CLINICAL STUDY PROTOCOL

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Executive summary

In May 2017, 2018, 2019 and over an extended screening period from May – November 2021, a global blood pressure (BP) screening survey (May Measurement Month [MMM]) was carried out across 100 countries, collecting data from approximately 5 million adult participants to raise awareness of the health issues surrounding raised BP.

Due to the COVID-19 pandemic, the survey was deferred in 2020. Following the success of the campaign in 2021 despite COVID-19, a fifth global cross-sectional BP campaign (MMM22) is planned. As per previous years, it will include volunteer adults (aged ≥ 18 years). The MMM22 survey is expected to be conducted in approximately 80 countries each incorporating a variable number of screening sites. Basic demographic and clinical information as well as BP measurements will be collected by volunteers throughout the month of May, however this may be extended where necessary depending on the status of the COVID-19 pandemic in each country.

BPs will be measured with participants in the sitting position and recorded 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 Amazon Web Services (AWS) DynamoDB database. Screenees whose BP readings are consistent with the current definition of hypertension (≥140 mmHg systolic and/or ≥90 mmHg diastolic and/or taking BP-lowering medication) will be provided with written dietary and lifestyle advice. They will also be provided with advice regarding referral to receive medications and/or follow up support, according to local facilities.

For MMM22, in addition to the standard BP screening services, a select number of countries will be invited to conduct atrial fibrillation (AF) screening at MMM sites.

1. Rationale

Raised blood pressure (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 (CV) disease, specifically coronary artery disease, heart failure, stroke and renal disease. Because CV disease affects approximately one third of adults globally, it represents the largest epidemic ever experienced by mankind. Raised BP currently causes approximately 10.8 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]. However, 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[3,4]. Furthermore, less than a third of those who are treated for hypertension get their BPs controlled to currently recommended targets[3,4]. Even assuming treatment and control rates are maximised among those currently diagnosed as being 'hypertensive'[3,4] it is clear that a huge beneficial impact on morbidity and mortality, and a massive reduction in the burden of disease attributed to raised BP, can be achieved by increasing awareness through enhanced screening for raised BP.

Successful BP screening campaigns, entitled May Measurement Month (MMM) were carried out in 2017[5], 2018[6], 2019[7] and 2021. These campaigns included 80, 89, 92 and 94 countries, in the first four campaigns respectively, and in total almost 5 million adults were screened.

Although the status of the COVID-19 pandemic cannot be definitively predicted during 2022, it seems likely that at some stage during the year most countries of the world will have the capacity to contribute to the campaign. Meanwhile, given the huge morbidity and mortality rates attributed to raised BP, it is important that the screening of this most punitive of risk factors should continue assuming the safety of all involved is maintained. Hence, whilst the timing of such screening will need to be flexible, and logistics regarding the safety of volunteers and screenees tailored to suit the conditions in each setting, MMM is expected to take place in 2022.

2. Aims

The aims of the May Measurement Month 2022 campaign are as follows:

1) To highlight the importance of measuring BP.

2) To identify and facilitate the reduction of BPs of those people who require intervention to lower their BP according to current guidelines.

3. Objectives

The objectives of the May Measurement Month 2022 campaign are as follows:

1) To target 1 million people aged ≥ 18 years (Target numbers may be affected by the ongoing COVID-19 pandemic).

2) To supply diet and lifestyle treatment advice to all those screened who have BPs in the high normal (130-139 / 80-89 mmHg) and hypertensive (≥140/90mmHg) ranges.

3) To provide advice on further follow-up of raised BP according to local facilities.

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. Methods

4.1 Inclusion criteria

i. Any adult aged ≥ 18 years

ii. Informed participant consent for participation given according to local requirements.

4.2 Patient materials

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, Chinese, Portuguese) and will be available to download from the maymeasure.org website.

4.3 Collection of site information and basic demographic information

a) All questionnaire 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) :

1a. Country

1b. City/Town/Village

2. Site ID and /or investigator email address
3. Type of location of screening site – Hospital/clinic/pharmacy, Workplace, Public Area (indoors), Public area (outdoors), Home, other
4. Date of measurement
5. How old are you in years?
6. What is your sex? Male, Female, Other
7. Ethnicity – Black, White, South Asian, East/South East Asian, Middle Eastern, Mixed, Other
8. When did you last have your blood pressure measured? Never, Over 12 months ago, Within the last 12 months
9. Have you participated in MMM at least once before? Yes, No

10a. Have you ever been diagnosed with high BP by a health professional (except in pregnancy)? Yes, No

10b. If yes, at what age were you diagnosed?

11. How many drug classes are you currently taking for your BP? 0, 1, 2, 3, 4, 5 +, Don't know
12. Do you usually pay fees for your consultations when you get your BP treated? Pay nothing, Pay Part, Pay Fully, Not sure if part or fully paid
13. Do you usually pay fees for your medication when you get your BP treated? Pay nothing, Pay Part, Pay Fully, Not sure if part or fully paid
14. Do you take you BP medication regularly? If not – why? I do, Too expensive, Not easily available, Side effects, Only take them when I need them, Prefer alternative medicine, I forget
15. Are you currently taking the following medication? Statins – Yes, No, Don't know; Aspirin - Yes, No, Don't know; Warfarin/oral anticoagulant (blood thinners) – Yes, No, Don't know
16. If female, are you pregnant? Yes/No
17. If female, have you had raised blood pressure in this or a previous pregnancy? Yes, No

18a. If female, are you currently taking: Hormonal contraception Yes, No

18b Hormone Replacement Treatment (HRT)? Yes, No

19. Do you use tobacco (including chewing tobacco, cigars and pipes)? Yes, No – but I did in the past, Never
20. Do you consume alcohol? Never/rarely, 1-3 times per month, 1-6 times per week, Daily
21. Have you been diagnosed as having diabetes by a health professional (except in pregnancy)? Y/N
22. Have you ever suffered from a:
    a) Heart attack - Yes, No
    b) Stroke - Yes, No
    c) Heart failure – Yes, No
    d) Irregular heartbeat – Yes, No
23. Have you had a positive test for COVID-19? If so when? No, Yes: 0-3mths ago, Yes: 3-6mths, Yes: 6-9mths, Yes: 9-12mths, Yes >12mths

23a. How long did your COVID symptoms persist? 0-3mths, 3-6mths, 6-9mths, 9-12mths, >12mths

24. Have you received the COVID-19 (Coronavirus) vaccination? No, Yes – 1st, Yes – 1st and 2nd, Yes – 1st, 2nd and 3rd
25. Do you take part in at least 150 mins of moderate exercise (brisk walking) or 75 mins of more vigorous exercise per week? Yes, No
26. How many years of education do you have? 0, 1-6 years, 7-12 years, Over 12 years
27. Weight (estimate if not measure) kg / lbs
28. What was your birthweight? kg / lbs
29. What is the manufacturer of the BP machines being used? OMRON / Other
30. Ideally 3, but at least 1 SBP, DBP, and pulse measurement
    Was the pulse regular? Yes, No

4.4 Collection of BP measurements

4.4.1 Type of BP machine

- BP should preferably be measured by an automated electronic device or, if this is not available, a conventional sphygmomanometer using a stethoscope can be used.
- 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 respectively.
- The brand of BP machine used to measure BPs will be recorded.

4.4.2 Cuff size

Measure the circumference of the arm (at the mid arm level) and ensure where possible that the correct size of arm cuff is used:

- For arms with circumferences 22 – 32 cm, use regular cuff
- For arms with circumference 32 – 42cm, use large cuff
- For arms with circumference > 42cm, use extra-large cuff
- For arms with circumference <22 cm use paediatric cuff

4.4.3 Taking BP measurements

- BP should be measured on the upper arm of one arm only, preferably left. The cuff should be placed at the heart level
- The patient's arm being used for the measurement should rest comfortably on a table
- Prior to measurement:

  The participant should be seated with their backs supported, legs uncrossed and feet flat on the ground for 5 min

  Participants should not have smoked immediately before or during the measurement and should not talk during and between BP measurements.
- Three (3) BP readings should be taken with 1 min between readings and recorded using one of the methods described below in Section 5.
- 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 below in Section 5. If the auscultatory method/sphygmomanometer is used, the heart rate should be established during the 1 minute after each BP reading, and also recorded via the app or other chosen data collection method.

4.5 Advice for high normal and 'hypertensive' BPs

Definition of high normal:

- the average SBP (mean of the last 2 of 3 readings) = 130-139 mmHg and/or
- the average DBP (mean of the last 2 of 3 readings) = 80-89 mmHg

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

Dietary and lifestyle information provided to those with high normal and 'hypertensive' BPs to include:-

a) reduce salt intake

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

c) don't smoke

d) reduce caffeine intake

e) reduce saturated fat and sugar intake

f) engage in regular physical exercise for at least 30 minutes on at least five 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.

4.6 Atrial Fibrillation Sub-study (for participating countries/sites only)

Raised blood pressure (BP) and atrial fibrillation (AF) are both major risk factors for stroke and AF is more common among those with raised BP. Both conditions, if detected and well treated, can reduce the risk of stroke and other cardiovascular disorders (eg dementia).

Both conditions are relatively easy to detect by routine screening and recently-produced medical devices allow for the detection of AF via a single lead ECG incorporated into a BP measuring device (eg. the OMRON Complete device).

The AF-Screen International Collaboration is a group of global experts with an interest in AF. Their aim is to promote discussion and research about screening for unknown or under-treated AF as a way to reduce stroke and death. They provide advocacy for implementation of AF screening programs, tailored to the medical systems of individual countries. The AF-Screen International Collaboration will work with the May Measurement Month (MMM) campaign in 2022 to carry out combined AF and BP screening in a subset of countries participating in MMM, in order to raise awareness of undiagnosed AF.

4.6.1 Methods

Approximately 38 countries that participate in MMM (see Appendix 1) have been identified as having active AF-Screen members. The MMM National Leads in those countries will collaborate with their local AF-screen members as appropriate to acquire ethics and agree screening sites that will participate in both the usual MMM protocol as well as the AF sub-study.

BP and AF screening will be carried out using the OMRON Complete devices on all BP screenees aged 60 and above.

The usual questionnaire administered with BP screening will be modified slightly by the addition of 2 extra questions as follows :-

31. Was Atrial Fibrillation detected in the current assessment? Yes, No
32. Have you ever been diagnosed as having Atrial Fibrillation by a health professional before? Yes, No

Those detected as having AF will be advised of their condition and provided written information about the causes and consequences of AF.

Those detected with AF will be referred to relevant medical facilities to arrange confirmation and management of the AF diagnosis as required.

Data regarding the treatment and follow up of those patients detected initially as having AF will be collected and analysed as part of the MMM 22 substudy (MMM/AFS 2022).

5. Data Management

5.1 Source Data

- Data will be collected directly from screenees and entered onto the bespoke MMM App (produced by Clarifi media) before and immediately after BP measurements. The data collected is anonymous, with no personally-identifiable information collected from the screenees.

- Investigators collecting or uploading data may use their own email address as the identification code for the site where screening takes place.

- The MMM App can be used where internet facilities are not available but will then need to be downloaded and registered in an area with internet connection. Where online access is available at the screening site, data will be uploaded automatically from the app to the central AWS DynamoDB database.

- If working offline, data will be uploaded by the app once internet access is 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 recorded either directly, or via entry from paper forms. These will be submitted to the MMM project team and stored in the same AWS Dynamo DB database.

5.2 Database

BP data records will be stored on Amazon Web Services (AWS). Data collected via the app will be stored in raw form in an AWS DynamoDB database and exports of the collected data will be stored as Comma Separated Value (CSV) files within AWS Simple Storage Service (AWS S3).

Access to AWS will be restricted to authorised users only who will require to use 2-factor authentication to sign into their accounts. Access to this password-protected drop-folder and to DynamoDB will be provided to the MMM statistician, project manager and those nominated by the MMM Management Board for the purposes of data analysis, for the duration of analysis.

5.3 Access to Data

The Study Principal Investigator on behalf of MMM will be the custodian of the data on behalf of all collaborating national investigators. National Lead MMM Investigators in each country may request the raw data via email to the project manager, which will be made available as soon as possible and ideally within 10 working days. Following cleaning of the data centrally, cleaned data will also be available to Lead MMM Investigators in each country on request as soon as possible and ideally within 10 working days. Access to the data for any other 3rd parties for research purposes is granted by the

MMM Publication committee on application via mail to the MMM Trustees. Any data supplied (except to National Lead Investigators) will exclude the screening site reference ID which may contain the email of the local MMM 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 proportion of screenees with previously undiagnosed hypertension at a national, regional, global and ethnic level.

ii) Age and sex stratified and standardised levels of systolic (S) BP, diastolic (D) BP, BP variability and the proportion of screenees with known and newly diagnosed hypertension generated at a national, regional and global level.

iii) The proportion of screenees with uncontrolled hypertension among those on treatment for hypertension.

iv) The association between the same BP parameters and site of data collection, age, sex, ethnic group, weekday and treatment status 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 Considerations

7.1 Informed Consent

In accordance with local requirements, informed consent will be acquired from all screenees having received a simple verbal explanation of what data are to be collected and why, including that collected data will be used for research purposes.

7.2 Ethical/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 authority before BP screening begins. Implications of COVID-19 may require adaptation of the screening period within each local setting.

7.3 Subject Confidentiality

All screenee data collected for MMM is anonymous and not traceable to the individual screenees.

7.4 Local COVID-19 compliance

National leaders and their delegates will be responsible for ensuring that the running of MMM22 within their country, is in line with all local laws and guidance measures regarding COVID-19.

In addition to ensuring all local regulations are adhered to, we also strongly recommend the following measures are adopted by volunteers who take BP measurements from screenees: appropriate social distancing measures, the use of face masks and visors, regular hand-washing and the use of anti-bacterial wipes and sanitising agents on the blood pressure cuffs in between screenees.

8 Study Management

8.1 Overall management structure

The MMM Trustees of the newly formed charity will provide global oversight for the project, collection, processing, analysis and interpretation of the data. They will be supported by the project management team to form the MMM Management Board. The MMM Management Board will also receive advice from external advisors appointed to the board for a defined period. These advisors will meet with the MMM Management Board twice per year plus on an ad-hoc basis if required. 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 the MMM Management Board via the Project Manager at harsha@maymeasure.org .

9 References

1. GDB 2019 Risk Factor Collaborators. Global, regional, and national comparative risk assessment of 874 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study Lancet 2020: 396(10258):1129-1306.

2. Poulter et al. Seminars in Hypertension. Lancet 2015: 386: 801-12.

3. Chow et al. Prevalence, awareness, treatment, and control of hypertension in rural and urban communities in high-, middle-, and low-income countries. JAMA 2013: 310: 959: 68.

4. Geldsetzer et al. The state of hypertension care in 44 low-income and middle-income countries: a cross-sectional study of nationally representative individual-level data from 1·1 million adults. Lancet 2019: 394: 652-66.

5. Beaney et al. May Measurement Month 2017: an analysis of blood pressure screening results worldwide. The Lancet Global Health. May 2018. 2018:6 e736-43.

6. Beaney et al. May Measurement Month 2018: a pragmatic global screening campaign to raise awareness of blood pressure by the International Society of Hypertension. Eur Heart J. 2019. 1;40(25):2006-2017.

7. Beaney et al. May Measurement Month 2019: The Global Blood Pressure Screening Campaign of the International Society of Hypertension. Hypertension. 2020; 76(2):333-341.

Appendix 1

Atrial Fibrillation Screening Countries

In the first instance, the countries listed below will be invited to participate in our Atrial Fibrillation Screening Programme in 2022.

1. Australia
2. Austria
3. Belgium
4. Brazil
5. Canada
6. China
7. Denmark
8. France
9. Germany
10. Greece
11. Hong Kong
12. India
13. Ireland
14. Israel
15. Italy
16. Japan
17. Malaysia
18. Mexico
19. Netherlands
20. New Zealand
21. Nigeria
22. Norway
23. Portugal
24. Romania
25. Saudi Arabia
26. Scotland
27. Serbia
28. Slovakia
29. South Korea
30. Spain
31. Sweden
32. Switzerland
33. Taiwan
34. Thailand
35. United Kingdom
36. USA
37. Uruguay