What Is the Best Mix of Population-Wide and High-Risk Targeted Strategies of Primary Stroke and Cardiovascular Disease Prevention?

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In arguably the most influential public health article ever written, "Sick Individuals and Sick Populations," Geoffrey Rose[1] described and appraised 2 mainstream strategies for primary prevention of disease: (1) the "high-risk" strategy, where the preventative strategy seeks to identify high-risk susceptible individuals to offer them some individual protection; and (2) the population "mass" strategy aimed to reduce the mean level of the determinants of disease, and thereby the incidence of disease, in the population as a whole. He concluded that a "high-risk" strategy is needed only as long as the underlying causes of incidence remain unknown or uncontrollable, and the priority in primary prevention should always be the discovery and control of the causes of incidence to shift the whole distribution of exposure in a favorable direction via a population strategy.

For the primary prevention of stroke and cardiovascular disease (CVD), the value of population screening to identify individuals at high risk of CVD was first publicly debated almost 20 years later.[2] Jackson et al,[3] the proponents of the high-risk strategies argued that the key for preventing CVD is well-targeted treatment with safe, inexpensive and effective drugs for patients at high risk and that this approach is more effective than population-wide interventions, such as reducing salt intake and managing obesity.[2,3] However, it was argued by Capewell,[4] the opponent of the high-risk strategy, that the "high-risk" approach lacks effectiveness and is associated with low uptake of the screening, inaccuracy of the CVD risk scoring systems in estimating an individual patient's risk, low adherence to treatment, medicalization of individuals, and high cost.[2,4] He warned that perhaps the greatest harm arising from the "high-risk" strategies is misleading health professionals and politicians into thinking they can tick the box "mission accomplished" (screening completed) and the problem of CVD prevention is solved. Therefore, the best strategy for preventing CVD is policy interventions aimed at reducing key modifiable CVD risk factors across whole populations.[2] However, at the time of the debate there was no robust evidence for or against either of these strategies. As the global burden and cost of stroke and CVD[5,6] is increasing, it is timely and necessary to critically review the current strategies of stroke and CVD prevention in light of the available evidence to inform future directions in primary stroke and CVD prevention (see Tables 1 and 2 for "Aims of This Viewpoint" and "Search and Selection Criteria").

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Table 1. Aims of This Viewpoint

- To outline a history of primary stroke and cardiovascular disease (CVD) prevention strategies development
- To outline advantages and disadvantages of "high-risk" and population-wide primary stroke prevention strategies
- To describe current trends in primary stroke prevention
- To provide evidence of effects of primary stroke and CVD "high-risk" and population-wide prevention strategies on stroke and CVD incidence and/or mortality
- To suggest priorities and funding sources for primary stroke and CVD prevention strategies
- To suggest future directions in primary stroke and CVD prevention strategies and research

Table 2. Search and Selection Criteria

We also searched MEDLINE, Embase, Google Scholar, and the Cochrane Library, as well as the internet (using Google and other search engines), for primary stroke and CVD prevention research published between January 1970 and September 2019 using the following key words in title or abstract: "stroke," "cerebrovascular disease," "isch(a)emic heart disease," or "cardiovascular disease" AND "prevention," "cost," "guidelines," "tax or taxation," "trial," "incidence," "prevalence," "mortality," "burden," or "outcomes." We concentrated on randomized controlled trials and population-based studies. Additionally, we manually searched the reference lists of relevant publications and consulted with experts in stroke, CVD, and other relevant stakeholders, to complement the electronic searches.

Current Trends in Primary Prevention Strategies

Over the past 2 decades, the advent of new and more accurate CVD risk scoring systems[7–11] has shifted focus from population-wide prevention strategies to more medicalized "high-risk" strategies.[11] Despite the lack of robust evidence for cost and medical effectiveness of the "high-risk" approach in terms of the reduction of stroke and CVD incidence on a population level,[12,13] virtually all guidelines on CVD prevention stress the importance of a total CVD risk-based screening approach,[14–19] and this strategy has become the focus of public health policy in several countries, including New Zealand,[17] Australia,[18] the United Kingdom,[20] and China.[21] The "high-risk" strategy is also advocated by the American Heart Association (AHA) in the Million Heart Cardiovascular Risk Reduction Programme,[22] and the identification of individuals at risk was emphasized as the focus of the national primary CVD prevention strategy in 2010.[23]

In the United States, the AHA has emphasized both the high-risk strategy and population or mass approach. For example, the AHA has launched the Million Hearts Initiative targeting improvement in both clinical preventative practice and community prevention.[24–26] The Million Hearts Initiative represents a partnership with a number of organizations including the US Centers for Disease Control and Prevention. The key components of the initiative are to improve clinical prevention by increasing appropriate aspirin use, hypertension control and cholesterol control, reducing smoking, aligning health information technology with key metrics across healthcare systems, advocating for clinical innovations in care, strengthening community prevention in the domains of tobacco and smoking control at state and local levels, supporting evidence-based interventions for preventative control, and improving overall nutrition in the population. Furthermore, the AHA has launched a Life's Simple 7 community campaign to improve cardiovascular health by educating the public on cardiovascular risks.[27] Life's Simple 7 includes rationale for a healthy cardiovascular lifestyle and how to manage blood pressure, control cholesterol, and reduce blood glucose; become more active and have a healthy diet; lose weight; and stop smoking. Finally, the most recent AHA guidance statements in 2018 and 2019 in relation to CVD prevention are based on treatment decisions for the individual patient according to cardiovascular risk estimation, but also advocate for healthy lifestyle across the life course of all individuals.[28]

Uncertain Value of "High-Risk" Strategies

The value of screening for high-risk CVD ("high-risk" strategy) to reduce incidence of stroke and CVD on a population level has been questioned for several reasons.[4,25,26]

First, by definition, the "high-risk" strategy leaves out the people with low and moderate CVD risk who ultimately make up 80% of all stroke and heart attacks.[29,30] Therefore, the majority of the population at large, who contribute the majority of future incident CVD events, are not prioritized for recognition, education, and other prevention interventions.

Second, labeling people as "low risk" may give them false reassurance that they are protected from stroke and heart attack, which may compromise their motivation to control their risk factors. This is particularly so for young people with high levels of risk factors and a high relative risk of stroke and CVD that requires at least intensive lifestyle advice, but in whom risk scores predict them to be at low absolute risk because of their age. Furthermore, clinicians often seek thresholds to trigger certain interventions. This concept is at odds with the fact that risk is a continuum, particularly for risk factors such as blood pressure and cholesterol, and there is no threshold at which certain interventions are automatically indicated. Therefore, it has been suggested that in

communicating absolute CVD risk, categorization of people into low, moderate (mild), and high risk should be abandoned.[31]

Third, with the exception of smoking, most behavioral risk factors that contribute a large proportion of stroke and CVD burden (unhealthy diet, sedentary lifestyle, and excessive alcohol intake),[32,33] are not included in the CVD risk screening systems. Independent genetic factors, which increase the risk of incident stroke by about one third,[34] are also not included in CVD screening systems. Therefore, the ability of the CVD screening to detect, control, and monitor important lifestyle factors for stroke and CVD prevention is limited. However, it is acknowledged that risk prediction may improve in the future with multimodal strategies that include new technologies such as machine learning (which can construct mathematical functions via automated analyses of large training data sets and create models that may more accurately predict risk of stroke and CVD),[35–37] although a recent systematic review showed no evidence of superior performance of machine learning over well-established logistic regression for clinical prediction models.[38]

Fourth, a microsimulation study[39] evaluating CVD screening to reduce burden from CVD reported that universal screening seems less effective than population-wide approaches in reducing CVD incidence, and emphasized that further research is needed to identify the best mix of population-wide and risk-targeted CVD strategies to maximize cost effectiveness and minimize inequalities.

Fifth, CVD screening programs require considerable efforts and cost from society and individuals and are unlikely to be widely implemented in countries with limited resources unless they are effective or linked to existing effective programs.[29] In some regions, such as Latin America, such "high-risk" strategies are not used.[40]

Sixth, there is no evidence that screening programs by themselves are effective in preventing stroke and CVD events. The Inter99 (Intervention 1999) randomized controlled trial (59 616 people aged 30 to 60 years followed for 10 years)[13] was specifically designed to determine effects of screening for CVD risk and risk factors and lifestyle counseling on incidence of ischemic heart disease in the general population and found no significant difference between the intervention and control groups in the risk of ischemic heart disease (hazard ratio, 1.03, 95% CI, 0.94–1.13), stroke (hazard ratio, 0.98; 95% CI, 0.87–1.11), combined ischemic heart disease and stroke (hazard ratio, 1.01; 95% CI, 0.93–1.09), and total mortality (hazard ratio, 1.0; 95% CI, 0.91–1.09). A subsequent Cochrane meta-analysis[12] of 15 randomized controlled trials comparing the effect of health checks (screening for >1 disease or risk factor) with no health checks in a total of 251 891 adults found there were no beneficial effects of general health checks over 1 to 15 years' follow-up for total mortality (risk ratio, 1.00; 95% CI, 0.97–1.03; I^2=0%), CVD mortality (risk ratio, 1.05; 95% CI, 0.94–1.16; I^2=65%), ischemic heart disease incidence (risk ratio, 0.98; 95% CI, 0.94–1.03; I^2=11%), or stroke incidence (risk ratio, 1.05; 95% CI, 0.95–1.17; I^2=53%).

These data suggest that health checks with systematic CVD screening and counseling are not, in isolation, effective in practice. However, supplementing risk factor screening with behavioral counseling and pharmacological treatment as appropriate, and linkage to community programs has been shown to lower CVD risk over the next year by 10% in 31.8% (95% CI, 26.9%–36.6%) of individuals at moderate baseline risk and by 25% in 47.9% (95% CI, 41.2%–54.6%) of individual at high baseline risk, as predicted by the Framingham Risk Score.[20]

Seventh, even if CVD screening systems are effective and identify all individuals in the population with a 10-year CVD risk of ≥30% (6% of the population), and all of these individuals are appropriately treated, the incidence of major CVD is estimated to be reduced by, at most, 11%.[41]

Finally, since many of the underlying causes of stroke and CVD are well established, identifiable, and controllable,[42–44] according to Rose,[1] there is not a major role for the "high-risk" strategy for primary prevention of stroke and CVD, but more a complementary role to the more powerful population strategy.

We are not advocating that screening for CVD risk be abandoned but that the "high-risk" approach should not be the prime focus of public health policy for primary stroke and CVD prevention. It should be used as an adjunct to the population-wide strategies and primarily for early detection of established risk factors,[45] objective monitoring of progress of individuals in controlling their risk of CVD, and for determining thresholds for the pharmacological management and its intensity at the physician and individual level (eg, blood pressure and lipid-lowering medicines, aspirin).[46–50] In addition, to be widely used, such screening should be simple and inexpensive. For example, integrating screening for hypertension into routine medical examinations and related coverage by health insurance was recently recommended as a potentially cost-effective tool for CVD prevention in Vietnam.[51] Although recently there were concerns raised as to the low applicability of the thresholds for pharmacological treatments in resource-poor countries,[52] there is a danger of medicalization instead of focusing on lifestyle risk factor control.[53] Health resources are too scarce to waste on proven ineffective and expensive screening strategies (that are not coupled with appropriate intervention) and, given the already huge and increasing stroke and CVD burden,[6] the importance of the use of effective population-wide primary stroke and CVD prevention strategies cannot be underestimated.

In several countries, there are ongoing or intermittent media campaigns educating people about stroke and heart disease recognition for secondary stroke prevention, particularly stroke signs and symptoms that necessitate calling emergency services (eg, Face, Arm, Speech, Time [F.A.S.T.]) There is compelling evidence that F.A.S.T. campaigns result in increased ambulance dispatches and public stroke awareness, at least in the short term.[54,55] Importantly, the medical attention was sought by a bystander in nearly 90% of cases, suggesting the importance of mass-media public education rather than focused programs in high-risk groups for stroke.[56] While the extensive 5-year F.A.S.T.-based public campaign in England cost $13.6 million and resulted in increased number of patients with major stroke who sought medical attention within 3 hours (odds ratio, 2.56; 95% CI, 1.11–5.90), it failed to improve the use of emergency medical services by people with transient ischemic attack and minor stroke (odds ratio, 0.79; 95% CI, 0.50–1.23).[57] The authors called for campaigns that are tailored to transient and less severe symptoms. However, in a recent review of 30 studies on public stroke education, such campaigns were shown to be costly, and their efficacy was either limited (in terms of improving stroke outcomes) or not present.[55] These results are in line with a systematic review of 11 studies examining effectiveness of the F.A.S.T. public campaign that showed that such campaigns may raise awareness of signs of stroke but have limited impact on behavior.[58] It was also shown that stroke education of children at schools has proven feasible and efficient in the United States and Japan.[55] Given the uncertainty about the long-term sustainability of stroke awareness knowledge and cost-effectiveness of F.A.S.T. public campaigns, especially for people with transient ischemic attack and minor stroke, further research into this important area of stroke education is needed. Clearly, primary and secondary stroke/CVD prevention campaigns should be viewed as complementary activities, with the priority given to primary stroke/CVD actions.

Resetting Priorities Toward a Population-Wide Strategy for Preventing Stroke and CVD

From the public health perspective, the best ultimate measure of effectiveness of the primary stroke and CVD prevention interventions is incidence, both in absolute (number of new people affected by the stroke and/or acute myocardial infarction) and relative (rate per 100 000 per year) terms,[59,60] while prevalence of stroke/CVD risk factors in the population and global CVD/stroke risk estimates are important intermediate measures of the effectiveness.[61] There is sufficient consistent, although modest, evidence of the effectiveness of population-wide strategies to reduce the burden from stroke and CVD in the United States,[62] Sweden,[63] Finland,[64,65] and Japan[66] to call for a review and resetting of priorities toward the population-wide strategy for preventing stroke and CVD. Modeling studies suggest that any intervention that achieves even a modest population-wide reduction in any major CVD risk factor would produce a net cost saving, as well as improving health.[67] An 80% reduction in CVD among the working-age population has been observed over 40 years in Finland concurrent with population-wide changes in lifestyle and environment.[68]

The population-wide approach for primary stroke and CVD prevention with the emphasis on elimination of artificial trans-fat, dietary sodium reduction, and effective treatment of elevated blood pressure was recently emphasized in the World Health Organization Global Hearts Initiatives[69] and CVD initiative "Resolve."[70] Another important evidence-based, feasible, and cost-effective strategy to prevent stroke and CVD, with the focus on population-wide prevention, is the World Health Organization "best-buy" interventions.[69,71] Among 36 studies (608 940 participants), 19 reported on the effectiveness of tobacco-related best buys, presenting good evidence for group interventions in reducing tobacco use but weaker evidence for interventions targeting individuals. There were fewer studies on smoking bans, warning labels, and mass media campaigns, and no studies on taxes or marketing restrictions. Fourteen of thebest buy interventions did not have any good evidence for effectiveness in low- to middle-income countries. Observational evidence from the Nurses' Health Study (71 243 women and 43 685 men free of CVD and cancer at baseline) suggested that controlling 5 lifestyle risk factors (smoking, physical activity, diet, alcohol consumption, weight) could reduce the risk of stroke by 47% (95% CI, 18–69) in women and by 35% (95% CI, 7–58) in men.[72,73]

Further population-based observational evidence from the UK Biobank Study of 306 473 adults who were followed for a median of 7.1 years suggest that adherence to a healthy lifestyle (nonsmoker, healthy diet, body mass index <30 kg/m^2, and regular physical exercise) could reduce the risk of stroke by up two thirds compared with an unfavorable lifestyle independent of genetic risk.[34]

A modeling study has estimated that a 30% reduction in population-wide sodium intake (World Health Organization recommended modest reduction) over 10 years could reduce the incidence of ischemic heart disease, ischemic stroke, and hemorrhagic stroke by about 7.3%, 7%, and 9.4%, respectively.[74] Applying these estimates to the Global Burden of Disease 2017 data,[75] it can be estimated that, globally, even this modest level of sodium intake reduction could annually prevent 776 500 cases of ischemic heart disease (95% uncertainty interval, 698 840–860 990), 541 660 cases of ischemic stroke (95% uncertainty interval, 486 580–

607 430), and 394 800 cases of hemorrhagic stroke (95% uncertainty interval, 358 820–432 450).

The increasing number of stroke cases throughout the world, particularly in low-income countries, demands that we review our strategies and opportunities for optimal stroke prevention.[60,61] Geoffrey Rose always maintained the population and high-risk approaches to prevention are not mutually exclusive but rather are complementary. We agree, but we are concerned that there has been a relative underutilization of population-wide prevention strategies and increasing focus on "high-risk" prevention strategies and that this imbalance may underpin suboptimal primary stroke and CVD prevention.[31]

Funding of Primary Prevention

To be sustainable, primary stroke and CVD prevention strategies should not only be effective but sufficiently funded. Organization for Economic Cooperation and Development countries allocate <3% of their health spending on average to public health and prevention activities, and a large proportion of this funding (about 44%) is spent on less cost-effective measures, such as healthy-conditions monitoring, including CVD screenings.[76] Just in England, annual costs of universal screening of 40- to 74-year-old adults for the risk of developing a chronic condition such as heart disease, stroke, kidney disease, type 2 diabetes mellitus, or dementia (NHS Health Check) amount to 165 million GBP.[77] A recent microsimulation study to estimate the potential impact of this universal screening for primary prevention of CVD showed its inferiority compared with alternative strategies, which incorporate population-wide approaches.[39] In our opinion, a much greater proportion of public health funds, or access to other funds, is required to implement effective population-wide strategies of prevention, minimize inequality in targets for prevention, and provide universal health coverage. However, the question is where to get additional funds for primary stroke and CVD prevention?

As taxation on tobacco, salt, sugar, and alcohol is one of the most efficient ways to reduce their consumption and promote healthy behaviors[78] (with the associated benefits for CVD and overall health at the population level)[78–81] and generate significant revenues for governments,[78] we believe these revenues can and should be reinvested back into the

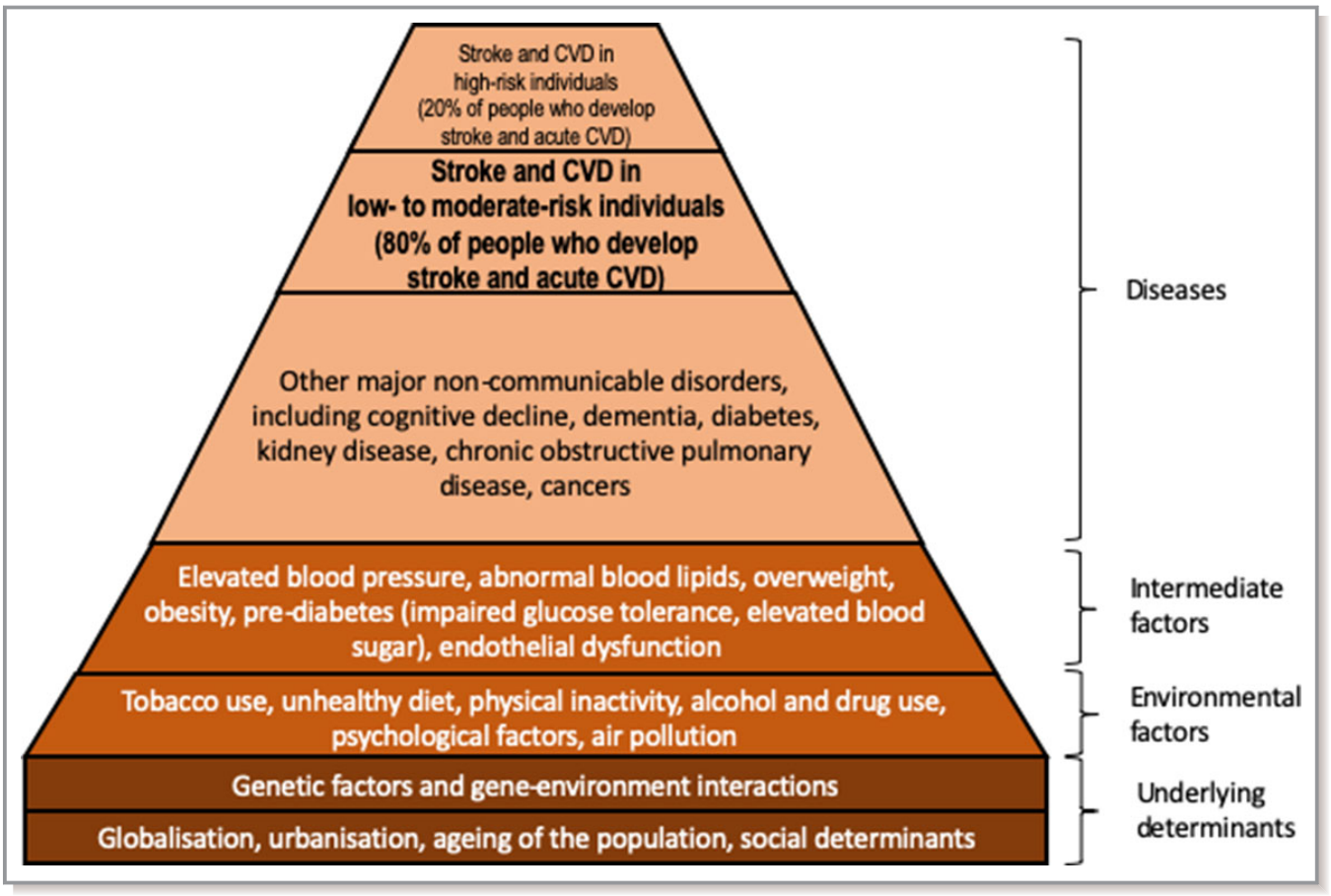

Figure. Theoretical models of causal pathways and benefits of population-wide primary stroke and CVD prevention strategies for preventing other noncommunicable diseases. CVD indicates cardiovascular diseases.

public health sector and health research to improve the health of the taxpayers, including appropriate funding of primary prevention strategies for stroke, CVD, and other major noncommunicable diseases. Such uses of the tax revenue would also be important to ensure public acceptability of these taxes.[82,83] It was also suggested that organizations committed to CVD control in high-income countries could provide some funding for resource-poor countries to help them with the development and implementation of primary prevention strategies.[84] The properly implemented primary prevention interventions will, in turn, generate significant additional cost savings from preventing diseases, which can be further used for improving well-being of the population and various social programs. Unique political, social, and financial circumstances in a given country or region may require scaling of the population approach to successfully meet such challenges in the domain of prevention.

Conclusions

Priority in the stroke and CVD primary prevention strategies should be given to the reduction of exposure to CVD risk factors of the whole population across the life course, regardless of the CVD risk, with the focus on behavioral and lifestyle risk factors (including tobacco use, unhealthy diet [excessive salt and sugar intake, lack of fruits and vegetables], physical inactivity, and the harmful use of alcohol), thus allowing an integrative approach that also targets other major noncommunicable diseases, such as dementia, diabetes mellitus, cancer, and pulmonary diseases.[31] This is because nearly everyone is at lifetime risk of developing these diseases. This cluster of diseases and risk factors was prioritized by the World Health Organization and its Global Action Plan on noncommunicable diseases,[85] and was also included in the 2011 United Nations Noncommunicable Disease Declaration, and the United Nations Post-2015 Sustainable Development Goals.[86] Focusing on the "high-risk group" alone will be addressing just the tip of the iceberg (Figure). Therefore, a multisectoral total population approach is recommended as the priority.

While advocating that the pendulum now has swung back toward population-wide prevention strategies, we emphasize that optimal stroke and CVD prevention requires a complementary 2-tiered population-based and high-risk approach, whereby measures and education about behavioral risk factors (diet, physical activity, alcohol and tobacco avoidance) are applied to the general population, and simple, inexpensive screening for a history of vascular disease and presence of modifiable vascular risk factors (particularly hypertension and smoking) is undertaken to identify those requiring the addition of prophylactic drug therapy to reinforced lifestyle and behavioral interventions (Table 3). Concurrently, global population exposure to improved social and environmental factors, including reduced exposure to air pollution, remain a priority for all. We agree with Kypridemos et al[39] that further research is required to determine the best mix of population-wide and high-risk targeted strategies for primary stroke and CVD prevention.

The last but not least important aspect of primary stroke/CVD prevention strategies is the evaluation of their effectiveness. Limiting criteria for evaluation of such strategies to just frequency estimates (eg, incidence, prevalence, mortality rates) is misleading, as it does not provide any information

Table 3. Overview and Summary of Policy Implications of this Viewpoint

Evidence of effectiveness of "high-risk" and population-wide strategies

- No randomized controlled trial evidence to support effectiveness of multifactorial "high-risk" strategies for reducing stroke and CVD incidence and mortality
- Growing body of observational evidence to support medical and cost effectiveness of population-wide strategies for reducing stroke and CVD incidence and mortality
- Uncertainty concerning the best balance of population-wide and "high-risk" CVD strategies

Policy implications

- Policy makers and politicians should prioritize population-wide strategies for primary stroke and CVD prevention
- As taxation on tobacco, salt, sugar, and alcohol is one of the most effective ways to reduce their consumption and promote healthy behaviors (with the associated benefits for CVD and overall health at the population level) and generate significant revenues for governments. These revenues can and should be re-invested back into the public health sector and health research to improve health of the taxpayers, including appropriate funding of primary prevention strategies for stroke, CVD, and other major noncommunicable diseases
- While measures and education about behavioral risk factors (diet, physical activity, alcohol, and tobacco avoidance) need to be applied to the general population, a simple, inexpensive screening for a history of vascular disease and presence of modifiable vascular risk factors (particularly smoking, obesity, and facilitated access to measurement of blood pressure and identification of hypertension) should be undertaken to reinforce lifestyle and behavioral interventions and identify those requiring the additional benefits of prophylactic drug therapies
- Global population exposure to improved social and environmental factors, including reduced exposure to air pollution should remain a priority for stroke and CVD prevention
- Evaluation of the effectiveness of the proposed preventative strategies should include monitoring of the prevalence of stroke/CVD risk factors, stroke/CVD frequency (incidence and prevalence), functional (eg, physical and mental impairment) and vital outcomes in both rates (eg, per 100 000 per year) and absolute numbers
- Further research is needed to identify the best balance of population-wide and risk targeted CVD strategies to maximize cost effectiveness and minimize inequalities

about the real-life impact of the diseases on the health system and society. If we look at the Global Burden of Disease estimates for stroke and CVD, their age-adjusted incidence, prevalence, mortality, and disability-adjusted life-years lost rates have been declining over the past 30 years in almost every country of the world (except some low- to middle-income countries), but the absolute number of people who develop, die from, or remain disabled from these disorders over the same period of time has increased dramatically,[44,87–89] largely due to population growth and aging[90] as well as unfavorable trends in the prevalence of some risk factors.[33,44] These are exactly the people who require medical attention and access to health resources. Therefore, from a public health perspective, the absolute number of people to care for is far more important for healthcare planning and resource allocation than their rates. However, monitoring rates allows determination of the changes in the risk of these disorders and their outcomes while age-adjusted rates allow comparisons between different localities and populations. Therefore, the proposed preventative strategies should include monitoring of the prevalence of stroke/CVD risk factors, stroke/CVD frequency (incidence and prevalence), functional (eg, physical and mental impairment), and vital outcomes in both rates (eg, per 100 000 per year) and absolute numbers.

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Disclosures

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References

1. Rose G. Sick individuals and sick populations. *Int J Epidemiol*. 1985;14:32–38.
2. Jackson R, Capewell S. Upfront: cardiovascular risk screening: targeting individuals or populations? *BMJ*. 2008;4. Available at: https://bpac.org.nz/BPJ/2008/October/upfront.aspx. Accessed April 28, 2019.
3. Jackson R, Wells S, Rodgers A. Will screening individuals at high risk of cardiovascular events deliver large benefits? Yes, *BMJ*. 2008;337:a1371. DOI: https://doi.org/10.1136/bmj.a1371.
4. Capewell S. Will screening individuals at high risk of cardiovascular events deliver large benefits? No. *BMJ*. 2008;337:a1395.
5. Johnson CO, Nguyen M, Roth GA, Nichols E, Alam T, Abate D, Abd-Allah F, Abdelalim A, Abraha HN, Abu-Rmeileh NM, et al. Global, regional, and national burden of stroke, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol*. 2019;18:439–458.
6. Kyu HH, Abate D, Abate KH, Abay SM, Abbafati C, Abbasi N, Abbastabar H, Abd-Allah F, Abdela J, Abdelalim A, et al. Global, regional, and national disability-adjusted life-years (DALYs) for 359 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2018;392:1859–1922.
7. Pylypchuk R, Wells S, Kerr A, Poppe K, Riddell T, Harwood M, Exeter D, Mehta S, Grey C, Wu BP, Metcalf P, Warren J, Harrison J, Marshall R, Jackson R. Cardiovascular disease risk prediction equations in 400 000 primary care patients in New Zealand: a derivation and validation study. *Lancet*. 2018;391:1897–1907.
8. Muntner P, Colantonio LD, Cushman M, Goff DC Jr, Howard G, Howard VJ, Kissela B, Levitan EB, Lloyd-Jones DM, Safford MM. Validation of the atherosclerotic cardiovascular disease Pooled Cohort risk equations. *JAMA*. 2014;311:1406–1415.
9. Lackland DT, Elkind MS, D'Agostino R Sr, Dhamoon MS, Goff DC Jr, Higashida RT, McClure LA, Mitchell PH, Sacco RL, Sila CA, Smith SC Jr, Tanne D, Tirschwell DL, Touze E, Wechsler LR. Inclusion of stroke in cardiovascular risk prediction instruments: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2012;43:1998–2027.
10. Hippisley-Cox J, Coupland C, Brindle P. Derivation and validation of QStroke score for predicting risk of ischaemic stroke in primary care and comparison with other risk scores: a prospective open cohort study. *BMJ*. 2013;346:f2573.
11. Parmar P, Krishnamurthi R, Ikram MA, Hofman A, Mirza SS, Varakin Y, Kravchenko M, Piradov M, Thrift AG, Norrving B, Wang W, Mandal DK, Barker-Collo S, Sahathevan R, Davis S, Saposnik G, Kivipelto M, Sindi S, Bornstein NM, Giroud M, Bejot Y, Brainin M, Poulton R, Narayan KM, Correia M, Freire A, Kokubo Y, Wiebers D, Mensah G, BinDhim NF, Barber PA, Pandian JD, Hankey GJ, Mehndiratta MM, Azhagammal S, Ibrahim NM, Abbott M, Rush E, Hume P, Hussein T, Bhattacharjee R, Purohit M, Feigin VL; Stroke Riskometer TMCWG. The Stroke Riskometer(TM) App: validation of a data collection tool and stroke risk predictor. *Int J Stroke*. 2015;10:231–244.
12. Krogsbøll LT, Jørgensen KJ, Gøtzsche PC. General health checks in adults for reducing morbidity and mortality from disease. *Cochrane Database Syst Rev*. 2019;1:CD009009.
13. Jørgensen T, Jacobsen RK, Toft U, Aadahl M, Glümer C, Pisinger C. Effect of screening and lifestyle counselling on incidence of ischaemic heart disease in general population: Inter99 randomised trial. *BMJ*. 2014;348:g3617.
14. Graham I, Atar D, Borch-Johnsen K, Boysen G, Burell G, Cifkova R, Dallongeville J, De Backer G, Ebrahim S, Gjelsvik B, Herrmann-Lingen C, Hoes A, Humphries S, Knapton M, Perk J, Priori SG, Pyorala K, Reiner Z, Ruilope L, Sans-Menendez S, Scholte op Reimer W, Weissberg P, Wood D, Yarnell J, Zamorano JL, Walma E, Fitzgerald T, Cooney MT, Dudina A; European Society of Cardiology Committee for Practice Group. European guidelines on cardiovascular disease prevention in clinical practice: executive summary: fourth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (Constituted by representatives of nine societies and by invited experts). *Eur Heart J*. 2007;28:2375–2414.
15. Genest J, McPherson R, Frohlich J, Anderson T, Campbell N, Carpentier A, Couture P, Dufour R, Fodor G, Francis GA, Grover S, Gupta M, Hegele RA, Lau DC, Leiter L, Lewis GF, Lonn E, Mancini GB, Ng D, Pearson GJ, Sniderman A, Stone JA, Ur E. 2009 Canadian Cardiovascular Society/Canadian guidelines for the diagnosis and treatment of dyslipidemia and prevention of cardiovascular disease in the adult—2009 recommendations. *Can J Cardiol*. 2009;25:567–579.
16. World Health Organization. Prevention of cardiovascular disease: guidelines for assessment and management of total cardiovascular risk. World Health Organization. 2007. Available at: http://www.who.int/iris/handle/10665/43685. Accessed May 3, 2019.

17. New Zealand Guidelines Group. The assessment and management of cardiovascular risk. 2003. Available at: https://www.health.govt.nz/system/files/documents/publications/cvd_risk_full.pdf Accessed May 3, 2019.
18. National Health and Medical Research Council of Australia. Guidelines for the management of absolute cardiovascular disease risk. Canberra: National Health and Medical Research Council of Australia; 2012. Available at: https://www.heartfoundation.org.au/images/uploads/publications/Absolute-CVD-Risk-Full-Guidelines.pdf. Accessed May 3, 2019.
19. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, Cooney M-T, Corrà U, Cosyns B, Deaton C, Graham I, Hall MS, Hobbs FDR, Løchen M-L, Löllgen H, Marques-Vidal P, Perk J, Prescott E, Redon J, Richter DJ, Sattar N, Smulders Y, Tiberi M, van der Worp HB, van Dis I, Verschuren WMM, Binno S; ESC Scientific Group. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: the Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts) Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Eur Heart J*. 2016;37:2315–2381
20. NICE Guideline. Cardiovascular disease: risk assessment and reduction, including lipid modification. 18 July 2014. Available at: https://www.nice.org.uk/guidance/cg181/resources/cardiovascular-disease-risk-assessment-and-reduction-including-lipid-modification-pdf-35109807660997. Accessed April 26, 2019.
21. Wu S, Wu B, Liu M, Chen Z, Wang W, Anderson CS, Sandercock P, Wang Y, Huang Y, Cui L, Pu C, Jia J, Zhang T, Liu X, Zhang S, Xie P, Fan D, Ji X, Wong KSL, Wang L, Wei C, Wang Y, Cheng Y, Liu Y, Li X, Dong Q, Zeng J, Peng B, Xu Y, Yang Y, Wang Y, Zhao G, Wang W, Xu Y, Yang Q, He Z, Wang S, You C, Gao Y, Zhou D, He L, Li Z, Yang J, Lei C, Zhao Y, Liu J, Zhang S, Tao W, Hao Z, Wang D, Zhang S; China Stroke Study C. Stroke in China: advances and challenges in epidemiology, prevention, and management. *Lancet Neurol*. 2019;18:394–405.
22. Sanghavi DM, Conway PH. Paying for prevention: a novel test of medicare value-based payment for cardiovascular risk reduction. *JAMA* 2015;314:123–124.
23. Lloyd-Jones Donald M, Hong Y, Labarthe D, Mozaffarian D, Appel Lawrence J, Van Horn L, Greenlund K, Daniels S, Nichol G, Tomaselli Gordon F, Arnett Donna K, Fonarow Gregg C, Ho PM, Lauer Michael S, Masoudi Frederick A, Robertson Rose M, Roger V, Schwamm Lee H, Sorlie P, Yancy Clyde W, Rosamond Wayne D. Defining and setting national goals for cardiovascular health promotion and disease reduction. *Circulation*. 2010;121:586–613.
24. Tomaselli GF, Harty MB, Horton K, Schoeberl M. The American Heart Association and the million hearts initiative: a presidential advisory from the American Heart Association. *Circulation*. 2011;124:1795–1799.
25. Sacco RL, Frieden TR, Blakeman DE, Jauch EC, Mohl S. What the million hearts initiative means for stroke: a presidential advisory from the American Heart Association/American Stroke Association. *Stroke*. 2012;43:924–928.
26. Benjamin RM. The million hearts™ initiative: progress in preventing heart attacks and strokes. *Public Health Rep*. 2012;127:558–560.
27. My Life Check- Life's Simple 7. Available at: https://www.heart.org/en/healthy-living/healthy-lifestyle/my-life-check–lifes-simple-7. Accessed June 5, 2019.
28. Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, Himmelfarb CD, Khera A, Lloyd-Jones D, McEvoy JW, Michos ED, Miedema MD, Munoz D, Smith SC Jr, Virani SS, Williams KA Sr, Yeboah J, Ziaeian B. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2019;74:1376–1414.
29. Brindle P, Emberson J, Lampe F, Walker M, Whincup P, Fahey T, Ebrahim S. Predictive accuracy of the Framingham coronary risk score in British men: prospective cohort study. *BMJ*. 2003;327:1267–1270.
30. Dalton ARH, Soljak M, Samarasundera E, Millett C, Majeed A. Prevalence of cardiovascular disease risk amongst the population eligible for the NHS Health Check Programme. *Eur J Prev Cardiol*. 2013;20:142–150.
31. Feigin VL, Norrving B, Mensah GA. Primary prevention of cardiovascular disease through population-wide motivational strategies: insights from using smartphones in stroke prevention. *BMJ Global Health*. 2017;2:e000306.
32. Johnson CO, Nguyen M, Roth GA, Nichols E, Alam T, Abate D, Abd-Allah F, Abdelalim A, Abraha HN, Abu-Rmeileh NME, et al. Global, regional, and national burden of stroke, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *The Lancet Neurology*. 2019;18(5):439–458.
33. Stanaway JD, Afshin A, Gakidou E, Lim SS, Abate D, Abate KH, Abbafati C, Abbasi N, Abbastabar H, Abd-Allah F, et al. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2018;392:1923–1994.
34. Rutten-Jacobs LCA, Larsson SC, Malik R, Rannikmäe K, Sudlow CL, Dichgans M, Markus HS, Traylor M. Genetic risk, incident stroke, and the benefits of adhering to a healthy lifestyle: cohort study of 306–473 UK Biobank participants. *BMJ*. 2018;363:k4168.
35. de Lemos JA, Ayers CR, Levine BD, deFilippi CR, Wang TJ, Hundley WG, Berry JD, Seliger SL, McGuire DK, Ouyang P, Drazner MH, Budoff M, Greenland P, Ballantyne CM, Khera A. Multimodality strategy for cardiovascular risk assessment: performance in 2 population-based cohorts. *Circulation*. 2017;135:2119–2132.
36. Than MP, Pickering JW, Sandoval Y, Shah ASV, Tsanas A, Apple FS, Blankenberg S, Cullen L, Mueller C, Neumann JT, Twerenbold R, Westermann D, Beshiri A, Mills NL. Machine learning to predict the likelihood of acute myocardial infarction. *Circulation*. 2019;140:899–909.
37. Rajkomar A, Dean J, Kohane I. Machine learning in medicine. *N Engl J Med*. 2019;380:1347–1358.
38. Christodoulou E, Ma J, Collins GS, Steyerberg EW, Verbakel JY, Van Calster B. A systematic review shows no performance benefit of machine learning over logistic regression for clinical prediction models. *J Clin Epidemiol*. 2019;110:12–22.
39. Kypridemos C, Allen K, Hickey GL, Guzman-Castillo M, Bandosz P, Buchan I, Capewell S, O'Flaherty M. Cardiovascular screening to reduce the burden from cardiovascular disease: microsimulation study to quantify policy options. *BMJ* 2016;353:i2793.
40. Martins SC, Sacks C, Hacke W, Brainin M, Figueiredo FDA, Pontes-Neto O, Lavados Germain PM, Marinho MF, Hoppe Wiegering A, Vaca McGhie D, Cruz-Flores S, Ameriso SF, Camargo Villareal WM, Durán JC, Fogolin Passos JE, Gomes Nogueira R, Freitas de Carvalho JJ, Sampaio Silva G, Cabral Moro CH, Oliveira-Fil J, Gagliardi R, Gomes de Sousa ED, Fagundes Soares F, de Pinho Campos K, Piza Teixeira PF, Gonçalves IP, Santos Carquin IR, Muñoz Collazos M, Pérez Romero GE, Maldonado Figueredo JI, Barboza MA, Celis López MÁ, Góngora-Rivera F, Cantú-Brito C, Novarro-Escudero N, Velázquez Blanco MA, Arbo Oze de Morvil CA, Olmedo Bareiro AB, Meza Rojas G, Flores A, Hancco-Saavedra JA, Pérez Jimenez V, Abanto Argomedo C, Rodriguez Kadota L, Crosa R, Mora Cuervo DL, de Souza AC, Carbonera LA, Álvarez Guzmán TF, Maldonado N, Cabral NL, Anderson C, Lindsay P, Hennis A, Feigin VL. Priorities to reduce the burden of stroke in Latin American countries. *Lancet Neurol*. 2019;18:674–683.
41. Emberson J, Whincup P, Morris R, Walker M, Ebrahim S. Evaluating the impact of population and high-risk strategies for the primary prevention of cardiovascular disease. *Eur Heart J*. 2004;25:484–491.
42. O'Donnell MJ, Chin SL, Rangarajan S, Xavier D, Liu L, Zhang H, Rao-Melacini P, Zhang X, Pais P, Agapay S, Lopez-Jaramillo P, Damasceno A, Langhorne P, McQueen MJ, Rosengren A, Dehghan M, Hankey GJ, Dans AL, Elsayed A, Avezum A, Mondo C, Diener HC, Ryglewicz D, Czlonkowska A, Pogosova N, Weimar C, Iqbal R, Diaz R, Yusoff K, Yusufali A, Oguz A, Wang X, Penaherrera E, Lanas F, Ogah OS, Ogunniyi A, Iversen HK, Malaga G, Rumboldt Z, Oveisgharan S, Al Hussain F, Magazi D, Nilanont Y, Ferguson J, Pare G, Yusuf S. Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study. *Lancet*. 2016;388:761–775.
43. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, McQueen M, Budaj A, Pais P, Varigos J, Lisheng L; Investigators IS. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet*. 2004;364:937–952.
44. Feigin VL, Roth GA, Naghavi M, Parmar P, Krishnamurthi R, Chugh S, Mensah GA, Norrving B, Shiue I, Ng M, Estep K, Cercy K, Murray CJ, Forouzanfar MH; Global Burden of Diseases I, Risk Factors S, Stroke Experts Writing G. Global burden of stroke and risk factors in 188 countries, during 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet Neurol*. 2016;15:913–924.
45. Arena R, Arnett DK, Terry PE, Li S, Isaac F, Mosca L, Braun L, Roach WH, Pate RR, Sanchez E, Carnethon M, Whitsel LP. The role of worksite health screening. *Circulation*. 2014;130:719–734.
46. Whelton PK, Carey RM, Aronow WS, Casey DE, Collins KJ, Dennison HC, DePalma SM, Gidding S, Jamerson KA, Jones DW, MacLaughlin EJ, Muntner P, Ovbiagele B, Smith SC, Spencer CC, Stafford RS, Taler SJ, Thomas RJ, Williams KA, Williamson JD. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults. A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2018;71:e127–e248.
47. Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher K, Blumenthal RS, Braun LT, de Ferranti S, Faiella-Tommasino J, Forman DE, Goldberg R, Heidenreich PA, Hlatky MA, Jones DW, Lloyd-Jones D, Lopez-Pajares N, Ndumele CE, Orringer CE, Peralta CA, Saseen JJ, Smith SC, Sperling L, Virani SS, Yeboah J. 2018

AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of Blood Cholesterol. *J Am Coll Cardiol*. 2019;73:3168–3209.

48. Mosca L, Benjamin EJ, Berra K, Bezanson JL, Dolor RJ, Lloyd-Jones DM, Newby LK, Piña IL, Roger VL, Shaw LJ, Zhao D, Beckie TM, Bushnell C, D'Armiento J, Kris-Etherton PM, Fang J, Ganiats T, Gomes AS, Gracia CR, Haan CK, Jackson EA, Judelson DR, Kelepouris E, Lavie CJ, Moore A, Nussmeier NA, Ofili E, Oparil S, Ouyang P, Pinn VW, Sherif K, Smith SC, Sopko G, Chandra-Strobos N, Urbina EM, Vaccarino V, Wenger NK. Effectiveness-based guidelines for the prevention of cardiovascular disease in women—2011 update. *Circulation*. 2011;123:1243–1262.
49. Pandian JD, Gall SL, Kate MP, Silva GS, Akinyemi RO, Ovbiagele BI, Lavados PM, Gandhi DBC, Thrift AG. Prevention of stroke: a global perspective. *Lancet*. 2018;392:1269–1278.
50. Brainin M, Feigin V, Martins S, Matz K, Roy J, Sandercock P, Teuschl Y, Tuomilehto J, Wiseman A. Cut stroke in half: polypill for primary prevention in stroke. *Int J Stroke*. 2018;13:633–647.
51. Nguyen TPL, Wright EP, Nguyen TT, Schuiling-Veninga CCM, Bijlsma MJ, Nguyen TBY, Postma MJ. Cost-effectiveness analysis of screening for and managing identified hypertension for cardiovascular disease prevention in Vietnam. *PLoS One*. 2016;11:e0155699.
52. Haase CB, Gyuricza JV, Brodersen J. New hypertension guidance risks overdiagnosis and overtreatment. *BMJ*. 2019;365:1657.
53. Godlee F. Pills or public health? *BMJ*. 2019;365:1791.
54. Bray JE, Mosley I, Bailey M, Barger B, Bladin C. Stroke public awareness campaigns have increased ambulance dispatches for stroke in Melbourne, Australia. *Stroke*. 2011;42:2154–2157.
55. Vondráčková L, Mikulík R. Public stroke education: current status worldwide and projects to increase awareness in the Czech Republic. *Cor et Vasa*. 2017;59:e546–e552.
56. Wolters FJ, Paul NLM, Li L, Rothwell PM; Oxford Vascular S. Sustained impact of UK FAST-test public education on response to stroke: a population-based time-series study. *Int J Stroke*. 2015;10:1108–1114.
57. Wolters FJ, Li L, Gutnikov SA, Mehta Z, Rothwell PM. Medical attention seeking after transient ischemic attack and minor stroke before and after the UK Face, Arm, Speech, Time (FAST) public education campaign: results from the oxford vascular study. *JAMA Neurol*. 2018;75:1225–1233.
58. Sudirman H, Yuliyanti C, Sari AI. Effectiveness of 'FAST' stroke campaign for fast stroke recognition and response: a systematic review. *Proc Int Conf Appl Sci Health* 2018;3:112–121.
59. Ryan GWAK. An overview of primary prevention. *J Mental Health*. 1998;7:441–449.
60. Pigeot I, De Henauw S, Foraita R, Jahn I, Ahrens W. Primary prevention from the epidemiology perspective: three examples from the practice. *BMC Med Res Methodol*. 2010;10:10.
61. Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, Himmelfarb CD, Khera A, Lloyd-Jones D, McEvoy JW, Michos ED, Miedema MD, Muñoz D, Smith SC, Virani SS, Williams KA, Yeboah J, Ziaeian B. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. *Circulation*. 2019;140:e596–e646.
62. Record NB, Onion DK, Prior RE, Dixon DC, Record SS, Fowler FL, Cayer GR, Amos CI, Pearson TA. Community-wide cardiovascular disease prevention programs and health outcomes in a rural county, 1970–2010. *JAMA* 2015;313:147–155.
63. Blomstedt Y, Norberg M, Stenlund H, Nyström L, Lönnberg G, Boman K, Wall S, Weinehall L. Impact of a combined community and primary care prevention strategy on all-cause and cardiovascular mortality: a cohort analysis based on 1 million person-years of follow-up in Västerbotten County, Sweden, during 1990–2006. *BMJ Open*. 2015;5:e009651.
64. Puska P. Successful prevention of non-communicable diseases: 25 year experiences with North Karelia project in Finland. *Public Health Med*. 2002;4:5–7.
65. Vartiainen E. The North Karelia Project: cardiovascular disease prevention in Finland. *Global Cardiol Sci Pract*. 2018;2018:13.
66. Miura K. Epidemiology and prevention of hypertension in Japanese: how could Japan get longevity? *EPMA J*. 2011;2:59–64.
67. Barton P, Andronis L, Briggs A, McPherson K, Capewell S. Effectiveness and cost effectiveness of cardiovascular disease prevention in whole populations: modelling study. *BMJ*. 2011;343:d4044.
68. Pekka P, Sameer B, Jagat N (eds.) The North Karelia Project. *Global Heart*. 2016;11:171–266.
69. From Burden to "Best Buys": Reducing the Economic Impact of Non-Communicable Diseases in Low- and Middle-Income Countries. World Health Organization, World Economic Forum and the Harvard School of Public Health. World Economic Forum, Geneva, Switzerland. 2011. Available at: http://www.who.int/nmh/publications/best_buys_summary.pdf. Accessed September 11, 2018.
70. Frieden TR, Bloomberg MR. Saving an additional 100 million lives. *Lancet*. 2018;391:709–712.
71. Allen LN, Pullar J, Wickramasinghe KK, Williams J, Roberts N, Mikkelsen B, Varghese C, Townsend N. Evaluation of research on interventions aligned to WHO "Best Buys" for NCDs in low-income and lower-middle-income countries: a systematic review from 1990 to 2015. *BMJ Global Health*. 2018;3:e000535.
72. Chiuve SE, Rexrode KM, Spiegelman D, Logroscino G, Manson JE, Rimm EB. Primary prevention of stroke by healthy lifestyle. *Circulation*. 2008;118:947–954.
73. Gorelick PB. Primary prevention of stroke: impact of healthy lifestyle. *Circulation*. 2008;118:904–906.
74. Aminde LN, Cobiac LJ, Veerman JL. Potential impact of a modest reduction in salt intake on blood pressure, cardiovascular disease burden and premature mortality: a modelling study. *Open Heart*. 2019;6:e000943.
75. Institute for Health Metrics and Evaluation (IHME). GBD Compare Data Visualization. Seattle, WA: IHME, University of Washington, 2019. Available at: https://vizhub.healthdata.org/gbd-compare/. Accessed October 8, 2019.
76. Gmeinder M, Morgan D, Mueller M. "How much do OECD countries spend on prevention?", OECD Health Working Papers, No. 101, OECD Publishing, Paris, 2017. https://doi.org/10.1787/f19e803c-en. Accessed May 19, 2019.
77. Robson J, Dostal I, Sheikh A, Eldridge S, Madurasinghe V, Griffiths C, Coupland C, Hippisley-Cox J. The NHS Health Check in England: an evaluation of the first 4 years. *BMJ Open*. 2016;6:e008840.
78. Sassi F, Belloni A, Mirelman AJ, Suhrcke M, Thomas A, Salti N, Vellakkal S, Visaruthvong C, Popkin BM, Nugent R. Equity impacts of price policies to promote healthy behaviours. *Lancet*. 2018;391:2059–2070.
79. Johnson RK, Appel LJ, Brands M, Howard BV, Lefevre M, Lustig RH, Sacks F, Steffen LM, Wylie-Rosett J. Dietary sugars intake and cardiovascular health a scientific statement from the American Heart Association. *Circulation*. 2009;120:1011–1020.
80. Martineau F, Tyner E, Lorenc T, Petticrew M, Lock K. Population-level interventions to reduce alcohol-related harm: an overview of systematic reviews. *Preventive Med*. 2013;57:278–296.
81. Mayor S. Taxes on alcohol, tobacco, and soft drinks are fair and produce health gains, review finds. *BMJ*. 2018;361:k1524.
82. Feigin VL, Norrving B, George MG, Foltz JL, Roth GA, Mensah GA. Prevention of stroke: a strategic global imperative. *Nat Rev Neurol*. 2016;12:501–512.
83. Wilson N. Salt tax could reduce population's salt intake. *BMJ*. 2004;329:918.
84. Yusuf S, Wood D, Ralston J, Reddy KS. The World Heart Federation's vision for worldwide cardiovascular disease prevention. *Lancet*. 2015;386:399–402.
85. World Health Organization. Global action plan for the prevention and control of noncommunicable diseases 2013–2020. Geneva: WHO; 2013. Available at: http://www.who.int/nmh/events/ncd_action_plan/en/. Accessed January 22, 2020.
86. Norrving B, Davis SM, Feigin VL, Mensah GA, Sacco RL, Varghese C. Stroke prevention worldwide–what could make it work? *Neuroepidemiology*. 2015;45:215–220.
87. Feigin VL, Vos T. Global burden of neurological disorders: from global burden of disease estimates to actions. *Neuroepidemiology*. 2019;52:1–2.
88. Feigin VL, Nguyen G, Cercy K, Johnson CO, Alam T, Parmar PG, Abajobir AA, Abate KH, Abd-Allah F, Abejie AN, Abyu GY, Ademi Z, Agarwal G, Ahmed MB, Akinyemi RO, Al-Raddadi R, Aminde LN, Amlie-Lefond C, Ansari H, Asayesh H, Asgedom SW, Atey TM, Ayele HT, Banach M, Banerjee A, Barac A, Barker-Collo SL, Bärnighausen T, Barregard L, Basu S, Bedi N, Behzadifar M, Béjot Y, Bennett DA, Bensenor IM, Berhe DF, Boneya DJ, Brainin M, Campos-Nonato IR, Caso V, Castañeda-Orjuela CA, Rivas JC, Catalá-López F, Christensen H, Criqui MH, Damasceno A, Dandona L, Dandona R, Davletov K, de Courten B, deVeber G, Dokova K, Edessa D, Endres M, Faraon EJA, Farvid MS, Fischer F, Foreman K, Forouzanfar MH, Gall SL, Gebrehiwot TT, Geleijnse JM, Gillum RF, Giroud M, Goulart AC, Gupta R, Gupta R, Hachinski V, Hamadeh RR, Hankey GJ, Hareri HA, Havmoeller R, Hay SI, Hegazy MI, Hibstu DT, James SL, Jeemon P, John D, Jonas JB, Jóźwiak J, Kalani R, Kandel A, Kasaeian A, Kengne AP, Khader YS, Khan AR, Khang Y-H, Khubchandani J, Kim D, Kim YJ, Kivimaki M, Kokubo Y, Kolte D, Kopec JA, Kosen S, Kravchenko M, Krishnamurthi R, Kumar GA, Lafranconi A, Lavados PM, Legesse Y, Li Y, Liang X, Lo WD, Lorkowski S, Lotufo PA, Loy CT, Mackay MT, Razek HMAE, Mahdavi M, Majeed A, Malekzadeh R, Malta DC, Mamun AA, Mantovani LG, Martins SCO, Mate KK, Mazidi M, Mehata S, Meier T, Melaku YA, Mendoza W, Mensah GA, Meretoja A, Mezgebe HB, Miazgowski T, Miller TR, Ibrahim NM, Mohammed S, Mokdad AH, Moosazadeh M, Moran AE, Musa KI, Negoi RI, Nguyen M, Nguyen QL, Nguyen TH, Tran TT, Nguyen TT, Ningrum DNA, Norrving B, Noubiap JJ, O'Donnell MJ,

Olagunju AT, Onuma OK, Owolabi MO, Parsaeian M, Patton GC, Piradov M, Pletcher MA, Pourmalek F, Prakash V, Qorbani M, Rahman M, Rahman MA, Rai RK, Ranta A, Rawaf D, Rawaf S, Renzaho AMN, Robinson SR, Sahathevan R, Sahebkar A, Salomon JA, Santalucia P, Santos IS, Sartorius B, Schutte AE, Sepanlou SG, Shafieesabet A, Shaikh MA, Shamsizadeh M, Sheth KN, Sisay M, Shin M-J, Shiue I, Silva DAS, Sobngwi E, Soljak M, Sorensen RJD, Sposato LA, Stranges S, Suliankatchi RA, Tabarés-Seisdedos R, Tanne D, Nguyen CT, Thakur JS, Thrift AG, Tirschwell DL, Topor-Madry R, Tran BX, Nguyen LT, Truelsen T, Tsilimparis N, Tyrovolas S, Ukwaja KN, Uthman OA, Varakin Y, Vasankari T, Venketasubramanian N, Vlassov VV, Wang W, Werdecker A, Wolfe CDA, Xu G, Yano Y, Yonemoto N, Yu C, Zaidi X, Zaki MES, Zhou M, Ziaeian B, Zipkin B, Vos T, Naghavi M, Murray CJL, Roth GA; 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;379:2429–2437.

89. James SL, Abate D, Abate KH, Abay SM, Abbafati C, Abbasi N, Abbastabar H, Abd-Allah F, Abdela J, Abdelalim A, et al. 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;392:1789–1858.

90. Roth GA, Forouzanfar MH, Moran AE, Barber R, Nguyen G, Feigin VL, Naghavi M, Mensah GA, Murray CJ. Demographic and epidemiologic drivers of global cardiovascular mortality. *N Engl J Med*. 2015;372:133–134.

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