Evaluation of diagnostic ultrasound use in a breast cancer detection strategy in Northern Peru

Segen Aklilu, Carolyn Bain, Pooja Bansil, Silvia de Sanjose, Jorge A. Dunstan, Vanessa Castillo, Vivien Tsu, Ines Contreras, Ronald Balassanian, Tara K. Hayes Constant, John R. Scheel

1 Department of Radiology, University of Washington, Seattle, Washington, United States of America, 2 PATH, Seattle, Washington, United States of America, 3 Instituto Nacional de Enfermedades Neoplásicas, Lima, Peru, 4 PATH, Lima, Peru, 5 Department of Global Health, University of Washington, Seattle, Washington, United States of America, 6 Department of Pathology, University of California San Francisco, San Francisco, California, United States of America, 7 Sea Mar Community Health Centers, Burien, Washington, United States of America

☯ These authors contributed equally to this work.

* jrs4yg@uw.edu

Abstract

To evaluate the diagnostic impact of point-of-care breast ultrasound by trained primary care physicians (PCPs) as part of a breast cancer detection program using clinical breast exam in an underserved region of Peru. Medical records and breast ultrasound images of symptomatic women presenting to the Breast Cancer Detection Model (BCDM) in Trujillo, Peru were collected from 2017–2018. Performance was measured against final outcomes derived from regional cancer center medical records, fine needle aspiration results, patient follow-up (sensitivity, specificity, positive, and negative predictive values), and by percent agreement with the retrospective, blinded interpretation of images by a fellowship-trained breast radiologist, and a Peruvian breast surgeon. The diagnostic impact of ultrasound, compared to clinical breast exam (CBE), was calculated for actual practice and for potential impact of two alternative reporting systems. Of the 171 women presenting for breast ultrasound, 23 had breast cancer (13.5%). Breast ultrasound used as a triage test (current practice) detected all cancer cases (including four cancers missed on confirmatory CBE). PCPs showed strong agreement with radiologist and surgeon readings regarding the final management of masses (85.4% and 80.4%, respectively). While the triage system yielded a similar number of biopsies as CBE alone, using the condensed and full BI-RADS systems would have reduced biopsies by 60% while identifying 87% of cancers immediately and deferring 13% to six-month follow-up. Point-of-care ultrasound performed by trained PCPs improves diagnostic accuracy for managing symptomatic women over CBE alone and enhances access. Greater use of BI-RADS to guide management would reduce the diagnostic burden substantially.
Introduction

The low awareness and lack of local access to medical imaging result in most women with breast cancer in low- and middle-income countries (LMICs) presenting at a late stage when treatment is largely unsuccessful [1–5]. A multi-organization consortium, including PATH, the Peruvian Ministry of Health, and the national and regional cancer centers (INEN and IREN-Norte), the University of Washington, and the University of California San Francisco, instituted the Breast Cancer Detection Model (BCDM) in Northern Peru using locally available resources [6, 7]. Peru was chosen because of the government-run Seguro Integral de Salud, which offers free cancer care in-country, and Plan Esperanza initiative which aids in educational activities. The BCDM focuses on improved access to accurate clinical breast exams (CBEs) in local communities by raising breast health awareness among women and providing education and training to midwives and primary care physicians (PCPs).

WHO defines early diagnosis of cancer as focusing on detecting symptomatic patients as early as possible, so they have the best chance for successful treatment (https://www.who.int/activities/promoting-cancer-early-diagnosis). This contrasts to screening, which occurs in asymptomatic women. Screening is a more advanced level of care delivery that requires more resources and must be preceded by an established early diagnosis program.

The BCDM also uses implementation science principles by introducing evidence-based interventions into a different clinical setting and evaluating their impact. Interventions include training to build skills and induce behavioral changes among health care providers. The overall aim is the adoption of improved CBE and ultrasound imaging, education to engage patients and stakeholder organizations, and revised management algorithms [8].

Previous research has shown that breast ultrasound is effective in LMICs to detect breast cancer, particularly in conjunction with CBE [9, 10]. Ultrasound use has reduced the rate of abnormal CBEs requiring tissue sampling by up to 75% [11]. Ultrasound also provides the PCP and patient with reassurance by identifying benign (e.g., cysts) or normal (e.g., ribs) findings that correspond to the abnormal CBE. Ultrasound was introduced into the BCDM patient care pathway as a low-cost approach to increase access at the point-of-care in the community and potentially reduce the number of women requiring fine needle aspiration (FNA) at more centralized health centers.

In the U.S., radiologists report ultrasound findings using the Breast Imaging Reporting and Data System (BI-RADS) [12]. Despite the wealth of data supporting BI-RADS use to improve interpretive accuracy, it is not clear that PCPs and technologists interpreting ultrasounds can use the full BI-RADS accurately to inform management of breast findings. Previous studies indicate that, among LMIC radiologists not fully trained using BI-RADS, use of BI-RADS can result in mis-characterization and mis-management of findings. However, standardized systems using fewer terms and decision points appear to result in more consistent and accurate management [7].

Program evaluations on breast imaging interpretation can improve accuracy and efficiency by addressing interobserver variability and providing practitioners with feedback [7, 10, 13, 14]. For example, variability in lesion margin description, a critical factor in the decision for biopsy, may affect biopsy rates and missed cancer rates [15]. Among U.S. radiologists, there are variable interobserver rates with fair agreement with respect to descriptors for lesion echo pattern or margin [16, 17], as well as fair or poor agreement in assigning some assessment categories [15, 18].

The purpose of the current assessment is to evaluate the ultrasound component of the BCDM, regarding the accuracy of breast ultrasound performance and interpretation by trained PCPs in the La Libertad region, and evaluate the diagnostic impact of adding
ultrasound to standard CBE. A secondary goal of this program evaluation is to assess the theoretical diagnostic impact of different reporting systems (triage, condensed BI-RADS, full BI-RADS). The results of this evaluation will provide data for the potential scalability of this model in other regions of Peru and help improve the program during the scale-up phase.

Methods

Ethics statement

This retrospective study was exempt from IRB review by the University of Washington and PATH due to its retrospective design and use of anonymized data. The original program was exempted from IRB review by the PATH IRB committee as the program provided standard of care to a region currently receiving no early diagnosis activities. This program was not intended for research and, therefore, women were not consented.

Study setting

La Libertad is a medically underserved region in northern Peru, 560 km north of the more resourced capital city of Lima. Trujillo is the largest city in La Libertad; here women have access to basic primary care services, but not routine mammography screening.

As part of BCDM, trained clinic-based midwives educated women on breast cancer and performed CBEs. Women with signs and symptoms of potential breast cancer (e.g., breast lump) in Trujillo were referred to a PCP for a CBE, ultrasound and an FNA. Clinic staff transport FNA samples to IREN-Norte for interpretation by a cytopathologist.

Patient and public involvement

There was a collaborative effort from the national government, the Peruvian Ministry of Health and other local and foreign health agencies. These entities were involved in the clinical algorithm/management, recruitment and conduct of the overall program.

Intervention

For this study, symptomatic women were defined as those presenting with either a self-detected symptom or a positive clinical finding by the midwife (e.g., lump, skin changes). The BCDM incorporated breast ultrasound in 2016; a trained PCP performed and interpreted the breast ultrasound after their CBE and prior to the decision regarding FNA. If either the ultrasound or the PCP CBE was positive, FNA was performed immediately. The addition of ultrasound to the program consisted of ultrasound training of the PCPs, quality assurance, a revised management algorithm, and data collection (S1 Fig).

Ultrasound training. A Peruvian breast surgeon from INEN with previous breast ultrasound experience trained for two weeks with a fellowship-trained breast radiologist at Seattle Cancer Care Alliance/University of Washington. Thereafter, the surgeon trained 15 PCPs (in two groups) in the La Libertad region. The training lasted eight hours a day for two days and included both didactic and practical components. After the training, a trained PCP from the first group mentored PCPs in the second group. This second group received oversight and BI-RADS training from the surgeon and were required to pass a written test before practicing independently. A similar multi-tiered training approach has been used in other countries [7].

Quality assurance. The breast surgeon reviewed ultrasound images to assure quality. Patients with a negative or benign interpretation by the PCPs subsequently interpreted as positive by the surgeon were contacted and received appropriate care. Interpretive performance (i.e., medical audit) was calculated using the BI-RADS Atlas guidelines [12].
Development of an algorithm for evaluating patients with ultrasound. A patient management algorithm (S2 Fig) was developed to standardize decision-making. To reduce the possibility of missing a cancer, the algorithm calls for ultrasound to be used as a triage tool to differentiate normal from abnormal breast tissue, with immediate FNA for all findings (BI-RADS 3, 4, and 5) except normal breast tissue and classically benign findings (BI-RADS 1 and 2).

Imaging
All ultrasound imaging was performed with high frequency linear transducers (>7.5 MHz) on either a VINNO E30 (Sozhou, China) or a SAMSUNG MEDISON ACUVIX XG (Seoul, Korea). Physicians recorded their ultrasound interpretation on standardized forms. Such forms have been shown previously to improve interpretation and management of findings by PCPs and facilitate learning of BI-RADS [7].

Data collection
In addition to clinical intake forms and ultrasound images, BCDM program staff collected medical records and patient follow-up details from IREN-Norte (cancer versus no cancer). Positive outcomes were defined as ultrasound examinations associated with a cancer diagnosis within 365 days. Ultrasound examinations not associated with a cancer diagnosis by FNA or after searching the IREN-Norte medical records after 365 days from ultrasound were considered negative [12]. The breast radiologist (7 years experience) and breast surgeon (1 year experience) retrospectively reviewed and interpreted anonymized ultrasound images, blinded to each others’ interpretations and the initial interpretations by the PCPs. Both reviewers completed the same ultrasound interpretation form used by the PCPs.

Statistical analysis
All statistical analyses are conducted in Stata 13.1 (StataCorp, College Station, TX). The distribution of mass characteristics (shape, internal echogenicity, margins, and size) were used to calculate the likelihood of malignancy [19]. Cancer detection rate (per 1,000 ultrasounds), abnormal interpretation rate, sensitivity, specificity, positive predictive values for ultrasound-positive women recommended for biopsy and for women actually biopsied (PPV2, PPV3), and negative predictive value (NPV), were calculated according to the 5th edition BI-RADS Atlas [12]. Performance was also calculated in terms of percent agreement between interpreting groups (radiologist and surgeon, surgeon and PCPs, and radiologist and PCPs) for the BI-RADS lexicon, findings, and management plans. The patient management algorithm recommended biopsy for all masses (Triage ultrasound), even those with probably benign findings. Therefore, BI-RADS 3, 4, and 5 findings were considered a positive interpretation. In contrast, when calculating the theoretical interpretive performance of using condensed or full BI-RADS system, masses with probably benign characteristics (BI-RADS 3) would be followed by repeat imaging six months later and, therefore, considered a negative interpretation in accordance with the BI-RADS Atlas [12].

The diagnostic impact of breast ultrasound was calculated by assuming that, in the absence of breast ultrasound, every suspicious CBE finding receives a standard-of-care referral for a surgical biopsy. Management changes after breast ultrasound, according to actual practice (i.e., triage) and potential practice (condensed or full BI-RADS), were determined.
Results

Patient population

From 2017–2018, 181 diagnostic ultrasounds were performed on symptomatic women referred to the BCDM PCP for evaluation (Fig 1). Ten (5.5%) were excluded: four repeat visits of women already included in the analysis and six missing a BI-RADS assessment. Out of 171, 156 (91.2%) were recommended for FNA (BI-RADS 3–5), 103 (66%) received an FNA within the program and 48 (30.8%) received appropriate follow-up outside the program. Five women (3.2%) recommended for FNA did not have FNA or appropriate follow-up documented. Twenty-three cancers were diagnosed during the study period.

S1 Table describes the distribution of characteristics for the 171 patients included in this program evaluation. Of the 171 women, 56% were 30–49 years old and 69% breast-fed their children. Many reported contraception use (40.1%), while few reported alcohol use (1.7%). Few women had family history (4.5%) and none had personal history of breast cancer.

Interpretive performance of PCPs

Table 1 shows the frequency of characteristics used by PCPs to describe masses, with associated likelihood of malignancy and benignity. Masses with oval/round shape (n = 83) were more common than irregular shape (n = 69) and were significantly less likely to represent malignancy (7.2% versus 24.6%, p = < 0.001). Similarly, circumscribed margins (n = 92) were more common than not circumscribed margins (n = 60) and were significantly less likely to be associated with malignancy (9.8% versus 23.3%, p = 0.049). All masses associated with cancer (n = 23) were assigned not hyperechoic for internal echogenicity. Larger masses were more likely to represent malignancy (p = 0.01).

There was strong agreement between all groups for identifying the correct finding (88–89%) (Table 2). The percent agreement for all BI-RADS lexicon characteristics for masses was highest for internal echogenicity (97–98%), followed by margins (60–86%), and shape (70–84%). Percent agreement between all groups for the final assessment of masses was highest using triage (80–85%), compared to full BI-RADS (47–54%) or condensed BI-RADS (50–56%).

![Flowchart for ultrasound examination results](https://doi.org/10.1371/journal.pone.0252902.g001)
Table 1. Characteristics used to describe masses on ultrasound (N = 156).

| Ultrasound Mass Characteristics | Number (%) | Number (%) with cancer diagnosis | Number (%) without cancer diagnosis | P value* |
|--------------------------------|------------|----------------------------------|------------------------------------|----------|
| Shape                          |            |                                  |                                    |          |
| Irregular                      | 69(44.2)   | 17 (24.6)                        | 52 (75.4)                          | <0.001   |
| Oval/round                     | 83(53.2)   | 6 (7.2)                          | 77 (92.8)                          |          |
| Missing                        | 4(2.6)     | 0 (0)                            | 4 (100.0)                          |          |
| Internal echogenicity          |            |                                  |                                    |          |
| Hyperechoic                    | 2(1.2)     | 0 (0)                            | 2 (100.0)                          | 0.70     |
| Not Hyperechoic                | 152(97.4)  | 23 (15.1)                        | 129 (84.9)                         |          |
| Missing                        | 2(1.2)     | 0 (0)                            | 2 (100.0)                          |          |
| Margins                        |            |                                  |                                    |          |
| Circumscribed                  | 92(58.9)   | 9 (9.8)                          | 83 (90.2)                          | 0.049    |
| Not Circumscribed              | 60(38.5)   | 14 (23.3)                        | 46 (76.7)                          |          |
| Missing                        | 4(2.6)     | 0 (0)                            | 4 (100.0)                          |          |
| Size                           |            |                                  |                                    |          |
| Size > 2 cm                    | 58(37.2)   | 15 (25.9)                        | 43 (74.1)                          | 0.010    |
| Size (2 cm or less)            | 91(58.3)   | 7 (7.7)                          | 84 (92.3)                          |          |
| Missing                        | 7(4.5)     | 1 (14.3)                         | 6 (85.7)                           |          |
| Total                          | 156 (100)  |                                  |                                    |          |

*Chi-squared P value

Triage ultrasound (BR 3,4,5 considered positive) identified four cancers considered not suspicious by the PCP—two called negative and two assigned for clinical follow-up (Table 3). Triage ultrasound was more sensitive than the PCP’s CBE (100% and 82.6% respectively). Furthermore, using ultrasound as a triage test also resulted in a somewhat higher sensitivity (100% versus 87%) and NPV (100%) than condensed and full BI-RADS, but with significantly lower specificity (10.1% versus 71.6%) (Table 4). The condensed and full BI-RADS would have resulted in 94 BI-RADS 3 (probably benign) masses being followed-up with repeat imaging later, rather than immediate biopsy, with 3.2% of them ending up being malignant (S2 Table).

Table 2. Inter-observer percent agreement for BI-RADS lexicon use and assessment.

|                      | BR vs. S | BR vs. PCPs | S vs. PCPs |
|----------------------|----------|-------------|------------|
| Overall Findings     | 88.5     | 88.4        | 88.3       |
| For masses           |          |             |            |
| Number of masses     | 137      | 146         | 143        |
| Type of Shape        | 70.3     | 83.9        | 71.5       |
| Type of Margin       | 85.8     | 64.2        | 59.5       |
| Internal Echogenicity| 97.7     | 97.1        | 98.4       |
| Assessment           |          |             |            |
| Number of women assessed | 156   | 164         | 153        |
| Full BI-RADS         | 53.8     | 48.8        | 47.1       |
| Condensed BI-RADS$   | 56.4     | 54.9        | 50.3       |
| Triage Ultrasound¶   | 79.5     | 85.4        | 80.4       |

BR: breast radiologist; S: Peruvian Breast Surgeon; PCPs: primary care physicians

§ Condensed BI-RADS: BI-RADS 1 and 2, BI-RADS 3, BI-RADS 4 and 5
¶ Triage Ultrasound: BI-RADS 1 and 2; BI-RADS 3 and 4 and 5

https://doi.org/10.1371/journal.pone.0252902.t001

https://doi.org/10.1371/journal.pone.0252902.t002
Table 3. Clinical management changes before and after breast ultrasound for all women.

| Physicians’ CBE management | Post-CBE Ultrasound Management |
|-----------------------------|--------------------------------|
| Management Category         | Triage System | Condensed System | Cancers detected |
| All women (N = 171)         |                  |                  |                  |
| Negative                    | 26 (15.2)       |                  |                  |
| Biopsy                      | 25 (96.1)       | 11 (42.3)        | 2                |
| Negative/ Benign            | 1 (3.9)         | 1 (3.9)          | 0                |
| Follow up                   | 14 (8.2)        |                  |                  |
| Imaging follow-up           | 0               | 8 (57.1)         | 0                |
| Biopsy                      | 11 (78.6)       | 3 (21.4)         | 2                |
| Negative/ Benign            | 3 (21.4)        | 3 (21.4)         | 0                |
| Referral with biopsy        | 131 (76.6)      |                  |                  |
| Imaging follow-up           | 0               | 72 (56.7)        | 3                |
| Biopsy                      | 120 (91.6)      | 46 (36.6)        | 16               |
| Negative/ Benign            | 11 (8.4)        | 11 (8.4)         | 0                |
| No. (%) Biopsies by Recommendation | 131 (76.6) | 156 (91.2) | 62 (36.2) | 23 (100) |
| False Positive Rate         | 85.4            | 85.3             | 67.7             |

Diagnostic impact of ultrasound on the management of symptomatic women

Based on the PCP’s CBE alone, 76.6% of the women would have been referred for ultrasound, while 8.2% and 15.2% would be designated as clinical follow-up (non-neoplastic abnormality) and negative (no follow-up needed) respectively (Table 3). In total, ultrasound changed the management after the PCP’s CBE in 29.2% of cases with triage (mostly increasing biopsies), and 66.7% with condensed and full BI-RADS (mostly decreasing biopsies). The false positive rate for biopsy recommendations was 85.4% for the PCP’s CBE alone, 85.3% for ultrasound triage, and 67.7% for condensed BI-RADS.

Discussion

Evaluating programs is a critical component of implementation science and involves quality assessment, improvement, and sustainability. Here, the impact of imaging was evaluated in the BCDM in an underserved region in Peru. This is one of the first studies–outside clinical trials–following the use of CBE, education, and point-of-care ultrasound that included multiple years

Table 4. Interpretive performance of primary care physicians based on actual and alternative reporting systems (N = 171).

|                        | Triage Ultrasound† | Condensed/Full BI-RADS‡ |
|------------------------|--------------------|-------------------------|
| Cancer Detection Rate (per 1,000 ultrasounds) | 147.4              | 322.6                   |
| Abnormal interpretation rate | 88.1               | 35.0                    |
| Sensitivity            | 100.0 (85.2–100.0) | 87.0 (66.4–97.2)        |
| Specificity            | 10.1 (5.8–16.2)    | 71.6 (63.6–78.7)        |
| PPV2                   | N/A                | 32.3 (20.9–45.3)        |
| PPV3                   | N/A                | 45.5 (30.4–61.2)        |
| NPV                    | 100.0 (78.2–100.0) | 97.2 (92.2–99.4)        |

†Triage ultrasound: BI-RADS 3,4,5 are positive interpretations and result in a biopsy recommendation
‡Condensed and full BI-RADS: BI-RADS 4,5 are positive interpretations and result in a biopsy recommendation
PPV2: BI-RADS 4 and 5 as positive interpretation; women recommended for biopsy with missing FNA results are assumed negative
PPV3: BI-RADS 4 and 5 as positive interpretation; women recommended for biopsy with missing FNA results are excluded
of program follow-up on patient outcomes and several generations of PCPs, trained by in-country trainers, performing ultrasound. The results suggest that PCP’s CBE followed by point-of-care triage ultrasound and tissue sampling with FNA performed by PCPs can increase clinical accuracy at the primary care level, reducing consumption of limited specialty care services in resource-limited settings. Further, different standardized reporting systems for ultrasound demonstrated important trade-offs to consider when starting similar programs.

Several groups have used education with point-of-care CBE and ultrasound at community health centers and through periodic camps to decentralize diagnostic services and increase access [7, 11, 20]. These efforts have limited sustainability without continued external resources or commitment from the government. By training a local breast surgeon in breast ultrasound who could train and support subsequent generations of PCPs, using pre-existing imaging equipment, and shifting ultrasound interpretation and FNA to PCPs, the program becomes more sustainable with local resources. The ability of PCPs to achieve improved results with ultrasound suggests this approach is viable. Although the level of agreement was reduced significantly when using more detailed BIRAD reporting systems (condensed and full BI-RADS), the disagreement was usually caused by ‘overcalling’ benign findings as probably benign, and probably benign as suspicious. This cautious approach among less experienced radiologists has been observed in the U.S. and normalizes with experience and feedback [21]. Further follow-up is necessary to confirm that PCP patient management agreement improves as experience increases, provided that examinations are linked to patient follow-up information. Ensuring continued improvement in image interpretation through increased training and feedback is necessary to maximize the impact of ultrasound.

Most diagnostic services in LMICs are centrally located in large cities, and women with late-stage breast cancer often cite distance from these tertiary diagnostic centers and limited knowledge about their locations as factors that contributed to delayed presentation [22]. In northern Peru, symptomatic women required further evaluation at distant tertiary hospitals. In our study, 89% received ultrasound and FNA by a trained PCP in the community close to where the women live. These rates were better than a similar program in rural Uganda (36%) that offered point-of-care ultrasound locally, but FNA at a tertiary hospital farther away [11]. These findings suggest that breast cancer detection services, linked to pathology services, closer to where women live can decrease the women’s burden and increase successful detection and follow-up. Importantly, reducing false positive evaluations and unnecessary biopsies saves women money, time, and anxiety, and may improve community participation in a breast cancer detection program over time. In this evaluation, point-of-care ultrasound performed by PCPs increased biopsies by 14.6% using the conservative triage algorithm (while improving sensitivity over PCP CBE), but could have reduced biopsies by 40.4% if the condensed BI-RADS had been used. Prior studies in High Income Countries and LMICs have shown ultrasound improves the sensitivity and specificity of CBE [9, 10, 23]. One study in Uganda showed ultrasound reduced false positive CBEs requiring tissue sampling by 75%. However, the median age of women in that study was 29 years—ten years younger than our study [11].

There are clear trade-offs between the simplicity of triage ultrasound and more complex condensed or full BI-RADS approaches. While the triage system was easier to learn and use consistently, it resulted in greater resource utilization by recommending biopsy of all masses (BI-RADS 3, 4, and 5); this is expensive and potentially unnecessary in LMICs where most women presenting for an evaluation (early adopters) are < 40 years old and thus relatively low risk for breast cancer. However, the recommendation to use imaging follow-up to manage probably benign masses (BI-RADS 3) instead of immediate biopsy relies on an assumption of <2% risk of malignancy [12] and an assurance that women have access to subsequent imaging follow-up. Using condensed BI-RADS would have resulted in short interval follow-up of three
masses that represented cancer (3.2%). Although this is above the cutoff level recommended in the U.S. [12], health systems will need to consider the tradeoff with the number of women who might not receive care due to the added burden of biopsying numerous benign masses. Each reporting system (triage, condensed BI-RADS, full BI-RADS) varies in complexity. One approach is to start with the simplest reporting system (triage) and gradually phase out FNA of “probably benign” findings, as quality assurance reviews provide evidence that it is safe to manage such findings without immediate FNA, as suggested by Lam et al. [24]. Program planners should initially anticipate providers needing greater support and oversight, gradually shifting towards a more comprehensive reporting system that allows imaging follow-up when the infrastructure and diagnostic performance are ready.

It is notable that one third of the cancers detected by the BCDM program were 2 cm or less. This observation is consistent with those from large randomized controlled trials in China and India, where approximately 45% and 19% of masses detected by a combination of awareness, self-detection, and CBE were less than 2 cm, respectively [25, 26]. These results support the argument that even in settings without mammography, breast cancer early diagnosis is feasible.

This study has limitations. While using BI-RADS 3 imaging follow-up, as an alternative to sampling all masses, will save money, data was not collected to calculate cost-effectiveness of this option and determine how many more women would receive care over use of triage ultrasound. Additionally, it is still possible, although unlikely given limited healthcare options in this region, that some women receive follow-up outside our program [6]. Patient follow-up information was obtained through the cancer center and repeat community visits, where possible, to reduce the likelihood of missed cancers and patients lost to follow-up. Searching records of local facilities found follow-up for eight additional women without FNA or follow-up results at our study facility. Lastly, the study results have potentially limited generalizability to older Peruvian women because only 45% of women included in this study were 40 years or older; however, all cancers detected were in this older group. Including a more significant proportion of women at higher risk for malignancy could likely show improved efficiency of cancer detection of our strategy. Nevertheless, although important, these limitations do not inhibit our ability to improve cancer detection in this region.

**Conclusion**

Adding point-of-care ultrasound with FNA to local breast education and CBE services may improve early breast cancer diagnosis and can potentially reduce unnecessary biopsies using more advanced ultrasound reporting systems. This strategy saves resources and improves early cancer detection over existing options in LMICs. Early diagnosis breast cancer programs should start with a basic standardized reporting system for ultrasound. Once infrastructure and experience are in place, it is possible to transition to more comprehensive and selective approaches to save resources.

**Supporting information**

S1 Fig. Translated clinical intake form for breast ultrasound.
(PDF)

S2 Fig. Flowchart of services in community program for breast health.
(PDF)
S1 Table. Population characteristics of symptomatic women presenting for a breast evaluation (N = 171).
(PDF)

S2 Table. Accuracy of PCP assessment in detecting cancers, by actual and potential reporting system (N = 171).
(PDF)

Acknowledgments
Trujillo physicians performing breast imaging (primary care physicians): Dr. Wilfredo Larios, Dr. Jose E. Seminario, Dr. Pedro E. Guevara, Dr. William J. Velazquez. The authors would also like to thank Dr. Benjamin O. Anderson (Fred Hutchinson Cancer Research Center, Seattle, WA) for his early support in designing the program in Peru, and Dr. Gaytri P. Scheel (Everett Clinic, Everett, WA) and Ms. Catherine O’Donnell (Seattle, WA) for their critical review of this manuscript.

Author Contributions
Conceptualization: John R. Scheel.
Data curation: Carolyn Bain, Pooja Bansil, Vanesa Castillo, Ines Contreras, Tara K. Hayes Constant, John R. Scheel.
Formal analysis: Segen Aklilu, Carolyn Bain, Pooja Bansil, Silvia de Sanjose, Vanesa Castillo, John R. Scheel.
Investigation: Jorge A. Dunstan, Vanesa Castillo, John R. Scheel.
Methodology: Pooja Bansil, Silvia de Sanjose, Jorge A. Dunstan, Ronald Balassanian, John R. Scheel.
Project administration: Carolyn Bain, Ines Contreras.
Software: Pooja Bansil.
Supervision: Silvia de Sanjose, Vivien Tsu, Ronald Balassanian, John R. Scheel.
Writing – original draft: Segen Aklilu, Carolyn Bain, Pooja Bansil, Ronald Balassanian, John R. Scheel.
Writing – review & editing: Segen Aklilu, Carolyn Bain, Silvia de Sanjose, Vivien Tsu, Ines Contreras, Ronald Balassanian, Tara K. Hayes Constant, John R. Scheel.

References
1. Martei YM, Pace LE, Brock JE, Shulman LN. Breast cancer in low- and middle-income countries: Why we need pathology capability to solve this challenge. Clin Lab Med. 2018; 38(1):161–73. https://doi.org/10.1016/j.cll.2017.10.013 PMID: 29412880
2. Ginsburg O, Rositch AF, Conteh L, Mutebi M, Paskett ED, Subramanian S. Breast cancer disparities among women in low- and middle-income countries. Curr Breast Cancer Rep. 2018; 10(3):179–86.
3. Scheel JR, Molina Y, Anderson BO, Patrick DL, Nakigudde G, Gralow JR, et al. Breast cancer beliefs as potential targets for breast cancer awareness efforts to decrease late-stage presentation in Uganda. J Glob Oncol. 2018; 4(4):1–9. https://doi.org/10.1200/JGO.2016.008748 PMID: 30241166
4. Scheel JR, Parker S, Hippe DS, Patrick DL, Nakigudde G, Anderson BO, et al. Role of family obligation stress on Ugandan women’s participation in preventive breast health. Oncologist. 2019; 24(5):624–31. https://doi.org/10.1634/theoncologist.2017-0553 PMID: 30072390
5. Shetty MK. Screening and diagnosis of breast cancer in low-resource countries: what is state of the art? Semin Ultrasound CT MR. 2011; 32(4):300–5. https://doi.org/10.1053/j.sult.2011.04.002 PMID: 21782120

6. Bain C, Constant TH, Contreras I, Vega AMB, Jeronimo J, Tsu V. Model for early detection of breast cancer in low-resource areas: The experience in Peru. J Glob Oncol. 2018; 4(4):1–7. https://doi.org/10.1200/JGO.17.00006 PMID: 30241230

7. Scheel JR, Peacock S, Orem J, Bugeza S, Muyinda Z, Porter PL, et al. Improving breast ultrasound interpretation in Uganda using a condensed breast imaging reporting and data system. Acad Radiol. 2016; 23(10):1271–7. https://doi.org/10.1016/j.acra.2016.05.018 PMID: 27325412

8. Handley MA, Gorukanti A, Cattamanchi A. Strategies for implementing implementation science: a methodological overview. Emerg Med J. 2016; 33(9):660–4. https://doi.org/10.1136/emermed-2015-205461 PMID: 26893401

9. Sood R, Rositch AF, Shakoor D, Ambinder E, Pool K-L, Pollack E, et al. Ultrasound for breast cancer detection globally: A systematic review and meta-analysis. J Glob Oncol. 2019; 5(5):1–17. https://doi.org/10.1200/JGO.19.00127 PMID: 31454282

10. Tsu V, PATH, Scheel J, Bishop A, Murray M, Weigl B, et al. Breast ultrasound following a positive clinical breast examination: Does it have a role in low- and middle-income countries? J Glob Radiol. 2015; 1(2):1–7.

11. Matovu A, Mubende Regional Referral Hospital, Scheel J, Shadrack P, Ssembatya R, Njeri A, et al. Pilot study of a resource-appropriate strategy for downstaging breast cancer in rural Uganda. J Glob Radiol. 2016; 2(1).

12. D’Orsi CJ, Sickles EA, Mendelson EB, Morris EA, et al. ACR BI-RADS Atlas, Breast Imaging Reporting and Data System. Reston, VA, American College of Radiology; 2013.

13. Hadley M, Mullen LA, Dickerson L, Harvey SC. Assessment and improvement strategies for a breast cancer early detection program in rural South Africa. J Glob Oncol. 2018; 4(4):1–12. https://doi.org/10.1200/JGO.18.00015 PMID: 30085890

14. Scheel JR, Nealey EM, Orem J, Bugeza S, Muyinda Z, Nathan RO, et al. ACR BI-RADS use in low-income countries: An analysis of diagnostic breast ultrasound practice in Uganda. J Am Coll Radiol. 2016; 13(2):163–9. https://doi.org/10.1016/j.jacr.2015.07.035 PMID: 26419306

15. Abdullah N, Mesurolle B, El-Khoury M, Kao E. Breast imaging reporting and data system lexicon for US: interobserver agreement for assessment of breast masses. Radiology. 2009; 252(3):665–72. https://doi.org/10.1148/radiol.2523080670 PMID: 19567644

16. Lee H-J, Kim E-K, Kim MJ, Youk JH, Lee JY, Kang DR, et al. Observer variability of Breast Imaging Reporting and Data System (BI-RADS) for breast ultrasound. Eur J Radiol. 2008; 65(2):293–8. https://doi.org/10.1016/j.ejrad.2007.04.008 PMID: 17531417

17. Lazarus E, Mainiero MB, Schepps B, Koelliker SL, Livingston LS. BI-RADS lexicon for US and mammography: interobserver variability and positive predictive value. Radiology. 2006; 239(2):385–91. https://doi.org/10.1148/radiol.2392042127 PMID: 16569780

18. Choi EJ, Lee EH, Kim YM, Chang Y-W, Lee JH, Park YM, et al. Interobserver agreement in breast ultrasound categorization in the Mammography and Ultrasonography Study for Breast Cancer Screening Effectiveness (MUST-BE) trial: results of a preliminary study. Ultrasonography. 2019; 38(2):172–80. https://doi.org/10.14366/usg.18012 PMID: 30458606

19. Hong AS, Rosen EL, Soo MS, Baker JA. BI-RADS for sonography: positive and negative predictive values of sonographic features. AJR Am J Roentgenol. 2005; 184(4):1260–5. https://doi.org/10.2214/ajr.184.4.01841260 PMID: 15788607

20. Matsumoto MM, Widemon S, Farfán G, Vidaurre T, Dunstan J, Krotish DE, et al. Earlier breast cancer detection in Peru: Establishing a comprehensive program in an underserved region. J Am Coll Radiol. 2020; 17(11):1520–2. https://doi.org/10.1016/j.jacr.2020.06.003 PMID: 32645288

21. Miglioretti DL, Gard CC, Carney PA, Onega TL, Buist DSM, Sickles EA, et al. When radiologists perform best: the learning curve in screening mammogram interpretation. Radiology. 2009; 253(3):632–40. https://doi.org/10.1148/radiol.2533090970 PMID: 19789234

22. Ambroggi M, Biasini C, Del Giovane C, Fornari F, Cavanna L. Distance as a barrier to cancer diagnosis and treatment: Review of the literature. Oncologist. 2015; 20(12):1378–85. https://doi.org/10.1634/theoncologist.2015-0110 PMID: 26512045

23. Lehman CD, Lee AT, Lee CI. Imaging management of palpable breast abnormalities. AJR Am J Roentgenol. 2014; 203(5):1142–53. https://doi.org/10.2214/AJR.14.12725 PMID: 25341156

24. Lam DL, Entezari P, Duggan C, Muyinda Z, Vasquez A, Huayanay J, et al. A phased approach to implementing the Breast Imaging Reporting and Data System (BI-RADS) in low-income and middle-income countries. Cancer. 2020; 126 Suppl 10(S10):2424–30.
25. Thomas DB, Gao DL, Ray RM, Wang WW, Allison CJ, Chen FL, et al. Randomized trial of breast self-examination in Shanghai: final results. J Natl Cancer Inst. 2002; 94(19):1445–57. https://doi.org/10.1093/jnci/94.19.1445 PMID: 12359854

26. Sankaranarayanan R, Ramadas K, Thara S, Muwonge R, Prabhakar J, Augustine P, et al. Clinical breast examination: preliminary results from a cluster randomized controlled trial in India. J Natl Cancer Inst. 2011; 103(19):1476–80. https://doi.org/10.1093/jnci/djr304 PMID: 21862730