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Auricular acupressure for nausea and vomiting in breast cancer: Feasibility outcomes from a Phase II trial with embedded qualitative insights

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ABSTRACT

Introduction: Auricular acupressure (AA) has been a popular complementary health approach for managing cancer-related symptoms, including chemotherapy-induced nausea and vomiting (CINV) in breast cancer (BC) patients. Despite its growing use, clinical evidence regarding the feasibility and acceptability of AA remains limited and not yet fully established. This study aims to evaluate the feasibility and acceptability of using an evidence-based AA intervention for managing CINV in BC patients.

Methods: This paper reports the feasibility outcomes from a Phase II randomised controlled trial (RCT) with embedded qualitative insights. The clinical trial equally assigned 114 participants to a true AA, placebo AA, or standard care group. Patient-reported outcomes were assessed using the MASCC Antiemesis Tool (MAT), the Index of Nausea, Vomiting, and Retching (INVR), and the Functional Assessment of Cancer Therapy-Breast (FACT-B). Study feasibility was evaluated through recruitment, implementation, outcome assessment, intervention feasibility and safety, and participants' satisfaction. Upon RCT completion, semi-structured interviews were conducted to explore participants' experiences with the RCT and the intervention.

Results: The RCT achieved a high completion with 110 participants. Most participants adhered strictly to the 5-day AA protocol. AA-related adverse events were mild and transient. Participants found the complementary healthcare approaches convenient and safe, reporting that the study questionnaires were easy to complete and effectively captured CINV symptoms using MAT. Most participants supported AA's benefits in managing CINV.

Conclusion: The RCT procedures for using AA to manage CINV in BC patients were feasible, with satisfactory recruitment and retention rates, good questionnaire acceptability, and adherence to the protocol. Qualitative findings enhanced understanding of RCT feasibility and protocol acceptability from patients' perspectives. Findings from the Phase II RCT and qualitative interviews supported AA as a safe and convenient intervention for a future Phase III RCT to evaluate its definite effects on CINV in BC patients.

Clinical Trial Registration: ClinicalTrial.Gov (NCT02403037).

1. Introduction

The randomised controlled trial (RCT) has been regarded as one of the most rigorous clinical study designs to explore the cause-and-effect relationship (the "causality") between a health intervention and certain outcomes. However, the implementation of an RCT usually involves a significant investment of time, energy, and money [1,2], which indicates that preparatory work is crucial for estimating and managing the RCT study schedule, ensuring smooth progress within budget and timeframe [2]. Before a formal assessment of a health intervention through a fully powered RCT, it is essential to examine the feasibility of the intervention and study procedures in a small group of

Abbreviations: AA, Auricular acupressure; CINV, Chemotherapy-induced nausea and vomiting; BC, Breast cancer; RCT, Randomised controlled trial; MAT, MASCC Antiemesis Tool; INVR, Index of Nausea, Vomiting, and Retching; FACT-B, Functional Assessment of Cancer Therapy-Breast; CHA, Complementary health approach; MRC, Medical Research Council.

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participants under particular settings that are similar to the future main study design, so that the proposed intervention and study procedures can be practically appropriate for implementation in the main RCT [2,3]. A "feasibility" or "pilot" study is usually conducted for this purpose.

"Feasibility study" and "pilot study" are often used interchangeably to describe preparatory work before a main study [4,5]. However, a feasibility study typically focuses on specific methodological components, such as subject recruitment, randomisation, outcome assessment, and participant adherence (The National Institute for Health Research Evaluation, Trials and Studies Coordinating Centre, as cited in [4,5]). In contrast, a pilot study acts as a scaled-down version of the future main study, examining the entire methodological process [4,5]. In clinical research, feasibility objectives are often integrated into a pilot study to assess both individual components and the entire methodological protocol, from recruitment to end-point data collection.

Complementary health approaches (CHAs) are regarded as complex interventions due to the multiple components, specific treatment sessions, and varying degrees of patient engagement required for optimal outcomes. Before a fully powered trial can test the effectiveness of CHAs, an early phase study assessing intervention feasibility and piloting methodological procedures is essential. *The Medical Research Council (MRC) Framework for Developing and Evaluating Complex Interventions* ("the MRC framework") recommends combining quantitative and qualitative methods to evaluate study feasibility and pilot procedures, examining participant response rates and identifying barriers to participation [3]. Qualitative research within a health interventional study offers insights into participants' experiences, aiding in analysing factors contributing to study success, identifying potential protocol limitations for future improvement, and further enhancing the rigour of design, implementation, and interpretation, leading to more robust and comprehensive conclusions [6–9].

Our team conducted a research project, guided by the MRC framework, to develop and evaluate an evidence-based auricular acupressure (AA) intervention—a non-invasive, cost-effective, and self-administered technique—for managing chemotherapy-induced nausea and vomiting (CINV) in breast cancer patients [10–12]. This project included a Phase II RCT designed to pilot the study intervention protocol and RCT methodological procedure (the feasibility outcomes) and preliminarily evaluate the effects of AA in mitigating CINV (the clinical outcomes). The clinical outcome analysis demonstrated a positive impact of AA, particularly in alleviating acute CINV [11]. To complement the RCT feasibility outcomes, a nested qualitative study was undertaken using semi-structured interviews following the RCT. This qualitative component aimed to provide in-depth insights into the feasibility of the AA intervention and the methodological procedures of the RCT, thereby offering a more comprehensive evaluation. Accordingly, this paper presents the feasibility assessment of the research project, integrating findings from both the Phase II RCT feasibility outcomes and the embedded qualitative insights to provide a comprehensive evaluation of the AA intervention's feasibility and implementation potential.

2. Methods

2.1. Overview of the research project

In alignment with the MRC framework, an AA intervention, incorporating both true and placebo AA, was developed based on systematic review findings, AA-related theoretical frameworks, clinical practice standards, the symptomatology of CINV, and expert consensus [12]. Comprehensive details of the AA protocol have been previously published [11,12]; a summary is provided as follows. The AA intervention was delivered during the first five days of participants' initial chemotherapy cycle. For true AA, seven acupoints ("Cardia," "Stomach," "Spleen," "Liver," "Shenmen," "Sympathetic," and "Subcortex") were targeted to alleviate CINV, using hypoallergenic tape-attached Vaccaria seeds for manual acupressure [12]. The participants self-administered the AA after being trained by the study investigators, who are registered nurses with AA training backgrounds; they were then instructed to perform AA three times daily and apply additional acupressure as needed. In the sham AA group, the same acupoints and duration were used; however, no manual acupressure was applied, and Vaccaria seeds were replaced with Junci Medulla to prevent consistent acupoint stimulation and specific treatment effects [12]. Participants used a daily log to record their daily AA practice (for true AA) and any AA-related adverse events, as well as for the study investigators to monitor their adherence to AA [11].

A Phase II RCT was conducted with a three-arm, parallel, partial-blind, and sham-controlled pilot trial design among 114 BC patients to evaluate the RCT methodological procedures, assess the feasibility of the AA, and explore its potential effects on CINV [10,11]. Following the RCT, a nested qualitative study involving semi-structured interviews with 27 participants was undertaken to examine their experiences with the RCT and the AA intervention. Clinical outcomes from the Phase II RCT provided preliminary evidence of AA's effects in managing CINV [10], which have been reported separately [11]. Findings from the RCT feasibility outcomes and qualitative study findings informed refinements to the protocol for a future large-scale study.

The current paper focuses on the feasibility assessment of the research project, reporting the feasibility outcomes from the Phase II RCT and the findings from the semi-structured interviews. This research project was registered via ClinicalTrial.Gov (NCT02403037) and approved by relevant ethics committees at The Hong Kong Polytechnic University (HSEARS20150213001), Fujian Provincial Cancer Hospital (2015–022–01), the Affiliated People's Hospital of Fujian University of Traditional Chinese Medicine (2015–031–01), and the Second Affiliated Hospital of Fujian University of Traditional Chinese Medicine (2015-KL007–02).

2.2. The Phase II RCT

2.2.1. Study sample, setting and procedures

Details of the RCT design and clinical outcomes regarding the preliminary evaluation of the AA effects on CINV have been separately reported and adhere to CONSORT guidelines [11]. In summary, the study was conducted in three tertiary medical centres in Fuzhou, Fujian. A total of 114 BC patients scheduled for their first chemotherapy cycle were randomly assigned to a true AA ($n = 38$), a placebo AA ($n = 38$), and a standard care group ($n = 38$) [11]. Female adult BC patients were eligible to participate if they had a confirmed diagnosis of stage I–III BC, were chemotherapy- and auricular therapy-naïve, able to communicate in Mandarin, had at least primary school education, provided written informed consent, and were scheduled to receive their first cycle of moderately-high to highly emetogenic chemotherapy, alongside standard antiemetics [11]. Exclusion criteria included significant frailty or immune deficiency, inability to comply with study procedures, concurrent radiotherapy or other treatments, enrolment in other clinical studies, interfering health conditions, or ear conditions unsuitable for AA [11]. All participants received standard antiemetic treatment and routine care, while the AA groups received an additional 5-day true AA or placebo AA, respectively. Follow-up lasted until the end of the first chemotherapy cycle. Clinical outcomes, including acute and delayed CINV (measured by the MASCC Antiemesis Tool [MAT]), anticipatory CINV (measured by the Index of Nausea, Vomiting, and Retching [INVR]), and quality of life (measured by the Functional Assessment of Cancer Therapy-Breast [FACT-B]), were assessed throughout [11]. The analysis showed that AA plus standard treatment was superior in reducing CINV, particularly acute CINV, compared to standard treatment alone [11]. The study indicated that AA's effects comprised both specific antiemetic and non-specific placebo effects [11]. Feasibility outcomes regarding RCT procedures and AA intervention were evaluated, including subject recruitment, implementation, outcome assessment, acceptability, safety, and participants' satisfaction with AA.

2.2.2. Feasibility outcomes

2.2.2.1. Feasibility of subject recruitment. The feasibility of subject recruitment was assessed by: **a)** the total recruitment period and average monthly recruitment; **b)** the eligibility rate (eligible patients divided by screened patients); **c)** the recruitment rate (actual participants divided by eligible patients); **d)** the retention rate (completed RCT participants divided by total participants); **e)** the attrition rate (dropouts divided by total participants). Reasons for discontinuation were also collected.

2.2.2.2. Feasibility of the study questionnaires. The percentages of missing values at both item-level and scale-level for the MAT, INVR, and FACT-B were estimated. Item-level missing values were identified by the proportion of participants not responding to each item. The scale-level missing values were indicated by the proportion of participants not responding to at least one item in the entire questionnaire.

2.2.2.3. Feasibility and acceptability of the AA intervention. Descriptive statistics were used to estimate: **a)** the total number of days AA conducted in the true AA and placebo AA groups (standard period: 5 days); b) the number of times self-acupressure performed in the true AA group (standard: 3 times on day 1, 12 times from day 2 to day 5, and 15 times over the 5-day period); **c)** the duration of each self-acupressure session in the true AA group during the acute CINV, delayed CINV, and 5-day AA period (standard duration: 4 to 7 min).

2.2.2.4. Safety of the study intervention. The participants recorded possible AA-related adverse events during the 5-day AA, which was reported in the RCT clinical outcome paper [11]. A senior acupuncturist determined causality, using the WHO-Uppsala Monitoring Centre System with six causality degrees: "certain," "probable/likely," "possible," "unlikely," "conditional/unclassified," and "unassessable/unclassifiable" [11,16].

2.2.2.5. Participants' satisfaction with the AA treatment. The participants in the true and placebo AA groups rated satisfaction with the AA by answering three questions, including **a)** satisfaction with the AA evaluated on a 10-point numeric rating scale [NRS] ("1″ = "very dissatisfied" and "10″ = "very satisfied"), **b)** consideration of further AA (10-point NRS, "1″ = "absolutely not" and "10″ = "absolutely yes"), and **c)** willingness to recommend AA to others (10-point NRS, "1″ = "absolutely not" and "10″ = "absolutely yes").

2.2.2.6. Daily log for recording AA practice. Participants in the true and placebo AA groups used a daily log to record AA-related feasibility assessment data. The true AA group log has three sections: a) the daily schedule for AA with detailed instructions; b) time, frequency, and duration of daily self-acupressure; and c) possible AA-related side effects. Participants' satisfaction with the AA was also assessed on the last day's log. The placebo AA group log only recorded potential adverse events and participants' satisfaction with the AA treatment [11].

2.2.3. Feasibility data analysis

Descriptive statistics were used to summarise recruitment, eligibility, retention, and attrition rates, as well as the completion rates of study questionnaires. Missing data from the study questionnaires were analysed to identify both item-level and scale-level missing values. Adherence to the AA intervention, including total AA days, self-acupressure frequencies, and session durations, was also evaluated using descriptive statistics. The Chi-square test or Fisher's exact test explored differences in the total number of AA days between true AA and placebo AA. Spearman's correlation coefficient examined correlations of AA treatment days, self-acupressure times, and average duration of self-acupressure with AA's antiemetic effects using the MAT scoring system [13,14]. A correlation coefficient (r) lower than 0.30 indicates a weak correlation; 0.30–0.59 represents a moderate correlation; greater than 0.60 indicates a strong correlation [15]. Some participants did not complete the entire 5-day AA during the delayed CINV period. For these participants, the estimation of their self-acupressure times and average duration was based on the actual days they performed AA. The between-group difference in the satisfaction score was assessed using the Independent *t*-test or the Mann-Whitney U test.

2.3. The semi-structured interviews

2.3.1. Study sample, setting and procedure

A purposive sampling approach was utilised to recruit interviewees until data saturation was achieved. Participants were BC patients from the Phase II RCT who met the following purposive sampling inclusion criteria: a) demonstrated high, moderate, or low expectations regarding the effects of AA, as measured on a 10-point numerical NRS, where "0″ indicates very low expectations and "10" signifies very high expectations; b) either adhered to or did not adhere to the AA protocol, as assessed by the study investigator; and c) had prior experience with CHAs other than AA or had none. All RCT participants were informed about the interview aims and procedures in advance. Eligible patients interested in both the RCT and interviews provided written informed consent. After completing RCT data collection, participants were asked to indicate their expectations of AA's effects on CINV and previous CHA experiences. Those meeting the purposive sampling inclusion criteria were labelled as "potential interviewees" and invited for interviews.

The study investigator (Tan JY, male, research doctoral candidate at the time of study) arranged suitable times and venues for the interviews, ensuring privacy. The interviews were conducted by the study investigator on a one-on-one basis with the interviewees. These took place in locations convenient for the participants, such as an interview room, demonstration room, or other suitable areas at the study site. Each interview lasted about one-third of an hour on average. Prior to commencing the research project, the study investigator completed a rigorous qualitative research methodology course, gaining the necessary skills to conduct semi-structured interviews and analyse qualitative data with methodological rigour. Participants were briefed about the study aims and procedures beforehand. A topic guide was used to direct the interview process, which was developed based on a series of qualitative or mixed-methods studies that explored patients' views and/or perceptions of using CHAs [7,17–20]. The interview guide comprised twelve open-ended questions, detailed in **Supplementary File A**, designed to explore participants' overall experiences of participating in the clinical trial and receiving the AA. These questions addressed various aspects, including their use of complementary health approaches, engagement with study questionnaires and instruments, adherence to daily AA practice, and symptom experiences throughout the study period. Interviewees shared their experiences and feelings about participating in the RCT, receiving AA or placebo AA, and their perceptions of AA's antiemetic effects. Probes were used to encourage further elaboration. Pilot interviews were conducted with the first three interviewees to determine the feasibility of the topic guide and if any modifications were needed.

2.3.2. Qualitative data analysis

The interviews were conducted in Mandarin and audio recorded. Field notes were taken during and immediately after each interview. The audio records were transcribed verbatim by a student nurse, the study investigator, and an independent qualitative researcher. Data analysis employed the six-phase thematic analysis [21], which includes "familiarizing yourself with your data (phase one)," "generating initial codes (phase two)," "searching for themes (phase three)," "reviewing themes (phase four)," "defining and naming themes (phase five)," and "producing the report (phase six)" [21] (p. 87), with reliability checking performed by an independent researcher. The qualitative data codes were summarised in a list [22], and the independent researcher matched

the codes with related sentences, achieving an appropriate match rate exceeding 80 % [22]. *The 15-Point Checklist of Criteria for Good Thematic Analysis* [21] ensured rigorous transcription, coding, analysis, and reporting of the qualitative data.

To maintain the trustworthiness of the study findings, transcribed scripts were checked against the original records for accuracy. Backward translation from English to Mandarin was conducted to ensure equivalence in the interviewees' descriptions. Identified themes/sub-themes were returned to some interviewees for confirmation, ensuring they accurately reflected their experiences in the RCT and receiving the AA [23,24]. Interview findings were compared with other qualitative research on acupuncture/acupressure trials to assess transferability to other CHA settings [24]. Ongoing communications among the study investigator, interviewees, and independent researcher during data analysis ensured interpretations reflected the interviewees' actual thoughts and views, rather than the study investigator's preferences [24].

3. Results

3.1. Feasibility outcomes of the Phase II RCT

3.1.1. Participants' baseline demographic and clinical characteristics

A total of 114 BC patients participated in the RCT, with 110 completing the study [11]. Baseline data were detailed in the clinical outcome paper: the mean age was 47.5 years, half had primary education, and 11.4 % completed tertiary education. Most participants had healthcare insurance, 57.0 % were at stage II BC [11], 71.1 % had undergone a modified radical mastectomy, and common chemotherapeutic regimens included epirubicin/cyclophosphamide and doxorubicin/cyclophosphamide [11]. For CINV management, 5-HT3 antagonists with or without dexamethasone were frequently used [11].

3.1.2. Feasibility of the subject recruitment

Subject recruitment over 15 months saw eight participants per month [11]. Eligibility rate was 66.2 %, recruitment rate 76.5 %, and retention rate 96.5 %, indicating minimal attrition at 3.5 % [11]. Of the four patients who dropped out, one from the true AA group did not complete the delayed CINV assessment via telephone, though she indicated her satisfaction scores and did not return for subsequent chemotherapy cycles. The other three participants (two from the true AA group and one from the standard care group) discontinued due to moving back to hometowns or switching to local hospitals for further treatment.

3.1.3. Feasibility of the study questionnaires

No missing values were found for the INVR and MAT assessments. However, the FACT-B showed a few missing values. At baseline, 11 of 37 FACT-B items had missing responses: 59.6 % of participants refused to answer FACT-B-GS7 ("I am satisfied with my sex life"), 20.2 % did not respond to FACT-B-B4 ("I feel sexually attractive"), and 6.1 % declined to answer FACT-B-B9 ("I am able to feel like a woman"). Other items had minor missing values (0.9 % to 3.5 %). Only 38 participants completed all FACT-B items at baseline. Post-intervention, similar patterns emerged: 63.6 % refused FACT-B-GS7, 23.6 % did not answer FACT-B-B4, and 7.3 % did not answer FACT-B-B9. Only 34.5 % completed all items post-intervention.

3.1.4. Acceptability of the AA intervention

3.1.4.1. Total number of days of AA treatment. Most participants in both the true (76.3 %) and placebo AA groups (84.2 %) completed the 5-day AA. No significant difference in AA days was found between groups ($p = 0.67$). Of the three dropouts in the true AA group, one completed the 5-day AA and log, while the others completed 2-day and 3-day AAs with corresponding logs.

3.1.4.2. Times and durations of self-acupressure in the true AA group. During the acute CINV period (day 1 of the chemotherapy cycle), 84.2 % of participants in the true AA group adhered to the study protocol, performing self-acupressure at least three times per day, and the average duration of each self-acupressure session was four minutes and above in 71.0 % of the participants. During the delayed CINV period (days 2 to 5, but a few did not complete all the 4-day AA), 60.5 % performed self-acupressure 12 times or more, with 65.8 % maintaining an average session duration of four minutes or more. Over the entire AA period (days 1 to 5, but a few did not complete all the 5-day AA), 52.6 % completed at least 15 sessions, and 63.2 % maintained an average session duration of four minutes or more (Table 1).

3.1.4.3. Relationship between the antiemetic effects of AA and the AA-related feasibility outcomes. Statistically insignificant correlations were shown between the AA-related feasibility outcomes and most of the MAT nausea and vomiting outcomes ($p > 0.05$). Weakly positive correlations were identified between the MAT scores and the average duration of each self-acupressure session during the acute CINV, the delayed CINV, and the entire AA period, with a few correlations in the acute CINV period achieving borderline statistical significance (Table 2).

Table 1
Times and durations of self-acupressure in the true AA group.

Times and Durations of AA	True AA ($n = 38$)[a] Number (%)
Times of ear acupressure during acute CINV	
<3 times	6 (15.8 %)
3 times (standard)	30 (78.9 %)
>3 times	2 (5.3 %)
Average duration of each acupressure session during acute CINV	
<2 min	5 (13.2 %)
>2 but <4 min	6 (15.8 %)
4–7 min (standard)	26 (68.4 %)
>7 min	1 (2.6 %)
Times of ear acupressure during delayed CINV (standard: 4-day) [b]	
<6 times	5 (13.2 %)
6–11 times	10 (26.3 %)
12 times (standard)	15 (39.5 %)
>12 times	8 (21.1 %)
Average duration of each acupressure session during delayed CINV (standard: 4-day) [b]	
<2 min	5 (13.2 %)
>2 but <4 min	8 (21.1 %)
4–7 min (standard)	24 (63.2 %)
>7 min	1 (2.6 %)
Total times of ear acupressure during the whole AA treatment (standard: 5-day) [b]	
<9 times	5 (13.2 %)
9–14 times	13 (34.2 %)
15 times (standard)	12 (31.6 %)
>15 times	8 (21.1 %)
Average duration of each acupressure session during the whole AA treatment (standard: 5-day)[b]	
<2 min	5 (13.2 %)
>2 but <4 min	9 (23.7 %)
4–7 min (standard)	23 (60.5 %)
>7 min	1 (2.6 %)

Note: AA=auricular acupressure; CINV=chemotherapy-induced nausea and vomiting; *a*=one of the three true AA group participants who dropped out of the preliminary RCT completed the five-day AA and provided via telephone her five-day AA daily log recordings that she completed at home, while the other two participants completed only a two-day AA and log recordings and a three-day AA and log recordings, respectively; *b*=the standard AA treatment days were five days in total including a one-day acute CINV phase and a four-day delayed CINV phase. However, a few participants failed to complete the entire five-day AA, particularly for the AA during the delayed CINV phase, and therefore for those participants who failed to complete the five-day AA, the computation of their times and average duration of each self-acupressure session was based on their actual number of days (e.g., 2 days, 3 days, or 4 days) of AA.

Table 2
Correlations between AA-related feasibility outcomes and the antiemetic effects of AA on CINV.

AA-related Feasibility Outcomes	Group	MAT Total and Domain Scores								
		Overall Total	Total Nausea	Total Vomiting	Acute CINV	Acute Nausea	Acute Vomiting	Delayed CINV	Delayed Nausea	Delayed Vomiting
Number of days of AA	**True AA**	−0.012 (p = 0.94)	0.032 (p = 0.85)	−0.158 (p = 0.35)	−0.077 (p = 0.65)	−0.030 (p = 0.86)	−0.101 (p = 0.55)	0.115 (p = 0.50)	0.090 (p = 0.60)	−0.012 (p = 0.94)
Number of days of AA	**Placebo AA**	−0.217 (p = 0.19)	−0.145 (p = 0.39)	−0.305 (p = 0.06)	−0.151 (p = 0.37)	−0.050 (p = 0.77)	−0.243 (p = 0.14)	−0.109 (p = 0.51)	−0.142 (p = 0.40)	−0.101 (p = 0.55)
Total times of ear acupressure during acute CINV period	**True AA**	−0.075 (p = 0.66)	−0.076 (p = 0.66)	−0.034 (p = 0.84)	−0.106 (p = 0.53)	−0.013 (p = 0.94)	−0.212 (p = 0.20)	−0.002 (p = 0.99)	−0.087 (p = 0.61)	0.156 (p = 0.36)
Total times of ear acupressure during delayed CINV period	**True AA**	0.076 (p = 0.66)	0.152 (p = 0.37)	−0.052 (p = 0.76)	−0.104 (p = 0.53)	0.066 (p = 0.69)	−0.369 (p = 0.02)	0.267 (p = 0.11)	0.268 (p = 0.11)	0.216 (p = 0.20)
Total times of ear acupressure during the entire AA treatment period	**True AA**	0.078 (p = 0.65)	0.140 (p = 0.41)	−0.021 (p = 0.90)	−0.098 (p = 0.56)	0.073 (p = 0.66)	−0.358 (p = 0.03)	0.266 (p = 0.11)	0.242 (p = 0.15)	0.257 (p = 0.13)
Average duration of each acupressure session during acute CINV	**True AA**	0.281 (p = 0.09)	0.220 (p = 0.19)	0.312 (p = 0.06)	0.298 (p = 0.07)	0.315 (p = 0.05)	0.122 (p = 0.47)	0.152 (p = 0.37)	0.030 (p = 0.86)	0.350 (p = 0.03)
Average duration of each acupressure session during delayed CINV	**True AA**	0.232 (p = 0.17)	0.186 (p = 0.27)	0.264 (p = 0.12)	0.228 (p = 0.17)	0.261 (p = 0.11)	0.060 (p = 0.72)	0.123 (p = 0.47)	0.027 (p = 0.88)	0.321 (p = 0.05)
Average duration of each acupressure session during the entire AA treatment period	**True AA**	0.261 (p = 0.12)	0.211 (p = 0.21)	0.285 (p = 0.09)	0.249 (p = 0.13)	0.274 (p = 0.10)	0.086 (p = 0.61)	0.160 (p = 0.34)	0.064 (p = 0.71)	0.333 (p = 0.04)

Note: AA=auricular acupressure; CINV=chemotherapy-induced nausea and vomiting; MAT=MASCC Antiemesis Tool.

3.1.5. Safety of the AA intervention

Eleven participants experienced minor to moderate adverse reactions to AA, deemed "probable/likely". Adverse events were transient, disappearing after AA tape removal without additional interventions [11].

3.1.6. Participants' satisfaction with the AA intervention

Seventy-four participants in the true and placebo AA groups indicated their satisfaction with the AA (response rate 97.4 %), showing general satisfaction. The mean score was 6.8 (SD=1.7) for true AA and 7.2 (SD=1.4) for placebo AA. For considering further AA treatment, the mean was 6.6 (SD=1.7) in true AA and 6.9 (SD=1.7) in placebo AA. Willingness to recommend AA to others scored 6.2 (SD=1.7) in true AA and 6.4 (SD=2.0) in placebo AA. No statistically significant difference in satisfaction scores was found between groups.

3.2. Results of the semi-structured interviews

3.2.1. Theme and sub-themes

The interviews were performed within two months after the participants completed the RCT. Twenty-seven participants were invited, and all agreed to interview. Table 3 shows the demographic and characteristics of the 27 interviewees. Five themes were identified, describing the interviewees' experiences of taking part in the RCT and receiving the AA. The main themes and sub-themes were presented, with representative data extracts summarised in the **Supplementary File B**.

3.2.1.1. Views on CHAs

3.2.1.1.1. Adjuvant approaches to conventional medicine. Most interviewees noted previous experiences with CHAs (e.g., acupuncture, massage, scraping therapy, herbal medicine) for themselves or their families. They viewed CHAs as promising adjuncts to conventional medicine for managing chemotherapy side effects, emphasising their holistic approach to regulating body functions and alleviating chemotherapy-induced symptoms. Interviewees commonly believed that the beneficial effects of CHAs were gradual and slow.

3.2.1.1.2. Relatively safe approaches with minor adverse events. Most interviewees viewed CHAs as relatively safe. Some described themselves as having a sense of security when receiving CHAs because of their conviction in the safety of CHAs. However, the interviewees had only a superficial understanding of the safety of CHAs. When asked to indicate from what aspects they believed CHAs were safe, none of them could provide any details and name specific side events that could be related to CHAs.

3.2.1.1.3. A desire to receive CHAs to manage chemotherapy-induced symptoms. Some interviewees expressed a desire to receive CHAs during chemotherapy to alleviate unpleasant symptoms. One suggested that the medical centre establish a dedicated unit offering tailored CHAs for hospitalised patients.

3.2.1.2. Experiences of completing the study questionnaires

3.2.1.2.1. Convenient and easy to understand. Most interviewees found the questionnaires easy to complete and considered the workload reasonable, as they were asked to fill in only a few questionnaires throughout the study period, not daily. One participant complained that frequent paperwork could be very annoying for patients already under distress from chemotherapy, and they would not want to bear additional burdens when feeling "really bad." Another interviewee mentioned a sensitive item in the FACT-B about her sex life, which she declined to answer due to personal privacy. However, she noted that this question did not bother her since the FACT-B clearly instructed patients to skip any items they preferred not to answer.

3.2.1.2.2. Recall of acute and delayed nausea and vomiting. Most interviewees recalled the frequency and severity of acute CINV on day 1 of the first chemotherapy cycle and the delayed symptoms in subsequent days. Some agreed that a one-time assessment for delayed symptoms was feasible. However, a few interviewees expressed difficulty providing accurate answers for delayed emesis due to memory lapses. One participant, with memory issues, preferred daily checks for more accurate symptom recording.

3.2.1.3. Adherence to the intervention protocol

3.2.1.3.1. Adherence to regular self-acupressure. Most interviewees in the true AA group confirmed regular self-acupressure. One mentioned additional acupressure upon feeling nauseous. Two demonstrated correct self-acupressure skills. Another participant initially followed

Table 3
Characteristics of the interviewees.

Demographic and Clinical Data		Number (%)
Group allocation of the preliminary RCT (n = 27)	True AA group	10 (37.0 %)
	Placebo AA group	11 (40.7 %)
	Standard care group	6 (22.2 %)
Age (years) (n = 27)	60–69	4 (14.8 %)
	50–59	5 (18.5 %)
	40–49	14 (51.9 %)
	30–39	2 (7.4 %)
	20–29	2 (7.4 %)
Education background (n = 27)	University/college degree or diploma	2 (7.4 %)
	Technical school or high school	1 (3.7 %)
	Secondary school	6 (22.2 %)
	Primary school	18 (66.7 %)
Employment status (n = 27)	Professional	2 (7.4 %)
	Manual work	8 (29.6 %)
	Housewife	14 (51.9 %)
	Admin or clerical work	1 (3.7 %)
	Retired	1 (3.7 %)
	Other	1 (3.7 %)
Marital status (n = 27)	Married	26 (96.3 %)
	Single	1 (3.7 %)
Stage of breast cancer (n = 27)	Stage III	7 (25.9 %)
	Stage II	18 (66.7 %)
	Stage I	2 (7.4 %)
Chemotherapy protocol (n = 27)	Doxorubicin + cyclophosphamide (AC) combination [a]	7 (25.9 %)
	Epirubicin + cyclophosphamide (EC) combination [a]	18 (66.7 %)
	Docetaxel+ cyclophosphamide (TC) combination	1 (3.7 %)
	Pirarubicin+ cyclophosphamide combination	1 (3.7 %)
Antiemetic medication (n = 27)	5-HT3 receptor antagonists + dexamethasone	14 (51.9 %)
	5-HT3 receptor antagonists only	13 (48.1 %)
Adherence to AA protocol (n = 21)	Rigid adherence	13 (61.9 %)
	Not rigid adherence	8 (38.1 %)
Expectations of AA treatment effects (0–10 numerical scale, n = 21)	Maximum score	10
	Minimum score	1
	Average score (mean)	5.95
Previous experiences with CHAs (n = 27)	Yes	16 (59.3 %)
	No	11 (40.7 %)

Note: RCT=randomized controlled trial; AA: auricular acupressure; a=these combinations were administered with or without sequential adjuvant therapy using paclitaxel or docetaxel; CHA: complementary health approach.

instructions on day 1 but, perceiving no effects of AA, chose not to strictly follow the protocol, thereafter, performing acupressure only occasionally when aware of "something in the ear."

3.2.1.3.2. Adherence to precautions and treatment duration of AA. Most of the interviewees in the true and placebo AA groups confirmed that they had kept the AA tapes in place for 5 days, and they followed the telephone instructions on day 6 to remove the AA tapes. Most of the interviewees had rigid adherence to the AA precautions. For instance, they were careful to prevent the AA tapes from getting wet when washing hair or taking a shower, and they also prudently cleaned their ears to prevent the AA tapes from falling off. Three interviewees receiving the placebo AA had inadvertently dropped a few AA tapes on day 3 or 4, but none reported to the study team.

3.2.1.4. Safety and convenience of the intervention

3.2.1.4.1. A relatively safe approach with minor irritations. Most interviewees did not experience any adverse events related to AA. A few reported minor irritations: three in the true AA group noted minor pain during self-acupressure, which ceased after removing the AA tapes. One placebo AA recipient mentioned mild ear itching, and another reported slight redness at the AA sites, though she did not log it as an adverse reaction or inform the study team. Only one true AA participant reported significant pain during self-acupressure but did not notify the study team, completing the 5-day AA despite the discomfort.

3.2.1.4.2. A convenient approach without disturbing routine treatments and activities. The interviewees generally found AA convenient, not interfering with routine treatments and activities. Following AA practice precautions, they could groom themselves without disturbing or wetting the tapes. One interviewee receiving true AA noted some inconvenience when sleeping laterally, as the pillow pressed against the ear. However, another mentioned that a soft pillow prevented earache and discomfort. Overall, the interviewees were satisfied with AA, with more than half hoping to continue using it for CINV and other issues like fatigue and sleep disturbances. One participant emphasised that the non-invasive nature of AA was a key factor in her decision to participate and consider further AA treatment.

3.2.1.5. Perceptions of the intervention effects

3.2.1.5.1. Perceptions of the intervention effects for nausea and vomiting. Most interviewees who received either the true or placebo AA reported mild or no CINV symptoms during the first chemotherapy cycle. Over half felt their symptoms were more alleviated during the first cycle with AA compared to subsequent cycles without AA. Participants were pragmatic about AA's effects, perceiving some beneficial impact on CINV relief. Their perceptions stemmed from experiences across different cycles, noting worse symptoms in the second cycle without AA. A few based their perceptions on previous CHA use or comparisons with other patients not using AA. One placebo AA user, familiar with complementary medicine patches for motion sickness, believed AA had a similar mechanism. Another true AA user cited a belief in AA's efficacy as a key motivator to complete the study.

3.2.1.5.2. Perceptions of the intervention effects on emotional well-being. Interviewees with minor or no CINV symptoms reported better emotional status during the first chemotherapy cycle. They noted that minor emesis did not significantly impact their appetite, reducing the physical and psychological burden of treatments and daily activities. Two participants felt relieved when they did not experience severe sickness like other patients and believed that reduced physical symptom distress contributed to their improved emotional status after discharge.

3.2.1.5.3. Perceptions of the placebo effects of the intervention. Several participants described the AA effects as "psychological comfort" or a "psychological effect," suggesting AA might boost patients' expectations of treatment. One interviewee mentioned hearing about the effectiveness of CHAs in alleviating sickness, which led her to believe she would not experience CINV symptoms after AA treatment. This belief was reinforced when she remained symptom-free during the study while others without AA experienced severe CINV symptoms.

4. Discussion

The MRC framework highlights the importance of integrating quantitative and qualitative methods to evaluate complex interventions [3]. In acupuncture/acupressure trials, qualitative studies often enrich the interpretation of quantitative data [6,7,20,25–27]. This study's quantitative component demonstrated the feasibility of an evidence-based AA for managing CINV in BC patients. The qualitative component enhanced the understanding of the RCT methodological procedures and the feasibility of the study protocol from the patients' perspectives, which are crucial for refining the study protocol for a

future main RCT to examine the definite effects of AA on CINV in BC patients.

The Phase II RCT demonstrated a 76.5 % recruitment rate, surpassing those in other cancer symptom management studies using non-pharmacological methods [28–33]. The retention rate was excellent, with only four patients dropping out. Existing evidence supports AA as a safe, convenient, and potentially effective method for managing CINV. This information was shared with potential participants to alleviate concerns about the intervention's benefits and safety. AA was administered during normal hospitalisation days, with outcomes collected on-site or via phone, saving participants' energy and time. These factors, along with participants' positive attitudes towards CHAs and the convenience of AA, likely contributed to the high recruitment and retention rates.

Most interviewees can accurately recall their CINV symptoms during the first chemotherapy cycle. However, some expressed concerns about accurately recording MAT symptoms due to memory lapses, especially for delayed symptoms, potentially undermining the validity of the MAT assessment. For older patients with memory issues, a simple daily record of CINV symptoms may help. This could be considered for the future main RCT.

Significant missing data were found in some FACT-B items, such as FACT-B-GS7 and FACT-B-B4. Interviews indicated these items involved "personal privacy," which is sensitive for some participants. Given China's conservative culture, particularly in rural areas, many participants declined to respond. Similarly, in Iran, most female cancer patients avoided EORTC QLQ-C30 items on sexual activities due to cultural reasons [26]. Additionally, FACT-B-GS7's missing data might result from questionnaire instructions allowing participants to skip sensitive questions, suggesting the author anticipated this and included strategies to handle missing data in the scoring guide.

Patients' adherence to the AA treatment was deemed appropriate, consistent with findings from other RCTs using similar interventions [34–37]. The convenience of AA practice likely contributed to this adherence, along with patient-related factors. Experiencing treatment effects quickly has been crucial for improving study adherence [38], while concerns about intervention risks and negative perceptions of its effects may hinder adherence [39,40]. During the interviews, most participants indicated that the perceived effectiveness and safety of AA for CINV were key motivators for completing the study. This aligns with Hopton et al. (2013) [6], who found that better chronic pain management using acupuncture may have (at least partially) contributed to the intervention's acceptability.

Weakly positive associations were found between MAT scores and the average duration of each self-acupressure session during the acute CINV, delayed CINV, and entire AA periods, with some correlations in the acute period achieving borderline statistical significance. This suggests that more severe symptom was positively correlated with a higher frequency of self-acupressure, particularly during the acute CINV period. A possible explanation is that BC patients with more severe symptoms on day 1 tended to perform self-acupressure more frequently for symptom relief.

This study identified a few AA-related side effects, mostly mild and transient, supporting AA as a relatively safe approach [11], consistent with prior research [41]. However, AA-related adverse events are likely underreported in the RCT. The qualitative study found three cases of minor pain in a small sample, while daily logs showed five cases in the true AA group. Additionally, one interviewee with placebo AA reported minor redness that was not recorded in the log. This non-adherence to recording might be due to the transient and mild nature of the adverse events, which participants might not have considered significant enough to report.

The interview findings revealed that participants with minimal or no CINV symptoms reported better emotional status, suggesting that less symptom distress might lead to improved psychological outcomes. Qualitative studies that focused on patients' experiences of receiving acupuncture reported that, in addition to improving targeted health conditions, acupuncture may have some beneficial effects on patients' physical and psychological well-being [42,43]. Alraek and Malterud (2009) [42] described these additional benefits of acupoint stimulation as a "positive side-effect," aligning with Traditional Medicine's holistic perspective. Future main RCT could consider psychological well-being as a secondary outcome.

Several interviewees mentioned the placebo effects of AA, believing its effects were "psychological comforts." The patients' expectations of the AA intervention may play a crucial role in generating the placebo effects, with "mental suggestion" strengthening if participants did not experience emesis after AA while observing others without AA suffering severe symptoms. This aligns with another qualitative study indicating that acupressure's antiemetic effects might be associated with placebo effects [7]. Despite perceiving AA as a "psychological comfort," interviewees acknowledged its symptom control benefits and expressed willingness for further AA treatment. This supports Segar's (2012) [44] assertion (cited in Hughes et al., 2013 [7]) that while CHAs' effects may be associated with some placebo effects, they remain attractive to patients.

This study has some limitations. Although favourable evidence supported the feasibility and acceptability of the AA intervention and RCT procedures, specific criteria for determining feasibility success were not defined during the study design phase. The study was designed and implemented prior to the development of the Study Within A Trial (SWAT) methodology, which may have limited opportunities for a more structured and systematic evaluation of trial processes. The semi-structured interviews shared a limitation with Hughes et al. (2013) [7], where recruitment and participation were voluntary. This suggests that participants with positive RCT outcomes were more likely to join the interviews, potentially biasing their experiences and views on study participation and AA. Despite using purposive sampling to enhance sample representativity, the selection criteria did not include patients with varying CINV symptom experiences post-AA, which might also introduce biases in the study findings.

5. Conclusion

This study employed a Phase II RCT and a qualitative study to explore the feasibility of an AA intervention for managing CINV in BC patients. The RCT procedures were feasible, with satisfactory recruitment and retention rates, and good acceptability of the intervention and outcome assessment. Interview findings further illuminated the feasibility and acceptability of the RCT procedures and the study protocol from the participants' perspectives. Results from the Phase II RCT and qualitative study complemented each other, suggesting that AA could be a safe and convenient intervention in a future fully powered Phase III RCT to evaluate its effects on CINV in BC patients.

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Jing-Yu (Benjamin) Tan: Writing – original draft, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Lorna K.P. Suen:** Writing – review & editing, Conceptualization. **Tao Wang:** Writing – review & editing, Formal analysis.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability statement

The study datasets contain sensitive personal information and are stored securely with restricted access. Access is subject to approval by the relevant ethics committees and data custodians.

Supplementary materials

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