

rise of flavivirus infections demands vaccines to protect people living in, and travelling to endemic countries. Lack of vaccine safety will dramatically affect the public trust in vaccines for flaviviruses and other diseases, as shown by the recent measles outbreak affecting thousands of unvaccinated children in the Philippines, after the risks of CYD-TDV dengue vaccine became apparent.¹¹ Vaccines are extremely safe and have saved millions of lives. The problems associated with the dengue vaccine CYD-TDV are therefore an unfortunate event. As a result, new tests are urgently needed to determine flavivirus serological status, ideally suitable for point-of-care testing to allow approaches that pair screening with vaccination.¹² However, the complexity of flaviviral immune interplay might require determination of other flaviviruses besides dengue, and at the very least semi-quantitative techniques including innovative tools for test interpretation that are currently entirely unavailable for point-of-care testing.

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- 1 Casey RM, Harris JB, Ahuka-Mundeke S, et al. Immunogenicity of fractional-dose vaccine during a yellow fever outbreak - final report. *N Engl J Med* 2019; **381**: 444–54.
- 2 Brady OJ, Osgood-Zimmerman A, Kassebaum NJ, et al. The association between Zika virus infection and microcephaly in Brazil 2015–2017: an observational analysis of over 4 million births. *PLoS Med* 2019; **16**: e1002755.
- 3 Wilder-Smith A, Hombach J, Ferguson N, et al. Deliberations of the Strategic Advisory Group of Experts on Immunization on the use of CYD-TDV dengue vaccine. *Lancet Infect Dis* 2019; **19**: e31–38.
- 4 Poland GA, Kennedy RB, Ovsyannikova IG, Palacios R, Ho PL, Kalil J. Development of vaccines against Zika virus. *Lancet Infect Dis* 2018; **18**: e211–19.
- 5 Rey FA, Stiasny K, Vaney MC, Dellarole M, Heinz FX. The bright and the dark side of human antibody responses to flaviviruses: lessons for vaccine design. *EMBO Rep* 2018; **19**: 206–24.
- 6 Pedroso C, Fischer C, Feldmann M, et al. Cross-protection of dengue virus infection against congenital Zika syndrome, northeastern Brazil. *Emerg Infect Dis* 2019; **25**: 1485–93.
- 7 Katzelnick LC, Gresh L, Halloran ME, et al. Antibody-dependent enhancement of severe dengue disease in humans. *Science* 2017; **358**: 929–32.
- 8 Sridhar S, Luedtke A, Langevin E, et al. Effect of dengue serostatus on dengue vaccine safety and efficacy. *N Engl J Med* 2018; **379**: 327–40.
- 9 Ministério da Saúde, Sinan Net. Dengue - notificações registradas no sistema de informação de agravos de notificação. <http://tabnet.datasus.gov.br/cgi/tabcgi.exe?sinanet/cnv/denguebr.def> 2007–13 (accessed June 4, 2019).
- 10 Ministério da Saúde, Sinan Net. Dengue - notificações registradas no sistema de informação de agravos de notificação. <http://tabnet.datasus.gov.br/cgi/deftohtm.exe?sinanet/cnv/denguebr.def> 2014–17 (accessed June 4, 2019).
- 11 Larson HJ, Hartigan-Go K, de Figueiredo A. Vaccine confidence plummets in the Philippines following dengue vaccine scare: why it matters to pandemic preparedness. *Hum Vaccin Immunother* 2019; **15**: 625–27.
- 12 Ariën KK, Wilder-Smith A. Dengue vaccine: reliably determining previous exposure. *Lancet Glob Health* 2018; **6**: e830–31.

Preparedness for emerging epidemic threats: a *Lancet Infectious Diseases* Commission



At any time, an emerging, lethal, and highly transmissible pathogen might pose a risk of being spread globally because of the interconnectedness of the global population.^{1,2} Emerging epidemic threats are occurring with increasing scale, duration, and effect, often disrupting travel and trade, and damaging both national and regional economies.^{3,4} Even geographically limited outbreaks such as the Ebola virus disease in Africa might have a global effect.

Preparing for epidemic threats is not a static or binary (prepared or unprepared) exercise, but a dynamic state reflecting the constantly changing world. Countries prepare in different ways based on their interpretation of disease risks and international agreements such as the International Health Regulations (IHR). The IHR were

introduced in 1969 to prevent spread of specific serious diseases between countries and set out preparedness measures at international borders to stop disease spread. The 2005 revisions to the IHR reflect changes across multiple dimensions, requiring countries to develop preparedness capacities to detect and respond to outbreaks where and when they occur, supported by international partners to respond when outbreaks cannot be contained locally.⁵ However, disruptive factors have emerged at a greater pace over the past decade, creating a new ecology that requires novel strategies for preparedness. These factors include dealing with the increasing human population density and connectivity, harnessing novel data streams and new technological advances to manage epidemics, mitigating false

	Disruptive factors	Examples of manifestations
Political and institutional	National governments; international agencies; non-governmental organisations and charities; corporate entities; academic institutions	Weakness in behavioural change guidance from national and international organisations; scarcity of sustainable leadership and financing in failed states leading to neglected or uncoordinated health systems; increasing duration and frequency of insecurity or conflict zones hindering efforts to recognise and respond to health threats; failure of countries to report disease outbreaks because of fear of economic consequences
Social	Travel patterns, migration, and interconnectivity; trade; technology and digital revolution, including those that affect human interaction; expansion and control of information; patterns of communication including social media; expectations and definition of expertise; social conflict and privacy	Failure of host countries to protect the health of refugees and migrants; epidemic of devastating rumours and fake news on social media due to increased digital connectivity; emergence of social influencers exerting influence on politicians and institutions; increased resistance and hesitancy within communities to health interventions because of opposition by local experts
Environment	Geography affecting biological diversity; planned and unplanned urbanisation; climate change; interaction between humans, animals, and vectors; human development; state of the economy; state of health systems	Climate change resulting in increased flooding with failed sanitation and safe water; altered distribution of zoonotic disease reservoirs and vectors; emerging zoonosis with increased agricultural production and human encroachment into animal environments; changing national priorities resulting in sharply reduced investment in health systems
Pathogenesis	Changing disease biomes; relationship between hosts and pathogens; pathogen evolution and changes; technologies such as synthetic biology, and the risks of manufacturing pathogens and their accidental or deliberate release; characteristics of a population such as underlying disease condition	Increased opportunities for mutation or reassortment of infectious agents; increasingly reduced effectiveness of conventional vaccines and therapeutics for prevention and treatment of diseases; failure of conventional control measures to break the chain of transmission of infectious agents

Table: Examples of disruptive factors and their manifestations that require mitigation for effective preparedness

information on social networks, to creating informal technical networks that can work together when political forces fail to do so.

Do the recent outbreaks of Ebola virus disease, Middle East respiratory syndrome coronavirus, and yellow fever reflect this changing context of disruptions requiring dynamic responses? These outbreaks show that countries are at various stages of preparedness, and many have underdeveloped preparedness plans and response capabilities with weak or non-existent strategies to mitigate disruptive factors.^{6,7} Many countries face severe difficulties in providing universal health coverage, for example, and might overlook timely investments for threats that demand greater health-care facility or workforce requirements.^{8,9} Other challenges include shifts in within-country and between-country cooperation, the evolving need for transdisciplinary, cross-sectoral approaches and social participation,^{2,3,8,9} and effective leadership, coordination, and financing of local national and international partners.¹⁰

Against this backdrop, the *Lancet Infectious Diseases* Commission on Preparedness for Emerging Epidemic Threats was formed in mid-2019 to examine the importance of this new ecology and its disruptive factors that have resulted in an underprepared world, whether current planning assumptions still hold, and what mitigation measures need to be introduced.

A sample of the new ecology, its disruptive factors, and how they manifest are shown in the table. Preparedness plans must take these factors into account to succeed and those that do not will not have the resilience and capability to fully respond. These factors are political and institutional factors that include influential stakeholders and decision-making forces; social factors that link individuals and communities, through exchange of goods and information, and building relationships that ensure societal cohesiveness; environmental factors that influence pathogens and hosts, contribute to biodiversity and how diseases emerge and spread, these factors affect interaction between humans, vertebrate animals, and arthropod vectors, and influence human development and health systems; and pathogenic factors that define the biological basis of epidemic emergence and antimicrobial resistance, host-pathogen interactions, and available interventions to address these epidemics.

The *Lancet Infectious Diseases* Commission will discuss disruptive factors and how preparedness planning must consider this new ecology by exploring current preparedness platforms and their vulnerability to disruptive factors; by addressing key disruptions, identifying possible solutions, and providing recommendations for countries to strengthen preparedness; by developing a multidisciplinary approach including

a strong role for social sciences and innovative technology; by challenging leaders and stakeholders to create sustainable preparedness platforms through collaborations and investment in established and novel recommendations; and by creating a community of practice to share new ideas and monitor outcomes.

To tackle the wide-ranging issues, the Commission has brought together experts from academic, public health, policy making, international, non-governmental, and corporate institutions. They bring local and global knowledge and experience, including policy-making and field response, human and animal health (including One Health) approaches, and novel developments in communications, information technology, analytics, public health, diagnostics, and therapeutics. The Commission aims to deliver the report by 2021 and will include key recommendations for countries and international stakeholders, and monitoring indicators to evaluate the effectiveness of preparedness initiatives over time.

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See Online for appendix

- 1 McCloskey B, Dar O, Zumla A, Heymann DL. Emerging infectious diseases and pandemic potential: status quo and reducing risk of global spread. *Lancet Infect Dis* 2014; **14**: 1001–10.
- 2 WHO. Global Preparedness Monitoring Board. A world at risk: annual report on global preparedness for health emergencies. Geneva: World Health Organization, 2019.
- 3 American Veterinary Medical Association. One Health: a new professional imperative. 2008. https://www.avma.org/KB/Resources/Reports/Documents/onehealth_final.pdf (accessed Nov 28, 2019).
- 4 The World Bank. From panic and neglect to investing in health security: financing pandemic preparedness at a national level (English). 2017. <http://documents.worldbank.org/curated/en/979591495652724770/From-panic-and-neglect-to-investing-in-health-security-financing-pandemic-preparedness-at-a-national-level> (accessed Nov 28, 2019).
- 5 WHO. International Health Regulations 2005. 2016. <https://www.who.int/ihr/publications/9789241580496/en/> (accessed Nov 28, 2019).
- 6 WHO. Global Health Observatory (GHO) data. 2019 <https://www.who.int/gho/ihr/en/> (accessed Nov 28, 2019).
- 7 Global Health Security Agenda. Implementing the Global Health Security Agenda: Progress and Impact from U.S. Government Investments. 2018. https://www.cdc.gov/globalhealth/healthprotection/resources/pdf/GHSA-Report_Feb-2018.pdf (accessed Nov 28, 2019).
- 8 Oshitani H, Kamigaki T, Suzuki A. Major issues and challenges of influenza pandemic preparedness in developing countries. *Emerg Infect Dis* 2008; **14**: 875–80.
- 9 Kluge H, Martín-Moreno JM, Emiroglu N, et al. Strengthening global health security by embedding the International Health Regulations requirements into national health systems. *BMJ Glob Health* 2018; **3** (suppl 1): e000656.
- 10 Jain V, Duse A, Bausch DG. Planning for large epidemics and pandemics: challenges from a policy perspective. *Curr Opin Infect Dis* 2018; **31**: 316–24.