May Measurement Month 2018: a pragmatic global screening campaign to raise awareness of blood pressure by the International Society of Hypertension


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Aims

Raised blood pressure (BP) is the biggest contributor to mortality and disease burden worldwide and fewer than half of those with hypertension are aware of it. May Measurement Month (MMM) is a global campaign set up in 2017, to raise awareness of high BP and as a pragmatic solution to a lack of formal screening worldwide. The 2018 campaign was expanded, aiming to include more participants and countries.

Methods and results

Eighty-nine countries participated in MMM 2018. Volunteers (≥18 years) were recruited through opportunistic sampling at a variety of screening sites. Each participant had three BP measurements and completed a questionnaire on demographic, lifestyle, and environmental factors. Hypertension was defined as a systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg, or taking antihypertensive medication. In total, 74.9% of screeners provided three BP readings. Multiple imputation using chained equations was used to impute missing readings. 1,504,963 individuals (mean age 45.3 years; 52.4% female) were screened. After multiple imputation, 502,079 (33.4%) individuals had hypertension, of whom 59.5% were aware of their diagnosis and 55.3% were taking antihypertensive medication. Of those on medication, 60.0% were controlled and of all hypertensives, 33.2% were controlled. We detected 224,285 individuals with untreated hypertension and 111,214 individuals with inadequately treated (systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg) hypertension.

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Introduction

Raised blood pressure (BP) continues to be the biggest contributor to the global burden of disease and mortality, with 10.4 million hypertension-related deaths in 2017. Hypertension affects over 1 billion adults worldwide and is forecast to affect over 1.5 billion by 2025. Despite the availability of effective treatments, only a small minority of those affected have their BPs controlled even to what are currently considered conservative targets (<140 mmHg systolic and <90 mmHg diastolic BP). This shortfall is largely due to the fact that only a minority of the hypertensive population receive BP-lowering treatment, which in turn reflects that the majority have not had their BP measured. As recognized by the World Heart Federation and the Lancet Commission on Hypertension, a critical route to maximize improvements in BP control among hypertensive adults is to enhance awareness of the condition.

Hence, in 2016 the International Society of Hypertension (ISH) announced its intention to initiate and lead a global campaign designed to raise awareness of the importance of BP and to act as a pragmatic temporary solution to the shortfall in BP screening programmes. This campaign, May Measurement Month (MMM) 2017, was designed to expand on and standardize the activities of the annual World Hypertension Day (17 May) which had been an international event since 2005. The initial MMM survey took place in 2017 in 80 countries, screening over 1.2 million adults. The positive feedback from global investigators and the finding of over 250,000 BP measurements between BP recordings. In 2017 and 2018, ~14,000 Omron BP devices (Omron Healthcare, Kyoto, Japan) were distributed to MMM sites where insufficient devices were available. In total, 87.3% of readings were taken using Omron devices. Otherwise, locally available devices were used to measure BP with a recommendation to use automated devices where possible.

Conclusion

May Measurement Month expanded significantly compared with 2017, including more participants in more countries. The campaign identified over 335,000 adults with untreated or inadequately treated hypertension. In the absence of systematic screening programmes, MMM was effective at raising awareness at least among these individuals at risk.

Methods

Study design

The MMM survey is a cross-sectional opportunistic study of BPs of volunteer adults aged 18 years or more. Over 100 countries were contacted either via those who had collaborated in MMM 2017 or via other national and international hypertension, cardiovascular or renal societies. In each country, one or more national leaders were identified to take the responsibility of acquiring national ethical clearance for the survey (if required) and to identify volunteer staff to set up screening sites and measure BPs. The protocol produced for MMM 2017 was updated and included training materials on BP measurement, and campaign promotional materials.

Data handling and statistical analysis

Data were entered via a bespoke MMM mobile application, available in eight languages (Arabic, Chinese, English, French, Hindi, Polish, Portuguese, and Spanish). Where, for logistic reasons or investigator preference, the mobile application was not used, data were entered on pre-prepared paper forms and transferred later to spreadsheets or the mobile application.

Volunteers were recruited at local sites using convenience sampling. Having been made aware of the availability of BP screening, those adults who wished to take advantage of the campaign attended one of the available MMM screening sites and were therefore self-referred. The campaign was targeted ideally at those who had not had their BP measured in the previous year, but participants who presented and had been screened more recently were not excluded from the study.

Appendix

Data were cleaned locally and/or centrally depending on local capacity, following rules with cut-off ranges devised and provided to all sites (see Supplementary material online, Appendix). Countries submitting fewer
than 10 screenees were excluded from analyses due to concerns over the validity of these screening sites.

Data from 89 countries were submitted, collated centrally, and analysed using Stata version 14.2 (StataCorp 2015). Countries were grouped into seven regions based on the UN geographical classification, with minor modifications to match the regions used in 2017.11 Classification of country economic income was derived from data from the World Bank.

Comparisons of the first, second, and third BP readings were made among the 1 126 495 individuals with all three readings available. For all further analyses, the mean of the second and third readings was used. Where one or more BP measurements were missing, multiple imputation by chained equations was used, assuming that missingness was dependent on the observed data (Missing At Random).

Multiple imputation was conducted for those with complete data on age, sex, ethnicity, and use of antihypertensive medication. The imputation model incorporated all variables included in the further analyses, required to avoid bias in the analyses.12 Each of the three systolic BP and three diastolic BP readings were also included in the model, along with the mean of the second and third readings, following the ‘just another variable’ approach.13 Twenty-five imputations were created, chosen on the basis of the percentage of missing data in the mean BP readings, and confirmed by the Monte Carlo errors of the estimates (at <10% of the standard errors).

In participants for whom the mean reading could not be imputed, due to missing one or more of age, sex, ethnicity, or antihypertensive medication, a reduced imputation model using only the individual BP readings was used. The primary analysis combined the data imputed using the complex and reduced model (n = 1 504 963). Sensitivity analyses were performed using the complete cases, reduced model, complex model, combination (primary) model, and also comparing the MMM 2017 imputation model. A full description of the imputation method, along with sensitivity analyses can be found in the Supplementary material online, Appendix.

For comparisons of BP across regions, age and sex standardization was carried out, based on the World Health Organization world age-standard population, and assuming an equal ratio of males to females.14 Measures of association were analysed using the complex imputation model (i.e. not including those with missing data in age, sex, ethnicity, or antihypertensive medication). Linear mixed models were run separately for systolic and diastolic BP with a random intercept model to account for country-level clustering. All models were adjusted for age, sex, and use of antihypertensive medication, with age incorporated as a restricted cubic spline with five knots, and inclusion of an interaction between age and sex. The association between BP and heart rate was analysed using linear mixed effects models which compared the BP with heart rate at each reading, and accounted for repeated measurement within each participant using a random intercept.

### Results

#### Participant characteristics

Data on 1 504 963 participants from 89 countries (see Supplementary material online, Appendix Table A2) were cleaned, collated, and analysed. Of these data, 12.4% were submitted via the bespoke mobile application. Rates of complete data collection for individual variables were improved compared with 2017, with only 0.9% missing data on sex, and only 2.1% missing data on age (for full details see Supplementary material online, Appendix Table A3). One-third of participants were screened in a hospital or medical clinic, and 105 009 (7.0%) screenees had been screened in MMM 2017.

Participants were stratified across seven regions with significant differences in mean ages and sex distribution across regions (Table 1). South Asia contributed the largest proportion of screenees (26%) and Europe the least (5.4%). More women than men were screened in all regions except South Asia and the North Africa and Middle East. Mean ages were lowest in the North African and Middle East region for both women (34.9 years) and men (36.6 years) and highest in the Americas for both women (49.5 years) and men (51.3 years). Use of antihypertensive medication also varied from 9.0% in sub-Saharan Africa, to 32.7% in the Americas. The differential distributions of age, sex, and medication use across the seven regions highlight the need for adjustment of these three variables when making comparisons among regions.

The percentages of participants from high-income, upper-middle, lower-middle, and low-income countries were 12.3%, 30.0%, 54.4%, and 3.4% respectively. Of 1 504 963 screenees, 111 374 (8.5%) reported having diabetes, 61 174 (4.6%) reported a history of myocardial infarction (MI), 42 010 (3.2%) reported a history of stroke,
167,487 (12.3%) reported current smoking, 59,210 (4.6%) reported alcohol consumption ≥ once per week, and 13,233 (1.7%) of women reported being pregnant. Both height and weight were recorded in 91.4% of participants, but at least one of height and weight was estimated rather than measured in 24.2% of screenees. The mean body mass indexes (BMIs) of men and women were 24.6 kg/m² (SD 4.5) and 24.3 kg/m² (SD 4.9), respectively (see Supplementary material online, Appendix Table A3).

Variation across blood pressure readings
Of all participants, 1,126,495 (74.9%) had all 3 BP readings recorded (see Supplementary material online, Appendix Table A1). Blood pressures decreased on average by 3.0/2.0 mmHg between the first and third readings (Table 2). Similarly, the proportion of screenees with hypertension decreased on subsequent readings with a 4.0% difference in hypertension prevalence based on the first and third reading. The lowest prevalence of hypertension was found using the mean of the second and third readings (Table 2).

For participants missing the second and/or third BP reading, multiple imputation was used to impute the mean of the two readings. Using the complex model (for those with age, sex, ethnicity, and anti-hypertensive use all documented), imputations were carried out for a total of 237,871 participants. For the remaining 137,556 participants, the simple imputation model was used. A total of 25 imputations were created.

Numbers with hypertension
After imputation, the mean BP worldwide was 123.1/77.9 mmHg (95% confidence interval 123.0/77.9–123.1/77.9). Mean unadjusted BPs ranged from 119.3/76.4 mmHg in East Asia to 127.3/79.3 mmHg in Europe (Table 3). After age and sex standardization according to the WHO population, East Asia still had the lowest mean BPs (117.0/75.4 mmHg), whilst South Asia and Europe had the highest levels (124.6/78.1 mmHg and 124.6/78.4 mmHg, respectively). Worldwide, the mean BP of all those not taking antihypertensive medication was 120.0/76.7 mmHg and of those taking antihypertensive medication was 127.7/80.0 mmHg.

Following imputation, 502,079 (33.4%) participants were found to have hypertension (95% confidence interval 33.3%–33.4%) (Table 4). Of these, 298,940 (59.5%) were aware of their condition and 277,794 (55.3%) were on treatment. Of those on treatment, 166,580 (60.0%) were controlled and hence 33.2% of all those with hypertension were controlled. Of all participants screened worldwide...
who were not on antihypertensive medication, 18.3% were found to have hypertension. Following standardization for age and sex, 17.9% of participants not on antihypertensive medication were found to have hypertension, with the lowest proportion in East Asia (13.9%) and the highest proportion in Northern Africa and the Middle East (21.4%) (Supplementary material online, Appendix Table A6).

Sensitivity analyses showed only minor differences in the mean BPs and in the proportions with hypertension. In the complete case analysis (before imputation), of 1 129 536 individuals with a mean of the second and third readings available, 33.6% were found to have hypertension (95% confidence interval 33.5%–33.7%). This compared with 33.4% using the 2017 imputation model, 33.4% using the reduced MI model, 33.0% using the complex MI model and 33.4% using the combined primary model. Full details of the results from the sensitivity analyses along with estimates of precision and Monte Carlo errors are shown in the Supplementary material online, Appendix Tables A4 and A5.

Differences in BP parameters and management were apparent across regions, with the lowest proportion of all hypertensive participants on medication in Northern Africa and the Middle East (32.1%), and the highest proportion in the Americas (70.6%). Of those on medication, control rates were lowest in sub-Saharan Africa (45.1%) and highest in South Asia (70.4%).

Of 105 009 (7.0%) of individuals who had also participated in MMM 2017, the proportion with hypertension was 45.1%, compared with 32.5% who did not participate in MMM 2017.

Of all participants, 43.3% had had a BP check within the last 12 months. Of those who had not had a BP check in the last year, the mean BP was significantly lower than in those who had (122.1/77.5 mmHg vs. 124.3/78.5 mmHg), with the proportion with hypertension lower in those not checked in the last 12 months (24.7% vs. 44.7%). Comparison across country income strata showed lower proportions on treatment and lower control rates among the treated in low-income countries relative to other income levels (see Figure 1).

**Blood pressure associations**

Based on linear mixed models, the global association between age and systolic BP in men and women who were not receiving antihypertensive treatment showed a linear increase, with the mean BP in women exceeding the mean BP in men at 75 years of age. For diastolic BP, the relationship shows an inverted U shape, with highest levels at age 50–55 years, and with BP in women lower than in men until aged 85–90 years (Figure 2).

After adjustment for age and sex (including an interaction between age and sex) systolic and diastolic BPs were significantly higher in people who were taking antihypertensive medications (Figure 3). Higher BPs were also seen in those who reported having previously been told they had high BP, independent of the association with medication use. After adjusting for age, sex, and antihypertensive medication, significantly lower systolic and diastolic BPs were seen in those with a history of diabetes, stroke, and MI, compared to those without.

Systolic and diastolic BPs were lower when measured on the left compared to the right arm, and in pregnant women compared to women who were not pregnant (Figure 4). Higher BPs were seen in alcohol drinkers, with a linear dose-dependent relationship, and slightly higher BPs were seen in those who were fasting at the time of meal.

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**Table 4** Key proportions for participants with hypertension, worldwide, and by region, after imputation

<table>
<thead>
<tr>
<th>Region</th>
<th>Number with hypertension</th>
<th>Proportion with hypertension (%)</th>
<th>Proportion of hypertensives aware (%)</th>
<th>Proportion of hypertensives on medication (%)</th>
<th>Proportion of those on medication with controlled BP (%)</th>
<th>Proportion of all hypertensives controlled (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>South Asia</td>
<td>132 173</td>
<td>33.8</td>
<td>59.5</td>
<td>56.9</td>
<td>70.4</td>
<td>40.0</td>
</tr>
<tr>
<td>East Asia</td>
<td>93 499</td>
<td>30.7</td>
<td>64.0</td>
<td>59.1</td>
<td>63.2</td>
<td>37.3</td>
</tr>
<tr>
<td>South-East Asia and Australasia</td>
<td>104 148</td>
<td>35.4</td>
<td>50.8</td>
<td>50.1</td>
<td>48.7</td>
<td>24.4</td>
</tr>
<tr>
<td>Americas</td>
<td>76 574</td>
<td>40.4</td>
<td>76.7</td>
<td>70.6</td>
<td>60.9</td>
<td>43.0</td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td>37 603</td>
<td>24.8</td>
<td>43.6</td>
<td>33.1</td>
<td>45.1</td>
<td>15.0</td>
</tr>
<tr>
<td>Northern Africa and Middle East</td>
<td>24 579</td>
<td>26.3</td>
<td>35.7</td>
<td>32.1</td>
<td>58.6</td>
<td>18.8</td>
</tr>
<tr>
<td>Europe</td>
<td>33 504</td>
<td>41.6</td>
<td>71.0</td>
<td>62.0</td>
<td>48.9</td>
<td>30.3</td>
</tr>
<tr>
<td>Worldwide</td>
<td>502 079</td>
<td>33.4</td>
<td>59.5</td>
<td>55.3</td>
<td>60.0</td>
<td>33.2</td>
</tr>
</tbody>
</table>

**Figure 1** Proportions of hypertensives not on medication, on medication and controlled, on medication and uncontrolled, by country income strata.
screening. Smokers showed no significant difference in BPs compared with non-smokers.

A strong linear relationship was seen between both systolic and diastolic BP and increasing levels of BMI (Figure 5), with a mean increase of ~6.7/4.1 mmHg comparing obese participants to those considered underweight. A sensitivity analysis found no significant difference in this relationship using BMIs that were measured compared with those that were estimated. A similarly strong linear relationship was seen between diastolic BP and heart rate (Figure 6). The association of systolic BP with heart rate was clear, but less pronounced.

Compared to hospital- or clinic-based measurements, BPs measured in pharmacies were significantly lower, while those taken in the workplace were significantly higher (Supplementary material online, Appendix Figure A1). Systolic BPs were highest on Saturday and lowest on Sunday.
on Tuesday, with diastolic BP highest on a Monday. However, although statistically significant, these effects were small being under 0.5 mmHg on average (Supplementary material online, Appendix A2). Additional adjustment for alcohol did not significantly affect the association with day of week. There was no clear relationship between BP levels and increasing levels of room temperature. Full
details of these analyses, along with coefficients and 95% confidence intervals, are shown in the Supplementary material online, Appendix.

Discussion

May Measurement Month 2018 expanded on the unique achievements of MMM 2017 by including over 1.5 million screenees from 89 countries, replacing MMM 2017 as the largest synchronized, standardized, and multinational screening campaign of any cardiovascular risk factor ever carried out. Equally importantly, the quality of data collected was greatly improved compared with MMM 2017, with less missing data, allowing a more rigorous and valid evaluation of the associations between BP and those variables recorded.

Over a third of a million adults were identified as having untreated (224 285) or inadequately treated (111 214) hypertension, reaffirming previously established low BP treatment and control rates3–5 and the findings of MMM 2017.9 In addition, 59.5% of participants identified with hypertension were aware of having had a previous diagnosis of hypertension. This was higher than the 46.5% awareness found in the PURE study and may reflect our more contemporary data and/or differential recruitment practices.3 However, with 40.5% of participants with hypertension unaware of having high BP, MMM can have a substantial impact in raising awareness in this group.

Using the hitherto standard definition of hypertension (>140 mmHg systolic or >90 mmHg diastolic or on treatment for hypertension), the proportion of screenees with hypertension was almost identical (33.4%) to that discovered in MMM 2017 (34.9%), despite a different source of participants in terms of countries included and the different relative distribution of numbers of screenees among the countries. The proportion with hypertension among the 105 009 participants screened in both MMM 2017 and MMM 2018, was higher than in the rest of the population who were not screened in 2017, suggesting that those found to have higher BPs in 2017 were more likely to return for screening.

In our study, ‘hypertension’ was based on a single set of three readings, contrary to optimal practice,15–17 but further measurements or ambulatory readings would not have been feasible due to both cost and logistics. We might therefore expect spuriously high rates of hypertension through inclusion of those with white coat hypertension. MMM 2018 data reaffirm that the most conservative (and therefore likely the most accurate) diagnostic criteria for hypertension when based on three serial BP recordings arose from the mean of the second and third BP readings, even though the third reading was on average lower than the second. We recommend that if treatment decisions have to be made on the basis of a single set of readings—sadly all too common—this approach gives the optimal conservative information unless further readings can be taken.

Screenees were recruited by opportunistic, convenience sampling and although sites generated a wide range of participants, comparison of prevalence of hypertension across regions is inappropriate. However, the associations of BP within the screened population are internally valid18 and given the magnitude of the study and diversity of participants, are likely to be externally valid. This is supported by the strong reaffirmation of the well-established associations seen between higher BP and increasing age,19 BMI20 and levels of alcohol intake21 and lower BP with pregnancy.22

The largest disparities in BP levels among subgroups were those observed across the range of BMIs (Figure 5), those who had previously been told they had high BP and those taking antihypertensive medication. A similarly strong relationship was found with heart rate, but the
effect was unexpectedly stronger with diastolic than with systolic BP. We also found a surprising relationship of reduced BP in participants with a history of diabetes, stroke, and MI after accounting for age, sex, and medication use. The reasons for this are not clear, but could reflect residual confounding, more aggressive BP treatment in these groups of patients, post-MI heart failure, or unrecorded use of BP-lowering medication (e.g. if thought to be for a different indication).

In 2018, Ramadan started in May and for this reason, we added a question on fasting status. Almost 100 000 MMM participants were fasting and were found to have slightly higher BPs than those who were not fasting—however, given the small difference observed, this appears to be consistent with previous studies showing no clinically significant effects of fasting in normotensive or hypertensive patients. As found in MMM 2017, readings taken on the right arm were higher than those measured on the left arm. Compared with BPs measured in hospitals or clinics, BPs were lower in all types of sites except the workplace. Whilst this might reflect a higher rate of hypertension among those screened in a medical setting it may also reflect a version of the ‘white-coat’ effect.

The relationship with ambient temperature was unclear and does not fit with recent findings of reduced BP with higher room temperatures. May Measurement Month results may have been confounded by inappropriate documentation of outdoor temperatures rather than indoor, or ignoring changes in room temperature throughout the day. As in MMM 2017, systolic BPs were highest on Saturday and lowest on Tuesday, but the size of the difference was small and the relationship was unaffected by adjusting for alcohol.

Limitations

Limitations of MMM 2018 include that, although efforts to train those measuring BPs were made, variations in the machines used and in the environment during measurement mean that standardization of measurement around the world was inevitably imperfect. While the mobile application and data input templates were designed to minimize errors during entry, inaccuracies did occur, requiring some measurements to be dropped during the cleaning process. Despite this, the strong corroboration in analyses based on estimated, compared to measured, height and weight, suggest a high degree of validity.

The study protocol required three BP measurements for each participant, but at least one of these three measurements was not taken or documented in a quarter of participants. The significant variation across the first, second, and third readings had the potential to cause a large impact in analysis and a possible over-diagnosis of hypertension. Our use of multiple imputation allowed us to mitigate this effect and accurately estimate the mean of the second and third reading from a single reading, with results robust to a range of different imputation models.

In keeping with most hypertension surveys, the diagnosis of hypertension was based on a single series of readings. This is not recommended practice for diagnosis at the individual level but sadly is all too commonly used in clinical practice.

A further limitation is that screenees were self-selected and opportunistic convenience sampling was used to include people who ideally, had not had their BPs measured in the previous year. Hence the study was, by design, not intended to give representative samples. A third of measurements were taken in medical settings which might result in the self-selection of a greater proportion of participants with hypertension.

However, as our results show, the absolute differences in mean BP taken in different settings was small (under 2 mmHg systolic/diastolic).

Due to the potential self-selection bias introduced through the sampling, underlying prevalence rates cannot be reported and compared, and differences between countries and regions should be interpreted in the context of the local characteristics of screening sites. Despite the limitations, our results are in line with published data in smaller cohorts demonstrating that 30–35% of adults have hypertension, with a high proportion being unaware and a small percentage being treated to target. In addition, the results do provide ‘real-world’ data on the characteristics of the participants who are likely to present to a volunteer-based screening campaign, which for many countries may be a more feasible option than a systematic screening programme.

The effect of diet and lifestyle advice given to all those with raised BP (treated or not) could not be evaluated in the cross-sectional design, and hence the post-survey impact on awareness could not be evaluated. However, plans to incorporate post-screening follow-up are in progress for MMM 2019 and subsequent years. Furthermore, at the individual level over 335 000 adults were made aware of their raised BP levels and, given the extensive promotion of MMM via television, radio, the media, and social media, we believe that awareness at the population level was also increased. Although large improvements in data quality were achieved in MMM 2018, only a minority (12.4%) of the data were collected through the bespoke mobile application. This resulted in slower data collection, cleaning, transfer, analyses, and publication of results. Further improvements in data collection are planned for MMM 2019.

Finally, for the logistic and financial reasons the survey was restricted to use a relatively short questionnaire to collect data from screenees. However, plans to extend and modify the questions each year are in place. Efforts to include more screenees from low-income countries will also be made in future years.

Future directions

May Measurement Month 2018 was achieved at a central cost of 14 cents per participant and 65 cents per identified case of untreated or treated but uncontrolled hypertension, although most costs were offset by having volunteer investigators, donated BP measurement devices and locally raised funds. May Measurement Month 2018 confirms that mass screening of BP is feasible around the world at a relatively low cost to raise awareness of BP in large numbers of people. Although the ultimate aim of the MMM campaign is to use the data to influence health policy on BP screening and management where it is needed most, meanwhile, it provides stand-alone benefits likely to reduce the health burden due to raised BP.

Further analyses of all individual national datasets from MMM 2018 are in progress to update and expand on those based on MMM 2017 national data. It is hoped that this will help to facilitate dissemination of local results and thereby potentially influence awareness and national policies related to the implications of BP screening and hypertension management.

Conclusion

The results from MMM 2018 show that significant numbers of people can be identified with untreated, or treated but uncontrolled,
hypertension from an opportunistic, volunteer-driven screening campaign. The growth from over 1.2 million screenees in 2017 to over 1.5 million in 2018 attests to the perceived efficacy amongst national investigators and volunteers in the ability of MMM to raise awareness of this major and growing global health burden, at least in the significant numbers found to have raised BP. Given the urgency to act, as long as large numbers of people with untreated or inadequately treated hypertension are identified, sufficient central support can be obtained, and suitable surveillance systems are still not available for many countries of the world, we believe MMM should continue on an annual basis.

**List of MMM Investigators**


**Supplementary material**

Supplementary material is available at European Heart Journal online.

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