

characterised and accounted for in future assessments of rabies control strategies.

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Knowledge advances and gaps on the demand side of vaccination



Vaccination is one of the most successful and cost-effective interventions for preventing and controlling infectious diseases. In addition to providing direct protection for vaccinated individuals, vaccination also induces indirect protection for the community by slowing transmission of diseases.¹ This effect, in turn, reduces the risk of infection among susceptible individuals and helps to prevent disease outbreaks. However, the success of vaccines depends on high levels of vaccination uptake. Supply-side factors, such as inadequate access to vaccines, remain important contributors to suboptimal vaccination uptake.² But, ensuring that individuals decide to take-up available vaccines is an additional challenge. Several studies have shown that increased numbers of individuals globally are questioning vaccines, seeking alternative vaccination schedules, and deciding to delay or refuse vaccination.³

Encouragingly, there is growing international focus on the demand side of vaccination. Various international working groups have been established in this regard—one on vaccine hesitancy within WHO,⁴ one on vaccine

confidence within the US National Vaccines Advisory Committee,⁵ and one on vaccine demand under the leadership of UNICEF.⁶ The 2017 Assessment Report of the Global Vaccine Action Plan also recommended that all countries develop strategies to increase acceptance and demand for vaccination.² Furthermore, academic publications examining the scope and drivers of vaccine demand have increased substantially over the past decade,³ together with the number of systematic reviews synthesising this evidence (appendix).

As an emerging focus and field of research, it is timely to reflect on the knowledge advances that have been made and the current gaps requiring attention going forward. A first major development has been the depolarisation of individuals as either anti-vaccines or pro-vaccines. Research in this area has shed light on the porous continuum of vaccine attitudes and behaviours, thus challenging previous perspectives of a simple dichotomy between vaccine acceptance and rejection. Various terms have been developed to capture this spectrum: hesitancy, confidence, trust, acceptance, demand, and uptake. However, there is

See Online for appendix

considerable ambiguity and inconsistency surrounding the definitions and usage of these terms. For example, vaccine hesitancy has been described as a psychological state,⁷ a behaviour,⁸ and a decision making process.⁹ The terms used to capture the demand side of vaccination are often also used interchangeably, without due regard to their theoretical relevance and distinctions. Therefore, there is a need for greater precision and agreement surrounding the concepts being used.⁷ How we use and define concepts matter, shaping how we understand the problem and how we focus our intervention efforts. Conceptual precision and consistency is also essential for tracking trends over time, and for enhancing the comparability of research results.

A second substantial development has been the recognition that vaccine attitudes and decision-making behaviours are complex and context-specific, shaped by multiple psychological and social factors. This understanding has highlighted the limitations of traditional knowledge-deficit approaches within public health, which tend to assume that vaccination delays or refusals are primarily driven by inadequate knowledge. Various contrasting conceptual frameworks have been developed to understand these multiple influencing factors, beyond knowledge. For example, WHO⁸ has proposed a three C framework, including axes of confidence, complacency, and convenience, which has subsequently been extended by others to contain two additional Cs or axes (calculating risks and collective responsibility).¹⁰ By contrast, Peretti-Watel and colleagues have reformulated the C framework into a two-dimensional decision-making process that depends on people's commitment to the risk culture of modern society and on their trust in mainstream medicine.⁹ Alternative approaches have drawn on ecological models of health to categorise explanatory factors across different levels of individual, interpersonal, and contextual influence.⁸

Although diverse perspectives are productive for propelling debate, having several conceptual frameworks makes it difficult for those charged with addressing demand-related challenges. Therefore, there is a need to test, adapt, and potentially integrate existing models to facilitate the translation of knowledge into practice. Moreover, although available models have provided important insights into what factors influence vaccine decision making, few provide an understanding of

how these factors operate. Therefore, theory building is needed to explain how different explanatory factors function and interact to influence vaccination decisions. This is essential for the design of more theoretically grounded and tailored interventions that are centred around causal mechanisms, thus improving their effectiveness and cost-efficiency. Because vaccine decision making is inevitably complex, theory development in this area would benefit from a multidisciplinary approach, integrating knowledge from various intellectual fields.

A final important development has been the increased number of systematic reviews focusing on the scope and drivers of vaccine demand. Synthesising evidence across different vaccines, settings, and populations, these reviews have been instrumental in revealing the rising trend of vaccine hesitancy, delays, and refusals, which can be used to inform immunisation decision making. However, the evidence base in the field is heavily skewed towards high-income countries (appendix). Because vaccine demand-related issues are thought to be context specific, it is unclear whether findings from high-income countries can be appropriately generalised to other settings. Indeed, most low-income and middle-income countries face substantial structural barriers to vaccination and, therefore, the relationship between supply-side and demand-side factors is likely to be more complex than that in high-income countries. Consequently, increased research focusing on the demand side of vaccination is needed in low-income and middle-income countries. This will help to distinguish such issues from other reasons why individuals are not vaccinated in these settings and enhance our understanding of how the nature and drivers of demand-related factors vary (or not) across global settings. Ultimately, this is essential for enhancing the generalisability of vaccination causal models and for addressing the rising demand-related challenges facing immunisation programmes worldwide.

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Towards the elimination of HTLV-1 infection in Japan



The reported high prevalence of human T-cell leukaemia virus type 1 (HTLV-1) among the Aboriginal population in Australia triggered an open letter to WHO by Fabiola Martin and colleagues, urging action against HTLV-1 infection in May, 2018.¹ Japan is well known for having 1 million people living with HTLV-1 infection, the largest number in the world.^{2,3} HTLV-1 infection is concentrated in the southern islands of Kyushu and Okinawa, but it has also spread to urban areas such as Tokyo and Osaka because of internal migration. Given the large burden of HTLV-1 in Japan, the Government of Japan has maintained its strong commitment towards the elimination of HTLV-1 and has been a leader in implementing various policies to address HTLV-1 infection and related diseases.

Japan has been taking a leading role in advancing science regarding HTLV-1, from the identification of mechanisms of HTLV-1 transmission to the discovery and treatment of HTLV-1-related diseases, including adult T-cell leukaemia-lymphoma, HTLV-1-associated myelopathy and tropical spastic paraparesis (HAM-TSP), and various inflammatory disorders.^{4–6}

Japan was the first country to implement two main strategies for prevention of HTLV-1 transmission. For the prevention of mother-to-child transmission (MTCT) through breastfeeding, antenatal HTLV-1 antibody screening and the recommendation for mothers with positive results to refrain from breastfeeding have been implemented in the Nagasaki prefecture in Kyushu since 1987;⁷ and HTLV-1 antibody screening of all donated blood in Japan has been implemented by the Japanese Red Cross since 1986.³

Efforts towards the elimination of HTLV-1 were further accelerated after the establishment of the HTLV-1 Task Force and endorsement of the Comprehensive Measures for HTLV-1 by the Japanese Government in 2010. The Comprehensive Measures consist of five main pillars. First, routine HTLV-1 antibody testing was incorporated into antenatal pregnancy screening throughout Japan in 2010. Second, counselling was made available for people living with HTLV-1 infection and associated diseases, and training materials and courses for health-care providers and counsellors were organised. Third, the coordination of care for HTLV-1-associated diseases was strengthened, with better coordination between health-care facilities that care for patients with HTLV-1-associated diseases and the development of guidelines for the management of adult T-cell leukaemia-lymphoma and HAM-TSP. Fourth, the website of the Ministry of Health, Labour and Welfare was updated to provide information on HTLV-1 infection and associated diseases, and communication materials were developed and distributed to raise public awareness. Fifth, research on epidemiology, pathophysiology, diagnosis, and therapy was strategically promoted, with JP¥10 billion (approximately US\$9 million) specifically assigned on a recurring annual basis for the research of HTLV-1-associated diseases.

To promote these five main pillars of policy, the Comprehensive Measures introduced the establishment of the HTLV-1 Control Promotion Council, consisting of patient groups, scientists, health-care professionals,