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Japan's vision for a peaceful and healthier world

Health is fundamentally a global issue. Recent outbreaks of Ebola virus disease and Middle East respiratory syndrome have reminded us that global health issues require collective action. The world must unite and countries must establish resilient and sustainable health systems, ensuring that each individual is secure and receives the highest attainable standard of health. Japan has been a longstanding advocate of human security¹ and has taken concrete action on the ground in support of this principle. Human security protects the vital core of all human lives in a way that enhances freedom, fulfilment, and capabilities^{1,2} and underlies Japan's policy of Proactive Contribution to Peace. Japan regards health as an indispensable element of human security.¹

In September, 2015, the United Nations General Assembly adopted the 2030 agenda for sustainable development, which includes universal health coverage (UHC), to which Japan attached great importance during the negotiation process.³ Achieving UHC requires comprehensive changes to systems, human resources, and public awareness. To catalyse such changes, leaders must commit to leave no one behind in the drive for the best attainable health gains. The Sustainable Development Goals (SDGs) have created an opportunity to connect sectors and empower individuals, families, and communities. It is crucial that we agree on a monitoring and evaluation framework so that the impact of UHC against investment is measurable and thus attainable.

Japan will host the first G7 Summit after the adoption of the SDGs in May, 2016. Alongside the G7 Health Minister's Meeting, and the Tokyo International Conference on African Development, Japan will create an opportunity for countries and partners to discuss concrete steps towards achieving new goals, while sharing Japan's relevant experiences, so that we can move forward together with this new agenda.

Japan's global health priorities are to construct a global health architecture that can respond to public health crises and to build resilient and sustainable health systems. To realise these goals, Japan has endorsed two new global health strategies: the Basic Design for Peace and Health⁴ and the Basic Guidelines for Strengthening Measures on Emerging Infectious Diseases.⁵ I would like to underline the importance of these priorities and foster succinct and relevant discussions during our G7 presidency in 2016.

First, in preparation for the G7 Summit, we will discuss how to address the challenges of public health emergencies. The existing global health architecture must be restructured to ensure prompt and effective responses to public health emergencies. Public and private partners, government, and civil society—at global, regional, country, and community levels—should reach agreement on their respective roles in advance of emergencies. Japan expects WHO to have the lead role in prompt detection and containment, especially in the early stages of a public health emergency, while acknowledging WHO's need for further reform and capacity strengthening. Japan is ready to support this reform process, including the launch of the Contingency Fund for Emergencies.⁶ Japan also fully supports the efforts of the World Bank's Pandemic Emergency Facility, and calls for coordination between WHO and the World Bank to ensure the two mechanisms have supplementary and complementary roles so that they increase efficiency and effectiveness in crises responses.

Second, we will discuss strategies to build resilient, sustainable national health systems. In the past 70 years, Japan's life expectancy increased by more than 30 years and, since the early 1980s, health outcomes have consistently been top ranked.⁷ These achievements are the result of the establishment of universal health insurance in 1961, favourable proximal determinants of health, such as healthy diet and access to clean water,



Japan's Prime Minister Shinzo Abe

and action on social determinants of health.⁷ Assuring equitable access to quality basic health care in Japan improved population health outcomes and boosted economic growth, social stability, equity, justice, and solidarity.⁸ Progress has been accomplished not only through socioeconomic development, but also through firm political will, even when countries have limited resources.⁹ Examples can be seen in countries such as Kenya, where a Japanese official development assistance loan is supporting the attainment of UHC.¹⁰

In pursuit of resilient and sustainable health systems, the International Health Regulations (IHR) also have a role in reducing the risk of emergencies and minimising their potential damage. In this context, we support the Global Health Security Agenda as a concrete mechanism to strengthen core country capacity stipulated in the IHR. Japan is well aware of the importance of the fight against communicable diseases, such as tuberculosis, as well as addressing the challenge of antimicrobial resistance.¹¹ We reiterate the importance of the One Health approach in the fight against antimicrobial resistance, and of supporting countries to comply with the WHO Global Action Plan on Antimicrobial Resistance,¹¹ as confirmed at the G7 Elmau Summit. Taking into account ever expanding global economic integration, especially in the Asia Pacific region, Japan is all the more responsible for addressing the threat of antimicrobial resistance as countries develop their own national action plans.

Moreover, Japan, the world's fastest-ageing society, is pioneering the response to the challenge of ageing by extending healthy life expectancy while maintaining a sustainable health system, on the basis of a life-course approach for all generations.^{4,12} *Health Care 2035*, a report by an advisory panel to the Health Minister of Japan, proposed a new health system for 2035 with the goal to deliver unmatched health outcomes through care that is both sustainable and contributes to prosperity in Japan and around the world.¹³

In strengthening health systems, we cannot afford to overlook common assets, such as health information systems and drug supply chains established by disease-specific approaches. For this reason, Japan aims to bring together expertise and resources, including those from disease-specific approaches, from donor countries and international organisations, including WHO, the World Bank, the Global Fund to Fight AIDS, Tuberculosis and

Malaria, and Gavi, the Vaccine Alliance, to support health-system strengthening in developing countries.

Japan has advocated for global health at previous summit meetings it hosted, including Kyushu-Okinawa in 2000 and Hokkaido-Toyako in 2008. Establishment of the Global Fund to Fight AIDS, Tuberculosis and Malaria in 2002 was a direct outcome of Japan's leadership on infectious disease in Okinawa. We have also led global health innovation through the new Japan Agency for Medical Research and Development and the Global Health Innovative Technology Fund.^{14,15} In addition, Japan has supported global resource mobilisation and private sector investment around poverty-related infectious disease, such as efforts towards polio eradication.

I reiterate that health issues are not purely the domestic concerns of individual countries. Health is a cross-border, global challenge. It is urgent that we all work to set up a framework for collaboration as soon as possible. At this crucial juncture for the future of global health, Japan will host an international conference, Universal Health Coverage in the New Development Era, on Dec 16, 2015, in Tokyo. In the lead-up to Japan's G7 presidency in 2016, this conference is expected to highlight global preparedness for health emergencies, as well as explore resilient and sustainable health systems under the SDGs. In a world more interconnected than ever before, leaders must strive to unite rather than divide, and enhance human security and peace through the pursuit of health and wellbeing for all. With the G7 presidency in 2016, Japan is determined to contribute further to galvanise renewed momentum for global health so that all people can receive the basic quality services they need, and are protected from health threats, without financial hardship. Through a series of meetings next year, I intend to prove Japan's firm commitment to a peaceful and healthier world.

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I am the Prime Minister of Japan. I declare no competing interests.

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Gene therapy for age-related macular degeneration



Age-related macular degeneration is the most common cause of untreatable blindness in the world, and its prevalence is increasing.¹ Current therapies for neovascular age-related macular degeneration aim to prevent growth of the abnormal retinal blood vessels that could leak and cause rapid visual loss in the later stages of the disease. This growth inhibition is achieved by regular injections into the eye of molecules that block the activity of vascular-endothelial growth factor (VEGF).² These drugs are expensive, and the requirement for regular and indefinite intraocular injections puts a substantial strain on health-care resources. In *The Lancet*, Elizabeth Rakoczy and colleagues³ present 1 year results from a phase 1 clinical trial to assess a single treatment, with gene therapy, as an alternative to regular injections for achieving long-term VEGF blockade.³

Rakoczy and colleagues used an adeno-associated viral (AAV) vector to deliver the gene encoding soluble Fms-related tyrosine kinase-1 (sFLT-1), a naturally occurring inhibitor of VEGF. A dose of 10^{10} vector genomes (vg) of rAAV.sFLT-1, increasing to 10^{11} vg, was administered by a single injection under the peripheral retina (avoiding the central macula) in two groups of three patients, with two control patients receiving no treatment. The hypothesis was that transduced cells would produce sufficient sFLT-1 protein to diffuse into the vitreous and inactivate VEGF.⁴ Treatment effects were assessed by a reduction in the need for further injections of the standard treatment (ranibizumab) and improvements in retinal anatomy during the 1 year study period. While there was no matched control group, comparisons with historical data from other studies were in keeping with a treatment effect from the procedure. There were no

safety concerns, such as retinal ischaemia or atrophy of the retinal tissue, which have been a concern with prolonged anti-VEGF therapy.⁵

Rakoczy and colleagues' trial is notable in exploring the use of gene therapy as a means of providing a so-called protein pump, which is particularly suited to the enclosed compartment of the eye. Although AAV gene therapy has shown promise for gene replacement in single-gene disorders,⁶ the use of gene therapy to reprogramme genetically normal cells of the retina to take on additional functions opens a new chapter in potential AAV applications. One of the very first trials of retinal gene therapy⁷ also used a viral vector as a pharmacological method for the sustained delivery of a therapeutic protein to block VEGF in age-related macular degeneration. The key difference with respect to the current trial³ is that the earlier study⁷ used an adenoviral vector to deliver the VEGF antagonist, which was predicted to have only a temporary effect. AAV vectors, in contrast, have evolved to evade the host immune system and have shown evidence of indefinite gene expression following human subretinal administration (figure).⁸

Other anti-VEGF approaches in clinical trials include administration of the AAV vector directly into the vitreous cavity rather than into the subretinal space (NCT01024998). Intravitreal injections are easier to perform, but most probably a higher vector dose would be needed and there could be more off-target effects due to transduction of retinal ganglion cells and a greater risk of inflammation.⁹ The study by Rakoczy and colleagues³ validates the subretinal approach. There are, however, outstanding questions, such as which

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