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Delays in follow-up among women with abnormal results: a retrospective study based on population-based breast cancer screening programme in China

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Abstract

Objective Timely diagnostic follow-up subsequent to abnormal results is crucial for the efficacy of breast cancer screening programs. We aimed to identify the frequency and women-level factors of loss or delay in the follow-up for screening abnormalities in China.

Methods This mixed-methods cohort study comprised a retrospective analysis of ultrasound based breast screening data collected from Boluo (site A), Lilin (site B), and Ordos (site C) in China from 2018 to 2021, and qualitative, semistructured interviews conducted with program leaders from the three local Maternal and Child Health (MCH) hospitals, respectively. According to the screening protocol, we assessed the follow-up of two screening results: (1) mammography after suspicious results in the ultrasound and (2) biopsy after positive results in the ultrasound or supplement mammography. The rates and timeliness of follow-up with diagnostic examinations were compared across the different sites and procedures, and logistic regression was employed to explore the women-level factors influencing failure or delay in follow-up.

Results Of 7,939 women with abnormal screening results, 5,943 (74.86%) received final diagnostic tests, while 4,631 (58.33%) got final diagnosis timely. The follow-up rate for mammography was higher than that for biopsy. Site A performed better in follow-up, with an overall follow-up rate of 98.01%, which may be related to the provision of free biopsy services and the establishment of a robust referral system. Women aged 45 to 54 years (ref: 35–44 years; aOR = 1.18; 95% CI: 1.01, 1.38; $P = 0.032$) were more likely to be lost to follow-up. Women who had never attended breast screening (ref: ever screened; aOR = 1.15; 95% CI: 1.00, 1.32; $P = 0.046$) were at high risk for delayed follow-up. Conversely, women with a high level of education (aOR = 0.66; 95% CI: 0.59, 0.73; $P < 0.001$) and those with abnormal

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clinical breast examination results (ref: with normal results; aOR = 0.79; 95% CI: 0.69, 0.92; $P = 0.002$) were more likely to get timely follow-up.

Conclusions The overall follow-up rate and quality among women with abnormal screening results showed significant regional variability, and still required to be improved. Moreover, women with higher age and lower educational levels were particularly at high risk for delayed follow-up care and deserved more attention.

Keywords Breast neoplasms, Early detection of cancer, Mass screening, Diagnostic delay

Introduction

Mammography (MAM)-based screening program has been verified to be effective in the reduction of breast cancer mortality through timely detection of early-stage disease [1–3]. A diagnostic follow-up after abnormal screening results entails additional MAM, ultrasound (US), or biopsy to determine a definitive diagnosis. Failure or delay in follow-up can negatively impact women's survival and diminish the overall efficacy of cancer screening programs [4–8]. One pooled study based on five organized breast cancer screening programs in Canada showed that the delayed diagnosis (>6 months) could increase the risk of the progression of breast carcinoma [9]. In addition, inadequate follow-up may also lead to increased emotional distress [7]. The previous study supported that anxiety about breast cancer might decrease participation in subsequent mammography screenings [10]. Therefore, breast diagnostic referral rates and timeliness of follow-up are listed as the candidate performance indicators for evaluating breast cancer screening programs among various European countries [11, 12].

To eliminate inequities in access to appropriately resourced and high-quality services for breast cancer prognosis, the World Health Organization launched the Global Breast Cancer Initiative (GBCI) in 2020. One of three pillars of the GBCI is timely breast cancer diagnosis, which stipulates that evaluation, imaging, tissue sampling, and pathology should be completed within 60 days [13]. Recently, a study showed the feasibility of timely diagnosis in the 21 member countries of the Asian National Cancer Centers Alliance (ANCCA). However, most ANCCA countries lacked national data, and the only institutional-level evidence was based on symptomatic people in hospitals [14]. Similarly, there is limited published literature on the timeliness of diagnostic follow-up among Chinese women, even though the national breast cancer screening program has been implemented over ten years.

Previous studies have identified various factors contributing to disparities in timely follow-up, including barriers at the health system, provider, and individual levels [15–17]. Identifying specific characteristics that heighten the risk of diagnosis delay, particularly at the women's level, provides the foundation for developing tailored strategies to improve adherence to prescribed follow-up care schedules. Currently, empirical evidence evaluating factors affecting diagnostic delay in China is scant, with existing research primarily concentrated on the management of breast cancer patients.

Therefore, the objectives of this retrospective study were to identify the frequency and underlying causes of the failure or delay in the follow-up of women with abnormal screening findings in China.

Materials and methods

Study design and population

We conducted a retrospective study based on the established population-based national breast cancer screening programs from three sites in east, central, and west China between 2018 and 2021, including Boluo (site A), Liling (site B), and Ordos (site C). The three sites included relatively well-established case information systems and, to some extent, with regional representation, could provide preliminary results about the current screening follow-up situation in China. Eligible women were 35 to 64 years of age and had lived in the local area for six months or more, while women with a history of breast cancer or refusal to participate in screening were excluded.

Information about screening participants, including demographic characteristics, risk factors of breast cancer, and the results of initial screening, diagnosis tests, and biopsy, were extracted from the information system of each site. Demographic characteristics and breast cancer risk factors were derived from self-reported questionnaires. Women with a confirmed diagnosis of breast cancer in a first- or second-degree relative were identified as having a family history of breast cancer.

Available facility-level characteristics included screening program protocol type, participating institutions, follow-up processes for women with abnormal screening results, and availability of information systems, which were collected through qualitative interviews with the program management staff.

Breast cancer screening program protocols

Site A launched a free breast cancer screening programme for rural women in 2009, while sites B and C started their programmes in 2016. Site A and site B were two national program sites with the same screening strategy, while site C performed a different screening strategy

as a regional program site. Women in the 35–64 years range were personally invited to undergo breast cancer screening every three years in all three sites, but the target population of the breast cancer screening program in Site C covered both urban and rural women, while the other two regions covered only rural women.

From 2018 to 2021, the screening targets for these three regions were 52,135, 86,090, and 192,000, respectively, which were set by the local health administration departments based on the total number of women of appropriate age. The screening process included firstly health education through new media, communities, village doctors, or other channels to inform women about the significance of breast cancer screening, as well as the screening procedures, and to encourage their participation. Screening facilities were responsible for administering questionnaires to participants, including information on breast cancer risk factors to the participants and providing clinical breast examinations (CBE), breast ultrasound, and mammography services. CBE and US were applied as the primary screening methods for sites A and B. The results of US and MAM were reported by the Breast Imaging Grading Assessment Reporting System (BI-RADS). Women with BI-RADS category 0 or 3 in US were provided with supplemental MAM. In contrast, those with BI-RADS category 4 or 5 in US or supplemental MAM were required to accept a biopsy. Based on this protocol, to facilitate the management of the screening program, women with ultrasound categories 0 and 3 were managed in a unified way and regarded as suspicious. Women with MAM categories 4 and 5 or ultrasound categories 4 and 5 were regarded as positive at sites A and B. Additionally, some women with BI-RADS 0 or 3 MAM underwent biopsy when it was deemed necessary by breast specialists after a comprehensive assessment, considering factors such as physical examination, imaging findings, and medical history [18]. The primary screening methods in site C were the same, but women with BI-RADS categories 0, 4, or 5 in US were required a diagnostic MAM. Only a biopsy was recommended for those with BI-RADS category 0, 4, or 5 on MAM [19]. Thus, to facilitate the management of referrals of abnormal women, we defined ultrasound categories 0, 4, or 5 as suspicious and MAM categories 0, 4, or 5 as positive at site C. The detailed flow chart of each site was described in Supplementary Figs. 1 and 2, respectively.

Identification of failure or delay in follow-up on abnormal breast cancer screening

Based on the different screening protocols, women with abnormal screening results would be recommended to re-visit the hospital to receive follow-up exams. We identified the specific potential gaps in follow-up on abnormal breast cancer screening of three sites, respectively. In site A and site B, the potential gaps included: (1) gap in obtaining a biopsy for those with a positive US result; (2) lack of a diagnostic MAM for those with a suspicious US result; (3) failure to receive a biopsy for those with a positive result of MAM. Although there might be a gap that women with BI-RADS category 0 or 3 on MAM failed to receive a biopsy as clinicians recommended, we did not include it in our analysis due to the lack of this information. For site C, the care delivery gaps referred to: (1) lack of a diagnostic MAM for those with a suspicious US result; (2) women with a positive result of MAM failed to attend a biopsy.

We defined failure to attend a follow-up visit for women with referral recommendations as no follow-up results in the local screening information system after one year of screening, as case closure time in the three regions was typically 3 to 6 months, and the reporting period for screening data was one year. Inevitably, there must be information gaps that may underestimate the follow-up rate. We calculated the time intervals of follow-up care between the date of two screening or diagnostic examinations with any procedures. A waiting time of more than 60 days was chosen as the threshold for a follow-up delay according to the second pillar of GBCI [13].

Women might have received a biopsy rather than a diagnostic MAM without following screening protocol, but they were still defined as having follow-up results. The failure or delay of follow-up was described in Fig. 1.

Statistical analysis

The demographic and clinical characteristics of screening participants were computed using frequencies (percentages). We used the Chi-squared test to compare baseline characteristics for screening participants among three sites. Follow-up rate, follow-up time interval (the median days and IQR), and the percentage of timeliness follow-up were used to display the gaps among screening procedures stratified by study sites and BI-RADS categories. Logistic regressions were applied to identify women-level factors related to failure or delay in the follow-up among abnormal screening women, and forest plots were used for logistic regression results. Regional variables were incorporated into the regression analysis to minimize the potential confounder resulting from regional disparities. In addition, we conducted stratified analyses across distinct referral subgroups, including women referred for mammography and biopsy. To mitigate the loss of statistical power due to reduced sample size and to explore the impact of missing data, we implemented multiple imputations with chained equations for incomplete variables. Educational level and race were excluded from imputation due to the lack of correlated variables necessary to construct predictive equations. Consequently, no more

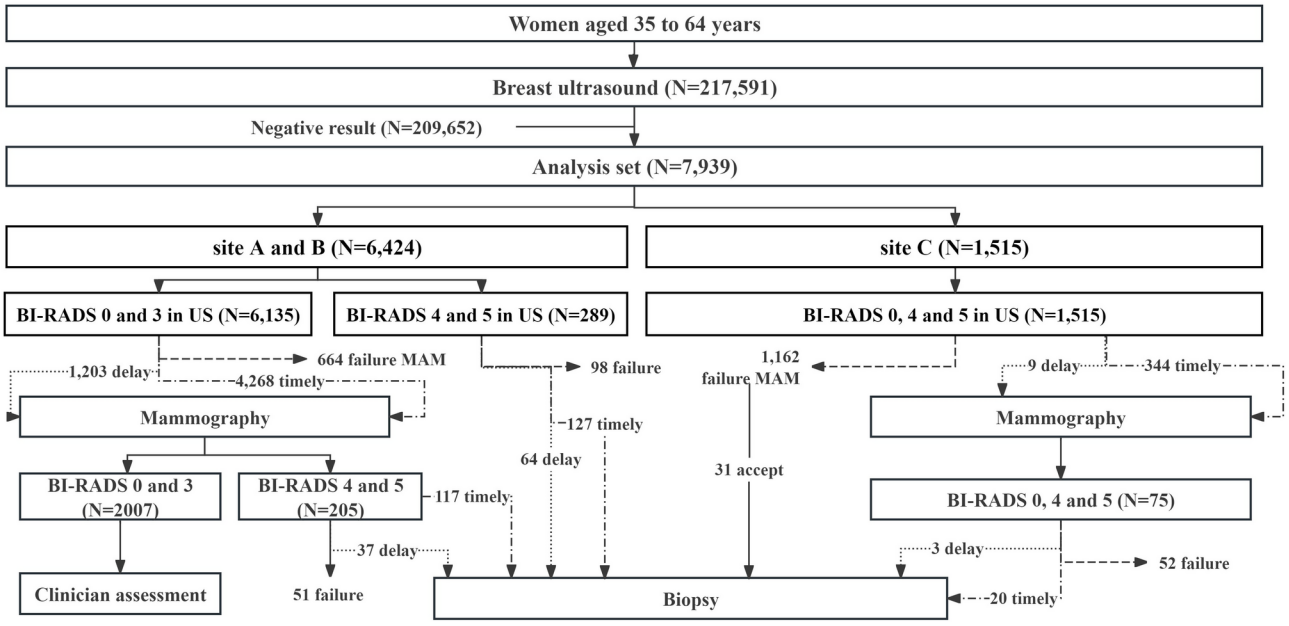


Fig. 1 Overview of gaps of the three screening sites

than 5% of the data were excluded from the multivariable regression analysis. All statistical analyses were conducted using R (version 4.4.1). A P-value < 0.05 was regarded as statistical significance.

Results

Between 2018 and 2021, 217,591 women (mean [SD] age, 47.38 [7.70] years) aged 35 to 64 years underwent breast screening at the three study sites (Supplementary Table 1). Of these, 7,939 women (3.65%) with abnormal screening results who required follow-up diagnostic examinations were included in the analysis. Nearly 56.91% of participants were aged 45 to 64 years, and 24.11% had an education level of primary school or below. The majority (75.82%) were premenopausal, and 23.50% reported having previously attended breast screening. The characteristics of women with abnormal screening results varied across the study sites, except for age at first delivery. Table 1 summarizes the baseline characteristics among women with abnormal screening results in detail.

Timeliness follow-up on abnormal screening results

We analyzed the rates of follow-up and timely follow-up among the different screening processes according to the screening protocols at each site. 5,943 (74.86%) completed a follow-up MAM or biopsy, while 4,631 (58.33%) of those with follow-up results received the diagnostic examination within 60 days. The rate of follow-up for US referral to MAM (76.13%) was higher than those for US referral to biopsy (66.09%) and MAM referral to biopsy (63.21%). A similar trend was observed in the timely follow-up rate.

Both Site A and B had higher follow-up rates for US to MAM sessions, 99.84% (2,533/2,537) and 81.66% (2,938/3,598), respectively. The follow-up rate in US to biopsy sessions at Site B is lower than that of Site A, at 47.34% (80/169). However, Site A had a lower referral rate (68.00%) for MAM to biopsy sessions. The follow-up rate for Site C was less than 50% for both US to MAM and MAM to biopsy sessions (23.30% [353/1,515] and 30.67% [23/75]). The difference in percentages with timely follow-up was similar to the follow-up rate among the three sites. Meanwhile, we evaluated the follow-up rate for the entire procedure between US and the diagnostic tests, which showed substantial regional variations among the three sites: 98.01% (2,604/2,657), 79.82% (3,007/3,767), and 21.91% (332/1,515) respectively. Analysis of the timeliness of follow-up among all participants (including those with and without follow-up results) revealed rates of 77.83%, 59.76%, and 20.59% for the three sites, respectively (Table 2).

In addition, we evaluated the timeliness of follow-up among women who completed referral examinations, excluding the population lost to follow-up. The proportion of women who received timely mammography or biopsy has increased to over 70%, especially at site C, where the timely referral rate for mammography and biopsy reached 97.43% and 86.96%, respectively.

Follow-up mechanisms for abnormal breast screening results among three sites

In the qualitative interviews, we summarized the processes for follow-up on abnormal screening tests in Table 3, which showed variability among the three sites.

Table 1 Characteristics of screening participants with abnormal results

Characteristics	Total (*N* = 7939)	Site A (*n* = 2657)	Site B (*n* = 3767)	Site C (*n* = 1515)	*P*-value
Age					<0.001
35–44	3421(43.09)	1295(48.74)	1526 (40.51)	600 (39.60)	
45–54	3440 (43.33)	1080 (40.65)	1711 (45.42)	649 (42.84)	
55–64	1078 (13.58)	282 (10.61)	530 (14.07)	266 (17.56)	
Educational level					<0.001
Primary school or below	1914 (24.11)	288 (10.84)	740 (19.64)	886 (58.48)	
Junior high school	2901 (36.54)	1434 (53.97)	1182 (31.38)	285 (18.81)	
High school	2267 (28.56)	259 (9.75)	1782 (47.31)	226 (14.92)	
College and above	500 (6.30)	327 (12.31)	63 (1.67)	110 (7.26)	
Missing	357 (4.50)	349 (13.14)	0 (0.00)	8 (0.53)	
Race					<0.001
Han	7477 (94.18)	2316 (87.17)	3735 (99.15)	1426 (94.13)	
Other	116 (1.46)	9 (0.34)	26 (0.69)	81 (5.35)	
Missing	346 (4.36)	332 (12.50)	6 (0.16)	8 (0.53)	
Age of menarche					<0.001
≤ 13	2857 (35.99)	660 (24.84)	2012 (53.41)	185 (12.21)	
14–15	3388 (42.68)	1268 (47.72)	1199 (31.83)	921 (60.79)	
≥ 16	1316 (16.58)	729 (27.44)	186 (4.94)	401 (26.47)	
Missing	378 (4.76)	0 (0.00)	370 (9.82)	8 (0.53)	
Menopause status					<0.001
Postmenopausal	1857 (23.39)	511 (19.23)	956 (25.38)	390 (25.74)	
Premenopausal	6019 (75.82)	2092 (78.74)	2811 (74.62)	1116 (73.66)	
Missing	63 (0.79)	54 (2.03)	0 (0.00)	9 (0.59)	
Previous childbirth					0.047
Yes	7854 (98.93)	2621 (98.65)	3738 (99.23)	1495 (98.68)	
No	85 (1.07)	36 (1.35)	29 (0.77)	20 (1.32)	
Age of first delivery					<0.001
≤ 35	7699 (96.98)	2592 (97.55)	3625 (96.23)	1482 (97.82)	
>35	52 (0.65)	25 (0.94)	18 (0.48)	9 (0.59)	
Missing	188 (2.37)	40 (1.51)	124 (3.29)	24 (1.58)	
Breastfeeding history					<0.001
Yes	7195 (90.63)	2384 (89.73)	3363 (89.28)	1448 (95.58)	
No	683 (8.60)	228 (8.58)	404 (10.72)	51 (3.37)	
Missing	61 (0.77)	45 (1.69)	0 (0.00)	16 (1.06)	
Family history of breast cancer					< 0.001
Yes	65 (0.82)	6 (0.23)	11 (0.29)	48 (3.17)	
No	7861 (99.02)	2648 (99.66)	3756 (99.71)	1457 (96.17)	
Missing	13 (0.16)	3 (0.11)	0 (0.00)	10 (0.66)	
Breast cancer screening history					< 0.001
Yes	1866 (23.50)	988 (37.18)	258 (6.85)	620 (40.92)	
No	5813 (73.22)	1634 (61.50)	3509 (93.15)	670 (44.22)	
Missing	260 (3.27)	35 (1.32)	0 (0.00)	225 (14.85)	
US results[#]					—
BI-RADS 0	436 (5.49)	9 (0.34)	77 (2.04)	350 (23.10)	
BI-RADS 3	6049 (76.19)	2528 (95.14)	3521 (93.47)	—	
BI-RADS 4	1437 (18.10)	114 (4.29)	163 (4.33)	1160 (76.57)	
BI-RADS 5	17 (0.21)	6 (0.23)	6 (0.16)	5 (0.33)	

[#]Women with BI-RADS category 3 in US were not defined as abnormal women in site C

Table 2 Follow-up rate and percentage with timely follow-up for women with screening abnormality stratified by screening processes

Screening processes	Total	Site A	Site B	Site C
US (suspicious) → MAM[a]				
Follow-up rate (%)	76.13(5824/7650)	99.84(2533/2537)	81.66(2938/3598)	23.30(353/1515)
Timely follow-up rate[e] (%)	60.29(4612/7650)	80.65(2046/2537)	61.76(2222/3598)	22.71(344/1515)
Follow-up time[e] (median, IQR)	27 (2, 238)	15(2, 52)	14(2,202)	> 365
Timely follow-up rate[f] (%)	79.19 (4612/5824)	80.77 (2046/2533)	75.63 (2222/2938)	97.45 (344/353)
Follow-up time[f] (median, IQR)	8 (1, 49)	15 (1, 52)	7 (1, 54)	2 (0, 5)
MAM (positive) → Biopsy[b]				
Follow-up rate (%)	63.21 (177/280)	68.00(85/125)	86.25(69/80)	30.67 (23/75)
Timely follow-up rate[e] (%)	48.93 (137/280)	53.60(67/125)	62.50(50/80)	26.67 (20/75)
Follow-up time[e] (median, IQR)	66 (20, > 365)	51 (20, >365)	40.5(9.5,88)	> 365 (36.5,>365)
Timely follow-up rate[f] (%)	77.40 (137 /177)	78.82 (67/85)	72.46 (50/69)	86.96 (20/23)
Follow-up time[f] (median, IQR)	25 (10, 53)	26 (15, 51)	25 (8, 62)	21 (8.5, 33)
US (positive) → Biopsy[c]				
Follow-up rate (%)	66.09 (191/289)	92.50(111/120)	47.34(80/169)	-
Timely follow-up rate[e] (%)	43.94 (127/289)	55.00(66/120)	36.09(61/169)	-
Follow-up time[e] (median, IQR)	89 (16, > 365)	49 (13.8, 111)	>365 (22,>365)	-
Timely follow-up rate[f] (%)	66.49 (127/191)	59.46 (66/111)	76.25 (61/80)	-
Follow-up time[f] (median, IQR)	31 (9, 84.5)	43 (11, 97)	20.5 (8, 57)	-
US (suspicious/positive) → Diagnostic examination (including MAM/biopsy)[d]				
Follow-up rate (%)	74.86 (5943/7939)	98.01 (2604/2657)	79.82 (3007/3767)	21.91 (332/1515)
Timely follow-up rate[e] (%)	58.33 (4631/7939)	77.83 (2068/2657)	59.76 (2251/3767)	20.59 (312/1515)
Follow-up time[e] (median, IQR)	33(3,>365)	19(2, 56)	18(2,214)	>365
Timely follow-up rate[f] (%)	77.92 (4631/5943)	79.42 (2068/2604)	74.86 (2251/3007)	93.98 (312/332)
Follow-up time[f] (median, IQR)	10 (1, 53)	18 (2, 54)	7 (1, 61)	2 (0, 8)

[a] Women with BI-RADS categories 0 or 3 in US (suspicious results) were provided with supplemental MAM in Site A and B, while those with BI-RADS categories 0, 4, or 5 in US (suspicious results) were referred to Site C; [b] Women with BI-RADS categories 4 or 5 in MAM (positive results) required a biopsy in Site A and B, but those with BI-RADS categories 0, 4, or 5 in US (positive results) in MAM were required in Site C; [c] Women with BI-RADS categories 4 or 5 in US (positive results) were directly referred for biopsy only at Site A and B; [d] The follow-up rate for the entire procedure between US and the diagnostic testings including: (1) US (with a positive result)→biopsy, (2) US (with a suspicious result)→MAM (with a negative result), (3) US(with suspicion result) →MAM (with a positive result)→biopsy, (4) US (with suspicion result)→biopsy (without following screening protocol); [e] Including women who did not complete follow-up; [f] Excluding women who did not complete follow-up

Site A and B could implement one-stop screening services in county maternal and child health hospitals, while only US and diagnostic MAM, excluding biopsy, were provided at Site C. Participants who required a biopsy had to go to hospitals at their own expense, except at Site A.

> *The local screening institution had not yet established a pathology department, and the professional level of screening staff was insufficient, limited to the diagnosis and treatment of common breast diseases. (Managers in Site C)*

To improve the accessibility and adherence to screening services among rural women, sites A and B implemented portable mobile ultrasound. At all three sites, screening physicians were responsible for the follow-up and management of women with screening abnormalities, primarily through telephone communication. In addition, Sites A and B implemented a door-to-door approach to hard-to-reach populations through multisectoral cooperation mechanisms, such as women's federation organizations and rural governments, to improve adherence to follow-up recommendations.

> *For women with screening abnormalities who had not accepted follow-up diagnostic examinations despite multiple invitations, the list would be provided to the health and family planning officers and the women's federation chairperson. The chairperson conducted home visits, to encourage them to complete the necessary follow-up. (Managers in Site B)*

Table 3 Characteristics of breast cancer screening procedures in the three analyzed sites

Dimensions	Site A	Site B	Site C
Economic regions	South	Central	East
Type of screening program protocols	National-level	National-level	Local-level
Places to provide screening/diagnostic tests			
Ultrasound and Mammography	County-level maternal and child health hospital alone	County-level maternal and child health hospital alone	County-level maternal and child health hospital
Biopsy			Higher-level hospitals (e.g., municipal/provincial general hospitals)
Service charges			
Ultrasound and Mammography	Free	Free	Free
Biopsy		Self-financed	Self-financed
Whether to provide a one-stop screening service			
Rural	No	No	No
Urban	Yes	Yes	
Follow-up processes			
Full-time staff responsible for follow-up management	Yes (Screening doctors and follow-up quality control team)	Yes (General examination doctors)	Yes (Screening doctors)
Referral mechanism with the superior	Yes	Yes	No
Follow-up forms	Send text message; Contact by phone; Create the WeChat groups	Send text message; Contact by phone	Contact by phone
Measures for women with overdue follow-up	Door-to-door visitation (Women's Federation Organizations; village doctors)	Door-to-door visitation (Women's Federation Organizations; Health and Family Planning Specialist)	Contact by phone
Measures to increase the follow-up rate of women with abnormal screening finding	Health education and peer education	Health education and peer education	Health education
Whether to establish the information system for follow-up	Yes	Yes	Yes

Women-level factors associated with failure or delay in follow-up

The results presented are based on the imputed data set (Fig. 2A and B). To determine the robustness of our primary outcomes, a comparison was made between the imputed results and the complete case. The initial regression models are detailed in Supplemental Fig. 3. Individuals that had abnormal clinical breast examination results (aOR = 0.80; 95% CI: 0.68, 0.95; $P = 0.012$) had a lower risk of failure to the follow-up examination. Otherwise, women with later age of menarche (14–15 vs. ≤13, aOR = 1.70, 95% CI: 1.46, 1.97, $P < 0.001$; ≥16 vs. ≤13, aOR = 1.27, 95% CI: 1.01, 1.60; $P = 0.043$) or who had never attended breast screening (aOR = 1.31; 95% CI: 1.08, 1.59; $P = 0.007$) had a higher risk of loss to follow-up. Moreover, women aged 45 to 54 years (aOR = 1.18; 95% CI: 1.01, 1.37; $P = 0.032$) seemed more likely to fail in follow-up.

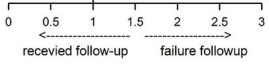
Women who were more likely to complete a follow-up testing within 60 days were those with higher educational levels (aOR = 0.66; 95% CI: 0.59, 0.73; $P < 0.001$) or abnormal clinical breast examination results (aOR = 0.79; 95% CI: 0.69, 0.92; $P = 0.002$). Women without a history of breastfeeding (aOR = 0.52; 95% CI: 0.43, 0.63; $P < 0.001$) had a lower risk of delay in follow-up. In contrast, opposite associations were observed among women with later age of menarche (14–15 vs. ≤ 13; aOR = 1.18; 95% CI: 1.04, 1.33; $P = 0.008$), or who had never attended breast screening (aOR = 1.15; 95% CI: 1.00, 1.32; $P = 0.046$). Referrals from ultrasound to mammography showed a similar pattern of women-level influencing factors to those affecting the acceptance of overall follow-up examinations(Supplementary Fig. 4). However, except for regional effects, only clinical breast examination results had a significant impact on the follow-up rate for referrals from mammography to biopsy (Supplementary Fig. 5).

Discussion

There remains a scarcity of evidence about the status of follow-up for abnormal breast cancer screening regarding the organized breast cancer screening program in China. In this retrospective multicenter study, we found that 74.86% of women with abnormal screening results got the final diagnosis, and 58.33% received diagnostic examinations within 60 days. There was considerable variation in follow-up

A

Characteristic	Received follow-up (N=5943)	Failure follow-up (N=1996)	aOR (95% CI)	p value
Age				
35-44	2652 (44.62)	769 (38.53)		
45-54	2537 (42.69)	903 (45.24)	1.18 (1.01 to 1.38)	0.032
55-64	754 (12.69)	324 (16.23)	1.18 (0.91 to 1.53)	0.211
Educational level*				
Junior high school or below	3434 (57.78)	1381 (69.19)		
High school or above	2162 (36.38)	605 (30.31)	0.87 (0.76 to 1.01)	0.062
Race*				
Han	5554 (93.45)	1923 (96.34)		
Other	55 (0.93)	61 (3.06)	0.69 (0.44 to 1.09)	0.113
Age of menarche*				
≤13	2395 (40.30)	462 (23.15)		
14-15	2309 (38.85)	1079 (54.06)	1.70 (1.46 to 1.97)	<0.001
≥16	961 (16.17)	355 (17.79)	1.27 (1.01 to 1.60)	0.043
Menopause status*				
Postmenopausal	1354 (22.78)	503 (25.20)		
Premenopausal	4534 (76.29)	1485 (74.40)	1.19 (0.98 to 1.45)	0.079
Previous childbirth				
Yes	5879 (98.92)	1975 (98.95)		
No	64 (1.08)	21 (1.05)	0.97 (0.46 to 2.07)	0.941
Breastfeeding history*				
Yes	5326 (89.62)	1869 (93.64)		
No	569 (9.57)	114 (5.71)	0.84 (0.66 to 1.08)	0.169
Family history of breast cancer*				
Yes	23 (0.39)	42 (2.10)		
No	5914 (99.51)	1947 (97.55)	0.79 (0.41 to 1.53)	0.487
Breast cancer screening history*				
Yes	1357 (22.83)	509 (25.50)		
No	4542 (76.43)	1271 (63.68)	1.31 (1.08 to 1.59)	0.007
Clinical breast examination*				
normal	2957 (49.76)	581 (29.11)		
abnormal	2971 (49.99)	1033 (51.75)	0.80 (0.68 to 0.95)	0.012
Site				
C	332 (5.59)	1183 (59.27)		
B	3007 (50.60)	760 (38.08)	0.08 (0.07 to 0.10)	<0.001
A	2604 (43.82)	53 (2.66)	0.01 (0.00 to 0.01)	<0.001



B

Characteristic	Timely diagnosis (N=4631)	Failure or delay to follow-up (N=3308)	aOR (95% CI)	p value
Age				
35-44	2108 (45.52)	1313 (39.69)		
45-54	1968 (42.50)	1472 (44.50)	1.07 (0.95 to 1.20)	0.245
55-64	555 (11.98)	523 (15.81)	1.22 (1.00 to 1.49)	0.055
Educational level*				
Junior high school or below	2545 (54.96)	2270 (68.62)		
High school or above	1778 (38.39)	989 (29.90)	0.66 (0.59 to 0.73)	<0.001
Race*				
Han	4286 (92.55)	3191 (96.46)		
Other	48 (1.04)	68 (2.06)	0.71 (0.46 to 1.08)	0.108
Age of menarche*				
≤13	1840 (39.73)	1017 (30.74)		
14-15	1814 (39.17)	1574 (47.58)	1.18 (1.04 to 1.33)	0.008
≥16	763 (16.48)	553 (16.72)	0.99 (0.84 to 1.18)	0.939
Menopause status*				
Postmenopausal	1024 (22.11)	833 (25.18)		
Premenopausal	3557 (76.81)	2462 (74.43)	1.11 (0.95 to 1.29)	0.175
Previous childbirth				
Yes	4583 (98.96)	3271 (98.88)		
No	48 (1.04)	37 (1.12)	1.58 (0.94 to 2.65)	0.085
Breastfeeding history*				
Yes	4083 (88.17)	3112 (94.07)		
No	506 (10.93)	177 (5.35)	0.52 (0.43 to 0.63)	<0.001
Family history of breast cancer*				
Yes	16 (0.35)	49 (1.48)		
No	4609 (99.52)	3252 (98.31)	0.60 (0.32 to 1.13)	0.113
Breast cancer screening history*				
Yes	1096 (23.67)	770 (23.28)		
No	3497 (75.51)	2316 (70.01)	1.15 (1.00 to 1.32)	0.046
Clinical breast examination*				
normal	2342 (50.57)	1196 (36.15)		
abnormal	2275 (49.13)	1729 (52.27)	0.79 (0.69 to 0.92)	0.002
Site				
C	312 (6.74)	1203 (36.37)		
B	2251 (48.61)	1516 (45.83)	0.21 (0.18 to 0.25)	<0.001
A	2068 (44.66)	589 (17.81)	0.07 (0.06 to 0.09)	<0.001

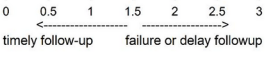


Fig. 2 Women-level factors associated with failure or delay in follow-up. (**A**) Factors associated with failure to complete follow-up after initial screening. (**B**) Factors associated with a waiting time of more than 60 days. * The raw data with missing data

rates and timeliness of diagnostic resolution across different sites (ranging from 21.91% to 98.01 and 20.59–77.83%, respectively). The variations in follow-up management quality were partly due to organizational differences between screening sites, such as healthcare delivery capacity. Women with older age, lower educational attainment, earlier menarche, and who had never attended breast screening or had breastfed were associated with failure or delay in diagnosis of breast cancer.

Effective follow-up of women with abnormal screening results is critical to ensuring the overall quality of screening programs. Many developed countries have established specific performance indicators to monitor the quality of follow-up care. The NHS Breast Screening Programme standards dictate that women with abnormal results referred for assessment should receive their first appointment at an assessment center within three weeks of their screening mammogram [20]. Similarly, the NBCCEDP required that 90% of women with abnormal breast screening results complete diagnostic evaluations within a referral interval of less than 60 days [21]. In China, management indicators such as follow-up rates for further examinations (≥ 90%) have been set in the Chinese National Breast and Cervical Cancer Screening Program (NBCCSP) [22]. However, our study indicates that there is still a considerable gap in fulfilling this requirement.

According to previous studies, the further assessment participation rates in China were significantly lower than in developed countries, where almost above 95% [23]. This disparity may be related to the public screening policy, which ensured sustained funds for screening programs, along with free screening tests and diagnostic tests provided. In our study, only site A offered free diagnostic tests, with the highest follow-up rate, particularly in the pathology referral. Furthermore, the screening information system of some well-established screening programs, such as the NHS Breast Screening Programme and BreastScreen Australia Program, could be linked to the national cancer registry system to achieve closed-loop information management from screening to diagnosis [24]. However, there were severe barriers across Chinese information systems, significantly increasing the difficulty of follow-up. Hence, system interoperability and data linkage need to be emphasized and strengthened [25].

The waiting times varied across procedures from screening to diagnosis. Given the higher false-positive rate in US, women with suspicious or abnormal results were recommended for MAM or referred for biopsy in China. Our study identified the significant care gaps in the screening process were US or MAM referral to the biopsy stage, and the diagnosis delay time was longer than US referral to MAM stage. The possible explanation for this finding was that screening was primarily conducted among maternity and child healthcare hospitals in China, where breast specialty and pathology departments were absent, resulting in the unavailability of pathology services [26]. Additionally, screening participants tended to go to high-level hospitals for diagnosis due to the low confidence level in the diagnostic capability of the pathology examination at the primary level. Therefore, this led to multiple visits to different healthcare providers and facilities, increasing the time to diagnosis, inconvenience, and anxiety for the women. Evidence from previous studies showed that the screening procedure involving fewer coordinators and external parties might be associated with a lower risk of failure in the follow-up of abnormal screening results [27]. The evidence supported that the increase in screening stages has, to some extent, led to missing visits in the population [28]. Similar results were found in our study, where the screening process of "US-MAM-biopsy" tended to result in delayed follow-up compared to "US-MAM".

We also observed the delay in follow-up among women with abnormal results differed among study sites. Site A and B performed better in follow-up compared to site C, which might be associated with a well-functioning referral system with higher-level facilities and a multi-sectoral collaboration mechanism, such as door-to-door visits. No pathology services and a lack of referral mechanisms linked to higher-level hospitals pose barriers to follow-up. Therefore, the waiting time to receive diagnosis testing (especially a biopsy) might be longer. Biopsy is the basic method for diagnosis of breast cancer. Healthcare institutions with limited service capacities could develop telepathology and strengthen cooperation with higher-level hospitals or third-party organizations to establish breast pathology capacity in limited resource settings [29, 30]. In addition, the application of easy biopsy methods (e.g. core needle biopsy replace open biopsy) may help to reduce the follow-up process and therefore the waiting time for a biopsy [31]. Notingly, although the follow-up rate and timeliness at site C were significantly lower than those in the other two regions, this discrepancy may be attributed to the reliance on telephone follow-up for collecting follow-up information. The failure of women to respond to calls or to provide follow-up results could have resulted in a lower follow-up rate in the region.

Patient-level characteristics significantly contributed to the discrepancy in follow-up rates. Consistent with other studies, our results indicated that age, education level, menarche age, screening history, and CBE results showed a close relationship with failure or delay in follow-up care. For example, one previous study conducted by Burack et al. showed that older women tend to receive follow-up care later compared with younger women [32]. Similarly, our study suggested that older women had a higher risk of failing or delaying follow-up compared with younger women. A recent study reported that women with higher

educational levels tend to get timely follow-ups within 60 days, which was also observed in our study [33, 34]. The explanation for this finding might be that these women have sufficient knowledge about breast cancer prevention and proactively seek medical care. Based on this, all three sites provided health education through lectures and mass media to improve the quality of follow-up visits. In addition, women with a history of breast screening may be more sensitive and responsive to breast changes, possibly because they have more health concerns [35]. A similar trend was observed in women with early age of menarche, which may be due to the risk factors related to breast cancer increasing the attention they place on screening results. Notably, women with abnormal CBE results were more likely to complete the follow-up for diagnostic exams within 60 days, which suggests that women paid more attention to follow-up depending on the degree of suspicion of cancer. A integrative literature review supported that patients presenting with breast symptoms were more likely to receive adequate follow-up, and a cross-sectional study in Sudanese also indicated the failure of doctors to suspect cancer at initial consultation was the leading cause of delayed diagnosis [15, 36]. In addition, the results of several studies based on delayed diagnosis of breast cancer have shown that, the appearance of symptoms that cannot be definitely linked to breast cancer, anxiety and fear, economic barriers, distance to the facility, and perceptions of other competing events taking precedence over personal health, such as work and family [37–41].

A specific strength of our study is that it is the first real-world study based on a government-supported mass breast cancer screening program in China, analyzing the status of loss or delay in follow-up among women with abnormal screening results, and proposing potential optimization recommendations. We explore the specific participant-level factors through multiple analyses and conduct qualitative interviews among three sites to complement institutional-level factors, which provide empirical evidence to help improve the effectiveness of a population-based screening program and identify the existing gap in achieving the goal of WHO GBCI in China. Moreover, our study was a multicenter study, and the three selected regions were located in the southern, central, and western economic regions, respectively. Although only one study site in each of the regions was included, it still provided a certain degree of regional representativeness, showing a preliminary overview of the current follow-up status of the organized breast screening programme in China.

This study has several limitations. Firstly, our data heavily relied on the screening information system, which was not integrated with other information systems, such as the national health insurance system. Staff obtained follow-up information and results of women through phone calls or their hospital information system and entered the relevant information into the screening system. Consequently, women who received follow-up examinations but whose subsequent information was not added into the system were regarded as loss of follow-up. This may result in the underestimation of the quality of follow-up to some extent. And inevitably, some women diagnosed with breast cancer concealed their diagnosis, leading to inaccurate breast cancer detection rates. Secondly, the risk factors related to women's level were all derived from self-reported questionnaires, which may introduce recall or reporting bias. Due to the lack of information on women's income levels, fear, anxiety, etc., the impact of financial burdens and psychological barriers on the loss of follow-up visits of abnormal women was not assessed. In addition, the proportion of incomplete cases reached 15.90% in our study. To address this, multiple imputations were performed for the missing data, and a sensitivity analysis was conducted for the primary outcomes by comparing the imputed data with the original data. However, slight differences were observed in the effects of certain variables, which may be related to the limited availability of relevant variables required to construct the imputation model and the data missing mechanism, such as not missing at random. Moreover, according to the screening protocol, further examinations of women with BI-RADS category 0 or 3 on MAM depended on the clinicians' assessment in site A and site B. However, these women were not included in the analysis due to the lack of assessment results, which may impact the accuracy of the biopsy referral rate.

Conclusion

Successful breast screening requires timely follow-up after abnormal US results in China. This study found that the overall follow-up rate and quality among women with abnormal screening results showed significant regional variability, and still required to be improved. The effective multi-sectoral cooperation mechanisms and an integrated service system may be essential to improve the timeliness of target groups to receive the full range of screening services. Vulnerable populations, such as older women and those with lower educational levels, are particularly at risk of delayed follow-up care and should be given more attention.

Abbreviations

MAM	Mammography
CBE	Clinical breast examination
US	Ultrasound
BI-RADS	The Breast Imaging Grading Assessment Reporting System
GBCI	Global Breast Cancer Initiative
OR	Odds ratio
IQR	Interquartile range

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12889-025-22879-x.

Supplementary Material 1

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Author contributions
Y.Z., F.Z., W.R., and L.Y. were the study conception initiators and designed the analysis. L.Z., F.W., J.C., Y.W., Y.X., G.Z., H.W., J.W., and H.L. collected the data. L.Y., W.R. performed the data analysis. L.Y., W.R., X.Z., and F.Z. participated in manuscript writing and interpretation. All authors provided constructive comments and revisions on the manuscript.

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Data availability
The datasets generated and/or analyzed during the current study are not publicly available to preserve anonymity of the respondents.

Declarations

Ethics approval and consent to participate
This study obtained the approval of the Ethics Committee of National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College (Beijing, China; reference number: 22/336–3542). All participants provided written informed consent before the screening procedures. The Ethics Committee approved the use of the database and the present study protocol and waived the informed consent from the individual as the data used in this study were obtained from a national program established by the government.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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