

## Evaluation of stress measurement using a wrist-worn device in volunteer subjects under Thai massage and cardio-exercise treatment

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### ABSTRACT

**Background:** Stress is one of the key factors leading to mood disorders. Screening for stress through questionnaires and heart rate variability (HRV) required delicate consideration and expertise for result interpretation. Nowadays, wrist-worn devices, a non-invasive and real-time monitoring technology for assessing stress levels, are widely used.

**Objective:** To evaluate wrist-worn devices for stress measurement and assess the stress responsiveness of Thai massage (TM) and cardio-exercise in volunteers.

**Materials and methods:** Device verification was inferred before distributing the wrist-worn device to volunteers. Fifty volunteers were randomly assigned to 1.5 hours of TM and 4 weeks of cardio-exercise in zones 1-2 as a stress relaxation program. The stress response rate was compared among 3 different stress measurement tools: an HRV device, cortisol level, and a wrist-worn device.

**Results:** Wrist-worn devices' step count and heart rate function were verified within an acceptable error of <5% and well correlated with the HRV device before starting the assignment. The significantly decreased value of the stress after TM indicated the responsiveness for stress relaxation within an 85% response rate by HRV ( $p < 0.001$ ) and 75% by wrist-worn devices ( $p = 0.002$ ). Higher response outcomes were achieved from the cardio-exercise program, resulting in an 80% response rate by cortisol ( $p < 0.001$ ), 83.3% by HRV device ( $p = 0.001$ ), and 90% by the wrist-worn device ( $p = 0.001$ ). Significant agreement of Kappa values for all paired devices under cardio-exercise reveals an acceptable similar response outcome from wrist-worn devices. The responsive outcome between TM and cardio-exercise programs in similar volunteer groups demonstrates no significant difference measured by HRV devices ( $p = 0.375$ ) and wrist-worn devices ( $p = 0.625$ ) using the McNemar test.

**Conclusion:** The data herein suggest that a wrist-worn device's stress monitoring provides satisfaction with real-time monitoring and long-term records comparable with HRV devices and cortisol measurements. Cardio exercise for 4 weeks of light and very light cardio is suggested as a continuous approach for stress relaxation. The TM program is a passive intervention that may help temporary relaxation compared to continuous cardio exercise according to subjective preference.

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### Introduction

Stress-induced mood disorder has been found to increase in all ages according to the complexity of work constraints and living lifestyles. Common stress symptoms

can affect mood, thoughts, and feelings, such as anxiety, restlessness, lack of motivation, and memory problems. Chronic stress can lead to many health problems, from less severe, such as headaches, high blood pressure, muscle tension, fatigue, stomach upset, and obesity, to chronic diseases such as heart disease, stroke, and diabetes. Self-mental resilience plays an essential skill in handling stress. Knowing stress or self-monitoring of stress occurrence can help to manage its effects using possible stress relaxation approaches, for example, regular physical activity on most days of the week, meditation, yoga, tai chi, or massage.

The stress score by questionnaire is commonly used as a simple screening approach for stress. However, the diversity of ethnicity and society should be considered when assessing its reliability.<sup>1</sup> Cortisol, a hormone secreted from the adrenal gland, plays a vital role in the stress response. Stress activation along the hypothalamic-pituitary-adrenal (HPA) axis releases corticotropin-releasing hormone (CRH) from the hypothalamus.<sup>2</sup> Stimulation of the anterior pituitary by CRH prompts the release of adrenocorticotrophin hormone (ACTH), which triggers the adrenal cortex to secrete cortisol into blood circulation.<sup>3</sup> Approximately a 9-fold increase in cortisol level was observed in stress compared to relaxed periods.<sup>4</sup> Also, the cortisol level is routinely used to diagnose abnormalities along the HPA axis, such as Cushing's syndrome, adrenal insufficiency, and hormone replacement in Addison's disease. Acute cortisol change can be reliably measured in saliva and blood, cortisol in urine can be used to establish daily cortisol secretion, and cortisol in hair can be used to gather long-term cortisol levels over weeks or months.<sup>5,6</sup> Assessment of cortisol in saliva captures acute cortisol production and is often used to measure daily stress because collection is relatively quick and easy. A high correlation between cortisol levels in blood and saliva has been reported.<sup>7</sup> Moreover, the sensitivity and specificity of salivary cortisol accounted for over 90%.<sup>8</sup> However, cortisol levels in the body fluctuate daily in response to stressors and circadian patterns that render salivary cortisol highest in the morning and lowest at night.<sup>7,9</sup>

The increase of stress hormones in blood circulation leads to an increase in heart rate and the elevation of blood pressure. Any alteration of heart rate due to the stress response can contribute to the fluctuation of successive heartbeats or R-R interval, described as heart rate variability (HRV).<sup>9</sup> HRV can be captured through different devices, including an electrocardiogram (ECG) with varying validity. An HRV device is equipped with an HRV measurement and analysis system, which reflects the heart activity and physiological changes and sensitivity to physical factors such as posture and movement while detected. Due to the data transformation from an ECG or HRV device, HRV is a sophisticated measurement that requires expertise for results interpretation. Collecting data reliably in a cost-efficient and ecologically valid way is difficult.

Nowadays, real-time monitoring and non-invasive methods for stress conditions have been introduced to

personal wearable devices. Wrist-worn device technology consists primarily of 3 primary sensors: a temperature sensor, a pulse rate sensor for physiological measurement, and an acceleration sensor for movement detection.<sup>10</sup> A combination of more sensors and algorithms were introduced to devices to enhance performance, such as an infrared blood flow sensor, heart rate monitoring sensor, photoplethysmography sensor, optical sensor, etc. HRV or pulse shape variability (PSV) has also been introduced to the device, and the results for stress detection are displayed on the screen.<sup>11</sup> The development of small, reliable, cost-effective sensor devices has increased consumer access and interest. However, the accuracy of commercially available devices could be improved, and data quality assessment is needed.

Thai massage (TM) and cardio-exercise have been used for stress relaxation and office syndrome treatment.<sup>12-15</sup> While the wrist-worn device has been well accepted as a friendly-to-use device for monitoring individuals' health, the validation of parameters acquired from the device remains limited.

This study evaluated wrist-worn devices harboring stress measurement functions compared to HRV devices and cortisol levels. TM and cardio-exercise were introduced as stress relaxation programs to volunteer subjects wearing wrist-worn devices, and the effectiveness of these stress-measuring devices was examined.

## Materials and methods

### Sample calculation

The absolute sample size for each intervention was found to be 22, which was calculated from the difference of two means formula. Participants were assigned to perform cardio-exercise zone 1 or 2 for 4 weeks. Stress parameters acquired from wrist-worn devices were substituted in the following equation:

$$n = \frac{(Z_{\alpha/2} + Z_{\beta})^2 \sigma_d^2}{\Delta^2}$$

The  $\sigma$  variance of stress parameters acquired from wrist-worn devices was 0.77, and the  $\Delta$  mean difference of stress parameters acquired from wrist-worn devices was 0.46. The  $Z_{\alpha/2}$  at 0.05 significant level was 1.96, whereas  $Z_{\beta}$  the 80% power was 0.84.

### Study subjects

The study was conducted under the approval of the Ethical Committee for Human Research, Khon Kaen University, Khon Kaen Province, Thailand (HE641321). Due to the GCP guidelines, the confidential information of volunteers was included, and consent forms were obtained from all participants. Inclusion criteria were specified for the healthy individuals, who had to be diagnosed by physicians with normal blood pressure, no medicinal use, and no alcoholic consumption. On the other hand, individuals with a history of conditions including mental disorders, neuropathy, Cushing's syndrome, Addison's syndrome, chronic diseases, hyperthyroid, pregnancy, and medication onset were excluded. Subjects between the mid-working age of 18 and 40 who fit the inclusion criteria

were screened for stress baseline using Suanprung Stress Test-20 (SPST-20) questionnaires. This study included fifty volunteers with moderate stress (stress score >24 points) for further assignments.

**Measurement parameters and devices**

The stress index parameter was measured in terms of HRV using an HRV Analyzer SA-3000P (Medicore Inc., Korea). In contrast, PSV was retrieved from the wrist-worn device from Zensorium (Thailand) Ltd. HRV is reflected as a time-domain measurement of heartbeat fluctuation in terms of R-R interval in minutes. The involvement of the sympathetic autonomic nervous system (ANS) during stress increases heart rate, decreasing the R-R interval of HRV.<sup>9</sup> The use of HRV assesses physical fitness and stress-coping ability. The physical stress index (PSI) reflects the load and pressure on the heart based on the R-R interval and heart rate, which indicates stress-related disorders such as fatigue, anxiety, dizziness, and depression.<sup>16</sup> The PSV enables real-time monitoring of waveform alteration obtained from the photoplethysmography (PPG) sensor in the wrist-worn device. The alteration of heart rate and breathing during stress affects the pulse wave feature, which the PPG sensor can identify.<sup>17</sup> The measurement of the PSV index will be displayed every 5 minutes. The alert of stress will indicate increased PSV. The computing of PSV from the device could be more transparent.

Cortisol level in saliva was also used as a biochemical-based, non-invasive method to compare the effectiveness of stress assessment devices. For both before and after the intervention, saliva was collected simultaneously before bedtime, as described by the manufacturer's procedure with the collection set (Salivette Cortisol, Sarstedt AG & Co. KG, Germany). After collection, the sample was immediately stored in a refrigerator (4-8°C) until use. The salivary cortisol was measured by electrochemiluminescence immunoassay (ECLIA) using a Cobas e801 Analyzer from Roche Diagnostics (Thailand) Ltd.

**Wrist-worn device verification**

Fifty wrist-worn devices were obtained from Zensorium (Thailand) Ltd. Before product delivery, the heart rate parameter between the Zensorium wrist-worn device and ECG was approved by the manufacturer and reported in mean absolute percent error (MAPE) with an acceptable value of ≤10% under ANSI/CTA-2065 standard.<sup>18</sup> The accuracy and precision of the 50 devices were retested for three functional modes, including step count, heart rate, and stress index, before being subjected to further experiments. Step count was compared between the displayed value on the screen device and the manual count. The difference between the manual count and the displayed values calculated inaccuracy regarding %bias. Imprecision was assessed in the percent of coefficient of variation (%CV) from 3 replicates of each device.

Heart rate measurement or pulse on the wrist-worn device was compared with manually counting the number of pulse beats at the wrist in one minute. The %bias and %CV were also calculated. In addition, the correlation of stress parameters obtained from wrist-worn devices and HRV devices among individual subjects (N=40) was also examined. The correlation coefficient and linear regression indicated the correlation between the two devices.

**Responsiveness evaluation of stress relaxation by TM and cardio-exercise in volunteer subjects wearing wrist-worn devices**

Regarding 50 recruited volunteers, only 40 subjects remained due to the dropout of subjects during the assignment, as shown in Supplement Table 1. These participants were randomly assigned to a short 1.5-hour Thai massage or 4-week cardio-exercise group as an independent group in a stress-relaxing program. Stress-responsive outcome was determined from the difference in stress values obtained before and after treatment. However, the final data of 36 volunteers (14 male and 22 female) remained. The age ranged from 20 to 38 years, with an average age of 28.6. The mean and standard deviation of BMI accounted 22.0±3.67.

**Table 1.** Verification data for imprecision and inaccuracy among the wrist-worn devices (N=50) used for step and heart rate parameters in this study.

Parameters	Precision (%CV)	Accuracy (%Difference or %Bias)
Step count (N=50)		
Mean	1.69	1.25
Range (min-max)	0-4.97	-3.50-2.00
Heart rate (N=50)		
Mean	1.25	1.38
Range (min-max)	0-3.21	-4.5-3.5

**Thai massage**

A total of 24 volunteers were assigned to receive regular TM treatment for 1.5 hours at the AMS Wellness Service Centre, Faculty of Associated Medical Science, Khon Kaen University. To minimize the variability of TM practitioners, only 1 staff member was assigned to treat all volunteers. Four volunteers were excluded due to incomplete data log records of the wrist-worn device, resulting in only 20 data obtained.

Stress parameter measurements were compared before and after TM was acquired from wrist-worn and HRV devices.

**Cardio-exercise**

A total of 30 volunteers were assigned to exercise according to their favorite program, e.g., running, badminton, etc., for four weeks to reach the acquired definition of cardio-exercise zones 1 or 2. The exercise period and frequency can be checked using data log records in a wrist-worn device to meet the criteria of 150 minutes per week.

Stress levels via HRV and wrist-worn devices were monitored during the period, as summarised in the experiment design in Figure 1. Moreover, cortisol levels in saliva were investigated on the starting date (week 0) as a baseline value and at the 4<sup>th</sup> week as the end point of intervention.

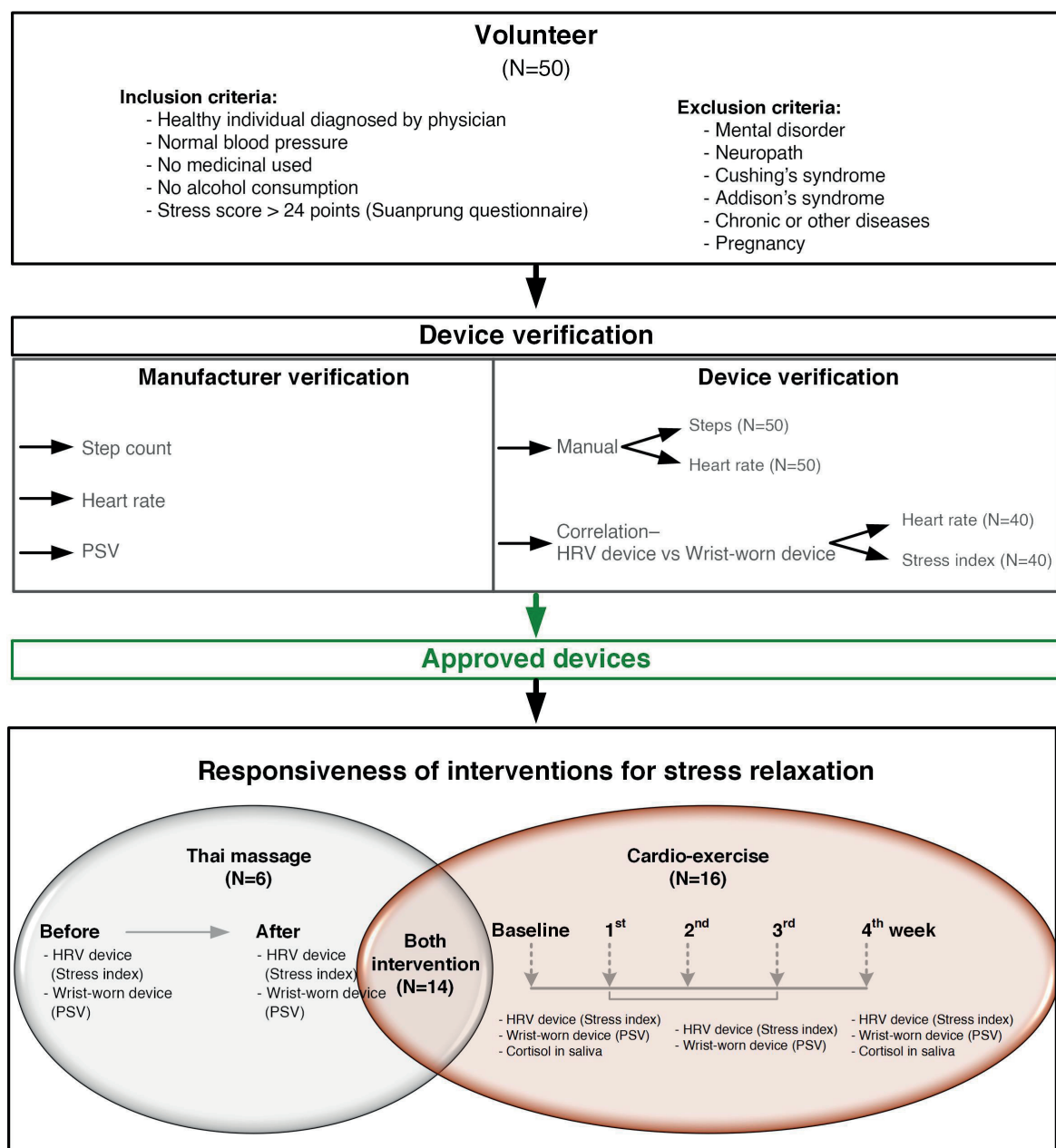


Figure 1. Experimental design of the study.

### Both interventions at different time

Among two interventions, 14 volunteers were selected to perform TM and cardio-exercise. To minimize the effect of each intervention in this group, volunteers who underwent TM once for at least 4 weeks prior were assigned to perform the cardio exercise.

The change in stress level between after and before intervention acquired from each detection method were recorded. A decrease in stress level after an intervention is indicated as a response case. On the other hand, an increased value and no change value after intervention indicated a non-response case.

### Statistical analysis

Statistical analysis was performed using IBM® SPSS® Statistics v.28 under Khon Kaen University license (IBM Corporation, IL, USA). The difference in stress levels obtained from each measurement method was calculated by subtraction before and after applying the intervention. The Shapiro-Wilk test was used to test the normality of differences. The statistical significance of stress values before and after intervention was determined using a paired t-test in the parametric dataset. At the same time, the Wilcoxon Signed Rank test was used for the nonparametric dataset with  $p \leq 0.05$ .

McNemar statistic was used to compare the conformity of the response outcome between TM and cardio-exercise in the same volunteers.

Cohen's kappa was introduced to determine the agreement of responsive outcome through each intervention (cardio-exercise and TM) using different stress measurement methods (cortisol, HRV, and wrist-

worn device). Levels of agreement, including none, minimal, weak, moderate, strong, and almost perfect, were classified by kappa values of 0-0.2, 0.21-0.39, 0.40-0.59, 0.60-0.79, 0.80-0.90, and  $>0.90$ , respectively,<sup>19</sup> while statistically significant responsiveness was indicated by a  $p \leq 0.05$ .

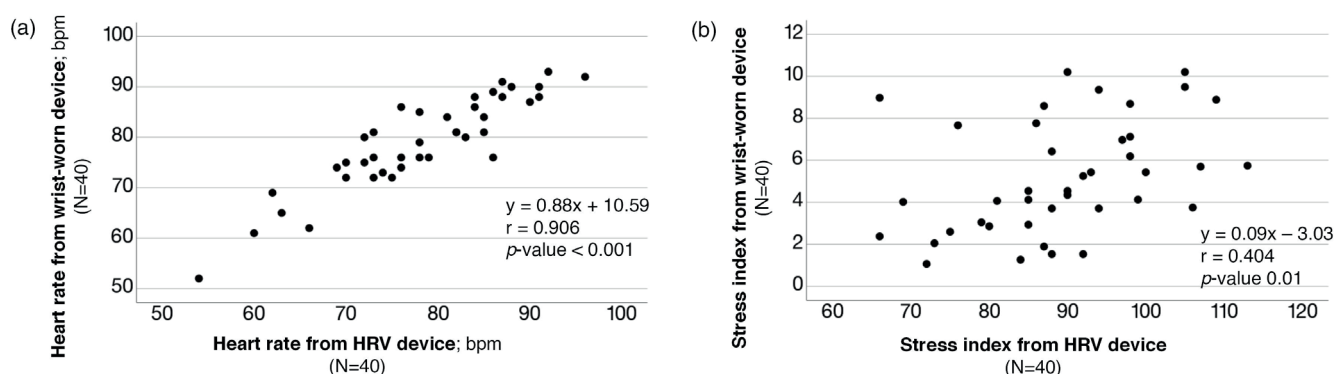
The power of the test was calculated to determine the sample size in each study group. A power of 80% or more is considered a sufficient sample size.

## Results

### Wrist-worn device verification

A total of 50 obtained wrist-worn devices were evaluated before being given to volunteers in two parameters: step count and heart rate functions. Averaged %CV and averaged %bias at 1.69% and 1.25% were observed for step count, whereas 1.25% and 1.38% were observed for heart rate function (Table 1). All wrist-worn devices were accepted as having acceptable imprecision and inaccuracy of  $\leq 10\%$ . These data agreed with the certificate of the product by Zensorium® wrist-worn devices using the comparison of heart rate measurement with ECG and reported in MAPE. Percent MAPE estimated from 6 physical activities, including walking, running, sitting, typical activities, cycling, and sleeping, were 7.41%, 8.48%, 2.40%, 5.71%, 9.71%, and 1.54%, respectively.

The heart rate and stress index of the wrist-worn devices were also compared with that of the HRV device (N=40). A positive and significant correlation of heart rate was found with  $r=0.906$ ,  $p<0.001$ , while stress index by the wrist-worn devices gave a lower correlation with  $r=0.404$ ,  $p=0.01$  (Figure 2).



**Figure 2.** Correlation between heart rate (a) and stress parameters (b) acquired from the HRV device and wrist-worn device.



### Agreement of stress-responsive outcome between wrist-worn devices and other devices

Stress monitoring parameters, including salivary cortisol level, stress index from HRV device, and PSV from wrist-worn device acquired from each subject, were categorized into response and non-response cases concerning the two different relaxation intervention programs, TM and cardio-exercise, as shown in Table S1. The response outcome is defined as the decreased stress parameters after intervention, whereas non-response is indicated whenever no change or increased stress values are found after intervention.

Methods were paired and compared using Cohen's kappa to evaluate the agreement level, as shown in Table 2.

Cortisol as a diurnal variation marker was excluded in TM because only 1.5 hours of TM was conducted as a short-term treatment. The wrist-worn devices demonstrated a high percentage of agreement at 80% under the TM program and 86.67-90% under the cardio-exercise program compared to other methods. A significant Kappa value was found for all paired devices under cardio exercise, indicating a similar response from wrist-worn devices. Higher agreement on stress-responsive outcome was found with moderate kappa ( $p < 0.001$ ) between the wrist-worn devices and cortisol values compared to weak kappa ( $p = 0.014$ ) by the HRV device. In addition, both HRV and cortisol levels, as compared to methods, were found to have significantly moderate agreement ( $p < 0.001$ ).

**Table 2.** Agreement analysis for stress responsiveness among different stress measurement methods.

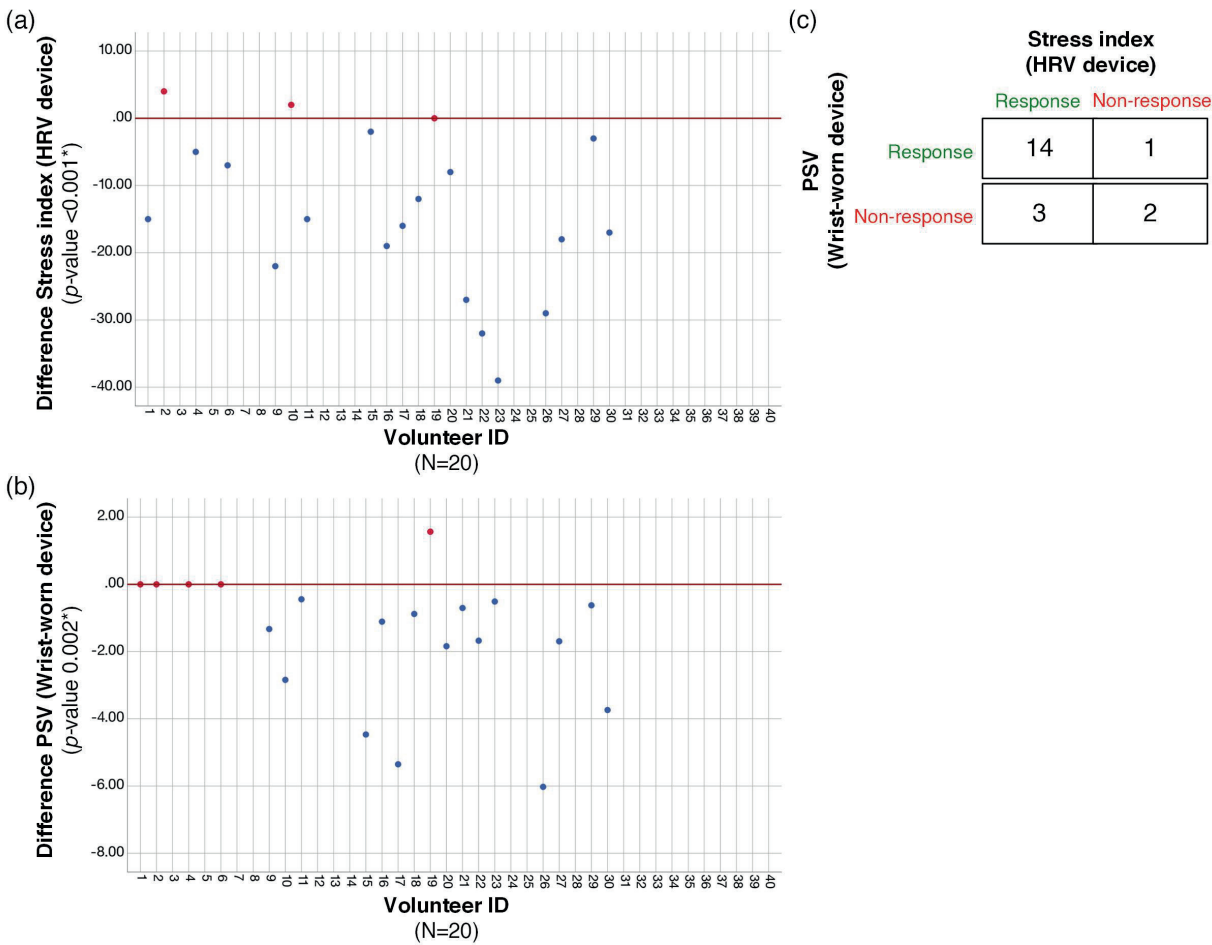
Comparison	%Agreement*	Kappa value (Level of agreement)	p value
Thai massage (N=20)			
Wrist-worn device vs HRV	80%	0.385 (Minimal agreement)	0.071
Cardio-exercise (N=30)			
Wrist-worn device vs Cortisol	90%	0.615 (Moderate agreement)	<0.001
Wrist-worn device vs HRV	86.67%	0.429 (Weak agreement)	0.014
HRV vs cortisol	90%	0.667 (Moderate agreement)	<0.001

**Note:** \*The percentage of agreement for each pair of devices was calculated from the number of similar outcomes in both response and non-response cases.

### The comparison of intervention programs for stress relaxation in volunteers wearing wrist-worn device

Stress measurement among 20 volunteers was monitored before and after being subjected to the TM program. Statistical significance of the different stress values after the intervention was found with both HRV ( $p < 0.001$ ) and wrist-worn devices ( $p = 0.002$ ), as shown in Figures 3a-3b. The decreased value of the stress index after TM indicated significant responsiveness for stress relaxation. HRV gave an 85% response rate (17/20), whereas a lower response rate of 75% (15/20) was found from wrist-worn devices (Figure 3c). A total of 3 cases of non-response outcomes (V2, V10, and V19) were found

from the HRV device, while 5 cases of non-response (V1, V2, V4, V6, and V19) were found by the wrist-worn device (see also supplement Table S1). Comparing the 2 methods, 14/20 individuals provided consensus response outcomes, while another 2/20 individuals were non-response to the intervention, accounting for 80% (16/20) conformity outcomes. The remaining 4 individuals (V1, V4, V6, and V10) with different outcomes revealed a 20% discrepancy between the two methods. Among the discrepancy outcomes, 3 cases (V1, V4, and V6) except V10 resulted in non-response detected by the wrist-worn device. This result indicates a higher sensitivity of HRV devices to detect stress than wrist-worn devices.

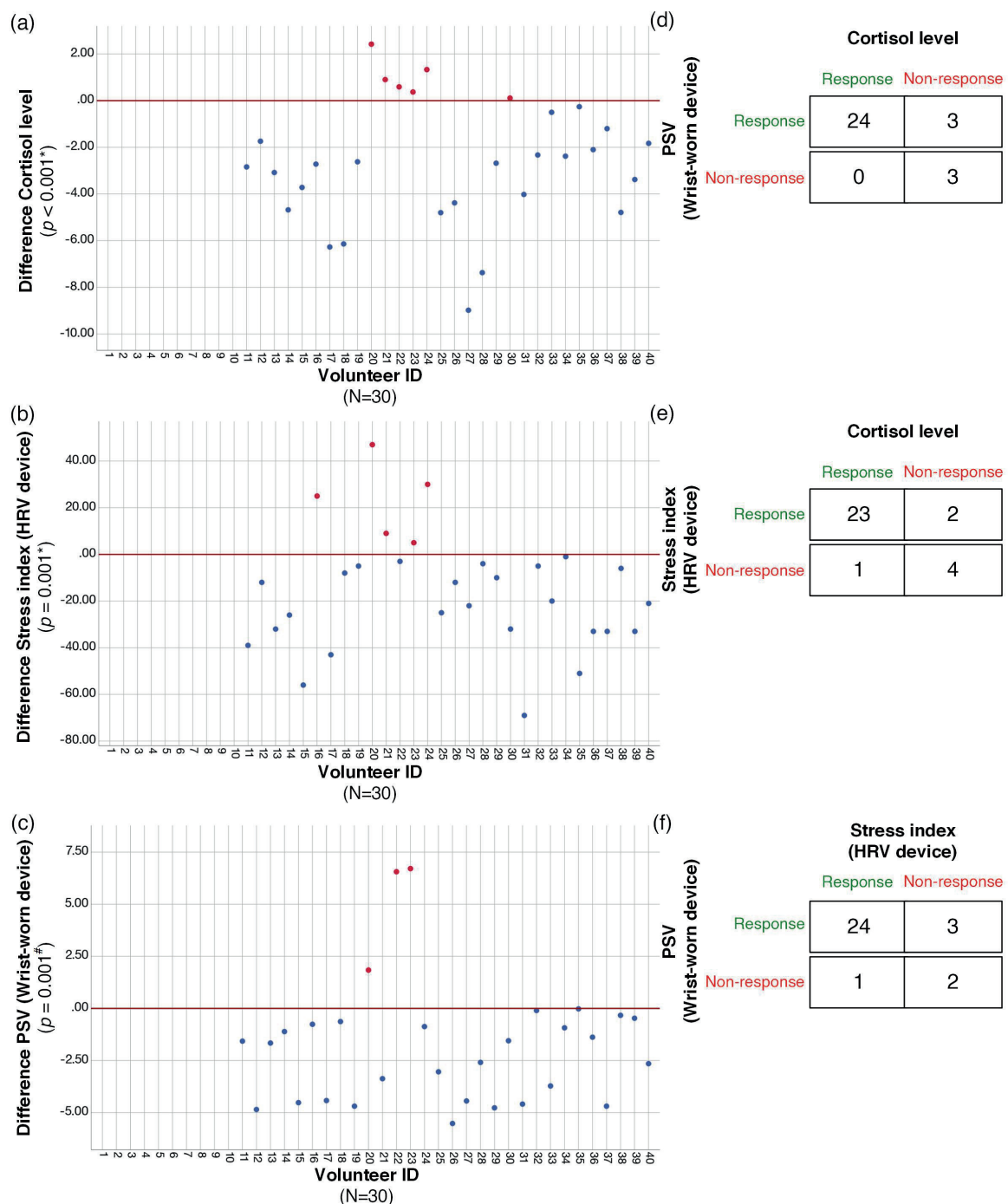


\*Pair t-test was used to compare the difference of stress responses before and after intervention.

**Figure 3.** Responsiveness of stress relaxation in volunteer subjects who acquired Thai massage intervention. The response outcome is defined as the decreased stress value after intervention, whereas non-response is indicated whenever no change or increased stress values are found after intervention. Spots indicate the difference in stress indication measured by (a) the HRV device and (b) the wrist-worn device, while blue indicates a response (negative value below zero line) and red indicates a non-response (zero or positive value at and upper the zero line), and (c) presents a confusion matrix comparing the outcome between HRV and wrist-worn device after treatment.

Figure 4 shows significant stress response outcomes after 4 weeks of the cardio-exercise program, resulting in 80% (24/30) response rate (blue dot) by cortisol level ( $p < 0.001$ , Figure 4a), 83.3% (25/30) response rate by HRV device ( $p = 0.001$ , Figure 4b) and 90% (27/30) response rate by wrist-worn device ( $p = 0.001$ , Figure 4c). The consensus outcome for stress response between method-pairing is

summarised in Figures 4d-4f. Figure 4d indicates a 10% discrepancy with 3 cases (V21, V24, and V30) between wrist-worn devices and cortisol pairing and an equal 10% discrepancy between HRV and cortisol pairing (Figure 4e), whereas 4 cases (V16, V21, V22 and V24) or 13.3% discrepancy was found when comparing wrist-worn devices and HRV (Figure 4f).



\*Pair t-test was used to compare the difference of stress responses before and after intervention.

<sup>#</sup>Wilcoxon signed rank test was used to compare the difference of stress responses before and after intervention.

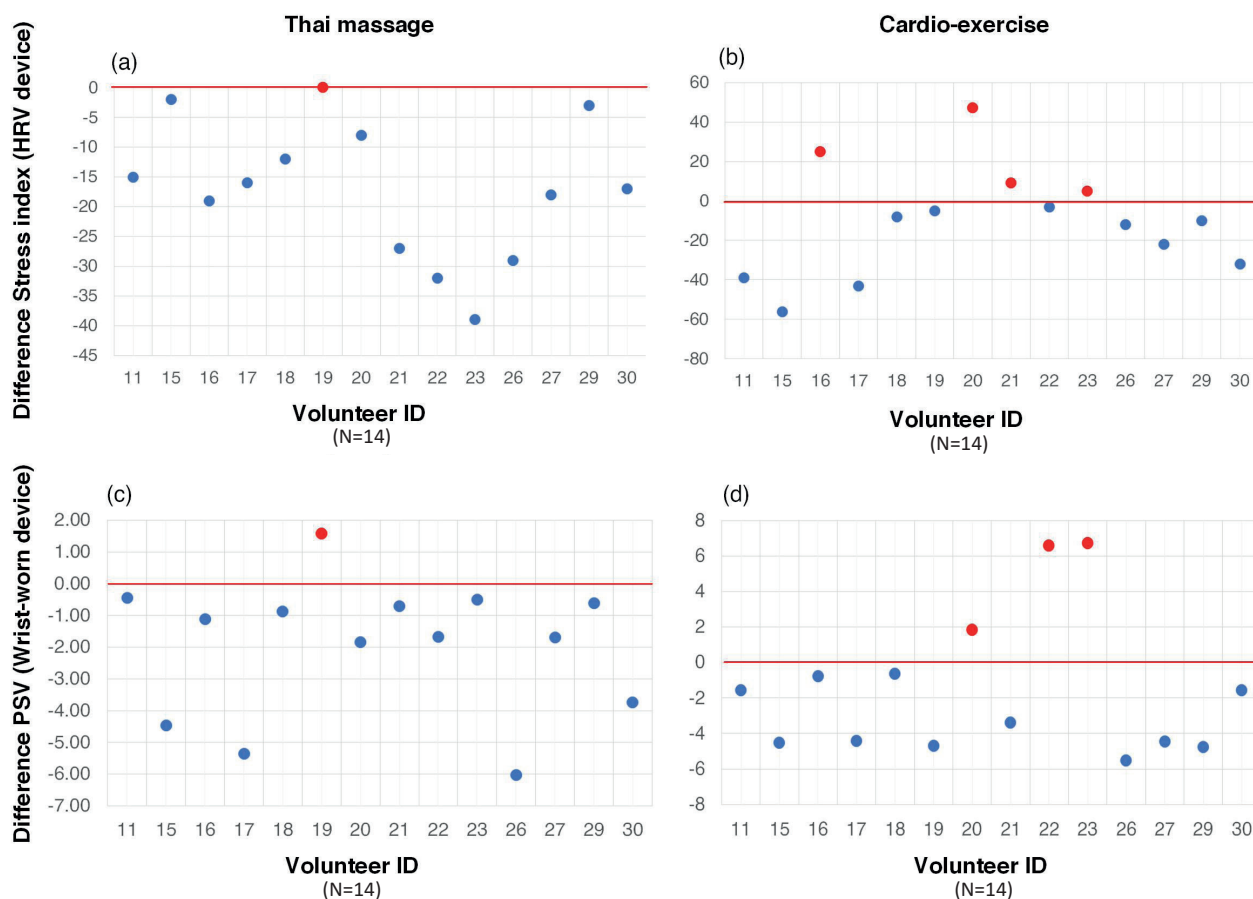
**Figure 4.** Discrepancy of response outcome for stress relaxation in 30 volunteer subjects who performed cardio-exercise intervention measured by (a) cortisol, (b) HRV device and (c) wrist-worn device. A blue dot indicates response (negative value below zero line), while a red dot indicates non-response (zero or positive value at and above the zero line). Two by two tables of paired methods were summarised between wrist-worn device & cortisol (d), cortisol & HRV device (e) and wrist-worn device & HRV device (f).



To minimize the confounding from different baselines of stress values in each subject, 14 volunteers were fixed and assigned to TM and cardio exercises using a similar stress measurement device, as shown in Figure 5. To avoid the interaction of 2 relaxing programs, a wash-out period of 4 weeks apart was strictly followed.

Out of a total of 14 volunteers, 5 cases (V16, V19, V20, V21, and V23) exhibited different outcomes, resulting

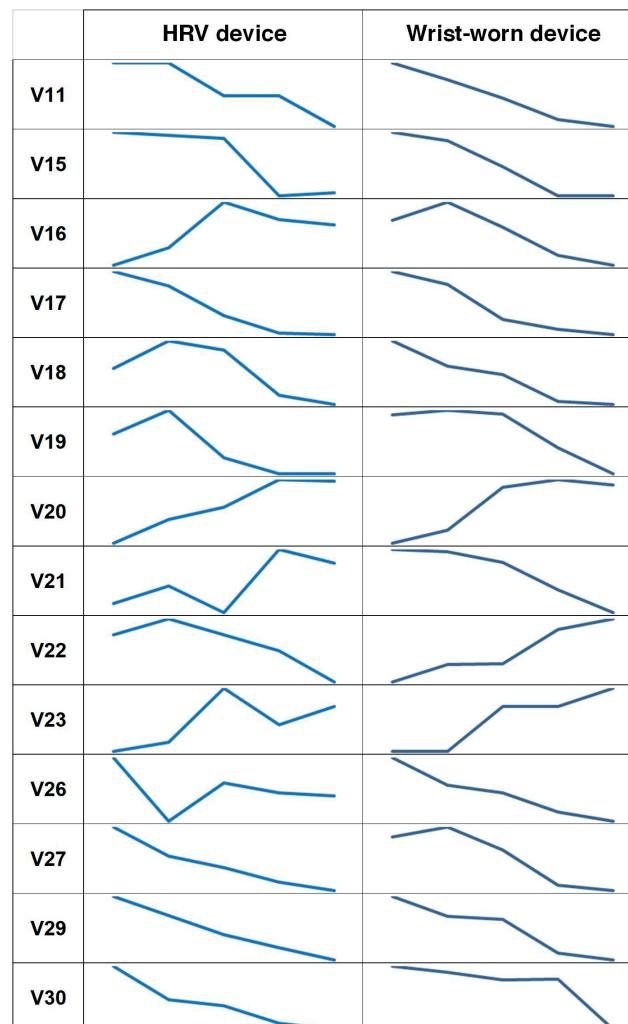
in a 35.7% discrepancy response between TM and cardio-exercise when the HRV device monitored stress without significant difference (Figure 5a-5b,  $p=0.375$ ). Only 4 cases (V19, V20, V22 and V23) showed a 28.6% discrepancy when using wrist-worn devices (Figure 5c-5d,  $p=0.625$ ). No significant difference between TM intervention (Figure 5a-5c) and cardio-exercise (Figure 5b-5d) measured by other devices was also found ( $p>0.05$ ) using the McNemar test.



**Figure 5.** Disconformity outcome between Thai massage and cardio-exercise program in similar volunteer groups (N=14) demonstrates no significant different measured by HRV device (a and b,  $p=0.375$ ) and wrist-worn devices (c and d,  $p=0.625$ ) using McNemar test.

Line plots of multi-point stress monitoring data using an HRV and wrist-worn device were compared among 14 volunteers for 4 weeks of cardio-exercise, as shown in Figure 6. The response rate detected by HRV and wrist-

worn devices was 71.4% (10/14) and 78.6% (11/14), respectively. This data confirmed comparable outcomes dependent on a relaxation program using either wrist-worn or HRV devices.



**Figure 6.** Stress monitoring of 14 subjects receiving 4 weeks of cardio-exercise program measured with 2 different methods including wrist-worn device (PSV) and HRV device.

## Discussion

The performance of all wrist-worn devices included in this study was qualified with inaccuracy and imprecision of less than 5% for step count and heart rate function following the ANSI/CTA-2065 standard. Heart rate measurement by the wrist-worn device was found to have a reasonable correlation ( $r=0.906$ ) with the HRV device. Taken together with the acceptable 10% MAPE certified by the manufacturer, all wrist-worn devices were approved for further investigation in the study. Moreover, a comparison study was conducted against different wearable devices in heart rate and energy expenditure parameters.<sup>20</sup> Variable levels of accuracy for heart rate measurement were activity-dependent, ranging from 2.44-10.76%. Although stress measurement between wrist-worn devices and HRV devices was found to have a lower correlation ( $r=0.404$ ), the difference in stress measuring units can be explained by the poor correlation between

both devices. HRV detects heart rate variables, but the wrist-worn device detects pulse shape variables.<sup>11,21</sup> The concordance of responsive outcome between TM and cardio-exercise using different devices by Kappa analysis is summarised in Table 2, indicating that significant agreement was found in wrist-worn devices with HRV and cortisol in the cardio-exercise program. Still, considerable agreement was being reached regarding the TM program. These data suggest that the wrist-worn devices provided an excellent and correlated responsiveness outcome with HRV and cortisol as the standard method. The results of the Kappa analysis confirmed the consensus outcome of stress response between method pairing, which showed HRV and cortisol provided comparable standard methods to evaluate the performance of wrist-worn devices under a cardio-exercise program. A similar finding also previously suggested an accuracy of HRV at 75% compared to EEG at 77.9%.<sup>22</sup>

Since the Kappa value demonstrated different agreements of stress-responsive outcomes among devices, the confounding factors from individual volunteers may contribute to the measurement discrepancy among controlled intervention programs. For TM, an HRV device can detect a higher response rate (17/20) than a wrist-worn device (15/20), suggesting that the HRV device is more sensitive to detecting changes in stress than a wrist-worn device. This finding can also be explained by the more comprehensive detectable range of HRV (60-120 units) compared to the smaller detectable range of PSV (1-10 units). In addition, the ineffectiveness of TM found in V2, V10, and V19 was explained by the experience of TM. V2 and V10 were unfamiliar with TM intervention, which may result in resistance to stress relaxation.

In contrast to V19, who suffered from office syndrome, only a short 1.5-hour TM may be insufficient to handle the stress.<sup>23</sup> Notably, the responsive outcome in cardio-exercise using a wrist-worn device gave the best response rate detection (27/30) compared to the HRV device (25/30) and cortisol (24/30). This finding suggests that a wrist-worn device for real-time monitoring can deliver more data supporting the actual stress for 4 weeks of intervention than the discrete monitoring of HRV devices and endpoint monitoring of cortisol.

To minimize the confounding effects among subjects underlying different stress baselines, a group of 14 subjects was assigned to both programs at various times (4 weeks apart). The comparison of stress responses of TM and cardio-exercise indicated no statistically significant difference between interventions with fixed devices and different devices with fixed intervention. However, 4 (V19, V20, V22, and V23) out of 14 (28.5%) shared the typical discrepant rate, implying that different outcomes may occur according to subject dependence on the relaxation program (Figure 5). Among the discrepancy cases, V19 suffered from long-term office syndrome, representing non-response outcomes by short period TM, while V20 carried over the restricted cardio-exercise zone 2; V22-V23 performed exercise longer than the recommended period (>200 min/week), which may have caused muscular strain and muscular fatigue. A heavy cardio zone may cause inappropriate muscle strain or exhaustion, resulting in relaxation resistance.<sup>24</sup> Moreover, various factors may affect stress levels, including the amount and duration of stress, genetic components, and patient history.<sup>25</sup> The success rate of stress relaxation with exercise depends on the duration period of regular exercise, which creates an accumulation effect compared to TM. Although TM is a traditional passive treatment with short-term response, the duration period and regular treatment might be important factors for successful response rates. The stress relaxation mechanism of cardio-exercise is associated with the neuroendocrine response to modulate cortisol hormone via an inactivation of cortisol into cortisone, an inert steroid. Increased anandamide (AEA) level, an endocannabinoid (eCB) during exercise, is a key induced increment in brain-derived neurotrophic factors that activate endorphin secretion, a positive mood hormone.

In addition, muscle activity during exercise increases tryptophan's uptake, crossing the blood-brain barrier and leading to increased serotonin, a neurotransmitter for sound emotional processing and memory function.<sup>26</sup>

To date, the American College of Sports Medicine (ACSM) guidelines have recommended that a minimal exercise program should consist of at least 20-30 min/per day, 3-5 days/week, for a total of 75-150 min/per week to develop and maintain cardiovascular fitness and reduce body fat.<sup>27</sup> A similar finding demonstrated susceptibility to stress reduction after zone 2 cardio-exercise (at least 30 min/day, 3-5 days/week for 8 weeks) in 30 nurse subjects and 55 physical therapy students.<sup>15,28</sup>

Trend analysis demonstrated that wrist-worn devices can provide slightly higher response rates than HRV. All data are recorded in real-time and kept in a data log, enabling a superior advantage for stress monitoring in personal use.

In this study, TM intervention was limited to only one short duration (1.5 hours), while the cardio exercise was delivered for 4 weeks. Thus, the cortisol could not be measured in TM intervention. Also, Kappa value of TM gave minimal agreement compared to moderate agreement of cardio-exercise. Moreover, cardio-exercise is recommended in cardio zones 1-2 but not limited to any specific sport. Some volunteers dropped out of the study due to insufficient periods of cardio zone 1-2. Some volunteers carried out heavy cardio zone 3, resulting in an exhausted status, which resisted the stress relaxation.

Moreover, more studies on wrist-worn devices using PPG sensors in the market are needed due to the limitation of raw data access. Processed data from most wrist-worn, for example, Apple, Garmin, or Fitbit bit, can be extracted using the Application Programming Interface (API); direct access to raw data is impossible. The performance evaluation study of standard wearable sensors for stress detection, including PPG sensors.<sup>29</sup> This study compared seven common wearable sensors by collecting data during baseline, stress, recovery and cycling from 32 participants. Machine learning algorithms were used to classify stress from all wearable sensors. The results demonstrated no significant different in accuracy. Therefore, the user's expectation preference and wearable comfort are considered when selecting a wearable for stress detection.

## Conclusion

The current analysis indicated that wrist-worn devices can help plan health assessment strategies and reduce stress. Stress monitoring by wrist-worn devices illustrates good performance comparable with HRV devices and cortisol levels. Stress measurement using a wrist-worn device offers advantages in real-time monitoring and long-term recording. Cardio exercise over 4 weeks was a better stress-relaxed approach than 1.5-hour TM. This finding supports the effectiveness of the proposed cardio-exercise program as a continuous and long-term activity with light and very light cardio zones. A heavy cardio zone may cause inappropriate muscle strain or exhaustion, increasing stress levels instead of

relaxation. Therefore, the suitable duration and exercise zone might be individually adjusted. Moreover, the TM program is exerted as a passive intervention that may help temporary relaxation compared to continuous cardio exercise according to subjective preference.

### Conflict of interest

The authors declare no conflicts of interest.

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