Human longevity : crosstalk between the brain and periphery

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CHAPTER 10

COMPARATIVE ANALYSIS OF THE EQUIVITAL EQ02 LIFEMONITOR WITH HOLTER AMBULATORY ECG DEVICE FOR CONTINUOUS MEASUREMENT OF ECG, HEART RATE AND HEART RATE VARIABILITY: A VALIDATION STUDY FOR PRECISION AND ACCURACY.

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ABSTRACT

The Equivital (EQ02) is a multi-parameter telemetric device offering both real-time and/or retrospective, synchronized monitoring of ECG, HR and HRV, respiration, activity and temperature. Unlike the Holter, which is the gold standard for continuous ECG measurement, EQO2 continuously monitors ECG via electrodes interwoven in the textile of a wearable belt. We aimed to compare EQ02 with the Holter for continuous home measurement of ECG, heart rate (HR) and heart rate variability (HRV).

Eighteen healthy participants wore, simultaneously for 24 hours, the Holter and EQ02 monitors. Per participant, averaged HR and HRV per 5 minutes from the two devices were compared using Pearson correlation, paired T-test and Blant-Altman analyses. Accuracy and precision metrics included mean absolute relative difference (MARD).

Artefact content of EQ02 data varied widely between (range 1.93% to 56.45%) and within (range 0.75% to 99.61%) participants. Comparing the EQ02 to the Holter, the Pearson correlations were respectively 0.724, 0.955 and 0.997 for datasets containing all data and data with <50% or <20% artefacts respectively. For datasets containing respectively all data, data with <50% or <20% artefacts, bias estimated by Bland-Altman analysis was -2.8, -1.0 and -0.8 beats per minute and 24h MARD was 7.08, 3.01 and 1.5. After selecting a three-hour stretch of data containing 1.15% artefacts, Pearson correlation was 0.786 for HRV measured as standard deviation of NN intervals (SDNN).

Although the EQ02 can accurately measure ECG and HRV, its accuracy and precision is highly dependent on artefact content. This is a limitation for clinical use in individual patients. However, the advantages of the EQ02 (ability to simultaneously monitor several physiologic parameters) may outweigh its disadvantages (higher artefact load) for research purposes and/ or for home monitoring in larger groups of study participants. Further studies can be aimed at minimizing the artefacts.

INTRODUCTION

With cardiovascular diseases still representing a leading cause of death globally, continuous electrocardiography (ECG) measurement is becoming increasingly important. Continuous ECG measurements yields valuable information on heart rate (HR) and its variability (HRV) that can be measured at a beat-to-beat level. Their direct clinical importance has been demonstrated in numerous studies. HR is a major risk factor for morbidity and mortality in cardiovascular diseases [1, 2]. Even in apparently healthy individuals, HR has predictive value for sudden cardiac death [3]. Furthermore, control of HR has become the focus of drug development for cardiovascular diseases [4]. In addition to HR, continuous measurement heart rate variability (HRV) serves as an index of cardiac sympathetic and parasympathetic activity [5]. HR and HRV associates with cardiac [3], physiological [6], psychological [7, 8] and sleep- related disorders [9]; and are being used as prognostic indicators for cardiac and non-cardiac diseases, such as idiopathic dilated myopathy [10], myocardial infarction [11], renal failure [12], end stage renal disease [13] and cancer [14].

ECG signals can be obtained from varying sources, such as Holter monitoring, bedside monitoring of vital parameters, systems for surface ECG, ergometric stress tests and systems for telemetry [15]. Of these, the Holter monitor (Holter) is the gold standard for continuous ECG measurement. The Holter records ECG signals via electrodes attached to the chest. However, over the years different innovative devices that are able to comfortably monitor ECG simultaneously with other physiological parameters for a prolonged period of time in freely moving subjects have become available. The Equivital EQ02 Lifemonitor (EQ02,) is a convenient and safe wireless ambulatory device that continuously measures ECG, HR and HRV via a chest-worn sensor belt embedding textile-based electrodes. In addition to cardiac parameters, EQ02 also measure breathing rate, body position and movement (accelerometry), and skin and core body temperature, all synchronized and time- stamped to provide contextual significance for possible diagnostic, therapeutic or research purposes. Although EQ02 has been used in several studies, e.g. for ambulatory monitoring of pilots, athletes and military personnel, both under physiological and extreme environmental conditions [16-20], EQ02 has not yet been validated against the gold standard for measurement of cardiac parameters.

Here for the first time, we compared the accuracy of EQ02 and Holter for continuous ECG, HR and HRV monitoring. The EQ02 and Holter were worn simultaneously for 24hours in home setting by an heterogeneous group of healthy male and female volunteers. Results were analyzed in point accuracy (including absolute and relative differences), monitor reliability and precision metrics for both devices.

METHODS

Ethics statement

This study was approved by the institutional review board of Leiden University Medical Center (LUMC) under protocol P11.116. All study participants gave written informed consent.

Study participants

The present study was embedded in the Switchbox Study, which was a sub-study of the Leiden Longevity Study (LLS). The LLS was originally designed to investigate genetic and phenotypic biomarkers associated with human longevity. A more detailed description of the study design and recruitment strategy for switchbox study [21] and the LLS [22] has been described elsewhere. The present study population consisted of 18 healthy adult male and female volunteers from the local population. The only exclusion criterion was presence of obvious chest deformity, which would impair lifemonitor belt fitting.

Apart from the 18 subjects, artefact percentage was determined in all raw Holter recordings that were collected in the department of cardiology of the LUMC in 2014. In total, artefact data from ECG recording of 4143 persons were used. Apart from the percentage of artefacts contained in the recordings, no other data from these individuals were used. Furthermore, similar raw artefact data were extracted from EQ02 recordings from 200 switchbox participants.

Experimental protocol

After body mass index and waist: hip ratio was measured, participants wore, simultaneously, the EQ02 monitor, a Holter and a Fitbit one™. These were turned on approximately concurrently. Participants undertook their usual daily activities, except swimming. They additionally kept a detailed diary of type and timing of all their activities.

Study devices

EQ02 monitoring

The EQ02 (Equivital EQ02, Hidalgo, UK) continuously measured ECG on two channels via three electrodes (table 1). The EQ02 monitoring system consists of a LM 1000 Lifemonitor sensor electronic module (SEM), Lifemonitor belts of varying sizes, a SEM lead and charging dock, a blue tooth USB dongle for laptop/ PC, and an Equivital Manager to configure SEMs and to download and export data. For this study, SEMs were configured in clinical mode, and data reported retrospectively at local time. Bluetooth connectivity was disabled and data transmission was at partial disclosure.

An appropriately sized lifemonitor belt held the SEM onto the subject's body. Its textile-based electrodes were moistened with water before making contact with the participant's skin. SEMs were charged for approximately one hour after 12 hours of recording. Upon study completion, SEM data was uploaded onto the Equivital manager; from where date- and time- stamped ECG, inter-beat interval and summary data of vital signs were extracted and exported.

Holter ECG monitoring

The Holter (SEER MC Holter monitor, GE Healthcare, USA) measured ECG on three channels. The Holter consisted of seven electrodes; color- coded lead wires and a battery operated, digital ECG recorder. Before placement of electrodes, participants' skin were prepared with alcohol and 3M red dot 2236 trace prep (3M Healthcare, Canada) to remove nonconductive skin layer and reduce skin impedance and eventual artefacts. Color- coded leads were clipped on to 3M electrodes (type 2271, 3M Healthcare, Canada) and placed as shown in figure 1.

TABLE 10.1 | Technical characteristics of the EQ02 and Holter monitors

	Holter	Equivital (EQ02) lifemonitor
Acceptance	Gold standard	Relatively new device
Parameters measured	ECG only	ECG, breathing rate, tri-axial accelerometry, skin temperature, core body temperature and energy expenditure, all fully synchronized.
Data presentation	Retrospective	Real- time (live) and retrospective (date- and time- stamped).
Recording modes	Ambulatory	Ambulatory and Clinical
Recording time	Usually 24- 48 hours	Fully charged battery lasts 24- 48 hours*. The internal memory of the recorder stores up to 50 days of data.
Channels	3	2
Electrodes	7	3
Type of Electrodes	Stick- on	Textile electrodes
Skin preparation	Necessary	
(Removal of non-conductive skin layer)	None	
Convenience	Can be cumbersome due to multiple lead wires, sensor pads, clips and/or re- enforcing tapes, carry-case	Easy to wear belt
Analysis software	MARS	Vivosense

**For this study, the monitors were charged after 12 hours of use*

Fitbit oneTM wireless activity and sleep tracker

The Fitbit oneTM (Fitbit, San Franscisco, USA) was worn on the waist (belt) during the day for tracking activity (step-counts) and on the sleep wrist- band at night for tracking sleep length and number and durations of awakenings. Upon study completion, data was downloaded via Fitbit dashboard. Sleep efficiency was extracted as a composite of time to fall asleep, number of awakenings and restless periods, total time in bed and the actual sleep time [23].

Data management

While data extracted from EQ02 were automatically time- and date stamped (date, time in hr., min., sec. & ms.), Holter data were not. Data from both devices were synchronized based

on the Equivital time stamp, by selecting aberrations (non-sinus beats) in two consecutive heart beats from the Holter that corresponded to those from EQ02, mostly around the start of the recording. Five-minute trends (averages) of HR, RR and HRV parameters from synchronized data were then extracted for analysis.

Data management: Holter monitor

Holter ECG data were analysed using MARS ambulatory Holter ECG analysis system (GE Healthcare, Milwaukee, WI, USA). After extraction, an exportable file was visible on MARS, which contained the annotations 'N' (normal sinus-rhythm), 'V' (ventricular-beat), 'S' (supraventricular-beat) or 'X' (artefact) (figure 1A). The software recognized and grouped QRS complexes on similarity. This process was manually checked and corrected when the recognition of QRS-location was faulty or the sinus/non-sinus labeling was wrong.

EQ02 data management: Vivosense

Raw ECG data from EQ02 was analyzed using Vivosense modular physiological monitoring and analysis platform (Vivonoetics, San Diego, USA). EQ02 data were visualized with Cardiac layout (figure 1B), for inspecting each ECG channel and derived R- wave markings, and artefact identification. This layout also contains accelerometer data channels for contextual interpretation.

The EQ02 unit provided two leads of ECG measurements that shared a common reference. These were denoted as SEM_ecg1 (primary raw ECG signal) and SEM_ecg2 (secondary raw ECG signal) respectively. Vivosense processed and performed QRS detection on both channels to generate two sets of R- wave markings. We chose SEM_ecg1, which was then scaled and filtered by Vivosense, as primary source ECG for derivation of RR, HR, and HRV parameters.

Artefacts in the ECG signals were identified and annotated. Artefacts were defined as (i) distorted signals and/ or (ii) segments of signal in which the different waves of the ECG complex could not be clearly identified. Vivosense offers an algorithm that automatically marks and calculates artefact percentage (figure 1B), and no-, low-, medium- and high-artefact cleaning/ noise reduction options. The automatic artefact-marking algorithm takes into account the minimum and maximum allowable heart rates, presence of ectopic beats, maximal interpolation length and signal noise. After removal of charging times, Vivosense automatic cleaning of the data in this study was performed by selecting the

timeframe to be cleaned, setting the sensitivity level of the automatic cleaning algorithm at medium noise filtering, and setting the minimal and maximal allowable HR limits to 30 and 220 beats per minutes respectively.

In addition, complete manual cleaning of EQ02 data was done for one participant, involving the time- intensive process of relocating incorrectly automatically recognized QRS-complexes to correct locations, and manually identifying and excluding artefacts.

Furthermore, Vivosense software calculated and displayed eight HRV indices, namely, average of NN-intervals (ANN), standard deviation of NN-intervals (SDNN), standard deviation of 5-minute averages of NN-intervals (SDANN), standard deviation of successive differences of NN-intervals (SDSD), square root of the mean squared differences of successive intervals (RMSSD), mean of the standard deviation of 5-minute NN-intervals (SDNNi), number of adjacent NN-intervals with a difference less than 50ms (NN50) and ratio of NN50 to total number of NN-intervals (pNN50).

Accuracy, precision and reliability metrics

The point accuracy of EQ02 was measured in terms of the relative difference (RD) and absolute relative difference (ARD) of HR measurements to assess respectively the bias (relative to the Holter) and the average error. The RD was calculated using the formula [(EQ02 HR – Holter HR)/Holter HR]. The ARD was calculated using the formula [|EQ02 HR – Holter HR|/Holter HR]. We additionally determined the mean absolute relative difference (MARD) of all paired points. The mean and standard deviation (SD) of MARDs from all 18 participants were computed for each synchronized 24h HR measurement, to assess respectively the accuracy and precision of EQ02 HR measurements.

Statistical analysis

Of the original 5182 paired data points of 5- minute HR averages from 18 participants, 4736 (91.4%) remained after exclusion of charging times. From these, three datasets were made containing: 1) raw data (all 4736 data points) 2) filtered data containing <50% artefacts (4059 (85.5%) data points) 3) filtered data containing <20% artefacts (3677 (77.6%) data points).

To analyze the strength of the linear relationship and agreement between both devices, synchronized data from both devices were analyzed with Pearson correlation analysis and Bland-Altman plots for all three datasets. To explore possible determinants of artefacts,

we stratified data based on sex, day and night, and tertiles of waist: hip ratios, tertiles of activity. The artefact distribution in strata was compared using Chi-square (X2) test. The association between BMI and artefact load was assessed using linear regression.

The per-participant estimates of HR and HRV derived from EQ02 and Holter monitors were compared with paired t-tests. For all paired points, RD, ARD and MARD were determined using aforementioned formulae.

Graphs were drawn using GraphPad Prism version 5 (GraphPad, San Diego, CA). All statistical analyses were performed using SPSS v.20 (SPPS Inc., Chicago, U.S.A.). Two-sided p-values below 0.05 were considered statistically significant.

RESULTS

Heart rate

Characteristics of study participants are summarized in table 2 and described in details per-person in supplementary table 1. The mean age of the participants was 27.6 years (range 19-57 years); 10 (55%) were males. The activity pattern of the participants was variable, ranging from 5,017 to 14,265 steps taken in 24 hours. Medical history showed that none of the participants had persistent chest pain, tiredness, dyspnea, lightheadedness, palpitations, cardiovascular diseases, hypertension, endocrine or other diseases. Two participants had hypothyroidism, for which they used levothyroxine (data not shown).

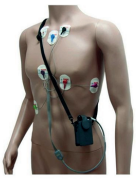
Different components of the cardiac cycle, including p-waves were clearly identifiable in the ECG tracings from both the EQ02 and Holter (figure 1).

TABLE 10.2 | Subject characteristics

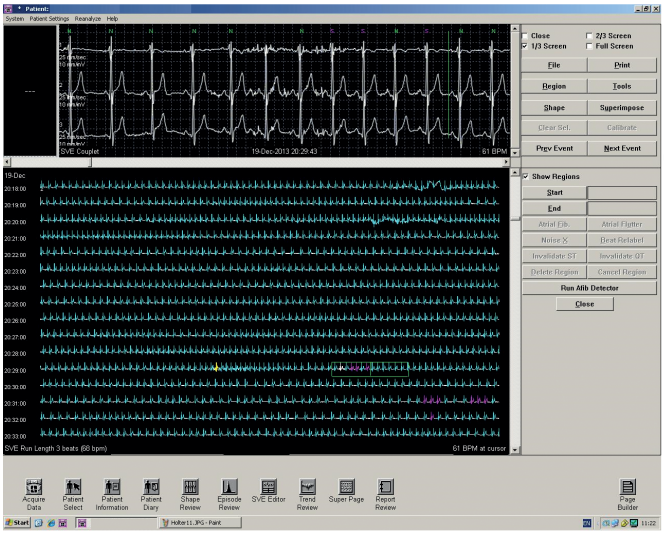
Demographics	**N=18**
Male n(%)	10(55)
Age, years	27.6(9.4)
Weight, kg	72(10.2)
BMI, kg/m2	22.5(2.4)
Waist: hip ratio	0.81(0.1)
Sleep (total hours)	580.2(156)
Step counts (total (mins) in 24 hours)	9635(2916)
% artefacts in raw EQ02 data*	19.0(14.7)

Data represent mean with standard deviation unless stated otherwise.

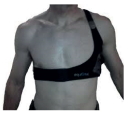
A. Holter ECG monitor

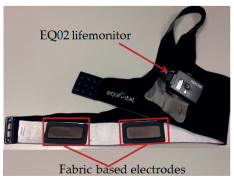


Holter data, analysed using MARS system



B. Equivital EQ02 lifemonitor





EQ02 data, analysed using Vivosense system

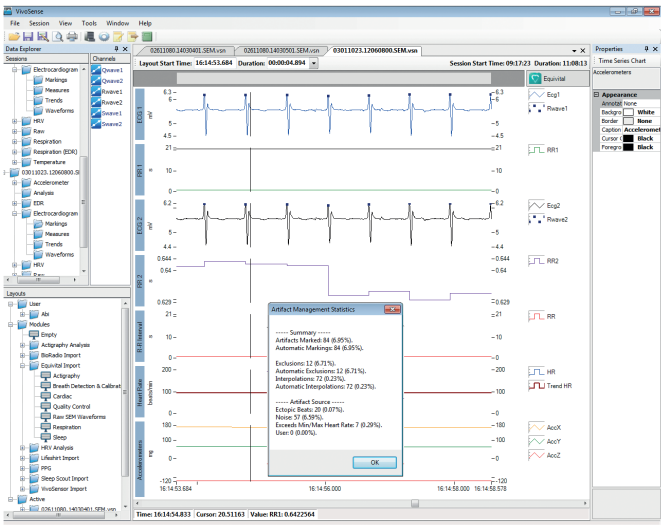


FIGURE 10.1 | Analysis software for Holter and EQ02 data management.

Figure 1A. shows the Holter monitor including its electrodes, lead wires, and its analytical software. Annotated tracings from the Holter can be seen on the MARS software. Figure 1B shows the EQ02 unit, consisting of the lifemonitor belt on which are three textile- based electrodes. ECG tracings are visualized on the cardiac layout of Vivosense software.

Artefact management

As shown in table 2, the average artefact percentage of the 24h EQ02 data was 19% (SD 14.7). However, marked differences existed in data quality (supplementary table 1) between participants (range 1.93% to 56.45%) and within participants (range 0.75% to 99.61%). Individual 24h graphs of Holter and EQ02 heart rate measurements of each of the 18 participants are shown in supplementary figure 1.

Figure 2 shows hourly averages of HR from the Holter, and EQ02 before cleaning, and after medium and high sensitivity cleaning for three representative participants with average artefact percentages over 24 hours of 1.93%, 56.45% and 22.15% respectively. Artefact percentages were variable throughout the day, but higher just around charging times, and lowest at night. At lower artefact percentages, there was good concordance between the EQ02 and Holter HR. In contrast, at higher artefacts percentages, there was discordance between the EQ02 and Holter HR values that persisted after applying the Vivosense automatic cleaning methods.

In addition, 24h EQ02 data for the participant in figure 2C was cleaned manually, which took 24 hours. Manual cleaning did not eliminate the discordance between Holter and EQ02 data at high artefacts percentages.

EQ02 sensor performance

Figure 3 display the Pearson correlation coefficients of HR measured using EQ02 and Holter for the three datasets sorted on artefact percentage. Pearson correlations were 0.724 for all data, and 0.955 and 0.997 for the datasets containing <50% and <20% artefacts respectively.

EQ02 point accuracy, mean accuracy and precision metrics

The point accuracy for EQ02 across the three datasets of varying artefact percentages are shown as RD and ARD distributions in figure 4A and B. For all data, 2246 of 4542 (49%) paired RD points had negative RD values. From the datasets containing <50% artefacts and <20% artefacts, respectively, 1802 of the 3882 (46%) and 1359 of the 3118 (43.6%) paired RD points had negative RD values. From the distribution of RD and ARD values shown in figure 4, the distribution of the underestimation extended over a broader range of HR values at higher artefact percentages.

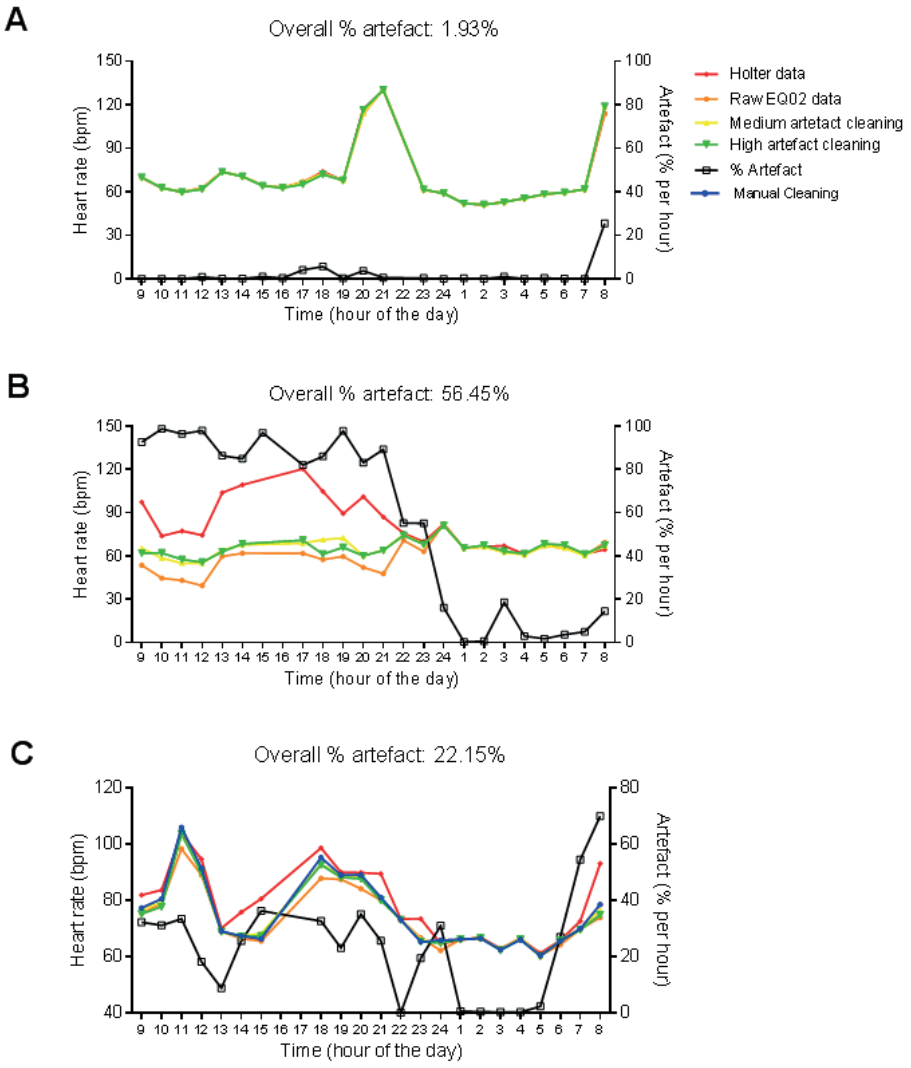


FIGURE 10.2 | 24h HR measurements by EQ02 and Holter.

Hourly averages of HR measured simultaneously using the EQ02 and Holter monitors for three participants (A, B and C). Raw EQ02 and automatically cleaned EQ02 data using the medium and high artefact sensitivity options of the Vivosense software are displayed. Artefact percentages over 24hours (above each graph) and per hour (right y-axis) are presented.

As an indicator of mean accuracy and precision of the EQ02, the MARD in EQ02 HR data relative to Holter HR over 24h are presented for the three data sets in figure 4C. The 24h MARD was 7.08±17% for all data, 3.01±10.55% for data containing <50% artefacts

and 1.5±10.51% for data containing <20% artefacts. As depicted by the SD of the MARD, while the precision did not markedly differ between <20% (SD 10.51) or <50% artefacts (SD 10.55), precision decreased at >50% artefacts (SD 17).

Agreement between devices

Bland- Altman plots of paired HR values from both devices are presented in figure 5, for the three datasets. Compared to the Holter, HR was on average lower when derived from EQ02, with respectively a mean (95% CI) difference of -2.8 (-29.8 to 24.3) beats per minute (bpm) for all data, -1.0 (-16.1 to 14.14) bpm for data <50% artefact and -0.8 (-13.5 to 11.8) bpm for data <20% artefacts.

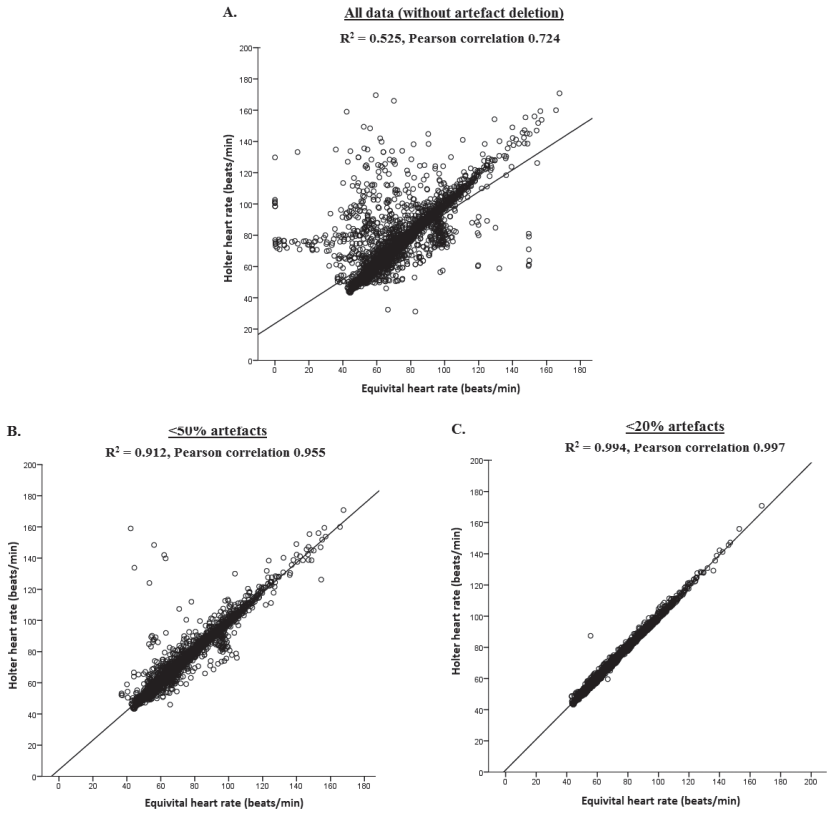


FIGURE 10.3 | Pearson correlations of HR measured by EQ02 and Holter.

Both R2 and Pearson correlation coefficients are shown for (A) all data, and filtered data containing (B) <50% artefacts and (C) < 20% artefacts.

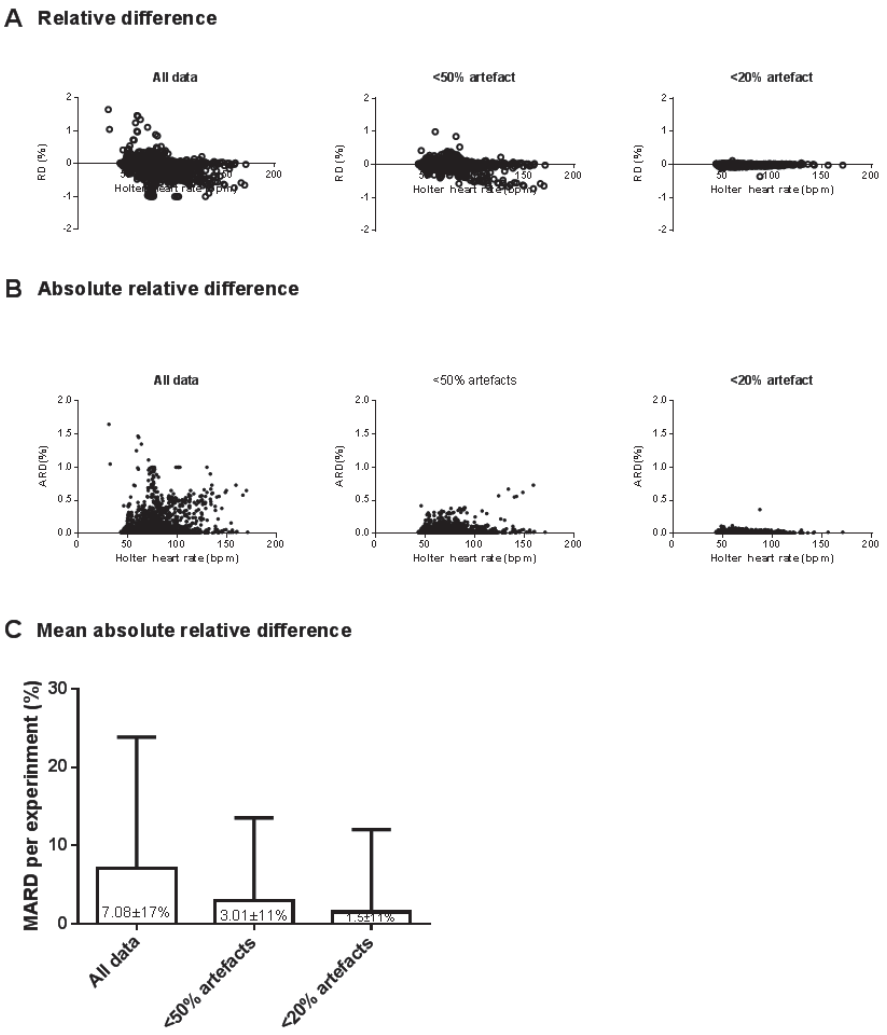


FIGURE 10.4 | Accuracy, precision and reliability of the EQ02 HR measurements.

The distribution, as a function of Holter values, of the relative difference (RD, panel A) and absolute RD (panel B) between each EQ02 HR measurement and its corresponding Holter HR value, for all data, and filtered data containing <50% and < 20% artefacts respectively. Panel C: MARD between EQ02- and Holter- derived HR values.

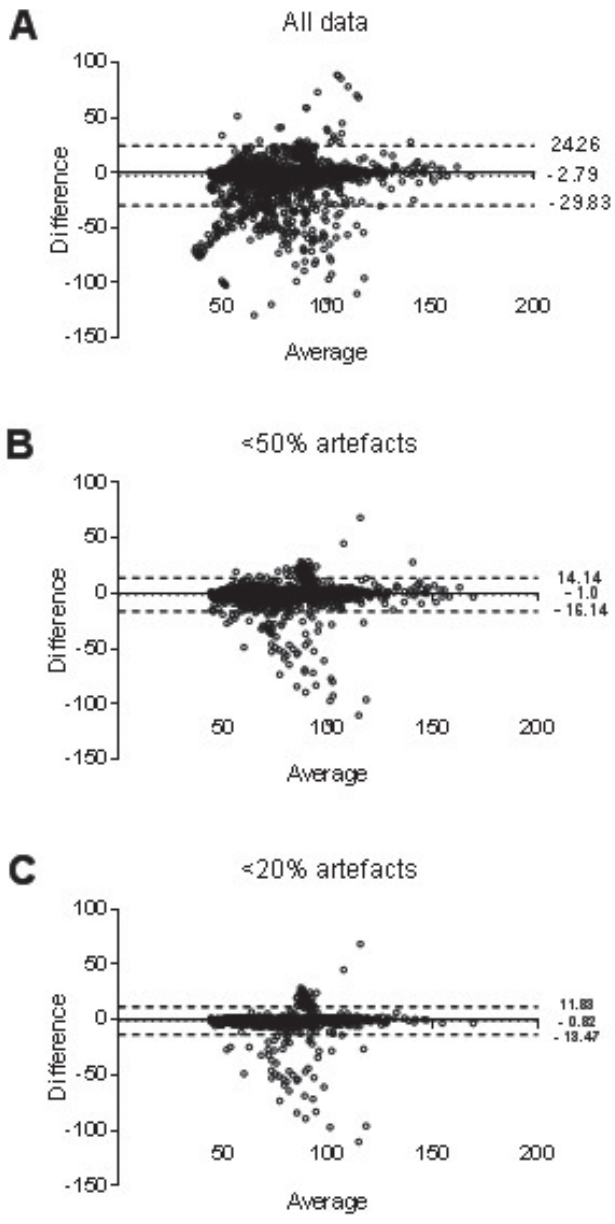


FIGURE 10.5 | Bland- Altman plots of HR measured by EQ02 and Holter.

Each dot represent paired (EQ02- Holter) HR values derived from all participants. The bias of the measurements (represented as solid lines) and the ± 1.96 SD (dotted lines) are presented for the measurements obtained for all data (A), filtered data containing <50% (B) artefacts and < 20% artefacts (C).

Evaluation of artefacts

In order to evaluate the artefact burden of the EQ02, we compared the artefact content of 24h Holter ECG recordings from 4,143 subjects with raw EQ02 data from 200 subjects. The average artefact percentage from the 4143 holter recordings was 2.95%, whereas the average artefact percentage from the 200 EQ02 recordings was 12.76%. Thus, the mean difference in artefact percentage in raw EQ02 compared to raw holter ECG was 10%. For the Holter, 77.9% of the 4,143 raw Holter ECG recordings had artefact percentage of ≤ 5%, whereas 65.5% of the 200 raw EQ02 ECG recordings had artefact percentage of ≤ 5%. The distribution of the artefacts is presented in figure 6.

Next, we evaluated possible sources of artefacts for the EQ02 recordings, including sex, waist: hip ratio, daytime versus nighttime (during which participants were asleep), activity (step counts) and BMI. The mean (SD) artefact percentages of male participants (19.4% (11.4)) was not significantly different (P=0.348) from that of females (15.9 (17.9)). When participants were divided into tertiles based on waist: hip ratio (w:h), tertile 1 (w:h range 0.71-0.76) had mean (SD) artefact percentage of 7.5 (3.5); tertile 2 (w:h range 0.77-0.83) had mean (SD) artefact percentage of 16.4 (6.0) while tertile 3 (w:h range 0.87-0.92) had mean (SD) artefact percentage of 29.7 (18.5) (P=0.014).

During the day, 62.9% of the data contained <20% artefacts, 17.15% contained 20-50% artefacts and 19.9% had 50-100% artefacts. In contrast, during the night, 82.7% of the data contained <20% artefacts, 12.4% contained 20-50% artefacts whereas 4.9% had 50-100% artefacts. Thus, there was considerably more artefacts during daytime compared to nighttime (p<0.001).

Furthermore, we also evaluated if activity of the participants, as measured using number of step counts taken during the study, had a bearing on artefacts percentage. Participants were divided into tertiles based on step counts, representing low activity (tertile 1, with 5017-8228 steps), medium activity (tertile 2 with 8229-11439 steps) and high activity (tertile 3 with 11440-14265 steps) respectively. For tertile 1 (least active), 73.3% of the data contained <20% artefacts, 11.8% contained 20-50% artefacts, and 14.9% of the data from the least active people contained 50-100% artefacts. For tertile 2 (medium active), 66.2% of the data contained <20% artefacts, 14.7% contained 20-50% artefacts, and 19.0% of the data contained 50-100% artefacts. Thus, there was comparatively more artefact in tertile 2 compared to tertile 1 (p<0.001). Similar significant result was obtained for comparison of tertile 3 (most active) to tertile 1 (p<0.001).

Finally, we assessed the association between BMI and artefact percentage. No significant association was found between BMI and artefact content of the EQ02 ECG recordings (P=0.256), data not shown.

Heart rate variability

Figure 7 graphically displays 10-minute averages of different HRV parameters for one participant (serial number 11, with overall average artefact percentage of 5.23%). Comparing HRV parameters from the two devices, the Pearson correlations were 0.967 for ANN, 0.393 for SDNN, 0.285 for rMSSD, 0.680 for SDANN and 0.982 for pNN50 for the 24-hour data. However, after selecting a three-hour stretch of data containing minimal artefacts (1.15% artefacts), the Pearson correlation for ANN remained the same. Except for pNN50 with Pearson correlation of 0.967 for 3- hour data, the Pearson correlation coefficients of the other HRV parameters improved to 0.786 for SDNN, 0.868 for rMSSD and 0.991 for SDANN for the 3 hour data with minimal artefacts (figure 8).

DISCUSSION

The EQ02 is a wireless device which can be used for monitoring multiple parameters, either real-time/live or offline/retrospectively. This is the first study to investigate the accuracy of EQ02 for continuous ECG measurement by comparing EQ02 with the gold standard (Holter). The major findings of this study are: 1) EQ02 is a convenient device for continuous measurement of ECG and its derivatives; 2) marked differences were observed in data quality between and within participants; 3) at lower artefacts percentages, HR and HRV measurements from EQ02 and Holter measurements were highly correlated; 4) artefacts percentages were lower during nighttime, when waist: hip ratio was lower, and at lower activity/ movement levels, as measured by step counts taken during the study.

EQ02 is relatively easy to wear in a home setting during habitual activities due to the design of the belt system with textile electrodes (the absence of wires). The use of wireless fabric electrodes in the a wearable belt provides comfort that makes the system suitable for prolonged and/ or frequent recordings [24]. However, this also imposes a limitation because textile electrodes are more prone to motion artefacts which interfere with R-wave detection [25]. Since textile– based electrodes do not have adhesives or clips, the instability

and misplacement of the electrodes can be a possible source of the relatively higher artefact percentages that we observed for the ECG recording from the EQ02 monitor. This validation study found marked differences in EQ02 data quality between and within participants, as determined by the percentage of artefacts. We found more artefacts just before EQ02 charging times. For this study, the EQ02 was charged for one hour for every 12 hours of use. Removal and replacement of the monitor around charging times is a possible reason for the increased artefacts around charging times. Known sources of artefacts for cardiac telemetric devices include electrode movement with respect to the skin interface (disrupting electrochemical equilibrium); muscle contraction resulting in unwanted electromyographic contamination that may share the desired signal frequency band; vocalizations; temperature changes; sensor-cross-talk; optical path length changes and electromagnetic induction [25, 26]. In literature, artefact load of cardiac telemetric devices have also been attributed to body movement, temporary impairment of skin electrode contact, loose electrode connections, broken leads, skeletal myopotentials, and ambient noise [27]. In line, we also found that higher artefacts were found at higher activity levels, since this involves increased body movement.

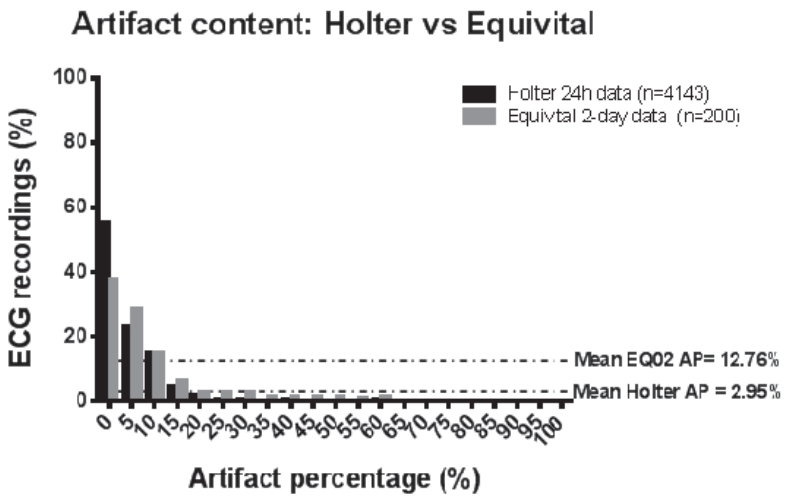


FIGURE 10.6 | Comparison of artefact content of raw Holter data to raw EQ02 data.

Bar chart showing content and distribution of artefact in raw (uncleaned) 24h Holter ECG recordings from 4,143 subjects with raw EQ02 data from 200 subjects. The average artefact percentage from the holter recordings was 2.95%, whereas the average artefact percentage from that 200 EQ02 recordings was 12.76%. AP: artefact percentage.

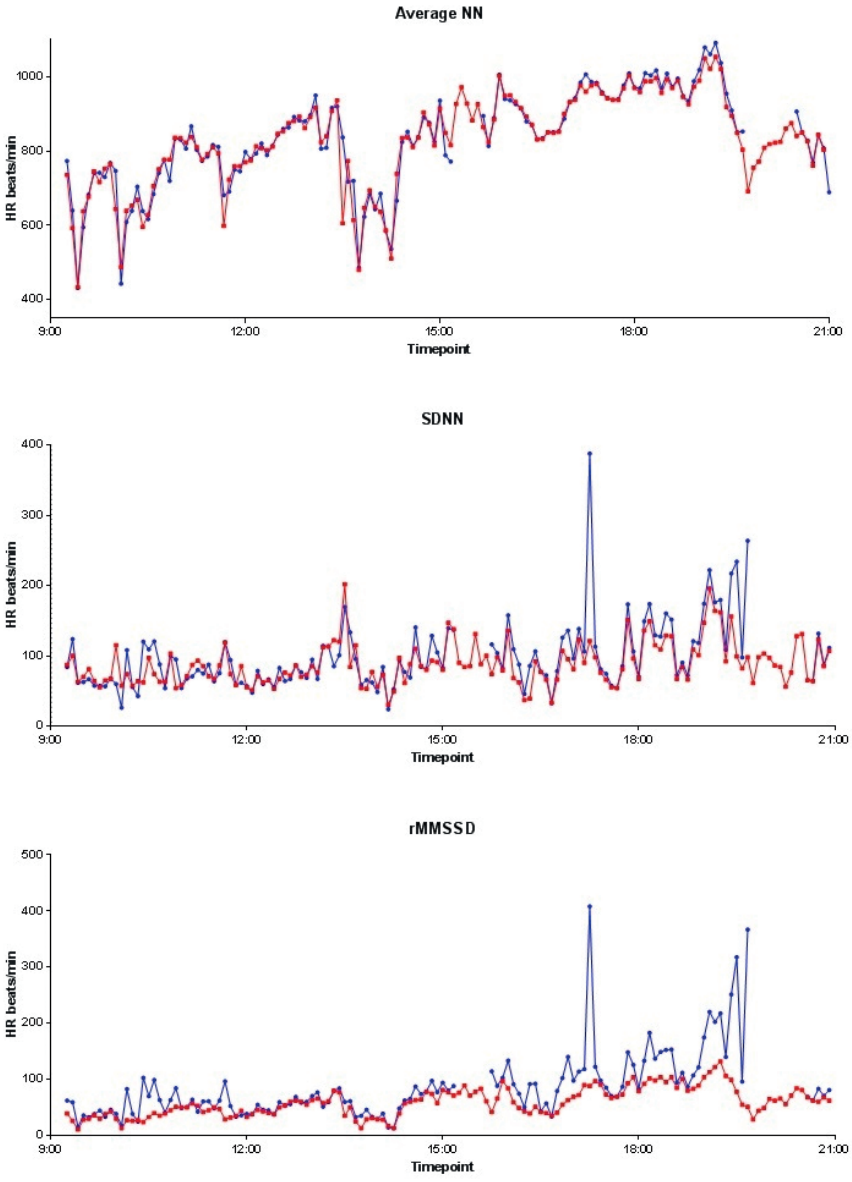


FIGURE 10.7 | 24- hour EQ02 and Holter HRV profile.

Average NN, SDNN and rMMSD of a participant over 24h, as recorded by the Holter (red) and EQ02 (blue).

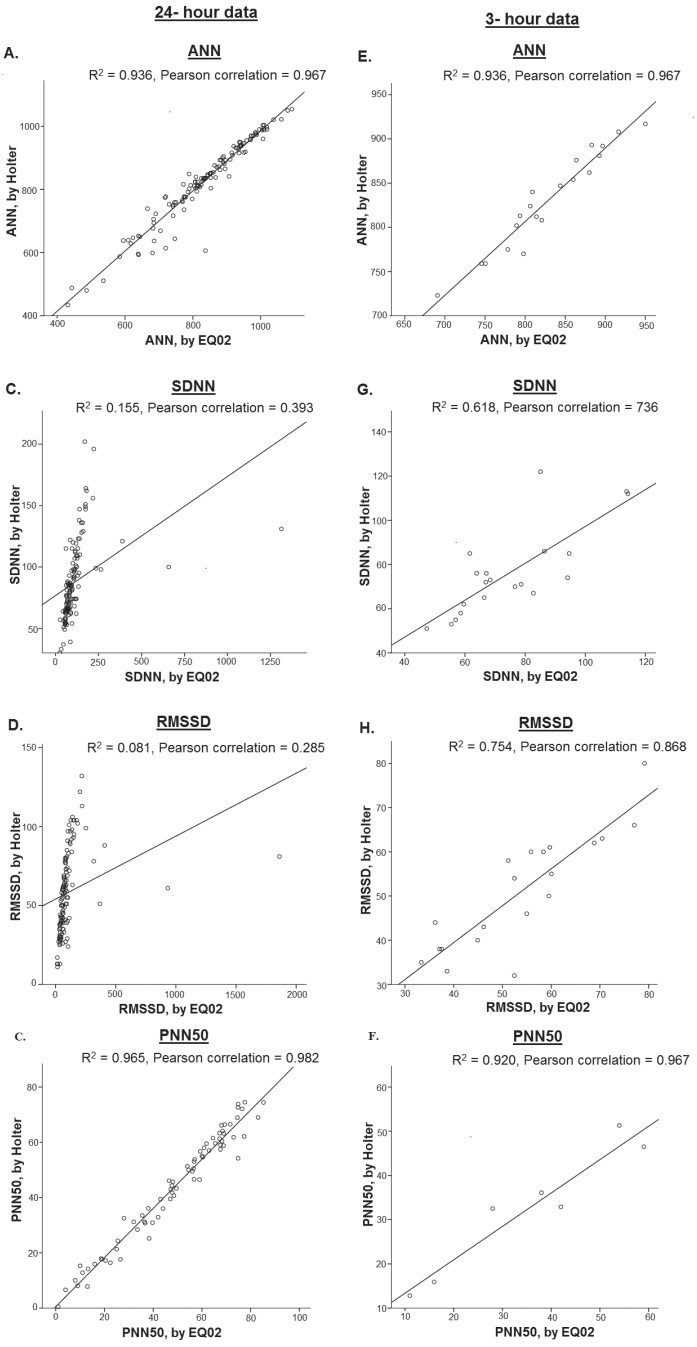


FIGURE 10.8 | Comparison between HRV parameters measured by EQ02 and Holter.

Correlation between ANN, SDNN, RMSSD and pNN50 in a participant from both devised over 24hr (A,B, C, D) and in a sub- selection of 3-hour data with artefact percentage 1.15% (E, F, G and H).

We demonstrated that at low artefact percentages, EQ02 can be used to reliably monitor ECG and its derivatives (HR, HRV) in relatively healthy participants. This is in accordance with a previous study [19] that compared HR derived from EQ02 and Polar S810i HR monitors under 10 minutes each of standing, lying and sitting. However, at higher artefact percentages (50% and higher), we found discordance between the EQ02 and Holter, which did not improve after application of the automatic cleaning options provided by Vivosense. Correlations improved by selecting data with <50% artefact or <20% artefacts. Similarly, HRV parameters (SDNN, RMSSD and pNN50) also showed markedly improved correlations after selection on a three- hour stretch of data with minimal artefacts. This further strengthens the finding that the quality of EQ02 is best at low artefact percentages. This agrees well with observations made by investigations into other mobile devices [28, 29]. For example, a validation study of the Actiheart found that HR values from Actiheart were in good agreement with those of other HR monitors during rest, but errors increased during exercises of higher intensity [28]. During high intensity movements, mobile devices are more prone to artefacts, in comparison to during rest. In line, whilst investigating potential determinants of artefacts, we found that artefact percentages were lower at lower activity levels (fewer step counts), at night, in subjects with lower waist: hip ratio and also somewhat lower in females. At night, participants were lying supine and mostly asleep which might result in better contact with electrodes and/ or decreased movement. Participants with lower waist: hip ratio also had significantly lower artefact percentages possibly because of better fitting of the Equivital belt. This could also have been the case in females, since female participants wore an extra layer of underwear over the Equivital belt, which might have potentially reduced belt displacements. This suggest that the artefact content of the EQ02 would most likely be attributable to motion artefacts and/or impaired skin- electrode contact.

One main limitation of our study is that it was conducted in eighteen relatively healthy participants without overt cardiac disease. A strength was that ECG was measured continuously and simultaneously using both devices over 24hours. More studies are needed to validate the EQ02 in specific groups, such as in the elderly, in large population studies and in patients with known cardiac disease. However, the susceptibility of the EQ02 to artefacts should be taken into account in such studies. Before application of Holter monitors, skin preparation is normally done with alcohol/KCl and red dot to remove nonconductive skin layer and reduce skin impedance to minimize artefacts. Perhaps

employing skin preparation techniques could also aid in minimizing artefacts with EQ02 recordings.

Summarily, we compared continuous ECG from EQ02 to the Holter over 24hours. Skin preparation, as well as clips used before application of the Holter electrodes prevents artefacts, whereas artefact management of EQ02 was done after data acquisition. We found that there was, on average, good agreement between HR and HRV values derived from EQ02 and Holter. However, its accuracy and reliability depended on the presence and quantity of artefacts. Presently, the artefact load of EQ02's ECG recordings exceeds that of the Holter. This would pose a serious limitation to its clinical use in individual patients, especially for measurements that are especially sensitive to artefacts. On the other hand, if artefacts can be properly managed, the EQ02's ability to monitor (live and/or retrospective), synchronize and store cardiac and other physiological parameters may offer potential benefits for home monitoring and/ or research purposes, as it could be useful for extensive continuous recording of ECG, HR, HRV and other physiologic data in large population studies.

Supporting information

The Supplementary Material for this article can be found online at:
http://journal.frontiersin.org/article/10.3389/fphys.2016.00391/full

Supplementary Table 1. Detailed characteristics of the study participants

Supplementary figure 1. 24h graphs of Holter and EQ02 heart rate measurements of individual study participants

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