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treatment of tuberculosis. New approaches to trial design, use of new drugs, and revisiting patient stratification might lead to shorter, effective treatment for tuberculosis.

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We declare no competing interests.

- Zumla AI, Gillespie SH, Hoelscher M, et al. New antituberculosis drugs, regimens, and adjunct therapies: needs, advances, and future prospects. *Lancet Infect Dis* 2014; **14**: 327–40.
- WHO. Priorities for tuberculosis research. 2013. http://apps.who.int/iris/bitstream/10665/85888/1/9789241505970_eng.pdf (accessed Nov 1, 2014).
- Johnson JL, Hadad DJ, Dietze R, et al. Shortening treatment in adults with noncavitary tuberculosis and 2-month culture conversion. *Am J Respir Crit Care Med* 2009; **180**: 558–63.
- A controlled trial of 3-month, 4-month, and 6-month regimens of chemotherapy for sputum-smear-negative pulmonary tuberculosis. Results at 5 years. Hong Kong Chest Service/Tuberculosis Research Centre, Madras/ British Medical Research Council. *Am Rev Respir Dis* 1989; **139**: 871–76.
- Ziganshina LE, Titarenko AF, Davies GR. Fluoroquinolones for treating tuberculosis (presumed drug-sensitive). *Cochrane Database Syst Rev* 2013; **6**: CD004795.
- Lounis N, Bentoucha A, Truffot-Pernot C, et al. Effectiveness of once-weekly rifapentine and moxifloxacin regimens against *Mycobacterium tuberculosis* in mice. *Antimicrob Agents Chemother* 2001; **45**: 3482–86.
- Jindani A, Harrison TS, Nunn AJ, et al. High-dose rifapentine with moxifloxacin for pulmonary tuberculosis. *N Engl J Med* 2014; **371**: 1599–608.
- Merle CS, Fielding K, Sow OB, et al. A four-month gatifloxacin-containing regimen for treating tuberculosis. *N Engl J Med* 2014; **371**: 1588–98.
- Gillespie SH, Crook AM, McHugh TD, et al. Four-month moxifloxacin-based regimens for drug-sensitive tuberculosis. *N Engl J Med* 2014; **371**: 1577–87.
- Jawahar MS, Banurekha VV, Paramasivan CN, et al. Randomized clinical trial of thrice-weekly 4-month moxifloxacin or gatifloxacin containing regimens in the treatment of new sputum positive pulmonary tuberculosis patients. *PLoS One* 2013; **8**: e67030.
- Phillips PP, Nunn AJ, Paton NI. Is a 4-month regimen adequate to cure patients with non-cavitary tuberculosis and negative cultures at 2 months? *Int J Tuberc Lung Dis* 2013; **17**: 807–09.
- Chang KC, Sterling TR, Yew WW. Are we ready to shorten the treatment duration for non-cavitary pulmonary tuberculosis? *Int J Tuberc Lung Dis* 2013; **17**: 712.
- Honeyborne I, Mtafya B, Phillips PP, et al. The molecular bacterial load assay replaces solid culture for measuring early bactericidal response to antituberculosis treatment. *J Clin Microbiol* 2014; **52**: 3064–67.
- Phillips PP, Gillespie SH, Boeree M, et al. Innovative trial designs are practical solutions for improving the treatment of tuberculosis. *J Infect Dis* 2012; **205** (suppl 2): S250–57.

Climate change and infectious disease: time for a new normal?

At present, there is a clarion call for action on climate change across the global health landscape.^{1,2} At the recent WHO-sponsored conference on health and climate (held in Geneva, Switzerland, on Aug 27–29, 2014) and the UN Climate Summit (New York, USA, on Sept 23, 2014), participants were encouraged to act decisively to change the current trajectory of climate disruption.³ Health inequalities, including those related to infectious diseases, have now been pushed to centre stage. This approach represents a step-change in thinking. But as we are urged toward collective action,² is it time to rethink our approach to research, especially in relation to climate change and infectious disease?

For a long time, climate change has been the proverbial unwanted guest at the global health table. Causal relations remain elusive to many researchers, even for infectious diseases with clear climate effects such as vector-borne, arboviral, and parasitic disease.⁴ An equally prevalent view was that climate change was the crucial game changer in terms of our understanding of infectious disease. Indeed, there

have been calls for global warming to be viewed as a health threat itself.⁵

Part of the problem is that much of the early research into climate change and infectious disease focused on proving how “coupled” or “decoupled” particular diseases are with climate effects.⁶ Thus, climate change was often viewed as a unique and discreet driver of disease.⁷ Unsurprisingly, this conceptualisation forged an evidence base that is both highly specific and often polarised.

Yet climate change is clearly an embedded context in which changes to the susceptibility and infectiousness of human and animal diseases—and thereby their emergence or transmission—occur. We know that climate change has direct and indirect effects on a range of diseases. Furthermore, climate disruption is likely to have multiplier effects between both diseases and drivers. Finally, climate warming could potentially forge a cascade of both biotic and abiotic events or factors leading to disease emergence and re-emergence. Such a cumulative or cascade effect could clearly set the scene for collective disease events in global health.



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These notions are not entirely new. In 1999, the International Red Cross predicted that climate change and poverty would trigger a decade of so-called super-disasters, including disease epidemics.⁸ More than two decades later, extreme weather events have caused a range of humanitarian crises. Although a cumulative or multiplier effect merging such events into a single super-disaster has not come to pass, the increasing frequency of these events raises the threat of such an occurrence. Similarly, the emergence of a range of global pandemics or zoonoses from severe acute respiratory syndrome to highly pathogenic avian influenza enables us to envision the potential effects on health services of multiple emerging infectious disease events.

From the outset, the identification of the forces behind such potential multiple disease events is likely to demand a deeper understanding of the inter-relationships and synergies between the myriad of factors important to change within the context of both human and animal health. Clearly in the context of multiple emerging infectious disease events, the additive effects of climate on a range of other drivers are what matters.

The recognition of key gaps in our knowledge has led to a call for transdisciplinary inquiries across global health.⁹ However, although such an approach is necessary, it is unlikely to be sufficient.¹⁰ Rather, to explore climate change as an embedded context demands that we explicate the synergies and inter-relationships between drivers, between diseases, and between both drivers and diseases. Ascertainment of the scope and direction of these interactions is an essential first step towards better elucidating the effect of climate change on infectious disease.

Therefore, perhaps it is time for a new “normal” in global health that views the human, wildlife, and livestock disease burden in any given geographical area as greater than the sum of its parts. In this approach, understanding the absence of a disease might be as important as identifying the specific factors driving disease emergence and transmission. Explorations of the collective disease burden across species might better

explain the role and interaction of climate than the current focus on specific drivers and individual diseases. In this approach, assessments of risk, vulnerabilities, and interactions across these collective versus absent disease states could begin to forge a wider understanding of the role and effect (both present and future) of climate change on disease.

To ascribe to such a wider framework is likely to only enhance, rather than limit, our understanding of the dynamics of infectious disease and climate change. Such an approach can certainly work in tandem with the recommendations from global conferences, meetings, and researchers.^{1,2,11} However, the creation of this new episteme will depend on our inherent flexibility to reach beyond existing constructs and explore absences in addition to emergences and synergies, and the direct drivers of infectious disease. The future is in our hands; is it time to forge a new normal?

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I declare no competing interests.

- 1 The Lancet. Climate change and health, action please not words. *Lancet* 2014; **384**: 1071.
- 2 Haines A, Ebi K, Smith K, Woodward A. Health risks of climate change: act now or pay later. *Lancet* 2014; **384**: 1073–75.
- 3 Chan M. Opening remarks on the conference on health and climate. WHO Conference on Health and Climate; Geneva, Switzerland; Aug 27–29, 2014.
- 4 Randolph S. Is expert opinion enough? A critical assessment of the evidence for potential impacts of climate change on tick-borne diseases. *Anim Health Res Rev* 2013; **14**: 133–37.
- 5 Costello A, Abbas, M, Allen A, et al. Managing the health effects of climate change. *Lancet* 2009; **373**: 1693–733.
- 6 McMichael A, Lindgren E. Climate change: present and future risk to health and necessary changes. *J Int Med* 2011; **270**: 401–13.
- 7 Woolhouse M, Gowtage-Sequeria S. Host range and emerging and re-emerging pathogens. *Emerg Infect Dis* 2005; **11**: 1842–47.
- 8 Red Cross. World Disasters Report 1999. Geneva: International Committee of the Red Cross, 1999.
- 9 Wilkinson K, Grant W, Green L, et al. Infectious diseases of animals and plants: an interdisciplinary approach. *Phil Trans R Soc B* 2011; **366**: 1933–42.
- 10 Jahn T, Bergmann M, Keil F. Transdisciplinarity: between mainstreaming and marginalization. *Ecol Econ* 2012; **79**: 1–10.
- 11 WHO. Health and climate conference plenary session. WHO Conference on Health and Climate; Geneva, Switzerland; Aug 29, 2014.