**Title**

Multimodal intervention for preventing peripheral intravenous catheter failure in adults (PREBACP study): A multicentre, cluster-randomised controlled trial.

Manuscript published in **The Lancet Haematology**

**DOI:**

**www.**

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## ABSTRACT

**Background**: Two billion peripheral intravenous catheters (PIVC) are inserted into inpatients worldwide year. Almost 1 in 2 PIVC failed for various reasons before completion of intravenous therapy. We aimed to determine the efficacy and costs of a multimodal intervention to reduce PIVC failure rates among hospitalised patients.

**Methods**: We conducted a cluster-randomised controlled trial at seven public hospitals in Spain. Clusters had at least 70% of permanent staff, being enrolled and randomly assigned (1:1) to the multimodal intervention or control arms. We concealed randomisation to allocation, without masking patients and professionals to the intervention arm. The protocol-prespecified primary outcomes were PIVC failure at 12 months (phlebitis, extravasation, obstruction or infections). Subsequently, we included dislodgment as part of PIVC failure, being a post-hoc modification. We registered this trial with the ISRCTN Registry, number ISRCTN10438530.

**Findings:** Between Jan 1, 2019, and March 1, 2020, we randomly assigned 22 eligible clusters to receive the multimodal intervention (n=11 clusters; 2196 patients; 2235 PIVCs, and 131 nurses) or usual practice in control group (n=11; 2282 patients, 2330 PIVCs, and 138 nurses). The intervention arm reduced the percentage of PIVC failure rates compared to the control group (37·10 [SD 1·32; HR = 0·81] vs 46·49 [SD 2·59; HR = 1·23]; mean difference -9·39 [95% CI -11·22 to -7·57; p<0·001]), as incurred less costs (€21·39 [SD 191·05] vs €40·89 [SD 389·55]) with a reduction of €-19·50 per PIVC (95% CI -37·20 to -1·80]; p=0.033) at 12 months. Per protocol-prespecified analysis of the primary outcome showed the intervention significantly reduced PIVC failure compared to the control group at 12 months. The median PIVC dwell time was 85 hours (IQR 55-110).

**Interpretation**: A multimodal intervention reduced PIVC failure, potentially serious complications for hospitalised patients, improved adherence to the best available evidence and savings for the National Health System.

**Funding:** This study is funded by The College of Nurses of the Balearic Islands under award number PI2017/0192.

**Keywords (MeSH)**: Implementation Science; Knowledge Management; Evidence-Based Practice; Peripheral Venous Catheterisation; Infection Control; Catheter-Related Infections; Randomised Controlled Trial.

**Panel: Research in context**

**Evidence before this study**

We searched MEDLINE, CINAHL, the Cochrane Collaboration databases, and ClinicalTrial.gov from database initiation until March 1, 2021, for intervention studies or randomised controlled trials focused on peripheral intravenous catheter (PIVC) failure. We constructed the searches using terms "peripheral", "intravenous/venous", "catheter/device/cannula", "failure", "complications", "phlebitis", "occlusion", "obstruction", "extravasation", "infiltration", "dislodgement", "accidental removal", "adverse events", "infection", "implementation", "guideline", "evidence-based practice", "intervention" and "multimodal intervention" with no language or date restrictions. We also searched the reference lists of identified articles. This search provided 12 relevant experimental studies reporting on multimodal interventions for reducing all-cause of PIVC failure rates and infections through recommendations from clinical practice guidelines. Regarding the quality of recommendations, we published a systematic review

in 2018 (last search April 2018) of seven clinical practice guidelines. Our study found that the quality of the reviewed was moderate. Clinical practice guidelines tend to centralise the knowledge of healthcare experts by offering well-described recommendations with different clinical management approaches. However, crucial elements such as "stakeholder involvement", "methodological rigour", and "applicability" received the lowest scores, highlighting a lack of interest in the implementation process and the inclusion of patient preferences to facilitate the adoption of best available evidence.

Another systematic review published in 2019 demonstrated that the effectiveness of 13 prospective multimodal studies was uncertain and variability, reinforcing the call that more randomised controlled trials with the assessment of adherence, sustainability and cost is needed.

We found no previous multicentre cluster-randomised studies that included the implementation process for preventing PIVC failure and complications (i.e., infections, phlebitis, obstructions, or extravasations) and improving the adherence to clinical practice guideline recommendations. Some studies conducted multimodal strategies to reduce PIVC failure and complications; moreover, other studies reported reduced PIVC-Bloodstream infections incidence. However, these studies had any limitation related to non-random assignment, non-equivalent groups, single-centre setting, or non-implementation process.

**Added value of this study**

We conducted a large cluster-randomized controlled trial in 22 hospital wards of seven hospitals that demonstrate the effectiveness of the multimodal intervention to reduce PIVC failure among inpatients, improve the adherence of healthcare professionals to the

best available evidence and reduce total costs and resources at 12 months, including an implementation model based on the integrated-Promoting Action on Research Implementation in Health Services (i-PARIHS) framework.

**Implications of all the available evidence**

The PREBACP multimodal intervention significantly reduced PIVC failure rates, potentially infectious complications for inpatients, and significant savings for health care systems. Our trial enabled a deeper understanding of decision-making, knowledge mobilisation and sense-making in routine clinical practice.

**Total word count**: 4916

## Background

Peripheral intravenous catheters (PIVC) are the most widely used medical devices during a hospital stay, with around two billion PIVCs used annually worldwide, mainly for short-term intravenous therapy [1]. These catheters result in remarkable adverse events, including unnecessary morbidity and ultimately mortality for patients, and increase clinical workloads and healthcare costs for the healthcare system [2]. PIVC failure is a frequent complication of PIVC use, with ~40 – 70% of these catheters removed prematurely due to mechanical and chemical complications (i.e. phlebitis, dislodgement, occlusion, infiltration) or infection before the completion of scheduled intravenous therapy [3–5].

To date, many studies using multimodal interventions have successfully reduced PIVC failure and complication rates, and the incidence of peripheral intravenous catheter-related to bloodstream infections [6–8]. However, the results from these studies must be interpreted with caution due to, for example, their use of unrandomized or non-equivalent groups, or the conduct on single sites, which would limit the generalisability of the results. Additionally, the implementation of evidence-based practice in healthcare remains a multifaceted and complex phenomenon where evidence, context and stakeholders are in permanent and dynamic interaction, demanding a thorough understanding of decision-making to integrate these key elements [9]. This implementation process should include strategies promoting the appraisal and fidelity to recommendations from clinical practice guidelines [10], healthcare professional expertise and patient preferences [11].

To date, no studies have integrated a multimodal intervention within a knowledge mobilisation model to reduce PIVC failure rates and improve the adherence to recommendations on the care of PIVC in European hospitals, drawing from the core elements of evidence, context, and facilitation present on the integrated-Promoting Action on Research Implementation in Health Services (i-PARIHS) framework [10,12]. The main

aim of this trial was to evaluate the efficacy of a multimodal intervention to reduce PIVC failure rates among inpatients. The secondary aims were adherence to quality indicators for insertion, maintenance, and management of PIVCs, and cost and resource utilisation to treat PIVC failures and complications.

# METHODS

## Study design and participants

We conducted a cluster-randomised controlled trial at seven public hospitals within the Spanish National Health System (Hospital Manacor, Hospital Comarcal de Inca, Hospital Sant Joan de Déu Palma, Hospital Can Misses, Hospital Regional Universitario de Málaga, Hospital Costa del Sol and Hospital Universitario Marqués de Valdecilla). We planned the recruitment with a minimum sample size of 20 clusters. After recruitment contacts to hospitals throughout 2018, we evaluated 28 hospital wards to participate in our study. We decided that four of them not eligible for randomisation due to the fact they did not meet the inclusion criteria for the implementation process, and two clusters declined participation. Finally, we recruited 22 hospital wards (12 medical, eight surgical, and two oncology) to the trial through local nurses collaborating in the project at each participating hospital. We included data from adult patients (18-years or older) with one or more PIVCs at the start of intravenous therapy, i.e., from PIVC insertion until intravenous therapy was completed or due to PIVC failure for any reason (infection, phlebitis, extravasation, obstruction, or dislodgement). However, we excluded data from palliative patients with an imminent terminal prognosis and patients where PIVC was used for less than 24 hours for intravenous therapy. Each ward enrolled in the study had at least 70% of permanent staff and low turnover of staff to avoid the chance of study contamination by personnel moving from one setting to other during the clinical trial, thus

ensuring as much homogeneity as possible between units. We involved all nursing staff providing direct PIVC care to inpatients in the participating wards.

## Randomisation and masking

The clusters (hospital wards) recruited were randomly assigned (1:1) to the multimodal intervention or the control group before the start of the trial, using a centralised web-based randomisation software, and stratified by type of setting (medical, surgical or oncology). Eight weeks before the study started, IB-M communicated the allocation details to the lead research nurse of each participating hospital, who informed the unit managers in December 2018. Hypothesis and endpoints were blinded to research assistants who obtained data during the trial to prevent selection bias. The assignment of control wards for the staff of the participating institutions was also blinded. We did not mask patients and hospital ward staff to allocation due to the nature of the intervention. MR-C supervised and audited data quality, randomisation, and masking compliance. PIVC endpoint data were obtained on the wards routinely by patient health records in all hospital wards. These data were collated by hospital informatics staff, who were not aware of the trial purpose. Trial statisticians were also unaware of intervention allocation.

## Procedures

We conducted data collection from January 2019 to March 2020. External research nurses external to each participating hospital collected outcome data from one or more PIVCs, provided patients were at the start of intravenous therapy, randomly and unannounced in both intervention arms. These nurses had more than five years of nursing experience and were recruited for their expertise and training in vascular access management. All of them received one week of face-to-face training on the study protocol and procedures to

complete a validated case report form previously published [13]. These standards aimed to homogenise the quality of the data collected, minimising biases and errors. Wards allocated to the intervention had access to this data via feedback of results. Control wards did not have access to the data and continued with standard PIVC care practices.

We collected primary and secondary outcomes on a secure database via the standardised form, and clinical and health outcomes for patients from the electronic health records. Additionally, we measured contextual factors related to the use of evidence-based practice at individual and team level with the Practice Environment Scale of Nursing Work Index (PES-NWI) [14] and the Evidence-Based Practice Questionnaire (EBPQ) [15]. Finally, we applied the PIVC Care Questionnaire (PIVCareQ) at baseline and after 12 months to determine routine practices related to the care of PIVCs. IB-M audited data quality, completeness, and protocol fidelity, monitoring all hospitals once a month. We observed that the margin of error was very low. However, we found some discrepancy related to the questionnaires. Therefore, we checked all questionnaires due to the optical reader from the university, used for transcription data of questionnaires to the database, exported a null result when the nurse had marked a wrong option in this question. **Appendix p 4** describes the indicators and requirements for PIVC care from clinical practice guideline recommendations. We obtained written informed consent from all patients or their legal representatives. The ethics and research committees of all participant hospitals and the Balearic Islands Ethic research Committee (IB3492/17PI) approved this study. The protocol trial was published in 2018 [16] and adhered to the CONSORT statement and its extension to C-RCTs.

## Appendix p 4. Indicators and requirements for the PIVC care from clinical practice guideline recommendations.

The intervention lasted 14 months (baseline 2 months, intervention period 12 months) (**Appendix p 1**) implementing a multimodal intervention underpinned by a knowledge mobilization model and including dissemination of up-to-date protocols, education for healthcare professionals and patients, and regular feedback on performance (**Appendix p 6**). A variety of local facilitators comprising patient representatives, healthcare professionals, lead nurse researcher and managers tailored the intervention to the local context, based on the findings of EBPQ, PIVCareQ and NWI questionnaires. Furthermore, these facilitators identified barriers and facilitators in the organization, promoting the best evidence of national and international clinical practice guideline recommendations during the intervention period. The control group did not receive any intervention during the trial, continuing with usual care.

## Appendix p 1. Timeline of PREBACP study

## Appendix p 6. Multimodal components of the PREBACP intervention for preventing peripheral intravenous catheter failure in adults.

We evaluated one or more PIVCs per patient during their hospital stay. PIVCs analysed were inserted by ward nurses according to existing standard operating procedures. Ultrasound-guided techniques were not used during the trial. Nurses were responsible for decision-making regarding the adequacy of the PIVC and all aspects related to their insertion, maintenance, and removal according to patient needs, and considering the existing policy on each study site. Skin disinfection pre-insertion was carried out with 2% chlorhexidine in 70% isopropyl alcohol at all sites. All PIVCs were Introcan Safety (non-

winged) IV catheter (B. Braun Medical Inc., Bethlehem, PA). A transparent dressing with polyurethane borders (Tegaderm, 3M, St. Paul, MN, U.S.A.) was applied at the insertion point to secure the PIVC *in situ*. Needle-free valves were connected to PIVCs directly, via a 10cm extension tubing ending in a three-way connector (Becton, Dickinson and Company, NJ, U.S.A.), or neutral displacement needleless connectors (ICU Medical Inc., San Clemente, CA, U.S.A.). Standard caps were placed on all needleless connectors to minimise accidental tubing disconnections. The existing policy did not include routine disinfection of PIVC caps as a preventive measure. The underlying technology or properties of the vascular devices used in this trial do not differ among the various brands commonly used worldwide.

Any replacement or additional use of PIVCs during the trial were documented for inclusion in the economic evaluation of the study. Nurses were responsible for decision-making about PIVC withdrawal at all trial sites, when intravenous therapy was completed, or complications occurred. However, the withdrawal of unnecessary PIVCs on completion of intravenous therapy as a therapeutic approach to prevent CRBSI was not included on any participating hospitals. Additionally, the routine replacement of PIVC every 72 - 96 hours was not in practice on any participating hospital. Therefore, the PIVC indwelling time could extend over 96 hours if patients had no complications or infection. To mitigate control bias, we used standardised case definitions for PIVC failure and adverse events, as per international guidelines for preventing PIVC failure and BSIs (Healthcare Infection Control Practices Advisory Committee, United States of America, United Kingdom, Spain) [17–19]. Clinicians requested the culture of PIVC tip on suspicion of PIVC-related bloodstream infection. Each nurse manager provided information to standardise PIVC removal, PIVC tip culture and haemoculture extraction. PIVC tips were cultured with a semiquantitative method by a microbiologist blinded to the study.

## Outcomes

The effect and process evaluation were measured at baseline, 3, 6, 9 and 12 months after the implementation of the multimodal intervention.

*Primary outcome: all-cause PIVC failure*

The primary outcome was all-cause PIVC failure, defined as unplanned removal of the PIVC due to any complication and before any scheduled intravenous therapy is completed. PIVC failure could result from the following events: phlebitis (defined as at least one of the following: persistent pain referred to PIVC, erythema, swelling, palpable thrombosis of the cannulated vein), extravasation (inadvertent leakage of a vesicant solution into surrounding tissue), dislodgement (entire PIVC dislodged from the patient's body), obstruction (complete PIVC occlusion, whereby neither aspiration nor infusion is possible) and CRBSI (primary BSI with laboratory-confirmed PIVC infection). Initially, we did not consider dislodgement within primary analysis in the published protocol. However, recent studies on PIVC failure legitimated us to include it due to their impact on intravenous therapy interruption and a substantial improvement in the description of PIVC failure. Therefore, we modified the primary endpoint by an amendment to the protocol approved on 25 July 2021, including both analyses in tables.

*Secondary outcome: PIVC care quality and resource utilisation*

Secondary outcomes were adherence to multimodal intervention content and dosage and ~~CPG~~ clinical practice guideline recommendations; PIVC use and CRBSI detection; material and human resource utilisation; and individual and contextual factors related to

evidence. Each month, research nurses assessed patients and PIVCs recruited to the study to evaluate outcomes.

Multimodal intervention content and dosage was measured by the number of posters with recommendations and video protocols used in each ward; the number of nurses who completed the face-to-face training session and e-learning; the number of hours of result feedback; and the number of internal facilitators in the intervention group. Adherence to clinical practice guideline recommendations was measured by the number of recommendations completed (patient knowledge about PIVC, adequacy and insertion of PIVC, visual inspection of the insertion site, dressing type and status, PIVC flushing, documentation of PIVC care) and PIVCs with all recommendations completed, all in **Appendix p 4**).

PIVC use were measured by unnecessary PIVC (defined when intravenous treatment is not administered for more than 24 h.); two or more PIVCs in situ per patient; and CRBSI identification was assessed by CRBSI type 1 (positive culture in tips removed from patients with local signs or symptoms compatible with an infection at the point of catheter insertion); CRBSI type 2 (primary BSI without laboratory-confirmed local PIVC infection and with clinical signs that improve within 48 hours of catheter removal); and CRBSI type 3 (primary BSI with laboratory-confirmed local PIVC infection), as per Clinical Practice Guideline of Centers for Disease Control and Prevention, USA. The local microbiologist monitored adverse events (i.e., CRBSI, death, or admission to the intensive care unit), following up each tip culture for seven days and evaluating clinical signs and other relevant cultures.

We conducted three questionnaires for evaluating individual and contextual factors related to evidence-based clinical practice (EBCP) and PIVCareQ. The PIVCareQ (general asepsis and cutaneous antisepsis, insertion of PIVC, care of PIVC, principles general of PIVC management, strategies of PIVC removal, Record of PIVC, patient and professional education) used a 4-point Likert scale (1-strongly disagreed and 4-strongly agree), and measured at baseline and twelve months; the EBCP environment measured by PES-NWI (nurses' participation in hospital affairs; quality of nursing care; nurse management's capacity, leadership, and support for nursing staff; size of the nursing workforce and adaptation of available human resources, and professional relation between doctors and nurses), using a 4-point Likert scale (1-strongly disagree and 4-strongly agree), and individual EBCP measured by EBPQ (knowledge/competence, use/practice and attitudes of nurses), nurse characteristics (gender, age, and years in employment), using a 7-point Likert scale (1-strongly disagree and 7-strongly agree).

We calculated total resource use and costs for intervention and control sites. This cost-analysis included: PIVC, add-on devices and dressings applied at PIVC insertion considering staff time to use the products; products used for replacement PIVCs and additional staff time for PIVC insertion; costs of treatments of any complications (non-infectious, local or CRBSI); and cost of the facilitation activities carried out by local facilitators to implementing the multimodal intervention. The direct costs were allocated using 2020 Spanish National Health System prices (Euros). We also estimated the average time for all PIVC insertion, based on a multicentre study in the Spanish context [20], as 9 minutes. The nursing staff time cost was based on published staff salaries, updated to 2020. The average cost of staff time was calculated based on weighted average times during catheter insertion, with the same cost in both trial arms. The direct costs for the

treatment of thrombophlebitis, local infections associated with PIVC and primary ~~PIVC-BSIs~~ peripheral intravenous catheter-related to bloodstream infections were based on data published and relevant to the Spanish National Health System (increase in the number of days of hospitalisation and antibiotic treatment y staff salaries) [21]. Furthermore, the intervention group incurred an additional cost, based on the weighted average times that each intervention hospital ward employed for the facilitation process during the trial. We estimated that each intervention ward spent 48 hours on this aspect of the trial.

## Statistical analysis

We based the sample size calculation on a previous observational study in which a PIVC failure rate of 44·1% was reported. Minimum sample size required was 3821 patients, accepting 80% power, with a two-sided alpha of 0·05. We estimated an intracluster correlation coefficient of 0·01, for the reduction of a 15% in the rate of PIVC failure. We checked missing data, outlier and improbable values with source data verification and corrections for around 10% of patients in the primary analysis. The estimated sample size was considered enough to be clinically significant. Further details of this sample size calculation have previously been reported [16].

Categorical data were summarised as proportions and subsequently converted into mean and standard deviation (SD) together with continuous data. Comparability of groups at baseline for risk of device failure was assessed using clinical criteria. We did not impute missing data for primary and secondary outcomes.

The primary analysis was by modified intention to treat, which included all randomly assigned hospital wards for whom data on the primary endpoint were available. Quantitative methods were used to analyse primary and secondary outcomes. To account for within-patient correlation, due to multiple measurements from the same patient with

PIVC use during assessment days, we implemented generalised estimating equation models with binary outcome and logic link for all rate outcome comparisons. The statistical analysis consisted of an exploration of the descriptive data of the sample, bivariate analysis with parametric and non-parametric tests, depending on the nature of the distributions (correlation, ANOVA, chi-square) and multivariable. The Cochran-Mantel-Haenszel test was used to compare proportions. A series of exploratory analyses were conducted on sub-groups and covariates' impact on estimated the intervention's effects and processes. Variables that reveal prognostic or effect modifying potential on the outcome suggested by univariate analysis were subsequently evaluated by the multivariable analysis. Odds ratios with corresponding 95% confidence intervals are reported. An external analysed the trial data without being aware of the assignment of the intervention allocation. We calculated survival of PIVC failure rates and illustrated by the Kaplan-Meier method and further analysed by the long rank test for univariate analysis.

We considered a p-value of <0·05 as statistically significant. A regression model was constructed to further explore the results obtained in the bivariate analysis, seeking to build an explanatory model on PIVC failure. All statistical analyses were performed on SPSS IBM Statistics version 25 (SPSS/IBM, Chicago, Illinois, USA). We registered this cluster-randomised clinical trial with the ISRCTN Registry, number ISRCTN10438530 and available at https://doi.org/10.1186/ISRCTN10438530.

## Role of the funding source

The funder of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. IB-M and EC-S had full access to all data. The principal author (IB-M) had final responsibility for the decision to submit for publication.

## RESULTS

Between Jan 1, 2019, and March 1, 2020, we recruited 22 clusters that had randomly assigned to the two groups of the study (**figure 1**), recruiting 4478 patients and 4565 PIVCs, of similar characteristics in terms of the ward and patient admission type. Initially, we assessed four clusters that did not meet inclusion criteria, and two declined to participate. The exclusion criteria were that these clusters did not guarantee rigour in the implementation process because they could not ensure at least 70% permanent nurse staffing during the trial.

The effect and process evaluation were performed at baseline, 3, 6, 9 and 12 months after the implementation of the multimodal intervention. We included from primary analysis 2196 (94·3%) of 2329 patients, 2235 (94·1%) of 2374 PIVCs, and 131 nurses in the intervention group; and 2282 (94·8%) of 2407 patients, 2330 (94·6%) of 2462 PIVCs, and 138 nurses in the control group, which completed the follow-up. We excluded from primary analysis 133 (6%) of 2106 patients, and 139 (6%) of 2235 PIVCs in the intervention group; and 125 (6%) of 2282 patients, and 132 (6%) of 2330 PIVCs in the control group, because they had no available data for primary or secondary endpoint. **Figure 2** shows the number of patients and PIVCs during the trial, including PIVC failure findings for each cluster.

**Figure 1. Flow diagram of trial profile.**

**Figure 2. Trial profile including PIVC failure for each cluster.**

The intervention and control groups were similar in characteristics, both in the effect and process evaluation, at baseline. However, there were significant differences related to cognitive impairment, with 14·46 [SD 9·93] in the intervention group vs 32·21 [SD 18·01] in the control group; mean difference at baseline -17·75 [95% -30·48 to 5·02; 0·009]. All data on hospital ward characteristics at baseline are provided in **Table 1**.

**Table 1. Baseline characteristics of hospital wards.**

Regarding the primary outcome measures, the PIVC failure rate in the intervention arm decreased more at 12months compared to the control group (45·3 [SD 1·97] at baseline to 37·10 [SD 1·32; HR = 0·81] at 12 months, intervention group vs 44·85 [SD 3·02] at baseline to 46·49 [SD 2·59; HR = 1·23] at 12 months, control group; mean difference at 12 months -9·39 [95% CI -11·22 to -7·57; $p < 0·001$; **Table 2** and **Appendix p 2**]. Per protocol-prespecified analysis of the primary outcome showed the PIVC failure rate in the intervention significantly reduced more compared to the control group at 12 months (33·47 [SD 2·98; HR = 0·85] vs 41·06 [SD 4·62; HR = 1·18]), with a mean difference of -7·59 [95% CI -11·05 to -4·13; $p < 0·001$].

Also, the intervention group obtained reductions in PIVC failure mean at 3, 6 and 9 months (42·58 [SD 2·71] at 3 months, 39·03 [SD 3·30] at 6 months and 39·60 [SD 2·37] at 9 months in the intervention group vs 46·63 [SD 4·19] at 3 months [$p = 0·014$], 48·30 [SD 5·36] at 6 months [$p < 0·001$] and 45·89 [SD 3·23] at 9 months [$p < 0·001$] in the control group; **Appendix p 7**). All data of the effect evaluation of multimodal intervention during the trial are provided in **Table 2, Supplementary Figure 4**, and **Appendix p 7**.

Regarding PIVC dwell time overall, the median was 85 hours (IQR 55-110) [95% CI 82·75 to 87·25; Log-rank, p = 0·79], and was not significantly different between intervention and control groups. The median dwell time was significantly higher at control site than intervention site (90 h [IQR 60–115] vs 75 h [50–110]; p < 0·001; Appendix p 9).

**Table 2. Effect and process outcomes of trial at 12 months.**

**Appendix p 2. Flow of effect evaluation and clinical outcomes during the trial.**

**Appendix p 7. Evolution of effect and process outcomes at 3, 6 and 9 months.**

**Appendix 9. Kaplan−Meier analysis of survival from PIVC failure**

The intervention arm improved adherence to clinical practice guideline recommendations completed at 12 months compared to the control group (63·86 [SD 12·57] at baseline to 73·14 [SD 8·71] at 12 months, intervention group vs 57·71 [SD 11·00] at baseline to 60·29 [SD 8·29] at 12 months, control group; mean difference at 12 months 12·57 [95% CI 5·14 to 20·14]; p = 0·002; **Table 2**). Further, the intervention group improved the mean difference of all recommendations completed per PIVC analysed at 12 months compared to the control group (9·51 [95% CI 1·66 to 17·36]; p = 0·020; **Table 2**), as well as visual inspection of the insertion site at 12 months (23·74 [95% CI 4·99 to 42·50]; p = 0·016; **Table 2**).

Regarding PIVC failure subtypes and other clinical outcomes related PIVC use, the intervention group had greater decrease mean of PIVC failure subtypes difference at 12

months of phlebitis (-3·57 [95% CI -6·91 to -0·24]; p = 0·037); extravasation (-2·80 [95% CI -5·53 to -0·07]; p = 0·045); and CRBSI (-0·12 [95% CI -0·37 to 0·13]; p = 0·329). The results per study timepoint are provided in **Appendix p 7**. The intervention group improved the adherence to recommendations completed at 3, 6 and 9 months (64·00 [SD 10·00] vs 59·43 [SD 9·43; p = 0·287] at 3 months, 72·00 [SD 7·43] vs 58·00 [SD 8·29; p < 0·001] at 6 months and 70·00 [SD 9·86] vs 58·71 [SD 6·43; p = 0·005] at 9 months in the control group. Further, the intervention group improved the percentage of PIVCs with all recommendations completed at 6 and 9 months (12·99 [SD 7·64] vs 3·64 [SD 3·15; p = 0·001] at 6 months, and 10·93 [SD 9·47] vs 2·94 [SD 3·27; p = 0·016] at 9 months); patient knowledge related to PIVC at 6 months (66·72 [SD 16·56] vs 49·35 [SD 18·93; p = 0·033]); visual inspection of insertion site at 6 and 9 months (71·29 [SD 14·20] vs 45·94 [SD 19·62; p = 0·002] at 6 months and 64·94 [SD 23·12] vs 42·24 [SD 20·49; p = 0·024] at 9 months); and dressing status at 6 months (66·37 [SD 16·17] vs 44·18 [SD 15·13; p = 0·003]) compared with the control group. All data of the process evaluation of the multimodal intervention during the trial are provided in **Table 2, Appendix p 3, and Appendix p 7**.

## Appendix p 3. Flow of adherence to recommendations during the trial

The assessment with the PIVCareQ showed that nurses in the intervention group at 12 months modified their routine PIVC care, improving general asepsis and cutaneous antisepsis (mean difference 0·38 [95% CI 0·17 to 0·59]; 0·001), PIVC insertion (0·46 [95% CI 0·31 to 0·61]; < 0·001), PIVC care (0·34 [95% CI 0·17 to 0·51]; < 0·001), principles general of PIVC management (0·34 [95% CI 0·22 to 0·47]; < 0·001), strategies of PIVC removal (0·34 [95% CI 0·19 to 0·49]; < 0·001), documentation of PIVC (0·35 [95% CI 0·16 to 0·53]; 0·001), patient education (0·21 [95% CI 0·09 to 0·34]; 0·002),

and professional education (0·40 [95% CI 0·05 to 0·75]; 0·028). All data of the assessment of the routine practice perception are provided in **Table 2.**

Statistically significant variables were introduced in an initial multivariable analysis of PIVC failure (**Appendix p 10**). Following adjusted analysis, the significant protective factors were no cognitive impairment [OR 0.651 (95% CI 0.566 to 0.749); p < 0·001]; PIVC insertion in forearm with 20-22-gauge [OR 0.785 (95% CI 0.694 to 0.887); p < 0·001]; visual inspection of insertion site [OR 0.856 (95% CI 0.746 to 0.981); p = 0·026]; transparent dressing [OR 0.597 (95% CI 0.472 to 0.755); p < 0·001]; optimal dressing status [OR 0·497 (95% CI 0·436 to 0·566); p < 0·001]; and Management of PIVC flushing [OR 0·534 (95% CI 0·461 to 0·619); p < 0·001].

**Appendix p 10. Multivariable analysis of PIVC failure.**

Overall costs incurred and resources utilized on the trial are reported in **Table 3**. The mean overall costs of trial were substantially lower for the intervention group at 12 months (€21·39 [SD 191·05] vs €40·89 [SD 389·55]) with a reduction of -€19·50 per PIVC (95% CI -37·20 to -1·80]; p = 0·033). In addition, again at 12 months, the intervention group reduced the mean difference of costs of initial and replacement PIVC when indicated (-€0·31 [95% CI -0·46 to -0·16]; p < 0·001), the treatment of PIVC complications (-€23·91 [95% CI -41·82 to -6·01]; p = 0·009), and treatment of PIVC-related primary bloodstream infections (-€16·76 [95% CI -32·17 to -1·35]; p = 0·033).

**Table 3. Economic evaluation of resources required during the clinical trial.**

## DISCUSSION

To our knowledge, this is the first multicentre cluster-randomised controlled trial [22] of a multimodal intervention underpinned by an implementation model to reduce PIVC failure and improve adherence to best PIVC care recommendations. Our multimodal intervention significantly reduced all-cause PIVC failure and improved adherence to clinical best practice and care, although 43·2% of patients still experienced a PIVC failure, in line with previous studies reporting 32 – 52·3% [8,23–25]. Nurses at intervention sites significantly improved their PIVC care, incorporating at 12-months all elements of PIVCareQ. Our findings also reflect significant differences between the study arms in terms of resources and expenditure associated with the replacement of failed PIVC, treatment of peripheral intravenous catheter-related to bloodstream infections, with the intervention sites saving up to €19·50 per PIVC inserted compared to controls. Implementing this multimodal intervention could potentially free up to €3.9 billion in unnecessary costs and resources to treat PIVC failures and infections.

We identified some independent factors protecting patients from PIVC failure, including insertion in the forearm with 20 – 22 gauge, visual inspection of insertion site, maintenance of transparent polyurethane PIVC dressing and optimal PIVC flushing, all in agreement with published reports [7,23,26,27]. In our study, the overall mean of dressing status was substantially higher for the intervention group compared to the control group at 12 months (66·86 [SD 17·10] vs 51·37 [SD 25·26]), a rate comparable to the 64 – 79% of dressings in optimal conditions reported previously [13,23,28].

The implementation of evidence-based practice is a complex, multifaceted process in continuous interactions between evidence and context that is deeply nested at multiple levels from micro, meso and macro-organisational perspectives. The facilitation process was essential to engage stakeholders on the implementation and clinical improvements

sought by the trial. At each intervention site, the local facilitator educated all stakeholders in PIVC care on the recommended quality components, and proactively promoted the removal by nurses of catheters no longer needed. This education fostered a safe space where patients and healthcare professionals were free to express and discuss their thoughts about decisions related to catheters. Prior to the intervention, we analysed the organisational culture using the EBPQ and PES-NWI questionnaires so we could tailor the implementation process to such local context, in view of its influence on the success of quality improvement interventions [29]. The findings of these questionnaires provided intelligence on crucial dimensions of nurse engagement and leadership, size of nursing teams and professional relationships, and the relation between healthcare professionals with evidence-based care processes and practice [30]. The local facilitators were then able to address any barriers hindering the adoption of intervention practices in the study by drawing on in-depth knowledge regarding decision-making and contextual factors [31], such as PIVC workload or dated, task-based nursing models [32].

Our study has strengths and limitations that warrant consideration. The use of multiple data sources to identify current clinical practice and its progress, as well as the implementation of a multimodal intervention based on i-PARIHS during the trial on multiple sites strengthen our findings [33]. The multicentric design including hospitals with different organisational characteristics and located in diverse geographic areas increased the richness of our data and the external validity of the findings. To ensure as much homogeneity as possible between intervention and control arms, we included mechanisms to avoid the possibility of study contamination by staff moving from one setting to another during the clinical trial. In this regard, we controlled who were delivered the multimodal intervention, identifying of nurse staff during the trial by middle managers.

Regarding the limitations, we decided to include both results to ensure the transparency of the trial, although we modified the endpoint of the published protocol. We observe that this modification does not influence the result interpretation. Furthermore, it provides a more detailed characterisation of the PIVC failure event. Other limitation of this trial, and in agreement with studies deploying multimodal interventions, we are not able to determine whether any of the components was responsible for most, or any or the effect, or the benefits instead are obtained through the synergy of elements, and future research should determine the relative contribution of each component. Although CRBSIs are life-threatening adverse events, peripheral intravenous catheter-related to bloodstream infections had a low incidence in our setting. We were aware of this limitation at 12-month comparing to the control group. Further, we conducted our study for 12 months and thus the longer-term sustainability and decay rate of any effects obtained remains to be seen. Despite this, the trial findings reinforce the protective effect of the multimodal intervention. The sustainability of the intervention effects will strongly depend on maintaining an active implementation process with regular refreshing sessions for healthcare professionals delivered by PIVC experts. However, we could not guarantee that the multimodal intervention has reached its peak, as each intervention depends on the characteristics of the environment. Our study also lacked explicit local leadership buy-in, diverging somewhat from the multimodal literature where such support is actively sought [34]. Local study site coordinators engaged with hospital leadership and management, however, to authorise the enrolment of the sites onto the study. Finally, we continue to explore the interplay between micro, meso and macro-organisational levels to understand why wards with similar contextual characteristics performed differently in the study. These findings would need to be evaluated through mixed methodologies to analyse their impact at meso organisational level from a realistic approach.

## CONCLUSION

Implementing a multimodal intervention reduced PIVC failure among inpatients, resulted in reduced clinical workload and substantial cost savings for the National Health System. The use of the facilitation model counterbalanced the perception impact by clinicians on decision-making regarding the care of PIVCs, improving the adherence to the best available evidence.

## LIST OF ABBREVIATIONS

Peripheral intravenous catheters (PIVCs), Catheter-related bloodstream infections (CRBSI), the integrated-Promoting Action on Research Implementation in Health Services (i-PARIHS), Facilitating Implementation of Research Evidence (FIRE), the practice environment scale of nursing work index (PES-NWI), evidence-based practice questionnaire (EBPQ), PIVC care questionnaire (PIVCareQ), Evidence-based clinical practice (EBCP), standard deviation (SD).

## DECLARATIONS

### Ethical approval and consent to participate

This study has received approval from the Balearic Islands Ethic Research Committee (reference number: IB3492/17PI) and data collection is currently underway.

### Consent for publication

This manuscript does not contain data from any individual person.

## Availability of data and materials

The datasets generated during and/or analysed during the current study are available upon request from group investigation. The data are available beginning 3 months and ending 5 years following article publication for to investigators, whose proposed use of data will have been approved by an independent review committee identified for to realise an individual participant data meta-analysis. Proposals may be submitted up to 36 months following article publication to IB-M (ianblanco@hmanacor.org) and EC-S (enrique.castro-sanchez@city.ac.uk).

## Competing interests

No conflict of interest has been declared by the authors.


## Funding

This study is funded by The College of Nurses of the Balearic Islands under award number PI2017/0192. The findings and conclusions in this study are those of the authors and do not necessarily represent the official positions of The College of Nurses of the Balearic Islands. ECS is affiliated with the National Institute for Health Research Health Protection Research Unit in Healthcare Associated Infection and Antimicrobial Resistance at Imperial College London in partnership with Public Health England. ECS is a National Institute for Health Research Senior Nurse and Midwife Research Leader, and acknowledges the support of the BRC. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR, the Department of Health, or Public Health England.


## Authors' contributions

IBM is the principal investigator of the study. All authors contributed to the original idea and design of the study. All authors are responsible for the conduct of the study. Only IB-M and EC-S had full access and verified to all data. IBM prepared the first draft of the manuscript. IB-M, IFF, JDP-G and ECS provided statistical expertise, revising findings of the primary statistical analyses. All authors provided critical commentary on drafts and approved the final manuscript.

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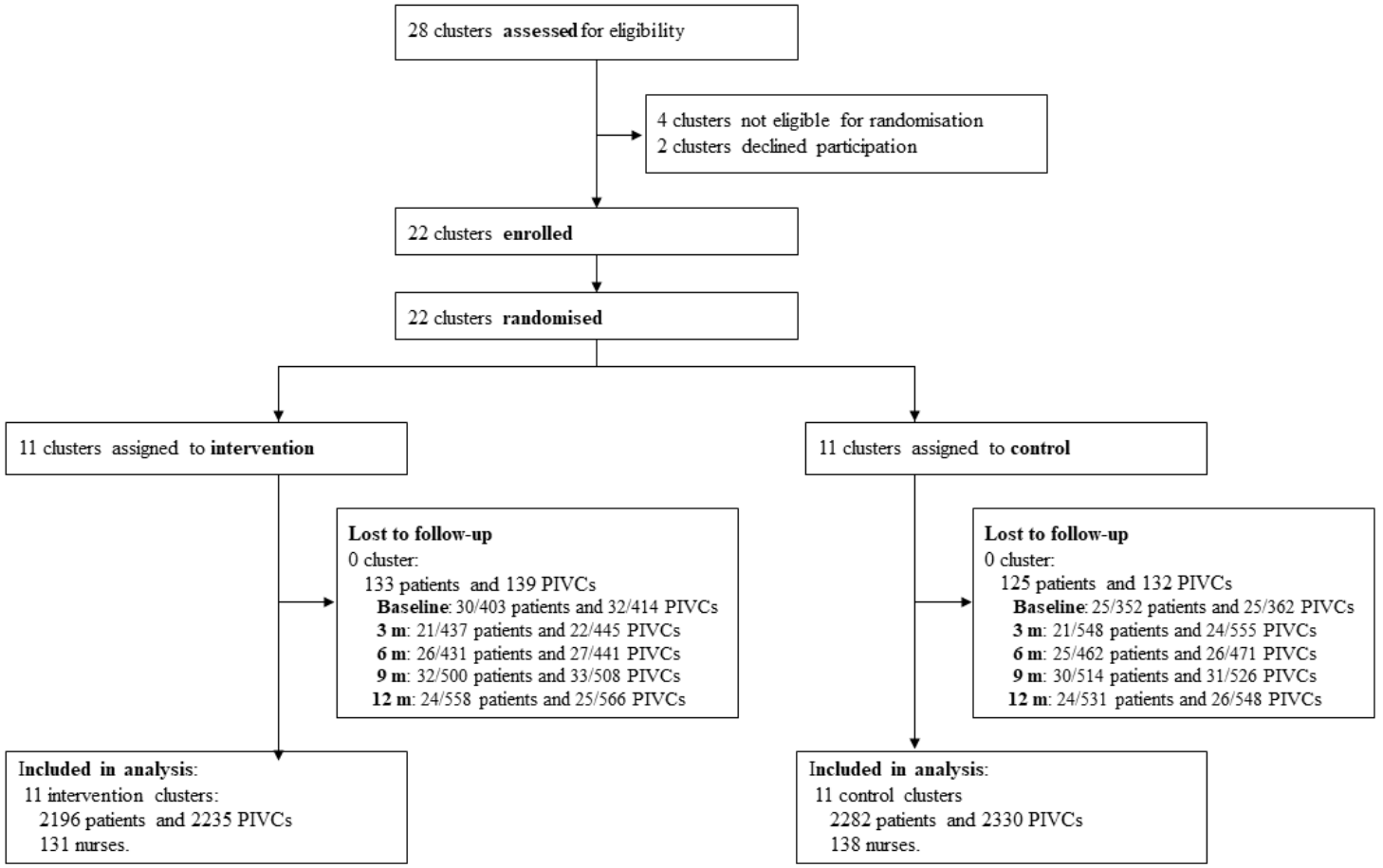
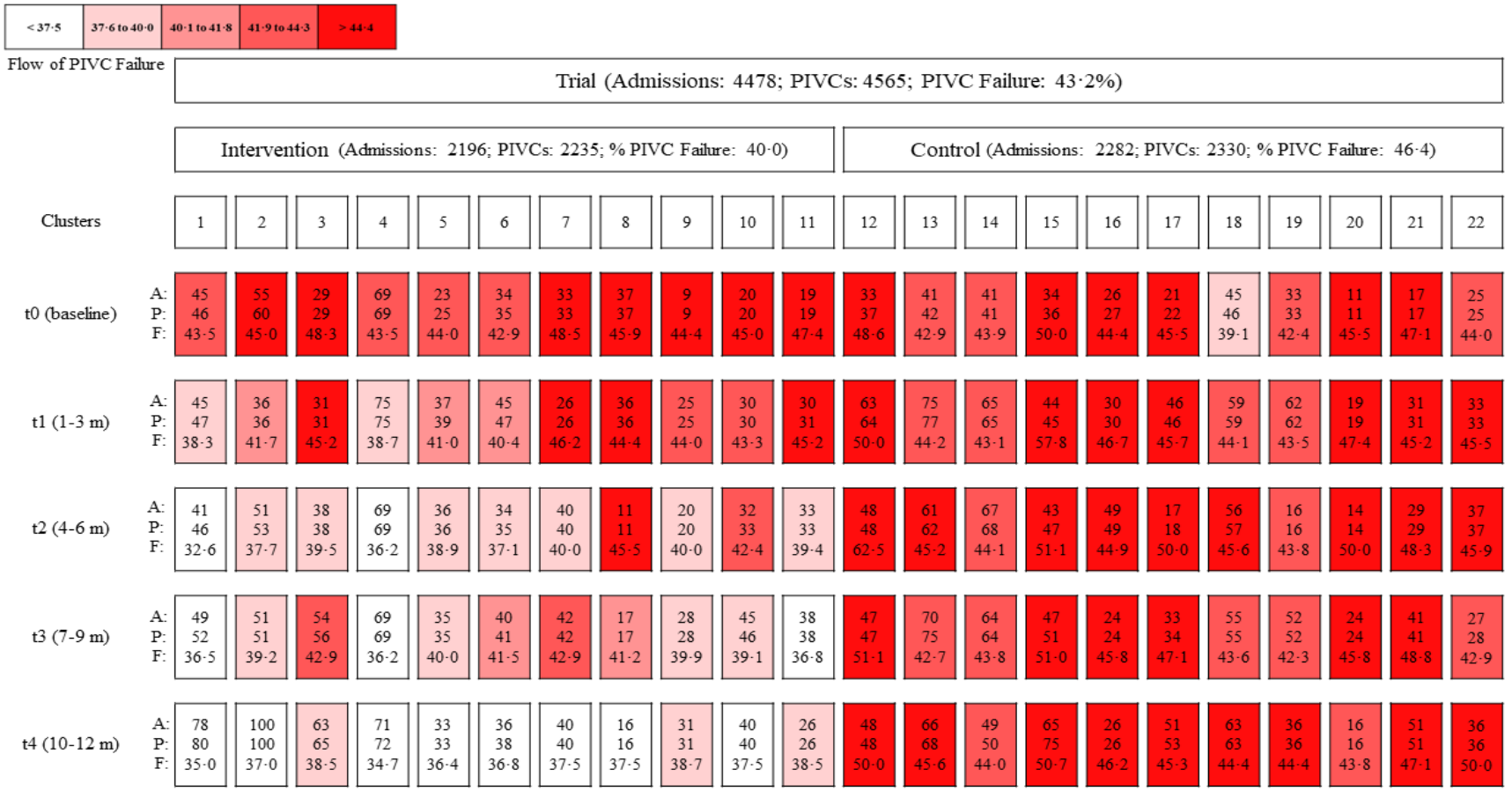
**Figure 1.** Flow diagram of trial profile.



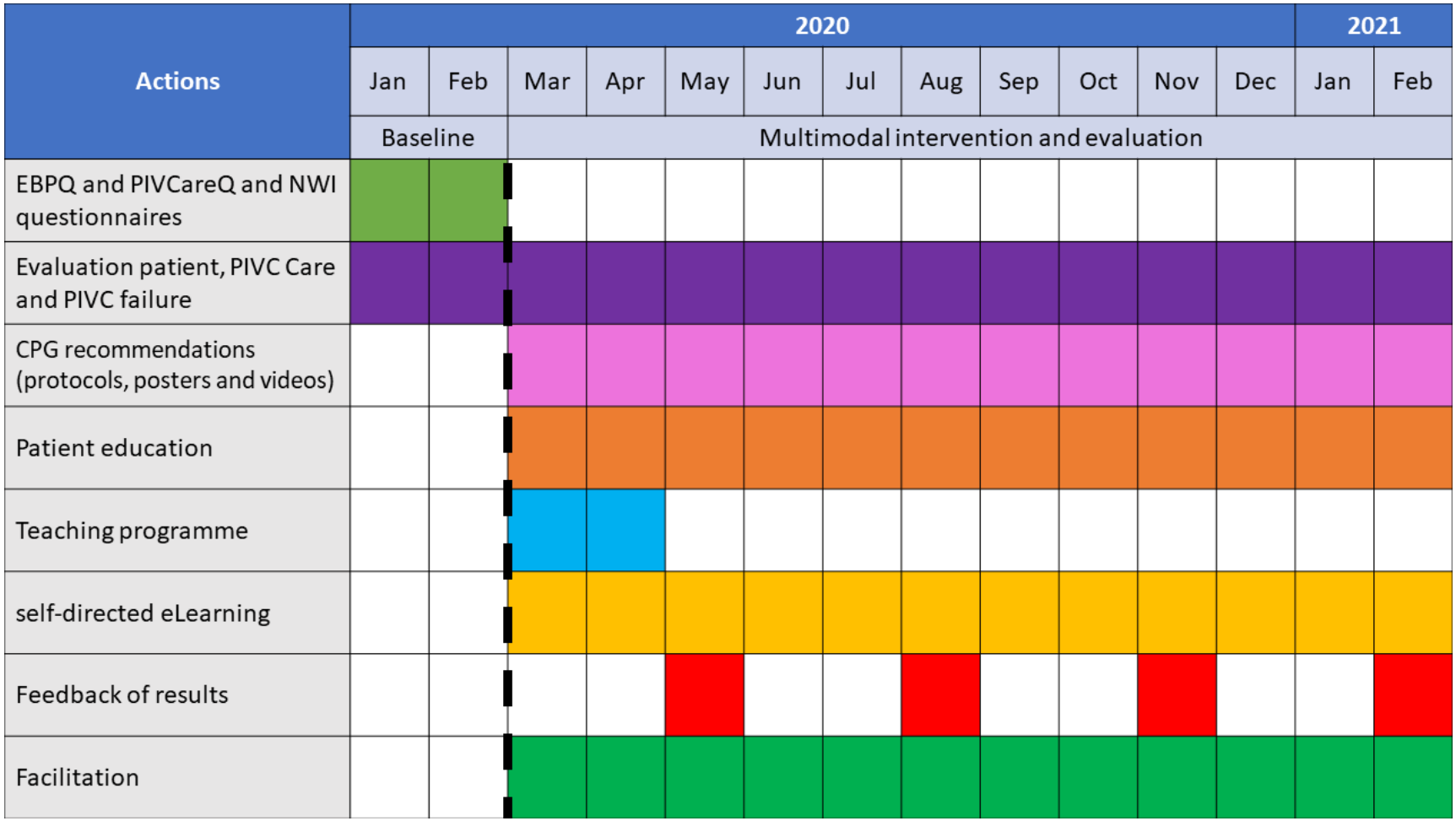

PIVC: Peripheral intravenous catheter; m: months

**Figure 2.** Trial profile including PIVC failure for each cluster.




A = number of patients who admitted during the trial. P = number of peripheral intravenous catheters included during the trial. F = % PIVC failure per hospital ward. t = time. m = month.

**Appendix p 1.** Timeline of PREBACP study.



**Appendix p 2.** Flow of effect evaluation and clinical outcomes during the trial.

| F | Ph | Ext | Obs | Dis | 2P | Unn | CRBSI |
|---|---|---|---|---|---|---|---|
| > 44·4 | > 23·0 | > 16·6 | > 10·7 | > 7·3 | > 5·0 | > 13·0 | > 1·2 |
| 41·9 to 44·3 | 19·4 to 22·9 | 13·8 to 16·5 | 8·1 to 10·16 | 6·1 to 7·2 | 3·6 to 4·9 | 11 to 12·9 | 0·8 to 1·1 |
| 40·1 to 41·8* | 16·0 to 19·3* | 11·2 to 13·7* | 5·9 to 8·0* | 4·9 to 6·0* | 2·0 to 3·5* | 9·5 to 10·9 | 0·4 to 0·7 |
| 37·6 to 40·0 | 12·4 to 15·9 | 8·4 to 11·1 | 3·3 to 5·8 | 3·7 to 4·8 | 0·6 to 1·9 | 7·5 to 9·4 | 0·1 to 0·3 |
| < 37·5 | < 12·3 | < 8·3 | < 3·2 | < 3·6 | < 0·5 | < 7·4 | 0 |

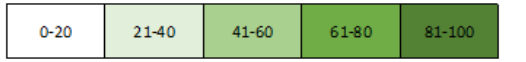
Flow of effect evaluation and clinical outcomes

| | Intervention | | | | | | | | Control | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | % PIVC failure | % phlebitis | % extravasation | % obstruction | % dislodgement | % 2 or more PIVCs in situ per patient | % unnecessary PIVC | % CRBSI | % PIVC failure | % phlebitis | % extravasation | % obstruction | % dislodgement | % 2 or more PIVCs in situ per patient | % unnecessary PIVC | % CRBSI |
| t0 (baseline) | 45·3 | 13·4 | 19·6 | 7·2 | 5 | 1·9 | 10·5 | 0·7 | 44·9 | 14·1 | 20·7 | 5·9 | 3·8 | 2·7 | 9 | 0 |
| t1 (1-3 m) | 42·6 | 12·7 | 18·9 | 6·2 | 4·8 | 1·5 | 11·4 | 0·5 | 46·6 | 18·5 | 16·8 | 4·6 | 6·6 | 0·6 | 12 | 0·6 |
| t2 (4-6 m) | 39 | 12 | 16·8 | 5·7 | 4·6 | 1·9 | 6·9 | 0 | 48·3 | 18·1 | 18·6 | 6·3 | 5·3 | 1·7 | 11·2 | 0·4 |
| t3 (7-9 m) | 39·6 | 15 | 16·3 | 3·9 | 4·5 | 1·3 | 5·8 | 0 | 45·9 | 15·4 | 20·3 | 4·7 | 5·5 | 1·9 | 11·3 | 0·4 |
| t4 (10-12 m) | 37·1 | 13·1 | 15·9 | 4·5 | 3·6 | 1·1 | 9·1 | 0 | 46·5 | 16·7 | 18·7 | 5·7 | 5·4 | 2 | 11 | 0·1 |

t: time period; m: months; F: % PIVC failure; Ph: % Phlebitis; Ext: % extravasation; Obs: % obstruction; Dis: % dislodgement; 2P: %2 or more PIVCs in situ per patient; Unn: % Unnecesary PIVC (when intravenous treatment is not administered for more than 24 h.); CRBSI: % Catheter-related bloodstream infection;

* Mean based on data of systematic review [5] and local evidence[4].

**Appendix p 3.** Flow of adherence to recommendations during the trial.



Flow of process evaluation (adherence of recommendations)

| | Intervention | | | | | | | | | Control | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | % RECs completed | % Patient knowledges related to PIVC | % PIVC adequacy and insertion | % Visual inspection of insertion site | % Dressing type | % Dressing status | % Management of PIVC flushing | % Record of PIVC care | % PIVCs with all REC completed | % RECs completed | % Patient knowledges related to PIVC | % PIVC adequacy and insertion | % Visual inspection of insertion site | % Dressing type | % Dressing status | % Management of PIVC flushing | % Record of PIVC care | % PIVCs with all REC completed |
| t0 (baseline) | 63·9 | 57·4 | 54·7 | 49·4 | 92·2 | 57·2 | 79·5 | 56·8 | 7·2 | 57·7 | 45·3 | 54·9 | 38·8 | 86·1 | 45·6 | 82·7 | 51 | 3·9 |
| t1 (1-3 m) | 64 | 56·8 | 55·3 | 57·8 | 88·2 | 53·8 | 72·9 | 63 | 7·6 | 59·4 | 54·2 | 46·7 | 43·7 | 91·9 | 47·2 | 80·8 | 51·5 | 4·9 |
| t2 (4-6 m) | 72 | 66·7 | 52·4 | 71·3 | 94 | 66·4 | 76·5 | 76·6 | 13 | 58 | 49·4 | 52·8 | 45·9 | 84·9 | 44·2 | 77·2 | 51·4 | 3·6 |
| t3 (7-9 m) | 70 | 62·2 | 53·6 | 64·9 | 94 | 60·3 | 78·4 | 76·4 | 10·9 | 58·7 | 50·9 | 49·7 | 42·2 | 89·6 | 46 | 79·2 | 53·8 | 2·9 |
| t4 (10-12 m) | 72·9 | 63·3 | 54 | 72·9 | 97 | 66·9 | 79·5 | 76·8 | 13·6 | 60·3 | 48·2 | 54·7 | 49·1 | 90·3 | 51·4 | 74·8 | 53·7 | 4·1 |

t: time period; m: months; REC: Recommendation; PIVC: peripheral intravenous catheter.

**Table 1.** Baseline characteristics of hospital wards.

| Baseline characteristics of hospital wards | Intervention (n = 11) | Control (n = 11) | Mean difference (95% CI) |
|---|---|---|---|
| | Mean (SD) | Mean (SD) | |
| Total patient admissions | 33·91 (17·29) | 29·72 (10·73) | 4·18 (-8·62 to 16·98) |
| Patient age (years) | 69·56 (4·29) | 69·92 (5·38) | -0·36 (-4·68 to 3·97) |
| % Patient gender female | 39·1 (12·11) | 41·03 (9·63) | -1·93 (-11·67 to 7·80) |
| % Patient gender male | 60·9 (12·11) | 58·97 (9·63) | 1·93 (-7·80 to 11·67) |
| % Comorbidity | 93·58 (6·37) | 92·75 (4·75) | 0·83 (-4·17 to 5·82) |
| % Cognitive impairment | 14·46 (9·23) | 32·21 (18·01) | -17·75 (-30·48 to 5·02) |
| % Use of antibiotics | 37·41 (12·84) | 34·62 (15·97) | 2·80 (-10·09 to 15·69) |
| Total nurses | 11·91 (1·92) | 12·55 (1·69) | -0·64 (-2·25 to 0·97) |
| % Nurses gender female | 84·42 (11·58) | 83·45 (17·58) | 0·97 (-12·27 to 14·21) |
| Nurse age (years) | 39·8 (4·72) | 40·07 (4·27) | -0·28 (-4·28 to 3·73) |
| Years employed as nurse | 16·22 (5·04) | 16·56 (4·66) | -0·33 (-4·65 to 3·99) |
| **Primary outcome modified intention-to-treat analysis** | | | |
| % PIVC failure | 45·30 (1·97) | 44·85 (3·02) | 0·45 (-1·81 to 2·72) |
| **Primary outcome per protocol-prespecified** | | | |
| % PIVC failure | 40·28 (4·23) | 41·09 (4·54) | -0·80 (-4·70 to 3·10) |
| **Secondary outcomes** | | | |
| Total PIVCs | 34·73 (17·89) | 30·64 (11·13) | 4·09 (-9·16 to 17·34) |
| PIVC length of time (days) | 3·55 (0·45) | 3·68 (0·45) | -0·13 (-0·54 to 0·27) |
| % Phlebitis | 13·43 (4·37) | 14·11 (3·39) | -0·68 (-4·16 to 2·80) |
| % Extravasation | 19·62 (3·54) | 20·70 (2·89) | -1·08 (-3·96 to 1·80) |
| % Obstruction | 7·23 (3·02) | 5·91 (3·53) | 1·32 (-1·60 to 4·24) |
| % Dislodgement | 5·02 (4·36) | 3·76 (3·15) | 1·25 (-2·13 to 4·63) |
| % CRBSI | 0·65 (1·28) | 0 | 0·65 (-0·16 to 1·45) |
| % 2 or more PIVCs in situ per patient | 1·94 (3·24) | 2·65 (3·39) | -0·71 (-3·66 to 2·24) |
| % Unnecessary PIVC | 10·48 (9·25) | 8·96 (8·85) | 1·52 (-6·54 to 9·57) |
| **Adherence to clinical practice guideline recommendations** | | | |
| % Recommendations completed | 63·86 (12·57) | 57·71 (11·00) | 6·14 (-4·43 to 16·57) |
| % Patient knowledge related to PIVC | 57·35 (23·30) | 45·28 (16·50) | 12·08 (-5·88 to 30·03) |
| % PIVC adequacy and Insertion | 54·66 (12·03) | 54·91 (15·01) | -0·24 (-12·34 to 11·86) |
| % PIVC inserted in | 42·69 (13·21) | 38·68 (13·38) | 4·02 (-7·81 to 15·84) |

| | | | |
|---|---|---|---|
| forearm | | | |
| % PIVC inserted with 20-22 gauge | 82·08 (18·82) | 81·53 (12·36) | 0·55 (-13·61 to 14·71) |
| % Visual inspection of insertion site | 49·39 (30·77) | 38·77 (17·80) | 10·62 (-11·74 to 32·98) |
| % Dressing type | 92·22 (19·04) | 86·12 (23·97) | 6·10 (-13·15 to 25·35) |
| % Dressing status | 57·17 (23·67) | 45·56 (18·34) | 11·61 (-7·22 to 30·44) |
| % Management of PIVC flushing | 79·46 (12·02) | 82·70 (8·95) | -3·24 (-12·67 to 6·18) |
| % Record of PIVC care | 56·75 (40·81) | 50·95 (42·03) | 5·80 (-31·05 to 42·64) |
| % PIVCs with all recommendations completed | 7·18 (10·12) | 3·90 (5·92) | 3·28 (-4·10 to 10·65) |
| **Environment Evidence-based clinical practice** | | | |
| PIVC care questionnaire (PIVCareQ) | | | |
| General asepsis and cutaneous antisepsis | 3·31 (0·23) | 3·23 (0·14) | 0·08 (-0·09 to 0·25) |
| Insertion of PIVC | 3·13 (0·17) | 3·04 (0·12) | 0·09 (-0·04 to 0·21) |
| Care of PIVC | 3·08 (0·10) | 3·00 (0·19) | 0·08 (-0·06 to 0·22) |
| General principles of PIVC management | 3·22 (0·11) | 3·16 (0·12) | 0·06 (-0·04 to 0·16) |
| Strategies of PIVC removal | 3·35 (0·14) | 3·23 (0·16) | 0·12 (-0·01 to 0·25) |
| Record of PIVC | 3·21 (0·18) | 3·21 (0·22) | 0·00 (-0·19 to 0·18) |
| Patient education | 2·92 (0·19) | 2·88 (0·35) | 0·04 (-0·21 to 0·29) |
| Professional education | 2·28 (0·40) | 2·20 (0·49) | 0·08 (-0·32 to 0·48) |
| EBCP Individual (EBPQ) | | | |
| Use/Practice | 4·19 (0·51) | 4·33 (0·43) | -0·14 (-0·56 to 0·28) |
| Attitudes | 5·10 (0·30) | 5·07 (0·29) | 0·03 (-0·24 to 0·29) |
| Knowledge/Competence | 4·32 (0·33) | 4·47 (0·36) | -0·15 (-0·46 to 0·15) |
| EBCP Context (PES-NWI) | | | |
| Nurses' participation | 2·32 (0·33) | 2·19 (0·30) | 0·13 (-0·14 to 0·41) |
| Quality of nursing care | 2·86 (0·46) | 2·77 (0·56) | 0·09 (-0·36 to 0·55) |
| Support of Nurse Manager | 3·26 (0·39) | 3·21 (0·36) | 0·05 (-0·29 to 0·38) |
| Staff and resources adequacy | 2·04 (0·35) | 2·01 (0·45) | 0·03 (-0·33 to 0·39) |
| Nurse/Physician relation | 2·51 (0·44) | 2·42 (0·41) | 0·09 (-0·29 to 0·47) |

Table 1. Baseline characteristics of hospital wards

**Table 2.** Effect and process outcomes of trial at 12 months.

| Characteristics of hospital wards to 12 months | Intervention (n = 11) | Control (n=11) | Mean difference (95% CI) | p value |
|---|---|---|---|---|
| | Mean (SD) | Mean (SD) | | |
| Total patient admissions | 48·55 (25·79) | 46·09 (16·16) | 2·45 (-16·69 to 21·60) | 0·792 |
| Patient age (years) | 67·79 (4·22) | 69·71 (5·86) | -1·92 (-6·46 to 2·62) | 0·389 |
| % Patient gender female | 51·07 (12·04) | 43·37 (13·08) | 7·70 (-3·48 to 18·88) | 0·166 |
| % Patient gender male | 48·93 (12·04) | 56·63 (13·08) | -7·70 (-18·88 to 3·48) | 0·166 |
| % Comorbidity | 90·88 (6·49) | 90·93 (9·22) | -0·05 (-7·14 to 7·04) | 0·989 |
| % Cognitive impairment | 22·08 (10·06) | 32·19 (18·89) | -10·11 (-23·57 to 3·35) | 0·133 |
| % Use of antibiotics | 35·74 (16·69) | 37·24 (14·22) | -1·50 (-15·29 to 12·29) | 0·823 |
| Total nurses | 12·09 (2·07) | 12·27 (2·28) | -0·18 (-2·12 to 1·76) | 0·847 |
| % Nurses gender female | 84·29 (10·92) | 81·82 (18·10) | 2·47 (-10·82 to 15·76) | 0·702 |
| Nurse age (years) | 39·80 (4·72) | 40·07 (4·27) | -0·28 (-4·28 to 3·73) | 0·887 |
| Years employed as nurse | 16·22 (5·04) | 16·56 (4·66) | -0·33 (-4·65 to 3·99) | 0·874 |
| **Primary outcome modified intention-to-treat analysis** | | | | |
| % PIVC failure | 37·10 (1·32) | 46·49 (2·59) | -9·39 (-11·22 to -7·57) | < 0·001 |
| Relative risk (95% CI) | HR 0·81 (0·72 to 0·92) | HR 1·23 (1·09 to 1·39) | - | - |
| **Primary outcome per protocol-prespecified** | | | | |
| % PIVC failure | 33·47 (2·98) | 41·06 (4·62) | -7·59 (-11·05 to -4·13) | <0·001 |
| Relative risk (95% CI) | HR 0·85 (0·75 to 0·96) | HR 1·18 (1·04 to 1·33) | - | - |
| **Secondary outcomes** | | | | |
| Total PIVCs | 49·18 (26·13) | 47·45 (17·85) | 1·73 (-18·17 to 21·63) | 0·858 |
| PIVC length of time (days) | 3·19 (0·51) | 3·66 (0·25) | -0·47 (-0·83 to 0·11) | 0·012 |
| % Phlebitis | 13·08 (3·54) | 16·66 (3·95) | -3·57 (-6·91 to -0·24) | 0·037 |
| % Extravasation | 15·93 (2·84) | 18·73 (3·28) | -2·80 (-5·53 to -0·07) | 0·045 |
| % Obstruction | 4·46 (2·45) | 5·67 (1·22) | -1·21 (-2·93 to 0·51) | 0·157 |
| % Dislodgement | 3·63 (3·11) | 5·43 (2·84) | -1·81 (-4·45 to 0·84) | 0·170 |
| % CRBSI | 0 | 0·12 (0·40) | -0·12 (-0·37 to 0·13) | 0·329 |
| % 2 or more PIVCs in situ per patient | 1·11 (1·78) | 2·00 (4·00) | -0·89 (-3·65 to 1·86) | 0·508 |
| % Unnecessary PIVC | 9·05 (11·38) | 11·04 (5·86) | -1·99 (-10·04 to 6·06) | 0·612 |
| **Multimodal intervention content and dosage** | | | | |
| Poster with recommendations | 5 | n/a | n/a | n/a |
| Video protocols | 3 | n/a | n/a | |
| E-learning (completed courses) | 33 | n/a | n/a | |
| Website (visits) | n/a | n/a | n/a | |
| Face-to-face training | No | n/a | n/a | |
| Feedback of results | 16 hours | n/a | n/a | |
| Nº of Internal facilitators | 5·36 (0·67) | n/a | n/a | |

| | | | | |
|---|---|---|---|---|
| **Adherence to clinical practice guidelines recommendations** | | | | |
| % Recommendations completed | 73·14 (8·71) | 60·29 (8·29) | 12·57 (5·14 to 20·14) | 0·002 |
| % Patient knowledge related to PIVC | 63·32 (15·32) | 48·21 (19·74) | 15·11 (-0·61 to 30·82) | 0·059 |
| % PIVC adequacy and insertion | 53·96 (14·70) | 54·67 (19·83) | -0·71 (-16·24 to 14·81) | 0·925 |
| % PIVC inserted in forearm | 45·09 (10·86) | 37·14 (15·01) | 7·95 (-3·70 to 19·60) | 0·170 |
| % PIVC inserted with 20-22 gauge | 82·26 (15·96) | 81·51 (14·38) | 0·75 (-12·77 to 14·27) | 0·909 |
| % Visual inspection of insertion site | 72·85 (20·67) | 49·11 (21·49) | 23·74 (4·99 to 42·50) | 0·016 |
| % Dressing type | 97·00 (5·07) | 90·31 (18·92) | 6·69 (-5·63 to 19·01) | 0·271 |
| % Dressing status | 66·86 (17·10) | 51·37 (25·26) | 15·49 (-3·69 to 34·68) | 0·108 |
| % Management of PIVC flushing | 79·47 (12·81) | 74·79 (14·33) | 4·69 (-7·40 to 16·78) | 0·428 |
| % Record of PIVC care | 76·82 (29·23) | 53·67 (39·00) | 23·14 (-7·51 to 53·80) | 0·131 |
| % PIVCs with all recommendations completed | 13·59 (11·54) | 4·08 (4·76) | 9·51 (1·66 to 17·36) | 0·020 |
| **PIVC care questionnaire (PIVCareQ)** | | | | |
| General asepsis and cutaneous antisepsis | 3·57 (0·22) | 3·19 (0·25) | 0·38 (0·17 to 0·59) | 0·001 |
| Insertion of PIVC | 3·49 (0·15) | 3·03 (0·19) | 0·46 (0·31 to 0·61) | < 0·001 |
| Care of PIVC | 3·39 (0·19) | 3·05 (0·19) | 0·34 (0·17 to 0·51) | < 0·001 |
| General principles of PIVC management | 3·54 (0·07) | 3·19 (0·18) | 0·34 (0·22 to 0·47) | < 0·001 |
| Strategies of PIVC removal | 3·54 (0·17) | 3·20 (0·17) | 0·34 (0·19 to 0·49) | < 0·001 |
| Record of PIVC | 3·50 (0·18) | 3·16 (0·24) | 0·35 (0·16 to 0·53) | 0·001 |
| Patient education | 3·10 (0·16) | 2·88 (0·10) | 0·21 (0·09 to 0·34) | 0·002 |
| Professional education | 2·88 (0·35) | 2·49 (0·43) | 0·40 (0·05 to 0·75) | 0·028 |

Table 2. Effect and process outcomes of intervention and control group at 12 months

**Table 3.** Economic evaluation of resources required at 12 months.

| Economic evaluation | Mean (SD), € | | Mean difference (95% CI) | p value |
|---|---|---|---|---|
| | Intervention (n = 2235) | Control (n=2330) | | |
| Cost of staff time for PIVC insertion [a, b] | 3·00 | 3·00 | - | - |
| Costs associated with PIVC first insertion and replacement | 7·31 (2·59) | 7·62 (2·61) | -0·31 (-0·46 to -0·16) | < 0·001 |
| Initial PIVC, dressing, add-on devices, and staff time [a, b] | 5·22 (0·23) | 5·21 (0·21) | 0·01 (0.00 to 0·03) | 0·015 |
| PIVC replacement, dressing, add-on devices, and staff time | 2·09 (2·56) | 2·41(2·60) | -0·32 (-0·47 to -0·17) | < 0·001 |
| Costs associated with treatment of complications | 9·35 (190·88) | 33·27 (389·29) | -23·91 (-41·82 to -6·01) | 0·009 |
| Treatment of PIVC-related primary bloodstream infections | 4·24 (147·85) | 21·00 (342·19) | -16·76 (-32·17 to -1·35) | 0·033 |
| Treatment of PIVC non-infectious complications | 5·12 (120·91) | 12·27 (187·00) | -7·16 (-16·33 to 2·03) | 0·126 |
| Total costs associated with insertion and removal PIVC | 16·67 (191·05) | 40·89 (389·55) | -24·22 (-42·14 to -6·30) | 0·008 |
| Costs of facilitation [a, c] | 4·72 | - | - | - |
| Total costs | 21·39 (191·05) | 40·89 (389·55) | -19·50 (-37·20 to -1·80) | 0·033 |
| Table 3. Economic evaluation of resources required during the clinical trial | | | | |

€ euro; [a] SDs not available because costs were calculated based on weighted mean times; [b] Mean calculated based on weighted average times during catheter insertion (9 minutes per catheter inserted); [c] Mean calculated based on weighted average times (each hospital ward in intervention group employed 48 hours for the trial; 1 hour = €20).

**Appendix p 4.** Indicators and requirements for the PIVC care from clinical practice guideline recommendations.

| Indicators | Requirements for compliance | Clinical practice guideline recommendations [17,19,35] |
|---|---|---|
| Patient knowledges related to PIVC | Patient receive education related to PIVC during admission by healthcare professional. | Patient education on treatment targets, administration, infusion, associated complications, care, and management of PIVC. |
| PIVC adequacy and insertion | Insertion site is to dorsum of hand, forearm, or upper arm. | Selection of the appropriate PIVC insertion site, assessing risks for infection, against the risks of mechanical complications and patient comfort unless clinically contraindicated or in an emergency. |
| | Intravenous cannula size is between 20 to 24 gauge for intravenous therapy. | Select the smallest-gauge peripheral catheter that will accommodate the prescribed therapy and patient need. |
| Visual inspection of insertion site | PIVC insertion site is visible through visual inspection at first sight and securement does not hinder their visualization | Inspection of the peripheral intravenous catheter insertion site at a minimum during each shift, recording the Visual Infusion Phlebitis score and/or infiltration score. |
| Dressing type | Dressing type is a sterile transparent bordered semi-permeable polyurethane. | Use of a sterile, transparent, semi-permeable polyurethane dressing to cover the intravascular insertion site. |
| Dressing status | Dressing is in perfect condition (intact, clean and dry). | Change of transparent, semi-permeable polyurethane dressings every 7 days, or sooner, if it is no longer intact or if moisture collects under the dressing. |
| Management of PIVC flushing | Nurses use of sterile normal saline for flushing PIVC and add-on devices, being clean without hematic residues | Use of sterile normal saline for injection to flush and lock catheter lumens that are accessed frequently.<br><br>Flushing of the peripheral intravenous catheter lumen with sterile normal saline with at least twice the volume of the catheter (and add-on devices), through push-stop-push technique. |
| Record of PIVC care | PIVC insertion and removal reason in the patient's health record is completed. | Record of peripheral intravenous catheter insertion, including assessment of insertion site and functionality. |

| | | |
|---|---|---|
| | | Record of peripheral intravenous catheter removal reason in the patient's health record. |
| Catheter removal and replacement strategies | PIVC failure occurs when the unplanned removal of the device due to mechanical complications (i.e., phlebitis, occlusion, infiltration) or infection before the completion of scheduled intravenous therapy. | Surveillance for the occurrence of unexplained fever or pain at the insertion site, examining for the occurrence of redness, erythema, or inflammation. |
| | | Removal of the peripheral intravenous catheter when complications occur, or as soon as it is no longer required. |
| | Unnecessary PIVC is when intravenous treatment is not administered for more than 24 h. | Removal of the unnecessary peripheral intravenous catheter when intravenous treatment is not administered after 24 h. |

Appendix p 4. Indicators and requirements for the PIVC care from clinical practice guideline recommendations.

Appendix p 6**.** Multimodal components of the PREBACP intervention for preventing peripheral intravenous catheter failure in adults.

| **Component** | **Description of the intervention** |
|---|---|
| Evidence | Implementation of clinical practice guideline recommendations [17,19] through up-to-date protocols, four posters with recommendations and three videos. |
| Users (Healthcare professionals and patients) | A teaching programme for professionals by PIVC experts, leaflets for patients and caregivers during the hospital stay by hospital nurses, which were designed by expert patients through a focal group, and self-directed eLearning (https://proyectoprebacp.wixsite.com/prebacp), on key topics related to care of PIVCs requiring a unique ID and password to avoid contamination between groups. We tailored the training to the needs identified at baseline on PIVCareQ outcomes. |
| Context | Face-to-face feedback with motivational messages to healthcare professionals every three months, on outcomes and to sustain adherence to recommendations. |
| Facilitation | Three nurses from each participating ward were trained on implementation of evidence-based practice, using the Facilitating Implementation of Research Evidence (FIRE) approach, and allocated as full-time local facilitators [9]. We empowered each local facilitator to tailor the multimodal intervention to the local ward context, resolving barriers and any on-site problems identified with the ward managers. We progressively deployed a co-facilitation model, increasing facilitator members depending on the local motivation of ward staff to mediate knowledge in decision-making with more professionals involved. |
| Appendix p 6. Multimodal components of the PREBACP intervention for preventing peripheral intravenous catheter failure in adults. | |

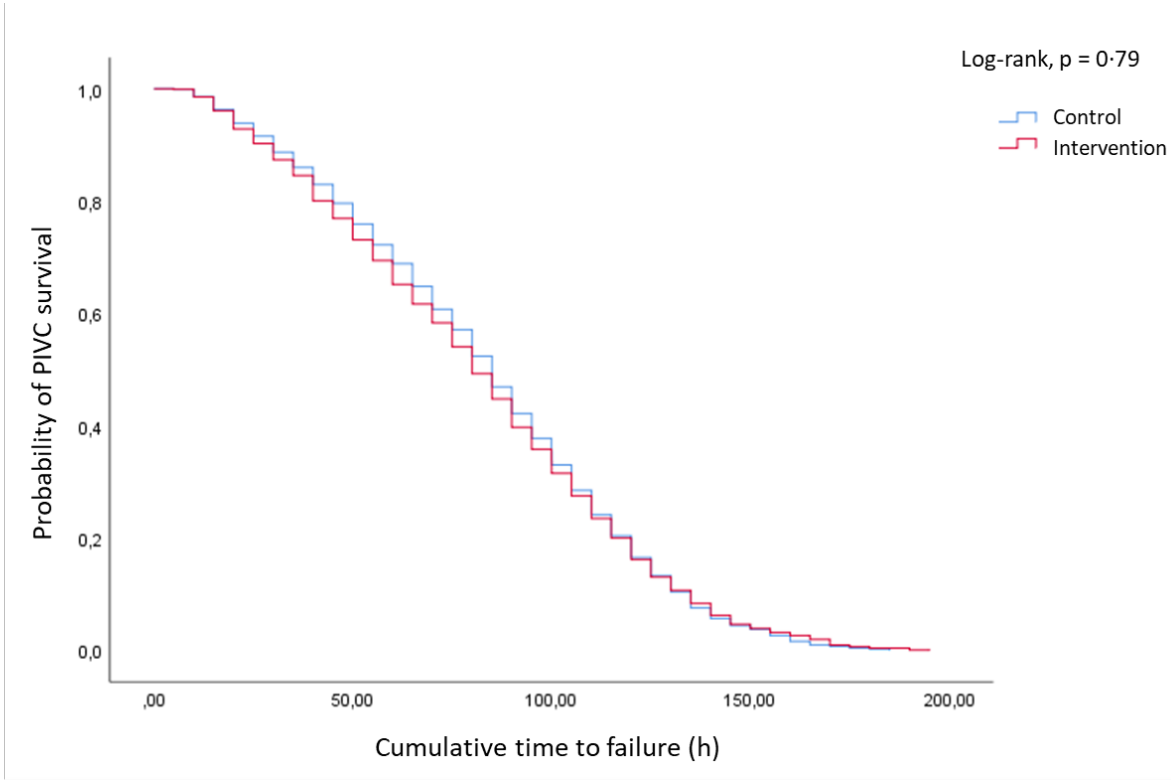
Appendix p 7. Evolution of effect and process outcomes at 3, 6 and 9 months.

| Characteristics of hospital wards | 3 months | | | 6 months | | | 9 months | | |
|---|---|---|---|---|---|---|---|---|---|
| | Intervention (n = 11) Mean (SD) | Control (n = 11) Mean (SD) | p-value | Intervention (n = 11) Mean (SD) | Control (n = 11) Mean (SD) | p-value | Intervention (n = 11) Mean (SD) | Control (n = 11) Mean (SD) | p-value |
| Total patient admissions | 37·82 (14·02) | 47·91 (18·05) | 0·159 | 36·82 (15·04) | 39·73 (18·68) | 0·692 | 42·55 (13·78) | 44·00 (15·81) | 0·820 |
| Patient age (years) | 68·27 (4·24) | 69·61 (5·95) | 0·548 | 67·56 (5·89) | 68·69 (8·26) | 0·716 | 68·66 (5·27) | 69·57 (6·47) | 0·722 |
| % Patient gender female | 47·68 (11·87) | 44·88 (12·95) | 0·602 | 44·64 (12·04) | 44·58 (13·24) | 0·576 | 43·86 (10·70) | 46·53 (14·58) | 0·630 |
| % Patient gender male | 52·32 (11·87) | 55·12 (12·95) | 0·602 | 52·36 (12·04) | 55·42 (13·24) | 0·576 | 56·14 (10·70) | 53·47 (14·58) | 0·630 |
| % Comorbidity | 91·64 (5·29) | 92·93 (5·58) | 0·585 | 93·12 (6·70) | 90·36 (9·78) | 0·449 | 94·22 (5·35) | 90·89 (6·54) | 0·205 |
| % Cognitive impairment | 20·66 (10·70) | 23·17 (14·15) | 0·643 | 22·31 (15·39) | 34·51 (19·22) | 0·116 | 26·59 (14·87) | 32·35 (17·47) | 0·415 |
| % Use of antibiotics | 37·51 (10·72) | 44·85 (13·44) | 0·172 | 33·71 (13·99) | 39·32 (13·47) | 0·349 | 37·71 (16·18) | 37·95 (14·47) | 0·972 |
| **Primary outcome modified intention-to-treat analysis** | | | | | | | | | |
| % PIVC failure | 42·58 (2·71) | 46·63 (4·19) | 0·014 | 39·03 (3·30) | 48·30 (5·36) | < 0·001 | 39·60 (2·37) | 45·89 (3·23) | < 0·001 |
| **Primary outcome per protocol-prespecified** | | | | | | | | | |
| % PIVC failure | 37·79 (2·83) | 39·99 (6·00) | 0·284 | 34·45 (1·89) | 42·98 (6·53) | <0·001 | 35·14 (3·34) | 40·41 (5·09) | 0·009 |
| Secondary outcome | | | | | | | | | |
| Total PIVCs | 38·45 (14·19) | 48·27 (18·42) | 0·177 | 37·64 (15·39) | 40·45 (19·01) | 0·706 | 43·18 (14·12) | 45·00 (16·61) | 0·785 |
| PIVC length of time (days) | 3·47 (0·69) | 3·75 (0·40) | 0·254 | 3·32 (0·63) | 3·61 (0·37) | 0·203 | 3·24 (0·45) | 3·51 (0·46) | 0·189 |
| % Phlebitis | 12·66 (2·72) | 18·53 (8·25) | 0·037 | 11·99 (2·95) | 18·13 (6·50) | 0·010 | 15·00 (5·03) | 15·39 (2·66) | 0·825 |
| % Extravasation | 18·91 (2·83) | 16·82 (3·23) | 0·122 | 16·77 (2·03) | 18·56 (2·79) | 0·100 | 16·26 (2·53) | 20·31 (3·66) | 0·007 |
| % Obstruction | 6·21 (1·99) | 4·64 (2·25) | 0·099 | 5·69 (1·62) | 6·32 (0·79) | 0·261 | 3·88 (2·13) | 4·72 (1·49) | 0·296 |
| % Dislodgement | 4·79 (3·61) | 6·64 (2·86) | 0·199 | 4·58 (2·23) | 5·32 (2·13) | 0·438 | 4·46 (3·23) | 5·48 (3·33) | 0·474 |
| % CRBSI | 0·45 (1·00) | 0·64 (1·17) | 0·679 | 0 | 0·43 (1·03) | 0·184 | 0 | 0·37 (0·83) | 0·152 |
| % 2 or more PIVCs in situ per patient | 1·53 (2·17) | 0·58 (1·02) | 0·202 | 1·87 (3·34) | 1·72 (2·80) | 0·911 | 1·27 (1·98) | 1·91 (2·95) | 0·555 |
| % Unnecessary PIVC | 11·35 (14·60) | 11·95 (7·53) | 0·904 | 6·91 (10·95) | 11·18 (9·67) | 0·345 | 5·78 (6·52) | 11·32 (6·65) | 0·062 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Multimodal intervention** | | | | | | | | | |
| Poster with recommendations | 4 | n/a | | 5 | n/a | | 5 | n/a | |
| Video protocols | 3 | n/a | | 3 | n/a | | 3 | n/a | |
| E-learning (completed courses) | 153 | n/a | | 21 | n/a | | 15 | n/a | |
| Website (visits) | n/a | n/a | n/a | n/a | n/a | n/a | n/a | n/a | n/a |
| Face-to-face training (1 per nurse) | 50 hours | n/a | | no | n/a | | no | n/a | |
| Feedback of results (1 per quarter) | 9 hours | n/a | | 9 hours | n/a | | 14 hours | n/a | |
| Number of Internal facilitators | 3 (0) | n/a | | 3 (0) | n/a | | 4·64 (1·03) | n/a | |
| **Adherence to clinical practice guideline recommendations** | | | | | | | | | |
| % Recommendations completed | 64·00 (10·00) | 59·43 (9·43) | 0·287 | 72·00 (7·43) | 58·00 (8·29) | < 0·001 | 70·00 (9·86) | 58·71 (6·43) | 0·005 |
| % Patient knowledges related to PIVC | 56·75 (21·75) | 54·23 (19·71) | 0·778 | 66·72 (16·56) | 49·35 (18·93) | 0·033 | 62·22 (20·09) | 50·94 (16·84) | 0·169 |
| % PIVC adequacy and insertion | 55·33 (16·52) | 46·74 (19·69) | 0·281 | 52·41 (12·27) | 52·84 (14·86) | 0·942 | 53·58 (11·92) | 49·68 (12·58) | 0·464 |
| % Visual inspection of insertion site | 57·78 (25·94) | 43·65 (18·27) | 0·155 | 71·29 (14·20) | 45·94 (19·62) | 0·002 | 64·94 (23·12) | 42·24 (20·49) | 0·024 |
| % Dressing type | 88·20 (17·72) | 91·85 (15·95) | 0·617 | 93·97 (10·77) | 84·86 (26·07) | 0·297 | 94·02 (12·16) | 89·61 (18·64) | 0·519 |
| % Dressing status | 53·77 (23·71) | 47·15 (19·54) | 0·484 | 66·37 (16·17) | 44·18 (15·13) | 0·003 | 60·34 (18·48) | 45·96 (17·21) | 0·073 |
| % Management of PIVC flushing | 72·87 (15·15) | 80·78 (11·34) | 0·181 | 76·48 (14·94) | 77·23 (12·57) | 0·901 | 78·36 (12·07) | 79·19 (13·23) | 0·879 |
| % Record of PIVC care | 63·00 (36·68) | 51·49 (41·78) | 0·500 | 76·56 (25·05) | 51·35 (40·34) | 0·093 | 76·44 (27·70) | 53·78 (38·66) | 0·130 |
| % PIVCs with all recommendations completed | 7·55 (7·43) | 4·94 (4·65) | 0·336 | 12·99 (7·64) | 3·64 (3·15) | 0·001 | 10·93 (9·47) | 2·94 (3·27) | 0·016 |

Appendix p 7. Evolution of effect and process outcomes at 3, 6 and 9 months.

Appendix 9. Kaplan−Meier analysis of survival from PIVC failure




| **Number at risk** | | | | | |
|---|---|---|---|---|---|
| Control | 1080 | 260 | 463 | 285 | 0 |
| Intervention | 893 | 240 | 371 | 247 | 0 |

**Appendix p 10.** Multivariable Analysis of PIVC failure.

| Outcomes | Unadjusted | | Adjusted (PIVC failure) | | |
|---|---|---|---|---|---|
| | OR | 95% CI | OR | 95% CI | p value |
| Multimodal intervention | 0·770 | 0·685 to 0·866 | ^ | ^ | ^ |
| Time period | 0·985 | 0·971 to 0·999 | ^ | ^ | ^ |
| Patient age | 1·002 | 0·998 to 1·005 | ^ | ^ | ^ |
| Patient gender male | 0·987 | 0·878 to 1·110 | ^ | ^ | ^ |
| 1 Comorbidity | 1·179 | 0·923 to 1·506 | ^ | ^ | ^ |
| 2 o more Comorbidities | 1·183 | 0·941 to 1·486 | ^ | ^ | ^ |
| No cognitive impairment | 0·677 | 0·592 to 0·774 | 0·651 | 0·566 to 0·749 | < 0·001 |
| Patient knowledge related to PIVC | 0·753 | 0·669 to 0·847 | ^ | ^ | ^ |
| PIVC adequacy and insertion (forearm and 20 – 22-gauge cannula) | 0·779 | 0·693 to 0·877 | 0·785 | 0·694 to 0·887 | <0·001 |
| PIVC inserted and maintained in the same hospital ward | 0·782 | 0·685 to 0·892 | ^ | ^ | ^ |
| Visual inspection of insertion site | 0·624 | 0·554 to 0·702 | 0·856 | 0·746 to 0·981 | 0·026 |
| Transparent dressing | 0·481 | 0·388 to 0·596 | 0·597 | 0·472 to 0·755 | < 0·001 |
| Optimal dressing status | 0·430 | 0·381 to 0·484 | 0·497 | 0·436 to 0·566 | < 0·001 |
| Management of PIVC flushing | 0·547 | 0·475 to 0·631 | 0·534 | 0·461 to 0·619 | < 0·001 |
| Record of PIVC care | 0·860 | 0·763 to 0·970 | ^ | ^ | ^ |
| All recommendations completed | 0·350 | 0·270 to 0·453 | ^ | ^ | ^ |
| **Appendix p 10.** Multivariable Analysis of PIVC failure | | | | | |

Hosmer-Lemeshow: $\chi$ 2: 6.58; p = 0.588; R2Nagelkerke: 0.10; ^ not part of the multivariable model as the results did not reach significance.