PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	The use and impact of point-of-care ultrasonography in general practice: a prospective observational study
AUTHORS	Aakjær Andersen, Camilla; Brodersen, John; Davidsen, Annette Sofie; Graumann, Ole; Jensen, Martin Bach

VERSION 1 - REVIEW

REVIEWER	David Barbic University of British Columbia, Canada
REVIEW RETURNED	24-Feb-2020

GENERAL COMMENTS	Title: suggest modifying the title for clarity. Instead of “Point-of-care ultrasonography in general practice affects patient care – a prospective observational study” consider “The use of point-of-care ultrasonography in general practice alters clinician diagnosis and patient management” General comments Excellent overall study considering not just the current use, but how the use impacts diagnostic certainty and overall patient care. Suggest changing from the abbreviation PoC-US to the recognized, and accepted POCUS. Abstract Page 3 [line 15-17] Primary and secondary outcome measures – “Using an online before-after PoC-US questionnaire” is a method and should likely be placed under “Design” These objectives require rewording for clarity Page 3 [line 26-32] How the proportion of PoC-US usage is reported should likely be changed to mean (with 95% CI) or median (with IQR). The current format is confusing. Page 3 [line 35-38] Suggest modifying the conclusions to something similar to “The clinical utilization of PoC-US was highly variable amongst the GPs included in this study” Strengths and Limitations Page 4 [line 10-12] suggest rewording this limitation to “This study may be subject to selection bias since the participating GPs likely constitute a subset of physicians with a special interest in ultrasonography”

	Introduction Minor grammar and syntax errors requiring correction. No major comments. Methods Study setting Page 5 [line 38-43] Suggest changing the second sentence to "Denmark has universal, publicly funded health care system, where almost patients are registered with a GP." Participating general practicitioners Suggest including inclusion criteria in a small box for clarity, such as: Box 1 Required Elements for GP participation 1. POCUS use for minimum 6 months 2. Use for anatomical regions 3. POCUS use on a daily basis 4. Formalized POCUS training 5. Minimum 1400 patients on roster 6. Etc etc etc Sample size and statistical analysis Page 6 [43-51] – please clarify what parameters (anticipated difference, alpha, beta, etc) were used to arrive that this projected sample size Ethical approval Page 6 [line 54-5] please clarify what "pseudo-anonymised" means. Was data completely anonymized, were those performing the statistical analysis blinded? Results Page 7 [line 11] Suggest changing the way this data is presented to something similar to "Twenty general practitioners from 18 clinics enrolled 574 patients (mean or median and 95% CI or IQR)" Page 7 [line 19-23] similar to above, suggest changing the reporting of results to means or medians depending on the distribution of the data. Page 7 [line 30-35] this paragraph is somewhat confusing. There aren't 834 different organs in the human body. A more appropriate representation of your findings would be to describe the most common system or combination of systems scanned by GPs, which is what Figure 3 shows. Page 8 [line 4-15] this data could be more clearly and succinctly presented in table form. Page 9 [line17-25] this data may actually be the most important of the entire manuscript. This speaks to improved diagnostic certainty on the part of GPs and improved patient care. Discussion Summary of main findings Page 8 [line 45] suggest changing "intended referrals from 49.2% to 25.6%" to a relative-risk reduction or hazard ratio. From what I can

	gather from the numbers presented, this is a relative risk reduction of 48%. Page 8 [line49-51] Was this qualitative work and pilot testing published? If so, please reference appropriately. Implications for Practice Page 9 [line 54-next page] Suggest modifying how this data is presented for clarity (see prior comments. Appendix 6 This is a major finding of this manuscript and should be modified to include as a Table.

REVIEWER	DR ADRIAN IONESCU MORRISTON CARDIAC CENTRE, UK
REVIEW RETURNED	19-Mar-2020

GENERAL COMMENTS	This is an excellent paper looking at the patterns of usage of point-of-care ultrasound (POCUS) among a cohort of Danish GPs. Its methodology is rigorous and the paper is clearly written and concise. It is very timely as POCUS is expanding outside the hospital settings. I only have one comment: the paper reports a large percentage of cases where the diagnosis was markedly changed by the application of POCUS. We have no idea whether allowing GPs (with a variable level of competence) the unrestricted use of POCUS results in better patient outcomes. This point obviously cannot be addressed n this paper, but it should be made in the discussion. The ideal trial design would be one that I have tried to get off the ground here in Wales and failed because no GPs were interested: Patients havd POCUS, the findings are documented but NOT ACTEF UPON; patients are then sent to have the scan (if deemed clinically indicated by the GP) in the hospital, and then accuracy, +ve and -ve predictive values of the GP scan are assessed. Only then can we confidently state that having POCUS widely available in the community is safe; at present we don't know. I think the discussion should address this topic.

REVIEWER	Gordian Lukas Schmid Department of General Practice, Medical Faculty of the University of Leipzig, Germany
REVIEW RETURNED	05-Apr-2020

GENERAL COMMENTS	This study explores the use of point-of-care ultrasound in Danish gerneral practice and the consequences for the diagnostic process. Methods and results are well described and discussed adequately. The study is an important contribution to the evidence-base for the future use of PoC-US in gerneral pratice. Especially, the measurents of the US-skills of the GPs included and the pre-post-comparison are very interesting. Nevertheless some minor points should be adressed before publication:

	1. Abstract: - line 15-17, language: please reduce the repetition of "PoC-US" 2. Abstract: - line 19-21: better use an alternative to "explore" e.g. "estimated" or "monitored" ... . From my point of view, the ability to produce Us images does not give an information about how US influences the diagnostic process. Please specify, change or explain this. 3. Abstract: - the very interesting findings about the reduction of referrals to specialists and hospitals should be mentioned in the abstract. 4. Strengths an limitations page 4, line 11-12: How do you think does this selection influence your findings? Please explain. 5. Methods, line 50: What does "some level" mean? Was any training enough? Please specify. 6. Results, page 7, line 20: I do not understand which numbers you reported here. The mean of minima and maxima? The use of median and IQR might be more appropriate here. Please clarify. 7. Results, line 24-26: What is the difference between answering a clinical question and exploring the reason for the patient's symptoms. Please explain and specify in the text. 8. Discussion, page 9, line 4-5: A comparison with all Danish GPs in respect to age, scientific degree and experience would be interesting here. One could expect participants to be younger and scientifically higher educated. Please add and discuss data describing the whole poulation of Danish GPs as far as possible. 9. Discussion, page 9, line 47: Better report the difference. e.g. "Reduced from XY to 25.9%" or "was reduced by XY%" 10. Figure 3: This figure looks somehow buisy and complex. Please consider to relocate the frequencies of the applications to the bottom or e.g. in brackets. Or simply replace the N of examinations by the frequencies as %. Then there would be space to enlarge the bars a little more and make a clear display of the interesting data. 11. Table 4: The data of figure 4 should better be presented as a table. 12. Appendix 1, line 10: shouldn't it be: "met the inclusion and missed the exclusion criteria"?

VERSION 1 – AUTHOR RESPONSE

Comment from reviewer 1 David Barbic University of British Columbia, Canada	Reply to comment
Title: suggest modifying the title for clarity. Instead of “Point-of-care ultrasonography in general practice affects patient care – a prospective observational study” consider “The use of point-of-care ultrasonography in general	Thank you. This is a fine suggestion for improving the title. The Editor also commented on the title. Below is a suggestion integrating both comments. “The use and impact of point-of-care

practice alters clinician diagnosis and patient management”	ultrasonography in general practice: a prospective observational study”
General comment: Excellent overall study considering not just the current use, but how the use impacts diagnostic certainty and overall patient care. Suggest changing from the abbreviation PoC-US to the recognized, and accepted POCUS.	Thank you for pointing to this. We have changed PoC-US to POCUS.
Abstract Page 3 [line 15-17] Primary and secondary outcome measures – “Using an online before-after PoC-US questionnaire” is a method and should likely be placed under “Design” These objectives require rewording for clarity	We have moved the design description and rephrased the primary and secondary outcome measures, which now reads: “We investigated the use of POCUS through the indication for use, the frequency of use, the time consumption, the extent of modification of the examination, and the findings.”
Abstract Page 3 [line 26-32] How the proportion of PoC-US usage is reported should likely be changed to mean (with 95% CI) or median (with IQR). The current format is confusing.	We have changed the reported frequency to median and IQR. The text now reads: “The GPs included 574 patients in the study. POCUS was used in patient consultations with a median frequency of 8.6% [IQR: 4.9-12.6]. Many different organs were scanned covering more than 100 different tentative diagnoses.”
Abstract Page 3 [line 35-38] Suggest modifying the conclusions to something similar to “The clinical utilization of PoC-US was highly variable amongst the GPs included in this study”	Thank you for this suggestion. We have rephrased the text: “The clinical utilization of POCUS was highly variable amongst the GPs included in this study both in terms of the indication for performing POCUS, organs scanned and frequency of use.”
Strengths and Limitations Page 4 [line 10-12] suggest rewording this limitation to “This study may be subject to selection bias since the participating GPs likely constitute a subset of physicians with a special interest in ultrasonography”	Thank you for this suggestion. We have changed the manuscript accordingly.
Introduction Minor grammar and syntax errors requiring correction. No major comments.	The manuscript have been through a thorough proofreading by a native speaker.
Methods Study setting Page 5 [line 38-43] Suggest changing the second sentence to “Denmark has universal, publicly funded health care system, where almost patients are registered with a GP.”	Thank you for this suggestion. We have changed the manuscript accordingly.
Participating general practicitioners Suggest including inclusion criteria in a small box for clarity, such as:	We agree this would increase clarity. If an additional box is allowed, we would be happy to include that. Considering the total number of tables/figures, we have listed the requirements

Box 1 Required Elements for GP participation 1. POCUS use for minimum 6 months 2. Use for anatomical regions 3. POCUS use on a daily basis 4. Formalized POCUS training 5. Minimum 1400 patients on roster 6. Etc etc etc	instead: "To be included in the study, GP had to: • Have used POCUS for a more than six months • Use POCUS for a minimum of two anatomical areas • Use POCUS on a daily basis • Have participated in formalized POCUS training e.g. an ultrasound course • Work in a practice with a patient population over 1400 • Work in the practice minimum 4 days a week"
Sample size and statistical analysis Page 6 [43-51] – please clarify what parameters (anticipated difference, alpha, beta, etc) were used to arrive that this projected sample size	Thank you for pointing to this. We have elaborated in the text: "Based on a questionnaire study[3], we estimate that there were around 75 GPs in Denmark, who would meet our inclusion criteria. We found it realistic to include 20 of the GPs in the study. Based on an interview study with Danish GPs[16], we estimated that the GPs would use POCUS 2-3 times a day. Assuming a participation rate of 80%, we expected to include 640 to 960 patients during the study period of one month."
Ethical approval Page 6 [line 54-5] please clarify what "pseudo-anonymised" means. Was data completely anonymized, were those performing the statistical analysis blinded?	Excellent point. We have clarified this in the text, which now reads: "Written informed consent was obtained from all participating GPs and patients and all data were pseudo-anonymized using de-identification numbers. Only the principal investigator (CAA) knew the identity of the GPs and only the GPs knew the identity of the participating patients."
Results Page 7 [line 11] Suggest changing the way this data is presented to something similar to "Twenty general practitioners from 18 clinics enrolled 574 patients (mean or median and 95% CI or IQR)"	Thank you for this suggestion. We have changed the text accordingly. It now reads: "Twenty general practitioners from 18 clinics each enrolled a median of 26 [IQR 17- 40] patients. Data from 574 patients were available for analysis, and in 528 patients, data were available for before-after comparison (figure 1)."
Results Page 7 [line 19-23] similar to above, suggest changing the reporting of results to means or medians depending on the distribution of the data.	Thank you for this suggestion. We have added the median and IQR. The text now reads: "Each GPs performed between 12 and 84 POCUS examinations (median: 32.0 [IQR: 17.8-42.8]) corresponding to an individual average between 0.6 and 3.9 ultrasound examinations per day. The GPs had between 13.0 and 24.4 face-

	to-face patient consultations per day (median: 15.9 [IQR: 14.2-17.8]). Hence, during the study period each GPs performed POCUS in between 3.7% and 20.8% of all face-to-face consultations [median: 8.6 [IQR: 4.9-12.6]).”
Results Page 7 [line 30-35] this paragraph is somewhat confusing. There aren’t 834 different organs in the human body. A more appropriate representation of your findings would be to describe the most common system or combination of systems scanned by GPs, which is what Figure 3 shows.	Thank you for your comment. We fully agree. We have changed the phasing “organ scanned” to “scanning modality” throughout the text. The text now reads: “POCUS was used to examine many different organs and structures (Figure 3). The GPs registered examining a total of 834 scanning modalities in 570 POCUS examinations (data missing in 4 patients); most commonly heart and lung in combination and different combinations of abdominal organs.”
Results Page 8 [line 4-15] this data could be more clearly and succinctly presented in table form.	We agree. However, we are afraid to exceed the number of tables that is accepted. Hence, we have not made any changes, but would be happy to add another table if the Editor allows this. No changes made.
Results Page 9 [line17-25] this data may actually be the most important of the entire manuscript. This speaks to improved diagnostic certainty on the part of GPs and improved patient care.	Thank you for pointing this out. We agree and we have emphasized these results by including Appendix 6 as Table 3.
Discussion Summary of main findings Page 8 [line 45] suggest changing “intended referrals from 49.2% to 25.6%” to a relative-risk reduction or hazard ratio. From what I can gather from the numbers presented, this is a relative risk reduction of 48%.	Thank you for this suggestion. We have included a relative-risk reduction in the text, which now reads: In the method section: “Relative-risk reduction in referrals for secondary care was calculated by considering referrals as events, the before-POCUS registrations as controls and the after-POCUS registrations as interventions.” In the results section: “Overall, there was an absolute reduction in intended referrals for secondary care from 49.2% to 25.6% corresponding to an absolute risk reduction of 23.6% and a relative-risk reduction of 48.0%,” And in the discussion section: “POCUS changed the intended management plan in 50.9% of patients, including a relative-risk reduction in planned referrals of 48%, and a change in the planned treatment of 26.5% of

	patients."
Discussion Page 8 [line49-51] Was this qualitative work and pilot testing published? If so, please reference appropriately.	Thank you for pointing to this. We have included the reference for the qualitative study (reference 16).
Implications for Practice Page 9 [line 54-next page] Suggest modifying how this data is presented for clarity (see prior comments.	Thank you for the suggestion. We have changed the text, which now reads: "POCUS was used in in the patient consultation with a median of 8.6% and with a median time consumption of five minutes"
Appendix 6 This is a major finding of this manuscript and should be modified to include as a Table.	Thank you for this suggestion. We agree and have added Appendix 6 as a Table 3
Comments from reviewer 2 DR ADRIAN IONESCU MORRISTON CARDIAC CENTRE, UK	Reply to comments
This is an excellent paper looking at the patterns of usage of point-of-care ultrasound (POCUS) among a cohort of Danish GPs. Its methodology is rigorous and the paper is clearly written and concise. It is very timely as POCUS is expanding outside the hospital settings. I only have one comment: The paper reports a large percentage of cases where the diagnosis was markedly changed by the application of POCUS. We have no idea whether allowing GPs (with a variable level of competence) the unrestricted use of POCUS results in better patient outcomes. This point obviously cannot be addressed n this paper, but it should be made in the discussion. The ideal trial design would be one that I have tried to get off the ground here in Wales and failed because no GPs were interested: Patients havd POCUS, the findings are documented but NOT ACTEF UPON; patients are then sent to have the scan (if deemed clinically indicated by the GP) in the hospital, and then accuracy, +ve and -ve predictive values of the GP scan are assessed. Only then can we confidently state that having POCUS widely available in the community is safe; at present we don't know. I think the discussion should address this topic.	Thank you for the comment. We agree that the issue regarding the quality of the GPs' scans is important and calls for more research. We have included this and rephrased the discussion: "Some studies have reported high diagnostic accuracies of GPs' POCUS examinations, when these were compared to repeated scans by imaging specialists[15,26]. However, these studies only included few scanning modalities, a rather small number of GPs, and the evaluation of accuracy was made shortly after participation in a training programme. Hence, we do not know if the results would be equally good if POCUS was applied for more applications, in a wider selection of GPs, or if long-term proficiency is achievable. Determining whether POCUS use in general practice results in better patient outcomes should include an evaluation of both the diagnostic accuracy (including potential overdiagnosis) of the performed examinations as well as the medical decision-making following the scan. In our baseline evaluation of the GPs scanning competences, we found that a few of the GPs lacked the practical skills for performing the scans, despite using POCUS regularly and having participated in training (Figure 2). Likewise, we found that the GPs described their POCUS findings as uncertain in 19.7% of examinations. Office-based GPs may be used to navigating in uncertainty and performing up to a certain level before referring patients on to more advanced care. Still, POCUS is a particularly user-dependent technology[23,27] and the ability to rule-in or rule-out, as well as the prevalence and

	interpretation of incidental findings, may differ between applications.[5,28.] Thus, there is a need for more research and evidence-based guidelines to support GPs in choosing what to scan and how to integrate findings into clinical care." In addition, the following is stated in the implication for practice session: "It remains to be investigated, if the change in patient management caused by POCUS actually improves patient care, or if it causes harm in terms of false positive findings, misdiagnosis, over-detection, and potential, subsequent overtreatment." One ekstra reference is added: Lindgaard K, Riisgaard L. PMC5592352; 'validation of ultrasound examinations performed by general practitioners'. Scand J Prim Health Care. 2017;35(3):256-261. and .)
Comments by reviewer 3: Gordian Lukas Schmid Department of General Practice, Medical Faculty of the University of Leipzig, Germany	Reply to comments
This study explores the use of point-of-care ultrasound in Danish general practice and the consequences for the diagnostic process. Methods and results are well described and discussed adequately. The study is an important contribution to the evidence-base for the future use of PoC-US in general practice. Especially, the measures of the US-skills of the GPs included and the pre-post-comparison are very interesting. Nevertheless, some minor points should be addressed before publication:	Thank you for the comment. We have addressed your points below.
1. Abstract: - line 15-17, language: please reduce the repetition of "PoC-US"	The Primary and secondary outcome measures have been rephrased and now reads: "We investigated the use of POCUS through the indication for use, the frequency of use, the time consumption, the extent of modification of the examination, and the findings."
2. Abstract: - line 19-21: better use an alternative to "explore" e.g. "estimated" or "monitored" ... . From my point of view, the ability to produce Us images does not give an information about how US influences the diagnostic process. Please specify, change or explain this.	Thank you for making this point. We have changed the word explored to estimated. The ability to produce US images were included under the domain POCUS influence on the diagnostic process under the assumption that the

	POCUS exam could only influence the diagnostic process, if the GP was able to produce the US images.
3. Abstract: - the very interesting findings about the reduction of referrals to specialists and hospitals should be mentioned in the abstract.	Thank you for the suggestion. We have included this finding in the abstract, which now reads: "Across applications and GPs, POCUS entailed a change in diagnoses in 49.4% of patients; increased confidence in a diagnosis in 89.2% of patients; a change in the management plan for 50.9% of patients including an absolute reduction in intended referrals to secondary care from 49.2% to 25.6%; and a change in treatment for 26.5% of patients."
4. Strengths an limitations page 4, line 11-12: How do you think does this selection influence your findings? Please explain.	Thank you for pointing to this. The text have been rephrased to: "This study may be subject to selection bias since the participating GPs most likely constitute a subset of physicians with a special interest in ultrasonography" And in the discussion, we have added: "Being a selected group of early-adapters of the technology, it is plausible that the participating GPs rely heavily on POCUS in their daily work and subsequently that the frequency of increased confidence and change in diagnosis, plan or treatment is higher in this particular group of GPs."
5. Methods, line 50: What does "some level" mean? Was any training enough? Please specify.	There is no official ultrasound education for GPs in Denmark. From the prospective qualitative study (reference 16) we knew that there was a large variation in the ultrasound education of GPs. Hence, our only requirement was that the GPs had received formalized training e.g. attended an ultrasound course or received structured formalized training during residency or other employment at a hospital department. To clarify this, we have added the following in the text: "…participated in some level of formalized POCUS training e.g. an ultrasound course."
6. Results, page 7, line 20: I do not understand which numbers you reported here. The mean of minima and maxima? The use of median and IQR might be more appropriate here. Please clarify.	Thank you for pointing to this. We have changed the text, which now reads: "Twenty general practitioners from 18 clinics enrolled a median of 26 [IQR 17- 40] patients.

	Data from 574 patients were available for analysis, and in 528 patients, data were available for before-after comparison (figure 1)."
7. Results, line 24-26: What is the difference between answering a clinical question and exploring the reason for the patient's symptoms. Please explain and specify in the text.	Thank you for pointing to this. We have clarified the distinction between the two by inserting a direct translation of the phrasing in the questionnaire. The text now reads: "When GPs were using POCUS, they aimed primarily to confirm or disconfirm a specific predefined clinical condition (73.1%), or to explore the reason for the patient's symptoms without having a specific predefined clinical condition in mind (20.2%), but they rarely planned to do both (1.6%)."
8. Discussion, page 9, line 4-5: A comparison with all Danish GPs in respect to age, scientific degree and experience would be interesting here. One could expect participants to be younger and scientifically higher educated. Please add and discuss data describing the whole poulation of Danish GPs as far as possible.	Thank you for this suggestion. We have added the following text to the discussion: "The participating GPs resembled the general GP population in Denmark in terms of the location and size of the clinic, but not in terms of age, gender or organization of the clinic. Specifically, the participants were younger, more often male and more often working in a partnership practice[19]."
9. Discussion, page 9, line 47: Better report the difference. e.g. "Reduced from XY to 25.9%" or "was reduced by XY%"	Thank you for pointing to this. We have changed the text accordingly. The text now reads: "This referral frequency was reduced from 49,2% to 25.69% by using POCUS"
10. Figure 3: This figure looks somehow busy and complex. Please consider to relocate the frequencies of the applications to the bottom or e.g. in brackets. Or simply replace the N of examinations by the frequencies as %. Then there would be space to enlarge the bars a little more and make a clear display of the interesting data.	Thank you for putting this to our attention. We have made a new version of the figure. Please see attached file [GULD BMJ open figure3 new ver.].
11. Table 4: The data of figure 4 should better be presented as a table.	We support the idea of presenting data in the best and most informative manner. We have made a table of the results. Hence Figure 4 becomes Table 3
12. Appendix 1, line 10: shouldn't it be: "met the inclusion and missed the exclusion criteria"?	Thank you for noticing. We have changed the text accordingly.

VERSION 2 – REVIEW

REVIEWER	Gordian Lukas Schmid Department of General pratice, Medical faculty, Universität Leipzig, Germany
REVIEW RETURNED	15-Jun-2020

GENERAL COMMENTS	Thank you for improving this important manuscript. A last comment came to my mind reading your revised paper: Abstract: It might be helpful to indicate, that the study was performed within a Danish cohort in the abstract.