CONFIDENTIAL

Relationship between blood pressure profiles measured by a wrist-type blood pressure monitor (HeartGuide) and left ventricular mass index.

HeartGuide BP LVMI study

Chief Investigator	Prof Bryan Williams
Contributing authors	Bryan Williams; Peter Lacy; Dawid Jedrzejewski; Ewan McFarlane.
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SPONSORS Number:	EDGE ID: 132948

Declarations

The undersigned confirm that the following protocol has been agreed and accepted and that the investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the Research Governance Framework 2005 (as amended thereafter), the Trust Data & Information policy, Sponsor and other relevant SOPs and applicable Trust policies and legal frameworks.

I (investigator) agree to ensure that the confidential information contained in this document will not be used for any other purposes other than the evaluation or conduct of the clinical investigation without the prior written consent of the Sponsor.

I (investigator) also confirm that an honest accurate and transparent account of the study will be given; and that any deviations from the study as planned in this protocol will be explained and reported accordingly.

Signature page

For and on behalf of the Trial Sponsor:		
Signature: 		Date: 09/12/2020.
Name (please print): Dr Maurice Griffin		
Position: Sponsorship Officer, Joint Research Office, University College London		
Chief Investigator:		
Signature: 		Date: 09/Dec/2020
Name: (please print): Professor Bryan Williams		

Key Trial contacts

Chief Investigator	Professor Bryan Williams. University College London & University College London NHS Trust Maple House, First Floor Suite A, 149 Tottenham Court Road, London, W1T 7DN 02076796639 Bryan.williams@ucl.ac.uk
Trial Manager	Mrs. Donna Moskal-Fitzpatrick University College London, Institute of Cardiovascular Science 3rd Floor, Roger Williams Building69-75 Chenies Mews WC1E 6HX 0207679883240 donna.moskal@ucl.ac.uk
Sponsor	UCL Joint Research Office
Funder(s)	Grant in Aid of Research Omron Healthcare Co. Ltd.

PROTOCOL VERSIONS

Version Stage	**Versions No**	**Version Date**	**Protocol updated & finalised by;**	**Appendix No detail the reason(s) for the protocol update**
Current	1.0	09/12/2020	B Williams, D Moskal Fitzpatrick UCL JRO	Ethics submission

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i. List of Abbreviations

ABPM	Ambulatory blood pressure monitoring
BP	Blood pressure
CAVI	Cardio-ankle vascular index
cMRI	Cardiac magnetic resonance imaging
ECG	Electrocardiogram
HBPM	Home blood pressure monitoring
LV	Left ventricle
LVMI	Left ventricular mass index
MRI	Magnetic resonance imaging
REC	Research ethics committee

ii. Key Words

HeartGuide wrist Blood Pressure Monitor

Left ventricular mass

Cardiac MRI

Ambulatory Blood Pressure.

iii. Trial Summary

Trial Title	Relationship between blood pressure profiles measured by a wrist-type blood pressure monitor (HeartGuide) and left ventricular mass index	
Internal ref. no. (or short title)	HeartGuide BP LVMI study	
Trial Design	Cross-sectional study	
Trial Participants	Men and Women ≥ 35 years old	
Planned Sample Size	50 study participants in the UK study. The data will be merged with a study conducted in parallel at the Jichi Medical University, Japan, using a similar protocol.	
Follow up duration	1 month	
Planned Trial Period	18 months; Anticipated start and end dates: 11 January 2021 – 10 July 2022 End of study defined as the last visit of the last participant	
	Objectives	Outcome Measures
Primary	Association between mean "out of office*" systolic blood pressure measured by the HeartGuide watch BP monitor and left ventricular mass index (LVMI) measured by cardiac MRI. **out of office" refers to blood pressure measurements made by the study participants in their home and work environments, i.e. away from the doctor's office.*	• LVMI by cardiac MRI • Mean of "out of office" systolic blood pressure measurements recorded by a wearable BP monitor (HeartGuide)
Secondary	1. Comparison of the relationships between BP indices measured by; (i) the HeartGuide watch BP monitor, or (ii) ABPM, or (iii) seated office BP, with	• LVMI and other cardiac / vascular indices by cardiac MRI • HeartGuide BP

	LVMI by cardiac MRI 2. Relationship between all BP indices and Cardiac Ankle Vascular index (CAVI). 3. Relationship between CAVI indices and cardiac MRI parameters including LVMI, cardiac volumes and vascular indices. 4. Relationships between all BP indices and ECG voltage criteria for left ventricular mass 5. The relationships and any significant differences between various BP indices	• 24-hour ABPM • CAVI • ECG voltage measures of LVMI • Brachial office BP
Data collected and storage	Analysis of the data will be done at University College London. Only processed data will be sent to Omron Healthcare Co Ltd., 53, Kunotsubo, Terado-Cho, Muko, Kyoto, Japan. Non-identifiable data will be collected on electronic tablet using an electronic case report form in REDCap. Data will be transferred to secure University College London computers and stored on a shared drive. No data will be stored on the electronic tablet. Identifiable data will be stored within Data Safe Haven at University College London or within the site file in a secure cabinet at the research offices (UCL).	

iv. Funding and Support

FUNDER	FINANCIAL SUPPORT GIVEN
Omron Healthcare Co Ltd., 53, Kunotsubo, Terado-Cho, Muko, Kyoto, Japan Post code: 617-0002 Contact details: Dr. Mitsuo Kuwabara, Tel: +81-75-925-2204 Fax: +81-75-925-2044 Mobile: +81-80-9596-5245 E-mail: mitsuo.kuwabara@omron.com	Grant to UCL in aid of investigator-led and designed research (£150,000) to cover the cost of the UK study

Key Roles and Responsibilities

SPONSOR: The sponsor is responsible for ensuring before a study begins that arrangements are in place for the research team to access resources and support to deliver the research as proposed and allocate responsibilities for the management, monitoring and reporting of the research. The Sponsor also has to be satisfied there is agreement on appropriate arrangements to record, report and review significant developments as the research proceeds, and approve any modifications to the design.

FUNDER: The funder is the entity that will provide the funds (financial support) for the conduction of the study. Funders are expected to provide assistance to any enquiry, audit or investigation related to the funded work.

CHIEF INVESTIGATOR (CI): The person who takes overall responsibility for the design, conduct and reporting of a study. If the study involves researchers at more than once site, the CI takes on the primary responsibility whether or not he/she is an investigator at any particular site.

The CI role is to complete and to ensure that all relevant regulatory approvals are in place before the study begins. Ensure arrangements are in place for good study conduct, robust monitoring and reporting, including prompt reporting of incidents, this includes putting in place adequate training for study staff to conduct the study as per the protocol and relevant standards.

The Chief Investigator is responsible for submission of annual reports as required. The Chief Investigator will notify the RE of the end of the study, including the reasons for the premature termination. Within one year after the end of study, the Chief Investigator will submit a final report with the results, including any publications/abstracts to the REC.

Background and Purpose of the Study

Blood pressure (BP) measurement is one of the commonest procedures conducted in routine medical care[1]. Identifying an elevated BP is important because a persistently elevated BP is associated with increased lifetime risk of myocardial infarction[2, 3], heart failure[2, 4], stroke[5, 6], dementia[7, 8], vascular disease[9, 10] and chronic kidney disease[11]. Indeed, global surveys have identified an elevated BP as the most important preventable cause of premature death[12, 13]. BP has traditionally been measured whilst seated and rested in the doctor's office using a cuff around the upper arm[1]. More recently, devices have become available that have allowed BP to be measured "out of office", i.e. in the patients' more usual environment such as at home or at work. This is done, either with an automated 24-hour BP monitor (ambulatory BP monitoring or ABPM)[14], programmed to measure BP multiple times over a 24-hour period using an upper arm cuff, whilst the patient is ambulant and when sleeping, or by patient self-measurement of BP using an upper arm cuff, multiple times whilst at home (whilst seated in the morning or the

evening for a minimum of 3 days), so called home BP monitoring (HBPM)[15]. With these out of office measurements (ABPM or HBPM), the multiple readings are averaged to provide a mean BP reading[16]. Recent guidelines on the clinical management of hypertension in the UK (NICE)[17], Europe[13] and the USA[18, 19] have all recommended that out of office BP measurement (either by ABPM or HBPM) should be undertaken to confirm the diagnosis of hypertension because (i) they can identify patients whose BP is only elevated in the doctors' office but not out of office, so called white coat hypertension, avoiding unnecessary treatment of patients with white coat hypertension[14]; (ii) when compared with seated office BP measurement, ABPM and HBPM readings are better correlated with pressure-mediated organ damage[20-22]; and (iii) when compared with seated office BP measurement, ABPM and HBPM readings are better correlated with clinical outcomes[23, 24], with ABPM providing the most compelling data.

Recently a wristwatch style monitor was developed for the measurement of out of office BP (HeartGuide, Omron, Japan)[25]. This is smaller, lighter and less intrusive than conventional ABPM monitors and does not depend on an upper arm cuff. Instead, the cuff is incorporated in the strap of the watch (see fig. 2) which allows the patient to activate self-measurement of their BP multiple times during the day, either whilst seated (e.g. similar to HBPM) or when ambulant (similar to ABPM). The device prompts the user via a short vibration at the wrist, to position their wrist at heart level, immediately prior to BP measurement. In a recent study, we showed that BP measured with this device correlated very well with BP measurements using upper-arm cuff-based ABPM when BP was recorded by the HeartGuide watch immediately after each activation of ABPM BP measurement[26]. The present study will extend these findings and evaluate whether average systolic BP measured using the HeartGuide watch is correlated with left ventricular mass index (LVMI) and a comparison of the strength of that correlation with that observed for 24-hour ABPM mean systolic BP and seated office clinic systolic BP. LVMI is the main outcome measure because hypertrophy of the left ventricle is a validated biomarker of elevated pressure and is itself potently correlated with increased risk of adverse cardiovascular outcomes and mortality[27-35]. The study will use cardiac MRI (cMRI) to measure LVMI because cMRI is recognised as the most accurate and reproducible means of measuring LVMI[36-41].

In addition to the measurement of LVMI as the primary outcome, this study will also examine the relationship between different BP parameters and vascular biomarkers of hypertensive injury using the non-invasive measurement of the Cardio-Ankle Vascular Index (CAVI).

The findings of this study will provide evidence of the validity of HeartGuide watch BP measurements when compared with conventional upper arm cuff-based BP measurements and for the first time evaluate the relationship between these various BP measurement techniques and markers of hypertension-mediated organ damage, specifically LVMI. These findings will be important to help define whether the HeartGuide watch BP monitor can provide an alternative means to characterise BP levels for the diagnosis of hypertension and monitoring the response of patients to antihypertensive therapy.

An interesting aspect of the study is that the measurement of BP with the HeartGuide watch BP monitor will be used to measure BP whilst rested and seated in the morning and evening, thereby mimicking the usual pattern of BP measurement recommended in guidelines for HBPM with a conventional upper-arm cuff-based device. However, the HeartGuide watch BP monitor also allows for BP measurements to be taken at other multiple times during the day. This is similar to the profile of BP measurements taken by ABPM but, with measurements over multiple days unlike ABPM which typically only measures BP over a single day. In this regard, the HeartGuide watch BP monitor will provide a different profile of BP measurement when compared to conventional HBPM or ABPM. It is a key additional objective of this study to define whether this new profile of BP measurement reveals any difference in the strength of the correlation between BP and LVMI.

This protocol describes the UK based study. A similar protocol will be used for a parallel study of similar size and design, developed with our collaborators at the Jichi Medical University in Japan. The plan is to evaluate the data from both studies independently but also combine the results of both studies to evaluate the relationship between BP measurement methods and indices and LVMI in different population cohorts representing Europe and Asia.

Objectives and outcome measures

Primary Outcome Measure

The association between mean "out of office" systolic BP measured by the HeartGuide watch BP monitor and LVMI measured by cMRI. "Out of office" refers to BP measurements made by the study participants in their home and work environments, i.e. away from the doctor's office.

Secondary Outcome Measures

1. Comparison of the relationships between mean BP indices measured by; (i) the HeartGuide watch BP monitor, or (ii) ABPM, or (iii) seated office BP, with LVMI by cMRI
2. The relationship between all BP indices as measured by all devices and the Cardio-Ankle Vascular Index (CAVI).
3. The relationships between CAVI indices and LVMI and corresponding cardiac and vascular indices by cMRI.
4. The relationships between all BP indices and ECG voltage criteria for left ventricular mass
5. The relationships and any significant differences between various BP indices

Study Design

This is a single centre cross-sectional study in 50 people with elevated systolic BP i.e. ≥ 130 mmHg, or receiving antihypertensive therapy. The study evaluates the relationships between BP measured with different validated and CE-marked devices, used for their intended purpose, and LVMI, measured by cMRI. The study does not involve any treatments or interventions.

A parallel study of similar design and purpose is also planned to be undertaken Jichi Medical University, Tochigi, Japan. This will allow for comparison of BP relationships with LVMI across two different population cohorts. To facilitate this two-centre analysis, non-identifiable data from both studies will be merged.

Trial setting

UCL Bloomsbury Phenotyping Centre, Roger Williams Building, 65-79 Chenies Mews, London WC1E 6HX. This is a purpose designed clinical research facility, incorporating the Chenies Mews Imaging Centre where MRI studies will also be performed.

Participant Selection

Study participants will have an elevated seated office systolic BP (≥130mmHg), or be receiving antihypertensive therapy for previously diagnosed hypertension and should meet the following criteria:

Participant Inclusion Criteria:

- Men or women aged ≥ 35 years or older
- Wrist circumference 16-19 cm (i.e. suitable for HeartGuide watch BP monitor)
- Seated Office systolic BP (Omron HEM-907) ≥ 130 mmHg or previously diagnosed with hypertension and currently taking anti-hypertensive medication.
- Willing and able to provide informed consent

Participant Exclusion Criteria:

- Unable or unwilling to provide informed consent
- Women who are pregnant
- Wrist circumference > 19 cm (unsuitable for the HeartGuide wrist monitor)
- Upper arm circumference > 42.0 cm (Unreliable cuff-based BP measurement)
- Unwilling or unable to undergo a cardiac MRI scan
- Current atrial fibrillation or other significant arrhythmia (makes BP measurement unreliable)
- Unwilling or unable to undertake 24-hour ambulatory blood pressure monitoring
- Unwilling or unable to undertake a minimum of 3 week-days of wrist blood pressure monitoring (HeartGuide watch BP monitor)
- Currently enrolled in another clinical trial or study

Study Processes

Each participant will be required to attend three outpatient visits for this study. The study visits can be performed on multiple days at the patient's convenience and according to their availability. Figure 1 summarises the design of the study and table 1 summarises the study visits and procedures. All study visits and procedures should ideally be performed within one month of visit 1.

Consent Procedure:

At least 24-hours prior to obtaining written informed consent, potential study participants identified at University College London Hospital (UCLH), will receive the study patient information leaflet. UCLH will act as a recruitment PIC site for this study. Immediately prior to obtaining written informed consent, the study objectives and procedures will be discussed with potential study participant by a member of the study team. If the study participant agrees to proceed with the study, the consent form will be signed by the study participant and co-signed by a GCP-trained and designated member of the study team. The study participant may withdraw consent at any time during the study.

Study visits

Visit 1:

- The study inclusion and exclusion criteria will be reviewed and the study objectives will be discussed prior to signing of informed consent
- Details of participant demographics and medical history will be recorded in the electronic study case report form. This will include; details of prior hypertension and other cardiovascular risk factors, i.e. smoking history, presence of diabetes, cholesterol levels (if known), brief dietary history, usual alcohol intake and exercise levels. History of any previous cardiac or kidney disease, or stroke, or any other significant medical history will be recorded. A list of current medications will be documented.
- Height and weight will be measured.
- A 12-lead electrocardiogram (ECG) will be recorded
- Seated clinic BP measurements will be taken (see below) and heart rate will be recorded.

- The Cardio-Ankle Vascular Index (CAVI) will be measured non-invasively (see below)
- The participant will then be trained in the use of the HeartGuide watch BP monitor (see below). After completion of training, study participants will be issued with the HeartGuide watch BP monitor and an event diary.
- The second study visit and third study visit for the cMRI scan will be scheduled.

No blood, urine or tissue samples will be collected for this study.

Visit 2:

This visit will ideally take place 7 days after visit 1

- Participants will return the HeartGuide BP watch and event diary
- The quality of the HeartGuide watch BP data will be reviewed to ensure that there is a minimum of 3 days of valid HeartGuide watch BP measurements. A minimum of 70% of successful HeartGuide readings will be required for a valid session. Individuals with insufficient BP data will be offered to have the HeartGuide measurement repeated.
- Seated office BP measurements will be recorded
- A 24-hour ABPM monitor will be applied and event diary issued.
- The cMRI booking will be confirmed

Visit 3:

- The ABPM and event diary will be returned and the quality of BP measurements reviewed – this can be scheduled to coincide with the cMRI or alternatively, the ABPM device can be returned after 24 hours by courier and visit 3 is then solely devoted to cMRI at patient convenience but within 1 month from visit 1
- The cMRI will be performed

Figure 1. Study design

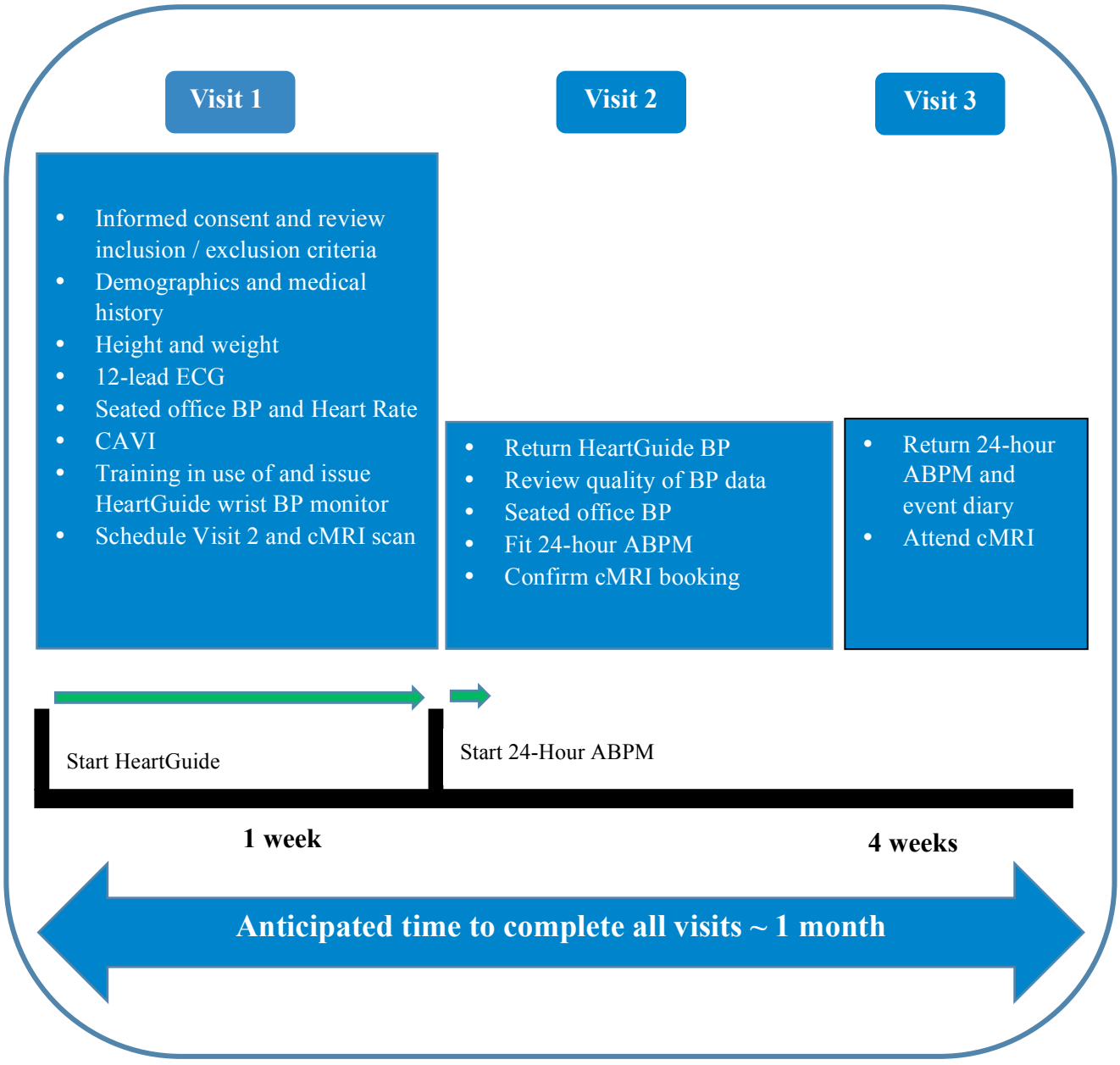


Table 1. Summary of study visits and procedures

Study Procedures	Visit 1	Visit 2	Visit 3
Informed Consent	X		
Demographics and Medical History	X		
Height and weight	X		
Seated blood pressure measurement	X	X	
Heart rate	X		
12-lead ECG	X		
Cardio-Vascular Ankle Index (CAVI)	X		
Issue HeartGuide watch BP monitor	X		
Schedule visit 2 and cardiac MRI	X		
Review quality of HeartGuide data		X	
Issue 24-hour ABPM monitor		X	
Cardiac MRI			X

Detailed Study Processes and Measurements

Seated Clinic blood pressure measurement:

Brachial clinic BP will be measured at the heart level over the upper arm with a suitably sized cuff, using a validated oscillometric monitor (HEM-907, Omron Healthcare Co. Ltd., Kyoto, Japan). Measurements will be taken with participants seated in a comfortable position with their arm supported at the level of the heart, legs uncrossed with feet flat on the floor. Measurements will be taken with the study staff in attendance. The BP monitor has an in-built timed protocol to standardise BP measurement. Once initiated, the participant will sit while the monitor counts down for 5 minutes, afterwards a pre-set protocol of 3 consecutive BP measurements spaced by 1 minute is started. Brachial systolic, diastolic and pulse are displayed by the device. BP measurements will be carried out on both arms and the mean of the last two blood pressures on the arm with the highest systolic BP will recorded as clinic BP. Data will be manually entered into the electronic data base.

HeartGuide watch BP measurement:

Participants will be provided with the HeartGuide watch BP monitor (figure 2). This is a CE-marked and validated BP monitor. Study participants will be shown how to operate and accurately apply this device to their wrist, charge the device, and use it to take accurate BP measurements. The watch will be worn on the non-dominant wrist.

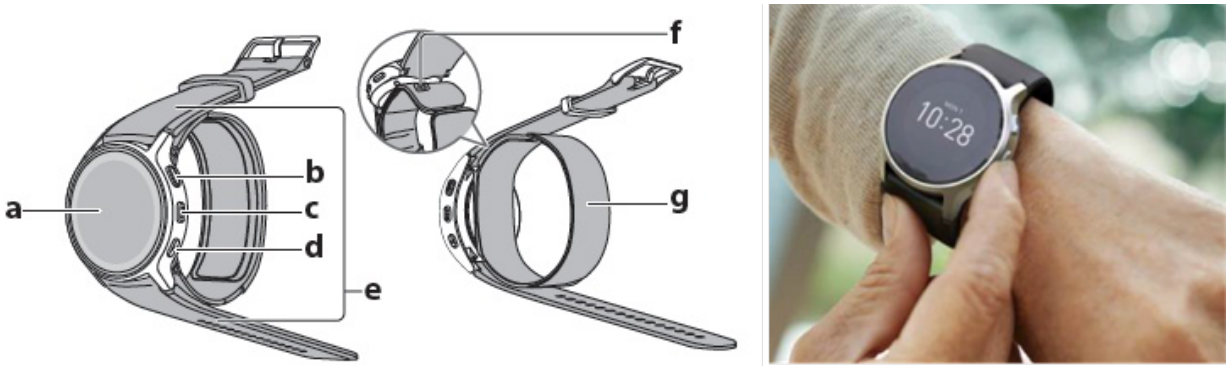
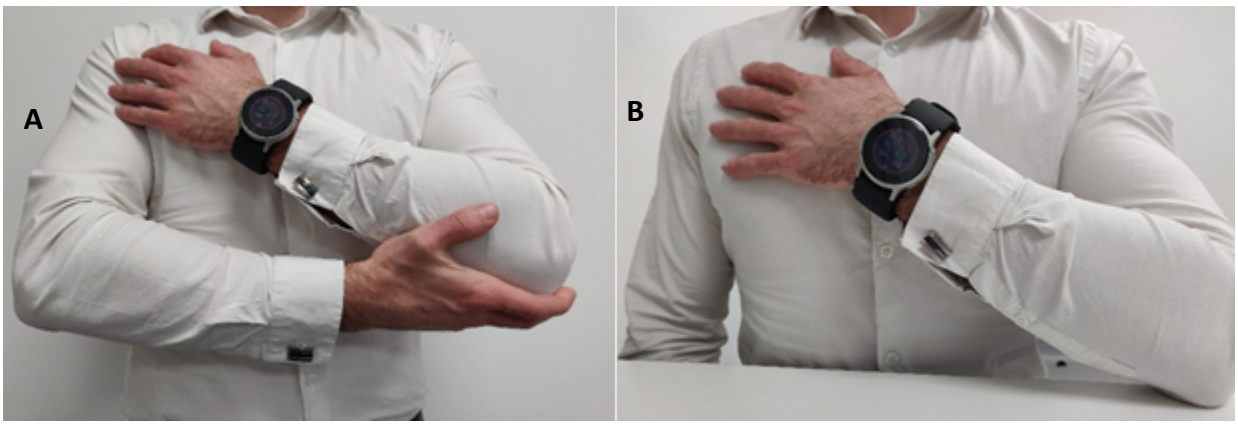


Figure 2, The HeartGuide BP watch device: a) display; b) start/stop button; c) forward button; d) home button; e) strap/band; f) charging port; g) cuff.

During study visit 1, participants will be briefed on what procedures need to be followed to acquire accurate BP readings including:

- Place the watch ~2.5 cm below the distal wrist crease
- Select the appropriate tightness of the watch using the manufacturer's guide
- Ensure that the watch is positioned in the centre of the wrist with help of the positioning mark located on the watch

For each measurement, the participant will be asked to keep the palm of the non-dominant arm in a neutral position, facing flat against the chest, keeping the watch away from the body and maintaining the centre of the palm still, at heart level. To minimise tension in the watch-wearing non-dominant arm, it should be supported using a tabletop or other solid surface whilst a measurement is being taken. Alternatively, the elbow of the non-dominant arm can be supported using the dominant arm if a supporting surface is not available e.g. whilst standing



(figure3).

Figure 3, Illustration of correct arm positioning for manually initiated HeartGuide BP measurements; A) with arm supported or B) arm rested on a solid surface.

All measurements will be manually initiated. In the morning after waking and in the evening before going to bed at which two measurements will be taken whilst seated, one minute apart, and following 5 minutes rest, mimicking the protocol for home BP measurement. Participants will also be asked to take single readings (whilst ambulant) at fixed time points during the day (10:00hrs, 12:00hrs, 14:00hrs, 16:00hrs, 18:00hrs), mimicking ambulatory blood pressure

measurement. Individual measurements can also be initiated at any other time point during the day (up to 5 times) and the reason for the additional readings should be recorded in the event diary.

Participants will be asked to take BP measurements using this procedure, for a minimum of 3 week days and up to a maximum of 7 days. The device will store up to a maximum of 100 measurements over the entire monitoring period, which is sufficient for the recommended monitoring schedule over a total of 7 days. To prevent damage to the watch, participants will be required to remove the watch when sleeping or when bathing. In addition, participants will be requested to selectively record their behavior, emotion, and location at the timing of each measurement.

The quality of the HeartGuide watch BP data will be reviewed at visit 2 to ensure that there is a minimum of 3 days of valid HeartGuide watch BP measurements. A minimum of 70% of successful HeartGuide readings will be required for a valid session. Individuals with insufficient BP data will be offered to have the HeartGuide measurement repeated.

24 hour Ambulatory Blood pressure measurement:

Ambulatory blood pressure measurement will be carried out using a validated oscillometric monitor (TM-2441, A&D Co. Ltd., Tokyo, Japan). Participants will be provided-with a suitably sized cuff to be worn on the non-dominant arm and ambulatory measurements will be collected over a maximum of 24 hours on a weekday. Individual measurements will be taken at 30 and 60-minute intervals during waking and sleeping hours, respectively. Participants will be instructed to keep their arm stable and in a relaxed position during each BP measurement. A diary will be provided to the participants to note any changes in activity and to record the time of going to sleep and waking for the period of monitoring. Upon returning the monitor to the study site, the BP data will be downloaded to a study-dedicated laptop and analysed for 24-hour, waking and sleeping BP averages using proprietary software. A minimum of 14 successful waking readings or ≥ 70% overall readings will be accepted for analysis[13]. If sufficient readings are not obtained for the analysis, participants will be offered to undergo another 24-hour ABPM measurement.

12-lead Electrocardiogram:

Study participants will lay supine for ~5 minutes prior to undergoing a 12-lead ECG (ASSY CAM-14 version 2; GE Medical Systems Information Technologies Inc., Wauwatosa, WI, USA). Data will be collected and sorted on the study-dedicated laptop using the GE Medical Systems Cardiosoft software (Cardiosoft version 6.73; GE Healthcare, Chicago, IL, USA).

Anthropometrics – height and weight:

Height and weight will be recorded using a stadiometer (Seca 274, Seca, Birmingham, UK) with electronic data capture. Participants will be asked to remove shoes for height and weight measurements.

Cardio-Ankle Vascular Index (CAVI):

Non-invasive assessment of arterial stiffness will be completed using the Cardio-ankle vascular index device (VS1500N, Fukuda Denshi, Tokyo, Japan). This device measures BP using cuffs placed over the upper arm and ankles, cardiac sounds using a phonograph placed on the sternum and a 2-lead ECG to gate readings. Vascular length is computed from body surface area and is used with pulse transit time from the aorta to ankle to derive pulse wave velocity. CAVI is computed by the device and is a scaled transformation of heart-ankle pulse wave velocity and is a surrogate of large artery stiffness[42]. Participants will be instructed to relax and lie supine for ~2 minutes to ensure heart sounds are detectable and ECG recordings are stable before measurements are taken. Two measurements will be taken consecutively with ~1 minute between measurements.

Cardiac MRI scan acquisition and analysis:

Cardiac MRI scans will be conducted at the Chenies Mews Imaging Centre. All scans will be performed on a 1.5T scanner (Magnetom Aera, Siemens Medical Solutions, Erlangen, Germany). Imaging of the heart will use an accelerated steady-state free precession protocol. Contrast will not be used in any imaging for this study. MRI scans will be conducted using standard NHS diagnostic and safety procedures.

Analysis of left ventricular (LV) mass will be undertaken using standard imaging software. The stack of LV images will be segmented to define the endocardial and epicardial borders. Summation of each individual slice will be calculated to determine LV mass. MRI scans will be

pseudo-anonymised so observers are not able to link any patient level data during analysis. MRI data will be manually entered into the study database. LV mass will be indexed to body surface area to derive the LVMI. For secondary outcomes additional MRI indices will be acquired, including cardiac volumes, functional parameters and aortic flow.

Statistical Analysis Plan and Data Analysis

Primary Outcome analysis and Sample size estimation

The primary outcome is the association between mean "out of office" systolic BP measured by the HeartGuide watch BP monitor and LVMI measured by cMRI. This relationship will be assessed by Pearson's correlation coefficient for normally distributed data. For the primary outcome, based on 50 cases, using an estimated Pearson's correlation coefficient of 0.30, using data on the relationship between 24-hour ABPM and cMRI LVMI from our prior studies[43], the power would be 0.56 at $P = 0.05$. With 50 cases and a correlation coefficient of 0.40, the power would be 0.83 at $P = 0.05$. For the full analysis with 100 cases (merged analysis with the Jichi Medical University study data), at a correlation coefficient of 0.30, the power is 0.86, and a correlation coefficient of 0.40, the power is 0.99 at $P = 0.05$.

Secondary Outcomes

Secondary outcomes will include:

1. Comparison of the relationships between LVMI/unindexed LV mass and BP indices measured by;
    a. The HeartGuide Watch BP monitor
    b. ABPM
    c. Seated clinic BP

2. Comparison of the relationships between CAVI parameters and BP indices measured by;
    a. The HeartGuide Watch BP monitor
    b. ABPM
    c. Seated clinic BP

3. Relationships between ECG voltage criteria for LV mass and BP indices measured by;

a. The HeartGuide Watch BP monitor
b. ABPM
c. Seated clinic BP

4. Relationship between CAVI indices and MRI parameters including;

    a. LVMI/unindexed LV mass
    b. Cardiac volumes
    c. Indices of vascular structure/function

5. Relationships and any significant differences between various BP indices measured by:

    a. The HeartGuide Watch BP monitor
    b. ABPM
    c. Seated clinic BP

All data will be analysed for distribution pattern and tested using appropriate methods. Summary statistics for continuous variables will be reported as means and standard deviation or 95% confidence intervals where appropriate. Categorical variables will be reported as n and percentage. Analysis of secondary outcomes will use similar techniques as used for the primary outcome i.e. Pearson's correlation coefficient calculated for the relationships between various BP parameters and cMRI measurements of LV mass, CAVI measurements or ECG voltage criteria for LV mass. The relationship between cMRI parameters and CAVI indices will also be determined using Pearson's correlation coefficient. Additionally, regression coefficients for all relationships will be calculated using linear regression models. Fisher's r to z transformation will be used to compare correlation coefficients between BP modes and MRI or CAVI or ECG-derived parameters. Direct comparison of BP indices will use student's t-tests, one-way ANOVA or other appropriate tests for non-normally distributed data. Data will also be plotted using Bland-Altman plots. Data may also be adjusted for potentially confounding demographic and anthropometric parameters where appropriate. A two-sided significance level of $P \leq 0.05$ will denote statistical significance. Effect size will also be reported. Due to the relatively small sample size, it is not anticipated that any sensitivity analyses will be carried out.

Data management

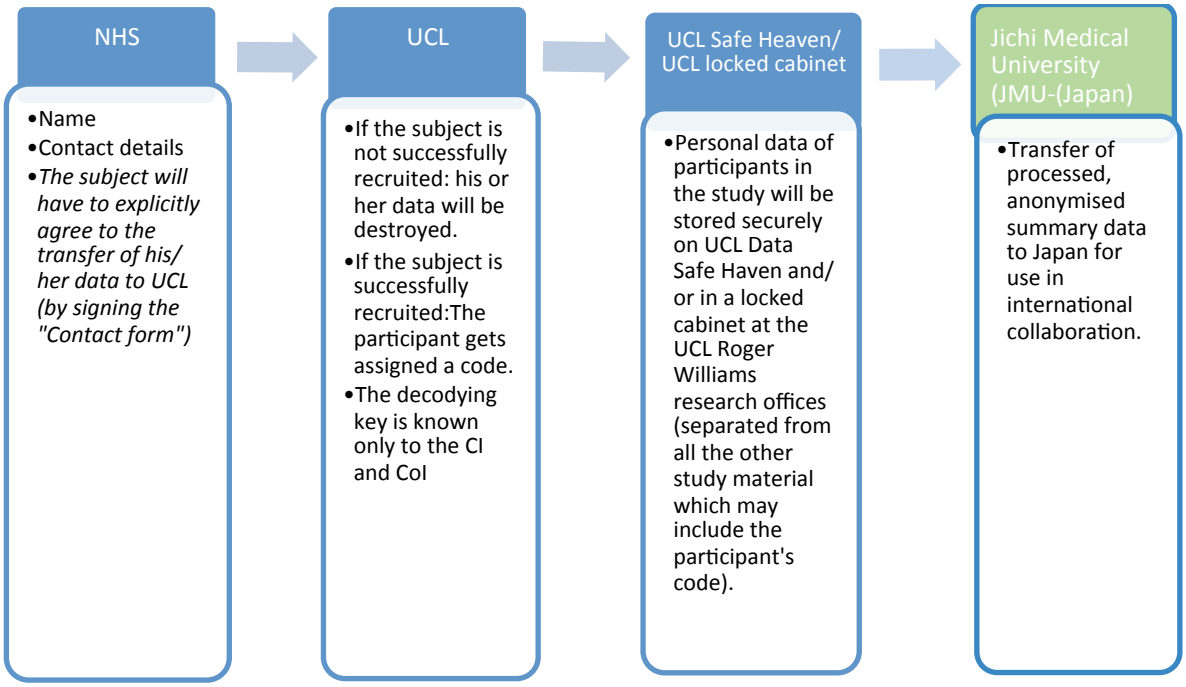
Personal data will be collected as part of this study and will be stored in a secure data environment at UCL (Data Safe Haven, DSH) and will only be accessible to study team members and authorised regulatory authorities. Stored personal data will only include participants' contact details (needed to book appointments and tests), their emergency contact details (needed in case of an emergency), their GP details (needed to inform the GPs about any relevant results and incidental findings) and signed and dated informed consent forms. All other study data will be pseudo-anonymised and stored electronically using a customised electronic database (Research Electronic Data Capture (REDCap)[44]) or on proprietary systems required for device data collection e.g. computers linked to the MRI scanner. The key to the pseudo-anonymised data will be stored in the UCL secure data environment (DSH). Pseudo-anonymised data from the REDCap database will be exported to statistical analysis systems (STATA, R-Studio) for processing and analysis. Pseudo-anonymised processed data from statistical analysis systems will be shared with collaborative investigators undertaking a similar parallel study at Jichi Medical University, Tochigi, Japan or with the study funder, Omron Healthcare Co. Ltd. Any data shared with collaborators or other investigators will be pseudo-anonymised and only include research results after statistical processing, and will not include personally identifiable information.

All study investigators and trial site staff will comply with the requirements of the General Data Protection Regulation (GDPR) and Data Protection Act 2018 with regards to the collection, storage, processing and disclosure of personal information. Study staff will safeguard the privacy of participants' personal data.

Personal data will be retained for up to one year following trial completion after which time it will be destroyed securely. All other non-identifiable data will be retained for up to ten years following trial completion after which time it will be archived according to standard UCL/UCLH procedures.

The study Chief Investigator will act as data custodian.

Data Flow Chart



Ethical and regulatory considerations

Prior to study commencement, local ethical approval for the study protocol and all other study procedures and documents will be sought and implemented via the National Research Ethics service / UK Health Research Authority. Evidence of ethical approval and all correspondence with the Research Ethics Committee (REC) will be maintained in the study site file. During the study, the REC will be notified of and required to approve any substantial or non-substantial protocol amendments prior to their implementation. Any deviations to protocol procedures will be reviewed and documented in the site file by the study Chief Investigator who will report these to the study sponsor where necessary. Study data will be monitored by the trial manager. Reports on study activities will be submitted to the study sponsor as required.

Peer and regulatory review

The study has been peer reviewed in accordance with the requirements outlined by UCL

- The Sponsor considers the procedure for obtaining funding from Omron Healthcare Co Ltd. to be of sufficient rigour and independence to be considered an adequate peer review.
- This study has been peer reviewed within UCL and by an independent and relevant peer reviewer during April 2020. The Sponsor has accepted these reviews as adequate evidence of peer review.

Safety Considerations

We are not anticipating any study-related adverse events as the study uses CE-approved devices and standard procedures for all other data collection. There are no invasive procedures or interventions used in this study. MRI will be performed using standard NHS procedures and contrast will not be used. Consequently, study-related adverse events are not anticipated. Non study-related adverse events will be recorded and addressed in accordance with standard NHS procedures.

Recording and reporting of events and incidents

16.1 Definitions of Adverse Events

Term	Definition
Adverse Event (AE)	Any untoward medical occurrence in a patient or study participant, which does not necessarily have a causal relationship with the procedure involved.
Serious Adverse Event (SAE).	Any adverse event that: • results in death, • is life-threatening*,

	• requires hospitalisation or prolongation of existing hospitalisation**, • results in persistent or significant disability or incapacity, or • consists of a congenital anomaly or birth defect
*A life- threatening event, this refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe. ** Hospitalisation is defined as an in-patient admission, regardless of length of stay. Hospitalisation for pre-existing conditions, including elective procedures do not constitute an SAE.	

16.2 Assessments of Adverse Events

Each adverse event will be assessed for severity, causality, seriousness and expectedness as described below.

16.2.1 Severity

Category	Definition
Mild	The adverse event does not interfere with the participant's daily routine, and does not require further procedure; it causes slight discomfort
Moderate	The adverse event interferes with some aspects of the participant's routine, or requires further procedure, but is not damaging to health; it causes moderate discomfort
Severe	The adverse event results in alteration, discomfort or disability which is clearly damaging to health

16.2.2 Causality

The assessment of relationship of adverse events to the procedure is a clinical decision based on all available information at the time of the completion of the case report form.

The following categories will be used to define the causality of the adverse event:

Category	Definition
Definitely:	There is clear evidence to suggest a causal relationship, and other possible contributing factors can be ruled out.
Probably:	There is evidence to suggest a causal relationship, and the influence of other factors is unlikely
Possibly	There is some evidence to suggest a causal relationship (e.g. the event occurred within a reasonable time after administration of the study procedure). However, the influence of other factors may have contributed to the event (e.g. the participant's clinical condition, other concomitant events).
Unlikely	There is little evidence to suggest there is a causal relationship (e.g. the event did not occur within a reasonable time after administration of the study procedure). There is another reasonable explanation for the event (e.g. the participant's clinical condition).
Not related	There is no evidence of any causal relationship.
Not Assessable	Unable to assess on information available.

16.2.3 Expectedness

Category	Definition
Expected	An adverse event which is consistent with the information about the procedure listed in the manual of Operation **or clearly defined in this protocol.**
Unexpected	An adverse event which is not consistent with the information about the procedure listed in the manual of operation **or clearly defined in this protocol.**

* this includes listed events that are more frequently reported or more severe than previously reported

16.3 Recording adverse events

All Adverse events will be recorded in the CRF following consent.

16.3.1 Procedures for recording and reporting Serious Adverse Events

All serious adverse events will be recorded in the medical records and the CRF, and the sponsor's AE log (the sponsors AE log is used to collate SAEs and AEs so that the CI can review all in one place for trend analysis. If this data will be collated on a database throughout the study, from which a line listing of the SAEs can be extracted for review, an AE log will not be required).

All SAEs (except those specified in section 16.5 as not requiring reporting to the Sponsor) must be recorded on a serious adverse event (SAE) form. The CI/PI or designated individual will complete an SAE form and the form will be preferably emailed to the Sponsor within 5 working days of becoming aware of the event. The Chief or Principal Investigator will respond to any SAE queries raised by the sponsor as soon as possible.

Where the event is unexpected and thought to be related to the procedure this must be reported by the Investigator to the Health Research Authority within 15 days.

Completed forms for unexpected SAES must be sent within 5 working days of becoming aware of the event to the Sponsor

Email forms to Research-incidents@ucl.ac.uk

16.4 Protocol deviations and notification of protocol violations

A deviation is usually an unintended departure from the expected conduct of the study protocol/SOPs, which does not need to be reported to the sponsor. The CI will monitor protocol deviations.

A protocol violation is a breach which is likely to effect to a significant degree –

(a) the safety or physical or mental integrity of the participants of the study; or

(b) the scientific value of the study.

The CI and sponsor will be notified immediately of any case where the above definition applies during the study conduct phase.

16.5 Reporting incidents involving a medical device(s)

Any adverse incident involving a medical device should be reported to the manufacturer of the device.

This is especially important where the incident has led to or, was it to occur again could lead to an event classified as serious (see section 9.1 for definition of SAE). Other minor safety or quality problems should be reported along with incidents that appear to be caused by human error.

All adverse incidents must be reported to Omron Healthcare Co Ltd.

Serious adverse events should be reported as soon as possible to the sponsor and manufacturer (usually within 24-hours of the incident being made known) using the form provided.

16.6 University incidents and near misses

An incident or near miss is any unintended or unexpected event that could have or did lead to harm, loss or damage that contains one or more of the following components:

a. It is an accident or other incident which results in injury or ill health.

b. It is contrary to specified or expected standard of patient care or service.

c. It places patients, staff members, visitors, contractors or members of the public at unnecessary risk.

d. It puts the University in an adverse position with potential loss of reputation.

e. It puts University property or assets in an adverse position or at risk.

Incidents and near misses must be reported to the University through DATIX as soon as the individual becomes aware of them.

A reportable incident is any unintended or unexpected event that could have or did lead to harm, loss or damage that contains one or more of the following components:

a) It is an accident or other incident which results in injury or ill health.
b) It is contrary to specified or expected standard of patient care or service.
c) It places patients, staff members, visitors, contractors or members of the public at unnecessary risk.
d) It puts the Trust and UCL in an adverse position with potential loss of reputation.
e) It puts the Trust and UCL property or assets in an adverse position or at risk of loss or damage.

Patient and Public involvement

Patient and public involvement will be used in the development, design and review of the patient information leaflet and for planning the dissemination and presentation of study results in a lay format.

Dissemination policy

At the end of the study, study participants and the study funder will receive an overview of the study data. Study results will also be submitted for publication in a peer-reviewed scientific journal and submitted for presentation at appropriate scientific meetings. Personal data will not be included in any study report.

Monitoring and Auditing

The Chief Investigator will ensure there are adequate quality and number of monitoring activities conducted by the study team. This will include adherence to the protocol, procedures for consenting and ensure adequate data quality.

The Chief Investigator will inform the sponsor should he/she have concerns which have arisen from monitoring activities, and/or if there are problems with oversight/monitoring procedures.

Funding and supply of Equipment

The funding arrangement of this study are summarized in this documents summary page and covered in detail in a separate document and collaborative agreement.

Training

The Chief Investigator will review and provide assurances of the training and experience of all staff working on this study. Appropriate training records will be maintained in the study files.

Indemnity Arrangements

University College London holds insurance against claims from participants for harm caused by their participation in this clinical study. Participants may be able to claim compensation if they can prove that UCL has been negligent. However, if this clinical study is being carried out in a hospital, the hospital continues to have a duty of care to the participant of the clinical study. University College London does not accept liability for any breach in the hospital's duty of care, or any negligence on the part of hospital employees. This applies whether the hospital is an NHS Trust or otherwise.

Archiving

UCL and each participating site recognise that there is an obligation to archive study-related documents at the end of the study (as such end is defined within this protocol). The Chief Investigator confirms that he/she will archive the study master file at University College London

for the period stipulated in the protocol and in line with all relevant legal and statutory requirements.

References

1. O'Brien E, Dolan E, Stergiou GS. Achieving reliable blood pressure measurements in clinical practice: It's time to meet the challenge. *Journal of clinical hypertension (Greenwich, Conn)* 2018;**20**:1084-8. https://doi.org/10.1111/jch.13323
2. Rapsomaniki E, Timmis A, George J, Pujades-Rodriguez M, Shah AD, Denaxas S*, et al.* Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1.25 million people. *Lancet* 2014;**383**:1899-911. https://doi.org/10.1016/s0140-6736(14)60685-1
3. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F*, et al.* Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet* 2004;**364**:937-52. https://doi.org/10.1016/s0140-6736(04)17018-9
4. McEvoy JW, Daya N, Rahman F, Hoogeveen RC, Blumenthal RS, Shah AM*, et al.* Association of Isolated Diastolic Hypertension as Defined by the 2017 ACC/AHA Blood Pressure Guideline With Incident Cardiovascular Outcomes. *JAMA : the journal of the American Medical Association* 2020;**323**:329-38. https://doi.org/10.1001/jama.2019.21402
5. Brown DW, Giles WH, Greenlund KJ. Blood pressure parameters and risk of fatal stroke, NHANES II mortality study. *American journal of hypertension* 2007;**20**:338-41. https://doi.org/10.1016/j.amjhyper.2006.08.004
6. Vishram JK, Borglykke A, Andreasen AH, Jeppesen J, Ibsen H, Jorgensen T*, et al.* Impact of age on the importance of systolic and diastolic blood pressures for stroke risk: the MOnica, Risk, Genetics, Archiving, and Monograph (MORGAM) Project. *Hypertension* 2012;**60**:1117-23. https://doi.org/10.1161/hypertensionaha.112.201400
7. Gottesman RF, Albert MS, Alonso A, Coker LH, Coresh J, Davis SM*, et al.* Associations Between Midlife Vascular Risk Factors and 25-Year Incident Dementia in the Atherosclerosis Risk in Communities (ARIC) Cohort. *JAMA neurology* 2017;**74**:1246-54. https://doi.org/10.1001/jamaneurol.2017.1658
8. Rovio SP, Pahkala K, Nevalainen J, Juonala M, Salo P, Kahonen M*, et al.* Cardiovascular Risk Factors From Childhood and Midlife Cognitive Performance: The Young Finns Study. *Journal of the American College of Cardiology* 2017;**69**:2279-89. https://doi.org/10.1016/j.jacc.2017.02.060
9. Chatziprodromou I, Tricoli A, Poulikakos D, Ventikos Y. Haemodynamics and wall remodelling of a growing cerebral aneurysm: a computational model. *Journal of biomechanics* 2007;**40**:412-26. https://doi.org/10.1016/j.jbiomech.2005.12.009
10. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. *Lancet* 2005;**365**:217-23. https://doi.org/10.1016/s0140-6736(05)17741-1
11. Tsai WC, Wu HY, Peng YS, Yang JY, Chen HY, Chiu YL*, et al.* Association of Intensive Blood Pressure Control and Kidney Disease Progression in Nondiabetic Patients With Chronic Kidney Disease: A Systematic Review and Meta-analysis. *JAMA internal medicine* 2017;**177**:792-9. https://doi.org/10.1001/jamainternmed.2017.0197

12. Lewington S, Clarke R, Qizilbash N, Peto R, Collins R. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet* 2002;**360**:1903-13.
13. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M*, et al.* 2018 ESC/ESH Guidelines for the management of arterial hypertension. *European heart journal* 2018;**39**:3021-104. https://doi.org/10.1093/eurheartj/ehy339
14. Parati G, Stergiou G, O'Brien E, Asmar R, Beilin L, Bilo G*, et al.* European Society of Hypertension practice guidelines for ambulatory blood pressure monitoring. *Journal of hypertension* 2014;**32**:1359-66. https://doi.org/10.1097/hjh.0000000000000221
15. Bliziotis IA, Destounis A, Stergiou GS. Home versus ambulatory and office blood pressure in predicting target organ damage in hypertension: a systematic review and meta-analysis. *Journal of hypertension* 2012;**30**:1289-99. https://doi.org/10.1097/HJH.0b013e3283531eaf
16. O'Brien E, Asmar R, Beilin L, Imai Y, Mallion JM, Mancia G*, et al.* European Society of Hypertension recommendations for conventional, ambulatory and home blood pressure measurement. *Journal of hypertension* 2003;**21**:821-48. https://doi.org/10.1097/01.hjh.0000059016.82022.ca
17. National Guideline C. National Institute for Health and Care Excellence: Clinical Guidelines. In: *Hypertension in adults: diagnosis and management*London: National Institute for Health and Care Excellence (UK); 2019. https://doi.org/https://www.nice.org.uk/guidance/ng136
18. Whelton PK, Carey RM, Aronow WS, Casey DE, Jr., Collins KJ, Dennison Himmelfarb C*, et al.* 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation* 2018;**138**:e426-e83. https://doi.org/10.1161/cir.0000000000000597
19. Whelton PK, Carey RM, Aronow WS, Casey DE, Jr., Collins KJ, Dennison Himmelfarb C*, et al.* 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation* 2018;**138**:e484-e594. https://doi.org/10.1161/cir.0000000000000596
20. Mancia G, Zanchetti A, Agabiti-Rosei E, Benemio G, De Cesaris R, Fogari R*, et al.* Ambulatory blood pressure is superior to clinic blood pressure in predicting treatment-induced regression of left ventricular hypertrophy. SAMPLE Study Group. Study on Ambulatory Monitoring of Blood Pressure and Lisinopril Evaluation. *Circulation* 1997;**95**:1464-70.
21. Sega R, Facchetti R, Bombelli M, Cesana G, Corrao G, Grassi G*, et al.* Prognostic value of ambulatory and home blood pressures compared with office blood pressure in the general population: follow-up results from the Pressioni Arteriose Monitorate e Loro Associazioni (PAMELA) study. *Circulation* 2005;**111**:1777-83. https://doi.org/10.1161/01.cir.0000160923.04524.5b
22. Ward AM, Takahashi O, Stevens R, Heneghan C. Home measurement of blood pressure and cardiovascular disease: systematic review and meta-analysis of prospective studies. *Journal of hypertension* 2012;**30**:449-56. https://doi.org/10.1097/HJH.0b013e32834e4aed
23. Clement DL, De Buyzere ML, De Bacquer DA, de Leeuw PW, Duprez DA, Fagard RH*, et al.* Prognostic value of ambulatory blood-pressure recordings in patients with treated hypertension. *The New England journal of medicine* 2003;**348**:2407-15. https://doi.org/10.1056/NEJMoa022273
24. Tucker KL, Sheppard JP, Stevens R, Bosworth HB, Bove A, Bray EP*, et al.* Self-monitoring of blood pressure in hypertension: A systematic review and individual patient data meta-analysis. *PLoS medicine* 2017;**14**:e1002389. https://doi.org/10.1371/journal.pmed.1002389
25. Kuwabara M, Harada K, Hishiki Y, Kario K. Validation of two watch-type wearable blood pressure monitors according to the ANSI/AAMI/ISO81060-2:2013 guidelines: Omron HEM-6410T-ZM and HEM-

6410T-ZL. *Journal of clinical hypertension (Greenwich, Conn)* 2019;**21**:853-8. https://doi.org/10.1111/jch.13499
26. Kario K, Shimbo D, Tomitani N, Kanegae H, Schwartz JE, Williams B. The first study comparing a wearable watch-type blood pressure monitor with a conventional ambulatory blood pressure monitor on in-office and out-of-office settings. *Journal of clinical hypertension (Greenwich, Conn)* 2020;**22**:135-41. https://doi.org/10.1111/jch.13799
27. Bang CN, Soliman EZ, Simpson LM, Davis BR, Devereux RB, Okin PM. Electrocardiographic Left Ventricular Hypertrophy Predicts Cardiovascular Morbidity and Mortality in Hypertensive Patients: The ALLHAT Study. *American journal of hypertension* 2017;**30**:914-22. https://doi.org/10.1093/ajh/hpx067
28. Dahlof B, Devereux RB, Kjeldsen SE, Julius S, Beevers G, de Faire U*, et al.* Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol. *Lancet* 2002;**359**:995-1003. https://doi.org/10.1016/s0140-6736(02)08089-3
29. Lindholm LH, Ibsen H, Dahlof B, Devereux RB, Beevers G, de Faire U*, et al.* Cardiovascular morbidity and mortality in patients with diabetes in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol. *Lancet* 2002;**359**:1004-10. https://doi.org/10.1016/s0140-6736(02)08090-x
30. Zhang H, Hu L, Wei X. Prognostic value of left ventricular hypertrophy in hypertensive patients: A meta-analysis of electrocardiographic studies. *Journal of clinical hypertension (Greenwich, Conn)* 2020;**22**:254-60. https://doi.org/10.1111/jch.13795
31. Brown DW, Giles WH, Croft JB. Left ventricular hypertrophy as a predictor of coronary heart disease mortality and the effect of hypertension. *American heart journal* 2000;**140**:848-56. https://doi.org/10.1067/mhj.2000.111112
32. Chatterjee S, Bavishi C, Sardar P, Agarwal V, Krishnamoorthy P, Grodzicki T*, et al.* Meta-analysis of left ventricular hypertrophy and sustained arrhythmias. *The American journal of cardiology* 2014;**114**:1049-52. https://doi.org/10.1016/j.amjcard.2014.07.015
33. Kannel WB. Left ventricular hypertrophy as a risk factor: the Framingham experience. *Journal of hypertension Supplement : official journal of the International Society of Hypertension* 1991;**9**:S3-8; discussion S-9. https://doi.org/10.1097/00004872-199112002-00002
34. Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP. Prognostic implications of echocardiographically determined left ventricular mass in the Framingham Heart Study. *The New England journal of medicine* 1990;**322**:1561-6. https://doi.org/10.1056/nejm199005313222203
35. Liao Y, Cooper RS, McGee DL, Mensah GA, Ghali JK. The relative effects of left ventricular hypertrophy, coronary artery disease, and ventricular dysfunction on survival among black adults. *JAMA : the journal of the American Medical Association* 1995;**273**:1592-7.
36. de Simone G, Izzo R, Chinali M, De Marco M, Casalnuovo G, Rozza F*, et al.* Does information on systolic and diastolic function improve prediction of a cardiovascular event by left ventricular hypertrophy in arterial hypertension? *Hypertension* 2010;**56**:99-104. https://doi.org/10.1161/hypertensionaha.110.150128
37. Devereux RB, Wachtell K, Gerdts E, Boman K, Nieminen MS, Papademetriou V*, et al.* Prognostic significance of left ventricular mass change during treatment of hypertension. *JAMA : the journal of the American Medical Association* 2004;**292**:2350-6. https://doi.org/10.1001/jama.292.19.2350
38. Lenstrup M, Kjaergaard J, Petersen CL, Kjaer A, Hassager C. Evaluation of left ventricular mass measured by 3D echocardiography using magnetic resonance imaging as gold standard. *Scandinavian journal of clinical and laboratory investigation* 2006;**66**:647-57. https://doi.org/10.1080/00365510600892233

39. Pattynama PM, De Roos A, Van der Wall EE, Van Voorthuisen AE. Evaluation of cardiac function with magnetic resonance imaging. *American heart journal* 1994;**128**:595-607. https://doi.org/10.1016/0002-8703(94)90636-x
40. Rodrigues JC, McIntyre B, Dastidar AG, Lyen SM, Ratcliffe LE, Burchell AE*, et al.* The effect of obesity on electrocardiographic detection of hypertensive left ventricular hypertrophy: recalibration against cardiac magnetic resonance. *Journal of human hypertension* 2016;**30**:197-203. https://doi.org/10.1038/jhh.2015.58
41. Vourvouri EC, Poldermans D, Schinkel AF, Koroleva LY, Sozzi FB, Parharidis GE*, et al.* Left ventricular hypertrophy screening using a hand-held ultrasound device. *European heart journal* 2002;**23**:1516-21. https://doi.org/10.1053/euhj.2002.3162
42. Shirai K, Utino J, Otsuka K, Takata M. A novel blood pressure-independent arterial wall stiffness parameter; cardio-ankle vascular index (CAVI). *Journal of atherosclerosis and thrombosis* 2006;**13**:101-7.
43. Williams B, McFarlane E, Jedrzejewski D, Lacy PS. Identifying and treating high blood pressure in men under 55 years with grade 1 hypertension: the TREAT CASP study and RCT *Efficacy and Mechanism Evaluation* 2019;**6**. https://doi.org/https://doi.org/10.3310/eme06130
44. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *Journal of biomedical informatics* 2009;**42**:377-81. https://doi.org/10.1016/j.jbi.2008.08.010