and middle-income countries are not taking it.¹¹ This suggests that strategies to initiate and maintain these drugs need to be as simple as possible. Such strategies might also have a role in high-income countries where the main alternative strategy (titrate treatment against risk factor levels) can result in undertreatment in practice.¹¹ Cost-effectiveness analysis suggests that a fixed-dose combination strategy is potentially cost-effective compared with treatment titration in a high-income setting.¹²

Although a polypill strategy might sit uncomfortably with precision medicine, there is now a substantial evidence base that such an approach is effective at reducing cardiovascular disease. Guideline writers and policy makers should consider how to incorporate this evidence base into quidelines and policies.

JM declares fees for academic advisory board membership for the Bristol-Myers Squibb-Pfizer-funded GUARD-AF trial of screening for atrial fibrillation, for Pfizersponsored education sessions on detection and diagnosis of atrial fibrillation, and for advice on a heart failure app for Omron. RJM declares working with Omron on the development and evaluation of a blood pressure telemonitoring system for which consultancy and licensing fees are paid to his institution.

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- 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.
- 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.
- Yusuf S, Hawken S, Ounpuu S, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries
- (the INTERHEART study): case-control study. Lancet 2004; **364:** 937-52. Wald NJ, Law MR. A strategy to reduce cardiovascular disease by more than 80%. BMJ 2003; **326**: 1419.
- Joseph P, Roshandel G, Gao P, et al. Fixed-dose combination therapies with and without aspirin for primary prevention of cardiovascular disease: an individual participant data meta-analysis. *Lancet* 2021; published online Aug 29. https://doi.org/10.1016/S0140-6736(21)01827-4.
- 6 Yusuf S, Joseph P, Dans A, et al. Polypill with or without aspirin in persons without cardiovascular disease. N Engl J Med 2021; 384: 216–28.
- Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *BMJ* 2002; **324**: 71–86.
- 8 Zheng SL, Roddick AJ. Association of aspirin use for primary prevention with cardiovascular events and bleeding events: a systematic review and meta-analysis. JAMA 2019; 321: 277–87.
- 9 Woo D, Haverbusch M, Sekar P, et al. Effect of untreated hypertension on hemorrhagic stroke. *Stroke* 2004; **35:** 1703–08.
- 10 Qiao Y, Yang T, Gan Y, et al. Associations between aspirin use and the risk of cancers: a meta-analysis of observational studies. BMC Cancer 2018; 18: 288.
- 11 Yusuf S, Islam S, Chow CK et al. Use of secondary prevention drugs for cardiovascular disease in the community in high-income, middle-income, and low-income countries (the PURE Study): a prospective epidemiological survey. Lancet 2011; **378**: 1231–43.
- 12 Jowett S, Barton P, Roalfe A et al. Cost-effectiveness analysis of use of a polypill versus usual care of best practice for primary prevention in people at high risk of cardiovascular disease. *PLoS One* 2017; **12**: e0182625.

Cerebral venous sinus thrombosis after vaccination: the UK experience

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An important but rare complication of COVID-19 vaccination is vaccine-induced immune thrombotic thrombocytopenia (VITT) associated with the adenovirus vector vaccines, Ad26.COV2.S (Johnson & Johnson) and ChAdOx1 (Oxford-AstraZeneca).¹⁻⁵ VITT occurs more commonly in women younger than 50 years who present within 5-24 days of vaccination with thrombosis in unusual sites-the majority with cerebral venous sinus thrombosis.^{1,6} Thrombocytopenia, elevated D-dimer, decreased fibrinogen, and positive antibodies against platelet factor 4 (PF4) are commonly observed.¹⁻⁶ Recommended treatments for VITT, based on similarities with autoimmune heparin-induced thrombocytopenia (HIT),⁷ include non-heparin anticoagulation, intravenous immunoglobulin, and avoidance of platelet transfusions.¹ Mortality associated with VITT is approximately 40%.¹

In *The Lancet*, Richard Perry and colleagues⁸ report on the largest series to date of patients with VITT-associated cerebral venous sinus thrombosis. In this multicentre cohort study, cerebral venous sinus thrombosis following COVID-19 vaccination was defined as VITT-associated if platelet count nadir was less than 150×10^{9} per L and, if measured, D-dimer concentration was greater than 2000 µg/L. Between April 1 and May 20, 2021, the study enrolled 70 patients with VITT-associated cerebral venous sinus thrombosis and 25 patients with cerebral venous sinus thrombosis that did not meet criteria for VITT from 43 hospitals in the UK, as well as a large historical cohort of patients with cerebral venous sinus thrombosis.

All cases of VITT-associated cerebral venous sinus thrombosis occurred after a first dose of the ChAdOx1 vaccine. 56 (97%) of 58 patients with VITT for whom



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