Center for General Practice at Aalborg University

Statistical analysis plan

The POCUS IN PRACTICE study Implementation of point-of-care ultrasonography in general practice: A stepped wedge cluster randomized trial

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Version number and date

Version 9. 19-12-2024

Content

1. Overview of analyses

This document contains the statistical analysis plan for 'The POCUS IN PRACTICE study Implementation of point-of-care ultrasonography in general practice: A stepped wedge cluster randomized trial'. The aim is to clarify analyses for the intended analyses. Therefore, the statistical analysis plan has been completed prior to the completion of the data collection. The overall purpose is to estimate the effect of a POCUS intervention for general practitioners. In the primary research article, the following outcomes are reported.

The primary outcomes are:

(P1) The number of registered reimbursement codes sent by the participating GP.

(P2) The number of referrals send to secondary care by the participating GP.

The secondary outcomes are:

S1. The number of consultations in primary care (e-mail, telephone, video, visits) managed by the participating GP.

S2. The GPs' perceived stress (Cohen's 10-item Perceived Stress Scale)

S3. The GPs' job satisfaction (Warr-Cook-Wall Job satisfaction Scale)

S4. The GPs burnout symptoms (Maslach Burnout inventory)

S7. To describe the number of adverse events reported by the participating GPs following the intervention

The tertiary outcome is:

T3. GPs' experiences of POCUS' influence on perceived stress, job satisfaction and burnout symptoms after the intervention.

The analysis intended for outcomes S5, S6, S8, T1 and T2 will not be specified in this statistical analysis plan, as these outcomes will be specified in elaborating study protocols and reported in separate articles.

The study design involves random and sequential crossover of clusters from control to intervention until all clusters are exposed (1). Participants (General Practitioners) have been recruited from 24th June 2022 to 1st September 2022 representing all five Danish regions. The GPs have been randomized to receive an education at different time-points.

year	2022	2022	2022	2023	2023	2023	2023	2023	2023	2023	2023	2023	2023	2023	2023	2024	2024	2024	2024	2024	2024
month	okt	nov	dec	jan	feb	mar	apr	may	jun	jul	aug	sep	okt	nov	dec	jan	feb	mar	apr	may	jun
cluster 1		#		x	x	x		#	*												
cluster 2			#		x	x	x		#	*											
cluster 3				#		x	x	x		#	*										
cluster 4					#		x	x	x		#	*									
cluster 5							#		x	x	x		#	*							
cluster 6									#		x	x	x		#	*					
cluster 7											#		x	x	x		#	*			
cluster 8												#		x	x	x		#	*		
cluster 9													#		x	x	x		#	*	
cluster 10														#		x	x	x		#	*
datacollection step	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21

	control period
	intervention including 3 course days
	intervention period
X	course days
*	patient questionnaire
#	GP questionnaire

Participating GPs are recruited from the five geographical regions in Denmark. Each geographical region is randomized to two clusters.
Eligible GPs from each geographical region are randomised to be enrolled in one of the two clusters assigned to the geographical region.

2. Background of the trial

Increased longevity results in more patients with a higher burden of disease and disability. These patients are complex to handle which increases the future need of healthcare services. Simultaneously, hospitals are becoming increasingly specialized and centralized with patients' length of stay shortened leading to a shift in healthcare services from hospitals to primary care. The general practitioner (GP) must therefore handle more complex patients, finalize the examination and treatment of more patients, and therefore GPs need the capabilities to refer to the correct sub-specialized department. This renders the diagnostic capacity and precision in the GP's office increasingly important. Point-of-care ultrasonography (POCUS) may be of benefit in this regard. We have previously developed an intervention to support GPs in performing POCUS. All participants will receive the educational intervention through attendance of a ultrasound course arranged by PLO-e (The organization of Danish General Practitioners). The educations intervention consists of three teaching seminars delivered over three months, a curriculum of 10 POCUS applications, an online learning platform providing educational support before, during, and after the teaching sessions. The online platform includes videos demonstrating the performance of POCUS, suggestions for additional literature, assignments

to support the development of skills, self-quizzes to focus attention of learning outcomes and specific action cards for each of the 10 POCUS applications framing the examinations in the clinical context. In addition, the online platform provides participants access to webinars and communication with other participants and teachers. The intervention is further described in the research protocol (ClinicalTrials.gov ID NCT05696821).

2.1. Eligibility

All GPs working in Danish general practice will be invited to participate in the study by newsletter invitation circulated by PLO to all PLO members. The newsletter will contain a link to a questionnaire in which the GPs will be asked to specify their name, practice, location of practice (region in Denmark), distance to nearest ultrasound scanning service, whether or not they are already using POCUS, whether or not they will have access to an ultrasound device during the educational intervention, and whether or not they are willing to share data. There will be a deadline (September 1st 2022) for responding to the invitation.

Following the deadline for signing up to participate in the study, the GPs reply to the questionnaires will be screened according to the inclusion and exclusion criteria to make a list of eligible participants fulfilling all inclusion and none of the exclusion criteria

Inclusion criteria:

1. GP, i.e., be a postgraduate medical doctor with a specialization in general practice
2. Work in office-based general practice in Denmark
3. Have access to an ultrasound device in the practice during the study period

Exclusion criteria:

1. GPs with a possible conflict of interest (e.g., industry affiliation related to the use of ultrasound)
2. No signed informed consent to participate.

All patients seen in general practice, that the GPs find relevant to examine with POCUS can be used in the data collection.

3. Adherence

Teachers at the educational intervention will support adherence to research protocols. The teacher will act as mentors for the participants during the educational intervention. The research team will reach out to participants who fail to submit data (GP questionnaires) but otherwise refrain from influencing practice.

4. Baseline characteristics

Tables of summary statistics will be produced in one group. The table will include:

The following participant characteristics will be collected in a baseline questionnaire:

Variable	Unit	Description
Age	years	Mean (SD[1]) and median (IQR[2])
Sex	male, female, other	frequency (%)
Experience as a medical doctor	years	Mean (SD) and median (IQR)
Experience as a GP[3]	years	Mean (SD) and median (IQR)
Experience with POCUS[4]	years	Mean (SD) and median (IQR)
Previous POCUS training	course participation, training during residency, experience from employment within another medical specialty, ad hoc training by colleague, other, no previous training	frequency (%)
Type of practice	solo-practice, partnership practice, solo-practice in collaboration, partnership practice in collaboration, other	frequency (%)
Location of practice	rural, city, mixed	frequency (%)
Distance to radiology department	kilometer	Mean (SD) and median (IQR)
Region	North Denmark Region, Central Denmark Region, Region of Southern Denmark, Region Zealand, Capital Region of Denmark	frequency (%)
Number of GPs working in the practice	1-20	Mean (SD) and median (IQR)
Number of patients listed with the clinic	1000-20000	Mean (SD) and median (IQR)

Note: The number of missing for each variable will be reported. [1] Standard Deviation, [2] Inter Quartile Range, [3] General Practitioner, [4] Point Of Care Ultra Sound

Characteristics of scanned patients

We will summarize the age and gender of patients being examined with ultrasound during the study according to the scanning-specific remuneration code bring used.

5. Outcomes

Following the use of POCUS in the general practice consultations the GPs will follow normal procedures for registration of activities in general practice using remuneration codes, fee-specific codes for using POCUS, and referrals in the medical record system. Prior to this study 11 fee-specific codes for 10 different POCUS examinations and one code for 'any other' POCUS examination will be installed in the medical record system.

For the data analysis of individual GPs activities (P1, P2 and S1), we will receive the number of monthly remuneration codes and referrals for each participating GP from October 2022 to June 2024.

For the data analysis of the GP questionnaires (S2, S3 and S4), we will include only GPs who have responded to both the BEFORE and AFTER questions related to the outcomes.

5.1. The primary outcomes

Outcome P1:

The number of monthly scanning-specific remuneration codes will be summarized for each participating GP from October 2022 to June 2024. In a stepped wedge analysis model, we will compare the number of scanning-specific remuneration codes BEFORE the intervention to the number of scanning-specific remuneration codes AFTER the intervention.

In addition, we will report the overall frequency of participating GPs, who use the scanning-specific remuneration codes in the end of the study (May and June 2024).

Outcome P2:

The number of monthly referrals will be summarized for each participating GP from October 2022 to June 2024. In a stepped wedge analysis model, we will compare the number of referrals sent by participating GPs BEFORE the intervention to the number of referrals sent AFTER the intervention.

5.2 Secondary outcomes

Outcome S1:

The number of monthly consultations will be summarized for each participating GP from October 2022 to June 2024. In a stepped wedge analysis model, we will compare the number of consultations sent from primary care BEFORE the intervention to the number of referrals sent AFTER the intervention.

Outcome S2:

We will summarize each participating GPs' answer to stress-related items in the BEFORE and AFTER questionnaire, to calculate the Cohen's PSS sum score (PSS-score).

We will report the mean(SD) er median [IQR] PSS-sum score BEFORE and AFTER for all participating GPs. In addition we will report the frequency of GPs with a PSS sum score ≥ 18 BEFORE and AFTER indicating a high level of stress (2).

Outcome S3:

We will summarize each participating GPs' answer to Job satisfaction-related items in the BEFORE and AFTER questionnaire, to calculate the Warr-Cook-Wall Job satisfaction sum score (WCW-score).

We will report the mean (SD) er median [IQR] WCW-sum score extracted from the 9 sub-items as well as the score of the one overall item BEFORE and AFTER for all participating GPs. In addition, we will report the frequency of GPs with a WCW-sum score ≤ 3 BEFORE and AFTER indicating low job satisfaction (2).

Outcome S4:

We will summarize each participating GPs' answer to burnout-related items in the BEFORE and AFTER questionnaire, to calculate the sum score of the three dimensions in the Maslach Burnout inventory (emotional exhaustion (9 items), de-personalization (5 items), and personal accomplishment (8 items)) (2).

We will report the mean(SD) er median [IQR] sum score for each dimension BEFORE and AFTER for all participating GPs.

Outcome S7:

We will summarize the total number of adverse events reported by the participating GP during the study in relation to the type of ultrasound examination performed.

5.3 Tertiary outcomes

Outcome T3:

We will summarize the participating GPs' experiences of POCUS' influence on perceived stress, job satisfaction and burnout symptoms after the intervention and report the frequency of GPs who report POCUS to have a positive impact(Very decreased or decreased sense of stress/jobsatisfaction/sense of burnout), no impact, or a negative impact(Very increased or increased sense of stress/jobsatisfaction/sense of burnout).

6. Data collection

Data will be collected as specified in the study protocol.

6.1. Register-based data

From PLSP, we will receive monthly aggregated data extracted from the medical-record system in the participating GPs' clinics from October 2022 to June 2024.
Data will be delivered as monthly aggregated data in separate models:

Model 1: including all scanning-specific remuneration codes registered in the participating clinics by participating GPs and for each code the corresponding age and gender of the patient.

Model 2.1: including the total number of consultations performed in the participating GPs' clinics further specified on the type of consultation.
Model 2.2: including the total number of scanning-specific remuneration codes performed in the participating GPs' clinics further specified on the 11 different codes.
Model 2.3: including the total number of referrals sent from the participating GPs' clinics further specified on the type of referral.
Model 3.1: including the total number of consultations performed by the participating GPs further specified on the type of consultation.
Model 3.2: including the total number of scanning-specific remuneration codes performed by the participating GPs further specified on the 11 different codes.
Model 3.3: including the total number of referrals sent by the participating GPs further specified on the type of referral.
Model 4: including all scanning-specific remuneration codes registered in the participating clinics by participating GPs and for each code, the corresponding type of consultation and any referral sent on the same patient on the same date as the on the same date as the scanning-specific remuneration code was used.
From PLSP, we will also receive a time-trend estimation based on all clinics in Denmark. This estimation will show the general development in number of remuneration code and referrals from October 2022 to June 2024. This data will be used to estimate the underlying time effect which is a confounder for the analysis.

6.2. GP questionnaires

The questionnaire will be collected through SurveyXact (Rambøll, Aarhus, Denmark).
Data from the BEFORE and AFTER questionnaire will be extracted from the online survey tool as excelfiles and merged in Stata prior to the analysis.

GPs report of adverse events will be extracted from SurveyXact as excelfiles.

7. Sample size

This is a pragmatic trial where size of the sample is given by the collective agreement between PLO and the Danish Regions. We plan to make post-hoc power calculations to discuss the needed of recruitment in future similar studies. The power calculation will not be used to discuss the results in current study (5,6).

8. Safety committee

A safety committee was set up to handle all reports of adverse and suspected adverse events (AEs) and serious adverse events (SAEs). Martin Bach Jensen headed the committee. The safety committee had the mandate to end the trial.

9. Statistical analysis

Data will be cleaned, and quality assurance will be performed to secure validity and completeness. All statistical analyses will be performed in Stata (IC version 18).

For the data analysis of P1, P2 and S1, we will receive individual GP data for the number of monthly remuneration codes (Scanning activity), referrals (Activity outside general practice) and consultations (Activity in general practice), from October 2022 to June 2024. For this period, we will also receive practice level data.

For outcomes P1, P2 and S1, we will use a linear regression mixed model adjusting for the random effect of clusters and participants, the fixed effect for steps in the analysis as well as the time trend (Data on the background population) and the effect coming from some participants' prior experience with POCUS. The time trend will be estimated from the variation in remuneration codes and referral in all GPs clinics in Denmark in the period October 2022 to June 2024.

All above mentioned analyses will be performed as complete case analyses. We will perform sensitivity analyses to (1) explore the effects of missing data using imputation of missing and (2) the time trend in our data compared to the time trend in the background population.

For the summarized data (S2, S3, S4, S7 and T3), we will use descriptive statistics. Data will be presented as mean (sd) and median [IQR] or n (%) and differences BEFORE and AFTER reported as differences in mean with 95% CI. For the data analysis of the GP questionnaires (S2, S3 and S4), we will include only GPs who have responded to both the BEFORE and AFTER questions related to the outcomes.

9.1. Flow chart

A detailed flow chart with number of invited, reasons for exclusions and reasons for dropouts will be reported for the participating GPs in a Figure.

9.2. Handling of missing data

Throughout the study period (21 months) participating GPs will be absent from the clinic due to vacation, short illness, course participation etc. This absence will result in variation in the GPs' activity (remunerations codes and referrals). For this study, we will assume that the participants' planned absence from the clinic is comparable. Still, extraordinary absence from the clinic due to e.g. long-term illness or longer vacation will result in missing data. Missing data for participants will also occur if a participant withdraws from the study or we are unable to extract data through the medical record system from a participant in a given month. Finally, missing data will occur if the clinic does not provide individual GP data to PLSP.

We will impute for missingness in two steps.

1)If individual data on a GP is missing, we will carry over data from the practice level. This can be done if the GP has no other colleagues participating in the study and if it will be reasonable to assume an overlap between the GPs data and practice level data.

2)In other cases of missingness, we impute data based on available data separately for each of the ten clusters based on available data from the cluster and the clinic.

10. Assignment of clusters

10.1 Allocation Sequence generation

When the GPs signed up to participate in the study, they were able to see the dates for the teaching seminars at each location, but they were not be able to choose between these (their assignment to a specific cluster was determined by randomization).

After 200 GP had been allocated to the five regions used in the SW-CRT, the 40 participants allocated to each region were randomized to participate in one of the two clusters: North Denmark Region (Aalborg or Sæby), Central Denmark Region (Aarhus or Herning), Region of Southern Denmark (Vejle or Odense), Region Zealand (Roskilde or Næstved) and Capital Region of Denmark (København V or Lyngby). Randomisation was performed on two levels – cluster order and individual participation at a specific time.

10.2 Order of clusters

First, the overall order of all clusters was randomized. I.e. the order of the clusters defined by each location was decided based on simple randomization -drawing an anonymous paper slip at random order with one of the following texts: Aalborg, Sæby, Aarhus, Herning, Vejle, Odense, Roskilde, Næstved, København V and Lyngby. From this an order for the delivery of courses was established (Figure 2). This randomization and the fixed timeline for the delivery of these courses was done on June 17th 2022 in order to plan and prepare the delivery of the intervention.

10.3 Participants' time of intervention

The randomization of participants at a given location to receive the intervention at one of two time points took place after the deadline for signing up for the course prior to the start of the data collection (October 2022). The randomizations were done by a research assistant not involved in assessment or delivery of the intervention (the randomization process was video documented). Following this randomization process, the GPs were offered participation in the SW-CRT by e-mail including a link for the PLO-e course allocated to the specific cluster.

11. Handling of data and blinding

A research assistant will help clean data and make data ready for analysis. She has no previous knowledge of participants. The researcher responsible for analyzing the primary outcome will have no knowledge of participants. He has a physiotherapy background and have never diagnosed or treated patients in general practice. They are both blinded to allocation in the study.

12. Ethics

The project was notified to the regional ethical committee (The North Denmark Region Committee on Health Research Ethics, registration number 96036), who responded that do ethical approval was necessary. The project is registered and conducted according to the regulations of the Danish Data Protection Agency (registration number ID-242-4).

13. References

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