growth. The assessment of antibody levels to prostate vaccine antigens was limited by the tests available. Almost all patients had pre-existing antibodies but few showed a booster response to the two antigens tested.[3]

There are three advantages of these new mRNA vaccines over previous DNA vaccines. They act in the cytoplasm rather than in the nucleus, and so there is no fear of integration into the host genome. The vaccine is lyophilised and said to be stable at up to 25°C for 3 years and at 40°C for 6 months. Finally, mRNA vaccines can be produced rapidly, which would be useful for an impending viral epidemic and especially to control an influenza pandemic, considering that the rate of manufacture of the present influenza vaccines is limited by the global supply of pathogen-free eggs.

If an injector device is essential for antiviral immunogenicity in human beings, a temperature stable mRNA vaccine could be ideal for mass vaccination using multidose vials. This approach would be preferable to virus-vectored vaccines, several of which are being investigated as potential new vaccines. Each vector virus—eg, a non-human primate adenovirus or a rhabdovirus, could only be used with confidence once in a population because immunity to the vector can inhibit the response to booster doses or to a different vaccine antigen in the same vector.[5]

An improved mRNA vaccine could be suitable as a rabies pre-exposure immunisation, which must induce immunity within weeks. The inclusion of rabies vaccine in WHO's Expanded Program on Immunization for children in areas with endemic dog rabies is, so far, an unaffordable ideal. An mRNA vaccine is unlikely to be useful as urgent prophylaxis after contact with a rabid dog. In this case, predictable rapid antibody induction is crucial to prevent the virus entering the CNS and causing encephalomyelitis and certain death.[6]

Before any predictions can be made, highly immunogenic viral mRNA vaccines must be devised. Let us hope that this innovation will not follow the path of DNA vaccines, which have not fulfilled the promise seen in animal experiments and have not been effective in human beings.[7]

Mary Warrell
Centre for Clinical Vaccinology & Tropical Medicine, Churchill Hospital, Oxford Vaccine Group, University of Oxford, Oxford, OX3 7LE, UK
mary.warrell@ndm.ox.ac.uk

I declare no competing interests.

1 Alberer M, Gnad-Vogt U, Hong HS, et al. Safety and immunogenicity of a mRNA rabies vaccine in healthy adults: an open-label, non-randomised, prospective, first-in-human phase 1 clinical trial. *Lancet* 2017; published online July 25. http://dx.doi.org/10.1016/S0140-6736(17)31665-3.
2 Weide B, Pascolo S, Scheel B, et al. Direct injection of protamine-protected mRNA: results of a phase 1/2 vaccination trial in metastatic melanoma patients. *J Immunother* 2009; **32:** 498–507.
3 Kübler H, Scheel B, Gnad-Vogt U, et al. Self-adjuvanted mRNA vaccination in advanced prostate cancer patients: a first-in-man phase I/IIa study. *J Immunother Cancer* 2015; **3:** 26.
4 Schnee M, Vogel AB, Voss D, et al. An mRNA vaccine encoding rabies virus glycoprotein induces protection against lethal infection in mice and correlates of protection in adult and newborn pigs. *PLoS Neg Trop Dis* 2016; **10:** e0004746.
5 Ertl HC. Viral vectors as vaccine carriers. *Curr Opin Virol* 2016; **21:** 1–8.
6 Warrell MJ, Warrell DA. Rabies: the clinical features, management and prevention of the classic zoonosis. *Clin Med (Lond)* 2015; **15:** 78–81.
7 Ertl HC. Rabies DNA vaccines for protection and therapeutic treatment. *Expert Opin Biol Ther* 2003; **3:** 639–44.

Health inequality across prefectures in Japan

Published Online July 19, 2017 http://dx.doi.org/10.1016/S0140-6736(17)31792-0

See Articles page 1521

Japan has exemplary records in human development as measured by a human development index of 0·903 in 2016 (ranked 17th in the world).[1] Universal access to health services with no financial barrier for every citizen in Japan launched in 1961 and has contributed to nearly equitable access and relatively small gaps in health status across regions and socioeconomic groups in the country.[2] Ageing is homogeneously distributed across all communities,[3] which has led to high demand for health care in all prefectures (provinces). Despite these achievements in the past, health inequity is increasing and has become a challenge for Japan.

In *The Lancet*, Shuhei Nomura and colleagues[4] use trend data for burden of disease between 1990 and 2015 to document comprehensive health measures on mortality, morbidity, and injuries and variations across prefectures in Japan. Between 1990 and 2015, average life expectancy has increased by 4·2 years. Although similar rises have occurred between men and women, the gap between the lowest and highest prefectures widened from 2·5 years in 1990 to 3·1 years in 2015. The average health-adjusted life expectancy (HALE) overall increased by 3·5 years over this period, but the disparity between HALEs in the highest and lowest performing prefectures


Indeed/Getty

has slightly widened across the period, from 2·3 years in 1990 to 2·7 years in 2015.

In Nomura and colleagues' study,[4] Japan performs well in reducing years of life lost (YLL) over time, probably driven by the reduction in mortality from cardiovascular diseases and neoplasms rather than by reducing the numbers of years living with disability (YLD) between 1990 and 2015. Age-standardised disability-adjusted life years (DALYs) were reduced by 19·8%: age-standardised YLDs contributed a 3·5% reduction and YLLs contributed a 33·4% reduction. Although mortality from other diseases is declining, both the numbers of deaths and age-standardised mortality from Alzheimer's disease and other dementias have increased; possibly leading to a slow down of progress in population health since 2005. There has also been a slow pace of reduction in age-standardised mortality rates from cardiovascular diseases since 2005 in Japan. Clearly health status progress overall has been hampered by a leveling off of mortalities from cardiovascular diseases, Alzheimer's disease, and other dementias after 2005. Primary prevention of Alzheimer's disease and dementias is therefore a major policy priority taken by the prefecture governments. Notably, Alzheimer's disease, breast cancer, and other neoplasms are the only three diseases that have little variation across prefectures.[4]

This study also shows prefecture variations in burden of diseases; for example, Shiga prefecture located in the western region of Honshu island has the highest number of diseases with mortality rates that are significantly lower than the national mean, hence Shiga has the highest life expectancy at birth in 2015. By contrast, Aomori prefecture in the most northern part of Honshu island has the highest number of diseases with mortality rates that are significantly higher than the national mean. For example, in Shiga the age-standardised mortality rate in 2015 for ischaemic heart disease was 39·8 deaths per 100 000 individuals, whereas in Aomori the mortality rate was 50·1 deaths per 100 000 individuals; the national average was 44·7 deaths per 100 000 individuals. Such large variations in age-standardised mortality rates across prefectures should prompt further investigation of the causes and policy interventions to minimise the prefecture gaps.

Although this study offers a comprehensive assessment of the health status trends and prefecture variations of mortality and DALYs in Japan, it provides little by way of what explains these variations. Exposure to risks, variations in lifestyle, and other socioeconomic and poverty trends and profiles in each prefecture are not fully analysed. That said, the study shows no significant correlation between age-standardised mortality rates or DALYs and health system indicators (health expenditure per capita in 2015 and health workforce density in 2014). But the 1-year cross-sectional health system factors might not be long enough to determine health status variations. Historical trends between 1990 and 2015 might offer some clues.

Disparities in socioeconomic status, material and social deprivations, poverty, and other lifestyle factors also contribute to health status variations, as well as a decade of economic recession in Japan.[5,6] A 2014 study,[7] showed that material factors (such as home ownership and living density); behavioural factors (such as sleep insufficiency, unbalanced diet, irregular meals, physical inactivity, excessive alcohol, and smoking); psychosocial factors, in particular perceived stress, and social relational factors (married or living alone) contribute to variations in difference in self-rated health status. These contributing factors, which may contribute to prefecture health disparities, were not fully assessed by Nomura and colleagues.[4] The findings from Nomura and colleagues[4] are similar to those of Fukuda and colleagues[8] of decreased geographical health inequalities before 1995 and increased inequalities thereafter—confirming the rising health inequality in Japan that needs to be investigated for contributing factors.

In addition to health determinants, political, socioeconomic, and environmental factors significantly contribute to health disparities;[9] and are often more considerable than health factors.[10] The lower socioeconomic classes have higher exposures to occupational hazards and injuries,[11] and risk-related lifestyle behaviours such as alcohol consumption, in particular binge drinking,[12] domestic violence and drug abuse,[13] and higher smoking prevalence.[14] Poverty and material deprivation can also result in less than needed access to health services.

Now is an opportune time to identify prefecture-specific social determinants of health inequity that will support the sustainable development goals, leaving no one behind and where all prefectures have equitable health status.

*Churnrurtai Kanchanachitra, Viroj Tangcharoensathien
Institute for Population and Social Research, Mahidol University, Thailand (CK); and International Health Policy Program, Ministry of Public Health, Thailand (VT)
churnrurtai.kan@mahidol.edu

We declare no competing interests.

1 United Nations Development Programme, Human Development Report 2016: Human Development for Everyone. 2016. http://hdr.undp.org/sites/default/files/2016_human_development_report.pdf (accessed May 30, 2017).
2 Ikeda N, Saito E, Kondo N, et al. What has made the population of Japan healthy? *Lancet* 2011; **378:** 1094–105.
3 Japan Statistics Bureau, Ministry of Internal Affairs and Communications. Japan statistical year book 2017. Population and Households. http://www.stat.go.jp/english/data/nenkan/66nenkan/1431-02.htm (accessed May 30, 2017).
4 Nomura S, Sakomoto H, Glenn S, et al. Population health and regional variations of disease burden in Japan, 1990–2015: a systematic subnational analysis for the Global Burden of Disease Study 2015. *Lancet* 2017; published online July 19. http://dx.doi.org/10.1016/S0140-6736(17)31544-1.
5 Sugisawa H, Harada K, Sugihara Y, et al. Socioeconomic status and self-rated health of Japanese people, based on age, cohort, and period. *Popul Health Metr* 2016; **14:** 27.
6 Kondo N, Subramanian SV, Kawachi I, Takeda Y, Yamagata Z. Economic recession and health inequalities in Japan: analysis with a national sample, 1986–2001. *J Epidemiol Community Health* 2008; **62:** 869–75.
7 Hiyoshi A, Fukuda Y, Shipley M, Brunner E. Health inequalities in Japan: The role of material, psychosocial, social relational and behavioral factors. *Soc Sci Med* 2014; **104:** 201–09.
8 Fukuda Y, Nakao H, Yahata Y, Imai H. Are health inequalities increasing in Japan? The trends of 1955 to 2000. *Biosci Trends* 2007; **1:** 38–42.
9 Crombie I, Irvine L, Elliott L, Wallace H. Closing the health inequalities gap: an international perspective. Copenhagen 2005. WHO Regional Office for Europe.
10 Marmot M, Allen J. Social determinants of health equity. *Am J Public Health* 2014: **104** (suppl 4)**:** S517–19.
11 Williams DR, Mohammed SA, Leavell J, Collins C. Race, socioeconomic status and health: complexities, ongoing challenges and research opportunities. *Ann N Y Acad Sci* 2010; **1186:** 69–101.
12 Fone DL, Farewell DM, White J, et al. Socioeconomic patterning of excess alcohol consumption and binge drinking: a cross-sectional study of multilevel associations with neighbourhood deprivation. *BMJ Open* 2013; **3:** e002337.
13 Nagassar RP, Rawlins JM, Sampson NR, et al. The prevalence of domestic violence within different socio-economic classes in Central Trinidad. *West Indian Med J* 2010; **59:** 20–25
14 Hiscock R, Bauld L, Amos A, Fidler JA, Munafò M. Socioeconomic status and smoking: a review. *Ann N Y Acad Sci* 2012; **1248:** 107–23.

Beating NCDs can help deliver universal health coverage

In WHO's drive to ensure good health and care for all, there is a pressing need to step up global and national action on non-communicable diseases (NCDs), and the factors that put so many people at risk of illness and death from these conditions worldwide. By action, we mean coordinated action that is led by the highest levels of government and that inserts health concerns into all policy making—from trade and finance to education, environment, and urban planning. Action needs to go beyond government and must bring in civil society, academia, business, and other stakeholders to promote health.

But governments have to take the initiative. Governments are in the driving seat when it comes to motivating, and obliging, the private sector to prioritise the healthy—not the profitable—option, particularly those industries (eg, manufacturers, retailers, and marketers of tobacco, alcohol, sugary drinks, or foods containing trans-fat and high levels of sodium) that make the products that jeopardise health. However, how can such action be achieved when the scale of the NCDs epidemic is so large—accounting for the premature deaths of 15 million people aged 30–69 years every year, including 7 million in low-income and lower-middle-income countries[1]—and the vested interests of powerful economic multinational operators so strong?

The answer is to prevent exposure to NCD-causing risks, such as tobacco smoke, harmful use of alcohol, physical inactivity, unhealthy diets, and air pollution, and to provide universal health coverage thereby ensuring all people can access needed preventive and curative health-care services, without falling into poverty.

WHO has developed a list of tried, tested, and affordable actions to improve prevention, early detection, treatment, and care of NCDs.[2,3] These include prioritising essential medicines, counselling, and care for people living with an NCD, no matter where they come from or how much money they have. WHO has also made recommendations for using laws to help prevent people developing NCDs in the first place. This action means regulating the amount of salt and sugar in processed foods and drinks that fuel the epidemics of cardiovascular diseases and diabetes,[4] and that are often cheaper than healthier options. Such regulation involves banning tobacco marketing, advertising, and promotion, and making all indoor public and workplaces smoke-free. Taxing tobacco, alcohol, and sugary drinks not only curbs consumption of unhealthy products, it can also generate revenue for disease prevention and treatment.

At the 70th World Health Assembly in May, 2017, governments endorsed the updated set of