CLINICAL STUDY PROTOCOL OUTLINE

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Lead organisations: International Society of Hypertension (ISH) and World Hypertension League (WHL)

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Executive summary:

ISH and WHL propose conducting a global cross-sectional blood pressure (BP) survey of volunteer adults (aged ≥ 18 years) who have not had their BPs measured for at least a year before the recruitment. 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 2017. 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) to a central database. Screenees whose BP readings are consistent with the current definition of hypertension will be provided with written dietary and lifestyle advice. Depending on local facilities they will also be provided with a referral to receive medications and/or follow up support.

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 coronary artery disease, stroke and renal disease. Raised BP currently causes approximately 9.4 million deaths each year worldwide (1) and this figure is expected to rise given an expanding and aging global population. Mankind has probably never experienced such a devastating epidemic. The aetiology of raised BP is largely explicable by identified environmental factors such as overweight, 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 cardiovascular (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)]. Less than a third of those who are treated for hypertension get their BPs controlled to currently recommended targets[(3)].

Even assuming sub-optimal treatment and control rates are maintained among those treated as 'hypertensive' [(3)] it is clear that a huge beneficial impact on mortality and reduction in this burden of disease 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 over 2 million people who require intervention according to current guidelines.

3. Objectives

3.1 To screen at least 25 million people aged ≥ 18 years who have not had their BPs measured for at least a year prior to recruitment.

3.2 To supply diet and lifestyle treatment advice to all those screened who have BPs in the

hypertensive range.

3.3 To use the data on untreated 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 ≥ 18 years

ii. consent for participation given

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.

ii. Collection of basic demographic information:

a) All information should be collected prior to BP measurements

b) The code of the participant should be first entered: COUNTRY/ SITE ID/ DATE/ CONSECUTIVE NUMBER. With the exception of Site ID, all other data will be collected automatically on the app (where it is used).

c) The following data should be collected on all screenees (core-dataset)

- Country code
- City
- Date
- Time of day
- Room temperature
- When was your blood pressure (BP) last measured? (MM/YYYY)
- What is your age? (estimated if necessary) What is your month and year of birth?

(MM/YYYY) (if known)

- What is your sex? (M/F)
- Self-declared ethnicity

- Are you currently on blood pressure/antihypertensive treatment? yes/no
- Do you have diabetes? yes/no/don't know
- Do you smoke? yes/no
- Have you had a heart attack in the past? yes/no
- Have you had a stroke in the past? yes/no
- Do you consume alcohol? (never or rarely/<once week/regularly)
- Which arm will be used to take the blood pressure reading? Left/right
- SBP (1-3)
- DBP (1-3)
- Heart rate (1-3)

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

- Measured or self-declared weight (kg/lbs)
- Measured or self-declared height (cm/inches)

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 correspond to 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 on the app, 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 on the mobile app.

k) 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.

l) 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) ≥ 140 mmHg and/or
- the average DBP (mean of the last 2 of 3 readings) ≥ 90 mmHg

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

a) reduce salt intake

b) reduce alcohol intake

c) engage in regular physical exercise for at least 30 minutes on most of the days of the week

d) have at least 5 portions of fruit and vegetables per day

e) reduce your weight aiming for a BMI target < 25 kg/m2

f) Other locally relevant advice…

A generic package of advice will be provided centrally for local adaptation and translated as 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. Where internet facilities are not available, data can be collected, handwritten and entered onto an EXCEL spreadsheet and thereafter transferred to the app which is available in 7 languages; English, Arabic, Chinese (Cantonese/Mandarin), French, Hindi, Portuguese and Spanish.

5.2 Database: The data will be held at Imperial Clinical Trials Unit (ICTU), School of Public Health, Imperial College London, Stadium House, 68 Wood Lane, London, W12 7RH.

5.3 Access to Data: The Study Principal Investigators representing ISH and WHL 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 Investigators.

6. Statistical Analysis

6.1 Sample size: The total of 25 million adults (18+years) was selected on the basis of being sufficient to represent the largest sample of BP data ever collected from each country involved and thereby guaranteed to raise awareness!

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 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.

iv) The association between the same BP parameters and previous CV disease, diabetes, smoking and alcohol intake and, where available, anthropometric variables.

7. Ethical Issues

7.1 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 and WHL 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 ISH–WHL Regional Advisory Groups (RAGs) which cover:

- Africa
- Asia and Australasia
- Central and South America
- Eastern Europe and Middle East

- North America
- Western Europe

9. References

1. Lim et al : Lancet 2012:380:2224-60
2. Poulter et al: Lancet 2015:386:801-12
3. Chow et al: JAMA 2013: 310:959:68