International Health Alerts 2017-4 Contents

International Health Alerts 2017-4 Abstracts

Sexual and Reproductive Health

Responses Practice Clinical updates: Diagnosis and management of postpartum haemorrhage
Chandraharan E. et al., edchandi@yahoo.co.uk

Postpartum haemorrhage remains the second leading direct cause of maternal deaths in the UK and the leading cause of maternal mortality in the world
Poor uterine tone accounts for about 80% of all cases of primary postpartum haemorrhage, whereas endometritis is the commonest cause of secondary postpartum haemorrhage presenting up to 12 weeks after delivery
Tranexamic acid is recommended for all women with atonic and traumatic postpartum haemorrhage as well as for ongoing haemorrhage during a caesarean section
Refer women with secondary postpartum haemorrhage after birth for ultrasonography to exclude retained products of conception or endometritis
Start broad spectrum antibiotics in women with secondary postpartum haemorrhage due to endometritis
Postpartum haemorrhage is a major cause of death during pregnancy and early motherhood, accounting for 25% of maternal deaths worldwide and is the second leading direct cause of maternal deaths in the UK. It is defined as blood loss of more than 500 mL from the female genital tract after delivery of the fetus (or >1000 mL after a caesarean section). Primary postpartum haemorrhage occurs within the first 24 hours of delivery, whereas secondary postpartum haemorrhage occurs between 24 hours and 12 weeks after delivery and is less common. For every maternal death due to postpartum haemorrhage, there are at least 10 "near-misses." Serious maternal morbidities include multiorgan failure, multiple blood transfusion, and peripartum hysterectomy. There have been recent advances in the management of postpartum haemorrhage secondary to coagulopathy and abnormal invasion of the placenta.
This review highlights the causes, diagnosis, and management of postpartum haemorrhage and is aimed at those involved in obstetric and postnatal care.

Where women go to deliver: understanding the changing landscape of childbirth in Africa and Asia
Montagu D. et al., Department of Epidemiology and Biostatistics, Global Health Sciences, University of California, San Francisco; dominic.montagu@ucsf.edu

Growing evidence from a number of countries in Asia and Africa documents a large shift towards facility deliveries in the past decade. These increases have not led to the improvements in health outcomes that were predicted by health policy researchers in the past. In light of this unexpected evidence, we have assessed data from multiple sources, including nationally representative data from 43 countries in Asia and Africa, to understand the size and range of changing delivery location in Asia and Africa. We have reviewed the policies, programs and financing experiences in multiple countries to understand the drivers of changing practices, and the consequences for maternal and neonatal health and the health

systems serving women and newborns. And finally, we have considered what implications changes in delivery location will have for maternal and neonatal care strategies as we move forward into the next stage of global action.

As a result of our analysis we make four major policy recommendations.

(1) An expansion of investment in mid-level facilities for delivery services and a shift away from low-volume rural delivery facilities.

(2) Assured access for rural women through funding for transport infrastructure, travel vouchers, targeted subsidies for services and residence support before and after delivery.

(3) Increased specialization of maternity facilities and dedicated maternity wards within larger institutions.

And (4) a renewed focus on quality improvements at all levels of delivery facilities, in both private and public settings.

Survival analysis of the association between antenatal care attendance and neonatal mortality in 57 low- and middle-income countries

Doku D.T. et al., School of Health Sciences, University of Tampere, Tampere, Finland. dokudavid@gmail.com

Background: Neonatal mortality is unacceptably high in most low- and middle-income countries (LMICs). In these countries, where access to emergency obstetric services is limited, antenatal care (ANC) utilization offers improved maternal health and birth outcomes. However, evidence for this is scanty and mixed. We explored the association between attendance for ANC and survival of neonates in 57 LMICs.

Methods: Employing standardized protocols to ensure comparison across countries, we used nationally representative cross-sectional data from 57 LMICs (N = 464 728) to investigate the association between ANC visits and neonatal mortality. Cox proportional hazards multivariable regression models and meta-regression analysis were used to analyse pooled data from the countries. Kaplan-Meier survival curves were used to describe the patterns of neonatal survival in each region.

Results: After adjusting for potential confounding factors, we found 55% lower risk of neonatal mortality [hazard ratio (HR) 0.45, 95% confidence interval (CI) 0.42–0.48] among women who met both WHO recommendations for ANC (first visit within the first trimester and at least four visits during pregnancy) in pooled analysis. Furthermore, meta-analysis of country-level risk shows 32% lower risk of neonatal mortality (HR 0.68, 95% CI 0.61–0.75) among those who met at least one WHO recommendation. In addition, ANC attendance was associated with lower neonatal mortality in all the regions except in the Middle East and North Africa.

Conclusions: ANC attendance is protective against neonatal mortality in the LMICs studied, although differences exist across countries and regions. Increasing ANC visits, along with other known effective interventions, can improve neonatal survival in these countries.

Child Health

News: WHO advises blanket anti-worming treatment for children despite lack of benefit
Nigel Hawkes

The World Health Organization has strongly recommended the mass treatment of hundreds of millions of children to eliminate worm infections, while admitting that evidence does not prove that it will do any good.

A Cochrane review published in 2015 by a team at the Liverpool School of Tropical Medicine found no evidence that eliminating intestinal worms by treating all children in an area where worms were endemic improved the children's average height, weight, or nutritional status. A Campbell review published in 2016 confirmed these findings.

Editorials: New cerebral findings in infants with congenital Zika syndrome

Nadia M Biassou, Division of Neuroradiology, Department of Radiology and Imaging Science, National Institutes of Health, Bethesda, MD, 20892, USA, biassoun@cc.nih.gov.

Calcification that resolves sets Zika apart from other congenital infections

Since the first outbreak of Zika virus infection in Uganda in 1947, the world has dealt with sporadic repeated outbreaks. But the most recent one in Brazil in 2015 was different. It appeared to be associated with an increased incidence of microcephaly among infants born to mothers infected with the virus during gestation, especially during the first trimester.

A series of seminal research papers convincingly correlated the presence of microcephaly with congenital Zika virus infection. The authors all described subcortical calcifications; abnormal development of central nervous system neurons, cortex, and white matter; and associated ventriculomegaly in affected infants. These findings were identified by both histopathological analyses and non-invasive neuroimaging.

In this issue, Aragao and colleagues) report new and important findings in the central nervous system on follow-up computed tomography (CT) scans from a series of 37 infants with confirmed or probable congenital Zika syndrome. Comparison of scans done soon after birth with follow-up scans done about one year later showed persistent evidence of cortical and white matter developmental abnormalities and subcortical calcifications, along with continued evolution of generalised cerebral volume loss and worsening ventriculomegaly. Microcephaly persisted in all infants.

Perhaps more importantly the authors report a surprising decrease in the overall number and size of subcortical calcifications at one year follow-up, which did not correlate with the degree of cerebral volume loss. Calcifications reduced in 34 infants, and, remarkably, disappeared altogether in one. These findings suggest that the sequelae of this strain of congenital Zika virus may be different from those of most other congenital infections (such as syphilis, toxoplasmosis, rubella, cytomegalovirus, herpesvirus, otherwise known as STORCH infections) in which bulky calcifications are often permanent.

The authors' longitudinal prospective study design allows within person comparison of neuroimaging findings and helps characterise the clinical course of congenital Zika syndrome, at least with respect to the appearance of cerebral pathology on non-invasive imaging. However, there at least three important caveats to consider. Firstly, this is a relatively small case series of just 37 infants, and confirmation is required. Secondly, these findings may be specific to the particular strain of Zika virus found in this region of Brazil, so the generalisability of the findings is unclear. Finally, as the authors state, none of the infants had follow-up magnetic resonance imaging scans, which limits a more detailed evaluation of the structural changes that may have occurred during follow-up. We are limited by the resolution and sensitivity of CT imaging (eg, we cannot tell whether these infants developed axonal changes).

Despite these caveats, the authors' intriguing findings will undoubtedly inspire more research to further characterise structural changes associated with the Brazilian strain of Zika virus and also to understand the underlying pathophysiological basis for these changes.

The authors report an intriguing hypothesis for their findings, informed by histological analyses of autopsy specimens from fetuses who died during different Zika outbreaks in Slovenia and Washington DC in the US. The specimens showed no evidence of inflammatory histological changes. Laboratory research in human cells and animal models also supports a non-inflammatory pathological mechanism of neuronal loss after Zika infection, and the authors hypothesise that the process involves non-inflammatory induced apoptosis of neuroprogenitor cells followed by phagocytosis by microglia (the brain's scavenger cells). They propose that calcium deposits are reduced by the same phaogcytic process.

Recent reports have described a non-inflammatory mechanism of neuronal injury for strains of Zika virus found in Asia, although these authors also suggest that a strain found in Africa may induce neuronal cell death through a classic inflammatory mechanism.

The pathophysiological hypothesis of Aragao and colleagues should encourage further research into the target cells affected and host's immune responses after gestational infections with the Brazilian strain of Zika virus. Their description of decreasing or complete resorption of calcifications in affected infants suggests that this imaging characteristic may be what sets congenital Zika syndrome apart from other congenital STORCH infections. Any implications for clinical improvement remain unclear.

For now, the most important conclusion from this study is that absence of subcortical calcifications on non-invasive neuroimaging should not be used to rule out a diagnosis of congenital Zika syndrome.

Analysis: Are the risks of treatment to cure a child with severe sickle cell disease too high?
de Montalembert M. et al., Department of Pediatrics, Reference Centre for Sickle Cell Disease, Hôpital Universitaire Necker-Enfants Malades, APHP, Paris, France. david.rees2@nhs.net

Haematopoietic stem cell transplantation from alternative donors is curative for children with sickle cell disease, but risk of death is high. David Rees and colleagues call for greater caution in its use. Curative treatment for sickle cell disease is potentially available to all patients using haematopoietic stem cell transplantation from alternative donors, but the risks of these procedures are very high. We don't know when these high risk transplants should be offered to children or how parents should be counselled to give appropriate consent

In high income countries, non-transplant treatments are being developed for sickle cell disease that are likely to improve prognosis. We need to develop safer transplants and to explore the ethics of offering high risk procedures to children with sickle cell disease and other chronic conditions. Sickle cell disease is one of the most common severe inherited conditions in the world. Around 300 000 babies are born with sickle cell disease each year, mostly in Africa, although there are roughly 100 000 affected people in the US and 50 000 in Europe. The prognosis for children born with the condition today varies enormously, particularly with geography: only about 20% of babies born in Africa survive to adulthood, whereas more than 93% of children survive to adulthood in Europe and the US, thanks to basic medical care, screening programmes, vaccinations, prophylactic antibiotics, blood transfusions, stroke prevention, and hydroxyurea. Median survival is 60 years in some high income countries, such as the UK

Neonatal sepsis
Shane AL et al., Division of Infectious Disease, Department of Pediatrics, Emory University School of Medicine and Children's Healthcare of Atlanta, Atlanta, GA, USA. ashane@emory.edu.

Neonatal sepsis is the cause of substantial morbidity and mortality. Precise estimates of neonatal sepsis burden vary by setting. Differing estimates of disease burden have been reported from high-income countries compared with reports from low-income and middle-income countries. The clinical manifestations range from subclinical infection to severe manifestations of focal or systemic disease. The source of the pathogen might be attributed to an in-utero infection, acquisition from maternal flora, or postnatal acquisition from the hospital or community. The timing of exposure, inoculum size, immune status of the infant, and virulence of the causative agent influence the clinical expression of neonatal sepsis. Immunological immaturity of the neonate might result in an impaired response to infectious agents. This is especially evident in premature infants whose prolonged stays in hospital and need for invasive procedures place them at increased risk for hospital-acquired infections. Clinically, there is often little difference between sepsis that is caused by an identified pathogen and sepsis that is caused by an unknown pathogen. Culture-independent diagnostics, the use of sepsis prediction scores, judicious antimicrobial use, and the development of preventive measures including maternal vaccines are ongoing efforts designed to reduce the burden of neonatal sepsis.

Research Methodology

Research Methods & Reporting: CONSORT-Equity 2017 extension and elaboration for better reporting of health equity in randomised trials
Welch V.A. et al., Methods Centre, Bruyère Research Institute, Ottawa, ON, Canada. vwelch@campbellcollaboration.org. CONSORT-Equity and Boston Equity Symposium

We outline CONSORT-Equity 2017 reporting standards, an extension to the CONSORT (Consolidated Standards of Reporting Trials) statement that aims to improve the reporting of intervention effects in randomised trials where health equity is relevant. Health inequities are unfair differences in health that can be avoided by reasonable action. We defined a randomised trial where health equity is relevant as one that assesses effects on health equity by evaluating an intervention focused on people experiencing social disadvantage or by exploring the difference in the effect of the intervention between two groups (or as a gradient across more than two groups) experiencing different levels of social disadvantage, or both. We held a consensus meeting with diverse potential users from high, middle, and low income countries, including knowledge users such as patients and methodologists. We discussed evidence for each proposed extension item from empirical studies, reviews, key informant interviews, and an online survey, aiming to improve clarity of reporting without imposing undue burden on authors. The new guidance contains equity extensions to 16 items from CONSORT 2010 plus one new item on research ethics reporting, with examples of good practice and a brief explanation and elaboration for each. Widespread uptake of this guidance for the reporting of trials where health equity is relevant will make it easier for decision makers to find and use evidence from randomised trials to reduce unfair inequalities in health. Summary points

The CONSORT statement provides a minimum set of 25 items to be reported with rationale and exemplars for all randomised trials
A multidisciplinary team used a consensus approach to develop CONSORT-Equity 2017, an extended CONSORT reporting guideline for better design and reporting of randomised trials where equity is relevant
CONSORT-Equity 2017 extends 16 items of the CONSORT statement and adds a new item on ethical concerns for transparently reporting information relevant to assessment of effects on health equity
The use of the CONSORT-Equity 2017 guideline will improve reporting of health equity in randomised trials and thereby facilitate greater use of this information in decision making

10 Best resources for community engagement in implementation research
Glandon D. et al., Johns Hopkins Bloomberg School of Public Health, Baltimore. dmglandon@jhu.edu

Implementation research (IR) focuses on understanding how and why interventions produce their effects in a given context. We identified a total of 59 resources by using a combination of online searches of the peer-reviewed and grey literature, as well as crowd-sourcing through the Health Systems Global platform. The authors then completed two rounds of rating the resources to identify the '10 best'. The resources were rated based on considerations of their relevance to IR, existence of an underlying conceptual framework, comprehensiveness of guidance, ease of application, and evidence of successful application in low- or middle-income countries or relevant contexts.
10 Best resources
- CARE Malawi. 2013. *The Community Score Card (CSC): A generic guide for implementing CARE's CSC process to improve quality of services*. Atlanta, Georgia: Cooperative for Assistance and Relief Everywhere, Inc. http://www.care.org/sites/default/files/documents/FP-2013-CARE_CommunityScoreCardToolkit.pdf
- CTSA Community Engagement Key Function Committee Task Force. 2011. *Principles of Community Engagement, Second Edition.* Bethesda, Maryland: National Institutes of Health. https://www.atsdr.cdc.gov/communityengagement/pdf/PCE_Report_508_FINAL.pdf
- Davies R, Dart J. 2005. *The 'Most Significant Change' Technique: A guide to its use*. www.mande.co.uk/docs/MSCGuide.htm
- Department of Environment and Primary Industries (DEPI), State of Victoria, Australia. 2014. The Engagement Toolkit, Version 4 - Effective Engagement: building relationships with community and other stakeholders. Melbourne, Australia: DEPI. http://www.dse.vic.gov.au/__data/assets/pdf_file/0003/105825/Effective_Engagement_4_-_Book_3_v3-01.pdf
- Douthwaite B, Alvarez S, Tehelen K, Cordoba D, Thiele G, Mackay R. 2008. Participatory impact pathway analysis: A practical method for project planning and evaluation. In: *Fighting poverty through sustainable water use*. Proceedings of the CGIAR Challenge Program on Water and Food 2nd International Forum on Water and Food, Vol. 4, Addis Ababa, Ethiopia, 10-14 November 2008, eds. R.S. Bayot and E. Humphreys; 31. Colombo, Sri Lanka: CGIAR Challenge Program on Water and Food. http://pipamethodology.pbworks.com/w/page/70283575/Home%20Page

- Holland J. 2013. *Who Counts? The Power of Participatory Statistics*. Institute of Development Studies. Warwickshire, UK: Practical Action Publishing. http://www.ids.ac.uk/publication/who-counts-the-power-of-participatory-statistics
- Norton A, Bird B, Brock K, Kakande M, Turk C. 2001. *A rough guide to PPAs: Participatory Poverty Assessment – an introduction to theory and practice*. London: Overseas Development Institute. https://www.odi.org/publications/1747-rough-guide-ppas-participatory-poverty-assessment-introduction-theory-practice
- Schiffer E. 2007. *Net-Map toolbox: influence mapping of social networks*. International Food Policy Research Institute. Paper presented at the Sunbelt Conference of the International Network of Social Network Analysis, Corfu, Greece, 01-06 May 2007. https://netmap.files.wordpress.com/2008/06/net-map-manual-long1.pdf
- WHO/TDR. 2014. *Implementation research toolkit*. Geneva, Switzerland: World Health Organization on behalf of the Special Programme for Research and Training in Tropical Diseases. http://www.who.int/tdr/publications/year/2014/9789241506960_workbook_eng.pdf
- Williams B, Hummelbrunner R. (2011). *Systems Concepts in Action: A Practitioner's Toolkit*. Stanford: Stanford University Press. http://www.sup.org/books/title/?id=18331

Malaria

The Impact of Introducing Malaria Rapid Diagnostic Tests on Fever Case Management: A Synthesis of Ten Studies from the ACT Consortium.
Bruxvoort KJ et al. London School of Hygiene & Tropical Medicine, London, United Kingdom.

Since 2010, the World Health Organization has been recommending that all suspected cases of malaria be confirmed with parasite-based diagnosis before treatment. These guidelines represent a paradigm shift away from presumptive antimalarial treatment of fever. Malaria rapid diagnostic tests (mRDTs) are central to implementing this policy, intended to target artemisinin-based combination therapies (ACT) to patients with confirmed malaria and to improve management of patients with nonmalarial fevers. The ACT Consortium conducted ten linked studies, eight in sub-Saharan Africa and two in Afghanistan, to evaluate the impact of mRDT introduction on case management across settings that vary in malaria endemicity and healthcare provider type. This synthesis includes 562,368 outpatient encounters (study size range 2,400-432,513). mRDTs were associated with significantly lower ACT prescription (range 8-69% versus 20-100%). Prescribing did not always adhere to malaria test results; in several settings, ACTs were prescribed to more than 30% of test-negative patients or to fewer than 80% of test-positive patients. Either an antimalarial or an antibiotic was prescribed for more than 75% of patients across most settings; lower antimalarial prescription for malaria test-negative patients was partly offset by higher antibiotic prescription. Symptomatic management with antipyretics alone was prescribed for fewer than 25% of patients across all scenarios. In community health worker and private retailer settings, mRDTs increased referral of patients to other providers. This synthesis provides an overview of shifts in case management that may be expected with mRDT introduction and highlights areas of focus to improve design and implementation of future case management programs.

Evaluation of Malaria Screening during Pregnancy with Rapid Diagnostic Tests Performed by Community Health Workers in Burkina Faso

Ruizendaal et al., Department of Medical Microbiology, Academic Medical Centre, Amsterdam, The Netherlands.

One of the current strategies to prevent malaria in pregnancy is intermittent preventive treatment with sulfadoxine-pyrimethamine (IPTp-SP). However, in order for pregnant women to receive an adequate number of SP doses, they should attend a health facility on a regular basis. In addition, SP resistance may decrease IPTp-SP efficacy. New or additional interventions for preventing malaria during pregnancy are therefore warranted. Because it is known that community health workers (CHWs) can diagnose and treat malaria in children, in this study screening and treatment of malaria in pregnancy by CHWs was evaluated as an addition to the regular IPTp-SP program. CHWs used rapid diagnostic tests (RDTs) for screening and artemether-lumefantrine was given in case of a positive RDT. Overall, CHWs were able to conduct RDTs with a sensitivity of 81.5% (95% confidence interval [CI] 67.9-90.2) and high specificity of 92.1% (95% CI 89.9-93.9) compared with microscopy. After a positive RDT, 79.1% of women received artemether-lumefantrine. When treatment was not given, this was largely due to the woman being already under treatment. Almost all treated women finished the full course of artemether-lumefantrine (96.4%). In conclusion, CHWs are capable of performing RDTs with high specificity and acceptable sensitivity, the latter being dependent on the limit of detection of RDTs. Furthermore, CHWs showed excellent adherence to test results and treatment guidelines, suggesting they can be deployed for screen and treat approaches of malaria in pregnancy.

Health Systems

Global Disease Detection-Achievements in Applied Public Health Research, Capacity Building, and Public Health Diplomacy, 2001-2016
Rao CY, et al.,

The Centers for Disease Control and Prevention has established 10 Global Disease Detection (GDD) Program regional centers around the world that serve as centers of excellence for public health research on emerging and reemerging infectious diseases. The core activities of the GDD Program focus on applied public health research, surveillance, laboratory, public health informatics, and technical capacity building. During 2015-2016, program staff conducted 205 discrete projects on a range of topics, including acute respiratory illnesses, health systems strengthening, infectious diseases at the human-animal interface, and emerging infectious diseases. Projects incorporated multiple core activities, with technical capacity building being most prevalent. Collaborating with host countries to implement such projects promotes public health diplomacy. The GDD Program continues to work with countries to strengthen core capacities so that emerging diseases can be detected and stopped faster and closer to the source, thereby enhancing global health security.

How do performance-based financing programmes measure quality of care? A descriptive analysis of 68 quality checklists from 28 low- and middle-income countries

Josephson E. et al., Sebastian Bauhoff, Center for Global Development (CGD), Washington, DC, USA sbauhoff@cgdev.org

This paper seeks to systematically describe the length and content of quality checklists used in performance-based financing programmes, their similarities and differences, and how checklists have evolved over time. We compiled a list of supply-side, health facility-based performance-based financing (PBF) programmes in low- and lower middle-income countries based on a document review. We then solicited PBF manuals and quality checklists from implementers and donors of these PBF mechanisms. We entered each indicator from each quality checklist into a database verbatim in English, and translated into English from French where appropriate, and categorized each indicator according to the Donabedian framework and an author-derived categorization. We extracted 8,490 quality indicators from 68 quality checklists across 32 PBF implementations in 28 countries. On average, checklists contained 125 indicators; within the same program, checklists tend to grow as they are updated. Using the Donabedian framework, 80% of indicators were structure-type, 19% process-type, and less than 1% outcome-type. The author-derived categorization showed that 57% of indicators relate to availability of resources, 24% to managing the facility and 17% assess knowledge and effort. There is a high degree of similarity in a narrow set of indicators used in checklists for common service types such as maternal, neonatal and child health. We conclude that performance-based financing offers an appealing approach to targeting specific quality shortfalls and advancing toward the Sustainable Development Goals of high quality coverage. Currently most indicators focus on structural issues and resource availability. There is scope to rationalize and evolve the quality checklists of these programs to help achieve national and global goals to improve quality of care.

Achieving accountability through maternal death reviews in Nigeria: a process analysis
de Kok B. et al., Department of Anthropology, University of Amsterdam. b.c.dekok@uva.nl

Maternal death reviews (MDRs) are part of the drive to increase accountability for maternal deaths and reduce their occurrence by identifying barriers to effective, quality care. However, conducting MDRs well is difficult; staff commitment and establishing a blame free environment are key challenges. By examining the communication strategies used in MDRs this study sought to understand how MDR members implement policy imperatives (e.g. 'no blame, no name') and manage the inevitable sensitivities of discussing a client's death in a multidisciplinary team. We observed and recorded four MDRs in Nigerian teaching hospitals and used conversation and discourse analysis to identify patterns in verbal and non-verbal interactions. MDRs were conducted in a structured way and had multidisciplinary representation. We grouped discursive strategies observed into three overlapping clusters: 'doing' no-name no-blame; fostering participation; and managing personal accountability. Within these clusters, explicit reminders, gentle enquiries and instilling a sense of togetherness were used in doing no-name, no-blame. Strategies such as questioning and invoking protocol were only partially successful in fostering participation. Regarding managing accountability, forms of communication which limit personal responsibility ('pass the buck') and resist passing the buck were observed. Detailed, lengthy eye witness accounts of dramatic events appeared to reduce staff's personal accountability. We conclude that interactional processes affect the meaningfulness of MDRs. In-depth, critical analysis depends on resisting 'passing the buck' by practitioners and chairs especially, who are also key to fostering participation and extracting value from multidisciplinary representation. Our

innovative methods provide detailed insights into MDRs as an interactional process, which can inform design of training aimed at enhancing MDR members' skills. However, given the multitude of systemic challenges we should also adjust our expectations of MDRs and the individual practitioners tasked to perform them in the name of enhancing accountability for maternal death reduction.

Municipal health services provision by local governments: a systematic review of experiences in decentralized Sub-Saharan African countries
Hilaire Zon, Milena Pavlova, Koiné Maxime Drabo, Wim Groot, National Laboratory of Public Health, Ministry of Health, Ouagadougou, Burkina Faso. hilairezon@yahoo.fr

'Four' types of decentralization are distinguished in health care: deconcentration when the shift in authority is to regional or district offices; devolution when the shift is to state, provincial or municipal governments; delegation when semi-autonomous agencies are granted new powers; and privatization when ownership is granted to private entities. This article systematically reviews the experiences of local governments of Sub-Saharan African countries with the provision of health services during and after decentralization reforms. The article highlights the achievements, challenges and issues associated with decentralization. The review shows that most countries have mainly focused on the process by enacting numerous policies, regulations and standards with mixed outcomes for health services delivery. Decentralization in general, and resource transfer from the central to local governments in particular, are a highly political issue that influences the health reform strategy on decentralization. The literature shows the complexity of implementing decentralization schemes which strongly impact the health service organization and delivery. The theory of decision space applied in a comparative analysis found that some functions, particularly financing, remain under the control of the central state. Despite the numerous challenges, this review identifies some good practices in resources transfer, key determinants being the type of decentralization and the government's will to make legislative and administrative changes required for the effectiveness of decentralization. The literature search, even though systematic, resulted in a limited number of relevant publications with evidence on the link between decentralization and health services delivery. This is a largely unexplored research area, especially the use of financial resources by local governments, the factors that drive local decision-making processes and the effects of decentralization on health care sector performance.

NCD's

The effect of physical activity on mortality and cardiovascular disease in 130 000 people from 17 high-income, middle-income, and low-income countries: the PURE study
Lear SA et al., Faculty of Health Sciences, Simon Fraser University, Burnaby and Division of Cardiology, Providence Health Care, Vancouver, BC, Canada. slear@providencehealth.bc.ca.

Background: Physical activity has a protective effect against cardiovascular disease (CVD) in high-income countries, where physical activity is mainly recreational, but it is not known if this is also observed in lower-income countries, where physical activity is mainly non-

recreational. We examined whether different amounts and types of physical activity are associated with lower mortality and CVD in countries at different economic levels. **Methods**: In this prospective cohort study, we recruited participants from 17 countries (Canada, Sweden, United Arab Emirates, Argentina, Brazil, Chile, Poland, Turkey, Malaysia, South Africa, China, Colombia, Iran, Bangladesh, India, Pakistan, and Zimbabwe). Within each country, urban and rural areas in and around selected cities and towns were identified to reflect the geographical diversity. Within these communities, we invited individuals aged between 35 and 70 years who intended to live at their current address for at least another 4 years. Total physical activity was assessed using the International Physical Activity Questionnaire (IPQA). Participants with pre-existing CVD were excluded from the analyses. Mortality and CVD were recorded during a mean of 6·9 years of follow-up. Primary clinical outcomes during follow-up were mortality plus major CVD (CVD mortality, incident myocardial infarction, stroke, or heart failure), either as a composite or separately. The effects of physical activity on mortality and CVD were adjusted for sociodemographic factors and other risk factors taking into account household, community, and country clustering. **Findings**: Between Jan 1, 2003, and Dec 31, 2010, 168 916 participants were enrolled, of whom 141 945 completed the IPAQ. Analyses were limited to the 130 843 participants without pre-existing CVD. Compared with low physical activity (<600 metabolic equivalents [MET] × minutes per week or <150 minutes per week of moderate intensity physical activity), moderate (600-3000 MET × minutes or 150-750 minutes per week) and high physical activity (>3000 MET × minutes or >750 minutes per week) were associated with graded reduction in mortality (hazard ratio 0·80, 95% CI 0·74-0·87 and 0·65, 0·60-0·71; p<0·0001 for trend), and major CVD (0·86, 0·78-0·93; p<0·001 for trend). Higher physical activity was associated with lower risk of CVD and mortality in high-income, middle-income, and low-income countries. The adjusted population attributable fraction for not meeting the physical activity guidelines was 8·0% for mortality and 4·6% for major CVD, and for not meeting high physical activity was 13·0% for mortality and 9·5% for major CVD. Both recreational and non-recreational physical activity were associated with benefits. **Interpretation**: Higher recreational and non-recreational physical activity was associated with a lower risk of mortality and CVD events in individuals from low-income, middle-income, and high-income countries. Increasing physical activity is a simple, widely applicable, low cost global strategy that could reduce deaths and CVD in middle age.

Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128·9 million children, adolescents, and adults
NCD Risk Factor Collaboration (NCD-RisC).

Background: Underweight, overweight, and obesity in childhood and adolescence are associated with adverse health consequences throughout the life-course. Our aim was to estimate worldwide trends in mean body-mass index (BMI) and a comprehensive set of BMI categories that cover underweight to obesity in children and adolescents, and to compare trends with those of adults. **Methods**: We pooled 2416 population-based studies with measurements of height and weight on 128·9 million participants aged 5 years and older, including 31·5 million aged 5-19 years. We used a Bayesian hierarchical model to estimate trends from 1975 to 2016 in 200 countries for mean BMI and for prevalence of BMI in the following categories for children and adolescents aged 5-19 years: more than 2 SD below the median of the WHO growth reference for children and adolescents (referred to as moderate

and severe underweight hereafter), 2 SD to more than 1 SD below the median (mild underweight), 1 SD below the median to 1 SD above the median (healthy weight), more than 1 SD to 2 SD above the median (overweight but not obese), and more than 2 SD above the median (obesity). **Findings**: Regional change in age-standardised mean BMI in girls from 1975 to 2016 ranged from virtually no change (-0·01 kg/m2 per decade; 95% credible interval -0·42 to 0·39, posterior probability [PP] of the observed decrease being a true decrease=0·5098) in eastern Europe to an increase of 1·00 kg/m2 per decade (0·69-1·35, PP>0·9999) in central Latin America and an increase of 0·95 kg/m2 per decade (0·64-1·25, PP>0·9999) in Polynesia and Micronesia. The range for boys was from a non-significant increase of 0·09 kg/m2 per decade (-0·33 to 0·49, PP=0·6926) in eastern Europe to an increase of 0·77 kg/m2 per decade (0·50-1·06, PP>0·9999) in Polynesia and Micronesia. Trends in mean BMI have recently flattened in northwestern Europe and the high-income English-speaking and Asia-Pacific regions for both sexes, southwestern Europe for boys, and central and Andean Latin America for girls. By contrast, the rise in BMI has accelerated in east and south Asia for both sexes, and southeast Asia for boys. Global age-standardised prevalence of obesity increased from 0·7% (0·4-1·2) in 1975 to 5·6% (4·8-6·5) in 2016 in girls, and from 0·9% (0·5-1·3) in 1975 to 7·8% (6·7-9·1) in 2016 in boys; the prevalence of moderate and severe underweight decreased from 9·2% (6·0-12·9) in 1975 to 8·4% (6·8-10·1) in 2016 in girls and from 14·8% (10·4-19·5) in 1975 to 12·4% (10·3-14·5) in 2016 in boys. Prevalence of moderate and severe underweight was highest in India, at 22·7% (16·7-29·6) among girls and 30·7% (23·5-38·0) among boys. Prevalence of obesity was more than 30% in girls in Nauru, the Cook Islands, and Palau; and boys in the Cook Islands, Nauru, Palau, Niue, and American Samoa in 2016. Prevalence of obesity was about 20% or more in several countries in Polynesia and Micronesia, the Middle East and north Africa, the Caribbean, and the USA. In 2016, 75 (44-117) million girls and 117 (70-178) million boys worldwide were moderately or severely underweight. In the same year, 50 (24-89) million girls and 74 (39-125) million boys worldwide were obese. **Interpretation**: The rising trends in children's and adolescents' BMI have plateaued in many high-income countries, albeit at high levels, but have accelerated in parts of Asia, with trends no longer correlated with those of adults.

Diabetes Trends in obesity and diabetes across Africa from 1980 to 2014: an analysis of pooled population-based studies
NCD Risk Factor Collaboration (NCD-RisC) – Africa Working Group Prof. Andre Pascal Kengne, Non-Communicable Diseases Research Unit, South African Medical Research Council, Cape Town. Andre.kengne@mrc.ac.za

Background: The 2016 Dar Es Salaam Call to Action on Diabetes and Other noncommunicable diseases (NCDs) advocates national multi-sectoral NCD strategies and action plans based on available data and information from countries of sub-Saharan Africa and beyond. We estimated trends from 1980 to 2014 in age-standardized mean body mass index (BMI) and diabetes prevalence in these countries, in order to assess the coprogression and assist policy formulation.
Methods: We pooled data from African and worldwide population-based studies which measured height, weight and biomarkers to assess diabetes status in adults aged 18 years. A Bayesian hierarchical model was used to estimate trends by sex for 200 countries and territories including 53 countries across five African regions (central, eastern, northern, southern and western), in mean BMI and diabetes prevalence (defined as either fasting plasma

glucose of 7.0 mmol/l, history of diabetes diagnosis, or use of insulin or oral glucose control agents).

Results: African data came from 245 population-based surveys (1.2 million participants) for BMI and 76 surveys (182 000 participants) for diabetes prevalence estimates. Countries with the highest number of data sources for BMI were South Africa (n = 17), Nigeria (n = 15) and Egypt (n = 13); and for diabetes estimates, Tanzania (n = 8), Tunisia (n = 7), and Cameroon, Egypt and South Africa (all n = 6). The age-standardized mean BMI increased from 21.0 kg/m2 (95% credible interval: 20.3–21.7) to 23.0 kg/m2 (22.7–23.3) in men, and from 21.9 kg/m2 (21.3–22.5) to 24.9 kg/m2 (24.6–25.1) in women. The age standardized prevalence of diabetes increased from 3.4% (1.5–6.3) to 8.5% (6.5–10.8) in men, and from 4.1% (2.0–7.5) to 8.9% (6.9–11.2) in women. Estimates in northern and southern regions were mostly higher than the global average; those in central, eastern and western regions were lower than global averages. A positive association (correlation coefficient ' 0.9) was observed between mean BMI and diabetes prevalence in both sexes in 1980 and 2014.

Conclusions: These estimates, based on limited data sources, confirm the rapidly increasing burden of diabetes in Africa. This rise is being driven, at least in part, by increasing adiposity, with regional variations in observed trends. African countries' efforts to prevent and control diabetes and obesity should integrate the setting up of reliable monitoring systems, consistent with the World Health Organization's Global Monitoring System Framework.

Global Burden of Disease

Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016.
GBD 2016 Risk Factors Collaborators.

Background: The Global Burden of Diseases, Injuries, and Risk Factors Study 2016 (GBD 2016) provides a comprehensive assessment of risk factor exposure and attributable burden of disease. By providing estimates over a long time series, this study can monitor risk exposure trends critical to health surveillance and inform policy debates on the importance of addressing risks in context. **Methods**: We used the comparative risk assessment framework developed for previous iterations of GBD to estimate levels and trends in exposure, attributable deaths, and attributable disability-adjusted life-years (DALYs), by age group, sex, year, and location for 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks from 1990 to 2016. This study included 481 risk-outcome pairs that met the GBD study criteria for convincing or probable evidence of causation. We extracted relative risk (RR) and exposure estimates from 22 717 randomised controlled trials, cohorts, pooled cohorts, household surveys, census data, satellite data, and other sources, according to the GBD 2016 source counting methods. Using the counterfactual scenario of theoretical minimum risk exposure level (TMREL), we estimated the portion of deaths and DALYs that could be attributed to a given risk. Finally, we explored four drivers of trends in attributable burden: population growth, population ageing, trends in risk exposure, and all other factors combined. **Findings**: Since 1990, exposure increased significantly for 30 risks, did not change significantly for four risks, and decreased significantly for 31 risks. Among risks that are leading causes of burden of disease, child growth failure and household air pollution showed the most significant declines, while metabolic risks, such as body-mass index and high fasting plasma glucose, showed significant increases. In 2016, at Level 3 of the hierarchy, the three

leading risk factors in terms of attributable DALYs at the global level for men were smoking (124·1 million DALYs [95% UI 111·2 million to 137·0 million]), high systolic blood pressure (122·2 million DALYs [110·3 million to 133·3 million], and low birthweight and short gestation (83·0 million DALYs [78·3 million to 87·7 million]), and for women, were high systolic blood pressure (89·9 million DALYs [80·9 million to 98·2 million]), high body-mass index (64·8 million DALYs [44·4 million to 87·6 million]), and high fasting plasma glucose (63·8 million DALYs [53·2 million to 76·3 million]). In 2016 in 113 countries, the leading risk factor in terms of attributable DALYs was a metabolic risk factor. Smoking remained among the leading five risk factors for DALYs for 109 countries, while low birthweight and short gestation was the leading risk factor for DALYs in 38 countries, particularly in sub-Saharan Africa and South Asia. In terms of important drivers of change in trends of burden attributable to risk factors, between 2006 and 2016 exposure to risks explains an 9·3% (6·9-11·6) decline in deaths and a 10·8% (8·3-13·1) decrease in DALYs at the global level, while population ageing accounts for 14·9% (12·7-17·5) of deaths and 6·2% (3·9-8·7) of DALYs, and population growth for 12·4% (10·1-14·9) of deaths and 12·4% (10·1-14·9) of DALYs. The largest contribution of trends in risk exposure to disease burden is seen between ages 1 year and 4 years, where a decline of 27·3% (24·9-29·7) of the change in DALYs between 2006 and 2016 can be attributed to declines in exposure to risks. **Interpretation**: Increasingly detailed understanding of the trends in risk exposure and the RRs for each risk-outcome pair provide insights into both the magnitude of health loss attributable to risks and how modification of risk exposure has contributed to health trends. Metabolic risks warrant particular policy attention, due to their large contribution to global disease burden, increasing trends, and variable patterns across countries at the same level of development. GBD 2016 findings show that, while it has huge potential to improve health, risk modification has played a relatively small part in the past decade.

Global, regional, and national age-sex specific mortality for 264 causes of death, 1980-2016: a systematic analysis for the Global Burden of Disease Study 2016.
GBD 2016 Causes of Death Collaborators.

Background: Monitoring levels and trends in premature mortality is crucial to understanding how societies can address prominent sources of early death. The Global Burden of Disease 2016 Study (GBD 2016) provides a comprehensive assessment of cause-specific mortality for 264 causes in 195 locations from 1980 to 2016. This assessment includes evaluation of the expected epidemiological transition with changes in development and where local patterns deviate from these trends. **Methods**: We estimated cause-specific deaths and years of life lost (YLLs) by age, sex, geography, and year. YLLs were calculated from the sum of each death multiplied by the standard life expectancy at each age. We used the GBD cause of death database composed of: vital registration (VR) data corrected for under-registration and garbage coding; national and subnational verbal autopsy (VA) studies corrected for garbage coding; and other sources including surveys and surveillance systems for specific causes such as maternal mortality. To facilitate assessment of quality, we reported on the fraction of deaths assigned to GBD Level 1 or Level 2 causes that cannot be underlying causes of death (major garbage codes) by location and year. Based on completeness, garbage coding, cause list detail, and time periods covered, we provided an overall data quality rating for each location with scores ranging from 0 stars (worst) to 5 stars (best). We used robust statistical methods including the Cause of Death Ensemble model (CODEm) to generate estimates for each location, year, age, and sex. We assessed observed and expected levels and trends of

cause-specific deaths in relation to the Socio-demographic Index (SDI), a summary indicator derived from measures of average income per capita, educational attainment, and total fertility, with locations grouped into quintiles by SDI. Relative to GBD 2015, we expanded the GBD cause hierarchy by 18 causes of death for GBD 2016. **Findings**: The quality of available data varied by location. Data quality in 25 countries rated in the highest category (5 stars), while 48, 30, 21, and 44 countries were rated at each of the succeeding data quality levels. Vital registration or verbal autopsy data were not available in 27 countries, resulting in the assignment of a zero value for data quality. Deaths from non-communicable diseases (NCDs) represented 72·3% (95% uncertainty interval [UI] 71·2-73·2) of deaths in 2016 with 19·3% (18·5-20·4) of deaths in that year occurring from communicable, maternal, neonatal, and nutritional (CMNN) diseases and a further 8·43% (8·00-8·67) from injuries. Although age-standardised rates of death from NCDs decreased globally between 2006 and 2016, total numbers of these deaths increased; both numbers and age-standardised rates of death from CMNN causes decreased in the decade 2006-16-age-standardised rates of deaths from injuries decreased but total numbers varied little. In 2016, the three leading global causes of death in children under-5 were lower respiratory infections, neonatal preterm birth complications, and neonatal encephalopathy due to birth asphyxia and trauma, combined resulting in 1·80 million deaths (95% UI 1·59 million to 1·89 million). Between 1990 and 2016, a profound shift toward deaths at older ages occurred with a 178% (95% UI 176-181) increase in deaths in ages 90-94 years and a 210% (208-212) increase in deaths older than age 95 years. The ten leading causes by rates of age-standardised YLL significantly decreased from 2006 to 2016 (median annualised rate of change was a decrease of 2·89%); the median annualised rate of change for all other causes was lower (a decrease of 1·59%) during the same interval. Globally, the five leading causes of total YLLs in 2016 were cardiovascular diseases; diarrhoea, lower respiratory infections, and other common infectious diseases; neoplasms; neonatal disorders; and HIV/AIDS and tuberculosis. At a finer level of disaggregation within cause groupings, the ten leading causes of total YLLs in 2016 were ischaemic heart disease, cerebrovascular disease, lower respiratory infections, diarrhoeal diseases, road injuries, malaria, neonatal preterm birth complications, HIV/AIDS, chronic obstructive pulmonary disease, and neonatal encephalopathy due to birth asphyxia and trauma. Ischaemic heart disease was the leading cause of total YLLs in 113 countries for men and 97 countries for women. Comparisons of observed levels of YLLs by countries, relative to the level of YLLs expected on the basis of SDI alone, highlighted distinct regional patterns including the greater than expected level of YLLs from malaria and from HIV/AIDS across sub-Saharan Africa; diabetes mellitus, especially in Oceania; interpersonal violence, notably within Latin America and the Caribbean; and cardiomyopathy and myocarditis, particularly in eastern and central Europe. The level of YLLs from ischaemic heart disease was less than expected in 117 of 195 locations. Other leading causes of YLLs for which YLLs were notably lower than expected included neonatal preterm birth complications in many locations in both south Asia and southeast Asia, and cerebrovascular disease in western Europe. **Interpretation**: The past 37 years have featured declining rates of communicable, maternal, neonatal, and nutritional diseases across all quintiles of SDI, with faster than expected gains for many locations relative to their SDI. A global shift towards deaths at older ages suggests success in reducing many causes of early death. YLLs have increased globally for causes such as diabetes mellitus or some neoplasms, and in some locations for causes such as drug use disorders, and conflict and terrorism. Increasing levels of YLLs might reflect outcomes from conditions that required high levels of care but for which effective treatments remain elusive, potentially increasing costs to health systems.

Measuring progress and projecting attainment on the basis of past trends of the health-related Sustainable Development Goals in 188 countries: an analysis from the Global Burden of Disease Study 2016

GBD 2016 SDG Collaborators.

Background: The UN's Sustainable Development Goals (SDGs) are grounded in the global ambition of "leaving no one behind". Understanding today's gains and gaps for the health-related SDGs is essential for decision makers as they aim to improve the health of populations. As part of the Global Burden of Diseases, Injuries, and Risk Factors Study 2016 (GBD 2016), we measured 37 of the 50 health-related SDG indicators over the period 1990-2016 for 188 countries, and then on the basis of these past trends, we projected indicators to 2030. **Methods**: We used standardised GBD 2016 methods to measure 37 health-related indicators from 1990 to 2016, an increase of four indicators since GBD 2015. We substantially revised the universal health coverage (UHC) measure, which focuses on coverage of essential health services, to also represent personal health-care access and quality for several non-communicable diseases. We transformed each indicator on a scale of 0-100, with 0 as the 2·5th percentile estimated between 1990 and 2030, and 100 as the 97·5th percentile during that time. An index representing all 37 health-related SDG indicators was constructed by taking the geometric mean of scaled indicators by target. On the basis of past trends, we produced projections of indicator values, using a weighted average of the indicator and country-specific annualised rates of change from 1990 to 2016 with weights for each annual rate of change based on out-of-sample validity. 24 of the currently measured health-related SDG indicators have defined SDG targets, against which we assessed attainment. **Findings**: Globally, the median health-related SDG index was 56·7 (IQR 31·9-66·8) in 2016 and country-level performance markedly varied, with Singapore (86·8, 95% uncertainty interval 84·6-88·9), Iceland (86·0, 84·1-87·6), and Sweden (85·6, 81·8-87·8) having the highest levels in 2016 and Afghanistan (10·9, 9·6-11·9), the Central African Republic (11·0, 8·8-13·8), and Somalia (11·3, 9·5-13·1) recording the lowest. Between 2000 and 2016, notable improvements in the UHC index were achieved by several countries, including Cambodia, Rwanda, Equatorial Guinea, Laos, Turkey, and China; however, a number of countries, such as Lesotho and the Central African Republic, but also high-income countries, such as the USA, showed minimal gains. Based on projections of past trends, the median number of SDG targets attained in 2030 was five (IQR 2-8) of the 24 defined targets currently measured. Globally, projected target attainment considerably varied by SDG indicator, ranging from more than 60% of countries projected to reach targets for under-5 mortality, neonatal mortality, maternal mortality ratio, and malaria, to less than 5% of countries projected to achieve targets linked to 11 indicator targets, including those for childhood overweight, tuberculosis, and road injury mortality. For several of the health-related SDGs, meeting defined targets hinges upon substantially faster progress than what most countries have achieved in the past. **Interpretation**: GBD 2016 provides an updated and expanded evidence base on where the world currently stands in terms of the health-related SDGs. Our improved measure of UHC offers a basis to monitor the expansion of health services necessary to meet the SDGs. Based on past rates of progress, many places are facing challenges in meeting defined health-related SDG targets, particularly among countries that are the worst off. In view of the early stages of SDG implementation, however, opportunity remains to take actions to accelerate progress, as shown by the catalytic effects of adopting the Millennium Development Goals after 2000. With the SDGs' broader, bolder development agenda, multisectoral commitments and investments are vital to make the health-related SDGs within reach of all populations.

Nations within a nation: variations in epidemiological transition across the states of India, 1990–2016 in the Global Burden of Disease Study

India State-level Disease Burden Initiative Collaborators

Background. 18% of the world's population lives in India, and many states of India have populations similar to those of large countries. Action to effectively improve population health in India requires availability of reliable and comprehensive state-level estimates of disease burden and risk factors over time. Such comprehensive estimates have not been available so far for all major diseases and risk factors. Thus, we aimed to estimate the disease burden and risk factors in every state of India as part of the Global Burden of Disease (GBD) Study 2016.

Methods. Using all available data sources, the India State-level Disease Burden Initiative estimated burden (metrics were deaths, disability-adjusted life-years [DALYs], prevalence, incidence, and life expectancy) from 333 disease conditions and injuries and 84 risk factors for each state of India from 1990 to 2016 as part of GBD 2016. We divided the states of India into four epidemiological transition level (ETL) groups on the basis of the ratio of DALYs from communicable, maternal, neonatal, and nutritional diseases (CMNNDs) to those from non-communicable diseases (NCDs) and injuries combined in 2016. We assessed variations in the burden of diseases and risk factors between ETL state groups and between states to inform a more specific health-system response in the states and for India as a whole.

Findings. DALYs due to NCDs and injuries exceeded those due to CMNNDs in 2003 for India, but this transition had a range of 24 years for the four ETL state groups. The age-standardised DALY rate dropped by 36·2% in India from 1990 to 2016. The numbers of DALYs and DALY rates dropped substantially for most CMNNDs between 1990 and 2016 across all ETL groups, but rates of reduction for CMNNDs were slowest in the low ETL state group. By contrast, numbers of DALYs increased substantially for NCDs in all ETL state groups, and increased significantly for injuries in all ETL state groups except the highest. The all-age prevalence of most leading NCDs increased substantially in India from 1990 to 2016, and a modest decrease was recorded in the age-standardised NCD DALY rates. The major risk factors for NCDs, including high systolic blood pressure, high fasting plasma glucose, high total cholesterol, and high body-mass index, increased from 1990 to 2016, with generally higher levels in higher ETL states; ambient air pollution also increased and was highest in the low ETL group. The incidence rate of the leading causes of injuries also increased from 1990 to 2016. The five leading individual causes of DALYs in India in 2016 were ischaemic heart disease, chronic obstructive pulmonary disease, diarrhoeal diseases, lower respiratory infections, and cerebrovascular disease; and the five leading risk factors for DALYs in 2016 were child and maternal malnutrition, air pollution, dietary risks, high systolic blood pressure, and high fasting plasma glucose. Behind these broad trends many variations existed between the ETL state groups and between states within the ETL groups. Of the ten leading causes of disease burden in India in 2016, five causes had at least a five-times difference between the highest and lowest state-specific DALY rates for individual causes.

Interpretation. Per capita disease burden measured as DALY rate has dropped by about a third in India over the past 26 years. However, the magnitude and causes of disease burden and the risk factors vary greatly between the states. The change to dominance of NCDs and injuries over CMNNDs occurred about a quarter century apart in the four ETL state groups. Nevertheless, the burden of some of the leading CMNNDs continues to be very high, especially in the lowest ETL states. This comprehensive mapping of inequalities in disease burden and its causes across the states of India can be a crucial input for more specific health

planning for each state as is envisioned by the Government of India's premier think tank, the National Institution for Transforming India, and the National Health Policy 2017.

Infectious Diseases

Local, national, and regional viral haemorrhagic fever pandemic potential in Africa: a multistage analysis.
Pigott DM. et al., Institute for Health Metrics and Evaluation, University of Washington, Seattle, WA, USA. sihay@uw.edu.

Background: Predicting when and where pathogens will emerge is difficult, yet, as shown by the recent Ebola and Zika epidemics, effective and timely responses are key. It is therefore crucial to transition from reactive to proactive responses for these pathogens. To better identify priorities for outbreak mitigation and prevention, we developed a cohesive framework combining disparate methods and data sources, and assessed subnational pandemic potential for four viral haemorrhagic fevers in Africa, Crimean-Congo haemorrhagic fever, Ebola virus disease, Lassa fever, and Marburg virus disease. **Methods**: In this multistage analysis, we quantified three stages underlying the potential of widespread viral haemorrhagic fever epidemics. Environmental suitability maps were used to define stage 1, index-case potential, which assesses populations at risk of infection due to spillover from zoonotic hosts or vectors, identifying where index cases could present. Stage 2, outbreak potential, iterates upon an existing framework, the Index for Risk Management, to measure potential for secondary spread in people within specific communities. For stage 3, epidemic potential, we combined local and international scale connectivity assessments with stage 2 to evaluate possible spread of local outbreaks nationally, regionally, and internationally.
Findings: We found epidemic potential to vary within Africa, with regions where viral haemorrhagic fever outbreaks have previously occurred (eg, western Africa) and areas currently considered non-endemic (eg, Cameroon and Ethiopia) both ranking highly. Tracking transitions between stages showed how an index case can escalate into a widespread epidemic in the absence of intervention (eg, Nigeria and Guinea). Our analysis showed Chad, Somalia, and South Sudan to be highly susceptible to any outbreak at subnational levels.
Interpretation: Our analysis provides a unified assessment of potential epidemic trajectories, with the aim of allowing national and international agencies to pre-emptively evaluate needs and target resources. Within each country, our framework identifies at-risk subnational locations in which to improve surveillance, diagnostic capabilities, and health systems in parallel with the design of policies for optimal responses at each stage. In conjunction with pandemic preparedness activities, assessments such as ours can identify regions where needs and provisions do not align, and thus should be targeted for future strengthening and support.

An update on Zika virus infection.
Baud D et al., Materno-fetal and Obstetrics Research Unit, Obstetric Service, Department "Femme-Mère-Enfant", University Hospital, Lausanne, Switzerland. Electronic address: david.baud@chuv.ch.

The epidemic history of Zika virus began in 2007, with its emergence in Yap Island in the western Pacific, followed in 2013-14 by a larger epidemic in French Polynesia, south Pacific,

where the first severe complications and non-vector-borne transmission of the virus were reported. Zika virus emerged in Brazil in 2015 and was declared a national public health emergency after local researchers and physicians reported an increase in microcephaly cases. In 2016, WHO declared the recent cluster of microcephaly cases and other neurological disorders reported in Brazil a global public health emergency. Similar clusters of microcephaly cases were also observed retrospectively in French Polynesia in 2014. In 2015-16, Zika virus continued its spread to cause outbreaks in the Americas and the Pacific, and the first outbreaks were reported in continental USA, Africa, and southeast Asia. Non-vector-borne transmission was confirmed and Zika virus was established as a cause of severe neurological complications in fetuses, neonates, and adults. This Review focuses on important updates and gaps in the knowledge of Zika virus as of early 2017.

Editorial: Cholera: ending a 50-year pandemic

The global annual cholera burden is estimated at around 2·9 million cases per year, resulting in 95 000 deaths. In 2017, these estimates could be far exceeded due to a number of devastating outbreaks, including those in Yemen and northern Nigeria. So far this year, 750 000 suspected cases, causing over 2000 deaths, have occurred in Yemen alone. Currently, there is concern about the risk of a cholera epidemic among Rohingya refugees in the Cox's Bazar region of Bangladesh. In response to this public health threat, the Global Task Force on Cholera Control (GTFCC), has brought together representatives from cholera-affected countries, donors, and technical experts to develop a Global Roadmap to 2030. Published on Oct 3, the document describes a multisectoral strategy that could reduce cholera deaths by 90% and eliminate the disease from a further 20 countries by 2030.

Cholera is endemic in 47 countries, particularly in areas where the water, sanitation and hygiene (WASH) infrastructure is poor. In these areas, children are particularly at risk. Epidemics occur both within and outside of endemic areas, often amid humanitarian crises, when WASH infrastructure breaks down or is overwhelmed. In situations where the population lacks immunity, a wider age range is affected, often with more severe clinical manifestations. Currently the worldwide cholera burden is high. 60–70% of cholera cases and deaths occur in endemic areas of Africa, which could increase as urbanisation, particularly the growth of slums, places increasing numbers at risk.

Fluid resuscitation as the core of cholera treatment is well established, but recent developments in disease prevention strategies underlie the GTFCC's roadmap. Improvements in WASH systems can eliminate cholera, but although the rate of return on investment is good, these are initially expensive, and the slow expansion of WASH provision has failed to tackle the burden of cholera and other water-borne diarrhoeal diseases. The pivotal change in cholera control has been the development of oral cholera vaccines (OCV), underpinned by an improved understanding of the mechanism of cholera immunity. In a series of landmark research developments over the past 10 years, the efficacy, safety, acceptability, and feasibility of these vaccines have been demonstrated. The creation of a growing global OCV stockpile by WHO, with long-term funding support from Gavi, signalled the step-change in cholera prevention strategies and, since 2013, 13 million vaccine doses have been deployed, mostly in the emergency control of epidemics.

The novelty of the GTFCC eradication strategy is based on three key axes. First, the emphasis on rapid response to outbreaks: controlling epidemics through community engagement, improved early warning surveillance, and the rapid delivery of cholera control kits, OCV, and WASH supplies. Second, the strategy implements a multisectoral approach in hotspots of

endemic cholera. OCV programmes will be used as a bridge, immediately reducing disease burden and mortality while long-term solutions are developed: sustainable WASH infrastructure, strengthened health systems able to anticipate epidemics, and strong community engagement required to stop transmission. The third axis is the coordination of operational support, local and global resourcing, and technical expertise delivered by GTFCC. Over the next 18 months, the task force will support six to eight countries to develop cholera control plans, develop an investment case on cholera, and create operational guidance on integrated prevention strategies ahead of a review meeting planned in 2019.
The technical ability to control cholera is within our capabilities. After 50 years, could the tide be finally turning on the seventh pandemic?

Seminar: Measles
Moss WJ

Measles is a highly contagious disease that results from infection with measles virus and is still responsible for more than 100 000 deaths every year, down from more than 2 million deaths annually before the introduction and widespread use of measles vaccine. Measles virus is transmitted by the respiratory route and illness begins with fever, cough, coryza, and conjunctivitis followed by a characteristic rash. Complications of measles affect most organ systems, with pneumonia accounting for most measles-associated morbidity and mortality. The management of patients with measles includes provision of vitamin A. Measles is best prevented through vaccination, and the major reductions in measles incidence and mortality have renewed interest in regional elimination and global eradication. However, urgent efforts are needed to increase stagnating global coverage with two doses of measles vaccine through advocacy, education, and the strengthening of routine immunisation systems. Use of combined measles-rubella vaccines provides an opportunity to eliminate rubella and congenital rubella syndrome. Ongoing research efforts, including the development of point-of-care diagnostics and microneedle patches, will facilitate progress towards measles elimination and eradication.

Poisoning

Effectiveness of household lockable pesticide storage to reduce pesticide self-poisoning in rural Asia: a community-based, cluster-randomised controlled trial
Pearson M et al., Pharmacology, Toxicology and Therapeutics, University/BHF Centre for Cardiovascular Science, and Centre for Pesticide Suicide Prevention, University of Edinburgh, Edinburgh, UK; South Asian Clinical Toxicology Research Collaboration (SACTRC), Faculty of Medicine, University of Peradeniya, Peradeniya, Sri Lanka

Background. Agricultural pesticide self-poisoning is a major public health problem in rural Asia. The use of safer household pesticide storage has been promoted to prevent deaths, but there is no evidence of effectiveness. We aimed to test the effectiveness of lockable household containers for prevention of pesticide self-poisoning.
Methods. We did a community-based, cluster-randomised controlled trial in a rural area of North Central Province, Sri Lanka. Clusters of households were randomly assigned (1:1), with a sequence computer-generated by a minimisation process, to intervention or usual practice (control) groups. Intervention households that had farmed or had used or stored

pesticide in the preceding agricultural season were given a lockable storage container. Further promotion of use of the containers was restricted to community posters and 6-monthly reminders during routine community meetings. The primary outcome was incidence of pesticide self-poisoning in people aged 14 years or older during 3 years of follow-up. Identification of outcome events was done by staff who were unaware of group allocation. Analysis was by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT1146496.

Findings. Between Dec 31, 2010, and Feb 2, 2013, we randomly assigned 90 rural villages to the intervention group and 90 to the control group. 27 091 households (114 168 individuals) in the intervention group and 26 291 households (109 693 individuals) in the control group consented to participate. 20 457 household pesticide storage containers were distributed. In individuals aged 14 years or older, 611 cases of pesticide self-poisoning had occurred by 3 years in the intervention group compared with 641 cases in the control group; incidence of pesticide self-poisoning did not differ between groups (293·3 per 100 000 person-years of follow-up in the intervention group vs 318·0 per 100 000 in the control group; rate ratio [RR] 0·93, 95% CI 0·80–1·08; p=0·33). We found no evidence of switching from pesticide self-poisoning to other forms of self-harm, with no significant difference in the number of fatal (82 in the intervention group vs 67 in the control group; RR 1·22, 0·88–1·68]) or non-fatal (1135 vs 1153; RR 0·97, 0·86–1·08) self-harm events involving all methods.

Interpretation. We found no evidence that means reduction through improved household pesticide storage reduces pesticide self-poisoning. Other approaches, particularly removal of highly hazardous pesticides from agricultural practice, are likely to be more effective for suicide prevention in rural Asia.

Health Policy

World Report: Health in Angola in the wake of the presidential election
Green A.

The progress that had been made to improve health for the Angolan people after a long civil war could be lost among an economic crisis.

Angola's economy has been devastated by a global collapse in oil prices and the country's health sector is suffering as a result, with widespread shortages of critical medicines and supplies. The health system had experienced uneven development in the wake of a decades-long civil war that ended in 2002, but the government and its partners had made advances in improving access to health services and reducing the spread of communicable diseases. Those accomplishments are now at risk.

Amid the economic downturn, the country has been struck by a series of humanitarian crises, including outbreaks of yellow fever and cholera and a spike in malaria cases. These emergencies, spurred by the already existing gaps, have combined with the rapid inflation to further decimate the country's health system, experts said.

It was no surprise that concerns about health care featured prominently in the country's August presidential election. The vote was especially significant because it would determine the replacement for President José Eduardo dos Santos, who held power for 38 years, and could potentially signal a new direction for the country.

Now Angolans will watch to see whether João Lourenço—the former defence minister and incoming president following the ruling People's Movement for the Liberation of Angola's (MPLA's) lopsided victory—can deliver on his promises to build new infrastructure, increase

the number of health workers, and improve disease control and preparedness, even as the economy continues to sputter.

Angola's civil war, which began immediately after it achieved independence from Portugal in 1975, pitted the MPLA against the National Union for the Total Independence of Angola (UNITA). By the time a lasting peace deal was struck between the two sides in 2002, much of the country had been decimated.

The 15 years since have been marked by the discovery of massive oil fields and the economic expansion it sparked. Until 2014, Angola had one of the world's fastest-growing economies—dependent almost entirely on crude oil sales—which vaulted the country into upper-middle-income status. Dos Santos' Government channelled this new wealth into glittering infrastructure, especially in the capital Luanda, which sits on the Atlantic Ocean.

Angola finished 164 of 176 countries in Transparency International's 2016 Corruption Perceptions Index.

Meanwhile, the government has expressed a commitment to improving social services like health, but experts said progress was uneven. There are now eight universities graduating doctors, up from one in the period after the civil war ended. But there are still less than 4500 physicians to cover a population of more than 28 million people, according to WHO.

Five new regional hospitals have opened in recent years, but the quality of service across the health system is extremely varied. In 2015, more than a fifth of the county's 2356 health facilities were not functioning, according to a UNICEF report, and many of those that did could not provide basic services.

And although state spending on health has increased over the years, from 1·7% of the country's gross domestic product in 2009 to 2·7% by 2014, according to WHO, the country's economic downturn and the devaluation of Angola's currency is now undercutting those increases. The country must now spend more to purchase the same number of drugs and commodities from the international market—even as the overall state budget shrinks.

At the same time, Angola's wealth meant traditional aid and development actors put their resources elsewhere.

The global health law trilogy: towards a safer, healthier, and fairer world
Gostin LO et al., O'Neill Institute for National and Global Health Law, Georgetown University, Washington, DC, USA. gostin@law.georgetown.edu.

Global health advocates often turn to medicine and science for solutions to enduring health risks, but law is also a powerful tool. No state acting alone can ward off health threats that span borders, requiring international solutions. A trilogy of global health law—the Framework Convention on Tobacco Control, International Health Regulations (2005), and Pandemic Influenza Preparedness Framework—strives for a safer, healthier, and fairer world. Yet, these international agreements are not well understood, and contain gaps in scope and enforceability. Moreover, major health concerns remain largely unregulated at the international level, such as non-communicable diseases, mental health, and injuries. Here, we offer reforms for this global health law trilogy.
Lessons for development of WHO norms:
The global health law trilogy, despite its weaknesses, offers proof that global health law can be a powerful tool. The new WHO Director-General should push for novel global health laws on major health hazards (eg, non-communicable diseases, mental health, and injuries) and new initiatives (eg, universal health coverage). The lessons learned from 21st century

international health law are that broad scope, robust compliance, inclusion of public and private actors, and sustainable financing are essential to success. Legal instruments must also be flexible, with the capacity to evolve with time, technological advancement, and scientific evidence. In an age of nationalistic populism, collective action remains crucial to ameliorate globalised health threats, helping to realise the right to health.

Global Development Goals

Editorial: Far from universal access to electricity

Sustainable development goal 7 ensures "access to affordable, reliable, sustainable and modern energy for all". Yet estimates from the UN conference on trade and development's Least Developed Countries Report 2017, published on Nov 22, show that in 2014, 1·06 billion people—54% of whom were living in the least developed countries (LDCs)—did not have access to electricity.

Access to electricity lays the foundations for exponential development. Lighting and energy to charge mobile phones increase security and promote education by extending time available to study. Electricity enables food refrigeration and can replace biomass fuels for heating and cooking, reducing carbon dioxide emissions and air pollution. It can be a vector towards the economic empowerment of women, by reducing the time spent on household tasks, and enables communication between dispersed cultural and indigenous groups. At the structural level, access to dependable electricity sources can be transformational, promoting agricultural development and opening the door to energy-expensive manufacturing. Frequent blackouts of unreliable electric grids also threaten health systems, spoil vaccines, and interrupt medical procedures.

To scale up modern energy provision without exacerbating import dependence, a domestic supply chain will need to emerge. However, 82% of people without access to electricity in LDCs live in rural areas. Connecting these remote areas to a centralised energy grid has been a key obstacle. Recent technological advancements have made decentralised renewable energy services, such as solar energy minigrid systems and solar-powered lamps and mobile device chargers, affordable and reliable. However, policy makers will have to weigh the cost and benefits of providing accelerated access to energy over the long-term strategy of expanding the centralised grid.

Achieving universal access to electricity will be difficult, and it will be expensive. LDCs have to increase their annual rate of electrification by 350%, otherwise only four of the 47 LDCs will achieve access to electricity by 2030. However, we cannot afford to leave LDCs behind. Careful investment by public funders can and must incentivise this transition.

What works in inclusion health: overview of effective interventions for marginalised and excluded populations.
Luchenski S et al., Centre for Public Health Data Science, Institute of Health Informatics, University College London, London, UK. s.luchenski@ucl.ac.uk.

Inclusion health is a service, research, and policy agenda that aims to prevent and redress health and social inequities among the most vulnerable and excluded populations. We did an evidence synthesis of health and social interventions for inclusion health target populations,

including people with experiences of homelessness, drug use, imprisonment, and sex work. These populations often have multiple overlapping risk factors and extreme levels of morbidity and mortality. We identified numerous interventions to improve physical and mental health, and substance use; however, evidence is scarce for structural interventions, including housing, employment, and legal support that can prevent exclusion and promote recovery. Dedicated resources and better collaboration with the affected populations are needed to realise the benefits of existing interventions. Research must inform the benefits of early intervention and implementation of policies to address the upstream causes of exclusion, such as adverse childhood experiences and poverty.

HIV

Nutritional status is the major factor affecting grip strength of African HIV patients before and during antiretroviral treatment
Filteau S et al., Faculty of Epidemiology and Population Health, London School of Hygiene & Tropical Medicine, London, UK.

Objectives: Low grip strength is a marker of frailty and a risk factor for mortality among HIV patients and other populations. We investigated factors associated with grip strength in malnourished HIV patients at referral to ART, and at 12 weeks and 2-3 years after starting ART.
Methods: The study involved HIV-infected Zambian and Tanzanian participants recruited to the NUSTART trial when malnourished (body mass index <18.5 kg/m2) and requiring ART. The relationship of grip strength to nutritional, infectious and demographic factors was assessed by multivariable linear regression at referral for ART (n = 1742) and after 12 weeks (n = 778) and 2-3 years of ART (n = 273).
Results: In analyses controlled only for sex, age and height, most nutrition and infection-related variables were associated with grip strength. However, in multivariable analyses, consistent associations were seen for fat-free mass index, mid-upper arm circumference, haemoglobin and systolic blood pressure, and a variable association with fat mass index in men. C-reactive protein and CD4 count had limited independent effects on grip strength, while receiving tuberculosis treatment was associated with weaker grip strength.
Conclusions: In this population of originally malnourished HIV patients, poor grip strength was more strongly and independently associated with nutritional than with infection and inflammation variables. Programmes to improve health and survival of HIV patients should incorporate nutritional assessment and management and could use grip strength as a functional indicator of improving nutrition.

The gendered micropolitics of hiding and disclosing: assessing the spread and stagnation of information on two new EMTCT policies in a Malawian village.
Verheijen J., Department of Cultural Anthropology and Development Sociology, Faculty of Social and Behavioural Sciences, Leiden University. jpeverheijen@gmail.com

Analysing why certain information spreads—or not—can be highly relevant for understanding an intervention's potential impact. Two recently implemented policy changes

related to EMTCT (elimination of mother-to-child transmission of HIV) in the Balaka district of Malawi give ample opportunity to assess how new information trickles through a targeted rural community. One of the policies entails the lifetime provision of ART (anti-retroviral therapy) to all HIV+ pregnant women—a governmental strategy to EMTCT first initiated in Malawi and now being expanded throughout the region. The second new policy concerns a pilot project in which women are financially rewarded for attending antenatal care and delivering in the hospital. An in-depth anthropological approach was used to assess what women in one village community know about the policy changes and how they had come to know about it. Although the policies were implemented more or less at the same time, awareness and knowledge levels among village women differed largely: In case of the first, awareness stagnated at the level of those who directly received the information from health professionals. In the case of the second, highly accurate and up-to-date knowledge had spread throughout the village community. I suggest three reasons for this divergence: (i) perceived talk-worthiness of (issues addressed by) the interventions, (ii) motives for hiding or disclosing involvement in either of the interventions and (iii) the visibility of each intervention, or in other words, the (im)possibility to hide involvement. I argue that these reasons for women's structural silence on one policy change and prompt sharing of information on another follow a distinctly gendered logic. The findings underline that the diffusion of new information is to a great extent shaped by the social particularities of the context in which it is introduced.

Editorial: The end of HIV: Still a very long way to go, but progress continues
Deeks S. et al., Department of Medicine, University of California, San Francisco; Steven.Deeks@ucsf.edu

Let's End It is the theme of this year's World AIDS Day, which falls on December 1. In the spirit of the event, PLOS Medicine is devoting **this special issue** to a discussion on advances in HIV prevention, treatment, and cure. Here, we describe many of the remaining barriers in ending the epidemic and highlight a number of accompanying studies that provide paths forward for overcoming some of these challenges. An estimated 75 million people have acquired HIV infection since the first reports of infection in the 1970s. Over 35 million people have died. With the advent of combination antiretroviral therapy (ART) in 1996, the life expectancy of HIV-infected adults in both high- and low income countries now approaches that of the general population but only in people who start therapy early in the disease process, who take therapy on a daily basis, and who have life-long access to drugs and monitoring of antiviral effects. The remarkably successful and ongoing global effort to provide treatment means that 20.9 million of the estimated 36.7 million people living with HIV globally are now receiving therapy.
ART not only improves health but it makes a person non-infectious; HIV-infected mothers on effective ART rarely transmit HIV to their infants, and HIV-infected adults on effective ART have been shown to not transmit the virus to their sexual partners. The significance of these achievements cannot be overstated: in the past 3 decades, global biomedical and public health programs not only discovered how HIV causes disease and developed effective strategies to prevent and treat the infection, but also built a global public health response that is unprecedented in its scale and effectiveness.
ART is the mainstay of treatment for people with HIV infection, and a crucial component of UNAIDS's global aims to achieve, by 2020, high proportions (90%) of people, respectively, tested for HIV infection, receiving ART, and with viral suppression (the so-called 90-90-90

initiative). Despite massive international efforts to achieve this goal, many challenges remain, particularly as many of the key affected populations are highly stigmatized and marginalized. In this issue of PLOS Medicine, various experts address aspects of the challenges facing infants, children and adolescents, female sex workers, transgender women, men who have sex with men (MSM), and people who inject drugs. In a Perspective on these issues, Wafaa El-Sadr and colleagues discuss the important topic of differentiated service delivery by which process interventions are combined and blended as appropriate for individual populations and settings.

For those who can access ART, residual concerns persist. For example, for reasons that remain largely undefined, HIV-infected adults on otherwise effective therapy have an excess risk of developing a number of non-AIDS complications. These complications include cardiovascular disease and kidney disease, and in a study based on the D:A:D collaboration, Mark Boyd and colleagues describe a multiplicative increase in events in people at high risk of cardiovascular and renal disease, which has implications for long-term management. Due in part to problems in retaining people in care and the apparent inability of ART to fully restore health, there is now a major global scientific effort to find a cure for HIV disease. Although ART prevents HIV from replicating, it does not eliminate a stable reservoir of infected cells that persists indefinitely. Approaches to reducing this reservoir include starting ART very early (before the reservoir is established) or reconstructing a new HIV-free immune system through hematopoietic stem cell transplantation. Timothy Henrich and colleagues report an extraordinary case of what happened when ART was initiated on essentially the first day an infection might be diagnosed, estimated to be roughly 10 days post-infection. The reservoir of replication-competent virus in this individual was several orders of magnitude lower than that observed when ART was started during chronic infection, but unfortunately the person was not cured as, even during this brief period of time, approximately 200 stably infected cells were established. A similar state of prolonged time to rebound, once ART was stopped, was achieved in an HIV-infected individual who received an allogeneic stem cell transplantation, as demonstrated by Andrew Badley and colleagues. For the initial 10 months off ART, virus was undetectable but eventually rebounded. Careful sequencing of the rebound virus did not match virus sequenced in blood prior to transplantation, highlighting the great challenge in understanding the main source of viral rebound off ART. Furthermore, it is now clear that simply reducing virus, even by several logs, will not lead to durable remission without ART.
The aspirational slogan Let's End It suggests that the goal of ending the epidemic is in our grasp and hinges only on our collective commitment to do so. However, the remarkable progress, activism, resources, ingenuity, and sheer fortitude that have brought us this far will be needed in at least equal measure to take us to the end. Only by harnessing the maximum available resources; innovating and implementing relentlessly; and applying the fruits of these processes without prejudice to all human populations, wherever they are needed, will we be able to start imagining an end to the HIV/AIDS epidemic.

Tuberculosis

Perspective: Improving tuberculosis diagnosis: Better tests or better healthcare? (Abridged)
Sumona Datta, et al. Imperial College London, and Wellcome Trust Imperial College Centre for Global Health Research, London, United Kingdom, carlton.evans@ifhad.org

Tuberculosis (TB) is a preventable and curable disease, but it kills more people than any other infection. Many people with TB are never diagnosed, and those who are diagnosed are often ill and contagious for many weeks or months before a diagnosis is made. Barriers to TB diagnosis are well described, often including poverty; stigma; marginalization; indolent, nonspecific symptoms; and poorly performing diagnostic tests. However, despite their central role in TB diagnosis, healthcare providers have been the subject of surprisingly little research. This week in PLOS Medicine, Sylvia and colleagues report findings with important implications for TB elimination. They trained and sent simulated "standardized patients," also known as "mystery clients," to healthcare providers at village clinics, township health centers, and county hospitals in China and found that the care provided in 274 consultations differed greatly from TB recommendations. The standardized patients reported classical TB symptoms, but only 15% of the providers mentioned TB, and only 41% of the providers tested or referred patients as recommended for TB. These differences between policy and practice were especially marked in the village clinics where most care was provided, and simulations suggested that a proposed system of managed referral with gatekeeping at the level of the village clinic would further reduce correct management, all of which makes for uncomfortable reading.

The "know-do gap"

Perhaps the most remarkable aspect of this study is that although the providers did not generally manage patients with typical TB symptoms as recommended, when village and township doctors were presented with the same symptoms described in clinical vignettes, 81% were managed according to TB recommendations. Thus, as in the authors' previous research, the providers generally seemed to know what policies recommended but in practice usually did something quite different. This "know-do gap" is a common observation in quality improvement studies, and research to understand the reasons for it is a priority for TB elimination. Closing the TB know-do gap will surely be more complex than knowledge transfer and should consider systems constraints, environmental factors, and personal experiences that impact human behavior.

Tuberculosis policy for the real world

Perhaps the greatest value of this research transcends the above points. A survey of TB research publications or the agenda for TB conferences give the impression that TB elimination depends upon the development of better tests and pills, whilst TB policy documents understandably describe a perfect model of optimal care. Sylvia and colleagues are to be commended for highlighting and characterizing the profound discord between these currently unrealizable goals, contrasted with the real-world experience of people with typical TB symptoms. TB principally affects poorer people who are cared for in poorly resourced places. Thus, to be effective, better tests, pills, and TB policies should be integrated with interventions addressing the factors limiting access to TB care and urgently require a greater emphasis on assessing and improving TB care as an integrated component of the basic healthcare that people receive in the real world.

Health Care in Humanitarian Crises

Evidence on public health interventions in humanitarian crises
Blanchet K et al.

This is the first in a Series of four papers about health in humanitarian crises.

Recognition of the need for evidence-based interventions to help to improve the effectiveness and efficiency of humanitarian responses has been increasing. However, little is known about the breadth and quality of evidence on health interventions in humanitarian crises. We describe the findings of a systematic review with the aim of examining the quantity and quality of evidence on public health interventions in humanitarian crises to identify key research gaps. We identified 345 studies published between 1980 and 2014 that met our inclusion criteria. The quantity of evidence varied substantially by health topic, from communicable diseases (n=131), nutrition (n=77), to non-communicable diseases (n=8), and water, sanitation, and hygiene (n=6). We observed common study design and weaknesses in the methods, which substantially reduced the ability to determine causation and attribution of the interventions. Considering the major increase in health-related humanitarian activities in the past three decades and calls for a stronger evidence base, this paper highlights the limited quantity and quality of health intervention research in humanitarian contexts and supports calls to scale up this research.

Other articles in this series
37 Public health information in crisis-affected populations: a review of methods and their use for advocacy and action

38 Recurrent failings of medical humanitarianism: intractable, ignored, or just exaggerated?