

CLINICAL STUDY PROTOCOL OUTLINE

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Lead organisation: International Society of Hypertension (ISH)

Sponsors and corporate partners: International Society of Hypertension, Centres for Disease Control and Prevention (CDC), Omron, Servier

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Executive summary:

In May 2017 and 2018, the ISH conducted a global blood pressure screening survey across over 100 countries, collecting data from over 2.7 million participants to raise awareness of the health issues surrounding raised blood pressure. Following the success of the campaign, in 2019, ISH proposes to

conduct a third global cross-sectional blood pressure (BP) survey of volunteer adults (aged ≥ 18 years) who ideally have not had their BPs measured for at least a year before BP screening. The survey will be conducted in approximately 100 countries each incorporating a variable number of screening sites. Basic demographic and clinical information as well as BP measurements will be collected by health profession volunteers throughout May 2019. Sitting blood pressure will be measured in triplicate according to standardised specified methods. The data will be anonymised, coded and transferred electronically (through a purpose-designed application or using an Excel spreadsheet) to a central AWS DynamoDB database. Screenees whose BP readings are consistent with the current definition of hypertension will be provided with written dietary and lifestyle advice. They will also be provided with a referral to receive medications and/or follow up support, according to local facilities.

1. Rationale

Raised BP is the biggest single contributing risk factor to global death⁽¹⁾ and to the global burden of disease⁽¹⁾. This impact is largely mediated through increased rates of cardiovascular disease, specifically coronary artery disease and stroke, and renal disease. Because cardiovascular (CV) disease affects approximately one third of adults globally, it represents the largest epidemic ever experienced by mankind. Raised BP currently causes approximately 10.4 million deaths each year worldwide⁽¹⁾ and this figure is expected to rise, given an expanding and aging global population. The aetiology of raised BP is largely explicable by identified environmental factors such as obesity, excessive intake of alcohol and dietary salt, and insufficient exercise⁽²⁾. Several drug classes have been shown to provide cost-effective BP lowering for the prevention of the adverse CV sequelae of raised BP.

Despite the availability of these antihypertensive medications, global data suggest that less than half of those classified as hypertensive are aware of their problem⁽³⁾. Furthermore, less than a third of those who are treated for hypertension get their BPs controlled to currently recommended targets⁽³⁾.

Even assuming treatment and control rates are maximised among those currently diagnosed as being 'hypertensive' ⁽³⁾ it is clear that a huge beneficial impact on morbidity and mortality, and massive reduction in this burden of disease attributed to raised BP, can be achieved by increasing awareness through enhanced screening for raised BP.

2. Aims

- 2.1 To highlight the importance of measuring blood pressure.
- 2.2 To identify and reduce the BPs of those people who require intervention to lower their BP according to current guidelines.

3. Objectives

- 3.1 To screen at least 1 million people aged ≥ 18 years who ideally have not had their BPs measured for at least a year prior to the current BP screening.

- 3.2 To supply diet and lifestyle treatment advice to all those screened who have BPs in the hypertensive range.
- 3.3 To provide advice on how best to receive BP-lowering medications (if required) and further follow-up of raised BP according to local facilities.
- 3.4 To use the data on untreated and inadequately treated hypertension to motivate governments to improve local screening facilities and policies, and thereby reduce the global burden of disease associated with raised BP.

4. Methodology

4.1 Inclusion criteria:

- i. age \geq 18 years
- ii. consent for participation given according to local requirements.

4.2 Procedures

- i. Providing information about the study and collecting consent for participation. All written materials to be used by screenees will use vocabulary in a language that is clearly understood at the study sites. These materials will be provided in several core languages (English, French, Spanish, Portuguese, Hindi, Chinese) and will be available to download from the maymeasure.com website.
- ii. Collection of site information and basic demographic information:
 - a) All information should be collected prior to BP measurements
 - b) Where the app is used, data that will remain the same throughout the screening session will only need to be entered once (e.g. date, location).
 - c) The following data should be collected on all screenees (core-dataset)
 - o Country
 - o City/Town/Village
 - o Date of measurement

- o Age
- o Sex
- o At least 1 SBP, DBP and heart rate

In addition, the following variables will be recorded when available/possible:

- o Site ID and/or email address of screening site
- o Type of location of screening site – hospital/clinic, pharmacy, workplace, other public area (indoors), other public area (outdoors), home, other
- o When did you last have your blood pressure measured? Never / over 12 months ago / within the last 12 months
- o Did you participate in May Measurement Month in either 2017 or 2018? yes/no
- o Have you been diagnosed with high blood pressure by a health professional (except in pregnancy)? yes/no
- o Are you currently taking prescribed blood pressure/antihypertensive treatment?
yes/no/don't know
 - If yes:
 - o How many drug classes do you take for your blood pressure? 1 / 2 / 3 / 4 / 5 or more
 - o Do you take a statin? yes/no
 - o Do you take aspirin? yes/no
- o If female, are you pregnant? yes/no
- o If female, have you had raised blood pressure in this or a previous pregnancy? yes/no
- o Self-declared ethnicity – Black / White / South Asian / East Asian / South-East Asian / Arabic / Mixed / Other
- o Are you currently fasting? yes/no
- o Do you have diabetes? yes/no/don't know
- o Do you use tobacco? yes/no

- o Do you consume alcohol? never or rarely/1-3 times per month/at least once per week
- o Have you had a heart attack in the past? yes/no/don't know
- o Have you had a stroke in the past? yes/no/don't know
- o Measured or self-declared weight (estimate if required)
- o Measured or self-declared height (estimate if required)
- o What is the manufacturer name of the BP device?
- o SBP (2-3)
- o DBP (2-3)
- o Heart rate (2-3)

iii. BP measurements

- a) BP should preferably be measured by an automated electronic device, but can also be measured by a conventional sphygmomanometer using a stethoscope.
- b) If a sphygmomanometer is used, the first and fifth Korotkoff sounds (the appearance and disappearance of sounds) will be recorded as the systolic and diastolic BP.
- c) BP should be measured on the upper-arm
- d) Measure the circumference of the arm (at the mid arm level) and ensure that the correct size of arm cuff is used
 - For arms with circumference < 32 cm, use regular cuff
 - For arms with circumference 32-42 cm, use large cuff
 - For arms with circumference >42 cm, use extra-large cuff
 - For arms with circumference <20cm use paediatric cuff
- e) The cuff should be placed at the heart level
- f) The patient's arm being used for the measurement should rest comfortably on a table
- g) BP should be measured on one arm only, preferably left, and the arm used should be recorded

h) Prior to measurement:

- The participant should be seated with their backs supported and with their legs resting on the ground and in the uncrossed position for 5 min
- Participants should not have smoked immediately before or during the measurement

i) Three (3) BP readings should be taken and recorded using one of the methods described in section iii) k) with 1 min between readings.

j) For each BP reading, the automated BP devices also provide data on heart rate, and this information should also be captured using one of the methods described in section iii) k).

k) Data collected on each participant should be recorded and submitted into the database via the MMM app (produced by Clarifi Media).

If it is not possible to use the app at the screening site, data should be collected on paper using the MMM data capture form provided by the MMM Project Team. The paper forms should then be manually loaded onto the app. If neither of the above options above are available at the screening site then it will be possible to submit data on an excel spreadsheet, the template for which will be provided by the MMM project team.

l) If the auscultatory method/sphygmomanometer is used, the heart rate should be established during the 1 minute after each BP reading, and also recorded on the mobile app.

m) Definition of hypertension:

- being on at least one antihypertensive medication taken for raised BP or
- the average SBP (mean of the last 2 of 3 readings) \geq 140 mmHg and/or
- the average DBP (mean of the last 2 of 3 readings) \geq 90 mmHg

n) The make of BP machine used to measure BPs will be recorded.

iv. Dietary and lifestyle information provided to 'hypertensive' patients to include

a) reduce salt consumption

b) don't drink too much alcohol – stick to local recommendations

- c) don't smoke
- d) reduce caffeine intake
- e) reduce fat and sugar intake
- f) engage in regular physical exercise for at least 30 minutes on most of the days of the week
- g) eat plenty of fruit and vegetables daily (including beetroot and beetroot juice where possible)
- h) maintain a healthy body weight
- i) avoid stress where possible and allow time for relaxation

A generic package of advice will be provided centrally for local adaptation and can be translated locally if required.

5. **Data Management**

5.1 Source Data: Data will be anonymised and collected directly from screenees and entered onto the bespoke MMM App before and immediately after BP measurements. The MMM App will need to be downloaded and registered in an area with internet connection, but can then be used where internet facilities are not available. Where a laptop or mobile device is not available, data can be collected, handwritten on to a template form, provided by the MMM project team, and then transferred into the database via manual input into the app. The app will be available in 8 languages: English, Arabic, Chinese (Cantonese/Mandarin), French, Hindi, Portuguese, Polish and Spanish. If use of the MMM app is not at all possible, then an Excel spreadsheet will be provided by the MMM project team and data can be submitted on that.

5.2 Database: Uploaded blood pressure records will be held in an AWS DynamoDB database in the UK. On a periodic basis, the database is exported to an AWS S3 drop-folder. Access to this drop-folder and to DynamoDB will be provided to the nominated MMM data analyst.

5.3 Access to Data: The Study Principal Investigator representing ISH will be custodians of the data on behalf of all collaborating national investigators. National, regional and global data will be available for research purposes on application to the Principal Investigator.

6. **Statistical Analysis**

- 6.1 Sample size: The total of >1 million adults (18+years) was selected on the basis of including a large enough sample of BP data in each participating country, sufficient to raise awareness at a national level.
- 6.2. Data Analysis: Analyses will include but not be restricted to:
- i) The prevalence of previously undiagnosed hypertension at a national, regional, global and ethnic level.
 - ii) Age and sex stratified levels of systolic (S) BP, diastolic (D) BP, BP variability and prevalence of known and newly diagnosed hypertension generated at a national, regional and global level.
 - iii) The prevalence of uncontrolled hypertension among those on treatment for hypertension.
 - iv) The association between the same BP parameters and room temperature, altitude, ethnic group, week day and time of day will be evaluated at an ethnic, regional and global level.
 - v) The association between the same BP parameters and previous CV disease, pulse rate, diabetes, smoking and alcohol intake and, where available, anthropometric variables.

7. **Ethical Issues**

- 7.1 In accordance with local requirements, informed consent will be acquired and recorded from all screenees having received a simple verbal explanation of what data are to be collected and why.
- 7.2 Regulatory Authority approval:
In those countries or regions where ethics approval is required for an anonymised screening project such authorisation will be obtained from the relevant Regulatory Authority before BP screening begins.
- 7.3 Subject Confidentiality:
All data collected on the MMM App will be anonymised and not traceable to the individual screenees.

8 **Study Management**

Overall management structure: The selected officers of ISH will act as the Executive Committee providing

global oversight for the project, collection, processing, analysis and interpretation of the data. The recruitment will be initiated, monitored and supervised by the national leaders (at least 1 per country). They will be responsible for identifying recruitment sites, each with a centre lead (experienced clinician/nurse/pharmacist). The national leaders will report directly to one of the ISH Regional Advisory Groups (RAGs) which cover:

- Africa
- Europe (including Cyprus and Uzbekistan)
- Americas
- South and West Asia and The Middle East
- North Asia, South-East Asia and Oceania

9. References

1. GDB 2017 Risk Factor Collaborators. The Global Burden of Disease Study 2017. *Lancet*. 2018; 392:1923-1994
2. Poulter et al: *Lancet* 2015;386:801-12
3. Chow et al: *JAMA* 2013; 310:959:68