

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	What do patients with heart failure disclose about medication adherence at home to their hospital and primary care doctors? Exploratory interaction-based observational cohort study
<b>AUTHORS</b>	Frigaard, Christine; Menichetti, Julia; Schirmer, Henrik; Bjørnstad, Herman; Breines Simonsen, Tone Helene; Wisloff, Torbjorn; Gulbrandsen, Pal; Gerwing, Jennifer

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Lauffenburger, Julie Brigham and Women's Hospital, Harvard Medical School, Division of Pharmacoepidemiology and Pharmacoeconomics
<b>REVIEW RETURNED</b>	04-Apr-2024

<b>GENERAL COMMENTS</b>	<p>This is an observational study of recorded conversations between patients with heart failure and their doctors in Norway. There are some interesting elements to this manuscript, but I have substantive comments below.</p> <p>Major comments:</p> <ul style="list-style-type: none"><li>- Recommend refraining from using inferential observational data analysis methods for the study. The sample size is too small in order to make conclusions about higher frequencies of conversations in some settings versus others. Instead, the study should focus describing the prevalence of MADICs and themes about the conversations rather than being comparative.<ul style="list-style-type: none"><li>o There are also correlations within patient (i.e., multiple visits/patient) that make comparative statistics fraught with clustering issues.</li><li>o Rather than these inferential statistics, recommend adding in illustrative quotes to support some of the findings in Table 5.</li></ul></li><li>- Frequency and rate statistics are tough to follow. I appreciate that they're adjusted for the length of the visit but makes it more difficult to follow. The visits themselves also seem pretty lengthy, which may reduce generalizability to other settings.</li></ul> <p>Minor comments:</p> <ul style="list-style-type: none"><li>- In the abstract, please provide the years of the study and its geographic location (i.e., 2022-2023, Norway).</li><li>- In the abstract background, please clearly indicate that the study population is heart failure to help reduce over-generalization.<ul style="list-style-type: none"><li>o Please also repeat this for the first paragraph of the Discussion.</li></ul></li><li>- The manuscript should include limitations about the presence of another individual during the encounters for recordings. It is not clear why a Dictaphone or similar method (without an extra person) could not have been used.</li></ul>
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	<ul style="list-style-type: none"> <li>- Recommend providing more detail on how the classification for whether the MADICI conversation was initiated was defined.</li> <li>- Please provide more information about the number of visits included per patient.</li> <li>- More detail should be provided about why “yes” or “no” answers were not included in MADICI conversations.</li> </ul>
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<b>REVIEWER</b>	JELÍNEK, Libor Palacky University Olomouc, Faculty of Medicine
<b>REVIEW RETURNED</b>	20-Apr-2024

<b>GENERAL COMMENTS</b>	<p>The present article is an interesting study of adherence in patients with heart failure. The conversation between patient and physician is the basis of patient care in general and is not often a topic of scientific inquiry. In order to improve patient care, it is necessary to have enough data to describe the exact circumstances. The use of a verbatim transcript of the interview and its subsequent analysis may be able to illuminate this scientific grey area. In the future, it would be good if a larger percentage of patients were successfully enrolled in the study; in this case, the relatively smaller sample of eligible patients limits the validity of the study because the vast majority of patients remain undescribed.</p>
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### VERSION 1 – AUTHOR RESPONSE

<b>Reviewer: 1, Dr. Julie Lauffenburger, Brigham and Women's Hospital, Harvard Medical School</b>		
#	Major Comments to author:	Our response:
2	<p>Recommend refraining from using inferential observational data analysis methods for the study. The sample size is too small in order to make conclusions about higher frequencies of conversations in some settings versus others. Instead, the study should focus describing the prevalence of MADICIs and themes about the conversations rather than being comparative.</p>	<p>We agree that using inferential observational data analysis methods and how we have presented these results in the manuscript may have been misleading. Based on reviewer’s comments we have therefore removed all results and references connected to Wesch’s test and chi-square test from the manuscript. Instead of reporting statistical tests, we used three different generalised linear mixed effects regressions with random effects on patient level to provide estimates and confidence intervals of differences to investigate some interesting observations further.</p> <p>This is an exploratory interaction-based observational study designed to generate ideas for communication-based interventions aimed to improve medication adherence among patients with heart failure. In general, interaction-based studies investigating the quality and quantity of talk about medication adherence is uncharted territory. Our study provides first evidence on how current practice works. For the qualitative aspects of the study,</p>

		the study has high information power (saturation of data is usually reached with 20 individual interviews, and multiple data increase information power, see <i>Malterud et al. Sample size in qualitative interview studies: guided by information power. Qual Health Res 2016; 26</i> ). We believe that our findings also allow for statistical investigations suitable to provide estimates of parameters needed for quantitative studies later on.
2.1	There are also correlations within patient (i.e., multiple visits/patient) that make comparative statistics fraught with clustering issues.	We have exchanged “Wesch’s test” and “chi-square test” with three different generalised linear mixed effects regressions with random effects on patient level to avoid this issue.
2.2	Rather than these inferential statistics, recommend adding in illustrative quotes to support some of the findings in Table 5.	Thank you for this suggestion. We have tried to make the link with the illustrative quotes for the findings/ the 6 types of red-flags in Table 3 (previously Table 4) clearer, by adding: “(see Table 3 for the specific red-flags definitions and examples)” at page 8.
3	Frequency and rate statistics are tough to follow. I appreciate that they’re adjusted for the length of the visit but makes it more difficult to follow. The visits themselves also seem pretty lengthy, which may reduce generalizability to other settings.	Thank you for pointing this out. We have rewritten how we present frequency and rate statistics in the Results section, page 7.  We have provided detailed results from each patient trajectory with length of visit in supplementary materials (supplementary file S5) to enable future researchers to scrutinise our findings and consider generalisability to their own healthcare setting. According to our clinical experience we find that the consultation times are within normal variation to be expected for hospital and GP visits in Norway (Norwegian GP visits are typically scheduled to 20 minutes per complaint).
#	Minor Comments to author:	Our response:
4	In the abstract, please provide the years of the study and its geographic location (i.e., 2022-2023, Norway).	We have added this information in the abstract.
5	In the abstract background, please clearly indicate that the study population is heart failure to help reduce over-generalization.	We have specified more clearly in the abstract that the study population is patients with heart failure.
5.1	Please also repeat this for the first paragraph of the Discussion.	We have specified more clearly in the discussion that the study population is patients with heart failure.
8	The manuscript should include limitations about the presence of another individual during the encounters for recordings. It is not clear why a Dictaphone or similar method (without an extra person) could not have been used.	We have added this information to make the need for an observer more clearly under Methods, page 3: The researchers collected audio-recordings using Olympus DS-9000 and used Livescribe Echo2Pen to make synchronised observation

		<p>notes. This combined solution was selected to (a) make data collection more feasible than it would have been with video-recordings, especially in the hospital setting and (b) still be able to record crucial information missing from the audio-recordings that might influence how we would interpret the speech (e.g., what happened during periods of silence, objects patients or doctors pointed to or showed each other, who was present and how they were positioned in the room).</p> <p>In addition, we have more clearly stated the presence of an observer in Limitations, page 12:  (2) participant reactivity to the study situation, especially due to an observer present during the consultation, may have led to more talk about medications and “best practice behaviour”.</p>
9	Recommend providing more detail on how the classification for whether the MADICI conversation was initiated was defined.	We have added an example to make this clearer, page 10.
10	Please provide more information about the number of visits included per patient.	Thank you for making us aware that this was unclear. We have added information to make this clearer throughout the manuscript.
11	More detail should be provided about why “yes” or “no” answers were not included in MADICI conversations.	We have included the following information to make this clearer under Results / Identifying MADICI, page 6: “The latter choice was conservative, but we deemed it necessary due to the ambiguity of the meaning of minimal verbal responses on audio-recordings, where any accompanying facial displays, or co-speech gestures were missing.”

<b>Reviewer: 2</b>		
<b>Dr. Libor JELÍNEK, Palacky University Olomouc, University Hospital Olomouc</b>		
<b>#</b>	<b>Comments to author:</b>	<b>Our response:</b>
12	The present article is an interesting study of adherence in patients with heart failure. The conversation between patient and physician is the basis of patient care in general and is not often a topic of scientific inquiry. In order to improve patient care, it is necessary to have enough data to describe the exact circumstances. The use of a verbatim transcript of the interview and its subsequent analysis may be able to illuminate this scientific grey area. In the	Thank you for acknowledging that our study explores a scientific grey area within medication adherence research. A sample of 25 patients with data at 3 time points is large enough for the exploratory nature of this study. We share with the reviewer the generalisability/validity concern (highlighted in the limitations of the study) and the hope that by describing current practice in three settings our results can be used to generate ideas for communication-based interventions to improve practice and

	<p>future, it would be good if a larger percentage of patients were successfully enrolled in the study; in this case, the relatively smaller sample of eligible patients limits the validity of the study because the vast majority of patients remain undescribed.</p>	<p>allow researchers to estimate parameters for future intervention studies.</p>
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**VERSION 2 – REVIEW**

<b>REVIEWER</b>	<p>Lauffenburger, Julie Brigham and Women's Hospital, Harvard Medical School, Division of Pharmacoepidemiology and Pharmacoeconomics</p>
<b>REVIEW RETURNED</b>	<p>03-Jun-2024</p>

<b>GENERAL COMMENTS</b>	<p>The authors have been sufficiently responsive.</p>
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