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## International Health Alerts 2018-3 Abstracts

### Child Health / iCCM

#### 1. *IJE* 2018;47(3):40–51

##### **Associations between key intervention coverage and child mortality: an analysis of 241 sub-national regions of sub-Saharan Africa**

Akachi Y et al., Swiss Tropical and Public Health Institute and University of Basel, Switzerland  
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**Background:** Reducing child mortality remains a key objective in the Sustainable Development Goals. Although remarkable progress has been made with respect to under-5 mortality over the last 25 years, little is known regarding the relative contributions of public health interventions and general improvements in socioeconomic status during this time period.

**Methods:** We combined all available data from the Demographic and Health Survey (DHS) to construct a longitudinal, multi-level dataset with information on subnational level key intervention coverage, household socioeconomic status and child health outcomes in sub-Saharan Africa. The dataset covers 562 896 child records and 769 region-year observations across 24 countries. We used multi-level multivariable logistics regression models to assess the associations between child mortality and changes in the coverage of 17 key reproductive, maternal, newborn and child health interventions such as bednets, water and sanitation infrastructure, vaccination and breastfeeding practices, as well as concurrent improvements in social and economic development.

**Results:** Full vaccination coverage was associated with a 30% decrease in the odds of child mortality [odds ratio (OR) 0.698, 95% confidence interval (CI) 0.564, 0.864], and continued breastfeeding was associated with a 24% decrease in the odds of child mortality (OR 0.759, 95% CI 0.642, 0.898). Our results suggest that changes in vaccination coverage, as well as increases in female education and economic development, made the largest contributions to the positive mortality trends observed. Breastfeeding was associated with child survival but accounts for little of the observed declines in mortality due to declining coverage levels during our study period.

**Conclusions:** Our findings suggest that a large amount of progress has been made with respect to coverage levels of key health interventions. Whereas all socioeconomic variables considered appear to strongly predict health outcomes, the same was true only for very few health coverage indicators.

#### 2. *Plos Med* 2018;15(7):e1002615

##### **Neurodevelopmental disorders in children aged 2–9 years: Population-based burden estimates across five regions in India**

Arora NK et al., The INCLIN Trust International, New Delhi, India <nkarora@inclintrust.org>

**Background.** Neurodevelopmental disorders (NDDs) compromise the development and attainment of full social and economic potential at individual, family, community, and country levels. Paucity of data on NDDs slows down policy and programmatic action in most developing countries despite perceived high burden.

**Methods and findings.** We assessed 3,964 children (with almost equal number of boys and girls distributed in 2–<6 and 6–9 year age categories) identified from five geographically diverse populations in India using cluster sampling technique (probability proportionate to population size). These were from the North-Central, i.e., Palwal (N = 998; all rural, 16.4% non-Hindu, 25.3% from scheduled caste/tribe [SC-ST] [these are considered underserved communities who are eligible for affirmative action]); North, i.e., Kangra (N = 997; 91.6% rural, 3.7% non-Hindu, 25.3% SC-ST); East, i.e., Dhenkanal (N = 981; 89.8% rural, 1.2% non-Hindu, 38.0% SC-ST); South, i.e., Hyderabad (N = 495; all urban, 25.7% non-Hindu, 27.3% SC-ST) and West, i.e., North Goa (N= 493; 68.0% rural, 11.4% non-Hindu, 18.5% SC-ST). All children were assessed for vision impairment (VI), epilepsy (Epi), neuromotor impairments including cerebral palsy (NMI-CP), hearing impairment (HI), speech and language disorders, autism spectrum disorders (ASDs), and intellectual disability (ID).

Furthermore, 6–9-year-old children were also assessed for attention deficit hyperactivity disorder

(ADHD) and learning disorders (LDs). We standardized sample characteristics as per Census of India 2011 to arrive at district level and all-sites-pooled estimates. Site-specific prevalence of any of seven NDDs in 2–<6 year olds ranged from 2.9% (95% CI 1.6–5.5) to 18.7% (95% CI 14.7–23.6), and for any of nine NDDs in the 6–9-year-old children, from 6.5% (95% CI 4.6–9.1) to 18.5% (95% CI 15.3–22.3). Two or more NDDs were present in 0.4% (95% CI 0.1–1.7) to 4.3% (95% CI 2.2–8.2) in the younger age category and 0.7% (95% CI 0.2–2.0) to 5.3% (95% CI 3.3–8.2) in the older age category. All-site-pooled estimates for NDDs were 9.2% (95% CI 7.5–11.2) and 13.6% (95% CI 11.3–16.2) in children of 2–<6 and 6–9 year age categories, respectively, without significant difference according to gender, rural/urban residence, or religion; almost one-fifth of these children had more than one NDD. The pooled estimates for prevalence increased by up to three percentage points when these were adjusted for national rates of stunting or low birth weight (LBW). HI, ID, speech and language disorders, Epi, and LDs were the common NDDs across sites. Upon risk modelling, noninstitutional delivery, history of perinatal asphyxia, neonatal illness, postnatal neurological/brain infections, stunting, LBW/prematurity, and older age category (6–9 year) were significantly associated with NDDs. The study sample was underrepresentative of stunting and LBW and had a 15.6% refusal. These factors could be contributing to underestimation of the true NDD burden in our population. **Conclusions.** The study identifies NDDs in children aged 2–9 years as a significant public health burden for India. HI was higher than and ASD prevalence comparable to the published global literature. Most risk factors of NDDs were modifiable and amenable to public health interventions.

## Communicable Diseases

3. *Am J TMH* 2018;98(6):1826-32

### **Estimating the Risk of Vertical Transmission of Dengue: A Prospective Study**

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The incidence of dengue worldwide is increasing rapidly. A better understanding of dengue transmission may help improve interventions against this major public health problem. The virus is mostly transmitted by vectors. There are, however, other modes of transmission, notably mother-to-child transmission or vertical transmission. We studied a prospective cohort of 54 women who had dengue while pregnant during the 2012-2013 epidemic in French Guiana to estimate the mother-to-child transmission rate and assess the clinical and biological presentation of neonatal dengue. The rate of vertical transmission was between 18.5% (95% confidence interval [CI]: 9.25-31.4) and 22.7% (95% CI: 11.5-37.8), depending on the calculation method used. Mother-to-child transmission occurred both in early and late pregnancy. There were 52 births, including three newborns who presented neonatal dengue with warning signs requiring platelet transfusion. This quantification of the mother-to-child transmission of dengue highlights three points: first, vertical transmission of dengue is not negligible; second, it is more frequent when maternal dengue occurs late during pregnancy near delivery; and third, reliable diagnostic tests must be used to allow the diagnosis of vertical transmission. Our findings indicate that if there is a known history of maternal dengue during pregnancy, or if there is fever during the 15 days before term, cord blood and placenta should be sampled after delivery and tested for the virus, and the newborn should be closely monitored during the postpartum period.

4. *Am J TMH* 2018;Jul 25. doi: 10.4269/ajtmh.18-0032. [Epub ahead of print]

### **Introductory Article on Global Burden and Epidemiology of Typhoid Fever**

Radhakrishnan A et al., Centre for Global Child Health, The Hospital for Sick Children, Toronto, Canada

This article is the introduction to a 12-paper supplement on global trends in typhoid fever. The Tackling Typhoid (T2) project was initiated in 2015 to synthesize the existing body of literature on typhoidal salmonellae and study national and regional typhoid fever trends. In addition to a global systematic review, eight case studies were undertaken to examine typhoid and paratyphoid fever

trends in endemic countries alongside changes in relevant contextual factors. Incidence variations exist both within and between regions with large subnational differences as well, suggesting that public health changes impacting typhoid and paratyphoid fevers in one setting may not have similar impacts in another. This supplement also brings to light the lack of national typhoid fever surveillance systems, inconsistencies in diagnostics, and the lack of typhoid fever associated morbidity and mortality data in many countries, making it difficult to accurately quantify and track burden of disease. To better understand typhoid fever there is a need for more high-quality data from resource-poor settings. The implementation of typhoid surveillance systems alongside the transition to blood-culture confirmation of cases, where possible, would aid in the improvement of data quality in low-income settings. The following supplement includes the results of our global systematic review, eight-country case study articles, a qualitative article informed by semistructured interviews, and a conclusion article on potential ways forward for typhoid control.

Other articles in the Serie:

- \* **Case Report: Typhoid Fever and Spotted Fever Group Rickettsiosis Presenting Concomitantly in an Indian Immigrant**
- \* **Typhoid Fever in Chile 1969-2012: Analysis of an Epidemic and Its Control**
- \* **The Control of Typhoid Fever in Vietnam**
- \* **Longitudinal Typhoid Fever Trends in India from 2000 to 2015**
- \* **Implementation of Interventions for the Control of Typhoid Fever in Low- and Middle-Income Countries**
- \* **Global Trends in Typhoidal Salmonellosis: A Systematic Review**
- \* **Typhoidal Salmonella Trends in Thailand**
- \* **Typhoid Fever: Tracking the Trend in Nigeria**
- \* **Typhoid Fever: Way Forward**
- \* **The Burden of Typhoid Fever in South Africa: The Potential Impact of Selected Interventions**

#### 5. [BMJ 2018;361:k2485](#)

News

#### **Sixty seconds on . . . Nipah virus**

Nipah what?

Move over Ebola and Zika, it's another scary zoonotic virus with a catchy name. Its reservoir is fruit bats and its home is in Asia. It recently broke out in northern Kerala in India, causing 18 confirmed infections and, so far, 17 deaths. And a good deal of panic.

Is this a new disease?

No, it was first identified in Malaysia in 1998, when bats infected pigs which then infected farmers. It killed 105 people, and more than a million pigs had to be slaughtered.

#### 6. [EID 2018;24\(9\):1748-50. doi: 10.3201/eid2409.170361](#)

#### **Symptomatic Dengue during Pregnancy and Congenital Neurologic Malformations**

Paixão ES et al., London School of Hygiene and Tropical Medicine, London, United Kingdom

Dengue virus infection during pregnancy increased the risk for any neurologic congenital anomaly in the infant by roughly 50% and for other congenital malformations of brain 4-fold. Our results show an association between dengue during pregnancy and congenital anomalies of the brain, suggesting that flaviviruses other than Zika virus are associated with such malformations.

#### 7. [Lancet 2018 Aug 17. pii: S0140-6736\(18\)31204-2. doi: 10.1016/S0140-6736\(18\)31204-2. \[Epub ahead of print\]](#)

#### **Leishmaniasis**

Burza S et al., Faculty of Infectious and Tropical Diseases, London School of Hygiene & Tropical Medicine, London, UK

Leishmaniasis is a poverty-related disease with two main clinical forms: visceral leishmaniasis and cutaneous leishmaniasis. An estimated 0.7-1 million new cases of leishmaniasis per year are reported

from nearly 100 endemic countries. The number of reported visceral leishmaniasis cases has decreased substantially in the past decade as a result of better access to diagnosis and treatment and more intense vector control within an elimination initiative in Asia, although natural cycles in transmission intensity might play a role. In east Africa however, the case numbers of this fatal disease continue to be sustained. Increased conflict in endemic areas of cutaneous leishmaniasis and forced displacement has resulted in a surge in these endemic areas as well as clinics across the world. WHO lists leishmaniasis as one of the neglected tropical diseases for which the development of new treatments is a priority. Major evidence gaps remain, and new tools are needed before leishmaniasis can be definitively controlled.

## Health Financing / Health Policy

### 8. *BMJ* 2018;361:k1716

#### **Analysis Universal Health Coverage**

Rethinking assumptions about delivery of healthcare: implications for universal health coverage

Das J et al., <ajha@hsph.harvard.edu>

Simply providing more resources for universal coverage is not enough to improve health, argue Jishnu Das and colleagues. We also need to ensure good quality of care

We are at an inflection point in global health. People are living longer, healthier lives than ever before, and we are rightly celebrating disease focused programmes that have greatly reduced or eradicated diseases such as smallpox and river blindness. Better diagnosis and treatment of HIV/AIDS, malaria, and other diseases have saved countless lives. Yet, as populations age and the burden of morbidity grows more complex, the limitations of programmes focused on single diseases have become increasingly evident.

Policy makers have shifted towards a broader “systems” view of universal health coverage (UHC)—one that seeks to provide all people with access to essential health services without financial hardship—as the defining approach to improve the health of the world’s poorest people. As one of the key focuses of the sustainable development goals, UHC has become a rallying principle for all countries. Indeed, the new director general of the World Health Organization has made UHC his top priority for the agency.

UHC can achieve its primary objective of creating better health, but to do so, patients must have access to services that are high quality. This idea of “effective UHC” is not new. It has long been recognised that translating healthcare into health outcomes requires that services meet some basic standard of quality. However, without systematic data on quality, the working assumption has been that adequately trained doctors and nurses with access to infrastructure (such as well equipped facilities and medicines) will be sufficient to guarantee adequate quality. Emerging data suggest that this understanding may be incorrect. For example, even when resources are in place in countries as far afield as Bangladesh and Uganda, health systems are unable to ensure that doctors show up to work, with absence rates ranging from 40% to 60%. And when they do, the services they provide are far below any acceptable standard.

### 9. *HPP* 2018;33(5):675–96

#### **The impact of cash transfers on social determinants of health and health inequalities in sub-Saharan Africa: a systematic review**

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Cash transfers (CTs) are now high on the agenda of most governments in low- and middle-income countries. Within the field of health promotion, CTs constitute a healthy public policy initiative as they have the potential to address the social determinants of health (SDoH) and health inequalities. A systematic review was conducted to synthesise the evidence on CTs’ impacts on SDoH and health inequalities in sub-Saharan Africa, and to identify the barriers and facilitators of effective CTs.

Twenty-one electronic databases and the websites of 14 key organizations were searched in addition to grey literature and hand searching of selected journals for quantitative and qualitative studies on CTs’

impacts on SDoH and health outcomes. Out of 182 full texts screened for eligibility, 79 reports that reported findings from 53 studies were included in the final review. The studies were undertaken within 24 CTs comprising 11 unconditional CTs (UCTs), 8 conditional CTs (CCTs) and 5 combined UCTs and CCTs. The review found that CTs can be effective in tackling structural determinants of health such as financial poverty, education, household resilience, child labour, social capital and social cohesion, civic participation, and birth registration. The review further found that CTs modify intermediate determinants such as nutrition, dietary diversity, child deprivation, sexual risk behaviours, teen pregnancy and early marriage. In conjunction with their influence on SDoH, there is moderate evidence from the review that CTs impact on health and quality of life outcomes. The review also found many factors relating to intervention design features, macro-economic stability, household dynamics and community acceptance of programs that could influence the effectiveness of CTs. The external validity of the review findings is strong as the findings are largely consistent with those from Latin America. The findings thus provide useful insights to policy makers and managers and can be used to optimise CTs to reduce health inequalities.

Key Messages:

- CTs have seen an exponential growth in sub-Saharan Africa (SSA) in the last decade with corresponding strengthening of evaluation, but there have been no systematic review of their impact on social determinants of health (SDoH) and health inequalities.
- Evidence from 53 studies covering 24 CTs indicate that CTs can tackle the SDoH in SSA.
- CTs have moderate impact on health and nutritional outcomes and this calls for the provision of supplementary services and behaviour change interventions to optimise their impact.
- The review identified a range of factors that may facilitate or hinder the performance and effectiveness of CTs especially the size of the transfer and irregularity of transfer payment.

#### 10. HPP 2018;33(6):715–28

##### **Priority setting for health in the context of devolution in Kenya: implications for health equity and community-based primary care**

McCollum R et al., Liverpool School of Tropical Medicine, Liverpool, UK  
<rosalindmccollum@gmail.com>

Devolution changes the locus of power within a country from central to sub-national levels. In 2013, Kenya devolved health and other services from central government to 47 new subnational governments (known as counties). This transition seeks to strengthen democracy and accountability, increase community participation, improve efficiency and reduce inequities. With changing responsibilities and power following devolution reforms, comes the need for priority-setting at the new county level. Priority-setting arises as a consequence of the needs and demand for healthcare resources exceeding the resources available, resulting in the need for some means of choosing between competing demands. We sought to explore the impact of devolution on priority-setting for health equity and community health services. We conducted key informant and in-depth interviews with health policymakers, health providers and politicians from 10 counties (n = 269 individuals) and 14 focus group discussions with community members based in 2 counties (n = 146 individuals). Qualitative data were analysed using the framework approach. We found Kenya's devolution reforms were driven by the need to demonstrate responsiveness to county contexts, with positive ramifications for health equity in previously neglected counties. The rapidity of the process, however, combined with limited technical capacity and guidance has meant that decision-making and prioritization have been captured and distorted for political and power interests. Less visible community health services that focus on health promotion, disease prevention and referral have been neglected within the prioritization process in favour of more tangible curative health services. The rapid transition in power carries a degree of risk of not meeting stated objectives. As Kenya moves forward, decision-makers need to address the community health gap and lay down institutional structures, processes and norms which promote health equity for all Kenyans.

#### 11. HPP 2018;33 Suppl. ii1–ii4

##### **Strengthening health system leadership for better governance: what does it take?**

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This editorial provides an overview of the six papers included in this special supplement on health leadership in Africa. Together the papers provide evidence of leadership in public hospital settings and of initiatives to strengthen leadership development. On the one hand, they demonstrate both that current leadership practices often impact negatively on staff motivation and patient care, and that contextual factors underpin poor leadership. On the other hand, they provide some evidence of the positive potential of new forms of participatory leadership, together with ideas about what forms of leadership development intervention can nurture new forms of leadership. Finally, the papers prompt reflection on the research needed to support the implementation of such interventions.

All the papers in the special supplement acknowledge that leadership and management can be seen as distinct, but related, areas of competence, and that health managers must always be ‘managers that lead’. Where managing entails a focus on coordinating resources and implementing activities to produce reliable performance, leading is about enabling those within and outside the system to face challenges and achieve results under complex conditions. /.../

Taken together these papers illuminate, first, the nature of existing public sector leadership practices in various African health system settings—showing that individual leaders often exercise power in quite authoritarian and hierarchical ways. They also clearly demonstrate that, across countries, the existing public sector context provides barriers to exercising the sort of participatory leadership called for by the Alliance for Health Policy and Systems Research (2016). /.../

... these papers suggest that it is not enough to train individuals; instead it is necessary to engage workplace teams in leadership development programmes—especially given the interdisciplinary requirements of health care and the need for intersectoral actions to promote health. It is also not enough to train leaders away from their workplaces; instead experiential skills and tacit knowledge must be developed within workplace teams. Finally, it is not enough to train people, it is necessary also to develop an organizational context that sustains new leadership practices. This requires both a critical mass of people with new leadership skills whose micropractices of governance work to change the context from within, and new structures of governance that spread decision-making power and encourage multiple forms of accountability. In other words, leadership and governance are intertwined. And strengthening leadership in complex health systems is a system-wide reform, requiring collaboration between current health system leaders, educators and other groups.

Article titles:

\* **Leadership and the functioning of maternal health services in two rural district hospitals in South Africa**

\* **Leadership styles in two Ghanaian hospitals in a challenging environment**

\* **Examining clinical leadership in Kenyan public hospitals through the distributed leadership lens**

\* **Strategic leadership capacity building for Sub-Saharan African health systems and public health governance: a multi-country assessment of essential competencies and optimal design for a Pan African DrPH**

\* **Achievements and challenges in developing health leadership in South Africa: the experience of the Oliver Tambo Fellowship Programme 2008–2014**

\* **Enabling relational leadership in primary healthcare settings: lessons from the DIALHS collaboration**

**12. HPP 2018;33(7):777–85**

**Public–private partnerships in practice: collaborating to improve health finance policy in Ghana and Kenya**

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Social health insurance (SHI), one mechanism for achieving universal health coverage, has become increasingly important in low- and middle-income countries (LMICs) as they work to achieve this goal. Although small private providers supply a significant proportion of healthcare in LMICs,

integrating these providers into SHI systems is often challenging. Public–private partnerships in health are one way to address these challenges, but we know little about how these collaborations work, how effectively, and why. Drawing on semi-structured interviews conducted with National Health Insurance (NHI) officials in Kenya and Ghana, as well as with staff from several international NGOs (INGOs) representing social franchise networks that are partnering to increase private provider accreditation into the NHIs, this article examines one example of public–private collaboration in practice. We found that interviewees initially had incomplete knowledge about the potential for cross-sector synergy, but both sides were motivated to work together around shared goals and the potential for mutual benefit. The public–private relationship then evolved over time through regular face-to-face interactions, reciprocal feedback, and iterative workplan development. This process led to a collegial relationship that also has given small private providers more voice in the health system. In order to sustain this relationship, we recommend that both public and private sector representatives develop formalized protocols for working together, as well as less formal open channels for communication. Models for aggregating small private providers and delivering them to government programmes as a package have potential to facilitate public–private partnerships as well, but there is little evidence on how these models work in LMICs thus far.

13. [Lancet 2018;391\(10136\):2236-71](#)

### **Measuring performance on the Healthcare Access and Quality Index for 195 countries and territories and selected subnational locations: a systematic analysis from the Global Burden of Disease Study 2016**

GBD 2016 Healthcare Access and Quality Collaborators

**Background:** A key component of achieving universal health coverage is ensuring that all populations have access to quality health care. Examining where gains have occurred or progress has faltered across and within countries is crucial to guiding decisions and strategies for future improvement. We used the Global Burden of Diseases, Injuries, and Risk Factors Study 2016 (GBD 2016) to assess personal health-care access and quality with the Healthcare Access and Quality (HAQ) Index for 195 countries and territories, as well as subnational locations in seven countries, from 1990 to 2016.

**Methods:** Drawing from established methods and updated estimates from GBD 2016, we used 32 causes from which death should not occur in the presence of effective care to approximate personal health-care access and quality by location and over time.

**Findings:** In 2016, HAQ Index performance spanned from a high of 97·1 (95% UI 95·8–98·1) in Iceland, followed by 96·6 (94·9–97·9) in Norway and 96·1 (94·5–97·3) in the Netherlands, to values as low as 18·6 (13·1–24·4) in the Central African Republic, 19·0 (14·3–23·7) in Somalia, and 23·4 (20·2–26·8) in Guinea-Bissau. The pace of progress achieved between 1990 and 2016 varied, with markedly faster improvements occurring between 2000 and 2016 for many countries in sub-Saharan Africa and southeast Asia, whereas several countries in Latin America and elsewhere saw progress stagnate after experiencing considerable advances in the HAQ Index between 1990 and 2000. Striking subnational disparities emerged in personal health-care access and quality, with China and India having particularly large gaps between locations with the highest and lowest scores in 2016. In China, performance ranged from 91·5 (89·1–93·6) in Beijing to 48·0 (43·4–53·2) in Tibet (a 43·5-point difference), while India saw a 30·8-point disparity, from 64·8 (59·6–68·8) in Goa to 34·0 (30·3–38·1) in Assam. Japan recorded the smallest range in subnational HAQ performance in 2016 (a 4·8-point difference), whereas differences between subnational locations with the highest and lowest HAQ Index values were more than two times as high for the USA and three times as high for England. State-level gaps in the HAQ Index in Mexico somewhat narrowed from 1990 to 2016 (from a 20·9-point to 17·0-point difference), whereas in Brazil, disparities slightly increased across states during this time (a 17·2-point to 20·4-point difference). Performance on the HAQ Index showed strong linkages to overall development, with high and high-middle SDI countries generally having higher scores and faster gains for non-communicable diseases. Nonetheless, countries across the development spectrum saw substantial gains in some key health service areas from 2000 to 2016, most notably vaccine-preventable diseases. Overall, national performance on the HAQ Index was positively associated with higher levels of total health spending per capita, as well as health systems inputs, but these relationships were quite heterogeneous, particularly among low-to-middle SDI countries.

**Interpretation:** GBD 2016 provides a more detailed understanding of past success and current challenges in improving personal health-care access and quality worldwide. Despite substantial gains since 2000, many low-SDI and middle-SDI countries face considerable challenges unless heightened policy action and investments focus on advancing access to and quality of health care across key health services, especially non-communicable diseases. Stagnating or minimal improvements experienced by several low-middle to high-middle SDI countries could reflect the complexities of re-orienting both primary and secondary health-care services beyond the more limited foci of the Millennium Development Goals. Alongside initiatives to strengthen public health programmes, the pursuit of universal health coverage hinges upon improving both access and quality worldwide, and thus requires adopting a more comprehensive view-and subsequent provision-of quality health care for all populations.

14. *TMIH* 2018;23(7):806-13

### **Can community health workers identify omphalitis? A validation study from Southern Province, Zambia**

Herlihy JM et al., Department of Pediatrics, School of Medicine, University of California Davis, Sacramento, CA, USA

**Objective:** Omphalitis, or umbilical cord infection, is an important cause of newborn morbidity and mortality in low-resource settings. We tested an algorithm that task-shifts omphalitis diagnosis to community-level workers in sub-Saharan Africa.

**Methods:** Community-based field monitors and Zambian paediatricians independently evaluated newborns presenting to health facilities in Southern Zambia using a signs and symptoms checklist. Responses were compared against the paediatrician's gold standard clinical diagnosis.

**Results:** Of 1009 newborns enrolled, 6.2% presented with omphalitis per the gold standard clinical diagnosis. Paediatricians' signs and symptoms with the highest sensitivity were presence of pus (79.4%), redness at the base (50.8%) and newborn flinching when cord was palpated (33.3%). The field monitor's signs and symptoms answers had low correlation with paediatrician's answers; all signs and symptoms assessed had sensitivity <16%.

**Conclusion:** Despite extensive training, field monitors could not consistently identify signs and symptoms associated with omphalitis in the sub-Saharan African setting.

## **HIV / AIDS**

15. *Lancet* 2018;391(10143):2296

### **World Report**

### **Changes to dolutegravir policy in several African countries**

Nakkazi E

Kenya has officially banned the use of the antiretroviral dolutegravir by HIV- positive women of reproductive age. Many governments in Africa had been transitioning towards dolutegravir- based regimens, which have been shown to be better than other regimens, to treat their HIV-positive populations, but some countries are now slowing the roll-out of the programmes, as they await the results a the study from Botswana.

On May 18, WHO issued recommendations for dolutegravir use by women of childbearing age living with HIV, after a preliminary unscheduled analysis of an ongoing observational study in Botswana found a significantly increased risk of neural tube defects in children born to women taking dolutegravir at the time of conception. The results of the study, which are needed to confirm or dispel these observations, are expected in early 2019.

The Kenyan Ministry of Health has stated that an efavirenz-based regimen is now the preferred first-line treatment for women of childbearing age (aged 15–49 years). Adolescents and men on efavirenz-based regimen will continue to be transitioned to dolutegravir-based regimens. According to local press reports, in a circular to the county health directors, Director of Medical Services Jackson Kioko said that dolutegravir should no longer be prescribed to pregnant and breastfeeding women.

A letter from the National Empowerment Network of People Living with HIV/AIDS in Kenya said the ministry is making decisions without meaningfully engaging the people living with HIV and women of reproductive age who are likely to be affected.

Uganda's roll-out of dolutegravir-based regimens to all eligible candidates by December, 2018, is to be delayed. Treatment guidelines will be modified to administer dolutegravir-based regimens to men, postmenopausal women, and women of reproductive age using long-term family planning only.

Joshua Musinguzi, manager of the AIDS Control Programme at the Ministry of Health of Uganda, said that 50% of the people living with HIV in Uganda will fall outside of the eligible group.

Botswana is also exercising caution as they prospectively look into whether more cases will confirm or dispel the preliminary findings.

"We are human and our lives matter too", said Martha Akello, communications officer for the International Community of Women Living with HIV Eastern Africa. Instead, Akello said WHO and health systems should provide women with comprehensive information, routine pregnancy tests, access to long-term contraception, counselling, and support.

"Women are not homogeneous", she said. "They are capable of making choices but need to be supported through this process". This was echoed in a statement by the African Community Advisory Board. "We do not think that women are getting enough credit to be able to make conception decisions, and we hear this rhetoric as the same rhetoric that denied Africans treatment in the past", said the statement.

Not changing the guidelines would also give women a chance to change their sex practices and would encourage health systems to explain the risks of taking the drug instead of making decisions for women, said Russell. "We are concerned that governments' own lack of willingness to aggressively tackle access to long-term and effective contraception is standing in the way of ending HIV", she said.

"Every women needs to be on dolutegravir if they want to; the only question should be what about those who want to be pregnant?" she said.

#### 16. *Lancet* 2018;392(10148):685-97

##### **HIV**

Ghoshn J et al., Inserm UMR-S 1136, Institut Pierre Louis d'Epidémiologie et de Santé Publique, Paris, France

The benefits of combination antiretroviral therapy (cART) for HIV replication and transmission control have led to its universal recommendation. Many people living with HIV are, however, still undiagnosed or diagnosed late, especially in sub-Saharan Africa, where the HIV disease burden is highest. Further expansion in HIV treatment options, incorporating women-centred approaches, is essential to make individualised care a reality. With a longer life expectancy than before, people living with HIV are at an increased risk of developing non-AIDS comorbidities, such as cardiovascular diseases and cancers. Antiretroviral strategies are evolving towards a decrease in drug burden, and some two-drug combinations have proven efficacy for maintenance therapy. Investigational immune checkpoint inhibitors and broadly neutralising antibodies with effector functions have energised the HIV cure research field as the search for an effective vaccine continues. In this Seminar, we review advances and challenges relating to the goal of an AIDS-free world.

#### 17. *Lancet* 2018;392(10148):698-710

##### **The global response and unmet actions for HIV and sex workers**

Shannon K et al., Gender and Sexual Health Initiative, University of British Columbia, Vancouver, BC, Canada <kate.shannon@ubc.ca>

Female, male, and transgender sex workers continue to have disproportionately high burdens of HIV infection in low-income, middle-income, and high-income countries in 2018. 4 years since our *Lancet* Series on HIV and sex work, our updated analysis of the global HIV burden among female sex workers shows that HIV prevalence is unacceptably high at 10.4% (95% CI 9.5-11.5) and is largely unchanged. Comprehensive epidemiological data on HIV and antiretroviral therapy (ART) coverage are scarce, particularly among transgender women. Sustained coverage of treatment is markedly

uneven and challenged by lack of progress on stigma and criminalisation, and sustained human rights violations. Although important progress has been made in biomedical interventions with pre-exposure prophylaxis and early ART feasibility and demonstration projects, limited coverage and retention suggest that sustained investment in community and structural interventions is required for sex workers to benefit from the preventive interventions and treatments that other key populations have. Evidence-based progress on full decriminalisation grounded in health and human rights—a key recommendation in our Lancet Series—has stalled, with South Africa a notable exception. Additionally, several countries have rolled back rights to sex workers further. Removal of legal barriers through the decriminalisation of sex work, alongside political and funding investments to support community and structural interventions, is urgently needed to reverse the HIV trajectory and ensure health and human rights for all sex workers.

18. *TMIH* 2018;23(6):678-90

### **Is home-based HIV testing universally acceptable? Findings from a case-control study nested within the HPTN 071 (PopART) trial**

Sabapathy K et al., London School of Hygiene and Tropical Medicine, London, UK

**Objective:** The HPTN 071 (PopART) trial is examining the impact of a package including universal testing and treatment on community-level HIV incidence in Zambia and South Africa. We conducted a nested case-control study to examine factors associated with acceptance of home-based HIV testing and counselling (HB-HTC) delivered by community HIV-care providers (CHiPs) in PopART intervention communities.

**Methods:** Of 295 447 individuals who were offered testing, random samples of individuals who declined HB-HTC (cases) and accepted HB-HTC (controls), stratified by gender and community, were selected. Odds ratios comparing cases and controls were estimated using multivariable logistic regression.

**Results:** Data from 642 participants (313 cases, 329 controls) were analysed. There were no differences between cases and controls by demographic or behavioural characteristics including age, marital or socio-economic position. Participants who felt they could be open with CHiPs (AOR: 0.46, 95% CI: 0.30-0.71,  $P < 0.001$ ); self-reported as not previously tested (AOR: 0.64; 95% CI: 0.43-0.95,  $P = 0.03$ ); considered HTC at home to be convenient (AOR: 0.38, 95% CI: 0.27-0.54,  $P = 0.001$ ); knowing others who had accepted HB-HTC from the CHiPs (AOR: 0.49, 95% CI: 0.31-0.77,  $P = 0.002$ ); or were motivated to get treatment without delay (AOR: 0.60, 95% CI: 0.43-0.85,  $P = 0.004$ ) were less likely to decline the offer of HB-HCT. Those who self-reported high-risk sexual behaviour were also less likely to decline HB-HCT (AOR: 0.61, 95% CI: 0.39-0.93,  $P = 0.02$ ). Having stigmatising attitudes about HB-HTC was not an important barrier to HB-HCT uptake. Men who reported fear of HIV were more likely to decline HB-HCT (AOR: 2.68, 95% CI: 1.33-5.38,  $P = 0.005$ ).

**Conclusion:** Acceptance of HB-HTC was associated with lack of previous HIV testing, positive attitudes about HIV services/treatment and perception of high sexual risk. Uptake of HB-HCT among those offered it was similar across a range of demographic and behavioural subgroups suggesting it was 'universally' acceptable.

## **Malaria**

19. *Am J TMH* 2018;99(1):17-23

### **Malaria Elimination: Time to Target All Species**

Lover AA et al., Malaria Elimination Initiative at the University of California, San Francisco, San Francisco, California

Important strides have been made within the past decade toward malaria elimination in many regions, and with this progress, the feasibility of eradication is once again under discussion. If the ambitious goal of eradication is to be achieved by 2040, all species of *Plasmodium* infecting humans will need to be targeted with evidence-based and concerted interventions. In this perspective, the potential barriers

to achieving global malaria elimination are discussed with respect to the related diversities in host, parasite, and vector populations. We argue that control strategies need to be reorientated from a sequential attack on each species, dominated by *Plasmodium falciparum* to one that targets all species in parallel. A set of research themes is proposed to mitigate the potential setbacks on the pathway to a malaria-free world.

20. *Lancet* 2018;391(10130):1608–21

### Seminar

### Malaria

Ashley EA et al.

Following unsuccessful eradication attempts there was a resurgence of malaria towards the end of the 20th century. Renewed control efforts using a range of improved tools, such as long-lasting insecticide-treated bednets and artemisinin-based combination therapies, have more than halved the global burden of disease, but it remains high with 445 000 deaths and more than 200 million cases in 2016. Pitfalls in individual patient management are delayed diagnosis and overzealous fluid resuscitation in severe malaria. Even in the absence of drug resistance, parasite recurrence can occur, owing to high parasite densities, low host immunity, or suboptimal drug concentrations. Malaria elimination is firmly back as a mainstream policy but resistance to the artemisinin derivatives, their partner drugs, and insecticides present major challenges. Vaccine development continues on several fronts but none of the candidates developed to date have been shown to provide long-lasting benefits at a population level. Increased resources and unprecedented levels of regional cooperation and societal commitment will be needed if further substantial inroads into the malaria burden are to be made.

21. *Lancet* 2018;392(10147):569–80

### Efficacy of Olyset Duo, a bednet containing pyriproxyfen and permethrin, versus a permethrin-only net against clinical malaria in an area with highly pyrethroid-resistant vectors in rural Burkina Faso: a cluster-randomised controlled trial

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**Background.** Substantial reductions in malaria incidence in sub-Saharan Africa have been achieved with massive deployment of long-lasting insecticidal nets (LLINs), but pyrethroid resistance threatens control. Burkina Faso is an area with intense malaria transmission and highly pyrethroid-resistant vectors. We assessed the effectiveness of bednets containing permethrin, a pyrethroid, and pyriproxyfen, an insect growth regulator, versus permethrin-only (standard) LLINs against clinical malaria in children younger than 5 years in Banfora, Burkina Faso.

**Methods.** In this two-group, step-wedge, cluster-randomised, controlled, superiority trial, standard LLINs were incrementally replaced with LLINs treated with permethrin plus pyriproxyfen (PPF) in 40 rural clusters in Burkina Faso. In each cluster, 50 children (aged 6 months to 5 years) were followed up by passive case detection for clinical malaria. Cross-sectional surveys were done at the start and the end of the transmission seasons in 2014 and 2015. We did monthly collections from indoor light traps to estimate vector densities. Primary endpoints were the incidence of clinical malaria, measured by passive case detection, and the entomological inoculation rate. Analyses were adjusted for clustering and for month and health centre. This trial is registered as ISRCTN21853394.

**Findings.** 1980 children were enrolled in the cohort in 2014 and 2157 in 2015. At the end of the study, more than 99% of children slept under a bednet. The incidence of clinical malaria was 2·0 episodes per child-year in the standard LLIN group and 1·5 episodes per child-year in the PPF-treated LLIN group (incidence rate ratio 0·88 [95% CI 0·77–0·99; p=0·04]). The entomological inoculation rate was 85 (95% CI 63–108) infective bites per transmission season in the standard LLIN group versus 42 (32–52) infective bites per transmission season in the PPF-treated LLIN group (rate ratio 0·49, 95% CI 0·32–0·66; p<0·0001).

**Interpretation.** PPF-treated LLINs provide greater protection against clinical malaria than do standard LLINs and could be used as an alternative to standard LLINs in areas with intense transmission of *Plasmodium falciparum* malaria and highly pyrethroid-resistant vectors.

22. *TMIH* 2018;23(6):582-8

**High folate levels are not associated with increased malaria risk but with reduced anaemia rates in the context of high-dosed folate supplements and intermittent preventive treatment against malaria in pregnancy with sulphadoxine-pyrimethamine in Benin**

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**Objectives:** To investigate whether high-dosed folate supplements might diminish the efficacy of malaria intermittent preventive treatment in pregnancy (IPTp) with sulphadoxine-pyrimethamine (SP) in a cohort of pregnant women in Benin, where malaria is holoendemic.

**Methods:** We followed 318 women during the entire pregnancy and analysed haematological and *Plasmodium falciparum* indicators in the context of an intermittent preventive treatment trial in Benin. During the follow-up, women received two-dose IPTp (1500/75 mg of SP per dose) at the maternity clinic and 600 mg of albendazole, 200 mg ferrous sulphate and 5 mg folic acid per day for home treatment.

**Results:** High folate levels were not associated with increased malaria risk (adjusted OR (aOR) = 0.51 (95% CI: 0.17; 1.56, P-value = 0.24)), nor with increased *P. falciparum* density (beta coefficient = -0.26 (95% CI: -0.53; 0.02), P-value = 0.07) in a randomised trial of IPTp in Benin. On the contrary, higher iron levels were statistically associated with increased odds of a positive blood smear (aOR = 1.7 95% CI (1.2; 2.3), P-value < 0.001) and *P. falciparum* parasite density (beta coefficient = 0.2 95% CI (0.1; 0.3), P-value < 0.001). High folate levels were statistically associated with decreased odds of anaemia (aOR = -0.30 95% CI (0.10; 0.88), P-value = 0.03).

**Conclusions:** High folate levels are not associated with increased malarial risk in a prospective longitudinal cohort in the context of both iron and high-dosed folate supplements and IPTp. They are associated with reduced risk of anaemia, which is particularly important because iron, also given to treat anaemia, might be associated with increased malaria risk.

## Non-Communicable Diseases

23. *IJE* 2018;47(3):942–52

**Rapidly increasing body mass index among children, adolescents and young adults in a transitioning population, South Africa, 2008–15**

Sartorius B et al., University of KwaZulu-Natal, Durban, South Africa <sartorius@ukzn.ac.za>

**Background:** There is a global epidemic of overweight and obesity; however, this rate of increase is even greater in some low- and middle-income countries (LMIC). South Africa (SA) is undergoing rapid socioeconomic and demographic changes that have triggered a rapid nutrition transition. The paper focuses on the recent rate of change of body mass index (BMI) among children, adolescents and young adults, further stratified by key sociodemographic factors.

**Methods:** We analysed mean BMI of 28 247 individuals (including children) from 7301 households by age and year, from anthropometric data from four national cross-sectional (repeated panel) surveys using non-linear fitted curves and associated 95% confidence intervals.

**Results:** From 2008 to 2015, there was rapid rise in mean BMI in the 6–25 age band, with the highest risk (3–4+ BMI unit increase) among children aged 8–10 years. The increase was largely among females in urban areas and of middle-high socioeconomic standing. Prominent gains were also observed in certain rural areas, with extensive geographical heterogeneity across the country.

**Conclusions:** We have demonstrated a major deviation from the current understanding of patterns of BMI increase, with a rate of increase substantially greater in the developing world context compared with the global pattern. This population-wide effect will have major consequences for national development as the epidemic of related non-communicable disease unfolds, and will overtax the national health care budget. Our refined understanding highlights that risks are further compounded

for certain groups/places, and emphasizes that urgent geographical and population-targeted interventions are necessary. These interventions could include a sugar tax, clearer food labelling, revised school feeding programmes and mandatory bans on unhealthy food marketing to children. The scenario unfolding in South Africa will likely be followed in other LMICs.

24. [Lancet 2018;391\(10134\):2019-27](#)

**Practice patterns and outcomes after stroke across countries at different economic levels (INTERSTROKE): an international observational study**

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**Background:** Stroke disproportionately affects people in low-income and middle-income countries. Although improvements in stroke care and outcomes have been reported in high-income countries, little is known about practice and outcomes in low and middle-income countries. We aimed to compare patterns of care available and their association with patient outcomes across countries at different economic levels.

**Methods:** We studied the patterns and effect of practice variations (ie, treatments used and access to services) among participants in the INTERSTROKE study, an international observational study that enrolled 13 447 stroke patients from 142 clinical sites in 32 countries between Jan 11, 2007, and Aug 8, 2015. We supplemented patient data with a questionnaire about health-care and stroke service facilities at all participating hospitals. Using univariate and multivariate regression analyses to account for patient casemix and service clustering, we estimated the association between services available, treatments given, and patient outcomes (death or dependency) at 1 month.

**Findings:** We obtained full information for 12 342 (92%) of 13 447 INTERSTROKE patients, from 108 hospitals in 28 countries; 2576 from 38 hospitals in ten high-income countries and 9766 from 70 hospitals in 18 low and middle-income countries. Patients in low-income and middle-income countries more often had severe strokes, intracerebral haemorrhage, poorer access to services, and used fewer investigations and treatments ( $p < 0.0001$ ) than those in high-income countries, although only differences in patient characteristics explained the poorer clinical outcomes in low and middle-income countries. However across all countries, irrespective of economic level, access to a stroke unit was associated with improved use of investigations and treatments, access to other rehabilitation services, and improved survival without severe dependency (odds ratio [OR] 1.29; 95% CI 1.14-1.44; all  $p < 0.0001$ ), which was independent of patient casemix characteristics and other measures of care. Use of acute antiplatelet treatment was associated with improved survival (1.39; 1.12-1.72) irrespective of other patient and service characteristics.

**Interpretation:** Evidence-based treatments, diagnostics, and stroke units were less commonly available or used in low and middle-income countries. Access to stroke units and appropriate use of antiplatelet treatment were associated with improved recovery. Improved care and facilities in low-income and middle-income countries are essential to improve outcomes.

25. [Lancet 2018;391\(10134\)](#)

**The Lancet Taskforce on NCDs and economics**

A Series of five papers about non-communicable diseases and economics

\* [Lancet 2018;391\(10134\):2029-35](#)

**Investing in non-communicable disease prevention and management to advance the Sustainable Development Goals**

Nugent R et al., Research Triangle Institute International, Seattle, WA, USA <rnugent@rti.org>

Reduction of the non-communicable disease (NCD) burden is a global development imperative. Sustainable Development Goal (SDG) 3 includes target 3.4 to reduce premature NCD mortality by a third by 2030. Progress on SDG target 3.4 will have a central role in determining the success of at least nine SDGs. A strengthened effort across multiple sectors with effective economic tools, such as price policies and insurance, is necessary. NCDs are heavily clustered in people with low socioeconomic status and are an important cause of medical impoverishment. They thereby exacerbate economic inequities within societies. As such, NCDs are a barrier to achieving SDG 1, SDG 2, SDG

4, SDG 5, and SDG 10. Productivity gains from preventing and managing NCDs will contribute to SDG 8. SDG 11 and SDG 12 offer clear opportunities to reduce the NCD burden and to create sustainable and healthy cities. Erratum in Lancet 2018 Apr 9.

\* Lancet. 2018;391(10134):2036-46

**Tackling socioeconomic inequalities and non-communicable diseases in low-income and middle-income countries under the Sustainable Development agenda**

\* Lancet. 2018;391(10134):2047-58

**Action to address the household economic burden of non-communicable diseases**

\* Lancet. 2018;391(10134):2059-70

**Equity impacts of price policies to promote healthy behaviours**

\* Lancet. 2018;391(10134):2071-78

**Investing in non-communicable diseases: an estimation of the return on investment for prevention and treatment services**

26. Lancet 2018;392(10142):161-74

**Acute rheumatic fever**

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Acute rheumatic fever is caused by an autoimmune response to throat infection with *Streptococcus pyogenes*. Cardiac involvement during acute rheumatic fever can result in rheumatic heart disease, which can cause heart failure and premature mortality. Poverty and household overcrowding are associated with an increased prevalence of acute rheumatic fever and rheumatic heart disease, both of which remain a public health problem in many low-income countries. Control efforts are hampered by the scarcity of accurate data on disease burden, and effective approaches to diagnosis, prevention, and treatment. The diagnosis of acute rheumatic fever is entirely clinical, without any laboratory gold standard, and no treatments have been shown to reduce progression to rheumatic heart disease. Prevention mainly relies on the prompt recognition and treatment of streptococcal pharyngitis, and avoidance of recurrent infection using long-term antibiotics. But evidence for the effectiveness of either approach is not strong. High-quality research is urgently needed to guide efforts to reduce acute rheumatic fever incidence and prevent progression to rheumatic heart disease.

## Sexual and Reproductive Health

27. HPP 2018;33(5):666–74

**Technical quality of delivery care in private- and public-sector health facilities in Enugu and Lagos States, Nigeria**

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Private-sector providers are increasingly being recognized as important contributors to the delivery of healthcare. Countries with high disease burdens and limited public-sector resources are considering using the private sector to achieve universal health coverage. However, evidence for the technical quality of private-sector care is lacking. This study assesses the technical quality of maternal healthcare during delivery in public- and private-sector facilities in resource-limited settings, from a systems and programmatic perspective. A summary index (the skilled attendance index, SAI), was used. Two-staged cluster sampling with stratification was used to select representative samples of case records in public- and private-sector facilities in Enugu and Lagos States, Nigeria. Information to assess criteria was extracted, and the SAI calculated. Linear regression models examined the relationship between SAI and the private and public sectors, controlling for confounders. The median SAI was 54.8% in Enugu and 85.7% in Lagos. The private for-profit sector's SAI was lower than and the private not-for-profit sector's SAI was higher than the public sector in Enugu [coefficient = -3.6 (P = 0.018) and 12.6 (P < 0.001), respectively]. In Lagos, the private for profit sector's SAI was higher and the private not-for-profit sector's SAI was lower than the public sector [3.71 (P = 0.005) and -

3.92 ( $P < 0.001$ )]. Results indicate that the technical quality of private for-profit providers' care was poorer than public providers where the public provision of care was weak, while private for-profit facilities provided better technical quality care than public facilities where the public sector was strong and there was a relatively strong regulatory body. Our findings raise important considerations relating to the quality of maternity care, the public–private mix and needs for regulation in global efforts to achieve universal healthcare.

## Tuberculosis

28. *Am J TMH* 2018;99(2):317-22

### **Utilization and Clinical Value of Diagnostic Modalities for Tuberculosis in a High HIV Prevalence Setting**

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Human immunodeficiency virus (HIV) infection is a major risk factor for the development of active tuberculosis (TB), one of the deadliest infectious diseases globally. The high mortality associated with the disease can be reduced by early diagnosis and prompt antituberculous treatment initiation. Facilities in TB-endemic regions are increasing the use of nucleic acid amplification (e.g., GeneXpert), which provides rapid results but may have suboptimal sensitivity in HIV-associated TB. Our objective was to evaluate the current practices for TB diagnosis at Edendale Hospital, a large regional hospital in KwaZulu-Natal, South Africa—a TB-endemic region with high HIV prevalence. In this cross-sectional study, all adult inpatients newly started on TB treatment at Edendale were identified over a 6-week period. Demographics, clinical information, diagnostic test results, and outcomes were documented. Pulmonary TB (PTB), extrapulmonary TB (EXTB), and PTB + EXTB were defined as disease evidence in the lungs, other organs, or both, respectively. Ninety-four cases were identified, of which 83% were HIV-associated. Only 30% of all TB patients were microbiologically confirmed, consisting of 7/16 (44%) HIV-uninfected and 21/78 (27%) HIV-infected TB patients. Smear microscopy and mycobacterial culture were seldom ordered. Ultrasound was performed in about one-third of suspected EXTB cases and was valuable in identifying abdominal TB. In this clinical setting with a high incidence of HIV-associated TB, TB diagnosis was more commonly based on clinical assessment and imaging results than on mycobacterial gold standard test confirmation.

29. *Lancet* 2018;392(10144):292-301

### **Rapid urine-based screening for tuberculosis in HIV-positive patients admitted to hospital in Africa (STAMP): a pragmatic, multicentre, parallel-group, double-blind, randomised controlled trial**

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**Background:** Current diagnostics for HIV-associated tuberculosis are suboptimal, with missed diagnoses contributing to high hospital mortality and approximately 374 000 annual HIV-positive deaths globally. Urine-based assays have a good diagnostic yield; therefore, we aimed to assess whether urine-based screening in HIV-positive inpatients for tuberculosis improved outcomes.

**Methods:** We did a pragmatic, multicentre, double-blind, randomised controlled trial in two hospitals in Malawi and South Africa. We included HIV-positive medical inpatients aged 18 years or more who were not taking tuberculosis treatment. We randomly assigned patients (1:1), using a computer-generated list of random block size stratified by site, to either the standard-of-care or the intervention screening group, irrespective of symptoms or clinical presentation. Attending clinicians made decisions about care; and patients, clinicians, and the study team were masked to the group allocation. In both groups, sputum was tested using the Xpert MTB/RIF assay (Xpert; Cepheid, Sunnyvale, CA, USA). In the standard-of-care group, urine samples were not tested for tuberculosis. In the intervention group, urine was tested with the Alere Determine TB-LAM Ag (TB-LAM; Alere, Waltham, MA, USA), and Xpert assays. The primary outcome was all-cause 56-day mortality.

Subgroup analyses for the primary outcome were prespecified based on baseline CD4 count, haemoglobin, clinical suspicion for tuberculosis; and by study site and calendar time. We used an intention-to-treat principle for our analyses. This trial is registered with the ISRCTN registry, number ISRCTN71603869.

**Findings:** Between Oct 26, 2015, and Sept 19, 2017, we screened 4788 HIV-positive adults, of which 2600 (54%) were randomly assigned to the study groups (n=1300 for each group). 13 patients were excluded after randomisation from analysis in each group, leaving 2574 in the final intention-to-treat analysis (n=1287 in each group). At admission, 1861 patients were taking antiretroviral therapy and median CD4 count was 227 cells per  $\mu\text{L}$  (IQR 79-436). Mortality at 56 days was reported for 272 (21%) of 1287 patients in the standard-of-care group and 235 (18%) of 1287 in the intervention group (adjusted risk reduction [aRD] -2.8%, 95% CI -5.8 to 0.3;  $p=0.074$ ). In three of the 12 prespecified, but underpowered subgroups, mortality was lower in the intervention group than in the standard-of-care group for CD4 counts less than 100 cells per  $\mu\text{L}$  (aRD -7.1%, 95% CI -13.7 to -0.4;  $p=0.036$ ), severe anaemia (-9.0%, -16.6 to -1.3;  $p=0.021$ ), and patients with clinically suspected tuberculosis (-5.7%, -10.9 to -0.5;  $p=0.033$ ); with no difference by site or calendar period. Adverse events were similar in both groups.

**Interpretation:** Urine-based tuberculosis screening did not reduce overall mortality in all HIV-positive inpatients, but might benefit some high-risk subgroups. Implementation could contribute towards global targets to reduce tuberculosis mortality.

30. [Plos Med 2018;15\(7\):e1002591](#)

### **Treatment and outcomes in children with multidrug-resistant tuberculosis: A systematic review and individual patient data meta-analysis**

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**Background:** An estimated 32,000 children develop multidrug-resistant tuberculosis (MDR-TB; *Mycobacterium tuberculosis* resistant to isoniazid and rifampin) each year. Little is known about the optimal treatment for these children.

**Methods and findings:** To inform the pediatric aspects of the revised World Health Organization (WHO) MDR-TB treatment guidelines, we performed a systematic review and individual patient data (IPD) meta-analysis, describing treatment outcomes in children treated for MDR-TB. To identify eligible reports we searched PubMed, LILACS, Embase, The Cochrane Library, PsychINFO, and BioMedCentral databases through 1 October 2014. To identify unpublished data, we reviewed conference abstracts, contacted experts in the field, and requested data through other routes, including at national and international conferences and through organizations working in pediatric MDR-TB. A cohort was eligible for inclusion if it included a minimum of three children (aged < 0.001 for all characteristics).

Overall, 764 of 975 (78%) had a successful treatment outcome at the conclusion of therapy: 548/731 (75%) of confirmed and 216/244 (89%) of clinically diagnosed children (absolute difference 14%, 95% confidence interval [CI] 8%–19%,  $p < 0.001$ ). Treatment was successful in only 56% of children with bacteriologically confirmed TB who were infected with HIV who did not receive any antiretroviral treatment (ART) during MDR-TB therapy, compared to 82% in children infected with HIV who received ART during MDR-TB therapy (absolute difference 26%, 95% CI 5%–48%,  $p = 0.006$ ). In children with confirmed MDR-TB, the use of second-line injectable agents and high-dose isoniazid (15–20 mg/kg/day) were associated with treatment success (adjusted odds ratio [aOR] 2.9, 95% CI 1.0–8.3,  $p = 0.041$  and aOR 5.9, 95% CI 1.7–20.5,  $p = 0.007$ , respectively). These findings for high-dose isoniazid may have been affected by site effect, as the majority of patients came from Cape Town. Limitations of this study include the difficulty of estimating the treatment effects of individual drugs within multidrug regimens, only observational cohort studies were available for inclusion, and treatment decisions were based on the clinician's perception of illness, with resulting potential for bias.

**Conclusions:** This study suggests that children respond favorably to MDR-TB treatment. The low success rate in children infected with HIV who did not receive ART during their MDR-TB treatment highlights the need for ART in these children. Our findings of individual drug effects on treatment outcome should be further evaluated.

31. *TMIH* 2018;23(8):870-8

### **How affordable is TB care? Findings from a nationwide TB patient cost survey in Ghana**

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**Objectives:** Tuberculosis (TB) is known as a disease of the poor. Despite TB diagnosis and care usually being offered for free, TB patients can still face substantial costs, especially in the context of multi-drug resistance (MDR). The End TB Strategy calls for zero TB-affected families incurring 'catastrophic' costs due to TB by 2025. This paper examines, by MDR status, the level and composition of costs incurred by TB-affected households during care seeking and treatment; assesses the affordability of TB care using catastrophic and impoverishment measures; and describes coping strategies used by TB-affected households to pay for TB care.

**Methods:** A nationally representative survey of TB patients at public health facilities across Ghana. Results: We enrolled 691 patients (66 MDR). The median expenditure for non-MDR TB was US\$429.6 during treatment, vs. US\$659.0 for MDR patients (P-value = 0.001). Catastrophic costs affected 64.1% of patients. MDR patients were pushed significantly further over the threshold for catastrophic payments than DS patients. Payments for TB care led to a significant increase in the proportion of households in the study sample that live below the poverty line at the time of survey compared to pre-TB diagnosis. Over half of patients undertook coping strategies.

**Conclusion:** TB patients in Ghana incur substantial costs, despite free diagnosis and treatment. High rates of catastrophic costs and coping strategies in both non-MDR and MDR patients show that new policies are urgently needed to ensure TB care is actually affordable for TB patients.

## Miscellaneous

32. *BMJ* 2018;361:k2286

### **Feature Humanitarian Aid**

#### **Reporting adverse events in a war zone**

Arie S., <sophiearie@fmail.co.uk>

How much harm does humanitarian healthcare cause patients by mistake? Medical aid agencies and others are increasingly aiming to improve the quality and safety of healthcare they deliver, finds Sophie Arie

In 2014, in the midst of the Syrian conflict, aid workers vaccinating children against measles killed 15 infants when they injected them with the muscle relaxant atracurium by mistake. The Syrian team could not read the English labels on the ampoules of the drug, which they mistook for the diluent used for mixing the measles vaccine.

The World Health Organization, which was coordinating the vaccination campaign with the United Nations children's agency Unicef, said that it was the biggest such tragedy in memory.

"The circumstances in which we work make it harder [than it is for Western health services] to avoid medical errors or pre-empt them," says Tammam Aloudat, deputy medical director for the humanitarian charity Médecins Sans Frontières (MSF) Switzerland, which was not involved in the Syria incident.

Extremely difficult and dangerous situations

The nature of aid agencies' work means they often have a high turnover of staff, and many are posted to places where they do not speak the language of the health workers or patients. They care for particularly vulnerable patients, working in extremely difficult and dangerous situations, under intense pressure and for long hours in makeshift or poorly equipped facilities. Their work takes them to remote or dangerous places where populations are on the move, communications are poor, and where it can be hard to keep drugs cold, replenish stocks, or win the trust of local communities.

Simultaneously, donors want them to minimise administrative costs and maximise the number of people helped. The result is that aid agencies know little about adverse incidents among the millions of patients they treat.

33. [Lancet 2018;391\(101370\):2301](#)

#### **Comment**

#### **Low back pain: a major global challenge**

Clark E and Horton R, The Lancet, London, UK <stephanie.clark@lancet.com>

Low back pain is a major problem throughout the world and it is getting worse—largely because of the ageing and increasing world population. It affects all age groups and is generally associated with sedentary occupations, smoking, obesity, and low socioeconomic status. Years lived with disability caused by low back pain have increased by more than 50% since 1990, especially in low-income and middle-income countries (LMICs). Disability related to low back pain is projected to increase most in LMICs where resources are limited, access to quality health care is generally poor, and lifestyle changes and shifts towards more sedentary work for some mean the risks will only increase.

These are some of the issues highlighted in a Lancet Series of two papers and a Viewpoint on low back pain by an international group of authors, led by Rachele Buchbinder from Monash University, Melbourne, VIC, Australia. In the first paper, Jan Hartvigsen, Mark Hancock, and their colleagues draw our attention to the complexity of the condition and the contributors to it, such as psychological, social, and biophysical factors, and especially to the problems in LMICs where health systems are not equipped to cope with the growing burden of low back pain. They discuss the challenges and causes of low back pain and make suggestions for the way forward in research.

In the second paper, Nadine Foster and colleagues outline recommendations for treatment and the scarcity of research into prevention of low back pain. The evidence they discuss comes almost exclusively from high-income countries, and whether guidelines based on this evidence would be suitable for LMICs is not known. They propose solutions to inappropriate treatment, such as the use of opioids, but admit that the evidence base for them is inadequate.

The last paper is a call for action by Buchbinder and colleagues who argue that persistence of disability associated with low back pain needs to be recognised and that it cannot be separated from social and economic factors and personal and cultural beliefs about back pain. They urge global organisations such as WHO to take action to try to reduce the increasing and costly effects of disabling low back pain. A major challenge will be to stop the use of harmful practices while ensuring access to effective and affordable health care for people with low back pain.

\* [Lancet 2018;391\(10137\):2356-2367](#)

#### **What low back pain is and why we need to pay attention**

\* [Lancet. 2018;391\(10137\):2368-2383](#)

#### **Prevention and treatment of low back pain: evidence, challenges, and promising directions**

\* [Lancet 2018; 391\(10137\): 2384–88](#)

#### **Viewpoint**

#### **Low back pain: a call for action**

Key messages

- Use the notion of positive health—the ability to adapt and to self-manage in the face of social, physical and emotional challenges—for the treatment of non-specific low back pain
- Avoid harmful and useless treatments by adopting a framework similar to that used in drug regulation—ie, only include treatments in public reimbursement packages if evidence shows that they are safe, effective, and cost-effective
- Address widespread misconceptions in the population and among health professionals about the causes, prognosis, and effectiveness of different treatments for low back pain, and deal fragmented and outdated models of care
- Policy, public health, health-care practice, social services, and workplaces must jointly tackle the low back pain paradox in low-income and middle-income countries, where improving social and economic conditions could prevent or reduce low back pain incidence, but at the same time create expectations and demands for medical investigations and low-value health care that increase the risk of long-term back-related disability

34. [Lancet 2018;392\(10147\):581–91](#)

## On the road to universal health care in Indonesia, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016

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**Background.** As Indonesia moves to provide health coverage for all citizens, understanding patterns of morbidity and mortality is important to allocate resources and address inequality. The Global Burden of Disease 2016 study (GBD 2016) estimates sources of early death and disability, which can inform policies to improve health care.

**Methods.** We used GBD 2016 results for cause-specific deaths, years of life lost, years lived with disability, disability-adjusted life-years (DALYs), life expectancy at birth, healthy life expectancy, and risk factors for 333 causes in Indonesia and in seven comparator countries. Estimates were produced by location, year, age, and sex using methods outlined in GBD 2016. Using the Socio-demographic Index, we generated expected values for each metric and compared these against observed results.

**Findings.** In Indonesia between 1990 and 2016, life expectancy increased by 8.0 years (95% uncertainty interval [UI] 7.3–8.8) to 71.7 years (71.0–72.3): the increase was 7.4 years (6.4–8.6) for males and 8.7 years (7.8–9.5) for females. Total DALYs due to communicable, maternal, neonatal, and nutritional causes decreased by 58.6% (95% UI 55.6–61.6), from 43.8 million (95% UI 41.4–46.5) to 18.1 million (16.8–19.6), whereas total DALYs from non-communicable diseases rose. DALYs due to injuries decreased, both in crude rates and in age-standardised rates. The three leading causes of DALYs in 2016 were ischaemic heart disease, cerebrovascular disease, and diabetes. Dietary risks were a leading contributor to the DALY burden, accounting for 13.6% (11.8–15.4) of DALYs in 2016.

**Interpretation.** Over the past 27 years, health across many indicators has improved in Indonesia. Improvements are partly offset by rising deaths and a growing burden of non-communicable diseases. To maintain and increase health gains, further work is needed to identify successful interventions and improve health equity.

35. *Lancet* 2018;392(10148):673-84

### Vulnerability to snakebite envenoming: a global mapping of hotspots

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**Background:** Snakebite envenoming is a frequently overlooked cause of mortality and morbidity. Data for snake ecology and existing snakebite interventions are scarce, limiting accurate burden estimation initiatives. Low global awareness stunts new interventions, adequate health resources, and available health care. Therefore, we aimed to synthesise currently available data to identify the most vulnerable populations at risk of snakebite, and where additional data to manage this global problem are needed.

**Methods:** We assembled a list of snake species using WHO guidelines.

**Findings:** We provide a map showing the ranges of 278 snake species globally. Although about 6.85 billion people worldwide live within range of areas inhabited by snakes, about 146.70 million live within remote areas lacking quality health-care provisioning. Comparing opposite ends of the HAQ Index, 272.91 million individuals (65.25%) of the population within the lowest decile are at risk of exposure to any snake for which no effective therapy exists compared with 519.46 million individuals (27.79%) within the highest HAQ Index decile, showing a disproportionate coverage in reported antivenom availability. Antivenoms were available for 119 (43%) of 278 snake species evaluated by WHO, while globally 750.19 million (10.95%) of those living within snake ranges live more than 1 h from population centres. In total, we identify about 92.66 million people living within these vulnerable geographies, including many sub-Saharan countries, Indonesia, and other parts of southeast Asia.

**Interpretation:** Identifying exact populations vulnerable to the most severe outcomes of snakebite envenoming at a subnational level is important for prioritising new data collection and collation, reinforcing envenoming treatment, existing health-care systems, and deploying currently available and future interventions. These maps can guide future research efforts on snakebite envenoming from both

ecological and public health perspectives and better target future estimates of the burden of this neglected tropical disease.