recruitment, exposure, follow-up, and data collection			
2	Participants	6	<p>(a) <i>Cohort study</i> - Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up</p> <p><i>Case-control study</i> - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls</p> <p><i>Cross-sectional study</i> - Give the eligibility criteria, and the sources and methods of selection of participants</p> <p>(b) <i>Cohort study</i> - For matched studies, give matching criteria and number of exposed and unexposed</p> <p><i>Case-control study</i> - For matched studies, give matching criteria and the number of controls per case</p>	<p>RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided.</p> <p>RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided.</p> <p>RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.</p>	<p>6.1. "Data sources" section (page 7)</p> <p>6.2. No validation studies were conducted.</p> <p>6.3. A graphic representation of the databases merge is included in Figure 1.</p>
3	Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	7.1. No confounders or effect modifiers were included. Exposures and outcomes are explained in the "outcomes" section (page 7)
4	Data sources/ measurement	8	For each variable of interest, give sources of data and details		

1		of methods of assessment (measurement).			
2		Describe comparability of			
3		assessment methods if there is			
4		more than one group			
5					
6	Bias	9	Describe any efforts to address		
7			potential sources of bias		
8	Study size	10	Explain how the study size was		
9			arrived at		
10	Quantitative	11	Explain how quantitative		
11	variables		variables were handled in the		
12			analyses. If applicable, describe		
13			which groupings were chosen,		
14			and why		
15					
16	Statistical	12	(a) Describe all statistical		
17	methods		methods, including those used to		
18			control for confounding		
19			(b) Describe any methods used		
20			to examine subgroups and		
21			interactions		
22			(c) Explain how missing data		
23			were addressed		
24			(d) <i>Cohort study</i> - If applicable,		
25			explain how loss to follow-up		
26			was addressed		
27			<i>Case-control study</i> - If		
28			applicable, explain how		
29			matching of cases and controls		
30			was addressed		
31			<i>Cross-sectional study</i> - If		
32			applicable, describe analytical		
33			methods taking account of		
34			sampling strategy		
35			(e) Describe any sensitivity		
36			analyses		
37					
38					
39					
40					
41	Data access and		..	RECORD 12.1: Authors should	12.1 'Data
42	cleaning methods			describe the extent to which the	sources' section.
43				investigators had access to the database	(page 7)
44					

				population used to create the study population. RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	12.2 “Data analysis’ section (quantitative component) (page 7)
Linkage		..		RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	12.3 “Data analysis’ section (quantitative component) (page 7)
Results					
Participants	13	(a) Report the numbers of individuals at each stage of the study (<i>e.g.</i> , numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram		RECORD 13.1: Describe in detail the selection of the persons included in the study (<i>i.e.</i> , study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	‘Biopsy and treatment initiation rates and delays’ section (page 10)
Descriptive data	14	(a) Give characteristics of study participants (<i>e.g.</i> , demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) <i>Cohort study</i> - summarise follow-up time (<i>e.g.</i> , average and total amount)			

1 2 3 4 5 6 7 8 9 10 11	Outcome data	15	<p><i>Cohort study</i> - Report numbers of outcome events or summary measures over time</p> <p><i>Case-control study</i> - Report numbers in each exposure category, or summary measures of exposure</p> <p><i>Cross-sectional study</i> - Report numbers of outcome events or summary measures</p>			
12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27	Main results	16	<p>(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included</p> <p>(b) Report category boundaries when continuous variables were categorized</p> <p>(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period</p>			
28 29 30 31 32	Other analyses	17	Report other analyses done— e.g., analyses of subgroups and interactions, and sensitivity analyses			
Discussion						
34 35	Key results	18	Summarise key results with reference to study objectives			
36 37 38 39 40 41 42 43 44	Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias		RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over	‘Discussion’ section (5 th paragraph).

				time, as they pertain to the study being reported.	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence			
Generalisability	21	Discuss the generalisability (external validity) of the study results			
Other Information					
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based			
Accessibility of protocol, raw data, and programming code		..		RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	See 'Data sharing statement' (page 24)

*Reference: Benchimol EI, Smeeth L, Guttman A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.

*Checklist is protected under Creative Commons Attribution ([CC BY](https://creativecommons.org/licenses/by/4.0/)) license.