Validation of the Lifelight Contactless Blood Pressure and Pulse Rate Monitor

Melissa Kapoor, Blair Holman, Carolyn Cohen

Submitted to: JMIR mHealth and uHealth
on: February 13, 2024

Table of Contents

Validation of the Lifelight Contactless Blood Pressure and Pulse Rate Monitor

Melissa Kapoor[1] DPhil, BSc; Blair Holman[2] MS; Carolyn Cohen[2]

[1]Mind over Matter Medtech Ltd London GB
[2]Element Materials Technology Boulder 80 Health Park Dr #20 Louisville US

Corresponding Author:
Melissa Kapoor DPhil, BSc
Mind over Matter Medtech Ltd
Kemp House
160 City Road
London
GB

Abstract

Background: Key to reducing the immense morbidity and mortality burdens of cardiovascular diseases is helping people keep their blood pressure at safe levels. This requires that more people with hypertension be identified, diagnosed and given the tools to lower their blood pressure. Blood pressure monitors are critical to hypertension diagnosis and management. However, there are characteristics of conventional blood pressure monitors (oscillometric cuff sphygmanometers) that hinder their ability to facilitate rapid and effective hypertension diagnosis and management. Lifelight is a novel, calibration-free, software-only medical device that contactlessly measures pulse rate and blood pressure by measuring remote photoplethysmography (rPPG) signals of a patient's face using a standard smartphone or tablet camera.

Objective: Demonstrate the accuracy of Lifelight for classifying the full range of clinically relevant blood pressures as hypertensive or non-hypertensive. Demonstrate its accuracy for measuring pulse rate and the blood pressure of people with blood pressures relevant to Stage 1 hypertension.

Methods: Lifelight was investigated in a study that followed the data collection and data analysis methodology outlined in ISO 81060-2:2018/AMD 1:2020 "Non-invasive Sphygmomanometers – Part 2: Clinical investigation of automated measurement type". This validation study was conducted by independent laboratory Element Materials Technology Boulder (formerly Clinimark), a global leader for clinical testing of vital sign data for medical devices and consumer wearable products. The study generated data from 85 people aged 18-85 with the wide-ranging distribution of blood pressures specified in ISO 81060-2:2018/AMD 1:2020. At least 20% were required to have Fitzpatrick scale skin tones of 5 or 6, i.e., dark skin tones. The accuracy of Lifelight's blood pressure measurements was assessed by comparing Lifelight's measurements with measurements made by dual-observer manual auscultation using the same-arm sequential method specified in ISO 81060-2:2018/AMD 1:2020. The accuracy of Lifelight's pulse rate measurements was assessed by comparing Lifelight's measurements with concurrent ECG-derived heart rate values.

Results: Lifelight measured pulse rate with Accuracy root-mean-square of 1.34 beats per minute. The sensitivity and specificity with which Lifelight determined that blood pressures exceeded the in-clinic systolic threshold for diagnosis of hypertension was 70.1% and 71.7%, respectively. These rates are consistent with those reported for conventional blood pressure monitors in a literature review by The National Institute for Health and Care Excellence (NICE). The mean error of Lifelight for measuring blood pressure in the range of normotension and Stage 1 hypertension (i.e., in 65 of the 85 study participants) was 6.48 ± 12.88 mmHg for systolic blood pressure, and 0.43 ± 10.64 mmHg for diastolic blood pressure. No device-related adverse events occurred.

Conclusions: Lifelight has been independently tested against ISO 81060-2:2018/AMD 1:2020. Its safety and performance demonstrated in this study suggests that it is a promising solution for rapid, scalable and effective screening and management of hypertension.

(JMIR Preprints 13/02/2024:57241)
DOI: https://doi.org/10.2196/preprints.57241

Preprint Settings

1) Would you like to publish your submitted manuscript as preprint?

✓ **Please make my preprint PDF available to anyone at any time (recommended).**
Please make my preprint PDF available only to logged-in users; I understand that my title and abstract will remain visible to all users.
Only make the preprint title and abstract visible.
No, I do not wish to publish my submitted manuscript as a preprint.

2) If accepted for publication in a JMIR journal, would you like the PDF to be visible to the public?

✓ **Yes, please make my accepted manuscript PDF available to anyone at any time (Recommended).**
Yes, but please make my accepted manuscript PDF available only to logged-in users; I understand that the title and abstract will remain v
Yes, but only make the title and abstract visible (see Important note, above). I understand that if I later pay to participate in <a href="http

Original Manuscript

Validation of the Lifelight Contactless Blood Pressure and Pulse Rate Monitor

Authors and affiliations

Melissa Kapoor, Mind over Matter Medtech Ltd

Blair Holman, Element Materials Technology Boulder

Carolyn Cohen, Element Materials Technology Boulder

Abstract

Background

Key to reducing the immense morbidity and mortality burdens of cardiovascular diseases is helping people keep their blood pressure at safe levels. This requires that more people with hypertension be identified, diagnosed and given the tools to lower their blood pressure. Blood pressure monitors are critical to hypertension diagnosis and management. However, there are characteristics of conventional blood pressure monitors (oscillometric cuff sphygmanometers) that hinder their ability to facilitate rapid and effective hypertension diagnosis and management. Lifelight is a novel, calibration-free, software-only medical device that contactlessly measures pulse rate and blood pressure by measuring remote photoplethysmography (rPPG) signals of a patient's face using a standard smartphone or tablet camera.

Objective

Demonstrate the accuracy of Lifelight for classifying the full range of clinically relevant blood pressures as hypertensive or non-hypertensive. Demonstrate its accuracy for measuring pulse rate and the blood pressure of people with blood pressures relevant to Stage 1 hypertension.

Methods

Lifelight was investigated in a study that followed the data collection and data analysis methodology outlined in ISO 81060-2:2018/AMD 1:2020 "Non-invasive Sphygmomanometers – Part 2: Clinical investigation of automated measurement type". This validation study was conducted by independent laboratory Element Materials Technology Boulder (formerly Clinimark), a global leader for clinical testing of vital sign data for medical devices and consumer wearable products. The study generated data from 85 people aged 18-85 with the wide-ranging distribution of blood pressures specified in ISO 81060-2:2018/AMD 1:2020. At least 20% were required to have Fitzpatrick scale skin tones of 5 or 6, i.e., dark skin tones. The accuracy of Lifelight's blood pressure measurements was assessed by comparing Lifelight's measurements with measurements made by dual-observer manual auscultation using the same-arm sequential method specified in ISO 81060-2:2018/AMD 1:2020. The accuracy of Lifelight's pulse rate measurements was assessed by comparing Lifelight's measurements with concurrent ECG-derived heart rate values.

Results

Lifelight measured pulse rate with Accuracy root-mean-square of 1.34 beats per minute. The sensitivity and specificity with which Lifelight determined that blood pressures exceeded the in-clinic systolic threshold for diagnosis of hypertension was 70.1% and 71.7%, respectively. These rates are consistent with those reported for conventional blood pressure monitors in a literature review by The National Institute for Health and Care Excellence (NICE). The mean error of Lifelight for measuring blood pressure in the range of normotension and Stage 1 hypertension (i.e., in 65 of the 85 study participants) was 6.48 ± 12.88 mmHg for systolic blood pressure, and 0.43 ± 10.64 mmHg for diastolic blood pressure. No device-related adverse events occurred.

Conclusions

Lifelight has been independently tested against ISO 81060-2:2018/AMD 1:2020. Its safety and performance demonstrated in this study suggests that it is a promising solution for rapid, scalable and effective screening and management of hypertension.

Keywords

Remote photoplethysmography; Vital signs; Calibration-free blood pressure monitor; Medical device; Hypertension screening; Home blood pressure monitoring

1. Introduction

Cardiovascular disease (CVD) is the largest cause of death worldwide, accounting for about 19 million deaths a year [1]. In the EU it accounts for almost one third of all deaths [2], and in England it accounts for one quarter of all deaths [3]. Health inequality related to CVD is pronounced, with people living in the most deprived areas of England being more than twice as likely to die from CVD than people in the least deprived areas [4]. In the USA, disparities in CVD prevalence between the richest and poorest populations are not only substantial but growing [5].

High blood pressure (BP) is the leading risk factor for CVD [6]: globally, 54% of strokes and 47% of heart attacks are attributable to hypertension [7]. Therefore, BP is the best single indicator for identifying people at risk of CVD; once someone is diagnosed with hypertension, they can receive clinical support (lifestyle changes and anti-hypertensive medication) to reduce their risk of CVD. Indeed, BP is also the most important aspect of health for a patient with diagnosed hypertension to try to control (i.e., keep at safe levels) to reduce their risk of CVD: every 10mmHg reduction in BP down to a systolic BP of 110mmHg results in 17% reduction in coronary heart disease, 27% reduction in stroke, 28% reduction in heart failure and 13% reduction in all-cause mortality [8].

The large number of deaths caused by CVD plus the high healthcare and societal costs of CVD events (heart attacks, strokes etc.) are driving a strong global push to identify people with undiagnosed hypertension and then ensure their hypertension is well controlled. In the USA, up to one in eight patients with hypertension may not be diagnosed [9]. In England, 29% of people with hypertension are undiagnosed. This equates to 4.2 million people with undiagnosed hypertension [10]. Nationally, a target has been set to increase the percentage of hypertension cases that are diagnosed to 80% by 2029 [11], a target that will be more challenging to meet than was originally expected because it is estimated that the COVID-19 pandemic prevented or delayed almost 500,000 diagnoses of hypertension across England, Scotland and Wales [12]. Rapidly identifying millions of the people with undiagnosed hypertension requires a highly innovative and rapidly scalable approach. This is particularly true where a patient's hypertension may be undiagnosed because they are less engaged with conventional healthcare services, such as NHS Health Checks in England and people without health insurance in the USA.

Novel approaches are needed to ensure patients with diagnosed hypertension control their BP to safe levels (systolic blood pressure <140mmHg and diastolic blood pressure <90mmHg). Rates of BP control achieved using current approaches (typically home blood pressure monitoring using an automated oscillometric blood pressure cuff) are repeatedly shown to be low; in the USA, 43.7% of people with treated hypertension have controlled BP [13]. In the UK, this number is even lower at about 38.1% [14].

Home blood pressure monitoring (HBPM) can help improve BP control, especially when it is in combination with co-interventions such systematic medication titration, patient education, or lifestyle counselling [15]. However, many people with diagnosed hypertension do not own a BP monitor: one UK study found the rate to be not much more than half of treated patients [16]. For many patients who do own a BP monitor, the challenges to using the monitor mean they do not measure their BP according to clinical instructions. These challenges include their inconvenience (bulky size, need to roll up sleeves, need for regular calibration), their difficulty to operate, and the discomfort that they

can cause, particularly to patients with learning difficulties, cognitive impairments, mental illness, or frailty. One study in the USA found that only 38.7% of people with diagnosed hypertension report that they regularly self-monitor their BP [17]. With almost 94 million diagnosed in the USA alone [18,13], there is an opportunity to improve the BP control of many millions of people by making a more convenient and pleasant-to-use monitors for measuring BP available.

Pulse rate (PR) is another vital sign that can be beneficial to monitor in people with hypertension. The COVID-19 pandemic highlighted the heightened risk of infectious diseases on people with hypertension; a 2.5-fold increase in severity and mortality was observed [19]. It has been shown that pre-symptomatic infection such as COVID-19 can be detected from regular monitoring of heart rate (HR) [20].

Xim Limited has developed the Lifelight artificial-intelligence software application that enables completely contactless spot measurements (i.e., one-off measurements without prior calibration) of PR and BP. Based on the science of remote photoplethysmography (rPPG), Lifelight works by detecting tiny changes in the colour of facial skin that occur every time the heart beats. All that is required to generate PR and BP measurements is that the software application is downloaded onto a computer device (e.g., smartphone or tablet) with a standard camera, and that the patient's face stays in the line of sight of the camera for up to 60 seconds.

In the USA, it is estimated that 92% of the population owned a smartphone in 2023 [21]. Smartphone ownership is also increasing in developing countries; it is predicted to reach 75% in India by 2026, for example [22]. This means that the majority of the world's population has the equipment needed to use on-demand digital health applications, helping to reduce health inequalities linked to access to and attitudes/behaviours towards specialist medical equipment. Software-only BP monitors that do not require calibration, such as Lifelight, have particular promise for enabling high-volume hypertension screening that is currently unfeasible with conventional BP monitors or innovative BP monitors that require initial user calibration using separate hardware. Contactless BP monitors that require no specialist equipment also have promise for improving adherence to HBPM. It is therefore reasonable to expect that software-only BP monitors can enable earlier and better detection of hypertension, and also improve rates of BP control among people with diagnosed hypertension, leading to better patient outcomes.

Central to making a new medical technology available is ensuring it has regulatory approval to be marketed. Element Materials Technology Boulder (formerly Clinimark) completed a clinical investigation of the Lifelight blood pressure monitor commissioned by Xim. This study forms the basis of regulatory approvals worldwide for Lifelight. The aim of the study was to assess the accuracy of Lifelight's performance for measuring PR and BP in 85 adult patients aged 18-85 years old. To this end, the study followed the data collection and data analysis methodology outlined in ISO 81060-2:2018/AMD 1:2020, International Standards Organization Non-invasive Sphygmomanometers – Part 2: Clinical investigation of automated measurement type. This paper presents results from Lifelight's study data that relate to the use cases of 1. hypertension screening, 2. HBPM of people with Stage 1 hypertension.

2. Methods

The procedure, data collection methods, and data analysis methods of the Lifelight validation study follow applicable sections of:

- **International Standard ISO 81060-2:2018/AMD 1:2020** Non-invasive sphygmomanometers — Part 2: Clinical investigation of intermittent automated measurement type, where relevant to the device under investigation
- **ISO 14155:2020** Clinical investigation of medical devices for human participants – Good clinical practice (as appropriate).
- **Medical Device Regulation (EU) 2017/745**
- **Code of Federal Regulations** for Nonsignificant Risk Devices

a. Ethics approval

The study was performed in accordance with the declaration of Helsinki, 21 CFR 50, and 21 CFR 812 for non-significant risk device study investigations. The study only commenced once approval was received from the Independent Review Board (IRB) for testing through Salus IRB.

b. Participants and recruitment

Participants were healthy volunteers aged 18 to 85 years old who received an invitation from Element Materials Technology Boulder via phone or email to take part in the study. The procedure was explained to each potential participant and an IRB-approved informed consent form was provided to them. Participants who were satisfied that all of their questions had been satisfactorily answered, who completed the informed consent and health screening, who met all of the inclusion criteria and none of the exclusion criteria, and who contributed towards remaining sample size requirements (skin tone and blood pressure) were enrolled into the study. The only direct benefit to participating in this study was being a paid volunteer.

Participants were excluded from the study if they were medically unsuitable for participation at time of visit, any heart dysrhythmias (except respiratory sinus arrhythmia) as confirmed with a 3 lead ECG, compromised circulation or peripheral vascular disease, clotting disorders, female participants who were pregnant or trying to get pregnant, excessive facial hair, and conditions that affect the skin, such as anaemia, jaundice, rosacea, psoriasis, acute acne, and erythropoietic protoporphyria.

Participants could choose to withdraw themselves from the study without prejudice or they could be withdrawn by study investigators for predetermined reasons. Data excluded from the analysis was documented with justifications.

c. Study procedures

The study was conducted from 18 May 2023 to 03 August 2023 in the Element Materials Technology in Louisville, CO USA in accordance with the study procedure. Study notes were made to describe the conditions of each test as well as deviations, device issues, and any adverse events. There was no additional follow up with the participants.

The same arm sequential method was used to assess Lifelight's accuracy for measuring BP against the dual auscultation reference data. The reference blood pressure measurements were made by two trained observers using a Digital Sphygmomanometer (with a maximum error of ±1 mmHg per NIST traceable calibration verification) with a released BP cuff and a dual auscultatory stethoscope to

listen to the Korotkoff sounds at the brachial artery of each participant's bare left arm. Each observer's recording of observations of the reference sphygmomanometer was not visible to the other observer and neither observer could see the measurements recorded by Lifelight. The actual reference BP measurements are the average of each consecutive pair of reference BP recordings (i.e., the recording made before a given measurement of BP using Lifelight and the measurement made afterwards). These reference BP measurements determine which BP band each measurement set contributes to (hypotension, normotension, Stage 1 hypertension or Stage 2/3 hypertension).

After the participants had rested in the seated position for at least 5 minutes with legs uncrossed, feet flat on the floor, and back, elbow, and forearm supported, one or two initial baseline reference blood pressure recordings were taken. Then, up to eight pairs of reference and Lifelight recordings (starting and ending with reference recordings) were taken sequentially to obtain a minimum of three valid paired reference and Lifelight BP measurements. At least 60 seconds elapsed between each BP determination.

Any pair of observers' reference BP recordings with a difference greater than 4 mmHg were excluded and additional pairs of measurements (up to eight in total) taken to ensure that no more than 10% of the participants had fewer than three valid pairs of blood pressure readings.

Simultaneous to the BP measurements, an FDA-cleared ECG HR monitor (GE Healthcare S5 Compact Monitor) recording Heart Rate at 0.2 Hz was used as reference for Lifelight-derived Pulse Rate measurements. This ECG recording was continuous; reference measurements were the average over the 60-second window that Lifelight was running simultaneously.

d. Sample size

The sample size calculation for the full dataset collected in this study is defined by ISO81060-2:2018/AMD 1:2020. The requirement for 85 participants originated from the early work of the AAMI blood pressure committee dating from 1987.

The range of reference BP measurements for the 85 participants is also defined by ISO81060-2:2018/ AMD 1:2020:

- At least 5% of participants with systolic pressure ≤ 100 mmHg (Hypotension).
- At least 20% of participants with systolic pressure ≥ 140 mmHg (Hypertension).
- At least 5% of participants with systolic pressure ≥ 160 mmHg (High hypertension).
- At least 5% of participants with diastolic pressure ≤ 60 mmHg (Hypotension).
- At least 20% of participants with diastolic pressure ≥ 85 mmHg (Hypertension).
- At least 5% of participants with diastolic pressure ≥ 100mmHg (High hypertension).

Additionally, the ISO standard requires that at least 30% of participants are males and at least 30% are females. We additionally set the requirement that at least 20% of the study population should have a Fitzpatrick score of 5 or 6 (as assessed using the Mexameter MX 18 Melanin Density meter Photonova). Although no standard related to blood pressure monitors or rPPG-based medical technologies have requirements on the skin tone distribution of validation study participants, the Food and Drug Administration (FDA) has issued guidance that pulse oximeters (a PPG technology) should be validated on a population where at least 15% of participants have dark skin tones [23]. We therefore set the requirement for at least 20% of the participants in our validation study to have

Fitzpatrick skin tones of 5 or 6 to exceed the requirement for pulse oximeters. Our protocol allowed us to recruit up to 200 volunteers in order to secure the requisite data for analysis from 85 participants.

For the PR analysis, this paper reports on the full dataset collected from study participants (i.e., data from 85 participants meeting all skin tone and blood pressure distribution requirements). For BP, we provide two sets of analyses: 1. Analyses related to the use case of hypertension screening, which is relevant to people with any blood pressure (from hypotension through to high hypertension), and 2. Analyses related to the use case of HBPM by people with Stage 1 hypertension (BP up to 160/100 mmHg). Therefore, the full dataset collected from study participants in the validation study is used for analyses related to the hypertension screening use case (i.e., data from 85 participants meeting all skin tone and blood pressure distribution requirements). However, for the analyses related to HBPM, only the normotensive and Stage 1 hypertensive BP measurements are included, i.e., reference systolic BP datapoints of 100 – 159 mmHg and reference diastolic BP datapoints of 60 – 99 mmHg. Therefore, the analyses related to HBPM reported in this paper are made using data from fewer than 85 participants.

e. Data analysis

All statistical analyses were performed using Python. We did not perform imputation of missing or implausible data, and any missing, implausible, or problematic readings were excluded from analysis. Where Lifelight was unable to detect the participant's face during the measurement period, this was recorded in the CRF and the measurements were not analysed. Data for a given participant were considered valid if the reference systolic blood pressure determinations did not differ by more than 12mmHg and the reference diastolic blood pressure determinations did not differ by more than 8mmHg over the range of readings once the participant had settled.

This paper reports the mean error and standard deviation of Lifelight's BP measurements in cases where BP is either normotensive or Stage 1 hypertensive. These metrics comprise the Criterion 1 performance requirements stated in ISO 81060-2:2018/AMD 1:2020, which are the clinically sought-after performance metrics for these two use cases. The full set of requirements stated in ISO 81060-2:2018/AMD 1:2020 form the basis of the endpoints of our analyses for gaining regulatory approval of Lifelight for BP use cases generally.

This paper also reports Lifelight's performance for measuring BP in terms of its accuracy for classifying a given measurement set (simultaneous systolic and diastolic BP measurements) as either normotensive or hypertensive. A hypertensive systolic BP measurement (≥ 140 mmHg) and/or a hypertensive diastolic BP measurement (≥ 85 mmHg) can determine a measurement set to be hypertensive. This performance metric is particularly relevant to the use case of screening people with any level of BP for hypertension.

For PR, Lifelight's PR measurements were compared to the reference 3-Lead ECG-derived HR measurements averaged over the same 60-second period. Lifelight's performance in this paper is reported as Accuracy root-mean-square (A_{rms}). The mean bias and R^2 values are also reported.

3. Results

129 volunteers were screened and enrolled into the study in order to generate data meeting the requirements of ISO 81060-2:2018/AMD 1:2020. There were no serious adverse events or serious adverse device effects during the study. There were no observed device deficiencies that could have led to serious adverse device effects.

Table 1 presents the demographic distributions of the 85 participants whose data progressed to the PR analyses and BP classification (hypertension screening) analyses. 44 participants were enrolled in the study but subsequently withdrawn because of device deficiencies, minor adverse events (unrelated to Lifelight), observers could not determine reference BP measurements, and the participant would not progress the study closer to reaching its BP distribution requirements.

Table 1: Demographics of the 85 participants providing study data for PR and hypertension screening analyses

Demographic factor	Distribution
Gender	28/85 (33%) Male 57/85 (67%) Female
Age	20-77 years of age
Systolic BP (determined from baseline reference measurement)	80.5-191.5 mmHg
Diastolic BP (determined from baseline reference measurement)	47.5-106.5 mmHg
Race Participants could report more than one race	Asian (11), American Indian/ Alaskan Native (3), Black / African-American (9), White (64), Other (3)
Ethnicity	Hispanic (9), Non-Hispanic (76)
Skin Tone	17/85 (20%) Fitzpatrick 5&6 68/85 (80%) Fitzpatrick ≤4

The detailed breakdown of BP distributions for these 85 participants is shown in Table 2. These distributions meet the requirements of ISO 81060-2:2018/AMD 1:2020. Hypotension is defined as systolic pressure ≤ 100 mmHg and diastolic pressure ≤ 60 mmHg. Stage 1 hypertension is defined as systolic pressure ≥ 140 mmHg but <160mmHg and diastolic ≥ 85 mmHg but <100mmHg. Stage 2/3 hypertension is defined as systolic pressure ≥ 160 mmHg and diastolic ≥ 100 mmHg.

Table 2: Systolic and diastolic BP distributions of the 85 participants

	Hypotensive	Stage 1 Hypertensive	Stage 2/3 Hypertensive
Systolic BP	13%	25%	5%
Diastolic BP	8%	35%	6%

Once measurements falling outside the normotensive and Stage 1 hypertensive ranges were excluded, 185 measurements from 65 participants were used to generate the results related to HBPM.

The demographic distributions of these 65 participants are shown in Table 3. The distributions of the normotensive/Stage 1 hypertensive reference systolic and diastolic blood pressure measurements from these 65 participants are shown in Table 4.

Table 3: Demographics of the 65 participants providing BP data for HBPM use case analyses (participants providing normotensive or Stage 1 hypertensive measurements only)

Demographic factor	Distribution
Gender	26/65 (40%) Male 39/65 (60%) Female
Age	20-72 years of age
Systolic BP (determined from baseline reference measurement)	100.25-159.0 mmHg
Diastolic BP (determined from baseline reference measurement)	61.5-99.5 mmHg
Race Participants could report more than one race	Asian (4), American Indian/ Alaskan Native (2), Black / African-American (5), White (51), Other (3)
Ethnicity	Hispanic (6), Non-Hispanic (59)
Skin Tone	11/65 (17%) Fitzpatrick 5&6 54/65 (83%) Fitzpatrick ≤4

Table 4: Distributions of BP measurements for HBPM use case analyses (normotensive and Stage 1 hypertensive measurements only)

	Normotensive	Stage 1 Hypertensive
Systolic BP	75%	25%
Diastolic BP	65%	35%

As shown in Figure 1, the mean error of Lifelight's measurements of systolic BP was 6.48 mmHg, with 12.88 mmHg standard deviation. Figure 2 shows that Lifelight's mean error for measuring diastolic BP was 0.43 mmHg, with 10.64 mmHg standard deviation.

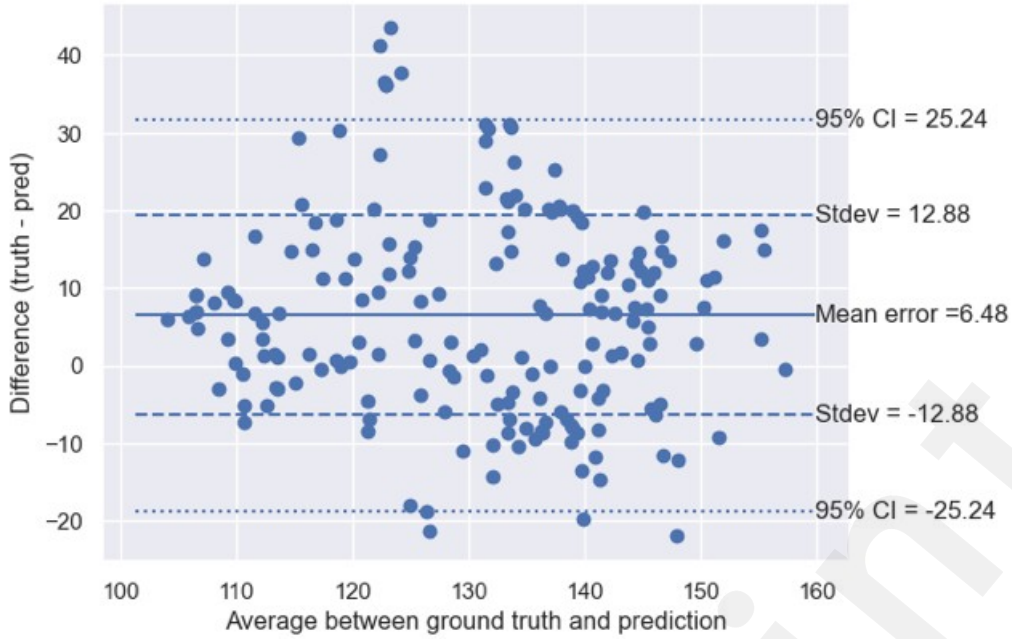


Figure 1: Bland-Altman plot of Lifelight's measurements of systolic blood pressure

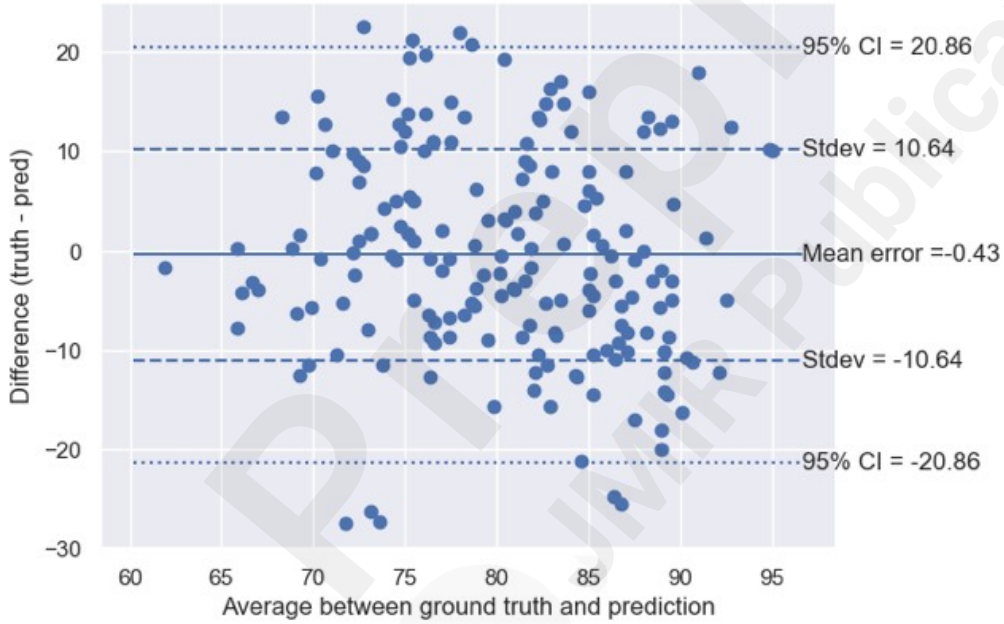


Figure 2: Bland-Altman plot of Lifelight's measurements of diastolic blood pressure

Lifelight correctly classified 70.1% of hypertensive systolic measurements (which could be from people with either Stage 1 hypertensive or Stage 2/3 hypertensive BP measurements) and 71.7% of non-hypertensive systolic measurements (which could be from people with either normotensive or hypotensive BP measurements). The confusion matrix for these classification results is shown in Figure 3.

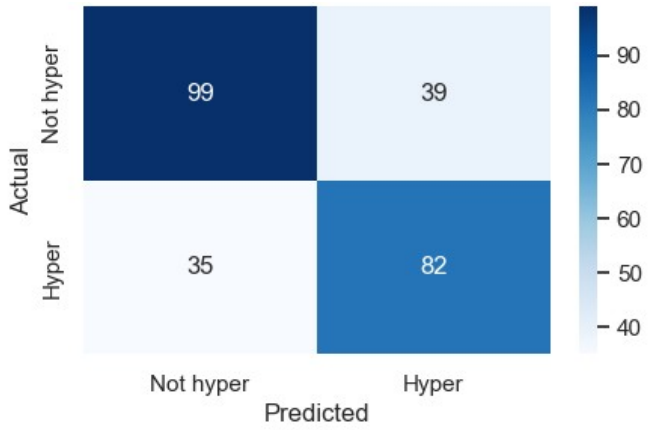


Figure 3: Confusion matrix for Lifelight's classification of BP (systolic and diastolic combined) as hypertensive or not

The scatterplot of Lifelight's measurements of PR is shown in Figure 4. The mean bias with which Lifelight measured PR across measurements from all 85 participants was 0.71 beats per minute (bpm) with R^2 of 0.9875. The A_{rms} was 1.34 bpm.

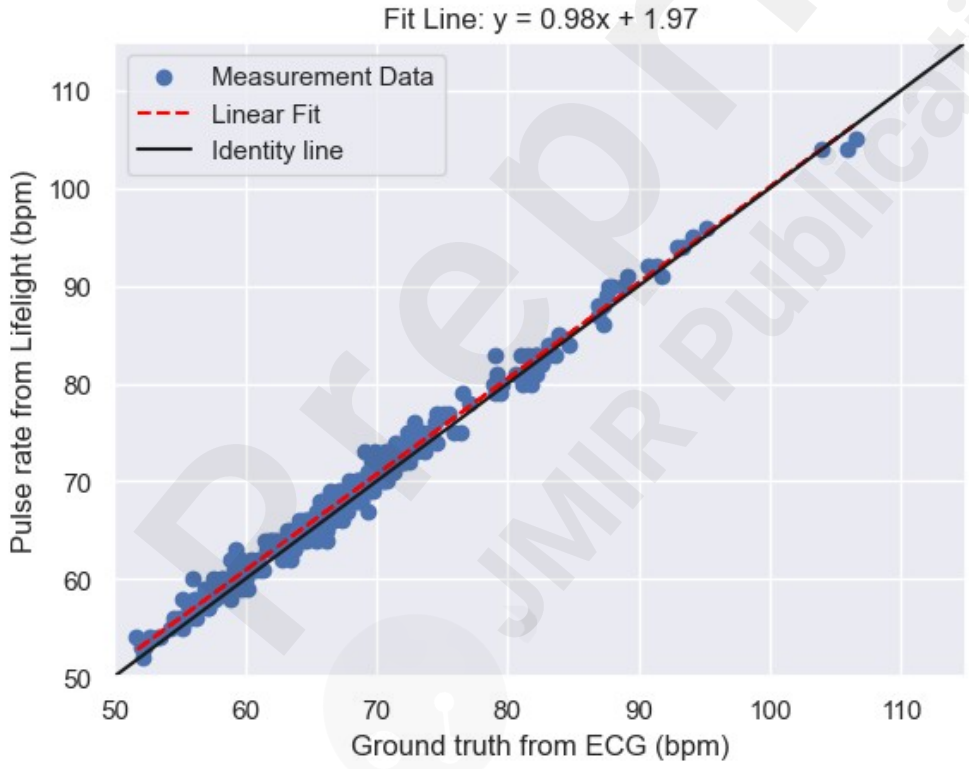


Figure 4: Scatterplot of Lifelight's PR measurements

4. Discussion

Establishing more effective and efficient ways for screening for hypertension, helping people with diagnosed hypertension to keep their BP controlled to safe levels via HBPM and providing a way to detect pre-symptomatic infectious disease in people with hypertension could help significantly reduce this global health burden.

Contactless and calibration-free vital signs monitors that require only ubiquitous equipment (e.g. a standard smartphone) are promising solutions for rapid, scalable, efficient and effective screening and management of people with hypertension. Intensive work is underway to introduce the contactless and calibration-free Lifelight BP and PR monitor in major markets. This rPPG technology works on standard smartphones and tablet devices.

This paper presents results from data collected in a recently completed validation study of Lifelight. The full study data adheres to relevant ISO standards and was conducted by the Element Materials Technology laboratory (i.e., independently of the manufacturer). The full study results will be the core clinical evidence used to support regulatory approval of Lifelight in major markets. For example, approval will be sought for Lifelight's PR measurement functionality on the basis that the study has shown that Lifelight measures PR with A_{rms} of 1.34 bpm.

The manufacturer, Xim, is planning and setting up a series of real-world evaluations of Lifelight in key clinical use cases of unmet need, starting with a randomised controlled trial of Lifelight HBPM among people with diagnosed (but not Stage 3) hypertension, and later with a trial of Lifelight for hypertension screening. These studies aim to demonstrate the clinical and cost-saving benefits of Lifelight in these key use cases.

The hypertension screening and HBPM use cases motivate focused investigation of the normotensive and Stage 1 hypertensive BP validation study data only. With mean error of 6.48 ± 12.88 mmHg for measuring systolic BP and 0.43 ± 10.64 mmHg for measuring diastolic BP among patients with normotensive or Stage 1 hypertensive BP, Lifelight appears to perform in line with the state of the art; a meta-analysis of regulated state-of-the-art BP monitors (devices that measure BP using contact-based PPG e.g. bracelets, or the volume-clamp method or tonometry at the finger) reported the mean error of these devices for measuring systolic BP (across the full range) to be 6.7 ± 15.3 mmHg and 5.5 ± 8.9 mmHg for measuring diastolic BP [24].

Moreover, Lifelight's accuracy must be considered in the light of the accuracy of the current standard of care, which are automated oscillometric BP cuffs and monitors. Automated oscillometric cuffs have inherent error mostly associated with the empirical algorithms used to derive BP from waveform pulsations. This inherent error is often compounded with errors arising because of incorrect operator use; one study found that only 62.8% of hypertensive patients place the cuff correctly and only 65.2% place it on a bare arm – a misuse that can cause BP measurement errors of up to 50 mmHg [25,26]. Another frequent operator use error is not calibrating the monitor as frequently as required (systematic error up to 9 mmHg after only 3 months) [27]. It is estimated that systematic errors due to uncalibrated blood pressure monitors accounts for 28% cases of undetected hypertension and 32% of false diagnoses of hypertension [28].

The National Institute for Health and Care Excellence (NICE) "Hypertension in adults: diagnosis and management - Evidence review for diagnosis 2019" (Guideline NG136) lists the evidence available on the sensitivities and specificities of BP monitors for discriminating hypertension from non-hypertension [29]. For measurements taken in the clinic, the sensitivities of the clinical studies included in NICE's evidence review range from 59% to 89.3%, and the specificities range from 41.4% to 81%. Therefore, the accuracy with which Lifelight distinguished hypertension from non-hypertension using data from across the full range of blood pressures in this study (70.1% sensitivity

and 71.7% specificity) creates hope that calibration-free and contactless technologies that only require ubiquitous equipment (e.g., standard smartphones) could enable rapid and scalable hypertension screening. Globally, 41% of women and 51% of men with hypertension are not diagnosed [30]. That means 580 million people could benefit from an accessible method for screening for hypertension.

As Lifelight's BP measurements are calculated using artificial intelligence (AI) algorithms, its accuracy for measuring BP will continue to improve as it is trained on more data. The effectiveness of the current Lifelight BP algorithms for helping patients with hypertension to control their BP to safe levels is being investigated in the VISION-RWE (real-world evaluation) study. The cost impacts of Lifelight for this HBPM is also being investigated in this UK-based real-world study.

Given that this study was conducted in the USA, it will be prudent to repeat elements of the study in the UK, to demonstrate accuracy on a UK population. Strengths of this study that future studies on Lifelight should aim to emulate include how well subject positioning was controlled with respect to their height, back angle and head angle relative to the camera, the consistency of the lighting through use of two photographic quality LED light panels with adjustable output, and the use of continuous ECG to ensure concurrent signal was available for the pulse rate analyses, eliminating the risk of physiological variation impacting the comparison. A weakness of this study was that over-recruitment was required to meet the demographic and blood pressure distribution requirements, particularly in the light of Lifelight "device deficiencies", i.e., inability to make a pulse rate and blood pressure measurement in some subjects; where the rPPG signal quality does not meet pre-specified thresholds, Lifelight returns no pulse rate and blood pressure measurements. Xim is currently undertaking extensive usability technical developments to improve the rate of successful pulse rate and blood pressure measurements with Lifelight.

5. Acknowledgements

The study protocol was co-developed by Element Materials Technology Boulder (formerly Clinimark), Mind over Matter Medtech, and Xim Limited. We especially thank Paul Batchelder, prior Chief Clinical Officer of Clinimark, for his advice on study design.

Study activities conducted at Element Materials Technology Boulder were funded by Xim Limited. Xim provided Element Materials Technology Boulder with tablet devices onto which the Lifelight application was already downloaded. Mind over Matter Medtech was funded by Xim Limited to conduct the data analyses and preparation of this manuscript.

6. Data Availability

The data generated and analysed during this study are commercially sensitive and are therefore not publicly available, as mandated by Xim's contractual obligations with its grant funders and investors. Furthermore, the informed consent provided by study participants only allows access to individual data, including in anonymized form, by authorized individuals of the research team based at the study sites, Xim, and Xim's authorized partners. Reasonable requests for access to the study data within these limitations will be considered by the corresponding author.

7. Conflicts of Interest

The authors have no conflicts of interest to declare.

8. Abbreviations

AI: artificial intelligence

A_{rms}: Accuracy root-mean-square

BP: blood pressure

bpm: beats per minute

ECG: electroencephalography

HBPM: home blood pressure monitoring

HR: heart rate

ISO: International Organization for Standardization

mmHg: millimetres of mercury

NICE: The National Institute for Health and Care Excellence

PR: pulse rate

R^2: coefficient of determination

rPPG: remote photoplethysmography

9. References

1. Roth, G. A., Mensah, G. A., Johnson, C. O., Addolorato, G., Ammirati, E., Baddour, L. M., Barengo, N. C., Beaton, A. Z., Benjamin, E. J., Benziger, C. P., Bonny, A., Brauer, M., Brodmann, M., Cahill, T. J., Carapetis, J., Catapano, A. L., Chugh, S. S., Cooper, L. T., Coresh, J., & Criqui, M. (2020). Global Burden of Cardiovascular Diseases and Risk Factors, 1990-2019: Update From the GBD 2019 Study. *Journal of the American College of Cardiology*, 76(25), 2982–3021. PMID:33309175
2. Eurostat. (2020). Cardiovascular diseases statistics. Accessed on 8th February 2024. https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Cardiovascular_diseases_statistics#Deaths_from_cardiovascular_diseases
3. Raleigh, V., Jefferies, D., & Wellings, D. (2022). Cardiovascular disease in England. Accessed 7th February 2024. https://www.kingsfund.org.uk/sites/default/files/2022-11/CVD_Report_Web.pdf
4. Office for National Statistics. (2023, March). Inequalities in mortality involving common physical health conditions, England. Accessed 7th February 2024. https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/healthinequalities/bulletins/inequalitiesinmortalityinvolvingcommonphysicalhealthconditionsengland/21march2021to31january2023
5. Abdalla, S. M., Yu, S., & Galea, S. (2020). Trends in cardiovascular disease prevalence by income level in the United States. *JAMA network open*, 3(9), e2018150-e2018150. PMID:32975572
6. Fuchs, F. D., & Whelton, P. K. (2019). High Blood Pressure and Cardiovascular Disease. Hypertension, 75(2), 285–292. PMID:31865786
7. Lawes, C.M., Vander Hoorn, S. and Rodgers, A., 2008. Global burden of blood-pressure-related

disease, 2001. The Lancet, 371(9623), pp.1513-1518. PMID:18456100
8. Ettehad, D., Emdin, C. A., Kiran, A., & Rahimi, K. (2016). Blood pressure lowering for cardiovascular disease – Authors' reply. *The Lancet*, 388(10040), 126–127. PMID:27411872
9. Ciemins, E. L., Ritchey, M. D., Joshi, V. V., Loustalot, F., Hannan, J., & Cuddeback, J. K. (2018). Application of a tool to identify undiagnosed hypertension—United States, 2016. *Morbidity and Mortality Weekly Report*, 67(29), 798. PMID:30048423
10. Office for National Statistics. (2023, April 27). Risk factors for undiagnosed high blood pressure in England. Accessed 8th February 2024. https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/healthandwellbeing/articles/riskfactorsforundiagnosedhighbloodpressureinengland/2015to2019#:~:text=An%20estimated%2032%25%20of%20adults
11. Public Health England and NHS England. (2019, February 14). Ambitions set to address major causes of cardiovascular disease. Accessed 7th February 2024. https://www.gov.uk/government/news/ambitions-set-to-address-major-causes-of-cardiovascular-disease&sa=D&source=docs&ust=1702428128016119&usg=AOvVaw2YFNniSrPLqyPwV-zyk_Pc
12. Dale, C. E., Takhar, R., Carragher, R., Katsoulis, M., Torabi, F., Duffield, S., Kent, S., Mueller, T., Kurdi, A., Le Anh, T. N., McTaggart, S., Abbasizanjani, H., Hollings, S., Scourfield, A., Lyons, R. A., Griffiths, R., Lyons, J., Davies, G., Harris, D., & Handy, A. (2023). The impact of the COVID-19 pandemic on cardiovascular disease prevention and management. *Nature Medicine*, 1–7. PMID:36658423
13. Muntner, P., Hardy, S. T., Fine, L. J., Jaeger, B. C., Wozniak, G., Levitan, E. B., & Colantonio, L. D. (2020). Trends in blood pressure control among US adults with hypertension, 1999-2000 to 2017-2018. *Jama*, 324(12), 1190-1200. PMID:32902588
14. Tapela, N., Collister, J., Clifton, L., Turnbull, I., Rahimi, K., & Hunter, D. J. (2021). Prevalence and determinants of hypertension control among almost 100 000 treated adults in the UK. *Open Heart*, 8(1), e001461. PMID:33707223
15. Tucker, K. L., Sheppard, J. P., Stevens, R., Bosworth, H. B., Bove, A., Bray, E. P., Earle, K., George, J., Godwin, M., Green, B. B., Hebert, P., Hobbs, F. D. R., Kantola, I., Kerry, S. M., Leiva, A., Magid, D. J., Mant, J., Margolis, K. L., McKinstry, B., & McLaughlin, M. A. (2017). Self-monitoring of blood pressure in hypertension: A systematic review and individual patient data meta-analysis. *PLOS Medicine*, 14(9), e1002389. PMID:28926573
16. Anbarasan, T., Rogers, A., Rorie, D. A., Grieve, J. W. K., Flynn, R. W. V., MacDonald, T. M., & Mackenzie, I. S. (2022). Factors influencing home blood pressure monitor ownership in a large clinical trial. *Journal of Human Hypertension*, 36(3), 325–332. PMID:33654240
17. Ostchega, Y., Zhang, G., Kit, B. K., & Nwankwo, T. (2017). Factors associated with home blood pressure monitoring among US adults: National Health and Nutrition Examination Survey, 2011–2014. American Journal of Hypertension, 30(11), 1126-1132. PMID:28633432
18. Tsao, C. W., Aday, A. W., Almarzooq, Z. I., Alonso, A., Beaton, A. Z., Bittencourt, M. S., ... & American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. (2022). Heart disease and stroke statistics—2022 update: a report from the American Heart Association. Circulation, 145(8), e153-e639. doi:10.1161/CIR.0000000000001052
19. Lippi, G., Wong, J., & Henry, B. M. (2020). Hypertension and its severity or mortality in Coronavirus Disease 2019 (COVID-19): a pooled analysis. *Polish Archives of Internal Medicine*. doi:10.20452/pamw.15272
20. Mishra, T., Wang, M., Metwally, A. A., Bogu, G. K., Brooks, A. W., Bahmani, A., Alavi, A., Celli, A., Higgs, E., Dagan-Rosenfeld, O., Fay, B., Kirkpatrick, S., Kellogg, R., Gibson, M., Wang, T., Hunting,

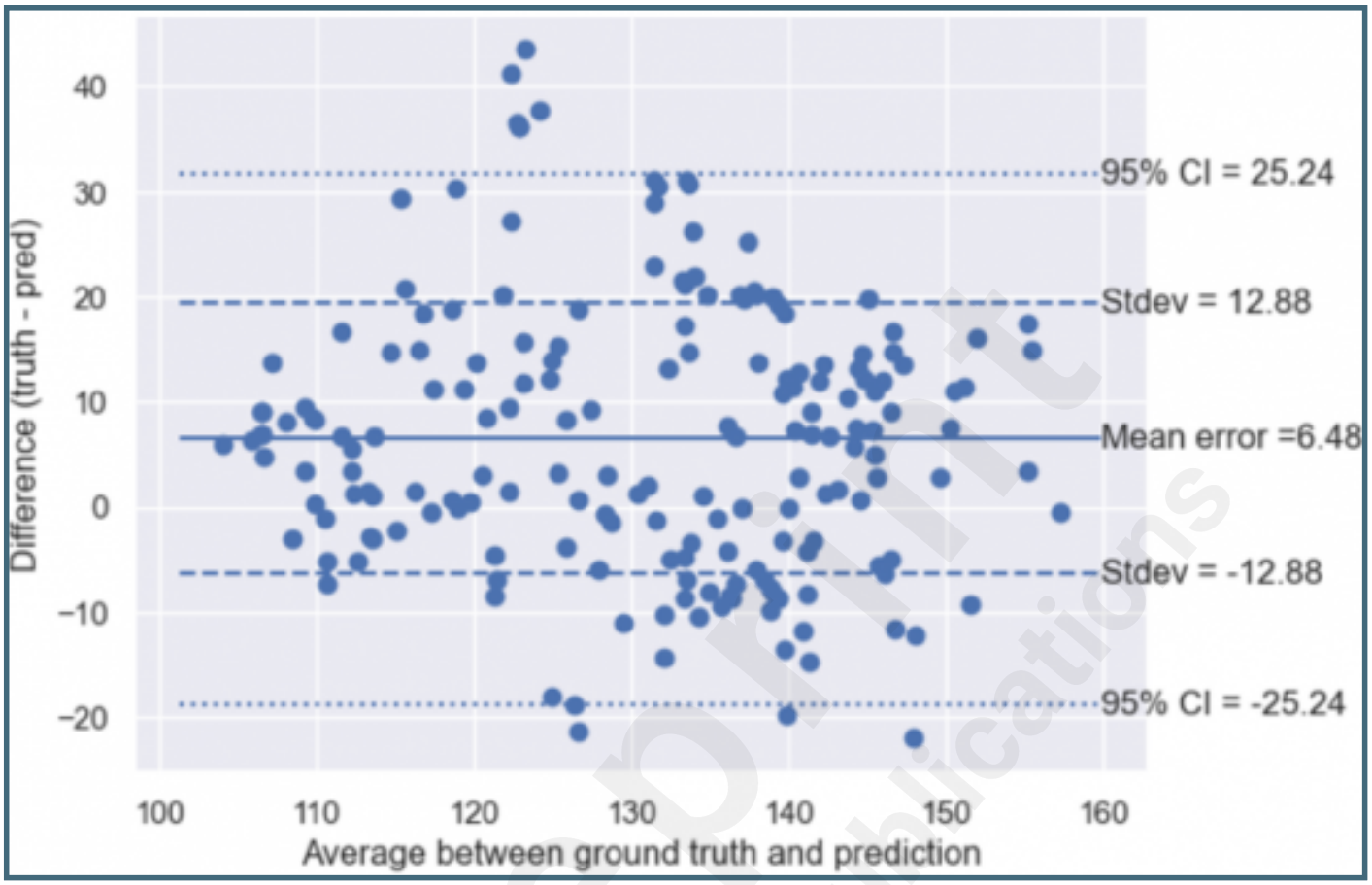
E. M., Mamic, P., Ganz, A. B., Rolnik, B., & Li, X. (2020). Pre-symptomatic detection of COVID-19 from smartwatch data. *Nature Biomedical Engineering*, 4(12), 1208–1220. PMID:33208926

21. Consumer Affairs. (2023). Cell phone statistics 2024. Accessed 7th February 2024. https://www.consumeraffairs.com/cell_phones/cell-phone-statistics.html
22. Deloitte. (2022). TMT Predictions 2022. Accessed 7th February 2024. https://www2.deloitte.com/content/dam/Deloitte/in/Documents/technology-media-telecommunications/in-TMT-predictions-2022-noexp.pdf
23. FDA. (2013, March). Pulse Oximeters – Premarket Notification Submissions [510(k)s], Guidance for Industry and Food and Drug Administration Staff. www.fda.gov/regulatory-information/search-fda-guidance-documents/pulse-oximeters-premarket-notification-submissions-510ks-guidance-industry-and-food-and-drug
24. Heiden, E., Jones, T., Brogaard Maczka, A., Kapoor, M., Chauhan, M., Wiffen, L., Barham, H., Holland, J., Saxena, M., Wegerif, S., Brown, T., Lomax, M., Massey, H., Rostami, S., Pearce, L., & Chauhan, A. (2022). Measurement of Vital Signs Using Lifelight Remote Photoplethysmography: Results of the VISION-D and VISION-V Observational Studies. *JMIR Formative Research*, 6(11), e36340. PMID:36374541
25. Flacco, M. E., Manzoli, L., Bucci, M., Capasso, L., Comparcini, D., Simonetti, V., Gualano, M. R., Nocciolini, M., D'Amario, C., & Cicolini, G. (2015). Uneven Accuracy of Home Blood Pressure Measurement: A Multicentric Survey. *The Journal of Clinical Hypertension*, 17(8), 638–643. PMID:25880129
26. Whelton, MD, S. P., Ebinger, MD, FACC , J., & Yang, MD, E. (2023, June 6). Why Is Cuff Size So Important and Other Factors That Affect Accurate Blood Pressure Measurement. *American College of Cardiology*. https://www.acc.org/Latest-in-Cardiology/Articles/2023/06/05/19/18/Why-Is-Cuff-Size-So-Important-and-Other-Factors-That-Affect-Accurate-BP-Measurement
27. Abderahman, H. N., Dajani, H. R., Miodrag Bolić, & Groza, V. (2016). An integrated system to compensate for temperature drift and ageing in non-invasive blood pressure measurement. *IEEE International Symposium on Medical Measurements and Applications (MeMeA)*. doi:10.1109/MeMeA.2016.7533751
28. Turner, M. J., Irwig, L., Bune, A. J., Kam, P. C., & Baker, A. B. (2006). Lack of sphygmomanometer calibration causes over- and under-detection of hypertension: a computer simulation study. *Journal of Hypertension*, 24(10), 1931–1938. PMID:16957551
29. NICE. (2019, August). Hypertension in adults: diagnosis and management - Evidence review for diagnosis NICE guideline NG136. Accessed 7th February 2024. https://www.nice.org.uk/guidance/ng136/evidence/a-diagnosis-pdf-6896748206
30. Zhou, B., Carrillo-Larco, R. M., Danaei, G., Riley, L. M., Paciorek, C. J., Stevens, G. A., Gregg, E. W., Bennett, J. E., Solomon, B., Singleton, R. K., Sophiea, M. K., Iurilli, M. L., Lhoste, V. P., Cowan, M. J., Savin, S., Woodward, M., Balanova, Y., Cifkova, R., Damasceno, A., & Elliott, P. (2021). Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. *The Lancet*, 398(10304). PMID:34450083

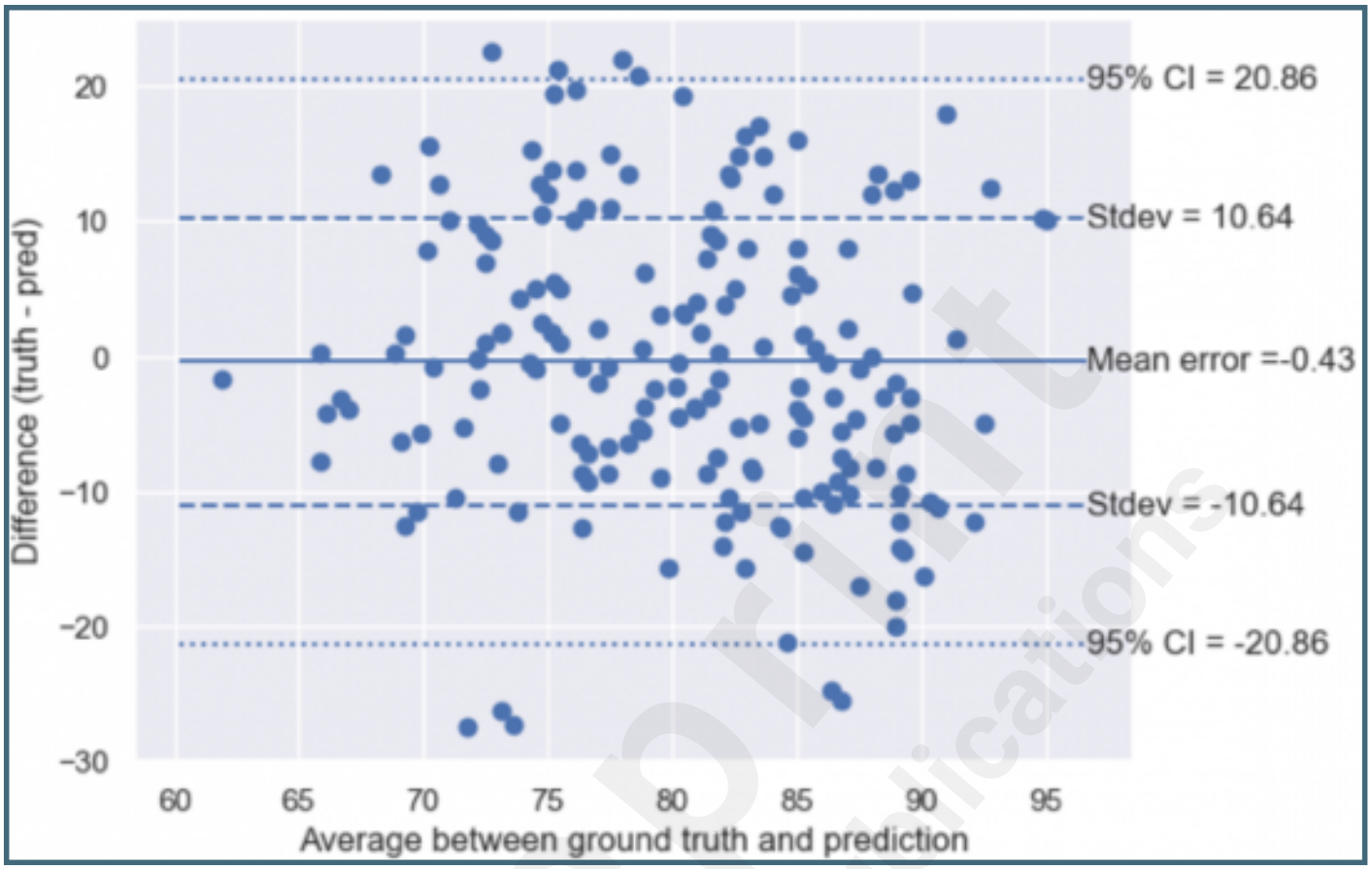
Supplementary Files

Figures

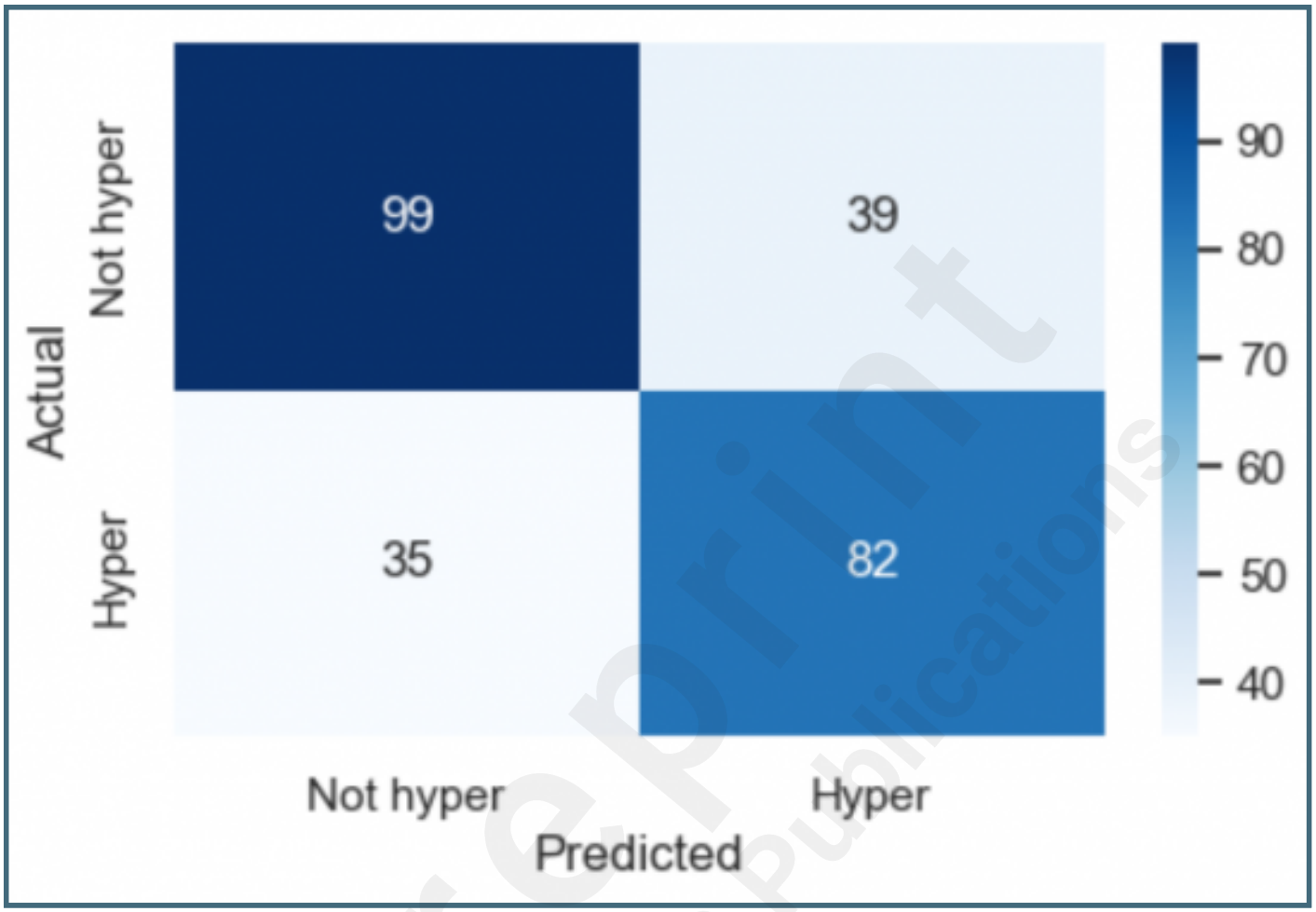
Bland-Altman plot of Lifelight’s measurements of systolic blood pressure.



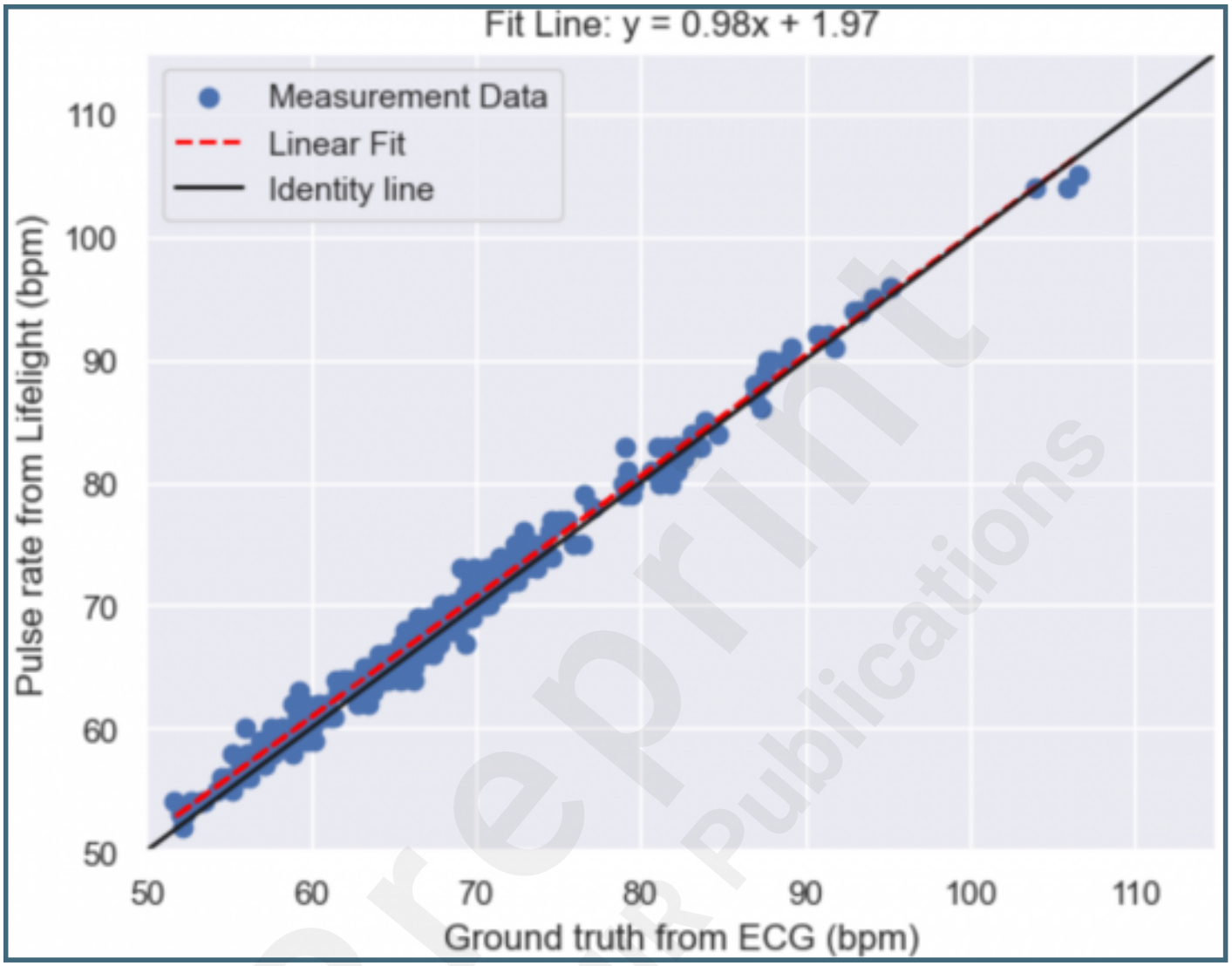
Bland-Altman plot of Lifelight's measurements of diastolic blood pressure.



Confusion matrix for Lifelight’s classification of BP (systolic and diastolic combined) as hypertensive or not.



Scatterplot of Lifelight’s PR measurements.



TOC/Feature image for homepages

Set up of the validation study for the Lifelight application.