PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Wireless monitoring of high-risk patients using a wearable patch sensor: a clinical validation study
AUTHORS	Breteler, Martine Huizinga, Erik van Loon, Kim Leenen, Luke Dohmen, Daan Kalkman, Cor Blokhuis, Taco

VERSION 1 – REVIEW

REVIEWER	Guanghao Sun The University of Electro-Communications
REVIEW RETURNED	09-Nov-2017

GENERAL COMMENTS	The author discuss the results of using a wearable sensor for wireless monitoring of vital signs i.e., heart rate and respiration rate at a clinical setting. The manuscript is not extremely innovative in the sense that the authors evaluated a product wearable sensor provided via a health IT company, which may considered as an advertising for this company and its product. I find the novelty and relevance to weak to recommend acceptance.

REVIEWER	Fang Zhao Medical College of Georgia at Augusta University, USA
REVIEW RETURNED	13-Nov-2017

GENERAL COMMENTS	This paper investigated a wearable patch sensor in actual high-risk patients. This work is significant for continuous vital sign monitoring. I noticed that before using median filtering, the agreement between the patch and the bedside monitoring system are large. Since the patch also has the position and movement data, can you check if most of the measurements with a great deviation are due to the movement?

VERSION 1 – AUTHOR RESPONSE

Dear Hemali Bedi, Assistant Editor

Dear Reviewers,

We would like to thank you for the opportunity to resubmit our manuscript entitled “Reliability of wireless monitoring using a wearable patch sensor in high-risk surgical patients in the step-down unit: a clinical validation study” (bmjopen-2017-020162) to BMJ Open. We are grateful to the reviewers for their helpful remarks and suggestions. Hereafter, we respond to their suggestions, which are now incorporated in the revised version of the manuscript. The revised manuscript has been read and approved by all authors.

We hope you will find the present version of our manuscript suitable for publication.

Yours sincerely,
Martine Breteler, MSc

Editorial Requirements
- Please revise your title to state the research question, study design, and setting (location). This is the preferred format for the journal.

The title has been revised to state the research question, study design and setting more explicitly to: “Reliability of wireless monitoring using a wearable patch sensor in high-risk surgical patients in the step-down unit: a clinical validation study”. We changed this on the title page on page 1.

- Please complete and include a STROBE check-list, ensuring that all points are included and state the page numbers where each item can be found: the check-list can be downloaded from here: http://www.strobe-statement.org/?id=available-checklists

We have completed and included the STROBE check-list for cohort studies to ensure that all points are included within the manuscript. All page numbers of each item of the STROBE checklist are enclosed.

Reviewer(s)' Comments to Author:

Reviewer 1#

1.1 The author discuss the results of using a wearable sensor for wireless monitoring of vital signs i.e., heart rate and respiration rate at a clinical setting. The manuscript is not extremely innovative in the sense that the authors evaluated a product wearable sensor provided via a health IT company, which may considered as an advertising for this company and its product. I find the novelty and relevance to weak to recommend acceptance.

We like to stress that we did not receive funding from the manufacturer of the wearable sensor (HealthPatch MD from manufacturer VitalConnect Inc.). Instead, we purchased the wearable sensor using institutional funds of our hospital to fully ensure an independent analysis in a clinically relevant setting. Therefore, we consider this study as a critical independent evaluation of this innovative product. That means there is no conflict of interest. In addition, the manufacturer neither had any insight or influence on drafting this manuscript.
We have added the following comment to the Competing interests section (page 11): To ensure independent analysis, the wearable sensor (HealthPatch MD) was purchased from VitalConnect Inc, the manufacturer of the HealthPatch MD.

Reviewer 2#

2.1 This paper investigated a wearable patch sensor in actual high-risk patients. This work is significant for continuous vital sign monitoring. I noticed that before using median filtering, the agreement between the patch and the bedside monitoring system are large. Since the patch also has the position and movement data, can you check if most of the measurements with a great deviation are due to the movement?

We fully agree with the reviewer that the agreement between the patch and the bedside monitoring system before median filtering might deviate more during periods of movement. We have considered to use position and movement data as well during this study, however this was not possible due to the following reasons. The movement data (raw accelerometer data streams) was not regulatory cleared for medical purposes (no CE clearance) and therefore, accelerometer data streams were disabled. The manufacturer now provides non-medical sensors for consumer purposes with the activity streams enabled, but these were not used in this study. In addition, we have collected position data, but these were of limited value since the manual posture calibration (within the settings of the HealthWatch application on the iPad) asks to calibrate while the patient is standing or sitting upright. The latter was not possible in this population of high-risk surgical patients in the early postoperative phase. Nonetheless, we agree with the reviewer that movement data may help to distinguish between valid data and artefacts.

Because of the aforementioned reasons, we were not able to ascertain if measurements with a large deviation were due to movement. We have revised the manuscript accordingly, since it was stated in the previous version of the manuscript that the “wireless sensor can measure position and movement”.

Reviewer 3#

Dear editor. Thank you for an opportunity to review this article that is generally well written and interesting describing novel technology used in real hospital and patient setting. The text is generally easy to read and statistics seem to be appropriate for showing the results. However, there are some questions raised by the manuscript and as they partly include revision of tables, figures and structure of introduction they can be considered as major revisions:

3.1 The abstract is clear and informative covering the most important findings and conclusions

We thank the reviewer for his compliment.

3.2 The introduction is concentrated on explaining the EWS and its importance in hospital patients. However, the findings from previous publications and technologies studying the same subject (such as wrist based sensors, respiratory rate measurement using different technologies, previous studies using this sensor in different setting) is not described well. Obviously at least some of the references 23-25 have been made with the same sensor?

We agree with the reviewer that the Introduction would benefit from more details from earlier published work. Reference 23 and 25 refer to the articles in which the same sensor was studied. We added the following comments on page 3 of the introduction: “Two studies reported satisfactory agreement between heart rate, respiration rate and their respective reference devices. However, these measurements were obtained from healthy participants in controlled conditions. Another study showed reliable heart rates and respiration rates in the majority of patients, but these data was limited

to short periods of measurements in patients with comorbid conditions[23-25]. As such, we cannot translate these findings accordingly to patients in a clinical environment at risk for complications".

3.3 Was the study registered in clinicaltrials.gov or similar prior to study measurements

No, since this study was not a randomized controlled trial we did not register it in clinicaltrials.gov. However, we have obtained formal approval for this study from our local ethical committee (number 15/550). We agree that for future studies registration is advisable even for observational studies.

3.4 p4 line 38 - The verification of the data was possible using remote monitoring. Was it done constantly to allow data verification?

Yes, we checked daily whether the sensor was still securely attached to the patient, whether no data loss occurred from transmission failure and whether there were any gross deviations from the reference monitor.
We added the following comment to the methods section on page 4: "Quality of the sensor data was verified several times by the researchers during data collection."

3.5 p5 line 16 Were the patients stationary during the movement period? Was invasive measurement part of the protocol, if not it might be left out or mentioned that patients were monitored with routine monitoring including ECG and impedance monitoring.

We thank the reviewer for this suggestion. We agree that the information regarding invasive measurement of blood pressure and arterial oxygen saturation via pulse oximetry is redundant as this was not part of the study protocol. Patients were monitored with a bedside routine monitoring system that uses ECG and impedance monitoring. We removed this sentence from the Methods section on page 5. Furthermore, it needs to be noted that patients were continuously monitored with the bedside reference system (wired), also during mobilizing on a chair next to bed.

3.6 p5 r28 data was resampled? Was the data averaged to 1-minute intervals or were there point measurements selected corresponding to reference monitor?

The data of the HealthPatch sensor was indeed resampled. The data was not averaged to 1-minute intervals as this may filter outliers. Instead, one point measurements per minute of the HealthPatch sensor were retained corresponding to the nearest time point of the reference monitor. Thus, less samples of the HealthPatch sensor were retained from a more frequently sampled signal (once every four seconds to once every minute). We realize that this requires clarification and added the following sentence in the Methods section on page 5: "(i.e., one sample per minute of the sensor was retained corresponding to the nearest time point of the reference monitor)".

3.7 p6 r 20 Was the data from reference monitor just corrupted or what was the problem with data retrieval? Please, comment.

We agree with the reviewer that this phrase requires clarification. Data from the reference monitor was not corrupted during patient measurements. The researchers received an automatically generated report every night with the vital signs data directly from the database server of the reference system. Unfortunately, we received a number of empty reports with no vital signs data due to malfunctioning of the database server. Since the data was only stored for 48 hours, we were not able to retrieve the vital signs data back. This resulted in data loss due to a database dropout without any consequences for actual patient monitoring on the stepdown unit.

3.8 p6 table 1. What is no? Does it refer to number (n)?
"No" indeed refers to number (n). We thank the reviewer and revised table 1 on page 6 accordingly.

3.9 The writers mention previous results here, but should also comment the results and their difference to the ones in the current study. Has the performance been better, worse or similar? Why?

We agree with the reviewer that results of our study needs to be better interpreted in relation to previous results. Therefore, we have adjusted the 'Strengths' section on page 10:
"Most studies were actually obtained under controlled laboratory conditions[25,27,33]. These studies demonstrated the ability of the HealthPatch sensor to accurately measure HR and RR in adult participants. Although the performance of heart rate under controlled conditions is similar, these results cannot be compared to our findings obtained in clinical practice. Hernandez et al. [24] reported a higher accuracy for HR and RR measurements with the SensiumVitals digital patch in stable patients with comorbid conditions for a limited time period (2h) compared to our study. Other studies used intermittent nurse observations on the ward as the only reference. Weenk et al. [34] reported that both HR and RR of the HealthPatch were in agreement with nurse measurements, although wide limits of agreement were found. Another study compared RR measurements of nurses with readings from the SensiumVitals digital patch and found inadequate agreement [35]. Although these studies showed the feasibility of wireless technology in clinical practice, comparison with nurse readings cannot validate the continuous performance of the wireless devices. Moreover, these wireless monitoring devices are not intended to deliver 'spot' readings for EWS, i.e., their use was evaluated for a purpose outside the intended scope of use"

3.10 Filtering. How was it decided? Was it tested before? Would continuous averaging work better? what would the results look like with that? The filtering should also be described in methods section.

We thank the reviewer for the valuable input and realize that the method and reasons for filtering need clarification. Applying a median filter over 15-minutes (a median over subsequent epochs of 15 minutes) was decided since both the reference method and the wireless sensor showed considerable variability in results, especially for RR measurements as can be seen in Figure 1. Such transient very high or low RR are often caused by movement artefacts. We were interested to see whether filtering would reduce these artefacts and increase the accuracy of measurements. Obviously the longer the filtering period, the more effective the artefact removal, but at the expense of early warning. We selected 15-minute median filtering period on clinical grounds to be still compatible with early warning and quick response times. Moreover, improved elimination of outliers could result in a higher proportion of epochs with reliable HR and RR resulting in lower false positive alarms. This is extremely important if remote patient monitoring with wearable sensors is to be deployed on general wards.

Table 1 (attached as supplementary file for Editor) shows the results of continuous averaging (a 'moving' median filter with a window of 15 minutes) on the accuracy of HR and RR. As compared to the median filtering over 15 minute epochs, reliability did not improve, neither deteriorate. To show the effect of both filters (median filter and moving median filter respectively) on HR and RR trend during the first four postoperative days of a patient, we added Figure 1B and Figure 1C in the Appendix section. We suggest not to include these figures within the manuscript, but it might be added as supplementary material.

Based on the comment of the reviewer we adjusted the Methods section on page 5: "a median filter over a 15-minute period was applied to study the effect on HR and RR outliers and to further explore

the potential of the wireless sensor in clinical practice. This filtering was calculated as a median over subsequent epochs of 15 minutes."

3.11 Filtering remains unclear for the reader. Does it mean continuous averaging within last 15 minutes, or that only every 15 minutes results were averaged as one number?

We agree that the filtering procedure needs more clarification. In accordance with our response on remark 3.10, the filtering over 15-minute data epochs was calculated as a median of every 15 minutes, i.e., not continuously averaged with a moving filter. Also, we decided not to use a mean, because a median better removes single outliers.

As noted in the previous remark 3.10 we have added the following sentence to the Methods section on page 5: "…a median filter over a 15-minute period was applied to study the effect on HR and RR outliers and to further explore the potential of the wireless sensor in clinical practice. This filtering was calculated as a median over subsequent epochs of 15 minutes…."

3.12 p11 r17 "wireless continuous monitoring…" Since the accuracy was rather poor, the potential of remote monitoring remains to be shown remains to be shown. Please word differently.

We agree with the reviewer that our wording should be rephrased. We have adjusted the conclusion on page 11 to the following: "Wireless continuous monitoring may have the potential to contribute to early recognition of physiological decline in high-risk patients. The tested wireless sensor was able to accurately record heart rate, but the accuracy of respiratory rate needs further optimization to reduce the incidence of false alarms and allow timely recognition of altered breathing patterns. "

3.13 Most figures refer to A and B but those are not marked in the figures.

We thank the reviewer and revised the figures accordingly.

3.14 Fig 1. Could 15 minutes averaging be included in the figure? It might visualize the difference between methods.

We thank the reviewer for this valuable suggestion. Including the results in the same figure reduced the clarity of Figure 1 and therefore we included an additional Figure 1B with the median filter over 15 minutes. In accordance to our response on 3.10 we also included an additional Figure 1C with a moving median filter of 15 minutes to show any differences in methods used. We suggest not to include these figures within the manuscript, but it might be added as supplementary material.

3.15 Reference 23 is incomplete. The paper or publication name is missing.

We thank the reviewer for his alertness. The reference has been adjusted accordingly.

VERSION 2 – REVIEW

REVIEWER	Jarkko Harju Tampere University Hospital
REVIEW RETURNED	28-Dec-2017

GENERAL COMMENTS	Thank you for the revised version that corrected the unclear parts of

	the manuscript. Based on authors suggestion and explanation figure 1c is not needed. I have no further comments for the manuscript.