# Hypertension in stroke survivors and associations with national premature stroke mortality: data for 2.5 million participants from multinational screening campaigns 

Queran Lin*, Tingxi Ye*, Pengpeng Ye, Claudio Borghi, Suzie Cro, Albertino Damasceno, Nadia Khan, Peter M Nilsson, Dorairaj Prabhakaran, Agustin Ramirez, Markus P Schlaich, Aletta E Schutte, George Stergiou, Michael A Weber, Thomas Beaneyt, Neil R Poultert

## Summary

Background Blood pressure control has a pivotal role in reducing the incidence and recurrence of stroke. May Measurement Month (MMM), which was initiated in 2017 by the International Society of Hypertension, is the largest global blood pressure screening campaign. We aim to compare MMM participants with and without a previous history of stroke and to investigate associations between national-level estimates of blood pressure management from MMM and premature stroke mortality.

Methods In this annual, global, cross-sectional survey, more than 2.5 million volunteers ( $\geq 18$ years) from 92 countries were screened in May, 2017, and May, 2018. Three seated blood pressure readings and demographic, lifestyle, and cardiovascular disease data were collected. Associations between risk factors and stroke history were analysed with mixed-effects logistic regression, and associations between national-level estimates of blood pressure management and premature stroke mortality based on Global Burden of Disease data were investigated with linear regression.

Findings $2222399(88 \cdot 4 \%)$ of 2515365 participants had recorded data on a history of stroke, of whom $62639(2 \cdot 8 \%)$ reported a previous stroke. Participants with a history of stroke had higher rates of hypertension $(77 \cdot 0 \% \mathrm{vs} 32 \cdot 9 \%$, $\mathrm{p}<0.0001$ ) and of treated $(90.2 \%$ vs $57.0 \%, \mathrm{p}<0.0001)$ and controlled $(55.9 \%$ vs $32.4 \%, \mathrm{p}<0.0001)$ hypertension than those without a history of stroke. A third of participants with a history of stroke had either untreated hypertension or treated but uncontrolled hypertension (blood pressure $\geq 140 / 90 \mathrm{~mm} \mathrm{Hg}$ ). Strong positive associations were found between national premature stroke mortality and mean systolic blood pressure ( $84 \cdot 3$ [ $95 \%$ CI $38 \cdot 8$ to $129 \cdot 9$ ] years of life lost [YLL] per 100000 people per mm Hg increase) and the percentage of participants with raised blood pressure ( $49 \cdot 1$ [ $22 \cdot 6$ to $75 \cdot 6$ ] YLL per 100000 people per $1 \%$ increase). Strong negative associations were found between national premature stroke mortality and the percentage of participants with hypertension on treatment ( -21.0 [ $-33 \cdot 0$ to $-8 \cdot 9$ ] YLL per 100000 people per $1 \%$ increase) and with controlled blood pressure ( -31.6 [ -43.8 to -19.4$]$ YLL per 100000 people per $1 \%$ increase).

Interpretation Blood pressure control remains suboptimal worldwide among people with a history of stroke. National estimates of blood pressure management reflect national premature stroke mortality sufficiently to prompt policy makers to promote blood pressure screening and management.

Funding International Society of Hypertension and Servier Pharmaceuticals.
Copyright © 2022 The Author(s). Published by Elsevier Ltd. This is an Open Access article under the CC BY 4.0 license.

## Introduction

In 2019, stroke was the second largest cause of death worldwide and the third leading cause of premature mortality. ${ }^{1}$ Globally, there were 12 million incident strokes in 2019 and a further 100 million people had a previous history of stroke. ${ }^{1}$ These values represented a $71 \%$ increase in the incident cases and an $82 \%$ increase in the prevalent cases reported annually in the 1990s. ${ }^{1}$ The global burden of stroke is expected to continue to increase and cause more than 7 million annual deaths by 2030. ${ }^{2}$ Economic costs associated with stroke are substantial, with direct annual medical costs to patients in the USA predicted to reach US $\$ 184$ billion by 2030 unless more effective preventive and therapeutic measures are instigated. ${ }^{3}$

Years of life lost as a result of stroke is highest in lowincome countries and lowest in high-income countries. ${ }^{1}$ However, to date, data on non-fatal stroke from lowincome and middle-income countries are scarce. ${ }^{4,5}$ The INTERSTROKE study ${ }^{6}$ established the contribution of ten potentially modifiable risk factors that provide $90 \%$ of the population attributable risk of stroke. Of these, hypertension was the largest contributor, accounting for $48 \%$ of the population attributable risk, with stroke risk almost three times higher in people with hypertension than in those without. ${ }^{6,7}$
Worldwide, between 1975 and 2015, the number of people with hypertension increased from 590 million to more than 1.1 billion, two-thirds of whom live in

Lancet Glob Health 2022; 10: e1141-49

See Comment page e1076
*Joint first authors
$\dagger$ Joint senior authors
Department of Primary Care and Public Health (Q Lin MPH, TYe MPH, T Beaney MSc) and Imperial Clinical Trials Unit (S Cro PhD, T Beaney, N R Poulter FMedSci), Imperial College London, London, UK; Guangdong Provincial Key Laboratory of Malignant Tumor Epigenetics and Gene Regulation (Q Lin) and Breast Tumor Center (Q Lin), Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, China; The George Institute for Global Health (PYe MPH, A E Schutte PhD) and School of Population Health (A E Schutte), University of New South Wales, Sydney, NSW, Australia; National Centre for Non-Communicable Disease Control and Prevention, Chinese Centre for Disease Control and Prevention, Beijing, China (PYe); Department of Medical and Surgical Sciences, IRCCS Azienda OspedalieroUniversitaria di Bologna, Bologna, Italy (C Borghi MD); Faculty of Medicine, Eduardo Mondlane University, Maputo, Mozambique (A Damasceno PhD); Department of Medicine, Center for Health Evaluation and Outcomes Sciences, University of British Colombia, Vancouver, BC, Canada (N Khan MD); Department of Clinical Sciences, Lund University, Skane University Hospital, Malmo, Sweden (P M Nilsson MD); Public Health Foundation of India and Centre for Chronic Disease Control, Haryana, India (D Prabhakaran DM); Hospital Universitario Fundación Favaloro, Buenos Aires, Argentina (A Ramirez MD);

Dobney Hypertension Centre, School of Medicine, Royal Perth Hospital Research Foundation, University of Western Australia, Perth, WA, Australia (M P Schlaich); Hypertension Center STRIDE-7, National and Kapodistrian University of Athens, School of Medicine, Third Department of Medicine, Sotiria Hospital, Athens, Greece (G Stergiou FRCP); Division of Cardiovascular Medicine, State University of New York, Downstate Medical Center,

New York, NY, USA
(M A Weber MD)
Correspondence to:
Dr Thomas Beaney, Department
of Primary Care and Public Health, Imperial College London, London W6 8RP, UK thomas.beaney@imperial.ac.uk

## Research in context

## Evidence before this study

We searched PubMed for articles related to blood pressure control among stroke survivors published in any language between Jan 1, 2010, and Aug 1, 2021, using the search terms "stroke", "risk factors", "stroke survivors", "post-stroke", "blood pressure", "hypertension", "control", "antihypertensive treatment/medication", "Global Burden of Disease", "global", "worldwide", "African countries", "European countries", "Asia", "smoking", "overweight", "obesity", "alcohol", "diabetes", "myocardial infarction", "age", and "sex". Combinations of the above terms were also searched. We screened more than 500 articles and found studies, including the Global Burden of Disease studies from 2016 and 2017, suggesting that hypertension is the most important risk factor for stroke, but data on stroke survivors and coverage of age range was poor. We also found studies that described suboptimal control of blood pressure in at least half of stroke survivors in several countries with small samples, whereas we found no research in a global context nor large-scale studies in low-income settings. Little is known about the control of blood pressure in people with a previous history of stroke worldwide.

## Added value of this study

Our study used data from 92 countries collected in 2017 and 2018 as part of May Measurement Month (MMM), the largest standardised, contemporary, global blood pressure screening
programme. Despite using opportunistic screening in many of the countries involved, these MMM data are the largest source of population blood pressure data available and contain data on more than 60000 stroke survivors. By analysing individual-level data from more than 2 million participants, we show that those with a previous history of stroke were much more likely than those without to have hypertension
( $77 \%$ vs $33 \%$ ) and, among stroke survivors, a third had untreated or inadequately treated raised blood pressure ( $\geq 140 / 90 \mathrm{~mm} \mathrm{Hg}$ ). After aggregating MMM data to the national level, parameters of blood pressure management were strongly and significantly associated with national premature stroke mortality rates, highlighting the crucial effect of blood pressure control on stroke mortality.

## Implications of all the available evidence

Our results show consistently poor blood pressure control among stroke survivors worldwide. Interventions tailored to the local context, including enhanced blood pressure screening facilities, are urgently needed to enable more effective blood pressure control. The strong associations between agestandardised measures of blood pressure management at the national level and premature stroke mortality could, in the absence of data arising from large, nationally representative samples, provide an impetus to policy makers to promote enhanced blood pressure screening and improved management of hypertension.

For MMM see
https://maymeasure.org
low-income and middle-income countries. ${ }^{8}$ Blood pressure control has a pivotal role in reducing the incidence ${ }^{6,7}$ and recurrence ${ }^{9}$ of stroke. Although a few studies, mostly in high-income countries, have found at least half of stroke survivors to have increased blood pressure ${ }^{10-13}$ little is known about the current status of blood pressure control in stroke survivors in most of the world.
The May Measurement Month (MMM) campaign is an annual, multinational, cross-sectional study, initiated in 2017 by the International Society of Hypertension, to raise awareness of the importance of blood pressure measurement. During the 2017 and 2018 campaigns, ${ }^{14,15}$ more than 2.7 million adults in 95 countries had their blood pressure screened. The MMM dataset is one of the largest sources of opportunistic data on blood pressure and related cardiovascular disease, arising from countries across the range of national income settings worldwide.
The first aim of this study was to compare cardiovascular risk factors, including the detection, management, and control of blood pressure, in MMM participants with and without a history of stroke. The second aim was to evaluate whether blood pressure and parameters of hypertension management at a national level based on MMM data were associated with national premature stroke mortality based on data from the

Global Burden of Diseases, Injuries, and Risk Factors Study (GBD).

## Methods

## Study design

The MMM campaign is an annual, global, cross-sectional survey of blood pressure that uses a single, standardised protocol and questionnaire across countries from seven UN geographical regions. ${ }^{16}$ Detailed descriptions of the methods used for setting up sites and promoting the campaign are available in previous MMM global reports ${ }^{14,15}$ and on the MMM website but local promotion included celebrity and government endorsement through media and social media. Self-referred participants 18 years or older were screened opportunistically using convenience sampling from May 1 to June 30, 2017, and from May 1 to June 30, 2018. Almost half (48.5\%) of participants were screened in health-care settings such as hospitals and pharmacies, $39.5 \%$ in indoor or outdoor public places such as supermarkets, education institutes, and playing fields, and $10 \cdot 1 \%$ in workplaces. ${ }^{14,15}$
Three seated blood pressure readings were collected at 1-min intervals and a questionnaire was completed for each participant. Details of blood pressure measurement are reported in previous MMM global reports. ${ }^{14,15}$ Measurements were made by volunteers trained in
standardised techniques through video recordings hosted on the MMM website and through face-to-face, on-site training. Blood pressure devices varied between sites, but $88 \cdot 1 \%$ of readings were measured with Omron devices. The questionnaire included questions on demographic information, lifestyle risk factors, and cardiovascular comorbidities (ie, stroke, myocardial infarction, and diabetes). Height and weight were measured, or estimated if equipment was unavailable. The questionnaire differed slightly between 2018 and 2017 (appendix pp 3-4); in 2018 a question regarding previous diagnosis of hypertension was added to enable awareness of hypertension to be evaluated. Alcohol consumption was treated as a binary variable ("never/rarely/1-3 times per month" or "at least once per week") in both 2017 and 2018 for consistency.
Data collected at screening sites were either entered into a web-based or mobile app available in six languages, or recorded on paper before being electronically transcribed. The data were collated centrally, cleaned, and analysed, except for data on 190955 participants from India who were screened in 2017, which were analysed locally for regulatory reasons and are not included in this analysis. Data cleaning rules and protocols for 2017 and 2018 remained consistent throughout all sites. ${ }^{14,15}$ Ethics approvals for the study were obtained where required by national investigators in each country. Informed oral consent was obtained from all participants.
Raised blood pressure was defined as a systolic blood pressure of at least 140 mm Hg , a diastolic blood pressure of at least 90 mm Hg , or both, on the basis of the mean of the second and third blood pressure readings. Hypertension was defined as a raised blood pressure or the taking of antihypertensive medication. Uncontrolled blood pressure was defined as raised blood pressure in participants who were taking antihypertensive medication. Body-mass index (BMI) was calculated as recorded weight (kg)/height ${ }^{2}(\mathrm{~m})$. Participants were categorised into four BMI groups (underweight, healthy weight, overweight, or obese) according to WHO categories. ${ }^{17}$

## Statistical analysis

Data were analysed using Stata version 15 IC. Three countries with insufficient data, defined as fewer than 50 participants, were excluded from the analysis, after which 92 countries remained. Descriptive statistics for participant characteristics are based on observed data. To reduce any bias from missing blood pressure readings, multiple imputation using chained equations was conducted to derive the missing mean of the second and third blood pressure readings, based on the assumption that the blood pressure readings were missing at random, using the approach developed previously for MMM. ${ }^{15}$ Two imputation models were applied and the results combined (appendix pp 5-6). The first imputation model was applied for participants for whom information on age, sex, ethnicity, and use of antihypertensive medication was complete. All variables included in the analysis
models were incorporated in the imputation model, including the three systolic and three diastolic blood pressure readings, the mean of the second and third blood pressure readings, and an interaction between age and sex. For the 733893 participants for whom records of age, sex, ethnicity, or antihypertensive medication were missing, a second imputation model was used, imputing on the basis of the recorded blood pressure readings alone (appendix pp 5-6). 25 sets of imputed data were generated, corresponding to the approximate proportion of participants for whom one or more blood pressure readings were missing. Hypertension parameters were standardised for age and sex on the basis of the WHO single age standard population, assuming an equal male-to-female ratio. ${ }^{18}$
We used mixed-effects logistic regression to estimate the odds ratios for different cardiovascular risk factors given a history of stroke, accounting for clustering within country using a random intercept model and assuming equal slopes. We selected variables for inclusion in the model using a theoretical approach, based on suspected confounders, but requiring a statistically significant association with both outcome and exposure. We constructed a basic multivariable model adjusted for age and sex alone and a fully adjusted model incorporating all potential confounders that were significantly associated with outcome and exposure from univariable models, except for myocardial infarction, which was excluded owing to multicollinearity with stroke. The fully adjusted model included age, sex, use of antihypertensive medication, smoking, alcohol intake, diabetes, and BMI category
To analyse the odds of a participant having raised blood pressure given a history of stroke, we applied univariable and multivariable mixed-effects logistic regression using a random intercept model for country and assuming equal slopes. Models were stratified by use of antihypertensive medication as a potential effect modifier. Two separate multivariable models were analysed: a basic model adjusted for age and sex alone, and a fully adjusted model that included age, sex, smoking, alcohol intake, diabetes, and BMI category.
We analysed the associations between national mean blood pressure levels and parameters of hypertension management from MMM and premature stroke mortality using national-level estimates of premature stroke mortality extracted from GBD data. ${ }^{19}$ We used agestandardised estimates of premature mortality, measured in years of life lost per 100000 people, standardised according to the world population age standard from GBD 2017 data. ${ }^{20}$ Results from MMM were aggregated to the national level, and linear regression was used to examine the associations between GBD national premature stroke mortality and the following national MMM parameters: mean systolic blood pressure, the proportion of all participants with raised blood pressure, the proportion of all participants with hypertension, the proportion of participants with hypertension taking antihypertensive

|  | $\begin{aligned} & \text { Previous stroke } \\ & (n=62639) \end{aligned}$ | No previous stroke $(\mathrm{n}=2159760)$ | p value* |
| :---: | :---: | :---: | :---: |
| Sex |  |  |  |
| Male | 33910 (54.5\%) | 978585 (45-7\%) | <0.0001 |
| Female | 28294 (45.5\%) | 1164674 (54.3\%) | <0.0001 |
| Age (years) | $51 \cdot 1(17 \cdot 4)$ | 45.0 (16.8) | <0.0001 |
| Age categories |  |  |  |
| <40 years | 16441 (28.6\%) | 843404 (41-7\%) | <0.0001 |
| 40-59 years | 20567 (35.7\%) | 724325 (35.8\%) | <0.0001 |
| 60-79 years | 17878 (31.1\%) | 411754 (20.3\%) | <0.0001 |
| $\geq 80$ years | 2645 (4.6\%) | 43678 (2.2\%) | <0.0001 |
| Diabetes | 23630 (38.8\%) | 153009 (7.4\%) | <0.0001 |
| Myocardial infarction | 36743 (59.5\%) | 57830 (2.7\%) | <0.0001 |
| Current smoker | 31718 (50.9\%) | 245826 (11.4\%) | <0.0001 |
| Alcohol consumption (at least once per week) | 5798 (10.0\%) | 127751 (6.4\%) | <0.0001 |
| BMI, $\mathrm{kg} / \mathrm{m}^{2}$ | 25.0 (4.9) | $24 \cdot 4$ (4.5) | <0.0001 |
| BMI categories |  |  |  |
| Underweight | 4146 (7.1\%) | 127921 (6.4\%) | <0.0001 |
| Healthy weight | 26406 (45.6\%) | 1078360 (54.0\%) | <0.0001 |
| Overweight | 18575 (32.1\%) | 580426 (29.0\%) | <0.0001 |
| Obese | 8788 (15.2\%) | 212182 (10.6\%) | <0.0001 |

Data are $n(\%)$ or mean (SD). Percentages given for each variable exclude participants for whom data were missing. For table with all denominators included, see appendix ( p 7 ). BMI=body-mass index. *p values are for the difference between estimates in participants with and without a previous stroke (calculated from $\chi^{2}$ tests for categorical variables or $t$ tests for continuous variables).

Table 1: Characteristics of 2222399 study participants with and without a history of stroke
medication, the proportion of participants taking antihypertensive medication with controlled blood pressure, and the proportion of all participants with hypertension who had controlled blood pressure.
Both univariable and multivariable linear regression models were constructed, with further adjustment for the national-level proportion of males and the proportions of participants with diabetes, who were current smokers, who consumed alcohol at least once per week, and who were overweight or obese. To remain consistent with the age standardisation used by GBD, each parameter was standardised according to the same GBD weights using 5 -year age groups. ${ }^{20}$ Countries with fewer than 50 participants using antihypertensive medication were excluded for the models that evaluated medication use. If data regarding the use of antihypertensive medication was missing, we assumed that these participants were not taking such medication when calculating national-level estimates. To assess the effect of this assumption, sensitivity analyses were conducted under two alternatives, assuming all participants for whom medication records were missing were either taking medication or excluded from the analysis.

## Role of the funding source

The funders of the MMM campaigns in 2017 and 2018 had no role in study design, data collection, data analysis,
data interpretation, or writing of the report, although several past or present officers of the International Society of Hypertension are coauthors.

## Results

Data were available for 2515365 participants from 92 countries. Of these, data on a history of stroke were recorded for 2222399 participants, of whom 896432 were screened in 2017 and 1325967 were screened in 2018. Participants ranged in age from 18 years to 99 years with a mean of $45 \cdot 1$ years (SD 16.9). Females accounted for $53.7 \%$ of participants, males comprised $45 \cdot 6 \%$, and the remaining participants (less than $0 \cdot 8 \%$ ) were recorded as "other" or the data were missing. Of the 2222399 respondents, $62639(2 \cdot 8 \%)$ reported a history of stroke.
Of participants with a history of stroke, 33910 (54.5\%) were male and 28294 ( $45 \cdot 5 \%$ ) were female ( $\mathrm{p}<0 \cdot 0001$; table 1). The mean age of participants with a history of stroke was 6 years older than those without ( 51.1 years vs 45.0 years, $\mathrm{p}<0 \cdot 0001$ ). Age-adjusted proportions of participants with a previous stroke were higher in males than in females $(3 \cdot 1 \%$ vs $2 \cdot 2 \%, p<0 \cdot 0001)$. In participants with a history of stroke, the proportions reporting diabetes, a previous myocardial infarction, current smoking, and consuming alcohol at least once per week were higher than in participants without a history of stroke (all p<0•0001). Participants with a history of stroke were also more likely to be underweight, overweight, or obese than those without ( $\mathrm{p}<0 \cdot 0001$ ). Characteristics by country are given in the appendix ( $\mathrm{pp} 8-13$ ).
Among 1764601 ( $79.4 \%$ ) participants for whom all three blood pressure readings and data on stroke history were recorded, mean systolic and diastolic blood pressure decreased from the first to the third readings (appendix p 13). The reduction was larger in participants with a previous stroke $(4.1 \mathrm{~mm} \mathrm{Hg}$ systolic; 3.2 mm Hg diastolic) than in participants without $(2.9 \mathrm{~mm} \mathrm{Hg}$ systolic; 1.8 mm Hg diastolic). Basing a definition of hypertension on each single reading, the absolute proportion of participants with hypertension reduced from $80 \cdot 6 \%$ using the first reading to $78 \cdot 7 \%$ using the third reading in participants with a previous stroke and from $38.3 \%$ to $34.2 \%$ in participants without. The lowest proportion of participants with hypertension was calculated from the mean of the second and third readings in both those with $(78 \cdot 6 \%)$ and without (33.3\%) a history of stroke.
After multiple imputation for missing blood pressure readings for 686147 participants with one or two missing readings, the mean of the second and third blood pressure readings was $129 \cdot 5 / 79.6 \mathrm{~mm} \mathrm{Hg}$ in those with a history of stroke and $123.0 / 77.9 \mathrm{~mm} \mathrm{Hg}$ in those without a history of stroke ( $\mathrm{p}<0 \cdot 0001$ ). Participants with a history of stroke who were not taking antihypertensive medication had significantly higher mean systolic and diastolic blood pressures than those without a history of stroke who were not taking antihypertensive medication

|  | Crude values |  |  | Standardised for age and sex |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Previous stroke | No previous stroke | $p$ value* | Previous stroke | No previous stroke | $p$ value* |
| Mean systolic/diastolic pressure, mm Hg | 129.5/79.6 | 123.0/77.9 | <0.0001 $\dagger$ | 124.4/77.8 | 124.0/78.4 | 0.059/<0.001 |
| Stratified mean systolic/diastolic pressure, mm Hg |  |  |  |  |  |  |
| Not on antihypertensive medication | 124.3/78.4 | 120.3/77.0 | <0.0001 $\dagger$ | 122.0/77.6 | 122.6/78.0 | 0.047/0.089 |
| On antihypertensive medication | 131.8/80.1 | 134.2/82.1 | <0.0001 $\dagger$ | 125.8/78.1 | 131-2/82.1 | <0.0001 $\dagger$ |
| Proportion of all participants with raised blood pressure | 33.9\% | 22.2\% | <0.0001 | 24.7\% | 23.2\% | 0.020 |
| Proportion of all participants with hypertension | 77.0\% | 32.9\% | <0.0001 | 70.1\% | 33.6\% | <0.0001 |
| Proportion of participants with hypertension on medication | 90.2\% | 57.0\% | <0.0001 | 89.7\% | 54.0\% | <0.0001 |
| Proportion of participants on medication with controlled blood pressure | 62.0\% | 56.8\% | <0.0001 | 72.9\% | 61.4\% | <0.0001 |
| Proportion of participants with hypertension with controlled blood pressure | 55.9\% | 32.4\% | <0.0001 | 64.8\% | 31.1\% | <0.0001 |
| Estimates are based on the mean of the second and third blood pressure readings, after multiple imputation. Raised blood pressure was defined as blood pressure $\geq 140 / 90 \mathrm{~mm} \mathrm{Hg}$. Hypertension was defined as blood pressure $\geq 140 / 90 \mathrm{~mm} \mathrm{Hg}$ or on antihypertensive treatment. Controlled blood pressure was defined as on antihypertensive treatment with blood pressure $<140 / 90 \mathrm{~mm} \mathrm{Hg}$. *p values are for the difference between estimates in participants with and without a previous stroke (calculated from $\chi^{2}$ tests for categorical variables or $t$ tests for continuous variables). $\dagger p<0.0001$ for both systolic and diastolic blood pressure values. |  |  |  |  |  |  |

(table 2). By contrast, of participants taking antihypertensive medication, those with a previous stroke had significantly lower mean blood pressures than those without (table 2). However, after standardisation for age and sex, the mean blood pressures of participants with and without a history of stroke in individuals not taking antihypertensive medication were similar. The proportion of participants with hypertension and the rates of treatment and control of hypertension were higher in those with a previous stroke, before and after standardisation for age and sex (all p<0•0001). In participants for whom hypertension awareness was recorded, awareness was significantly higher in the 32960 participants with a previous stroke than in those without ( $93 \cdot 8 \%$ vs $57 \cdot 2 \%, \mathrm{p}<0 \cdot 0001$ ). Sensitivity analyses showed that estimates were not substantially affected by assumptions regarding missing data on medication use (appendix p 14).
Associations of comorbidities and risk factors with a history of stroke were examined using univariable and multivariable mixed-effects logistic regression (figure 1). After adjustment for age and sex alone, participants with a history of stroke had $5 \cdot 9$ times ( $95 \%$ CI 5•8-6.0, $\mathrm{p}<0 \cdot 0001$ ) increased odds of having diabetes and 9.9 times ( $9 \cdot 7-10 \cdot 1, \mathrm{p}<0 \cdot 0001$ ) increased odds of being current smokers than those without a previous stroke-associations which, although attenuated, remained significant after full adjustment. Significant modification of this effect by age was also observed, with the odds of current smoking in participants with a history of stroke being significantly higher in the 18 -39-year age group than in other age groups after full adjustment (appendix p 15).
Participants with a history of stroke were more likely than those without to consume alcohol at least once per week and to be underweight, overweight, or obese
after adjustment for age and sex. However, in the fully adjusted model, participants with a history of stroke were at a lower risk of being overweight (odds ratio 0.89 [ $95 \%$ CI $0.87-0.91], \quad \mathrm{p}<0 \cdot 0001$ ) or obese ( 0.92 [0.89-0.95], $\mathrm{p}<0 \cdot 0001$ ) than those with no recorded history of stroke.
Overall, the odds of having raised blood pressure were 1.72 times ( $95 \%$ CI 1.69-1.75, p<0.0001) higher in participants with a previous stroke than in participants without. However, the use of antihypertensive medication modified this effect. The unadjusted odds of raised blood pressure in participants with a previous stroke compared with those without was higher for participants not taking medication, but not in those taking medication (appendix p 16). After adjustment for age and sex, the strength of this association was reduced in participants not taking medication and, after full adjustment, only a small but significant increase in the odds of raised blood pressure remained. However, in participants taking medication, full adjustment had only a small effect on the association with raised blood pressure: the odds of raised blood pressure in participants with a previous stroke was $9 \cdot 3 \%$ lower than in those without.
At the national level, several significant associations were seen between estimates of premature stroke mortality and mean systolic blood pressure, the percentage of participants with raised blood pressure, and other parameters of hypertension management in both univariable and multivariable models (table 3, figure 2, and appendix pp 17-18). In univariable models, premature stroke mortality increased, on average, by 84.3 ( $95 \%$ CI $38 \cdot 8-129 \cdot 9$ ) years of life lost per 100000 people for each 1 mm Hg increase in the mean systolic blood pressure of participants in each country ( $\mathrm{p}<0.0001$; table 3). Premature stroke mortality also increased
significantly for each $1 \%$ increase in the percentage of participants with raised blood pressure ( $\mathrm{p}<0 \cdot 0001$; table 3). Similarly, national parameters of hypertension treatment and control were strongly associated with national estimates of premature stroke mortality, such that higher percentages of participants with hypertension on treatment and higher percentages of participants with controlled blood pressure were associated with lower rates of premature stroke death. However, no significant association was found between national premature stroke mortality rates and estimates of the percentage of participants with hypertension in each country. Multivariable adjustment for sex, alcohol intake, smoking, diabetes, and the proportion of participants who were overweight or obese did not significantly alter the strength of these associations (table 3).
The proportion of the variance $\left(R^{2}\right)$ explained by each of the univariable models ranged from $0 \%$ for the


Figure 1: Forest plot of adjusted odds ratios for cardiovascular risk factors given a history of stroke from basic and fully adjusted mixed-effects logistic regression models
Basic adjustment=adjusted for age and sex. Full adjustment=adjusted for age, sex, use of antihypertensive
medication, diabetes, smoking, alcohol intake, and body-mass index (BMI) categories. *BMI categories analysed as binary outcomes compared with healthy weight as the reference group.
proportion of participants with hypertension to $24 \%$ for the proportion of participants with controlled hypertension. In multivariable models, $R^{2}$ values ranged from $31 \%$ to $44 \%$ (table 3). Sensitivity analyses indicated that assumptions regarding medication missingness did not affect the direction or the strength of these associations (appendix p 17).

## Discussion

In this study of more than 2.2 million adults with recorded data on stroke history and whose blood pressure was recorded in one of two consecutive MMM campaigns ${ }^{14,15}$ in 92 countries, $62639(2 \cdot 8 \%)$ reported a history of stroke. Participants who reported a history of stroke were 6 years older on average than those who did not, and age-adjusted proportions of stroke were higher in men than in women.
Participants with a history of stroke were significantly more likely at the time of blood pressure screening to have diabetes, smoke, consume alcohol regularly, and be underweight, associations that remained after adjustment for confounders. Given the cross-sectional nature of the MMM campaign, the temporal sequence of the association between stroke and subsequent risk factors seen in figure 1 cannot be established. However, given the established strong predictive links between diabetes and smoking and subsequent stroke, ${ }^{6,21}$ these findings are likely to largely reflect the carryover of prestroke propensity for stroke and the persistence of lifestyle habits. The small positive association between being overweight or obese and having a history of stroke is consistent with the recent findings from the FASTMAG trial, which reported that being overweight or obese after stroke was associated with better survival. ${ }^{22}$ However, this apparent association disappeared after adjustment in our study.
Stroke survivors were significantly more likely to have hypertension than participants without a history of stroke ( $77 \%$ vs $33 \%$ ), which was largely unaffected by accounting for differences in age and sex (table 2). However, among

|  | Univariable linear regression |  |  | Multivariable linear regression |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Mean change in premature stroke mortality per unit increase ( $95 \% \mathrm{Cl}$ )* | $p$ value | $R^{2}$ | Mean change in premature stroke mortality per unit increase ( $95 \% \mathrm{Cl}$ )* | $p$ value | $R^{2}$ |
| Mean systolic blood pressure, mm Hg | 84.3 (38.8 to 129.9) | <0.0001 | 0.138 | 85.1 (46.2 to 124.0) | <0.0001 | 0.441 |
| Proportion of all participants with raised blood pressure | 49.1 (22.6 to 75.6) | <0.0001 | 0.138 | 37.8 (14.6 to 61.0) | 0.002 | 0.385 |
| Proportion of all participants with hypertension | 9.0 (-16.5 to 34.5) | 0.484 | 0.006 | $13 \cdot 3$ (-8.4 to 35.0) | 0.227 | 0.311 |
| Proportion of participants with hypertension on medication | -21.0 (-33.0 to -8.9) | 0.001 | 0.140 | -20.4 (-34.0 to -6.8) | 0.004 | 0.373 |
| Proportion of participants on medication with controlled blood pressure | -31.4 (-46.6 to -16.2) | <0.0001 | 0.186 | -26.3 (-40.5 to -12.1) | <0.0001 | 0.409 |
| Proportion of participants with hypertension with controlled blood pressure | $-31 \cdot 6(-43 \cdot 8$ to $-19 \cdot 4)$ | <0.0001 | 0.237 | $-29 \cdot 9(-43 \cdot 6$ to $-16 \cdot 3)$ | <0.0001 | 0.441 |

Multivariable models adjusted for age-standardised proportions of male participants, current smokers, consuming alcohol at least once per week, diabetes, and the proportion who are overweight or obese. *Data are the mean ( $95 \% \mathrm{Cl}$ ) change in premature stroke mortality (years of life lost per 100000 people) per 1 mm Hg increase in mean systolic blood pressure or per $1 \%$ increase in proportion of participants.

Table 3: Associations between age-standardised premature stroke mortality from the Global Burden of Disease and age-standardised blood pressures and parameters of hypertension management from May Measurement Month from univariable and multivariable linear regression models
participants who were classified as hypertensive, those with a previous stroke were more likely to be on antihypertensive treatment, and have lower mean blood pressures, and have controlled blood pressure than those without a previous stroke (table 2).
Crude mean blood pressures in participants who were not treated for hypertension were significantly higher in those with a previous stroke than in those without, although only a small difference was apparent after standardisation for age and sex. Taken together, these findings suggest that participants with a previous stroke were more likely than those without to be on antihypertensive medication, and more likely to achieve stricter blood pressure control. Higher treatment rates in those with a previous stroke could be due to a greater likelihood of medical investigation and therefore higher diagnosis rates in participants with a history of stroke than in the general population, whereas stricter control could relate to both patient and clinician factors. Nevertheless, almost $40 \%$ of participants with a history of stroke who were on antihypertensive treatment did not have blood pressures controlled to less than $140 / 90 \mathrm{~mm} \mathrm{Hg}$ (table 2), which is currently viewed as a conservative, suboptimal target. ${ }^{23,24}$ In total, a third of those with a previous stroke had either untreated or inadequately treated blood pressure.
The significant associations between national blood pressure levels and markers of hypertension management and the associated proportions of the variance in premature stroke mortality are notable given the opportunistic convenience sampling used in the MMM campaigns. Only the national proportions of participants classed as having hypertension were not significantly associated with premature stroke mortality. This finding could, in part, reflect that a third of the population classed as having hypertension had normalised blood pressures (table 2). In univariable analyses, the other five parameters contributed between $14 \%$ and $24 \%$ of the variance in national premature stroke mortality, with proportions of controlled blood pressure among all participants with hypertension detected being the biggest independent contributor to the variance (figure 2, table 3).
A limitation of the GBD data is the absence of primary data for some countries and causes of death, and the use of modelling approaches, such as Bayesian meta-regression, to impute data from neighbouring countries. ${ }^{1.25}$ Modelling will inevitably incorporate some inaccurate estimates and comparative studies have shown differences in estimates compared with other data sources. ${ }^{26,27}$ Consequently, the already high estimated proportions of the stroke mortality variance arising from the MMM blood pressure parameters probably represent underestimates. That MMM only involved convenience sampling through opportunistic screening, rather than including representative samples of the countries included, could be considered a limitation of the associations observed between MMM-based measures


Figure 2: Scatter plots and predicted regression lines of national age-standardised premature stroke mortality from the Global Burden of Disease and age-standardised blood pressures and parameters of hypertension management from May Measurement Month from univariable linear regression models
of blood pressure management and national stroke mortality. However, the use of non-representative samples would probably dilute the true associations between measures of blood pressure control and stroke mortality at a national level. Meanwhile, in many of the countries involved with the MMM campaigns, systematic screening is not available and MMM represents the most comprehensive contemporary blood pressure data available. ${ }^{14,15}$ Consequently, pending the availability of representative data, and given the strong associations between raised blood pressure and subsequent premature mortality due to stroke, MMM data should help to persuade policy makers of the need for improved blood pressure screening and management in their countries-one of the objectives of the MMM campaign.
Other limitations of these analyses are that MMM data include only non-fatal strokes, stratification by stroke type (ischaemic or haemorrhagic) was not possible, and other details of stroke causes and management were not
available. Furthermore, data on stroke were self-reported and the duration since the reported stroke event was not recorded, which could affect the associations with subsequent risk factors. In common with all surveys of blood pressure carried out on a single occasion, the blood pressure data collected in the MMM campaigns are likely to overestimate rates of hypertension and uncontrolled blood pressure. Most clinical hypertension guidelines recommend that hypertension is diagnosed on the basis of repeated recordings measured on at least two evaluation visits, in an attempt to reduce the effect of acclimatisation to measurement and the white-coat effect. Missing data on the use of antihypertensive medication has the potential to confound the relationships between stroke, cardiovascular risk factors, and blood pressure, but sensitivity analyses showed that different assumptions regarding the missingness did not materially affect the results.
The key strengths of these analyses are that the data are derived from the largest standardised contemporary blood pressure screening campaign synchronised across 2 years in 92 countries and include a large number of contemporary prevalent stroke cases across a wide age range. Blood pressures were measured using standardised techniques and other data were collected in the same questionnaire following a common protocol.
In conclusion, blood pressure among stroke survivors is not adequately treated, with a third of those in our study having untreated or undertreated blood pressure. Furthermore, the MMM-based measures of blood pressure management at a national level correlated with premature stroke death sufficiently to allow policy makers to promote more efficient blood pressure screening and management.

## Contributors

TB and NRP conceived the study. QL, TY, SC, TB, and NRP developed the methodology. QL, TY, PY, SC, and TB had access to and verified the data, and conducted the analyses. All authors contributed to the interpretation of the results. QL, TY, TB, and NRP wrote the draft of the manuscript, and all authors contributed to the critical revision of the manuscript and approved the final version. The first two and last two authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

## Declaration of interests

GS reports lecture and consulting fees from AstraZeneca, Menarini, Microlife, Omron, and Servier; research study payments to his institution from Braun, InBody, Maisense, and Microlife; and honoraria for lectures and presentations from AstraZeneca, Boehringer, Menarini, Novartis, and Servier; all outside the submitted work. All other authors declare no competing interests.

## Data sharing

Anonymised participant data from MMM are available for research purposes subject to approval by the May Measurement Month
Management Board with a Data Use Agreement in place. Further details on applying for data access are available at https://www.maymeasure.org or by email to the corresponding author.

## Acknowledgments

The central coordination of MMM was funded by the International Society of Hypertension and Servier Pharmaceuticals. We thank the many MMM investigators worldwide who collected data for this study and the millions of participants who volunteered for screening, Omron
for the donation of blood pressure measurement devices, and Servier for support through the Institut la Conference Hippocrate. We thank Judith Bunn, former MMM project manager (Conference Collective), and Ranjit Rayat, editing assistant (School of Public Health, Imperial College London) for their support in the campaign, and Fei Li (Laboratory of Data Discovery for Health) for assisting with the figure designs. TB is supported by the National Insitute for Health Research Applied Research Collaboration North-West London. NRP was supported by the National Institute for Health Research Senior Investigator Awards, Biomedical Research Centre funding, and the British Heart Foundation Research Centre Excellence Award. The views expressed in this publication are those of the author(s) and not necessarily those of the funding organisations.

## References

1 GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet 2020; 396: 1204-22.
2 Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med 2006; 3: e442.
3 Ovbiagele B, Goldstein LB, Higashida RT, et al. Forecasting the future of stroke in the United States: a policy statement from the American Heart Association and American Stroke Association. Stroke 2013; 44: 2361-75.
4 GBD 2016 Stroke Collaborators. Global, regional, and national burden of stroke, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol 2019; 18: 439-58.
5 GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2018; 392: 1789-858.
6 O'Donnell MJ, Chin SL, Rangarajan S, et al. Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study. Lancet 2016; 388: 761-75.
7 The GBD 2016 Lifetime Risk of Stroke Collaborators. Global, regional, and country-specific lifetime risks of stroke, 1990 and 2016. N Engl J Med 2018; 379: 2429-37.

8 NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in blood pressure from 1975 to 2015: a pooled analysis of 1479 population-based measurement studies with $19 \cdot 1$ million participants. Lancet 2017; 389: 37-55.
9 PROGRESS Collaborative Group. Randomised trial of a perindoprilbased blood-pressure-lowering regimen among 6105 individuals with previous stroke or transient ischaemic attack. Lancet 2001; 358: 1033-41.
10 Towfighi A, Markovic D, Ovbiagele B. Abstract 3356: half the stroke survivors in the United States have poorly controlled hypertension. Stroke 2012; 43 (suppl 1): A3356 (abstr).
11 Wang YJ, Li ZX, Gu HQ, et al. China stroke statistics 2019: a report from the National Center for Healthcare Quality Management in Neurological Diseases, China National Clinical Research Center for Neurological Diseases, the Chinese Stroke Association, National Center for Chronic and Non-communicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention and Institute for Global Neuroscience and Stroke Collaborations. Stroke Vasc Neurol 2020; 5: 211-39.
12 Wahab KW, Kolo PM, Salawu FK, Sanya EO. Blood pressure control among hypertensive stroke survivors in Nigeria. J Stroke Cerebrovasc Dis 2017; 26: 1222-27.
13 Stevens E, Emmett E, Wang YZ, McKevitt C, Wolfe C. The burden of stroke in Europe. 2020. https://www.stroke.org.uk/sites/default/ files/the_burden_of_stroke_in_europe_-_challenges_for_policy_ makers.pdf (accessed June 15, 2021).
14 Beaney T, Schutte AE, Tomaszewski M, et al. May Measurement Month 2017: an analysis of blood pressure screening results worldwide. Lancet Glob Health 2018; 6: e736-43.
15 Beaney T, Burrell LM, Castillo RR, 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; 40: 2006-17.

16 UN. Standard country or area codes for statistical use (M49). 1999. https://unstats.un.org/unsd/methodology/m49/ (accessed May 15, 2020).
17 WHO. Body mass index—BMI. http://www.euro.who.int/en/ health-topics/disease-prevention/nutrition/a-healthy-lifestyle/body-mass-index-bmi (accessed May 15, 2020).
18 Surveillance Epidemiology and End Results Program. Standard populations-single ages. 2013. https://seer.cancer.gov/ stdpopulations/stdpop.singleages.html (accessed May 15, 2020).
19 Institute for Health Metrics and Evaluation. GBD results tool. 2020. http://ghdx.healthdata.org/gbd-results-tool (accessed May 15, 2020).
20 GBD 2017 Mortality Collaborators. Global, regional, and national age-sex-specific mortality and life expectancy, 1950-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2018; 392: 1684-735.
21 Di Angelantonio E, Bhupathiraju SN, Wormser D, et al. Body-mass index and all-cause mortality: individual-participant-data metaanalysis of 239 prospective studies in four continents. Lancet 2016; 388: 776-86.
22 Liu Z, Sanossian N, Starkman S, et al. Adiposity and outcome after ischemic stroke: obesity paradox for mortality and obesity parabola for favorable functional outcomes. Stroke 2021; 52: 144-51.

23 Unger T, Borghi C, Charchar F, et al. 2020 International Society of Hypertension Global Hypertension Practice Guidelines. Hypertension 2020; 75: 1334-57.
24 Williams B, Mancia G, Spiering W, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH) Eur Heart J 2018; 39: 3021-104.
25 Murray CJL, Lopez AD. Measuring the global burden of disease. N Engl J Med 2013; 369: 448-57.
26 McLain AC, Frongillo EA, Hess SY, Piwoz EG. Comparison of methods used to estimate the global burden of disease related to undernutrition and suboptimal breastfeeding. Adv Nutr 2019; 10: 380-90.
27 Kovacs SD, Mullholland K, Bosch J, et al. Deconstructing the differences: a comparison of GBD 2010 and CHERG's approach to estimating the mortality burden of diarrhea, pneumonia, and their etiologies. BMC Infect Dis 2015; 15: 16.

