PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

Title (Provisional)

HOW DO DOCTORS ADDRESS HEART FAILURE PATIENTS' DISCLOSURES OF MEDICATION ADHERENCE PROBLEMS DURING HOSPITAL AND PRIMARY CARE CONSULTATIONS? An exploratory interaction-based observational cohort study

Authors

Frigaard, Christine; Menichetti, Julia; Schirmer, Henrik; Wisloff, Torbjorn; Bjørnstad, Herman; Breines Simonsen, Tone Helene; Gulbrandsen, Pal; Gerwing, Jennifer

VERSION 1 - REVIEW

Reviewer	**1**
Name	**JELÍNEK, Libor**
Affiliation	**Palacky University Olomouc, Faculty of Medicine**
Date	**22-Jan-2025**
COI	**None**

Thank you for the opportunity to review an interesting study.

Adherence has become one of the main problems in the treatment of chronic diseases.

This study looks at the conversation between patient and physician and attempts to analyze its course. The design of the study is very unconventional and innovative.

An interesting detail is the difference in experience and gender between the two groups of physicians. The time spent with patients in the ward and in the outpatient clinic is also different. A section is devoted to this issue in the discussion.

For the reproducibility of the study, a complete protocol of the analysis of the interviews with all the red flags and their selection methodology should be included (at least in the supplement).

Limitations are the lack of generalisability and limited applicability in a health system other than the local one. To really reveal common practice, it would be very interesting to compare the results with interviews that are not clearly recorded (of course, there would be a

question of research ethics). On the other hand, the interview examples could be virtually the same in a practice almost anywhere in the world.

Reviewer **2**

Name **Lauffenburger, Julie**

Affiliation **Brigham and Women's Hospital, Harvard Medical School, Division of Pharmacoepidemiology and Pharmacoeconomics**

Date **17-Mar-2025**

COI **None**

Major comments:

- Were patients selected based on non-adherence? This otherwise seems to be a highly heterogeneous population.

- Much of the conclusions and results presented throughout are more comparative or quantitative in nature than the study design really allows; in particular, it is difficult to consider prevalence-based statistics for a cohort of n=25 that are likely highly selected. This is not well-recognized throughout. Related to this, the authors also state that these are consultations based on authentic patient-doctor consultations; it is true that these are real consultations, but more caution should be exhibited in describing these as extensively generalizable as patients still presumably needed to provide consent to participate in the study and have their information audio-recorded. Overall, it seems this this manuscript should be presented more in the context of a qualitative study as fundamentally the transcripts and their analysis are more closely aligned with those methods.

Minor comments:

- The abstract conclusion does not align with the results presented in there; at a minimum, it should be clearer which types of problems are unintentional versus unintentional. And, the conclusion suggests that comparative statistics were used, but only descriptive statistics were used. Recommend striking all such comparative language (e.g., “more likely to address”).

- How many researchers coded each transcript? This is not clear from the data provided.

- A framework for ‘intentional’ versus ‘unintentional’ non-adherence would be helpful; a prior paper is cited but this is not particularly clear.

VERSION 1 - AUTHOR RESPONSE

Reviewer: 1, **Dr. Libor JELÍNEK, Palacky University Olomouc, University Hospital Olomouc**		
#	Comments to author:	Our response:

1	For the reproducibility of the study, a complete protocol of the analysis of the interviews with all the red flags and their selection methodology should be included (at least in the supplement).	Thank you for pointing out that we should include more information about our first study, to make it clearer how results from this study were generated from the audio-recorded consultations. Following up on your suggestion, we have included our MADICI Codebook with illustrative examples into the supplementary materials and have also included more information in the methods section of the manuscript to explain how we recognised patients' Medication Adherence Disclosures In Clinical Interactions and patient utterances indicating (potential) non-adherence problems = red flags. See page 4.

Reviewer: 2 **Dr. Julie Lauffenburger, Brigham and Women's Hospital, Harvard Medical School**		
#	Major Comments to author:	Our response:
2	Were patients selected based on non-adherence? This otherwise seems to be a highly heterogeneous population.	Patients were selected according to the inclusion and exclusion criteria presented under Methods, page 2 and 3, and in no way was non-adherence a factor that affected inclusion in the study. The study sample is heterogenous, and as heterogenous as one might expect for a heart failure population in need of an emergency admittance to hospital. However, comparing the characteristics of the patients in our cohort with patient characteristics used to describe HF patients in general, for example in the recent ESC position paper on how to handle polypharmacy in HF [1] and the Norwegian nationwide study by Ødegaard et al. from 2023[2], our cohort display similarities on several key areas: Men > Women Patients have ≥3 coexisting comorbidities, and like our cohort, atrial fibrillation is a common co-morbidity. Patients' prescriptions at discharge from hospital include many of the four medications in the HF guideline-directed medical therapy

		Polypharmacy is frequent (≥5 medications), which is frequently encountered in contemporary HF care. To address your comment, we have added information about this under limitations, page 18.
3	Much of the conclusions and results presented throughout are more comparative or quantitative in nature than the study design really allows; in particular, it is difficult to consider prevalence-based statistics for a cohort of n=25 that are likely highly selected. This is not well-recognized throughout.	Our understanding of "prevalence" is that it is about the occurrence of a health condition, and if we were studying that in an epidemiological setting, indeed this sample size would be far too small to say anything meaningful. However, the comparisons we provide in the results fit with the quantitative nature of the analysis and are intended to report elucidating patterns in these interactions, not to say anything more generalisable beyond that. We have attempted to make this point clearer throughout. Though there are 25 patients in the cohort, it is also relevant that they have individually met with one of the 23 hospital doctors at the first ward visit when their health situation was poor, then with one of the 23 hospital doctors at the discharge visit when they were well enough to resume self-care at home, before meeting with one of the 25 general practitioners at the follow-up visit after they had been home for a week and had gained experience with any changes that were initiated at the hospital. The longitudinal design means that the patients' situations have changed over time, which means that each consultation has a separate agenda; the patient's health situation has changed, their medications may be changed, and who is responsible for administering medications is also changed along the care transitions. Therefore, the results presented in this study are based on analysis of how the 48 different doctors responded to patients' problem disclosures in 74 different and unique consultations (since one patient received the first ward visit and discharge visit together). We have tried to make this point clearer throughout. We have also included a short section about the analysis method- Microanalysis of Clinical Interactions [3](MCI), page 4, aiming to clarify how the method is constructed with a qualitative and quantitative phase, both considered important, and how quantitative results should be interpreted.

		We hope that this, together with several edits in our manuscript and the added information under limitations (page 18), will address your concerns and meet your approval.
4	Related to this, the authors also state that these are consultations based on authentic patient-doctor consultations; it is true that these are real consultations, but more caution should be exhibited in describing these as extensively generalizable as patients still presumably needed to provide consent to participate in the study and have their information audio-recorded.	We have noted your concern, and have reread our manuscript with this in mind, and have edited our text so that results are presented without encouraging unwarranted and extensive generalisation. We have also added a note of caution regarding interpretation of quantitative findings due to the size and selection of the study population under limitations, see page 18. We would like to follow up on your feedback: We agree that patients and doctors in this study are influenced by the study setting, leading to more talk about medication use. Due to the recruitment process, we believe that the patients in our cohort are less frail than the average patient admitted to the hospital for HF treatment, something we have accounted for under limitations of the study. We believe patients with lower functional levels would have more problems. Similarly, we believe that the doctors too were influenced by participation in the study. Having an observer present and being audio-recorded is likely to have resulted in the doctors trying to show their very best practice in line with their professional training – leading to doctors being more vigilant, more patient centred in their approach, addressing more, rather than less, of the patients' disclosed adherence problems. Therefore, we believe that the presence of our phenomena of interest that we could observe in the audio-recorded consultations (patients' medication adherence disclosures, doctors addressing actions, patients' negative feedback) is higher than what we would expect under "normal practice". Even if "best practice" deviates from "normal practice", results are suitable to indicate quality levels and generate ideas for improvement efforts.
5	Overall, it seems this this manuscript should be presented more in the context of a qualitative study as fundamentally the transcripts and their analysis are more closely aligned with those methods.	We do not agree that the analysis of interaction is necessarily aligned with qualitative research. Clinical communication literature includes both qualitative and quantitative approaches. However, we feel we were not clear in our initial description of the method and have attempted to explain it in the manuscript in more detail.

		In addition, the study was not designed to provide thick descriptions or deep insight into whether or how clinicians address patient disclosures about medication adherence at home. Instead, it stayed at the surface level of what happened in the interactions. We have attempted to include more information about the analysis method to be clearer about how we moved from an inductive approach (which could appear qualitative in orientation) to clear definitions, coding, quantification, and comparison within the sample. We feel presenting this study under a qualitative frame might misrepresent our approach and analysis and create unmet expectations from readers.
#	Minor Comments to author:	Our response:
6	The abstract conclusion does not align with the results presented in there; at a minimum, it should be clearer which types of problems are unintentional versus unintentional. And, the conclusion suggests that comparative statistics were used, but only descriptive statistics were used. Recommend striking all such comparative language (e.g., "more likely to address").	Thank you for pointing out that we needed to improve the coherence between results and conclusion in the abstract. We have rewritten the abstract, providing examples of problems that are intentional/unintentional, added the results from our calculation of odds ratio using mixed effects logistic regression, and made several edits to emphasise that this is an explorative study.
7	- How many researchers coded each transcript? This is not clear from the data provided.	Thank you for pointing out that this was unclear. We have rewritten how the coding was conducted under Methods, page 5.
8	- A framework for 'intentional' versus 'unintentional' non-adherence would be helpful; a prior paper is cited but this is not particularly clear.	Thank you for pointing out that it would be helpful with more information about Rob Horne's "perceptions and practicalities" framework (PAPA)[4]. We have revised our manuscript to clarify our analysis and findings to readers under Methods, page 5. In addition, we have redesigned Table 2 (page 8) to clarify the links between the topic of patients' adherence problem disclosure and categorisation according to the PAPA Framework. Also, we have made available how we have described and categorised all of the 62 redflag-topics in the supplementary materials, file S2, page 50.

1. How to handle polypharmacy in heart failure. A clinical consensus statement of the Heart Failure Association of the ESC. *Eur J Heart Fail* doi: 10.1002/ejhf.3642

2. Ødegaard KM, Lirhus SS, Melberg HO, et al. Adherence and persistence to pharmacotherapy in patients with heart failure: a nationwide cohort study, 2014–2020. *ESC Heart Fail* 2023;10(1):405-15. doi: 10.1002/ehf2.14206
3. Gerwing J, Healing S, Menichetti J. Microanalysis of Clinical Interaction (MCI) (2023) in Bigi, S. & Rossi, M. G. (Eds.) *A pragmatic agenda for healthcare: fostering inclusion and active participation through shared understanding*: John Benjamins Publishing Company; 2023:43-74.
4. Horne R, Cooper V, Wileman V, Chan A. Supporting Adherence to Medicines for Long-Term Conditions: A Perceptions and Practicalities Approach Based on an Extended Common-Sense Model. *Eur Psychol* 2019;24(1):82-96. doi: 10.1027/1016-9040/a000353