# Towards Anger Phenotyping of Indian Perimenopausal Females with Lyfas Anger Screening Optical Biomarker Instrument LASI

**Subhagata Chattopadhyay** ( subhagata.chattopadhyay2017@gmail.com )
Acculi Labs Pvt. Ltd. Bangalore
**Rupam Das**
Acculi Labs Pvt. Ltd. Bangalore

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## Abstract

# Background

Anger phenotyping in perimenopausal women is a complex task due to multifactor involvement. Anger sets sympathetic overdrive and affects the sympathovagal balance. Lyfas is a novel smartphone-based non-invasive optical biomarker instrument. It captures short Heart rate variability (HRV) and its correlated optical biomarkers using the method of arterial photoplethysmography and assesses the sympathovagal balance.

# Aims

This study is designed to mine the significant optical biomarkers (SDNN, RMSSD, pNN50, SD1/SD2, and LF/HF) and physical parameters (Age, HR, BMI, systolic and diastolic BP, estradiol, TSH, HbA1c, and cortisol) to construct a novel hybrid **L**yfas **A**nger **S**creening **I**nstrument (LASI) and then validated against the well-acclaimed **C**linical **A**nger **S**cale (CAS) in anger phenotyping. **Settings and Design**: It is a case-control study with a total of 415 perimenopausal women (case: 205 and healthy control: 210).

# Methods and material:

Lyfas tests were performed thrice/day for 2 weeks and their biomarkers' scores are captured. During the same period, they have also recorded the anger episodes as per the CAS scoresheet. **Statistical analysis used**: LASI is constructed using Spearman's correlation (ρ and p-values) and validated against the CAS instrument with Bland Altman's inter-rater reliability assessment by noting the strength of agreement.

# Results

BMI, BP, TSH, and HbA1c shows a significant positive correlation with anger. LASI scores high for recall (95%), specificity (75%), precision (92%), accuracy (71%), Youden's index (J-statistic, 74%), and fscore (74%).

# Conclusion

LASI is qualified to be used in the clinical setup in anger screening and monitoring.

## Introduction

Mental health has been perceived as the most important facet to take care of, especially during the corona pandemic. Mental health largely influences the sympathovagal balance or physiological homeostasis of the body and perturbed mental health during the ongoing pandemic mandates screening of likely disorders, if any. In general, mental illness screening tools are largely questionnaire-based, which are either self-rated or to be filled up by the mental health workers. A hybrid approach of clinical examination, laboratory tests, and response to therapeutic management are essential to arrive at an appropriate diagnosis by curbing the chance of human bias. During the corona pandemic, meeting a psychiatrist or going to the laboratory for tests are restricted to prevent catching the virus. Hence, on 25/3/2020, Govt. of India legalized the telemedicine model of healthcare delivery with guidelines, where patients and medical doctors can communicate with each other online. [1]

Phenotyping is a method of determining the characteristics based on observational or exhibiting traits. Anger is a protective emotional trait and is quite prevalent in modern days and its management is even a larger challenge during this pandemic phase due to a lack of social interactions, socioeconomic turmoil, uncertain future, high incidence of morbidity-mortality, and administrative decisions made, which some section of the population thinks unjustified, as found in the work of Smith et al. (2021). [2] Anger is more prevalent in males in society as mentioned in the research of Leonard (2020), [3] however, during this pandemic period, a good number of perimenopausal females complain of intractable but suppressed anger episodes, as shown by Suh et al (2021) in their study [4] due to various reasons and they have reported to the authors. Anger trait has genetic trait through the expression of the MAO-A gene, evident in the study of Mentis et al (2021), [5] endocrine irregularities e.g., estrogen and progesterone depletion, mentioned by Denson et al. (2018), [6] substance abuse described by Lesser (2021) [7], several environmental factors shown by Doyle et al. (2021), [8] and mental illnesses that show high grades of anger issues mentioned in the study of Roy et al. (2020). [9] The neurophysiology of anger shows that emotion, the orbital, medial, and ventrolateral frontal cortex are the key brain regions implicated in anger response and hence emotion tagged with anger is expressed more in these regions, as evident in the work of Blair (2012). [10] Reactive anger is also due to an aberration in the amygdala-hypothalamus-periaqueductal gray matter. [10]

Applications of smartphones in healthcare are gaining popularity across the world due to the increased number of smartphone users, cheaper mobile data, patient-centric delivery, higher version of data privacy, and its pervasive nature. [11] It's a new industry and the estimated market size will be $213.6 billion by 2025 from $50.8 billion in 2020 at a CAGR of 33.3%. [11] Using the optical sensor of the smartphone's rear main camera and the in-built LED light, these can measure the capillary blood flow and volume of the index fingers, when these are gently pressed on the camera. [12] The principle of arterial photoplethysmography, photochromatography, and signal processing play key roles to filter out capillary signals such as Pulse wave velocity (PWV) and Pulse rate variability (PRV). [13]. PRV is synonymous with Heart rate variability (HRV). HRV and its related cardiovascular biomarker (CVb) correlate as a surrogate for the Cardiac autonomic modulation (CAM) of the heart, which in turn gives a measure of mind-body homeostasis. *Lyfas* is not only such a smartphone-based

optical biomarker instrument, it is a quantum digital health platform containing several mental health instruments and tools that anybody can use at any time from anywhere. The instruments help measure the sign symptoms and the corresponding score, while the tool helps in clustering/classification of the state of the art mental health. [13] Its proprietary AI-ML algorithm gives downloadable mind-body analytics of the test-takers in just five minutes and it has been used in screening subclinical depression in the vulnerable population with its cascading other mental health effects such as insomnia and negative thoughts. [14]

The *objectives* of the study are as follows:

a) Creating and testing a set of *digital biomarker-physical parameter hybrid model* **L**yfas **A**nxiety **S**creening **I**nstrument (**LASI**) in a syndrome condition, where multiple systems and organs are involved,

b) Mining significant optical biomarkers and physical parameters and the construction of LASI, and

c) Examining reliability and validity of LASI to the Clinical Anger Scale (**CAS**).

# The novelty of the study

Anger phenotyping with optical biomarkers has never been attempted so far to the best of the knowledge of the authors. In this work, using Lyfas, which is a smartphone-based optical biomarker instrument, an attempt has been made to investigate the anger trait in perimenopausal women who pass through the endocrine-induced physiological and psychosocial stress during the premenopausal state of the mind and body. [15]

## Material And Method

# Statement of Ethics clearance

The study protocol submitted by Acculi Labs Pvt. Ltd., R. R. Nagar, Bangalore, Karnataka, India was approved by the Vagus Institutional Ethics Committee, Bengaluru, Malleswaram, Karnataka, India review board, which is registered with the Central Drugs Standard Control Organization, Ministry of Health and Family Welfare, Govt. of India (No. ECR/1181/Inst/KA/2019, dated 30-01-2020). [16]

# Declaration of patients' consent

Signed informed consents of all participants' have been taken on the organization letterhead according to the *declaration of Helsinki* by the research team prior test. [17]

# Study Design

# Coding and computation

Computations are done using Python 3.9.8 (64-bits) on IDLE editor in Windows 10 OS.

# Perimenopausal condition check

All web-enrolled subjects are checked for the signs symptoms of perimenopausal syndrome under the guidance of two trained gynecologists having an average experience of 20 years. Key signs and symptoms considered in this work are – (i) irregular menstruation (onset, duration, and flow), (ii) hot flush, and (iii) mood swings (stress, anger-anxiety, and depression or SAAD issues) as mentioned by Du et al. (2020) [18] Subjects with these conditions over the *previous 6 months* are recruited for the study.

# Clinical Anger Scale (CAS)

CAS is a gold-standard screening and grading instrument, developed by Snell et al. (1995) which is reliable. [19] It has 21-items each with a four-point scale (0, 1, 2, 3). The sum of the scores gives the total score for the subject. Overall, there are four grades based on the CAS scores as (i) Minimal (score: 0–13), (ii) Mild (score: 14–19), (iii) Moderate (Score: 20–28), and (iv) Severe (Score: 29–63). [20] In this paper, CAS scores are the '*dependent*' variables or *responses*, which are divided into four groups of CAS, mentioned below.

# Lyfas

*Lyfas* is a novel smartphone-based, and non-invasive optical biomarker capturing tool. The tool has been developed using the principle of digital signal processing. [21] It can capture a total of 101 different digital biomarkers and is commercially available. These functional biomarkers are indicative of the psychophysiological state of an individual. [21] *Lyfas* works on two principles, Photoplethysmography (PPG) and Photochromatography (PCG). PPG measures blood volume changes in the microvasculature, while PCG measures the reflected light from various blood components such as cells and solutes. [21] The process is carried out using an optical sensor on the camera and its flashlight acting as an information capturing layer. [21] The next layer is a signal processing layer, which consists of the proprietary mathematical modeling and algorithms (a combination of heuristics-ML-AI), which converts the input signal into actionable metrics, which in turn captures the functional biomarker parameters system-wise [21]. These parameters were then validated in clinical settings (history, physical examination, and laboratory investigations) to detect several electromechanical and physiological activities, such as cardiovascular mechanics, hemodynamics, hemorheology, indicative hematology, and biochemistry in the test takers. [21] The study by Das and Chattopadhyay (2021), Lyfas

has also been found reliable in predicting the cardiac risks in (i) Duchenne muscular dystrophy [22] and (ii) Chronic Obstructive Pulmonary Disease (Chattopadhyay and Das (2022)). [23] In another study by Chattopadhyay and Das (2022), Lyfas has also been found reliable in phenotyping the triad of hypertension-anger-anxiety in a vulnerable adult sample. [24]

The *working principle of Lyfas* has been elaborated step-by-step:

**Step-1**

Placing the index finger and lightly pressing on the rear main camera of the smartphone with the Android version 7 and above operating system, pre-loaded with *Lyfas* application

**Step-2**

Relaxed position with normal breathing and start the test after ticking the consent box and then follow the voice-guided steps of the test

**Step-3**

The camera light captures the capillary blood volume using the principle of Photoplethysmography (PPG), Arterial photoplethysmography (APPG), Photo chromatography (PCG), short Heart Rate Variability (120 seconds HRV), Mobile Spirometry (SPM), and Maneuvers like Orthostatic homeostasis to extract 101 clinically established digital biomarkers

**Step-4**

Grouping of biomarkers into various organ systems using its proprietary heuristics, ML, and finally AI algorithm

**Step-5**

AI-enabled analytics of these biomarkers to assess several psychophysiological states of the body and visualization, and finally

**Step-6**

Correlating analytics with clinical conditions.

# Rationale of parameter-selection

HRV and its correlated *optical biomarkers* surrogate for cardiac autonomic modulation (CAM) to maintain psychophysiological homeostasis. Mental illnesses may cause cardiac autonomic neuropathy (CAN) by disturbing the sympathovagal balance. Therefore, the heightened sympathetic drive is reflected through high LF/HF and SD1/SD2, low pNN50, RMSDD, SDNN, which may be noted in the disorders with high sympathetic drive, e.g., generalized anxiety disorders, [25] schizophrenia, [26] obsessive-compulsive disorders, [27] bipolar disorders, [28] and in many other. A relatively elevated parasympathetic drive is evident in severe degree depression, where the sympathetic drive lowers but the parasympathetic drive remains unaltered. [29]

On the other hand, *physical parameters*, such as middle-Age, HR (increased vasomotor response to hormonal imbalance [30]), BMI (usually gained weight towards obesity [31]), systolic and diastolic BP (often elevates as essential hypertension settles in the body as age advances [32]), estradiol (which is a measure of the hypothalamus-pituitary axis, usually drops [33]), TSH (often is elevated to compensate for the increased demand of thyroxin in the body [34]), HbA1c (rises as type-2 diabetes settles down in the body [35]), and cortisol (a measure of the hypothalamus-pituitary-adrenal axis is often elevated due to the increment of stress [36]) have direct or indirect relationships with the perimenopause stage in the women's life.

# Construction of LASI

*Optical biomarkers* (SDNN, RMSSD, pNN50, SD1/SD2, and LF/HF), obtained by the Lyfas test and *physical parameters* (Age, HR, BMI, systolic and diastolic BP, estradiol, TSH, HbA1c, and cortisol), obtained by the laboratory test and physical examination are the '*independent*' variables or *factors*. Statistically significant ($p < 0.05$, CI 95%) independent variables using Spearman's correlation scores are used to construct **L**yfas **A**nger **S**creening **I**nstrument (LASI), which is then validated against CAS. It is important to mention here that, based on LASI parameters, the *severity of anger* has been graded/classified as 'minimal', 'mild', 'moderate', and 'severe' by a team of three psychiatrists (average experience of 10 years, each), based on their professional experience, who have no clue (i.e., blind) about the respective CAS scores. Table 4 shows the sample LASI data and the corresponding anger grade, which is then matched with that of the CAS scores to evaluate the efficiency of LASI in anger grading (see Table 5).

# Pilot study

A total of 415 perimenopausal females are recruited through web invitations from the company website from October – to December 2021. Out of which 205 consists of the '*case*' as they have a history of anger episodes as per the CAS. Among the cases, for the past *six months*, roughly about 36% have had angry outbursts **(severe CAS)**, 24% have occasional but manageable anger episodes **(moderate CAS)**, while the remaining 40% have 'suppressed' anger, i.e., they feel angry but never show up or express **(moderate-to-severe CAS)**. The remaining 210 samples consist of the '*healthy control*' group having minimal or mild anger episodes **(minimal-to-mild CAS or nil anger)**. *Informed consent* has been obtained from each subject before the study. A recent (*a month-old*) laboratory data of HbA1c (to note the chances of insulin resistance, normal range < 5.7%), serum estradiol (E2, normal range 30–400 pg/ml), [37] TSH (normal range 0.35–4.94 mIU/L), [38] and cortisol (normal range 10–20 mcg/dl when taken between 6–8 am) [39] are collected. Heart rate (normal range 60–100 bpm), Age of the

subject, BMI (normal range 18.4–24.9), systolic BP (SBP, normal value is less than or equals 110–120 mmHg), diastolic BP (DBP, normal value is less than or equals to 68–80 mmHg) levels are also noted at the time of the test. HRV biomarkers, such as SDNN (normal range 50–60 ms), RMSSD (normal range 60–80 ms), pNN50 (normal range 20–40%), SD1/SD2 (normal range 1–3), and LF/HF (normal range 1-1.8) are captured by Lyfas tests, [40] [41] [42] which are taken three times a day – 7 am, 2 pm, and 10 pm for the *same period* for examining the differences in readings at different times of a day. Anger episodes are noted daily as per the **Clinical Anger Scale (CAS)** [19] for the same *two weeks* period.

# Statistics

# z-score normalization

In this work, factor/parameter-wise *z-score normalization* is performed before conducting data analysis. Data normalization is an important pre-processing step to convert the values of the attributes within the same scale. The z-score method of normalization normalizes each value of the dataset in such a way that the mean of all values is '0' and the standard deviation is '1'. [43] The advantage of z-score normalization is that it handles outliers better compared to the max-min normalization method. [44] Appendix-1 shows the data matrix following z-score normalization.

# Data analysis

*Descriptive data analysis* (estimation of mean, median, max-value, min-value, and standard deviations) has been performed to note the spread of the original (i.e., non-normalized) data and can be seen in Table 1. [45] *Kolmogorov-Smirnov tests*, *skewness*, and *kurtosis* are performed to conduct the normality test [46] and data internal consistency or fidelity has been tested by computing *Cronbach's alpha* (α) and can be seen in Table 2. [47] Later on, the strength of correlations (ρ, see Fig. 2) and the statistical significance ($p < 0.05$, CI 95%, see Table 3) of each LASI-factor/parameter with that of the CAS scores are obtained with the help of *Spearman's rank correlation* (ρ). [48] Afterward, the strengths of agreements between each significant parameter of LASI and CAS scores are estimated using *Bland Altman's reliability assessment (BARA)* [49] presented in Fig. 3 (BARA). Finally, the *efficacy* (classification metrics) of LASI in terms of recall (R), specificity (SP), precision (P), accuracy (A), Youden's index or j-stat (J), and fscores (F) are evaluated as the validation method (see Table 5). Figure 1 shows the flow diagram of the material and method applied in the study.

## Results

Appendix 1 shows the whole data matrix following *z-score* normalization.

Table 1
Descriptive statistics of all variables

| | count | mean | std | min | 25% | 50% | 75% | max | Skewness | Kurtosis |
|---|---|---|---|---|---|---|---|---|---|---|
| Age (yr.) | 415 | 49.21 | 3.65 | 43 | 46 | 50 | 52 | 55 | -0.07763 | -1.18204 |
| BMI | 415 | 25.42 | 5.20 | 18 | 21 | 25 | 29 | 36.8 | 0.34035 | -0.97904 |
| SBP (mmHg) | 415 | 125.98 | 21.55 | 100 | 111 | 118 | 140 | 180 | 0.969504 | -0.19382 |
| DBP (mmHg) | 415 | 84.74 | 17.89 | 65 | 72 | 78 | 93 | 130 | 1.110605 | 0.114337 |
| HR (bpm) | 415 | 82.83 | 11.80 | 65 | 74 | 80 | 88.5 | 110 | 0.896958 | -0.24427 |
| E2 (pg/ml) | 415 | 213.96 | 103.88 | 30 | 132 | 209 | 308 | 400 | 0.009137 | -1.09263 |
| CORTISOL (mcg/dl) | 415 | 15.03 | 3.15 | 10 | 12 | 15 | 18 | 20 | 0.008659 | -1.24934 |
| HbA1c (%) | 415 | 4.91 | 1.90 | 1.01 | 3.68 | 5 | 6 | 8 | -0.25417 | -0.69569 |
| TSH (mIU/L) | 415 | 4.14 | 2.18 | 0.51 | 2.48 | 4 | 6 | 8 | 0.186331 | -0.98786 |
| SD1/SD2 | 415 | 1.96 | 0.62 | 0.9 | 1.51 | 1.98 | 2 | 3 | 0.519975 | -0.66687 |
| LF/HF | 415 | 2.44 | 1.31 | 1.00 | 1.41 | 1.79 | 3 | 5 | 0.829643 | -0.7295 |
| SDNN (ms) | 415 | 60.70 | 13.42 | 39.7 | 50 | 60 | 70 | 90 | 0.354393 | -0.7326 |
| RMSSD (ms) | 415 | 63.05 | 14.18 | 40 | 52 | 61 | 70.15 | 95 | 0.496375 | -0.58328 |
| pNN50 (%) | 415 | 30.68 | 17.33 | 5 | 19 | 25 | 38 | 75 | 1.058462 | 0.123574 |
| CAS | 415 | 21.06 | 19.55 | 1 | 5 | 10 | 37 | 63 | 0.763034 | -0.89878 |

Table 2
Results of Kolmogorov-Smirnov (KST) and the Cronbach's α test

| | k-stat | p-value | α |
|---|---|---|---|
| **Age** | 0.10023 | 0.00044 | 0.8253 |
| **BMI** | 0.0967 | 0.00078 | |
| **SBP** | 0.2190 | 5.7312 | |
| **DBP** | 0.2190 | 5.7421 | |
| **HR** | 0.1809 | 2.3092 | |
| **E2** | 0.0730 | 0.0226 | |
| **CORTISOL** | 0.1211 | 9.0472 | |
| **HbA1c** | 0.1014 | 0.0003 | |
| **TSH** | 0.1009 | 0.0003 | |
| **SD1/SD2** | 0.2625 | 9.7698 | |
| **LF/HF** | 0.2460 | 1.3197 | |
| **SDNN** | 0.0688 | 0.0373 | |
| **RMSSD** | 0.0876 | 0.0031 | |
| **pNN50** | 0.2096 | 1.7728 | |
| **CAS** | 0.2253 | 5.4069 | |

Table 3
Spearman 'significant' ($p < 0.05$)correlation

| | p-value |
|---|---|
| **Age** | 0.0362 |
| **BMI** | 5.57e-64 |
| **SBP** | 2.02e-52 |
| **DBP** | 4.81e-50 |
| **HR** | 2.32e-14 |
| E2 | *0.9150* |
| CORTISOL | *0.1668* |
| **HbA1c** | 7.234e-56 |
| **TSH** | 4.600e-63 |
| **SD1/SD2** | 8.206e-71 |
| **LF/HF** | 4.735e-74 |
| **SDNN** | 3.133e-05 |
| **RMSSD** | 3.365e-23 |
| **pNN50** | 3.020e-08 |

Table 4
LASI 'sample' data matrix with CAS and LASI anger grades

| Age | BMI | SBP | DBP | HR | E2 | CORTISOL | HbA1c | TSH | SD1/SD2 | LF/HF | SDNN | RMSSD | pNN50 | CAS | CAS-grade | LASI-grad |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 45 | 32.8 | 151 | 98 | 92 | 42 | 16 | 5 | 7 | 0.9 | 2.5 | 44.2 | 57.6 | 24 | 18 | Mild | Mild |
| 46 | 30.5 | 161 | 124 | 83 | 156 | 10 | 7 | 8 | 1.1 | 2.2 | 39.7 | 47.7 | 10 | 33 | Severe | Mode |
| 48 | 36.4 | 130 | 82 | 71 | 55 | 11 | 6 | 6 | 1.8 | 2.9 | 47.4 | 62.7 | 10 | 60 | Severe | Seve |
| 49 | 20.3 | 131 | 126 | 68 | 290 | 19 | 7 | 7 | 1.4 | 2.5 | 48.6 | 70.3 | 10 | 56 | Severe | Seve |
| 50 | 20.2 | 125 | 97 | 107 | 335 | 11 | 6 | 7 | 1.3 | 3.2 | 56.1 | 73.4 | 13 | 56 | Severe | Mild |
| 51 | 36.8 | 155 | 77 | 72 | 345 | 18 | 5 | 5 | 1.3 | 3 | 58.8 | 85.5 | 64 | 11 | Minimal | Minir |
| 43 | 32.4 | 111 | 93 | 76 | 188 | 13 | 6 | 4 | 1.8 | 2.8 | 55 | 74.4 | 43 | 54 | Severe | Seve |
| 44 | 20.9 | 126 | 72 | 92 | 214 | 13 | 7 | 8 | 0.9 | 1.4 | 57.9 | 78.4 | 75 | 38 | Severe | Seve |
| 45 | 19.5 | 122 | 91 | 88 | 147 | 12 | 5 | 6 | 0.9 | 1.3 | 42 | 63.2 | 14 | 47 | Severe | Seve |
| 49 | 22.9 | 156 | 85 | 89 | 158 | 10 | 5 | 5 | 1.1 | 2.6 | 55 | 84.1 | 15 | 14 | Mild | Mild |
| 54 | 26 | 140 | 76 | 106 | 97 | 11 | 6 | 8 | 2 | 2 | 41 | 86 | 34 | 24 | Moderate | Mode |
| 54 | 35 | 133 | 68 | 83 | 123 | 12 | 6 | 6 | 3 | 5 | 61 | 50 | 52 | 27 | Moderate | Mode |

Table 5
Classification metric for measuring the efficiency of LASI (N = 415)

| TP | FP | TN | FN | R | SP | P | A | F | J |
|---|---|---|---|---|---|---|---|---|---|
| 297 | 23 | 82 | 13 | 0.958065 | 0.780952 | 0.928125 | 0.715663 | 0.942857 | 0.739017 |

## Discussions

As a usual occurrence with biopsychosocial data, the data used in this work is also not normally distributed as evident from the results of skewness, kurtosis, k-statistic, and p-values of KST. Spearman's correlation (ρ) study shows that all the parameters are statistically significant ($p < 0.05$, CI 95%) to predict anger, except the E2 and Cortisol. However, studies reveal that E2 and progesterone levels are raised during anger [50] so as with the Cortisol level as an adaptive response to the anger-induced threat mechanism. [51] *High positive* correlations can be seen between CAS and BMI (overweight often leads to mood swings), which is corroborated by the study of, CAS and LF/HF (high sympathetic or less parasympathetic drive) each has a ρ score of 0.65; followed by TSH ($\rho = 0.62$, high mood swing seen in hypothyroidism); HbA1c (mood disorders associated with diabetics), SBP, DBP (mood issues and irritations found with hypertensives), and SD1/SD2 (reflects heightened anxiety episodes with $\rho = 0.61$), each; while *negative correlations* are found in SDNN ($\rho = -0.23$) as high SDNN reflects good mental health, and *no correlation* is evident in E2, Age, and Cortisol (ρ close to 0). Results of BARA show the average proportional bias close to 0.0 and a standard deviation of 1.1597, which supports the fact that the inter-rater reliability of LASI is a novel instrument is very high when tested to a gold-standard champion instrument CAS.

The efficiency of LASI in grading the anger episodes has been compared to the CAS. Results show that LASI has 95% recall, 78% specificity, 92% precision, 71% accuracy, 94% fscores, and 74% J-stat score, which argues in favor of using LASI as a novel hybrid and efficient instrument for anger screening and monitoring in a clinical setup.

Lyfas can be used as an optical biomarker tool along with other physical parameters in the clinical setup for anger screening and monitoring. Appropriate mental health support can be provided to the sufferers to reduce it to the socially acceptable level towards improving their quality of life, which is often hampered by anger issues. *Bodyweight* control by regular exercise and dieting, regular *hormonal studies*, controlling *hypertension* and *diabetes*, taking appropriate measures in reducing *anxiety*, and Lyfas tests that provide the psychophysiological snapshots through *high LF/HF* and *SD1/SD2*, and *low SDNN* estimations as a tale-tell instrument, are some important correlates found in the study that influences anger to occur.

## Conclusion

Lyfas is a novel, pervasive, and non-invasive smartphone application that provides psychophysiological insights based on optical cardiovascular biomarkers, which surrogate for the cardiac autonomic modulation due to mental and metabolic dysregulations of the body. Biomarkers, such as LF/HF, SD1/SD2, SDNN gives important snapshots of the mental faculty of the test takers. The perimenopausal phase of a woman is stressful due to hormonal imbalance and associated metabolic disorders or comorbidities. Anger is a prevalent mental state in them as one of the outcomes of mood dysregulation. To date, there is no direct instrument to measure their anger states. Questionnaire-based instruments have their drawbacks. Therefore, given this scenario, Lyfas may be a clinical option for detecting the state of anger at a much early state and managing appropriately.

## Declarations

**Competing interest**

The authros affirm no competing interet.

### Author contribution

SC has designed and conducted the study, gathered, cleaned, and analyzed the data. RD has validated the results and written the paper.

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## Figures

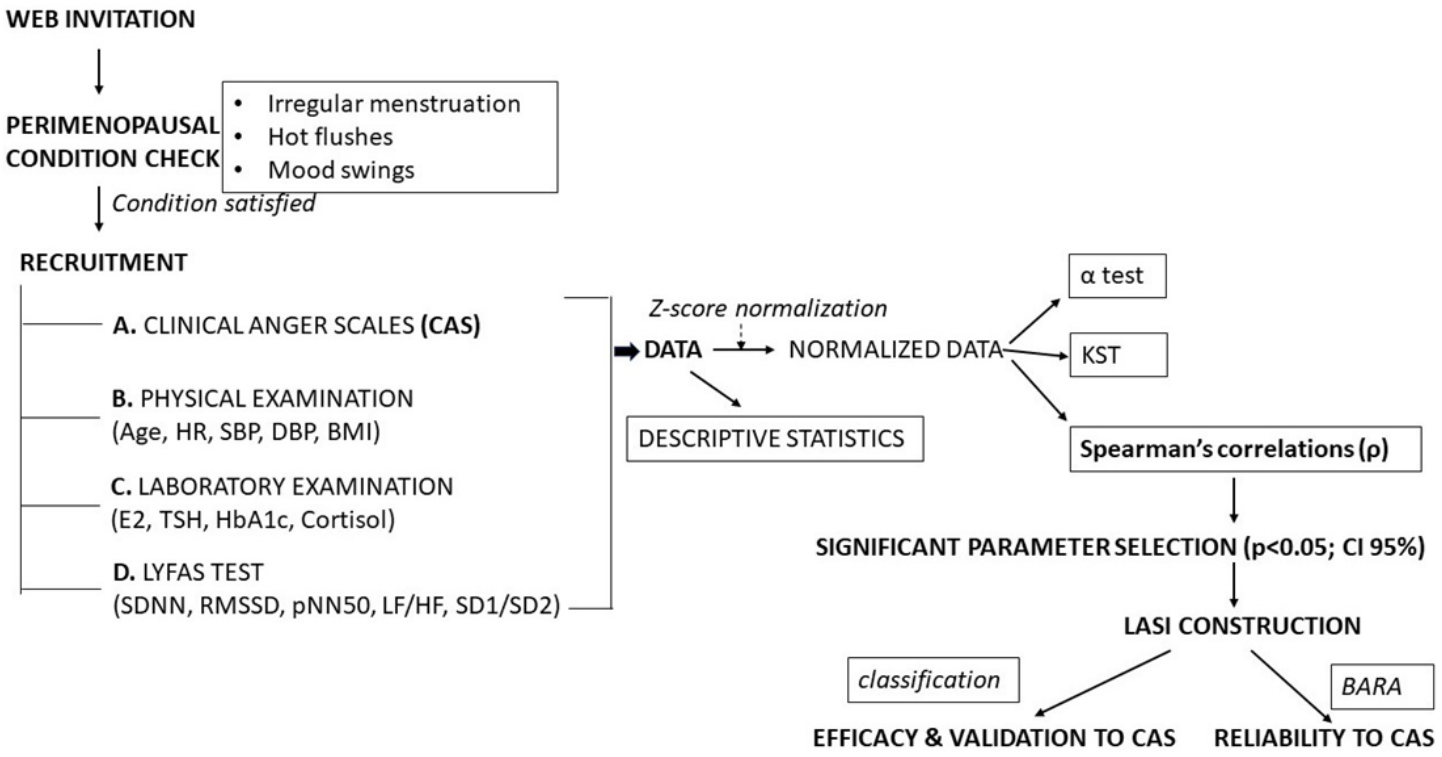


Figure 1

Flow diagram of the pilot study.

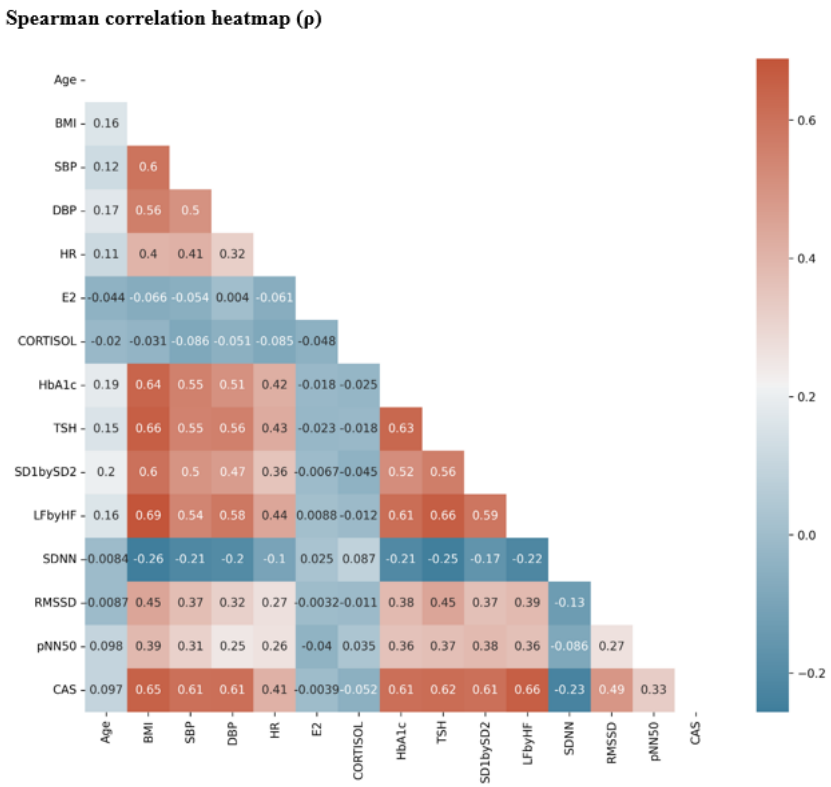


Figure 2

Spearman's correlation heatmap.

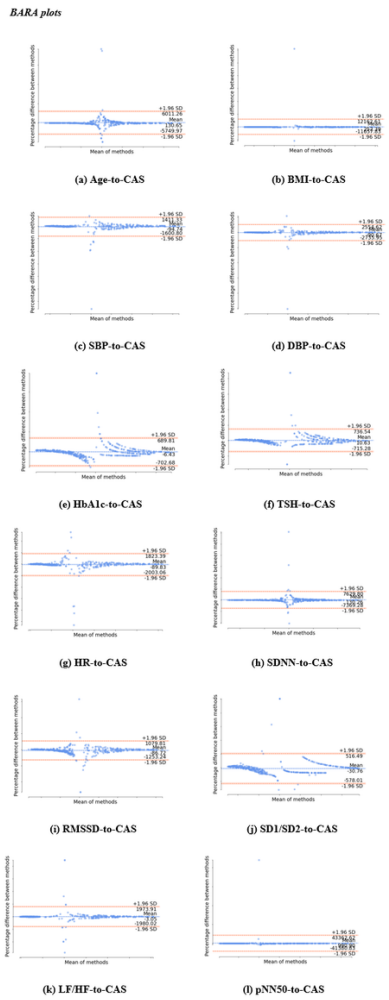


Figure 3

BARA inter-reliability plots of LASI parameters (novel instrument) to CAS (gold-standard champion instrument).

## Supplementary Files

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