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REVIEW

Application of patient navigation programs across the entire continuum of breast cancer care: a GRADE-assessed systematic review with meta-analysis

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Abstract

Background Patient navigation programs (PNPs) have been increasingly applied in breast cancer (BC) care of underserved clients, as they can significantly assist them with coordinating services across the care continuum. However, existing evidence has produced inconclusive findings regarding the empirical adequacy of BC-related caring interventions developed from PNPs. Hence, the aim of the present systematic review and meta-analysis was to clarify the benefits of PNPs across all phases of the BC care continuum. Primary outcomes comprised care-continuum indicators extracted predominantly from medical records, while secondary outcomes included client-reported healthcare measures.

Methods Five electronic data sources were searched for randomized controlled trials (RCTs) that investigated the effectiveness of PNPs across the BC care continuum from 1995 to January 10, 2025, with no restrictions on clients' sociodemographic characteristics. A random-effects model, using both the DerSimonian-Laird (DL) method and the Hartung-Knapp (HK) adjustment, was applied to estimate standardized mean differences (SMDs) for continuous outcomes and odds ratios (ORs) for dichotomous outcomes, with 95% confidence intervals (CIs).

Results Thirty-seven RCTs met the inclusion criteria, including four cluster RCTs and 33 individual RCTs. Quantitative synthesis was not feasible for time-to-resolution, adherence to adjuvant or post-treatment follow-up care, timely treatment initiation, treatment completion, satisfaction with care, or psychological distress; therefore, the effectiveness of PNPs for these outcomes remains uncertain. Meta-analyses of individual RCTs, all conducted using a DL random-effects model, indicated that PNPs significantly improved diagnostic follow-up compliance (OR, 2.42; 95% CI, 1.64, 3.59; $P<0.001$); screening mammogram adherence (OR, 2.18; 95% CI, 1.71, 2.77; $P<0.001$); and timely diagnostic resolution (OR, 2.51; 95% CI, 1.21, 5.24; $P=0.014$). Using the same DL model, PNPs also improved quality of life (SMD, 0.44; 95% CI, 0.09, 0.79; $P=0.014$) and reduced anxiety (SMD, −0.94; 95% CI, −1.66, −0.22; $P=0.010$). However, no statistically significant effects were observed under the DL model for depression (SMD, −0.34; 95% CI, −0.71, 0.04; $P=0.076$) or BC knowledge (SMD, 0.27; 95% CI, −0.19, 0.73; $P=0.247$). Substantial heterogeneity was observed across most pooled outcomes ($I^2=63.9\%–93.0\%$), accompanied by wide prediction intervals that included the null value. After applying the HK adjustment, the previously observed beneficial effects of PNPs on timely diagnostic resolution, quality of life, and anxiety were no longer statistically significant.

Conclusion Although initial analyses suggested that PNPs may improve several BC-related outcomes, these observed benefits were reduced in magnitude and, in some cases, no longer statistically significant after applying more conservative adjustment methods. Moreover, substantial heterogeneity across studies and the overall low methodological quality limit the certainty of the evidence. Therefore, the current findings should be interpreted cautiously, and further high-quality RCTs are needed to draw more definitive conclusions about the effectiveness of PNPs across the BC care continuum.

PROSPERO registration CRD42023487495.

Keywords Breast neoplasms · Evidence-based nursing · Healthcare disparities · Patient navigation

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Background

Breast Cancer (BC) is a significant global health burden, affecting women in both low- and middle-income countries [1]. According to the latest global cancer statistics, BC is the most commonly diagnosed cancer among women worldwide, accounting for approximately one in four cancer cases and one in six cancer deaths in women [2]. Fortunately, there have been promising advancements along the BC care continuum [3]. However, there are still persistent disparities in BC outcomes across different ethnic, racial, and socioeconomic groups [4]. Based on a recent report, it is more challenging for women with lower incomes or from disadvantaged racial and ethnic populations to benefit from BC screening, potentially leading to delayed BC detection and treatment, as well as increasing the associated risk of death [5]. This can be attributed to various factors, including economic issues, social environments, obstacles associated with BC care and treatment, and client-healthcare provider communication [6]. BC disparities can also be substantially affected by healthcare delivery systems [7].

Addressing disparities and promoting equity in BC care for underserved and vulnerable populations requires a well-designed healthcare delivery approach along with a culturally tailored care coordination or navigation program [8]. In this context, the patient navigation program (PNP) has emerged, ensuring timely and equitable access to healthcare generally, and more specifically, along the cancer care continuum [9]. This initiative was first introduced in 1990, when Harold Freeman designed a PNP at Harlem Hospital (New York, USA) to decrease the exceedingly high rate of disparities in BC care among the underserved local community of Black women [10].

PNP is defined as any formal or informal systematic process delivered by a multidisciplinary team of professional navigators (e.g., nurses, social workers, and health educators) or trained lay navigators; it involves different approaches based on individualized assessment and identification of clients' specific preferences, beliefs, needs, resources, and barriers to care [11]. In this client-centered healthcare delivery approach, navigators utilize their specialized knowledge, experiences, or skills to reduce cancer health disparities among medically underserved clients by providing a variety of services and activities, including but not limited to assisting with scheduling appointments, helping with financial or insurance constraints, providing language interpretation, facilitating communication between clients and team specialists inside and outside the healthcare system, coordinating transportation services, providing education and explaining information about different care aspects, and presenting clients with psychosocial advocacy and support [12, 13].

Since the inception of PNP, it has become a widely applied approach for effective care in different oncology fields [14], with BC presenting an ideal field for PNP due to the known survival benefits of early diagnosis through clinical breast examination (CBE) and mammography, early interventions, and the nature of treatments, which often require multidisciplinary modalities [15]. Hence, in recent decades, scientific studies have increasingly investigated the consequences of PNP across the continuum of BC care [16]. Studies have supported the potential for PNP to increase knowledge of BC, improve acceptance of and adherence to screening exams, reduce time to diagnosis, facilitate timely diagnosis, augment compliance with appropriate follow-up appointments after suspicious findings, raise adherence rates to treatment regimens, boost satisfaction with care, and enhance psychosocial outcomes related to abnormal findings, all of which benefit client care [17, 18].

Despite the increasing use of PNP, most available data on the value of its application in BC care have been anecdotal and based on practice-based evidence [11]. Randomized Controlled Trials (RCTs) and systematic reviews have also reported contradictory and inconsistent findings on the applicability of BC-related interventions developed on the basis of PNP, making it challenging to include this approach in BC-related care guidelines [17]. Previous related reviews have mostly synthesized BC along with other cancers [14, 16, 19–26]. Those that specifically addressed BC tended to be systematic in design, to synthesize the evidence at different levels, or to be weighted toward screening or diagnosis phases [17, 27–29]; this has made an evidence-based conclusion challenging. In light of the need for evidence-based nursing approaches to evaluate care program effectiveness and guide practice [30], this study aimed to systematically summarize and quantitatively synthesize available RCTs evaluating PNP interventions across the entire BC care continuum.

Methods

Design and registration

The design and reporting of this study were in compliance with the latest Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [31]. The study protocol was also recorded in the International Prospective Register of Systematic Reviews (PROSPERO, CRD42023487495).

Inclusion criteria

The eligibility criteria were based on the review question: "Do interventions based on PNP improve the quality of BC

care?" We included prospective RCTs published in English if they met the following criteria:

1) Were performed on women aged ≥ 18 years at any phase along the continuum of BC care;
2) Applied a caring intervention in community-based sites or medical settings based on PNP in the experimental group, meaning that a professional and/or non-professional navigator sought to achieve the following goals typical of the operationalization of a PNP: systematic screening and addressing of clients' specific needs and barriers related to health, providing services for clients more at risk of treatment or care delays, and supporting clients across the care continuum [32];
3) Implemented any form of health promotion intervention without PNP in the comparison group (e.g., an approach that clients regularly followed in order to access procedures, appointments, and healthcare professionals without a navigator);
4) Measured outcomes related to the BC care continuum through medical records or client-reported healthcare data: The primary outcomes of interest, predominantly derived from medical record data, included adherence to screening exams, adherence to diagnostic follow-up care, Timely Diagnostic Resolution (TDR), Time-to-Resolution (TTR), compliance with adjuvant treatment or post-treatment follow-up, timely initiation of treatment, and time to completion of treatment. These variables were carefully selected to provide a comprehensive evaluation of both the quality and timeliness of care, with an emphasis on objective and reliable metrics. To complement this clinical data, secondary outcomes included patient-reported variables, which offered valuable insights into the patient experience. These outcomes included knowledge of BC, satisfaction with care or treatment, Quality of Life (QoL), and psychological consequences (including distress, anxiety, and depression) (Table 1).

Based on a preliminary search, we decided to avoid restricting clients' sociodemographic characteristics in the inclusion criteria. When possible, differences in intervention effects across client-related subgroups were explored through subgroup analyses.

Exclusion criteria

Studies that used promotora-based or case management interventions were only retained in the sample if they clearly addressed navigation activities, because these interventions and PNP-driven interventions are commonly used

Table 1 The study outcomes regarding the effects of the PNPs on the BC care continuum

Outcomes		Definition
Primary	Adherence rate to a screening exam	The proportion of women who completed an age-appropriate mammogram or CBE as recommended
	Adherence rate to diagnostic follow-up care	The proportion of women with abnormal/suboptimal BC screening/diagnostic exams who completed all scheduled diagnostic follow-up care appointments for consultation or diagnostic procedures (i.e., mammogram, ultrasound, fine needle aspiration, biopsy, or CBE)
	TTR	The number of days from an abnormal BC screening/diagnostic exam to confirmation of a definitive diagnosis, either benign or malignant
	TDR	The proportion of women who achieved a definitive diagnosis (malignant or benign) within a specified time from the detection of abnormal results to diagnostic resolution
	Adherence rate to adjuvant treatment/or post-treatment follow-up care	The proportion of women who completed chemotherapy and/or radiation therapy, or a follow-up care appointment after these treatments
	Time to completion of treatment	The number of days from cancer diagnosis to completion of initial chemotherapy and/or radiation therapy
	Timely start of treatment	The proportion of women who initiated treatment within a predetermined time after a definitive diagnosis
Secondary	Knowledge of BC	Knowledge of women regarding BC and/or screening before and after the administration of a PNP
	Satisfaction with care or treatment	Overall satisfaction among women regarding BC-related care or treatment following the administration of a PNP
	QoL	QoL of women before and after the administration of a PNP
	Psychological consequences	Distress, anxiety, and depression among women following the administration of a PNP

BC breast cancer, *CBE* clinical breast examination, *PNP* patient navigation program, *QoL* quality of life, *TDR* timely diagnostic resolution, *TTR* time-to-resolution

interchangeably despite being dissimilar [33]. Trials were also excluded if they met the following criteria:

1) Included clients aged < 18 years;
2) Addressed BC in both genders, unless data were reported for female patients separately or the sample size of male patients compared to female patients was substantially lower;
3) Investigated BC in addition to other types of cancer, unless the sample size and data analysis were reported for BC separately;
4) Administered PNP along with other non-routine or alternative caring interventions (e.g., tailored educational DVD, health worker-guided smartphone application, or health outreach), unless the comparison group received the same non-routine or alternative caring interventions as the PNP group;
5) Implemented any intervention for the control participants, either using low-intensity navigation or with the help of the navigator employed in the PNP group;
6) Only evaluated study outcomes in the PNP group (e.g., satisfaction with care or treatment);
7) Were non-experimental, quasi-experimental, or modeling studies; qualitative syntheses; protocols; pilot trials; conference presentations; reviews; or without available full texts.

Information sources and search strategy

The Clarivate Web of Science, Scopus, and PubMed databases were systematically searched from the starting date of 1995, when the first study on PNP was published. Furthermore, the Cochrane Central Register of Controlled Trials was screened to find additional related trials. We also searched for trial protocols registered in the International Clinical Trials Registry Platform (ICTRP). The reference lists of the included studies were also checked manually to identify studies that might have been overlooked.

Two independent investigators conducted the searches; substantial agreement was found between them during this process (Kappa coefficient, 0.81–0.89). The first search was performed on August 13, 2024, and then updated on January 10, 2025. The search strategy consisted of the three principal components of "PNP," "BC," and "RCT" connected by "AND." For PubMed, medical subject headings were used to select appropriate key terms and synonyms. A combination of identified keywords was used for the other databases. The search syntax for each database was devised in coordination with a librarian to ensure a balance between specificity and inclusivity (Supplementary Table 1).

Screening and selection process

The search results of the selected databases were exported into reference management software (Endnote© version X8). Duplicate studies were then removed, and the remaining records were sent to Microsoft Word for initial screening. To this end, the two researchers independently screened all the titles and abstracts of the retrieved sources and removed irrelevant studies. In the following stage, the researchers meticulously screened the full texts of all retained articles based on the inclusion and exclusion criteria. Finally, the eligible articles were selected. The researchers resolved any disagreements in the study selection process through discussion; if the conflicts were not resolved, this discussion was extended to other researchers.

Data extraction

Two independent researchers initially extracted the main study characteristics using a standardized electronic data extraction form, and any discrepancies were resolved through discussion with other members of the research team. When data were missing or unclear, study authors were contacted to obtain the necessary information.

For dichotomous or binary outcomes, we extracted the number of events along with percentages or odds ratios (ORs) with 95% confidence intervals (CIs). To pool ORs in the meta-analysis, when a study reported only numbers with percentages, the OR was estimated using a standard formula. For continuous outcomes, mean changes from baseline to follow-up were extracted along with their corresponding standard deviations (SDs) or 95% CIs. When studies reported only 95% CIs, these were converted to SDs to enable data pooling. For studies that did not report change scores directly, the mean change was calculated as the difference between baseline and follow-up means, and the SD of change was computed using the following formula: $\sqrt{(\text{SD-pre}^2 + \text{SD-post}^2 - 2 \times r \times \text{SD-pre} \times \text{SD-post})}$, assuming a pre-post correlation (r) of 0.50 [34]. For studies with multiple follow-up time points, the longest available follow-up was selected to reflect the sustained effects of the interventions, in line with methodological guidance indicating that later assessments generally provide more stable estimates of intervention effects [35]. No harmonization of score direction was required for continuous outcomes, as all measures were consistently oriented across included studies. Higher scores were interpreted as indicating better QoL, satisfaction, and knowledge, as well as higher levels of anxiety, depression, and stress.

In multi-arm trials with two PNP groups (i.e., face-to-face vs. telephone-based, full-intensity vs. limited-intensity navigation), the two intervention arms were pooled into a single group for comparison with the control condition to prevent double counting and ensure that each study contributed only once per outcome. For trials evaluating PNP in combination with an active or alternative intervention and comparing it with both the active or alternative intervention

alone and standard care, the active or alternative intervention alone was considered the comparator, and effect estimates were derived from comparisons between the combined intervention (PNP plus co-intervention) and the co-intervention alone.

When available, adjusted effect estimates accounting for potential confounders (e.g., sociodemographic characteristics or baseline measures) were extracted to minimize confounding bias. Furthermore, where intention-to-treat analyses were applied to handle missing data, these estimates were preferentially used to reduce bias associated with incomplete outcome data. For cluster Randomized Controlled Trials (cRCTs), cluster-adjusted relative effect estimates (e.g., ORs) along with their corresponding measures of precision (e.g., CIs or standard errors (SEs)) were preferentially extracted. In cases where cluster-adjusted estimates were not explicitly reported, adjustments for clustering were undertaken, where feasible, using available parameters such as the intracluster correlation coefficient (ICC) and average cluster size to approximate the design effect. If neither direct extraction nor valid reconstruction of cluster-adjusted estimates was possible (e.g., due to missing ICC, cluster size, or variance estimates), the studies were excluded from the quantitative synthesis and retained for qualitative analysis only.

Quality assessment

The two investigators independently appraised and rated the quality of each eligible study. In cases of disagreement between the two corresponding investigators, a consensus was reached through conversation with other investigators. The revised Cochrane collaboration risk of bias tool for RCTs (RoB 2) was applied to assess the individual RCTs [36]. For cRCTs, the RoB 2-cRCT tool, specifically developed for this trial design, was used [37].

The certainty of evidence was assessed using the Grading of recommendations assessment, development, and evaluation working group (GRADE) approach. Evidence was downgraded based on RoB, inconsistency, indirectness, imprecision, and publication bias. No upgrading of evidence certainty was performed for any outcome, including for large or very large magnitude of effect [38]. Absolute effects were not calculated because baseline risks were not consistently reported and varied substantially across studies, precluding the derivation of a single representative control risk and meaningful absolute effect estimates.

Data synthesis and analysis

Data synthesis was performed concurrently with data extraction by two independent investigators, and any disagreements were resolved through discussion with other members of the research team. All statistical analyses were conducted in STATA version 14.0 (Stata Corp, College Station, TX), and statistical significance was set at $P < 0.05$.

A random-effects model was applied to all pooled analyses to account for between-study heterogeneity. The DerSimonian-Laird (DL) method was selected as the primary estimator due to its widespread use and established applicability in clinical research. This method enables estimation of both within-study and between-study variance components, thereby capturing heterogeneity in Effect Sizes (ESs) and allowing studies with greater precision (i.e., smaller SEs) to contribute more heavily to the pooled estimate [39]. However, given evidence that the DL approach may yield overly narrow CIs, sensitivity analyses were conducted using the Hartung-Knapp (HK) adjustment, which provides more conservative interval estimates and reduces the risk of overestimating precision [40]. The combined use of DL and HK methods was intended to enhance the robustness and credibility of the findings.

For dichotomous outcomes, ESs were expressed as ORs, while continuous outcomes were summarized using Standardized Mean Differences (SMDs) derived from Hedges' g, with correction for small-sample bias applied where appropriate. Only pre-post change scores were synthesized; post-intervention values were not combined with change scores. The SD of change scores was imputed assuming a pre-post correlation coefficient of $r = 0.50$, and sensitivity analyses were performed using alternative plausible values ($r = 0.25$ and $r = 0.75$) to assess the stability of the results.

Between-study heterogeneity was evaluated using τ^2, Cochran's Q statistic, and the I^2 index. In addition, 95% prediction intervals (PIs) were calculated to estimate the range of true effects expected in future studies. To investigate potential sources of heterogeneity, subgroup analyses were conducted for categorical moderators, and meta-regression analyses were performed for continuous variables [41]. Publication bias was assessed through visual inspection of funnel plots and Egger's test when at least 10 studies were available. For analyses including fewer than 10 studies, publication bias was evaluated qualitatively [42]. In cases of notable publication bias, the trim-and-fill method was applied to estimate bias-adjusted pooled ESs [43].

Results

Study identification

The flow diagram for the identification and study selection process is shown in Supplementary Fig. 1. In the initial search, 2180 records were obtained from the databases. Eleven further citations were found through citation searching of the retrieved studies and previous reviews. After

removing 652 duplicates, 1539 records were evaluated in the initial screening. Subsequently, 1435 irrelevant records were excluded through screening of titles and abstracts, leaving 104 eligible for the secondary screening. We could not retrieve the full text of one publication [44], and 66 further articles were excluded following full-text evaluation and application of the eligibility criteria (Supplementary Table 2). Finally, 37 studies were included in the final sample for the current review.

Characteristics of included studies

Table 2 summarizes the included study information. All studies were published between 1997 and 2023. Except for four studies, all were done in various parts of the United States of America (USA); the remainder were conducted in Denmark [45, 46], Malaysia [47], and Bangladesh [48]. Most studies employed a two-arm design, while six used three- or four-arm designs [48–53]. In terms of study design, the majority were individually randomized parallel-group trials, whereas four studies used a cluster-randomized design [52, 54–56]. Among the identified cRCTs, only one study was considered potentially eligible in principle because clustering was appropriately addressed [55]; however, it was ultimately excluded from the pooled analysis due to limited comparability and insufficient information to derive a pooled effect estimate. The remaining cRCTs were excluded from quantitative synthesis because they lacked cluster-adjusted effect measures or sufficient statistical detail to enable valid reconstruction of effect estimates for pooling (Supplementary Table 3).

Study participants came from different racial and ethnic minorities or medically underserved groups who were adversely affected by health disparities. They were recruited from diverse settings (e.g., hospitals, community-based health clinics or centers, and primary care or outpatient clinics) and geographic locations (e.g., urban, suburban, and rural). All study samples covered women alone, except for one study, which included both genders. This study was not excluded due to the small sample size of male patients compared to female patients (99.0% vs. 1.0%) [56]. Thirteen of the included studies investigated BC in addition to other types of cancer [52–55, 57–65]. Sample sizes ranged from 9 to 22,425 clients.

The studies investigated different phases along the continuum of BC care targeted by PNP (prevention or screening = 18, diagnosis = 10, treatment = 7, and survivorship = 2). Twenty studies reported a non-professional navigator-delivered model of PNP, utilizing trained community or lay health workers or peer navigators. Meanwhile, eight trials used professional navigators, mostly from nursing and social work backgrounds. Two studies recruited both professional and non-professional navigators [58, 66]. The navigator model was not mentioned in the other seven studies [52–54, 61, 65, 67, 68]. Navigation services were delivered face-to-face and/or remotely (i.e., by telephone calls, text messages, smartphone- or web-based applications, and emails). The services varied widely across studies but typically included activities involving the following: (1) addressing and assessing barriers to care or treatment; (2) educational sessions and materials; (3) appointment scheduling, reminders, attendance, and follow-up; (4) psychological support; (5) social, financial, and insurance issues; (6) translation needs; and (7) transportation arrangements. Comparison conditions included usual care alone ($n = 16$), alternative intervention alone ($n = 2$), usual care plus alternative intervention ($n = 5$), educational intervention alone ($n = 9$), delayed PNP or alternative intervention alone ($n = 2$), and delayed PNP or alternative intervention along with usual care ($n = 3$). The intervention duration and frequency ranged from a single session on 1 day to multiple sessions over 42 months.

Study outcomes

Screening outcomes

Eighteen studies measured the adherence rate to a screening exam. Of these, 15 studies addressed adherence to a mammogram among women who were overdue for this exam ($n = 13$), were candidates for a re-screening mammogram ($n = 1$), or had/had not undergone a prior screening mammogram ($n = 1$) [49, 50, 53–55, 57–59, 65, 68–73]. Two other trials documented the uptake of a screening mammogram among Medicare beneficiaries, without reporting any history of previous mammograms [60, 74]. One trial considered the uptake of screening CBE [47]. According to the qualitative synthesis, four of the 18 included studies demonstrated no significant difference between the study groups in adherence rate to screening exams [50, 54, 57, 65] (Table 2).

Excluding the single study that assessed CBE [47], a total of 17 studies were eligible for meta-analysis to evaluate the association between improved adherence to screening mammography and receiving PNP interventions. Of these, one study did not report the sample size of the control group, which would have allowed estimation of OR; hence, its inclusion in the meta-analysis was not possible [50]. Another study that measured a re-screening mammogram was also not included in the meta-analysis, because it was inconsistent with the rest of the studies [69]. Thus, 15 studies were deemed potentially eligible for quantitative synthesis. Of these, two were cRCTs, one of which was excluded due to the absence of cluster-adjusted effect estimates [54], while the other was not included because of methodological concerns, including a substantially larger ES and limited comparability with other studies, raising the possibility of disproportionate influence on the pooled estimate in the context

Table 2 Summary of the included studies on the effects of the PNPs on outcomes of the BC care continuum

Authors, publication year (location, design)	Population						Study arms: Sample size (age*)
	Condition	Race/ ethnicity	Primary language	Income/insurance	Education	Setting	
Atlas et al., 2023 (USA, 4-arm cRCT[1])	Women, aged 40-80 y, with abnormal BC screening results (BI-RADS: 3-5)[2]	Diverse (White, Hispanic or Latino: mostly)	English: mostly	Insured: mostly	nr.	46 Primary care practices in Massachusetts and New Hampshire	PNP: 220 (~61.0; 54.0-69.0) RP: 243 (~61.0; 52.0-69.0)
Bidstrup et al., 2023 (Denmark, 2-arm individual RCT)	Women, aged >18 y, with BC and moderate-to-severe distress	Danish: 100.0%	Danish: 100.0%	nr.	Higher education: mostly	Department of Breast Surgery in Rigshospitalet, Copenhagen	PNP: 156 (55.8±11.1) RP: 153 (56.7±11.4)
Schliemann et al., 2023 (Malaysia, 2-arm individual RCT)	Women, aged 40-74 y, without experiencing BC symptoms	Asian (Malay: 66.1%)	nr.	LI: 97.3%	HS: 75.2%	Two sub-districts of Segamat: Sungai Segamat, a town area & Jabi, a rural area	PNP: 122 (40-49: 39.3%) RP: 144 (40-49: 41.0%)
Wyatt et al., 2023 (USA, 2-arm individual RCT)	Women, aged 40-75 y, overdue for a mammogram[2, 3]	Muslims (South Asians: 62.1%)	Non-English: mostly	Insured: mostly	<HS: mostly	Local community-based organizations and mosques, New York	PNP: 173 (~53.8±9.1) RP: 175 (~45.1±9.1)
Champion et al., 2022 (USA, 3-arm individual RCT[4])	Women, aged 50-74 y, overdue for a mammogram[3]	White: 97.4%	English: 100.0%	MI: 41.3%; insured: 88.0%	≥HS: 82.8%	96 rural Indiana and Ohio counties	PNP: 162 (50-54: 37.0%) RP: 157 (50-54: 35.0%)
Fernandez et al., 2022 (USA, 2-arm individual RCT)	Women, aged ≥40 y, overdue for a mammogram[3]	Black: mostly	English or Spanish: nr.	LI & uninsured: mostly	≥HS: mostly	Houston and Weslaco, Texas	PNP: nr. RP: nr.
Dixit et al., 2021 (USA, 2-arm individual RCT)	Women who survived BC	Diverse (Asian: 41.0%)	English, Spanish, or Cantonese: nr.	LI: nr.; insured: 82.0%	≥HS: 64.0%	A public hospital in California	PNP: 20 (nr.) RP: 20 (nr.)
Savas et al., 2021 (USA, 2-arm individual RCT)	Women, aged ≥40 y, overdue for a mammogram[2, 3]	Latinas: 100.0%	Spanish or English: nr.	LI: 60.8%; uninsured: 91.8%	Highest grade completed: 9.0±3.1	El Paso, Texas	PNP: 194 (49.2±7.5) RP: 196 (49.5±7.4)
Glassgow et al., 2019 (USA, 3-arm individual RCT[5])	Women, aged ≥18 y, with an abnormal screening/diagnostic mammogram (BI-RADS: 0, 4, or 5)	Black (African American): 85.8%	nr.	Insured: 57.8%	nr.	Three hospitals in Chicago, Illinois	PNP: 809 (58.9±13.3) RP: 829 (58.5±12.6)
Margulies et al., 2019 (USA, 2-arm individual RCT)	Women with/without a prior screening mammogram	Diverse (Hispanic/ Latino: 44.8%)	Spanish/English: nr.	Insured: 100.0%	≥HS: 65.3%	A safety net hospital, New York	PNP: 25 (53.4±nr.) RP: 24 (55.2±nr.)
Molina et al., 2018 (USA, 2-arm individual RCT)	Women, aged 50-74 y, who were referred for a follow-up screening mammogram	Black (African American): 76.0%	nr.	$41,082; uninsured: 15.1%	nr.	Three hospitals in Chicago, Illinois	PNP: 741 (50-59: 50.0%) RP: 1,795 (50-59: 50.0%)

Table 2 (continued)

Slater et al., 2018 (USA, 2-arm individual RCT)	Women, aged 50-74 y, overdue for a mammogram[2, 3]	Diverse (White: 67.9%)	English: 83.0%	LI: 42.7%; insured: 100.0%	≤HS: 85.5%	Minnesota Department of Health	PNP: 11,077 (57.8±6.3) RP: 11,036 (58.9±6.4)
Han et al., 2017 (USA, 2-arm cRCT)	Women, aged 21-65 y, overdue for a mammogram[2, 3]	Korean Americans: 100.0%	Non-English: mostly	LI & uninsured: mostly	≥College: mostly	23 ethnic churches in the Baltimore, Maryland-Washington	PNP: 198 (~45.8±8.6) RP: 201 (~46.4±8.4)
Lee et al., 2017 (USA, 2-arm individual RCT)	Women, aged 40-79 y, overdue for a mammogram[3]	Korean Americans: 100.0%	Korean: 100.0%	LI: 56.6%	≥College: 52.5%	Masonic Cancer Center, Minnesota	PNP: 60 (51.3±8.7) RP: 60 (51.8±10.3)
Mertz et al., 2017 (Denmark, 2-arm individual RCT)	Women, aged >18 y, with BC and moderate-to-severe distress	Danish: 100.0%	Danish: 100.0%	nr.	Higher education: 84.0%	Copenhagen University Hospital, Copenhagen	PNP: 21 (50.9±12.1) RP: 20 (55.0±9.8)
Giese-Davis et al., 2016 (USA, 2-arm individual RCT)	Women, aged 20-85 y, with BC (BI-RADS: 0-4)	White: 88.5%	English: 100.0%	LI: 46.2%	≤HS: 48.1%	Santa Cruz County, California	PNP: 52 (55.3; nr.) RP: 52 (51.7; nr.)
Marshall et al., 2016 (USA, 2-arm individual RCT)	Women, aged ≥65 y, enrolled in Medicare Parts A and B	Black (African American): 100.0%	nr.	LI: 53.5%; insured: 100.0%	≥HS: 73.0%	Baltimore, Maryland	PNP: 638 (≤75: 71.5%) RP: 720 (≤75: 70.0%)
Ruddy et al., 2016 (USA, 2-arm individual RCT)	Women, aged ≥18 y, who had survived BC	Diverse (White: 83.3%)	English: 100.0%	HI: 57.2%; insured: nr.	≥College: 80.2%	A large Massachusetts-based hospital network	PNP: 47 (57; 50-64) RP: 49 (52; 45-63)
Braun et al., 2015 (USA, 2-arm individual RCT)	Women, aged ~67.5 y, enrolled in Medicare Parts A and B[2]	Asian and Pacific Islander (native Hawaiian: mostly)	English: mostly	LI: nr.; insured: 100.0%	≤HS: mostly	Moloka'i General Hospital, rural island of Moloka'i, Hawai'i	PNP: 128 (~68.4±nr.) RP: 132 (~66.7±nr.)
Freysteinson et al., 2015 (USA, 2-arm individual RCT)	Women, aged ≥18 y, who were scheduled for a mastectomy due to BC	Non-white: mostly	English: 100.0%	HI: mostly	≤HS: mostly	5 hospitals in Texas	PNP: 10 (55.1±12.0) RP: 9 (62.0±11.3)
Atlas et al., 2014 (USA, 2-arm cRCT)	Women, aged 42-74 y, overdue for a mammogram[2, 3]	Diverse (African American: mostly)	English: mostly	Insured: mostly	nr.	18 practices in an academic primary care network, Massachusetts	PNP: 22,425 (~49.7±10.1) RP: 20,439 (~47.5±10.0)
Fortuna et al., 2014 (USA, 4-arm individual RCT[6])	Women, aged 40-74 y, overdue for a mammogram[2, 3]	Diverse (non-Hispanic white: 38.3%)	nr.	MI: 42.2%; insured: 92.8%	nr.	An urban internal medicine practice in Rochester, New York	PNP: 153 (40-49: 53.0%) RP: 157 (40-49: 47.1%)
Ginsburg et al., 2014 (Bangladesh, 3-arm individual RCT[7])	Women, aged 25-88 y (mean: 38 y), with an abnormal CBE	Asian (Bengali: 100.0%)	Bengali: 100.0%	LI: mostly	≤HS: mostly	Catchment area of Khulna Division, Bangladesh	PNP: 246 (~38.3±10.6) RP: 240 (~37.4±10.7)

Table 2 (continued)

Lee et al., 2013 (USA, 2-arm cRCT)	Women, aged >18 y, with an abnormal screening test, predominantly a mammogram (BI-RADS: 0, 3-5)	Diverse (Hispanic: 60.4%)	Non-English: 54.8%	LI: 88.3%; uninsured: 54.2%	<HS: 54.6%	10 community-based primary care clinics, Tampa Bay, Florida	PNP: 494 (~41.0±11.4) RP: 545 (~47.6±13.0)
Fiscella et al., 2012 (USA, 2-arm individual RCT)	Women, aged >18 y, with BC[2]	Diverse (White: mostly)	English: mostly	LI & insured: mostly	≤HS: mostly	A hospital and multiple health center sites in Denver, Colorado & oncology practices in Rochester, New York	PNP: 183 (60 y: mostly) RP: 170 (60 y: mostly)
Hendren et al., 2012 (USA, 2-arm individual RCT)	Women with BC(BI-RADS: 0-4)[2]	Diverse (White: mostly)	English: mostly	HI & insured: mostly	≥HS: mostly	13 oncology and primary care practices, Rochester, New York	PNP: 134 (> 60 y: ~38.8%) RP: 119 (> 60 y: ~40.3%)
Raich et al., 2012 (USA, 2-arm individual RCT)	Women with an abnormal screening test, mostly mammogram (BI-RADS: 0, 3-5)[2]	Diverse (Hispanic: mostly)	English: mostly	LI & insured: mostly	≤HS: mostly	A public safety net for the City and County of Denver, Colorado	PNP: 308 (40-49: ~30.0%) RP: 320 (40-49: ~31.0%)
Phillips et al., 2011 (USA, 2-arm individual RCT)	Women, aged 51-70 y (mean 60 y), overdue for a mammogram[3]	Diverse (African American: 47.0%)	English: 77.0%	LI: nr.; insured/ uninsured: 63.0%	≥HS: 55.0%	3 internal medicine practices of an academic safety-net hospital, Boston	PNP: 1,817 (60.0±5.0) RP: 2,078 (60.0±5.0)
Bastani et al., 2010 (USA, 2-arm individual RCT)	Women, aged >18 y, with breast abnormalities	Hispanic/Latina: 76.0%	Spanish or English: nr.	LI: nr.	nr.	Two public hospitals in Los Angeles	PNP: 838 (n.r) RP: 833 (n.r)
Maxwell et al., 2010 (USA, 2-arm individual RCT)	Women, aged 40-73 y (mean: 52 y), with abnormal/suboptimal BC screening results	Korean American: 100.0%	Korean: 93.0%	LI: 80.0%; uninsured: 84.0%	≥HS: 85.0%	Two clinics in Koreatown, Los Angeles	PNP: 58 (40-49: 40.0%) RP: 58 (40-49: 35.0%)
Ell et al., 2009 (USA, 2-arm individual RCT)	Women, aged ≥18 y, with BC (BI-RADS: 0-3)[2]	Hispanic: 71.3%	Spanish: 73.8%	LI: n.r.; insured: 77.2%	<HS: 51.4%	An urban public safety net medical center, Los Angeles	PNP: 123 (≥50: 55.0%) RP: 114 (≥50: 56.0%)
Crump et al., 2008 (USA, 2-arm individual RCT)	Women, aged >25 y, with an abnormal mammogram (BI-RADS: 4 or 5)	Diverse (Black, African-American: 95.1%)	n.r.	LI: n.r.	n.r.	An urban hospital, Atlanta, Georgia	PNP: 48 (≥50 y: 47.9%) RP: 35 (≥50 y: 54.3%)
Ferrante et al., 2008 (USA, 2-arm individual RCT)	Women, aged >21 y, with an abnormal mammogram (BI-RADS: 4 or 5)	Diverse (Black, African-American: 59.0%)	English: 100.0%	LI: n.r.; uninsured: 60.0%	≤HS: 76.2%	An urban university hospital, Newark, New Jersey	PNP: 55 (49.9±12.2) RP: 50 (50.3±11.1)

Table 2 (continued)

Ell et al., 2007 (USA, 2-arm individual RCT)	Women, aged 19-79 y, with an abnormal mammogram (BI-RADS: 3-5)	Latino: 73.0%	Non-English: 71.0%	LI: nr.; non-insured: mostly	nr.	An urban public safety net medical center, Los Angeles	PNP: 96 (40-79: 86.0%) RP: 108 (40-79: 84.0%)
Paskett et al., 2006 (USA, 2-arm individual RCT)	Women, aged >40y, overdue for a mammogram[3]	Diverse (Native American: 42.0%)	nr.	LI: nr.; insured: 71.0%	>HS: 56.0%	A rural county (Robeson), North Carolina	PNP: 433 (54.5±10.7) RP: 418 (55.6±11.5)
Dignan et al., 2005 (USA, 3-arm individual RCT[8])	Women, aged ≥40 y (mean: 54.2 y), overdue for a mammogram[3]	American Indian: 100.0%	nr.	nr.	≥HS: 87.3%	Denver metropolitan urban area, Colorado	PNP: 157 (>65 y: 41.0%) RP: nr. (nr.)
Weber and Reilly, 1997 (USA, 2-arm individual RCT)	Women, aged 52-77 y (mean: 63 y), overdue for a mammogram[3]	Diverse (African American: 40.0%)	nr.	LI: 60.0%; insured: 90.0%	nr.	6 primary care practices, Rochester, New York	PNP: 186 (63.0±nr.) RP: 190 (63.0±nr.)

Authors, publication year (location, design)	Interventions details				Outcome (data collection method and time)	Findings**	RoB***
	Common intervention between PNP and RP groups	PNP group	RP group	Length of intervention			
Atlas et al., 2023 (USA, 4-arm cRCT[1])	Care as usual + alternative interventions (i.e., visit-based electronic health record reminders, phone call or mailed reminders for completing follow-up)	Common intervention + PNP (trained PNs presented navigation services by phone calls: 1) provided follow-up calls to assess women's social barriers to care; 2) scheduled and assisted with completing the recommended follow-up by addressing any barriers identified; 3) used an online network of verified social service programs to help women connect with services available in their community)	Common intervention alone	2 m	Adherence to diagnostic follow-up care (MRR: 4 m after enrollment)	N/S	Low
Bidstrup et al., 2023 (Denmark, 2-arm individual RCT)	Care as usual + alternative interventions (i.e., nurse support at appointments, municipality-based rehabilitation, including physical training and support groups)	Common intervention + PNP (a trained NN presented navigation services by phone calls and in-person visits: 1) assessed and prioritized needs for support; 2) provided empathetic dialogue and formed an alliance; 3) performed a joint analysis of the situation; 4) presented psychoeducation and debriefing; 5) developed goals setting; 6) addressed agreements, homework, and planning)	Common intervention alone	8 m	QoL (FACT-B: T1, baseline; T2, 6 m after T1; T3, 12 m after T1; T4, 18 m after T1)	Sig. ↑ at T3	Low
					Distress & anxiety (distress thermometer, GAD-7: T1, baseline; T2, 6 m after T1; T3, 12 m after T1; T4, 18 m after T1)	N/S	
					Depression (PHQ-9: T1, baseline; T2, 6 m after T1; T3, 12 m after T1; T4, 18 m after T1)	Sig. ↓ at T2	

Table 2 (continued)

Schliemann et al., 2023 (Malaysia, 2-arm individual RCT)	-	PNP (A- a data collector sent a text message with a link to a website, including information on BC screening; B- trained CHWs presented navigation services by phone calls or in-person visits: 1) called women to make sure they received the text message sent by the data collector, discussed BC symptoms and CBE, addressed barriers to screening, and asked whether they were interested in attending a CBE at the clinic; 2) scheduled a CBE appointment; 3) provided follow-up information for women with normal/abnormal CBE results and those who refused or did not attend the CBE appointment)	Care as usual (e.g., the usual option to access opportunistic screening via local clinics)	1 m	Adherence to screening CBE (self-report for the RP group and MRR for the PNP group: the end of 1-m intervention)	Sig. ↑	Some concern
Wyatt et al., 2023 (USA, 2-arm individual RCT)	Education, mostly on cancer screening, presented by a CHW and/or a LHW before randomization	Common intervention + PNP (trained LHWs presented navigation services by phone calls or in-person visits: 1) women informed the LHWs of scheduled and completed screening appointments and any difficulties in making the appointments; 2) LHWs explained the screening exams, motivated the women to be screened, and helped them make appointments)	Common intervention alone (women had no further contact with LHWs after randomization)	4 m	Adherence to screening mammogram (self-report: T1, baseline; T2, 4 m after T1) Knowledge of BC (a validated/non-validated test: T1, baseline; T2, 4 m after T1)	N/S N/S	Some concern
Champion et al., 2022 (USA, 3-arm individual RCT[4])	Education, mostly on cancer screening, presented via an interactive tailored DVD	Common intervention + PNP (trained SWs presented navigation services by phone calls and mailings: 1) assessed screening knowledge and barriers; 2) provided information about the benefits of screening and the availability of transportation to a clinic)	Common intervention alone	12 m	Adherence to screening mammogram (MRR: the end of 12-m intervention)	Sig. ↑	Some concern

Table 2 (continued)

Fernandez et al., 2022 (USA, 2-arm individual RCT)	Care as usual (i.e., standard referral protocol)	Common intervention + PNP (trained PNs presented navigation services by phone calls: 1) provided logistical support such as scheduling appointments and arranging transportation to care; 2) increased women's motivation to complete the needed service by addressing both psychosocial and structural barriers)	Common intervention alone	nr.	Adherence to screening mammogram (MRR: 3 and 6 m after enrollment)	N/S	Low
Dixit et al., 2021 (USA, 2-arm individual RCT)	Care as usual + alternative intervention (i.e., survivorship care planning)	Common intervention + PNP (a trained LPN presented navigation services by phone calls and in-person visits: 1) discussed survivorship care planns and survivorship issues; 2) encouraged women to discuss healthcare issues with their oncology providers and primary care providers; 3) accompanied women to their first primary care appointment; 4) assisted women in completing important forms; 5) provided information about community resources)	Common intervention alone	6 m	QoL (FACT-B: T1, baseline; T2, 6 m after T1)	N/S	Low
Savas et al., 2021 (USA, 2-arm individual RCT)	Education, mostly on cancer screening	PNP (A- a trained LHW presented in-person education using a flip chart and video; B- a professional PN presented navigation services by phone calls: 1) provided follow-up cues for action and logistical support; 2) scheduled cancer prevention screenings; 3) addressed women's barriers; 4) verified screening appointments and results)	Common intervention alone (presented via printed materials)	6 m (mean: 5.4 m)	Adherence to screening mammogram (self-report: the end of 6-m intervention)	Sig. ↑	Some concern

Table 2 (continued)

Glassgow et al., 2019 (USA, 3-arm individual RCT[5])	Care as usual	Common intervention + PNP (a trained LHW provided navigation services by phone calls, mailings, or in-person visits: 1) called women to ensure they understood the instructions for the mammogram preparation and helped them identify and solve any potential barriers to the appointment; 2) called women again to remind them about their appointment and re-assessed any potential barriers to attending the appointment; 3) met women at their appointments to answer their questions and provide any additional needed information; 4) worked with the hospital staff to ensure that screening results were delivered to women and that they understood them, along with the recommended follow-up; 5) attempted to contact women with abnormal screening results immediately to provide support until a diagnostic resolution was achieved; 6) provided support and addressed barriers to care throughout treatment for women with a definitive BC diagnosis)	Common intervention alone	~12 m	TTR (MRR: nr.)	Sig. ↓	Some concern
Margulies et al., 2019 (USA, 2-arm individual RCT)	Informational pamphlets	Common intervention + PNP (trained medical students presented navigation services: 1) educated women on BC and mammograms; 2) engaged women in motivational interviewing to overcome existing barriers; 3) escorted women to the radiology suite for a walk-in mammogram appointment)	Common intervention alone	3 w	Adherence to screening mammogram (MRR: 2 w after the end of 3-w intervention)	Sig. ↑	Some concern

Table 2 (continued)

Molina et al., 2018 (USA, 2-arm individual RCT)	Care as usual + alternative intervention (i.e., email reminders for the screening appointments)	Common intervention + PNP (a trained LHW presented navigation services by phone calls, mailings, or in-person visits: 1-3) the same as Glassgow *et al.*, 4) presented email reminders for subsequent mammogram appointments; 5) presented services to address women's comprehension and barriers through a shared decision-making process)	Common intervention alone	24 m	Adherence to follow-up screening mammogram (MRR: within 24 m after initial mammogram)	Sig. ↑	High
Slater et al., 2018 (USA, 2-arm individual RCT)	-	PNP (A- study staff sent women persuasive and innovative email materials coupled with a $20 incentive for using their Medicaid benefit to get screened; B- a professional PN presented navigation services via a PN-staffed call center: 1) addressed barriers; 2) scheduled appointments)	Delayed intervention (i.e., PNP after study completion)	10 w	Adherence to screening mammogram (MRR: 12 w after enrollment)	Sig. ↑	Some concern
Han et al., 2017 (USA, 2-arm cRCT)	Education, mostly on cancer screening	PNP (a trained CHW presented navigation services by phone calls, mailings, or in-person visits: 1) sent an individually tailored brochure via email; 2) provided health literacy training in a group setting; 3) called women monthly to provide consultation and address their individualized barriers)	Common intervention alone (presented via a publicly available educational brochure)	6 m	Adherence to screening mammogram (MRR: the end of 6-m intervention) Knowledge of BC (a validated test: T1, baseline; T2, 6 m after T1)	Sig. ↑ N/S	High
Lee et al., 2017 (USA, 2-arm individual RCT)	-	PNP (a trained LHW presented navigation services by a smartphone application: 1) helped women obtain the necessary resources, appointments, or transportation to receive a mammogram; 2) provided cancer screening information; 3) sent messages daily on various topics, including BC, screening, communication strategies, follow-up for test results, and information on local clinics; 4) sent questions as prompts to encourage women to schedule mammogram appointments)	Education on BC screening and community resources, presented via a mailed print brochure	1 w	Knowledge of BC and screening (a validated test: T1, baseline; T2, 1 w after T1) Adherence to screening mammogram (self-report: 6 m after enrollment) Satisfaction with care (a non-validated tool: 1 w after enrollment)	N/S Sig. ↑ Sig. ↑	Low

Table 2 (continued)

Mertz et al., 2017 (Denmark, 2-arm individual RCT)	Care as usual + alternative intervention (i.e., screening for distress before surgery, referring to the local rehabilitation center primarily for physical training)	Common intervention + PNP (a trained NN presented navigation services by phone calls and in-person visits: 1) provided systematic symptom screening; 2) motivated and supported women in self-managing their symptoms and using existing rehabilitation services; 3) discussed a wide range of subjects, including anxiety, sleeping problems, fatigue, family concerns, and physical problems)	Common intervention alone	4-6 m (mean: 5 m)	Satisfaction with treatment (a non-validated tool: 12 m after enrollment)	Sig. ↑	Some concern
					QoL (EORTC QLQ-C30: T1, baseline; T2, 6 m after T1; T3, 12 m after T1)	N/S	
					Distress, anxiety & Depression (distress thermometer, HADS: T1, baseline; T2, 6 m after T1; T3, 12 m after T1)	Sig. ↓ at T3	
Giese-Davis et al., 2016 (USA, 2-arm individual RCT)	Care as usual (i.e., a one-time visit with an oncology nurse who offered information and answered questions about different subjects)	Common intervention + PNP (a trained peer navigator presented navigation services by phone calls, emails, and in-person visits: 1) provided emotional support through active listening; 2) helped women to find community resources; 3) provided monthly clinical supervision and trauma-informed training)	Common intervention alone	6 m (mean: 5.16 m)	QoL (FACT-B: T1, baseline; T2, 3 m after T1; T3, 6 m after T1; T4, 12 m after T1)	Sig. ↑ at T1 vs. T4	Some concern
					Depression (CES-D: T1, baseline; T2, 3 m after T1; T3, 6 m after T1; T4, 12 m after T1)	N/S	
Marshall et al., 2016 (USA, 2-arm individual RCT)	Education, mostly on cancer screening	Common intervention + PNP (a trained LHW presented navigation services by phone calls and in-person visits: 1) reviewed women's baseline cancer screening status; 2) discussed printed educational materials; 3) considered predisposing factors to cancer screening; 4) identified potential barriers; 5) arranged appointments; 6) accompanied women to screenings; 7) enhanced interactions between women and healthcare providers by coaching women on potential questions to ask their care providers)	Common intervention alone	24 m (mean: 17.8 m)	Adherence to screening mammogram (self-report: the end of 24-m intervention)	Sig. ↑	Some concern

Table 2 (continued)

Ruddy et al., 2016 (USA, 2-arm individual RCT)	-	PNP (an NN presented navigation services by phone calls, emails, and in-person visits: 1) provided survivorship care planning, such as details about the therapies received and screening recommendations; 2) attempted to meet with women to coordinate their care; 3) attempted to dissuade women from redundant breast/chest wall examinations and unnecessary non-plastic surgery visits; 4) made suggestions for visits that could be postponed; 5) managed symptoms as needed)	Care as usual	12 m	Satisfaction with care (PSQ-18: T1, baseline; T2, 12 m after T1) QoL (SF-12: T1, baseline; T2, 12 m after T1)	N/S N/S	High
Braun et al., 2015 (USA, 2-arm individual RCT)	Education, mostly on cancer screening	PNP (trained LPNs presented navigation services by phone calls, emails, and in-person visits: 1) provided education; 2) made appointments; 3) sent reminders; 4) arranged transportation to appointments; 5) communicated with care providers; 6) helped women find financial support; 7) helped women complete paperwork)	Common intervention alone	12 m	Adherence to screening mammogram (self-report: the end of 12-m intervention)	Sig. ↑	Low
Freysteinson et al., 2015 (USA, 2-arm individual RCT)	-	PNP (a trained NN presented navigation services by in-person visits: 1) educated and emotionally supported women before surgery on the use of a mirror to view their mastectomy site during the initial post-operative and subsequent dressing changes; 2) provided a written handout on body image and mirror-viewing interventions)	Care as usual	nr.	QoL (SF-36: T1, baseline pre-operatively; T2, 1-2 weeks post-operatively)	N/S	High

Table 2 (continued)

Atlas et al., 2014 (USA, 2-arm cRCT)	An intervention presented via a web-based IT application to manage screening mammography	Common intervention + PNP (a PN presented navigation services by the application: 1) contacted women frequently, 2) explored individual barriers to screening, 3) educated women on different topics, 4) provided reminder calls, 5) arranged transportation, 6) assisted with visit preparation, 7) accompanied women to visits)	Common intervention alone (i.e., the application automatically sent customized reminder letters to overdue women and transferred them to practice delegate lists for follow-up)	12 m	Adherence to screening mammogram (MRR: T1, baseline; T2, 12 m after T1)	Sig. ↑ at T1	High
Fortuna et al., 2014 (USA, 4-arm individual RCT[6])	-	PNP (a trained health worker presented navigation services by phone calls and emailing: 1) sent personalized email reminders regarding screening schedules; 2) called women to remind them that they were overdue for screening, encouraged them to undergo screening, offered assistance with scheduling appointments, introduced referrals for a free mammogram, as well as provided relevant phone numbers)	Care as usual (i.e., personalized email reminders regarding screening time)	38 w	Adherence to screening mammogram (MRR: 13 m after enrollment)	Sig. ↑	Low
Ginsburg et al., 2014 (Bangladesh, 3-arm individual RCT[7])	An intervention presented by a smartphone application to manage CBE	Common intervention + PNP (trained CHWs presented navigation services by the application: 1) addressed potential barriers to seeking care; 2) suggested accompanying woman to their appointment or returning at a more suitable time to facilitate discussion with family members)	Common intervention alone (i.e., the application guides interviews, reports data, shows motivational video, and offers appointments for women with an abnormal CBE)	4 m	Adherence to diagnostic follow-up care (MRR: the end of 4-m intervention)	Sig. ↑	Low
Lee et al., 2013 (USA, 2-arm cRCT)	-	PNP (trained LPNs presented navigation services by phone calls, mailings, or in-person visits: 1) provided educational information on BC; 2) worked with community-based health and social service organizations to act on the identified barriers to diagnosis or treatment; 3) provided support and guidance to facilitate women's timely and high-quality care)	Care as usual	42 m	TTR (MRR: T1, within 42-m intervention; T2, <3 m after enrollment; T3, >3 m after enrollment) TDR (MRR: T1, 1 m after enrollment; T2, 12 m after enrollment)	Sig. ↓ at T3 Sig. ↑ at T2	Some concern

Table 2 (continued)

Fiscella et al., 2012 (USA, 2-arm individual RCT)	-	PNP (trained LHWs presented navigation services by phone calls, mailings, or in-person visits: 1) helped women identify and overcome treatment barriers collaboratively; 2) made supportive contact; 3) identified and linked women to social or financial resources and appropriate community supports; 4) helped with paperwork, obtaining records, scheduling appointments, and following up on test scheduling or results; 5) accompanied women to appointments)	Care as usual	12 m	Days to completion of treatment Satisfaction with care (PSCC: 3 m after enrollment) Distress (IES: 3 m after enrollment)	N/S N/S N/S	High
Hendren et al., 2012 (USA, 2-arm individual RCT)	-	PNP (a trained LPN presented navigation services by phone calls or in-person visits: 1) identified and assessed barriers; 2) provided appointment scheduling and reminders; 3) arranged transportation; 4) accompanied women to appointments; 5) helped women prepare a list of questions and take notes to improve communication)	Care as usual	12 m	QoL (FACT-B, FACT-G: T1, baseline; T2, 3 m after T1; T3, 6 m after T1; T4, 9 m after T1; T5, 12 m after T1)	N/S	Some concern
Raich et al., 2012 (USA, 2-arm individual RCT)	-	PNP (trained LPNs presented navigation services by phone calls, mailings, or in-person visits: 1) identified and assessed barriers to completing the diagnostic test or treatment; 2) provided social support; 3) ensured that the required examinations were scheduled; 4) communicated with clinic staff regarding women's needs and concerns; 5) accompanied women to their appointments; 6) assessed women's understanding of diagnostic test results and linked them to clinic staff for further explanation and to address their concerns)	Care as usual	~12 m	TTR (MRR: nr.) TDR (MRR: ~12 m)	Sig. ↓ for BI-RADS 3 Sig. ↑	Some concern

Table 2 (continued)

Phillips et al., 2011 (USA, 2-arm individual RCT)	-	PNP (trained PNs presented navigation services by phone calls, mailings, or in-person visits: 1) interacted directly with women and healthcare providers to coordinate care; 2) informed women of their need for a mammogram and the availability of the navigator to support them; 3) identified and helped women to overcome their barriers to care; 4) scheduled appointments and tracked women through completion of their mammograms)	Care as usual + delayed PNP	9 m	Adherence to screening mammogram (MRR: T1, baseline; T2, 9 m after T1)	Sig. ↑ at T2	Some concern
Bastani et al., 2010 (USA, 2-arm individual RCT)	-	PNP (a professional health worker and an LHW presented navigation services by phone calls and mailings: 1) the professional health worker contacted women to establish a relationship with them, provide information on breast abnormalities, and help them with emotional barriers to attending follow-up appointments; 2) two commercially available education pamphlets were mailed to women; 3) provided ongoing informational, emotional, and social support, encouragement to attend clinic appointments, and assistance in navigating the system)	Care as usual	6 m	TDR (MRR: the end of 6-m intervention)	N/S	Some concern

Table 2 (continued)

Maxwell et al., 2010 (USA, 2-arm individual RCT)	Care as usual (i.e., a case manager called women and presented a letter to urge them to make an appointment for a follow-up exam)	Common intervention + PNP (a trained peer navigator presented navigation services by phone calls and in-person visits: 1) reminded women before an appointment; 2) explained the need for and the nature of the diagnostic follow-up exams; 3) met women at the referral clinic and helped them at the hospital; 4) helped women to fill out forms; 5) provided information and emotional support; 6) provided translation and transportation services; 7) rescheduled follow-up appointments; 8) made home visits)	Common intervention alone	6 m	Adherence to diagnostic follow-up care (self-report: the end of 6-m intervention)	Sig. ↑	Some concern
Ell et al., 2009 (USA, 2-arm individual RCT)	Education, mostly on cancer screening, community resources, and depression, presented via a written educational pamphlet	Common intervention + PNP (A- a trained PN presented navigation services by phone calls and/or in-person visits: 1) provided adherence risk/barrier assessment, health education, psychosocial counseling, problem-solving, and support; 2) tracked women's follow-up; 3) called to remind women of appointments; B- an SW provided brief depression or anxiety counseling and/or referrals to community health resources)	Common intervention alone	12 m	Adherence to adjuvant treatment/post-treatment follow-up care (MRR: the end of 12-m intervention) QoL (FACT-G: T1, baseline; T2, 12 m after T1)	N/S N/S	Some concern
Crump et al., 2008 (USA, 2-arm individual RCT)	-	PNP (a trained CHW presented navigation services by phone calls, mailings, or in-person visits: 1) reminded women of their follow-up appointments; 2) explained the importance of timely follow-up for the abnormal mammogram; 3) identified potential barriers to follow-up and assisted in removing barriers through referral to appropriate resources; 4) accompanied women to the follow-up appointments as needed)	Care as usual (i.e., a reminder telephone call the day before a scheduled biopsy)	27 w	Adherence to diagnostic follow-up care (MRR: within 6 m after enrollment)	Sig. ↑	High

Table 2 (continued)

Ferrante et al., 2008 (USA, 2-arm individual RCT)	Care as usual	Common intervention + PNP (an SW presented navigation services by phone calls or in-person visits: 1) assisted women with emotional and social support; 2) helped women with scheduling and arriving at appointments on time; 3) connected women with resources and support systems; 4) facilitated interaction and communication between women and healthcare providers)	Common intervention alone	2 m	TTR (MRR: nr.) TDR (MRR: the end of 2-m intervention) Satisfaction with care (SHCQ: 1 m after final resolution) Anxiety (SAS: T1, baseline; T2, 1 m after final resolution)	Sig. ↓ Sig. ↑ Sig. ↑ Sig. ↓ at T2	Some concern
Ell et al., 2007 (USA, 2-arm individual RCT)	-	PNP (A- a trained PN presented navigation services by phone calls and in-person visits: 1) provided adherence risk/barrier assessment, health education, and psychosocial counseling; 2) tracked women's follow-up; 3) called for appointment reminders; B- an SW provided brief assessment, counseling, and referrals for mental health services in the community)	Care as usual	8 m	TDR (MRR: 2 and 6 m after enrollment), adherence to diagnostic follow-up care (MRR: nr.), timely start of treatment (MRR: within 30 d of diagnosis)	Sig. ↑	Some concern
Paskett et al., 2006 (USA, 2-arm individual RCT)	-	PNP (trained LHAs presented navigation services by phone calls/messages, mailings, and in-person visits: 1) identified and discussed important screening barriers; 2) provided education on BC; 3) provided financial and social support; 4) reminded women about their mammogram appointments)	Delayed intervention (participants were invited to receive a brochure about mammography 3 months after completing the follow-up assessment)	9-12 m	Knowledge of BC screening (a validated/non-validated test: T1, baseline; T2, 12-14 m after T1) Adherence to screening mammogram (MRR + self-report: 12-14 m after enrollment)	N/S Sig. ↑	Low
Dignan et al., 2005 (USA, 3-arm individual RCT[8])	-	PNP (a trained LPN presented navigation services by phone calls, mailings, or in-person visits: 1) provided information regarding BC, the importance of mammograms, and adherence to guidelines via a tailored education brochure or breast self-examination cards; 2) provided strategies for overcoming barriers to obtaining mammograms and follow-up care; 3) reinforced women's efforts to schedule and keep appointments)	Care as usual + delayed education presented via a tailored education brochure	One 20-90-min session	Adherence to screening mammogram (self-report: T1, baseline; T2, 6 m after T1)	N/S	High

Table 2 (continued)

Weber and Reilly, 1997 (USA, 2-arm individual RCT)	Personalized mail reminders to complete mammograms	Common intervention + PNP (trained CHWs presented navigation services by phone calls, mailings, and in-person visits: 1) provided education and reminders to complete mammograms; 2) identified and removed barriers to care, such as facilitating appointment scheduling, transportation, dependent care, and obtaining financial assistance)	Common intervention + care as usual + delayed PNP	4 m	Adherence to screening mammogram (MRR: T1, baseline; T2, 4 m after T1)	Sig. ↑ at T2	High

Abbreviations: *BC* breast cancer, *BI-RADS* breast imaging reporting and data system, *CBE* clinical breast examination, *CES-D* Center for Epidemiologic Studies Depression Scale, *CHW* community health worker, *cRCT* cluster-randomized trial, *DVD* digital video disc, *EORTC QLQ-C30* European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire, *FACT-B* Functional Assessment of Cancer Therapy-Breast, *FACT-G* Functional Assessment of Cancer Therapy-General, *GAD-7* Generalized Anxiety Disorder 7-item scale, *HADS* Hospital Anxiety and Depression Scale, *HI* high income, *HN* health navigator, *HS* high school, *IES* Impact of Events Scale, *IQR* interquartile range, *IT* information technology, *LI* low income, *LHA* lay health advisor, *LHW* lay health worker, *LPN* lay patient navigator, *m* month(s), *MI* middle income, *MRI* magnetic resonance imaging, *MRR* medical record review, *NN* nurse navigator, *N/S* not significant, *nr.* not reported, *PHQ-9* Patient Health Questionnaire-9, *PSCC* Patient Satisfaction with Cancer Care Questionnaire, *PSQ-18* Short-Form Patient Satisfaction Questionnaire, *PN* patient navigator, *PNP* patient navigation program, *QoL* quality of life, *RCT* randomized controlled trial, *RoB* risk of bias, *RP* routine program, *SAS* Zung Self-Rating Anxiety Scale, *SF-12* 12-item Short Form Survey (modified Medical Outcomes Study), *SF-36* 36-Item Short Form Survey (Medical Outcomes Study), *SHCQ* Satisfaction with Hospital Care Questionnaire, *Sig.* significant, *SW* social worker, *T* time, *TDR* timely diagnostic resolution, *TTR* time to resolution, *USA* United States of America, *w* week(s), *y* year(s), ~approximately, ↑ increase or higher, ↓ lower or fewer

*Reported as mean ± standard deviation, median; interquartile range, or highest range: percentage

**Outcomes in the patient navigation program arm compared with the routine program arm

***The revised Cochrane Risk of Bias tool for randomized trials (RoB 2): (1) low: the study is believed to be at low risk of bias for all domains; (2) some concern: the study raises some concerns in at least one domain, but not at high risk of bias for any domain; and (3) high: the study is judged to be at high risk of bias in at least one domain, or has some concerns in multiple domains that substantially lower confidence

[1]Investigated four groups: (1) standard care, (2) visit-based electronic health record reminders, (3) visit-based electronic health record reminders with population health outreach, and (4) visit-based electronic health record reminders, population health outreach, and a patient navigation program. We extracted and compared data from groups 3 and 4

[2]Investigated breast cancer in addition to other cancers; included in the current review because data for breast cancer were reported separately

[3]Included women with no record of a mammogram in the prior 12, 18, or 24 months

[4]Investigated three groups: (1) patient navigation program plus a tailored educational digital video disc, (2) tailored educational digital video disc alone, and (3) usual care alone. We extracted and compared data from groups 1 and 2

[5]Investigated three groups: (1) full navigation, (2) limited contact with patient navigators, and (3) no contact with patient navigators. We extracted and compared data from groups 1 and 3 because pooling data from groups 1 and 2 was impossible as women were not randomly assigned to group 2

[6]Investigated four groups: (1) reminder letters alone, (2) reminder letters and automated telephone messages, (3) reminder letters, automated telephone messages, and point-of-service prompts, and (4) reminder letters and personal telephone calls. We considered group 1 as control condition and compared it with group 4 because it was the only group with a patient navigator intervention

[7]Investigated three groups: (1) patient navigation program plus a community health worker (CHW)-guided smartphone application, (2) CHW-guided smartphone application alone, and (3) usual care alone. We extracted and compared data from groups 1 and 2

[8]Investigated three groups: (1) face-to-face patient navigation program, (2) telephone-based patient navigation program, and (3) control condition. We pooled data from groups 1 and 2 and compared them with group 3

of substantial heterogeneity [55]. Consequently, data from 13 individually RCTs conducted across diverse regions of the USA were pooled to evaluate screening mammography adherence among predominantly overdue women.

The meta-analysis, conducted using the DL random-effects model, yielded a pooled OR of 2.18 (95% CI, 1.71, 2.77; 95% PI, 0.94, 5.05; $P < 0.001$), indicating that women in the PNP intervention group ($n \approx 15{,}130$) were more than twice as likely to complete screening within the predefined follow-up period (typically 6–12 months) compared with those in the control group ($n \approx 15{,}443$). Substantial between-study heterogeneity was observed under the DL framework ($I^2 = 79.9\%$; $\tau^2 = 0.13$; Cochran's Q test $P < 0.001$) (Fig. 1). Following adjustment using the HK method ($t_{0.975,12} = 2.179$), the main association between the PNP intervention and screening uptake remained statistically significant (OR, 2.18; 95% CI, 1.67, 2.85). Subgroup analyses based on the DL random-effects model showed consistent results according to the method of data collection, with significant effects observed in studies relying on self-reported data (95% CI, 1.45; 3.37) as well as those using medical record reviews (95% CI, 1.55; 3.29) (Supplementary Table 4).

Diagnosis outcomes

Five studies addressed adherence rate to diagnostic follow-up care among low-income women of diverse ethnicity, who had abnormal BC screening results [48, 52, 67, 75, 76]. Based on qualitative synthesis, one study did not report any substantial difference between the PNP and control groups [52]; nonetheless, the remaining four trials revealed a significant between-group difference in favor of PNP (Table 2). After excluding one cRCT for which the effect estimate could neither be derived nor imputed due to insufficient data [52], the meta-analysis of four individually randomized trials, conducted using the DL random-effects model, yielded a pooled OR of 2.42 (95% CI, 1.64, 3.59; 95% PI, 0.67, 8.80; $P < 0.001$), implying that women receiving the PNP intervention ($n = 482$) were significantly more likely than those in the control group ($n = 467$) to adhere to diagnostic follow-up appointments within the predefined timeframe (typically 4–6 months). Heterogeneity, estimated using the DL random-effects model, was low to moderate and not statistically significant ($I^2 = 33.4\%$; $\tau^2 = 0.05$; Cochran's Q test $P = 0.212$) (Fig. 2a). Following adjustment using the HK method ($t_{0.975,3} = 3.182$), the association between the PNP intervention and adherence to diagnostic follow-up remained statistically significant (OR, 2.42; 95% CI, 1.28, 4.57). In sensitivity analyses under the DL random-effects model, after excluding one study based on self-reported data [76], the results from the remaining three studies using medical record-based data extraction remained statistically significant (95% CI, 1.58; 5.16) (Supplementary Table 5).

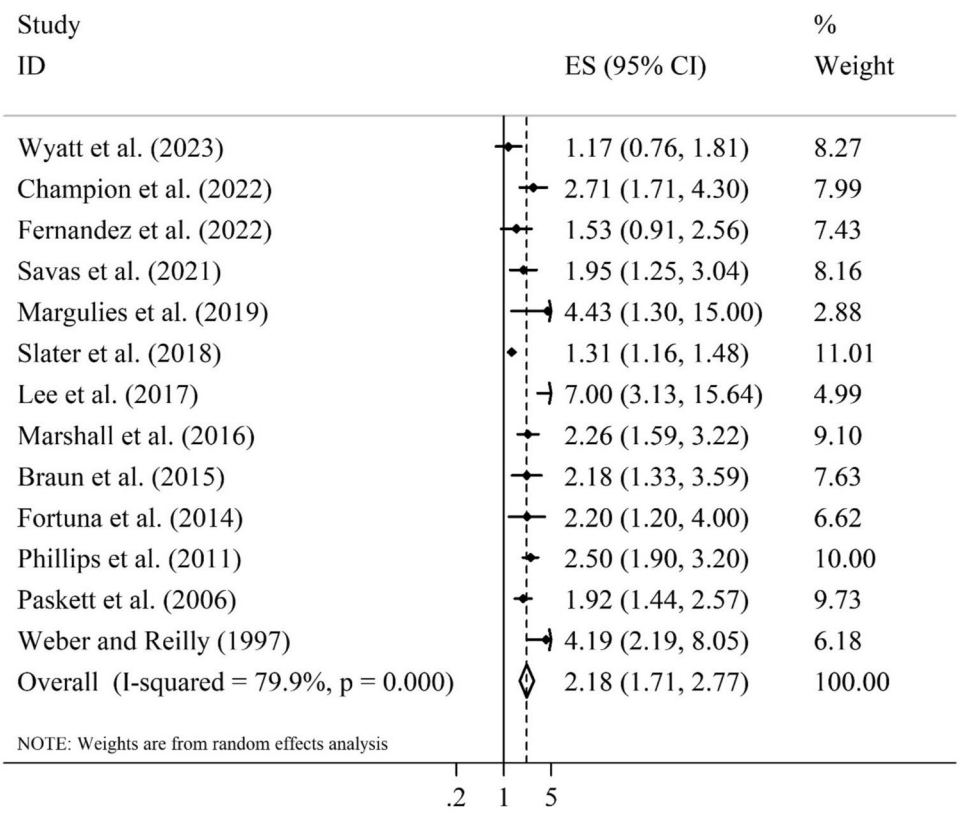

Fig. 1 Forest plot for the effect of PNPs versus control interventions on adherence to screening mammography among women who were predominantly overdue for a mammogram

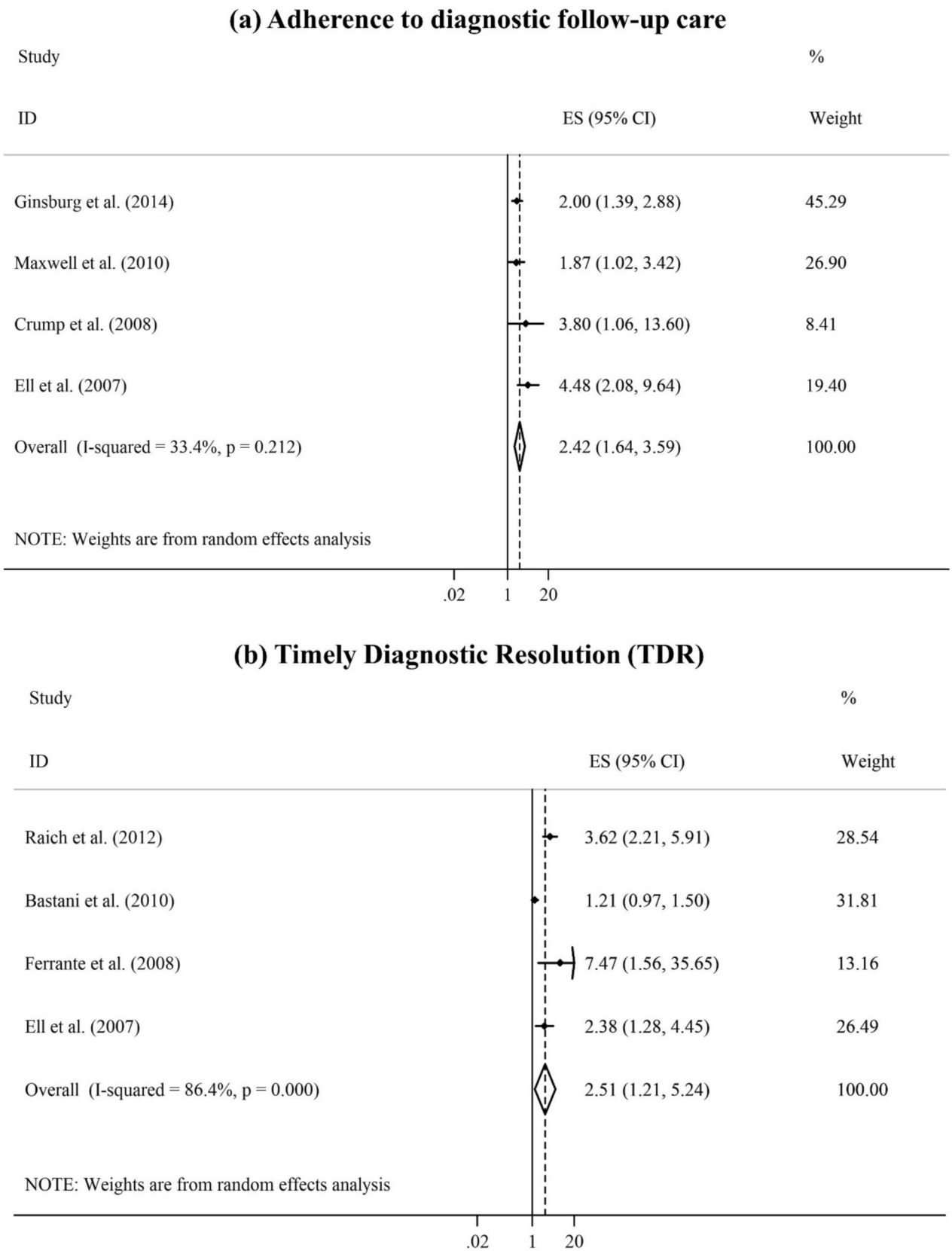

Fig. 2 Forest plots for the effects of PNPs versus control interventions on adherence to diagnostic follow-up and TDR among women with abnormal BC screening results

Five of the included two-arm RCTs, all conducted in the USA, reported TDR based on medical record review among low-income women with breast abnormalities who received a diagnostic resolution [56, 64, 66, 67, 77]. Based on qualitative synthesis, four trials revealed a significant between-group difference in favor of PNP, but one study did not find any considerable difference between groups [66] (Table 2). Following exclusion of one cRCT with insufficient data to derive or impute an effect estimate [56], the meta-analysis of four individually randomized trials demonstrated a pooled OR of 2.51 (95% CI, 1.21, 5.24; 95% PI, 0.10, 62.7; $P = 0.014$), showing that a significantly higher proportion of women in the PNP intervention group ($n = 1027$) achieved TDR within the predefined follow-up period (predominantly 6–12 months) compared with those receiving usual care ($n = 1311$). However, substantial between-study heterogeneity was observed under the DL random-effects model ($I^2 = 86.4\%$; $\tau^2 = 0.42$; Cochran's Q test $P < 0.001$) (Fig. 2b). After applying the HK adjustment ($t_{0.975,3} = 3.182$), the direction of the association between the PNP intervention and TDR achievement remained positive, but the effect estimate was no longer statistically significant (OR = 2.51; 95% CI, 0.76, 8.25).

Four included studies reported TTR among women with abnormal BC screening results who received a diagnostic resolution. Of these, two studies reported mean TTR [51, 77], while the remaining two reported median TTR [56] or presented TTR using Kaplan–Meier curves [64]. Hence, a quantitative analysis was impossible due to heterogeneity in reporting data. Conflicting results were obtained based on the qualitative synthesis (Table 2). Two studies showed that women in the PNP group experienced a significantly shorter TTR than women in the usual care group [51, 77]. In another study, the PNP group had a shorter TTR than the routine care group, but the effect of PNP was different according to the BI-RADS (breast imaging reporting and data system), as the impact was meaningful only for BI-RADS 3 [64]. Another study also found no significant between-group difference in TTR in the first 3 months; however, beyond 3 months, the navigated women showed a significantly shorter TTR than the non-navigated women, who had received only the usual care [56].

Treatment outcomes

Three included studies addressed treatment-related variables; however, performing a quantitative analysis was impossible due to the dissimilarities of variables (Table 2). Based on the qualitative synthesis, one trial reported no significant difference between women who received a written educational pamphlet and those who received PNP in terms of compliance rate to adjuvant treatment or post-treatment follow-up care [61]. Another study showed that usual care and PNP groups were not significantly different in terms of the time to completion of treatment [62]. However, in another study, women in the PNP group had a substantially higher rate of timely start of treatment than those in the usual care group [67].

Knowledge of BC

Four two-arm RCTs performed in various community settings around the USA addressed knowledge of BC and/or screening before and after lay health worker-led PNP and control educational interventions among middle-aged women, predominantly with no English proficiency and low income, who were overdue for a mammogram [55, 57, 70, 71]. Based on the qualitative synthesis, the study groups were not significantly different in knowledge score (Table 2).

After excluding one cRCT with insufficient statistical information to derive a comparable ES [55], the meta-analysis of three individually randomized trials, using a DL random-effects model, yielded a pooled SMD of 0.27 (95% CI, −0.19, 0.73; 95% PI, −5.34, 5.88; $P = 0.247$), suggesting that women receiving the PNP intervention ($n = 681$) showed a greater improvement in knowledge scores from baseline to last follow-up compared with those receiving educational interventions alone ($n = 675$); however, the difference was not statistically significant. Considerable between-study heterogeneity was observed under the DL model ($I^2 = 93.0\%$; $\tau^2 = 0.14$; Cochran's Q test $P < 0.001$) (Fig. 3). Following application of the HK adjustment ($t_{0.975,2} = 4.303$), the direction of the association between the PNP intervention and improvement in knowledge scores remained positive; however, the effect estimate was statistically non-significant (SMD = 0.27; 95% CI, −0.74, 1.28).

Satisfaction with care or treatment

Five two-arm RCTs compared overall satisfaction with cancer-related care or treatment following the administration of a PNP and control intervention [45, 62, 70, 77, 78]. Nevertheless, variations in data reporting methods made it impossible to pool data quantitatively. The controversial findings were also obtained from qualitative synthesis (Table 2). In one study among women with a definitive diagnosis of BC, usual care and PNP groups were not significantly different concerning the proportion of women reporting higher satisfaction within 3 months of enrollment [62]. Also, standard care alone and PNP were not different in terms of satisfaction with care among BC survivors [78]. However, one study found that women with an abnormal mammogram who received a PNP had higher mean satisfaction scores than those who received usual care alone within 1 month of final resolution [77]. In another study among women overdue for a mammogram, the percentage of women with better

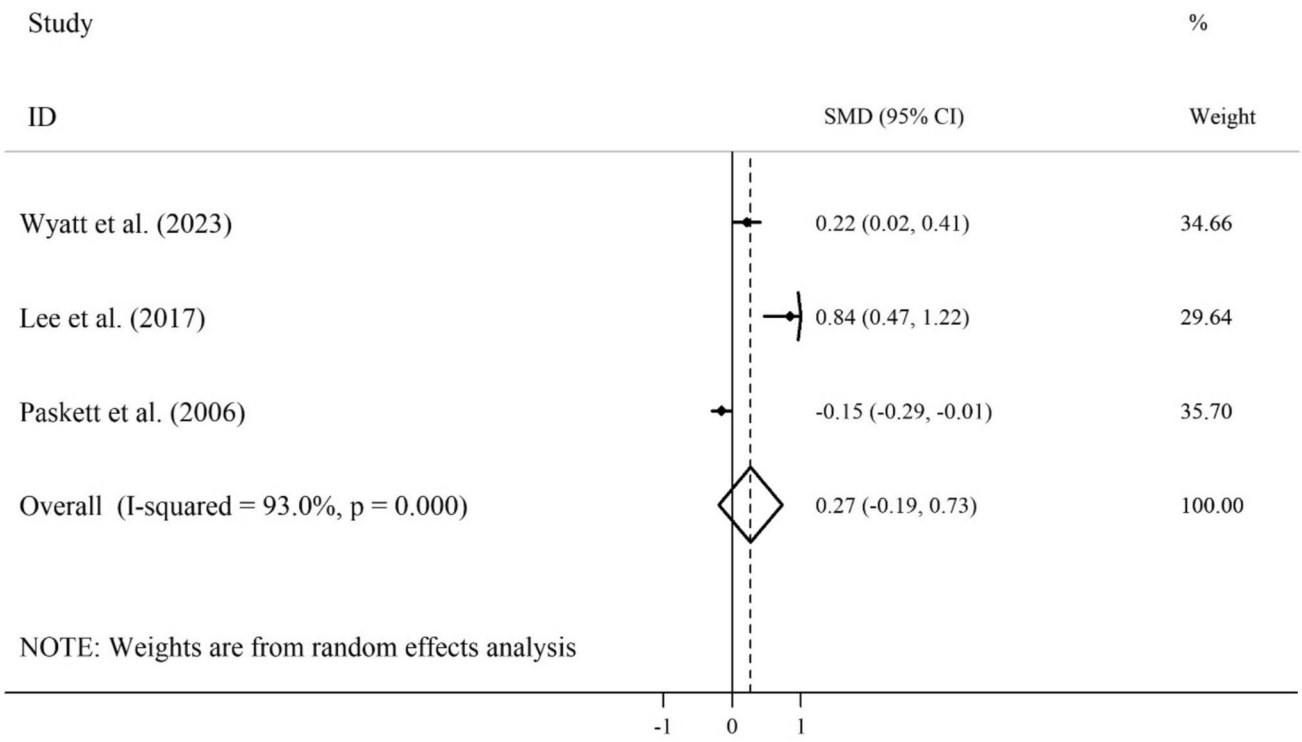

Fig. 3 Forest plot for the effect of PNPs versus educational interventions alone on changes in knowledge scores from baseline to follow-up among women who were overdue for a mammogram

satisfaction regarding received care was significantly higher in the PNP group than in the control group, who received the usual intervention [70]. A similar result was reported in another study among women with a definitive diagnosis of BC, who received either PNP or usual care plus an alternative intervention [45].

Health-related QoL

Eight studies assessed pre- and post-intervention QoL among women who were newly diagnosed with BC ($n=5$), BC survivors ($n=2$), or scheduled for mastectomy due to BC ($n=1$) [45, 46, 61, 63, 78–81]. Based on the qualitative synthesis, mixed findings were obtained (Table 2).

Out of eight included RCTs, two did not document the numerical data [61, 79] and two reported data only as median [78, 80]; hence, they were impossible to include in the meta-analysis. Finally, four two-arm individual RCTs were appropriate for pooled analysis; these had been conducted among women with newly diagnosed BC, who were in the treatment phase. Using the DL random-effects model, a pooled SMD of 0.44 was observed across the four RCTs (95% CI, 0.09, 0.79; 95% PI, −1.48, 2.38; $P=0.014$), indicating a statistically significant improvement in QoL scores from baseline to the end of follow-up among women who received PNP through both face-to-face and remote delivery methods ($n=363$) compared with those receiving control interventions ($n=344$). However, substantial between-study heterogeneity was detected under the DL model ($I^2=77.7\%$; $\tau^2=0.09$; Cochran's Q test $P=0.004$) (Fig. 4). Following application of the HK adjustment ($t_{0.975,3}=3.182$), the direction of the association between the PNP intervention and improvement in QoL remained positive, although the effect estimate was no longer statistically significant (SMD = 0.44; 95% CI, −0.13, 1.01).

Psychological consequences

The psychological effects of PNP among women with definitive BC ($n=4$) or abnormal mammogram ($n=1$) were documented in some studies. These studies addressed depression [45, 46, 81], anxiety [45, 46, 77], or distress [45, 46, 62], with overall mixed results (Table 2). Of the three RCTs examining distress, one reported a dichotomous outcome [62], precluding inclusion in a meta-analysis. However, meta-analysis was feasible for the three individual RCTs reporting anxiety and depression outcomes.

For anxiety, using the DL random-effects model, the pooled SMD was −0.94 (95% CI, −1.66, −0.22; 95% PI, −3.72, 1.84; $P=0.010$), indicating a statistically significant reduction in anxiety scores from baseline to the end of follow-up among women from urban populations who

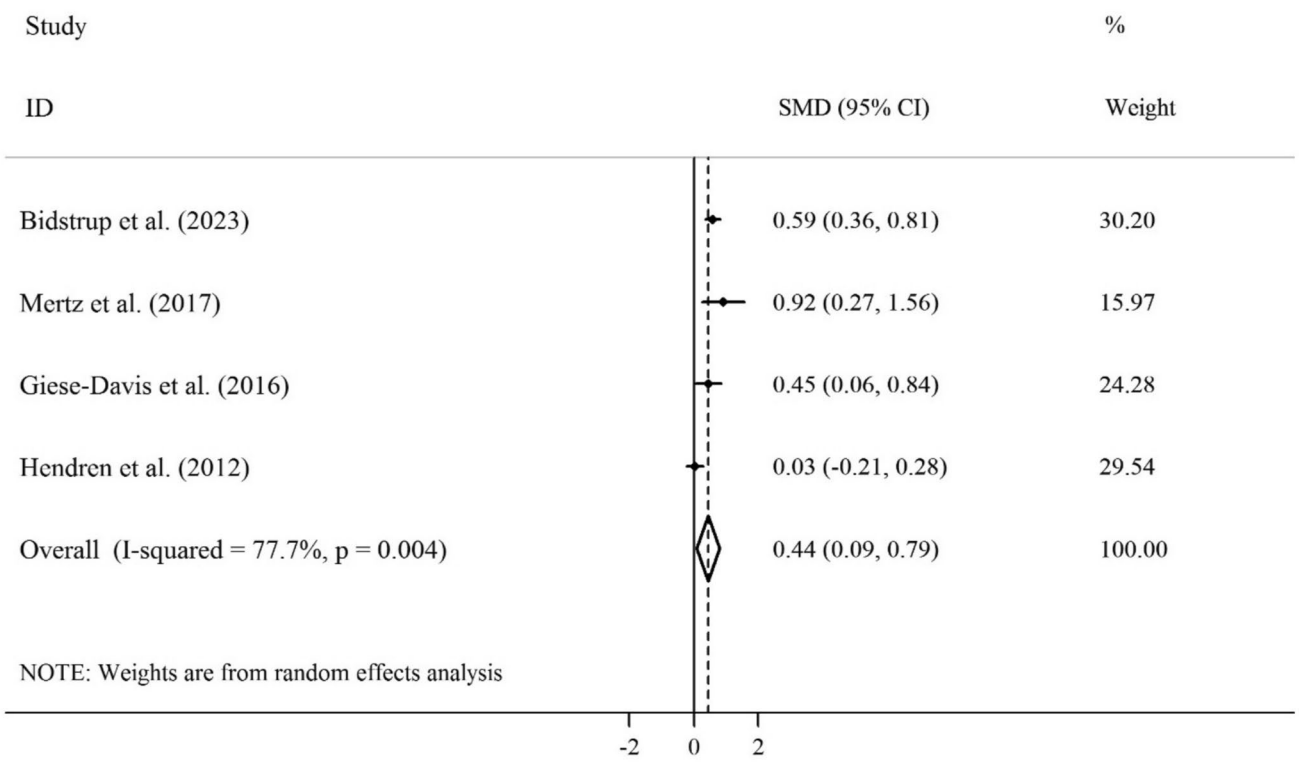

Fig. 4 Forest plot for the effect of PNPs versus control interventions on changes in QoL scores from baseline to follow-up among women with newly diagnosed BC

received PNP via combined face-to-face and remote delivery modalities ($n=213$), compared with those receiving control interventions ($n=224$). However, substantial between-study heterogeneity was observed under the DL model ($I^2=89.0\%$, $\tau^2=0.34$; Cochran's Q test $P<0.001$) (Fig. 5a). Following application of the HK adjustment ($t_{0.975,2}=4.303$), the direction of the association between the PNP intervention and anxiety reduction remained negative, but the effect estimate was no longer statistically significant (SMD = −0.94; 95% CI, −2.52, 0.64).

In contrast to the anxiety outcome, the meta-analysis of three studies on depression, conducted using the DL random-effects model, showed that the pooled SMD was −0.34 (95% CI, −0.71, 0.04; 95% PI, −1.72, 1.04; $P=0.076$), suggesting a non-significant trend toward lower depression scores from baseline to the 12-month follow-up among women with newly diagnosed BC who received the PNP intervention via a combination of face-to-face and remote delivery modalities ($n=229$), compared with control participants ($n=225$). Moderate-to-substantial between-study heterogeneity was observed under the DL model ($I^2=63.9\%$; $\tau^2=0.06$; Cochran's Q test $P=0.062$) (Fig. 5b). Following application of the HK adjustment ($t_{0.975,2}=4.303$), the direction of the association between the PNP intervention and depression reduction remained negative and not statistically significant (SMD = −0.34; 95% CI, −1.16, 0.48).

Sensitivity analysis

The results of the sensitivity analyses are summarized in Supplementary Table 5 and Supplementary Figs. 2–4. Overall, the pooled effect estimates were robust and were not substantially influenced by the exclusion of individual studies for outcomes including adherence rate to screening mammography, adherence to diagnostic follow-up care, TDR, knowledge of BC, and depression. However, some variability in the primary meta-analysis results was observed for QoL and anxiety outcomes, indicating potential sensitivity of these estimates to study inclusion.

Furthermore, for BC knowledge, QoL, anxiety, and depression outcomes in which the SD of change scores was imputed, additional sensitivity analyses were performed using plausible pre-post correlation coefficients of $r=0.25$ and $r=0.75$. The pooled effect estimates remained stable across these correlation scenarios, indicating that the findings were robust to the primary assumption of $r=0.50$.

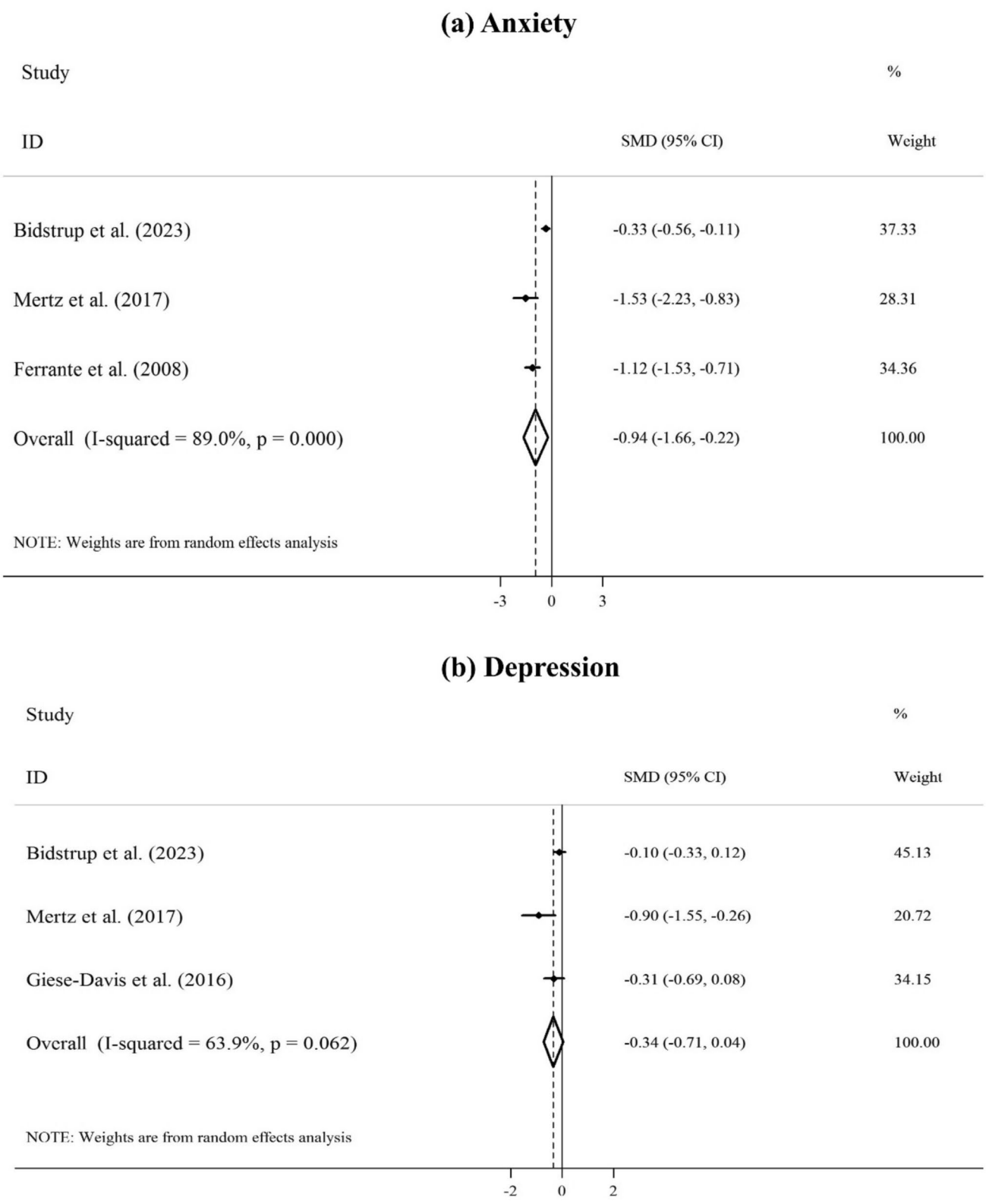

Fig. 5 Forest plots for the effects of PNPs versus control interventions on changes in anxiety and depression scores from baseline to follow-up among women with newly diagnosed BC or with an abnormal mammogram

Subgroup and meta-regression analyses

Overall, the results demonstrated high between-study heterogeneity for most outcomes. In contrast, depression and diagnostic follow-up adherence showed moderate and low-to-moderate heterogeneity, respectively, accompanied by relatively lower estimates of true between-study variance, suggesting more stable effect estimates across studies for these outcomes.

Subgroup analyses suggested that heterogeneity could be attributed to differences in study design (e.g., country, number of arms, setting, data collection and analysis methods, methodological quality, study duration, and whether BC was investigated alongside other cancers); participants' characteristics (e.g., age, race/ethnicity, residence, primary language, income, health insurance, education, and BI-RADS); and intervention features (e.g., type of navigator, mode of navigation delivery, and control intervention) (Supplementary Table 4). However, meta-regression indicated that none of the continuous variables significantly explained the observed heterogeneity (Supplementary Table 6).

Publication bias

Based on the visual inspection of the funnel plot (Supplementary Fig. 5), an asymmetry was revealed for the pooled ESs of adherence to a screening mammogram; this was also confirmed by Egger's test ($P = 0.004$). However, the ES was not affected by the trim-and-fill method, showing that the results were not modified by publication bias. For other outcomes with fewer than 10 studies, qualitative assessment revealed no clear evidence of publication bias.

Quality of studies

Based on the Cochrane RoB2, 20 studies had moderate quality, while the others had either low or high quality ($n = 9$ and $n = 8$, respectively) (Table 2). The risk of randomization process was the leading reason for high RoB (Supplementary Figs. 6 and 7). The investigators' decisions regarding RoB in each study are presented in Supplementary Table 7.

Based on the GRADE approach, most outcomes were rated as low-to-moderate in terms of evidence quality, as seen in Table 3. Inconsistency and serious RoB were the primary reasons for downgrading the certainty of evidence.

Discussion

Since 1990, after a drift from its original clinical setting, PNP now includes interventions across the BC continuum [82]. However, most available data on the effectiveness of PNP-driven interventions in BC care outcomes have been anecdotal and based on practice-based evidence, making it necessary to address the sustainability and scalability of the program before incorporating it into routine practice [11]. Recent RCTs have more extensively evaluated the efficacy of PNP for BC-related care outcomes; however, the results are controversial [17]. Also, a growing number of systematic reviews have recently been published regarding the consequences of PNP in improving BC outcomes; however, they have reported equivocal and inconclusive evidence of PNP efficacy, underscoring the need for more evidence-based studies. Hence, we conducted this systematic review with meta-analysis to make a critical assessment and synthesize currently available RCTs, thus establishing reliable evidence-based results on how PNP affects the BC care continuum.

In the present study, PNP was found to double the chances of screening mammogram adherence. This finding contributes to the growing body of evidence evaluating the benefit of PNP in improving BC screening rates [16, 83]. Based on a meta-analysis of nine RCTs from 2010 to 2018, PNP significantly improved the likelihood of completing population-based BC screening [17]. Likewise, a meta-analysis of 10 RCTs from the USA published from 1997 to 2016 indicated significantly higher BC screening rates in the PNP group compared with the usual or alternative care comparison group among populations adversely affected by health care disparities [14]. On the other hand, a meta-analysis of three studies with different designs showed an improvement in BC screening in Muslim immigrant and refugee women as a result of PNP using both mammography and CBE [84]. Our finding is in line with the benefits observed in the above-mentioned meta-analyses; however, we observed a higher ES, which might be due to the larger number of pooled ESs ($n = 13$).

Regarding diagnostic outcomes, the evidence synthesis suggests that PNP may potentially reduce the TTR of abnormalities suspicious for BC. PNP was associated with a twofold increase in adherence to diagnostic follow-up care. Women receiving PNP were also more likely to achieve a TDR within 6–12 months following the detection of a breast abnormality compared with those without PNP. However, this observed benefit was no longer statistically significant after the application of more conservative adjustment methods. Consequently, the robustness of this effect appears sensitive to the analytical approach and warrants further investigation.

Similar to our findings, previous reviews have yielded controversial diagnostic outcomes. A meta-analysis of RCTs published from 2008 to 2012 indicated that PNP significantly shortened the average time to BC diagnostic resolution compared to control interventions; however, it did not significantly improve the diagnostic resolution rate [17]. Furthermore, a prospective meta-analysis among minority and low-income

Table 3 GRADE evidence profile: Effects of the PNPs on outcomes across the BC care continuum

Outcomes (number of studies)	Quality assessment					Summary of findings			
	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Number of participants		Effect (95% CI)	Quality of evidence
						PNP group	RP group		
Adherence to a screening mammogram (13 RCTs)	Serious[1]	Serious[2]	No serious[3]	No serious[4]	Detected[5]	≈ 15,130	≈ 15,443	OR: 2.18 (CI: 1.71 to 2.77)	⊕⊖⊖⊖ Very low[6]
Adherence to diagnostic follow-up care (4 RCTs)	Serious[1]	No serious[7]	No serious[3]	No serious[4]	Undetected[8]	482	467	OR: 2.42 (CI: 1.64 to 3.59)	⊕⊕⊕⊖ Moderate[9]
Timely diagnostic resolution (4 RCTs)	Serious[1]	Serious[2]	No serious[3]	No serious[4]	Undetected[8]	1027	1311	OR: 2.51 (CI: 1.21 to 5.24)	⊕⊕⊖⊖ Low[10]
Knowledge of breast cancer (3 RCTs)	Serious[1]	Serious[2]	No serious[3]	No serious[4]	Undetected[8]	681	675	SMD: 0.27 (CI: −0.19 to 0.73)	⊕⊕⊖⊖ Low[10]
Quality of life (4 RCTs)	Serious[1]	Serious[2]	No serious[3]	No serious[4]	Undetected[8]	363	344	SMD: 0.44 (CI: 0.09 to 0.79)	⊕⊕⊖⊖ Low[10]
Anxiety (3 RCTs)	Serious[1]	Serious[2]	No serious[3]	No serious[4]	Undetected[8]	213	224	SMD: −0.94 (CI: −1.66 to −0.22)	⊕⊕⊖⊖ Low[10]
Depression (3 RCTs)	Serious[1]	No serious[8]	No serious[3]	No serious[4]	Undetected[8]	229	225	SMD: −0.34 (CI: −0.71 to 0.04)	⊕⊕⊕⊖ Moderate[9]

CI confidence interval, I^2 I-squared statistic, *RCTs* randomized controlled trials, *OR* odds ratio, *PNP* patient navigation program, *RP* routine program, *SMD* standardized mean difference

(1) No upgrading of evidence certainty was performed for any outcome, including those with large or very large effect estimates; (2) absolute effects were not calculated due to the variability and inconsistent reporting of baseline risks across studies

[1]A high proportion of risk-of-bias domains across the included studies were rated as having unclear or high risk of bias

[2]$I^2 > 70.0\%$

[3]Studies were sufficiently similar with respect to the population, intervention protocols, comparator, and intended outcomes

[4]The confidence interval included the overall treatment effect, but the optimal information size was met

[5]Egger's test ($P < 0.05$)

[6]We have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimated effect

[7]$I^2 = 50.0–70.0\%$

[8]Publication bias was evaluated qualitatively, and no evidence of publication bias was observed

[9]We are moderately confident in the effect estimate; the true effect is likely to be close to the estimate, but it remains possible that it is substantially different

[10]Our confidence in the effect estimate is limited; the true effect may be substantially different from the estimated effect

women with BC screening abnormalities showed no statistically significant effect of PNP compared to the usual care program in terms of achieving TDR at 60 days and 180 days; however, a benefit of PNP was reported at 365 days [29]. In another prospective meta-analysis comparing the efficacy of PNP and usual care in terms of TTR for clients with breast, cervical, colorectal, or prostate screening abnormalities and/or cancers, a benefit of PNP was seen from 91 to 365 days, but no positive effect was observed in the initial 90 days of care [19]. A meta-analysis of RCTs and non-RCTs further indicated that the screening-to-diagnosis phase of different cancer types was significantly shorter in nurse-navigated groups than usual care groups. It also showed a higher likelihood (45.0%) of completing diagnostic resolution in the navigated group than the non-navigated group; yet, the ES was not significant statistically [26]. We included only RCTs that specifically addressed PNP for BC. However, most of the aforementioned reviews exhibited heterogeneity in terms of cancer type and study design.

Regarding treatment outcomes, we did not perform a meta-analysis, as the outcomes were not homogeneous for pooled analysis. According to the qualitative synthesis, PNP can affect the timeliness of treatment initiation, but it had no substantial effect on adherence to treatment or time to treatment completion following a diagnosis. These findings augment the earlier related reviews. A systematic review of studies with different designs demonstrated that PNP could increase adherence rates to post-treatment surveillance mammography; however, little evidence supported its effectiveness in improving the treatment outcomes in BC (e.g., timeliness of treatment initiation and adherence rates to treatment) [28]. Furthermore, in a systematic review of the effectiveness of PNP in treatment initiation and treatment adherence of clients with different cancer types, a significant improvement in outcomes was reported [21]. In another systematic review addressing PNP for BC and gynecological cancer, the program helped women initiate treatment sooner and receive proper treatment [85]. In a meta-analysis of RCTs and non-RCTs, the length of time between the diagnosis and the first treatment visit among individuals with different cancer types was reduced significantly by nurse-led navigation. It also showed that cancer treatment was more likely (13.0%) to be initiated by nurse-navigated group participants than those in the control group; however, the ES was insignificant [26]. The benefits of PNP compared to usual care for treatment initiation among clients with prostate, breast, colorectal, or cervical screening cancers and/or abnormalities were documented by a prospective meta-analysis [19]. The studies mentioned above employed data from studies with different designs and covering different types of cancer; hence, it is difficult to compare these studies' findings with ours.

Although studies investigating client-reported outcomes following PNP are in their infancy, we tried to address these outcomes through data pooling. The meta-analyses indicated that women who received PNP reported significantly higher QoL and significantly lower levels of anxiety. However, these effects were no longer statistically significant after applying more conservative adjustment methods. Participants in the PNP group also demonstrated lower levels of depression and greater knowledge of BC, although the between-group differences were not statistically significant. Based on the qualitative synthesis, PNP appeared to have a positive influence on reducing distress and improving satisfaction with care. These findings can contribute to limited reviews evaluating the efficacy of PNP on these outcomes. A systematic review of RCTs and non-RCTs published between 1995 and 2016 demonstrated that the effect of PNP on care satisfaction among patients with various types of cancer was either positive (i.e., increased satisfaction) or neutral (i.e., no effect). Pooled analysis findings of the above review showed a statistically significant increase in satisfaction following PNP in one included RCT, while satisfaction and PNP were not significantly associated in the four non-RCTs [20]. Furthermore, in another systematic review of studies with different designs, 87.0% of studies showed significant benefits of PNP in terms of the satisfaction of clients with different cancers [21]. Meanwhile, a meta-analysis of studies with different designs showed patients' overall psychological outcomes were not significantly or positively affected by nurse navigators. However, the systematic review of the above-mentioned study indicated that nurse navigators had substantial potential to increase the satisfaction of clients with different cancer types [26]. There was heterogeneity in the studies included in the above-mentioned reviews in terms of cancer type and study design; meanwhile, we synthesized RCTs that addressed PNP for BC. Hence, comparisons must be made with caution.

Research strengths

This is the most comprehensive systematic review of PNP research about the entire continuum of BC care. Previous pertinent systematic reviews mostly addressed BC along with other cancers, while we focused specifically on BC. Related meta-analyses were also commonly weighted toward screening and diagnosis phases, while we considered all phases of the BC care continuum. We were the first to investigate the effects of PNP through a meta-analysis approach utilizing some client-reported health outcomes (i.e., knowledge of BC, QoL, anxiety, and depression). Unlike most previous reviews, which synthesized the evidence with different levels (i.e., RCTs, non-RCTs, prospective or retrospective cohort studies), we investigated only RCTs in order to reduce bias and misinterpretation in the obtained results. Furthermore, we evaluated the methodological quality of included RCTs using the latest version of the Cochrane RoB tool to appraise the RCTs, while previous reviews utilized either the old version of the Cochrane RoB assessment tool or other appraisal methods. Similarly, the quality of evidence was assessed using the GRADE approach, which was largely overlooked in previous meta-analyses.

Research limitations

The interpretation of findings from this review should consider certain limitations. First, limiting the studies to peer-reviewed English-language journals may have led to missing some related studies. Likewise, we excluded some studies that synthesized data on BC with other types of cancers, as well as gray literature (e.g., conference abstracts or unpublished studies). Second, most studies were conducted in the USA, which likely limits the generalizability of findings.

Also, the inadequacy of data reporting in the included studies can limit the study findings. Even though we scanned the registered protocol of all eligible studies and requested any needed information from their corresponding authors, we sometimes did not receive feedback; therefore, we made estimations by consensus. Third, due to the limited number of studies or heterogeneity in reporting data, estimating the pooled effects of the intervention on satisfaction with care or treatment, distress, and TTR was not possible. Fourth, most outcomes were supported by low-quality evidence. The absence of consistent baseline risk data across studies not only prevented the calculation of absolute effects but also contributed to residual uncertainty regarding the magnitude of the intervention's impact, as reflected in the GRADE assessment. Furthermore, several RCTs employed unclear or suboptimal randomization procedures, which further weakened the internal validity of the included evidence. Finally, high statistical heterogeneity was observed across multiple pooled analyses, which may have limited the robustness of evidence-based conclusions. To address this, we employed a random-effects model and conducted subgroup analyses to account for between-study variability and explore potential sources of heterogeneity. However, pooling data across different endpoint definitions may have further contributed to this heterogeneity.

Implications for practice and research

This review makes a meaningful contribution to informing future research and clinical practice. The meta-analysis demonstrated that PNPs have notable effects in improving adherence to screening mammography and diagnostic follow-up care, as well as in reducing TDR, with very low, moderate, and low certainty of evidence, respectively. Additionally, PNP was associated with significant reductions in clients' anxiety and improvements in QoL, although these findings were supported by low-certainty evidence. The intervention may also contribute to non-significant reductions in depression and modest increases in patient knowledge, with moderate and low certainty, respectively. Despite these promising findings, the results should be interpreted cautiously in the context of BC care due to variability in evidence certainty. Notably, after applying the HK adjustment, previously observed beneficial effects of PNPs on TDR, QoL, and anxiety were no longer statistically significant. These inconsistencies underscore ongoing concerns regarding the robustness of evidence supporting PNP effectiveness and highlight the need for further investigation.

The first concern is the lack of rigorous design in the included studies. Out of the 37 RCTs, only nine had low RoB in all domains of the Cochrane RoB2. The main reason for the observed high RoB was unclear reporting or inappropriate methodology in the randomization process. The subgroup analyses in low-quality studies showed PNP to be more effective in producing adherence to diagnostic follow-up care and screening mammograms. Moreover, GRADE showed low to moderate evidence quality for most outcomes. Thus, it is advisable that future studies be conducted with higher methodological quality and lower RoB, especially in the randomization sequence generation and concealment domain. Since improving outcomes of diagnostic and screening phases was the goal of employing PNP in most included studies, further trials within the realm of treatment and survivorship outcomes would be merited. Also, it was impossible to observe the effects of the intervention on TTR, treatment outcomes, satisfaction with care, and psychological distress using meta-analysis; there is a need for more assessments regarding these outcomes. Likewise, as PNP was not significantly effective on curbing clients' depression and increasing their knowledge, it is necessary to conduct more studies on these outcomes. In addition, because we found the country of origin to be a heterogeneity source for QoL and anxiety and because most studies had been conducted in the USA, where the first PNP emerged, it would be useful to perform similar trials in other regions that do not regularly apply PNP. Additionally, as none of the included studies evaluated the cost-effectiveness of PNPs, future research should prioritize examining their economic feasibility compared with usual care in relation to BC outcomes. Employing standardized economic metrics is recommended to ensure rigorous and transparent economic evaluations in forthcoming trials.

The second concern is the difficulty of identifying key components relevant to effective PNP. We found heterogeneity among PNPs in terms of the healthcare setting, the delivery format and duration of the intervention, as well as the type and qualification of the navigator. The included studies mainly examined the effectiveness of navigation services presented via both face-to-face and remote methods by non-professional navigators among urban populations selected from either medical or community settings. Our subgroup analyses showed that the intervention was more effective for QoL when administered by a nursing assistant for a duration of 8–12 months than when administered by a lay navigator for a duration of 5 months. Additionally, control interventions had more significant effects on improving QoL in studies that used a combination of usual care and alternative intervention in the control group compared to those that used usual care alone. We also found contradictory results relating to the healthcare setting. Therefore, ascertaining an optimal caring protocol that should be followed to obtain the most significant consequences would be a useful next step. To this end, multiple-arm trials are recommended to compare an intervention's effectiveness in cases of different navigation activities and formats, navigators with different

backgrounds and qualifications, healthcare settings and geographical locations, and control intervention types. Additional investigations are also suggested to compare different intervention durations and thus ascertain the optimal length of PNP.

Conclusion

Implementing PNP-driven interventions across the BC care continuum may enhance adherence to screening mammography and improve compliance with diagnostic follow-up. Additionally, favorable but non-significant trends were observed in depression and knowledge outcomes. Further potential benefits were suggested for TTR, patient satisfaction, and psychological distress; however, evidence for treatment-related outcomes remains limited. PNP involvement was also associated with significant improvements in TDR and QoL, as well as reductions in anxiety; however, these effects lost statistical significance under more conservative adjustments, warranting cautious interpretation. Overall, the certainty of evidence is constrained by the limited number of trials for several outcomes, methodological concerns in many included RCTs, substantial heterogeneity, and the lack of cost-effectiveness evaluations. Hence, further well-designed RCTs across diverse settings, particularly in the treatment and survivorship phases, are needed to enable more valid evidence-based decisions about the benefits of PNP along the continuum of BC care.

Abbreviations *BC*: Breast cancer; *BI-RADS*: Breast imaging reporting and data system; *CBE*: Clinical breast examination; *CI*: Confidence interval; *cRCT*: Cluster randomized controlled trials; *DL*: DerSimonian-Laird; *ES*: Effect size; *GRADE*: Grading of recommendations assessment, development, and evaluation working group; *HK*: Hartung-Knapp; *ICC*: Intracluster correlation coefficient; *ICTRP*: International clinical trials registry platform; *OR*: Odds ratio; *PI*: Prediction interval; *PNP*: Patient navigation program; *PRISMA*: Preferred Reporting Items for Systematic Review and Meta-Analysis; *PROSPERO*: International Prospective Register of Systematic Reviews; *QoL*: Quality of life; *RCT* : Randomized controlled trials; *RoB2*: Cochrane collaboration's risk of bias assessment tool for RCTs; *SD*: Standard deviation; *SE*: Standard error; *SMD*: Standardized mean difference; *TDR*: Timely diagnostic resolution; *TTR*: Time-to-resolution; *USA*: United States of America

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Data availability Data and materials are available by contacting the corresponding author.

Declarations

Ethics approval and consent to participate The Shahid Beheshti University of Medical Sciences, Tehran, Iran (School of Pharmacy and Nursing & Midwifery Local Research Ethics Board) approved this study (No. IR.SBMU.PHARMACY.REC.1402.051). Informed consent was not required for this study, as data were collected from earlier investigations in which verbal or written consent had already been received by the study authors.

Consent for publication No individual data are included in this study.

Declaration of generative AI in scientific writing While preparing this manuscript, the authors used ChatGPT and Grammarly to improve the language, clarity, and readability of the text. After using these tools, the authors carefully reviewed and edited the manuscript as needed and take full responsibility for the content of this publication.

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