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Child Health / iCCM

1. Am J TMH 2019 Jan 2. doi: 10.4269/ajtmh.18-0846

Mass Azithromycin Distribution to Prevent Childhood Mortality: A Pooled Analysis of Cluster-Randomized Trials

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Mass drug administration (MDA) with azithromycin may reduce under-5 child mortality (U5M) in sub-Saharan Africa. Here, we conducted a pooled analysis of all published cluster-randomized trials evaluating the effect of azithromycin MDA on child mortality. We pooled data from cluster-randomized trials randomizing communities to azithromycin MDA versus control. We calculated mortality rates in the azithromycin and control arms in each study, and by country for multisite studies including multiple countries. We conducted a two-stage individual community data meta-analysis to estimate the effect of azithromycin for prevention of child mortality. Three randomized controlled trials in four countries (Ethiopia, Malawi, Niger, and Tanzania) were identified. The overall pooled mortality rate was 15.9 per 1,000 person-years (95% confidence interval [CI]: 15.5-16.3). The pooled mortality rate was lower in azithromycin-treated communities than in placebo-treated communities (14.7 deaths per 1,000 person-years, 95% CI: 14.2-15.3 versus 17.2 deaths per 1,000 person-years, 95% CI: 16.5-17.8). There was a 14.4% reduction in all-cause child mortality in communities receiving azithromycin MDA (95% CI: 6.3-21.7% reduction, P = 0.0007). All-cause U5M was lower in communities receiving azithromycin MDA than in control communities, suggesting that azithromycin MDA could be a new tool to reduce child mortality in sub-Saharan Africa. However, heterogeneity in effect estimates suggests that the magnitude of the effect may vary in time and space and is currently not predictable.

2. Lancet 2018;392(10164):2567-82

Health impacts of parental migration on left-behind children and adolescents: a systematic review and meta-analysis

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Background: Globally, a growing number of children and adolescents are left behind when parents migrate. We investigated the effect of parental migration on the health of left behind-children and adolescents in low-income and middle-income countries (LMICs).
Methods: For this systematic review and meta-analysis we searched MEDLINE, Embase, CINAHL, the Cochrane Library, Web of Science, PsychINFO, Global Index Medicus, Scopus, and Popline from inception to April 27, 2017, without language restrictions, for observational studies investigating the effects of parental migration on nutrition, mental health, unintentional injuries, infectious disease, substance use, unprotected sex, early pregnancy, and abuse in left-behind children (aged 0-19 years) in LMICs. We excluded studies in which less than 50% of participants were aged 0-19 years, the mean or median age of participants was more than 19 years, fewer than 50% of parents had migrated for more than 6 months, or the mean or median duration of migration was less than 6 months. We screened studies using systematic review software and extracted summary estimates from published reports independently. The main outcomes were risk and prevalence of health outcomes, including nutrition (stunting, wasting, underweight, overweight and obesity, low birthweight, and anaemia), mental health (depressive disorder, anxiety disorder, conduct disorders, self-harm, and suicide), unintentional injuries, substance use, abuse, and infectious disease. We calculated pooled risk ratios (RRs) and standardised mean differences (SMDs) using random-effects models. This study is registered with PROSPERO, number CRD42017064871.
Findings: Our search identified 10 284 records, of which 111 studies were included for analysis, including a total of 264 967 children (n=106 167 left-behind children and adolescents; n=158 800 children and adolescents of non-migrant parents). 91 studies were done in China and focused on effects of internal labour migration. Compared with children of non-migrants, left-behind children had increased risk of depression and higher depression scores (RR 1·52 [95% CI 1·27-1·82]; SMD 0·16 [0·10-0·21]), anxiety (RR 1·85 [1·36-2·53]; SMD 0·18 [0·11-0·26]), suicidal ideation (RR 1·70 [1·28-2·26]), conduct disorder (SMD 0·16 [0·04-0·28]), substance use (RR 1·24 [1·00-1·52]), wasting (RR 1·13 [1·02-1·24]) and stunting (RR 1·12 [1·00-1·26]). No differences were identified between left-behind children and children of non-migrants for other nutrition outcomes, unintentional injury, abuse, or diarrhoea. No studies reported outcomes for other infectious diseases, self-harm, unprotected sex, or early pregnancy. Study quality varied across the included studies, with 43% of studies at high or unclear risk of bias across five or more domains.
Interpretation: Parental migration is detrimental to the health of left-behind children and adolescents, with no evidence of any benefit. Policy makers and health-care professionals need to take action to improve the health of these young people.

3. TMIH 2019;24(1):11-22

Packed red cells versus whole blood transfusion for severe paediatric anaemia, pregnancy-related anaemia and obstetric bleeding: an analysis of clinical practice guidelines from sub-Saharan Africa and evidence underpinning recommendations

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Objective: Blood component transfusion is increasingly promoted in sub-Saharan Africa (SSA), but is resource-intensive so whole blood is often used. We examined SSA recommendations about whole blood and packed red cell transfusions for pregnancy-related bleeding or anaemia, and paediatric anaemia, and evaluated the evidence underpinning these recommendations.
Method: Relevant SSA guidelines were identified using five electronic databases, websites for SSA Ministries of Health, blood transfusion services and WHO. To facilitate comparisons, indications for transfusing packed red cells or whole blood within these guidelines and reasons given for these recommendations were recorded on a pre-designed matrix. The AGREE II tool was used to appraise guidelines that gave a reason for recommending either packed red cells or whole blood. We systematically searched MEDLINE, CINAHL, Global Health, Cochrane library and NHSBT Transfusion Evidence Library, using PRISMA guidelines, for clinical studies comparing whole blood with packed red cells or combined blood components in obstetric bleeding or anaemia, or paediatric anaemia. Characteristics and findings of included studies were extracted in a standardised format and narratively summarised.
Results: 32 English language guidelines from 15 SSA countries mentioned packed red cell or whole blood use for our conditions of interest. Only seven guidelines justified their recommendation for using packed red cells or whole blood. No recommendations or justifications had supporting citations to research evidence. 33 full-text papers, from 11 234 citations, were reviewed but only one study met our inclusion criteria. This was a single-centre study in post-partum haemorrhage.
Conclusion: Evidence comparing whole blood and packed red cell transfusion for common paediatric and maternal indications is virtually absent in SSA. Therefore, it is unclear whether policies promoting red cells over whole blood transfusion are clinically appropriate. Building a relevant evidence base will help develop effective policies promoting the most appropriate use of blood in African settings.

4. TMIH 2019 Jan;24(1):31-42

Distance to care, care seeking and child mortality in rural Burkina Faso: findings from a population-based cross-sectional survey

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Objective: Although distance has been identified as an important barrier to care, evidence for an effect of distance to care on child mortality is inconsistent. We investigated the association of distance to care with self-reported care seeking behaviours, neonatal and post-neonatal under-five child mortality in rural areas of Burkina Faso.
Methods: We performed a cross-sectional survey in 14 rural areas from November 2014 to March 2015. About 100 000 women were interviewed on their pregnancy history and about 5000 mothers were interviewed on their care seeking behaviours. Euclidean distances to the closest facility were calculated. Mixed-effects logistic and Poisson regressions were used respectively to compute odds ratios for care seeking behaviours and rate ratios for child mortality during the 5 years prior to the survey.
Results: Thirty per cent of the children lived more than 7 km from a facility. After controlling for confounding factors, there was a strong evidence of a decreasing trend in care seeking with increasing distance to care ($P \leq 0.005$). There was evidence for an increasing trend in early neonatal mortality with increasing distance to care ($P = 0.028$), but not for late neonatal mortality ($P = 0.479$)

and post-neonatal under-five child mortality (P = 0.488). In their first week of life, neonates living 7 km or more from a facility had an 18% higher mortality rate than neonates living within 2 km of a facility (RR = 1.18; 95%CI 1.00, 1.39; P = 0.056). In the late neonatal period, despite the lack of evidence for an association of mortality with distance, it is noteworthy that rate ratios were consistent with a trend and similar to or larger than estimates in early neonatal mortality. In this period, neonates living 7 km or more from a facility had an 18% higher mortality rate than neonates living within 2 km of a facility (RR = 1.18; 95%CI 0.92, 1.52; P = 0.202). Thus, the lack of evidence may reflect lower power due to fewer deaths rather than a weaker association.
Conclusion: While better geographic access to care is strongly associated with increased care seeking in rural Burkina Faso, the impact on child mortality appears to be marginal. This suggests that, in addition to improving access to services, attention needs to be paid to quality of those services.

Communicable Diseases

5. Am J TMH 2019 Jan 7. doi: 10.4269/ajtmh.18-0705

WASH for WORMS: A Cluster-Randomized Controlled Trial of the Impact of a Community-Integrated Water, Sanitation, and Hygiene and Deworming Intervention on Soil-Transmitted Helminth Infections

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Water, sanitation, and hygiene (WASH) interventions have been proposed as an important complement to deworming programs for sustainable control of soil-transmitted helminth (STH) infections. We aimed to determine whether a community-based WASH program had additional benefits in reducing STH infections compared with community deworming alone. We conducted the WASH for WORMS cluster-randomized controlled trial in 18 rural communities in Timor-Leste. Intervention communities received a WASH intervention that provided access to an improved water source, promoted improved household sanitation, and encouraged handwashing with soap. All eligible community members in intervention and control arms received albendazole every 6 months for 2 years. Primary outcomes, such as infection with each STH, were measured using multiplex real-time quantitative polymerase chain reaction. We compared outcomes between study arms using generalized linear mixed models, accounting for clustering at community, household, and individual levels. At study completion, the integrated WASH and deworming intervention did not have an effect on infection with Ascaris spp. (relative risk [RR] 2.87, 95% confidence interval [CI]: 0.66-12.48, P = 0.159) or Necator americanus (RR 0.99, 95% CI: 0.52-1.89, P = 0.987), compared with deworming alone. At the last follow-up, open defecation was practiced by 66.1% (95% CI: 54.2-80.2) of respondents in the control arm versus 40.2% (95% CI: 25.3-52.6) of respondents in the intervention arm (P = 0.005). We found no evidence that the WASH intervention resulted in additional reductions in STH infections beyond that achieved with deworming alone over the 2-year trial period. The role of WASH on STH infections over a longer period of time and in the absence of deworming remains to be determined.

6. Am J TMH 2019 Feb;100(2):280-86. doi: 10.4269/ajtmh.18-0399

Characteristics of Subpatent Malaria in a Pre-Elimination Setting in Southern Zambia

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To achieve and sustain malaria elimination, identification and treatment of the asymptomatic infectious reservoir is critical. Malaria rapid diagnostic tests (RDTs) are frequently used to identify asymptomatic, Plasmodium-infected individuals through test-and-treat strategies, but their sensitivity is low when used in low transmission settings. Characteristics of individuals with subpatent (RDT-negative but polymerase chain reaction [PCR]-positive) Plasmodium parasitemia were evaluated in southern Zambia where malaria transmission has declined and efforts to achieve malaria elimination are underway. Simple random sampling based on satellite imagery was used to select households for participation in community-based, cross-sectional surveys between 2008 and 2013. Questionnaires were administered to collect information on age, gender, recent history of malaria symptoms, and recent antimalarial drug use. Blood samples were collected by finger prick for Plasmodium falciparum histidine-rich protein 2 RDT, blood smears for microscopy, and dried blood spots for molecular analysis to detect malaria parasites and their sexual stage. Of 3,863 participants with complete data, 102 (2.6%) were positive by microscopy, RDT, or PCR. Of these, 48 (47%) had subpatent parasitemia. Most individuals with subpatent parasitemia were asymptomatic (85%). Compared with individuals without parasitemia, individuals with subpatent parasitemia were significantly more likely to be aged 5-25 years. Approximately one quarter (27%) of those with subpatent parasitemia had detectable gametocytemia. These findings suggest that strategies based on active or reactive case detection can identify asymptomatic individuals positive by RDT, but more sensitive diagnostic tests or focal drug administration may be necessary to target individuals with subpatent parasitemia to achieve malaria elimination.

7. Am J TMH 2019 Feb;100(2):256-63. doi: 10.4269/ajtmh.17-0546

Evaluating Response Time in Zanzibar's Malaria Elimination Case-Based Surveillance-Response System

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As countries transition toward malaria elimination, malaria programs rely on surveillance-response systems, which are often supported by web- and mobile phone-based reporting tools. Such surveillance-response systems are interventions for elimination, making it important to determine if they are operating optimally. A metric to measure this by is timeliness. This study used a mixed-methods approach to investigate the response time of Zanzibar's malaria elimination surveillance-response system, Malaria Case Notification (MCN). MCN conducts both passive and reactive case detection, supported by a mobile phone-based reporting tool called Coconut Surveillance. Using data obtained from RTI International and the Zanzibar Malaria Elimination Program (ZAMEP), analysis of summary statistics was conducted to investigate the association of response time with geography, and time series techniques were used to investigate trends in response time and its association with the number of reported cases. Results indicated that response time varied by the district in Zanzibar (0.6-6.05 days) and that it was not associated with calendar time or the number of reported cases. Survey responses and focus groups with a cadre of health workers, district malaria surveillance

officers, shed light on operational challenges faced during case investigation, such as incomplete health records and transportation issues, which stem from deficiencies in aspects of ZAMEP's program management. These findings illustrate that timely response for malaria elimination depends on effective program management, despite the automation of web-based or mobile phone-based tools. For surveillance-response systems to work optimally, malaria programs should ensure that optimal management practices are in place.

8. BMJ Global Health: bmjgh-2018-001271

Commentary - Improving emergency preparedness and response in the Asia-Pacific

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The severe acute respiratory syndrome (SARS) outbreak in 2002/2003, which affected 37 countries and resulted in nearly 800 deaths, prompted a critical re-think of the global health security architecture. Recognition of the threat posed by emerging infectious diseases (EIDs) and the need to improve national and global surveillance and outbreak response systems motivated the World Health Assembly to adopt the International Health Regulations (IHR) in 2005. In the interim, the fateful tsunami of 2004 provided another turning point, emphasising the need for emergency preparedness in order to respond to and recover from major natural disasters. Against this backdrop, WHO's Western Pacific and South-East Asia regions adopted an all-hazards approach, encompassing disease outbreaks and natural disasters such as cyclones, tsunamis and earthquakes in order to strengthen their health emergency programmes.

Summary box

- Addressing regional health security threats require functional health systems that have integrated surveillance and response capacity, as specified by the International Health Regulations (IHR).
- Country-level IHR implementation is often suboptimal with limited intra-regional and inter-regional coordination and collaboration.
- Joint external evaluations provide multidimensional country-level assessments, but human and animal disease surveillance data are poorly integrated and subnational vulnerability is rarely considered.
- Retaining political commitment in between outbreaks/disasters requires better informed leadership and recognition of Health Security as a standing priority.
- Weak health systems require increased domestic investment, coordinated international assistance and a commitment to universal health coverage, including investment in quality-assured laboratory infrastructure and reporting systems.

9. BMJ Global Health: bmjgh-2018-001157

Research - Assessing global preparedness for the next pandemic: development and application of an Epidemic Preparedness Index

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Introduction Robust metrics for national-level preparedness are critical for assessing global resilience to epidemic and pandemic outbreaks. However, existing preparedness assessments focus primarily

on public health systems or specific legislative frameworks, and do not measure other essential capacities that enable and support public health preparedness and response.
Methods We developed an Epidemic Preparedness Index (EPI) to assess national-level preparedness. The EPI is global, covering 188 countries. It consists of five subindices measuring each country's economic resources, public health communications, infrastructure, public health systems and institutional capacity. To evaluate the construct validity of the EPI, we tested its correlation with proxy measures for preparedness and response capacity, including the timeliness of outbreak detection and reporting, as well as vaccination rates during the 2009 H1N1 influenza pandemic.
Results The most prepared countries were concentrated in Europe and North America, while the least prepared countries clustered in Central and West Africa and Southeast Asia. Better prepared countries were found to report infectious disease outbreaks more quickly and to have vaccinated a larger proportion of their population during the 2009 pandemic.
Conclusion The EPI measures a country's capacity to detect and respond to infectious disease events. Existing tools, such as the Joint External Evaluation (JEE), have been designed to measure preparedness within a country over time. The EPI complements the JEE by providing a holistic view of preparedness and is constructed to support comparative risk assessment between countries. The index can be updated rapidly to generate global estimates of pandemic preparedness that can inform strategy and resource allocation.

10. Lancet 2019 pii: S0140-6736(18)32277-3. doi: 10.1016/S0140-6736(18)32277-3

Scaling up prevention and treatment towards the elimination of hepatitis C: a global mathematical model

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Background: The revolution in hepatitis C virus (HCV) treatment through the development of direct-acting antivirals (DAAs) has generated international interest in the global elimination of the disease as a public health threat. In 2017, this led WHO to establish elimination targets for 2030. We evaluated the impact of public health interventions on the global HCV epidemic and investigated whether WHO's elimination targets could be met.
Methods: We developed a dynamic transmission model of the global HCV epidemic, calibrated to 190 countries, which incorporates data on demography, people who inject drugs (PWID), current coverage of treatment and prevention programmes, natural history of the disease, HCV prevalence, and HCV-attributable mortality. We estimated the worldwide impact of scaling up interventions that reduce risk of transmission, improve access to treatment, and increase screening for HCV infection by considering six scenarios: no change made to existing levels of diagnosis or treatment; sequentially adding the following interventions: blood safety and infection control, PWID harm reduction, offering of DAAs at diagnosis, and outreach screening to increase the number diagnosed; and a scenario in which DAAs are not introduced (ie, treatment is only with pegylated interferon and oral ribavirin) to investigate the effect of DAA use. We explored the effect of varying the coverage or impact of these interventions in sensitivity analyses and also assessed the impact on the global epidemic of removing certain key countries from the package of interventions.
Findings: By 2030, interventions that reduce risk of transmission in the non-PWID population by 80% and increase coverage of harm reduction services to 40% of PWID could avert 14·1 million (95%

credible interval 13·0-15·2) new infections. Offering DAAs at time of diagnosis in all countries could prevent 640 000 deaths (620 000-670 000) from cirrhosis and liver cancer. A comprehensive package of prevention, screening, and treatment interventions could avert 15·1 million (13·8-16·1) new infections and 1·5 million (1·4-1·6) cirrhosis and liver cancer deaths, corresponding to an 81% (78-82) reduction in incidence and a 61% (60-62) reduction in mortality compared with 2015 baseline. This reaches the WHO HCV incidence reduction target of 80% but is just short of the mortality reduction target of 65%, which could be reached by 2032. Reducing global burden depends upon success of prevention interventions, implementation of outreach screening, and progress made in key high-burden countries including China, India, and Pakistan.
Interpretation: Further improvements in blood safety and infection control, expansion or creation of PWID harm reduction services, and extensive screening for HCV with concomitant treatment for all are necessary to reduce the burden of HCV. These findings should inform the ongoing global action to eliminate the HCV epidemic.

11. Lancet 2018;392(10161):2313-24

Chronic hepatitis B virus infection

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Chronic hepatitis B virus infection is a global public health threat that causes considerable liver-related morbidity and mortality. It is acquired at birth or later via person-to-person transmission. Vaccination effectively prevents infection and chronic hepatitis B virus carriage. In chronically infected patients, an elevated serum hepatitis B virus DNA concentration is the main risk factor for disease progression, although there are other clinical and viral parameters that influence disease outcomes. In addition to liver biochemistry, virological markers, and abdominal ultrasonography, non-invasive assessment of liver fibrosis is emerging as an important assessment modality. Long-term nucleos(t)ide-analogue therapy is safe and well tolerated, achieves potent viral suppression, and reduces the incidence of liver-related complications. However, a need to optimise management remains. Promising novel therapies are at the developmental stage. With current vaccines, therapies, and an emphasis on improving linkage to care, WHO's goal of eliminating hepatitis B virus as a global health threat by 2030 is achievable.

12. Lancet 2018;392(10163):2425

World Report - WHO keeps polio on the international health emergency list

Zarocostas J.

After years of major gains, the fight to eradicate polio is facing setbacks marked by a spike in wild poliovirus type 1 cases in Afghanistan, stagnation in Pakistan, and the spread of circulating vaccine-derived poliovirus in several countries. Concerns of a possible resurgence of the disease worldwide are heightened, an emergency committee of WHO has warned.

13. Lancet 2019;393(10169):350-63

Seminar - Dengue

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Mortality from severe dengue is low, but the economic and resource burden on health services remains substantial in endemic settings. Unfortunately, progress towards development of effective therapeutics has been slow, despite notable advances in the understanding of disease pathogenesis and considerable investment in antiviral drug discovery. For decades antibody-dependent enhancement has been the prevalent model to explain dengue pathogenesis, but it was only recently demonstrated in vivo and in clinical studies. At present, the current mainstay of management for most symptomatic dengue patients remains careful observation and prompt but judicious use of intravenous hydration therapy for those with substantial vascular leakage. Various new promising technologies for diagnosis of dengue are currently in the pipeline. New sample-in, answer-out nucleic acid amplification technologies for point-of-care use are being developed to improve performance over current technologies, with the potential to test for multiple pathogens using a single specimen. The search for biomarkers that reliably predict development of severe dengue among symptomatic individuals is also a major focus of current research efforts. The first dengue vaccine was licensed in 2015 but its performance depends on serostatus. There is an urgent need to identify correlates of both vaccine protection and disease enhancement. A crucial assessment of vector control tools should guide a research agenda for determining the most effective interventions, and how to best combine state-of-the-art vector control with vaccination.

Health Policy

14. Am J TMH 2019 Feb;100(2):460-469. doi: 10.4269/ajtmh.18-0529

The Effect of Text Message Reminders to Health Workers on Quality of Care for Malaria, Pneumonia, and Diarrhea in Malawi: A Cluster-Randomized, Controlled Trial

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The use of mobile technologies in medicine, or mHealth, holds promise to improve health worker (HW) performance, but evidence is mixed. We conducted a cluster-randomized controlled trial to evaluate the effect of text message reminders to HWs in outpatient health facilities (HFs) on quality of care for malaria, pneumonia, and diarrhea in Malawi. After a baseline HF survey (2,360 patients) in January 2015, 105 HFs were randomized to three arms: 1) text messages to HWs on malaria case management; 2) text messages to HWs on malaria, pneumonia, and diarrhea case management (latter two for children < 5 years); and 3) control arm (no messages). Messages were sent beginning April 2015 twice daily for 6 months, followed by an endline HF survey (2,536 patients) in November 2015. An intention-to-treat analysis with difference-in-differences binomial regression modeling was performed. The proportion of patients with uncomplicated malaria managed correctly increased from 42.8% to 59.6% in the control arm, from 43.7% to 55.8% in arm 1 (effect size -4.7%-points, 95% confidence interval (CI): -18.2, 8.9, P = 0.50) and from 30.2% to 50.9% in arm 2 (effect size 3.9%-points, 95% CI: -14.1, 22.0, P = 0.67). Prescription of first-line antibiotics to children < 5 years with clinically defined pneumonia increased in all arms, but decreased in arm 2 (effect size -4.1%-points,

95% CI: -42.0, 33.8, P = 0.83). Prescription of oral rehydration solution to children with diarrhea declined slightly in all arms. We found no significant improvements in malaria, pneumonia, or diarrhea treatment after HW reminders, illustrating the importance of rigorously testing new interventions before adoption.

15. BMJ Global Health: bmj-2018-001145

Analysis - Global health security and universal health coverage: from a marriage of convenience to a strategic, effective partnership

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Global health security and universal health coverage have been frequently considered as “two sides of the same coin”. Yet, greater analysis is required as to whether and where these two ideals converge, and what important differences exist. A consequence of ignoring their individual characteristics is to distort global and local health priorities in an effort to streamline policymaking and funding activities. This paper examines the areas of convergence and divergence between global health security and universal health coverage, both conceptually and empirically. We consider analytical concepts of risk and human rights as fundamental to both goals, but also identify differences in priorities between the two ideals. We support the argument that the process of health system strengthening provides the most promising mechanism of benefiting both goals.

Summary box

What is already known about this subject?

Universal health coverage (UHC) and global health security (GHS) are frequently being used in tandem by policymakers, recognising that there are synergies between the two parallel agendas.

What are the new findings?

UHC and GHS goals are in tension. The research and practice communities that represent these two streams need to engage so that smart strategies can be identified to improve both aims simultaneously using codependent, but distinct policy.

Risk and human rights are two areas of convergence between UHC and GHS.

Divergence appears in the conceptualisation of risk at the collective or individual level, and the prioritisation of domestic or global activity.

What are the recommendations for policy and practice?

Health systems strengthening can be the policy mechanism which, brings GHS and UHC together, elevating health and mitigating risk for all.

16. BMJ Global Health: bmjgh-2018-001013

Health systems changes after decentralisation: progress, challenges and dynamics in Pakistan

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Decentralisation is widely practised but its scrutiny tends to focus on structural and authority changes or outcomes. Politics and process of devolution implementation needs to be better understood to evaluate how national governments use the enhanced decision space for bringing improvements in the health system and the underlying challenges faced. We use the example of Pakistan’s radical, politically driven provincial devolution to analyse how national structures use

decentralisation opportunities for improved health planning, spending and carrying out transformations to the health system. Our narrative draws on secondary data sources from the PRIMASYS study, supplemented with policy roundtable notes from Pakistan.
Our analysis shows that in decentralised Pakistan, health became prioritised for increased government resources and achieved good budgetary use, major strides were made contextualised sector-wide health planning and legislations, and a proliferation seen in governance measures to improve and regulate healthcare delivery. Despite a disadvantaged and abrupt start to devolution, high ownership by politicians and bureaucracy in provincial governments led to resourcing, planning and innovations. However, effective translation remained impeded by weak institutional capacity, feeble federal–provincial coordination and vulnerability to interference by local elites.
Building on this illustrative example, we propose (1) political management of decentralisation for effective national coordination, sustaining stable leadership and protecting from political interfere by local elites; (2) investment in stewardship capacity in the devolved structures as well as the central ministry to deliver on new roles.
Summary box
A process analysis of response to decentralisation in Pakistan and its consequences on health systems comes up with five main findings:

- Devolution led to increased government health allocations, sector-wide planning and governance innovations.
- Enthusiasm and ownership within subnational political–bureaucratic circles provided support.
- Weak national coordination capacity at centre and insufficient stewardship capacity in provinces impeded progress.
- Health systems became more vulnerable to local political interference requiring active management.
- Decentralisation implementation requires continued centre-province discussion on unresolved boundaries.

17. BMJ Global Health: bmjgh-2018-001084

Task shifting to improve the provision of integrated chronic care: realist evaluation of a lay health worker intervention in rural South Africa

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Introduction Task shifting is a potential solution to the shortage of healthcare personnel in low/middle-income countries, but contextual factors often dilute its effectiveness. We report on a task shifting intervention using lay health workers to support clinic staff in providing chronic disease care in rural South Africa, where the HIV epidemic and an ageing population have increased demand for care.
Methods We conducted a realist evaluation in a cluster randomised controlled trial. We conducted observations in clinics, focus group discussions, in-depth interviews and patient exit interviews, and wrote weekly diaries to collect data.
Results All clinic managers had to cope with an increasing but variable patient load and unplanned staff shortages, insufficient space, poorly functioning equipment and erratic supply of drugs. These conditions inevitably generated tension among staff. Lay health workers relieved the staff of some of

their tasks and improved care for patients, but in some cases the presence of the lay health worker generated conflict with other staff. Where managers were able to respond to the changing circumstances, and to contain tension among staff, facilities were better able to meet patient needs. This required facility managers to be flexible, consultative and willing to act on suggestions, sometimes from junior staff and patients. While all facilities experienced an erratic supply of drugs and poorly maintained equipment, facilities where there was effective management, teamwork and sufficient space had better chronic care processes and a higher proportion of patients attending on their appointed day.
Conclusion Lay health workers can be valuable members of a clinic team, and an important resource for managing increasing patient demand in primary healthcare. Task shifting will only be effective if clinic managers respond to the constantly changing system and contain conflict between staff. Strengthening facility-level management and leadership skills is a priority.

18. BMJ Global Health: bmjgh-2018-001159

Trends and drivers of government health spending in sub-Saharan Africa, 1995–2015

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Introduction Government health spending is a primary source of funding in the health sector across the world. However, in sub-Saharan Africa, only about a third of all health spending is sourced from the government. The objectives of this study are to describe the growth in government health spending, examine its determinants and explain the variation in government health spending across sub-Saharan African countries.
Methods We used panel data on domestic government health spending in 46 countries in sub-Saharan Africa from 1995 to 2015 from the Institute for Health Metrics and Evaluation. A regression model was used to examine the factors associated with government health spending, and Shapley decomposition was used to attribute the contributions of factors to the explained variance in government health spending.
Results While the growth rate in government health spending in sub-Saharan Africa has been positive overall, there are variations across subgroups. Between 1995 and 2015, government health spending in West Africa grew by 6.7% (95% uncertainty intervals [UI]: 6.2% to 7.0%) each year, whereas in Southern Africa it grew by only 4.5% (UI: 4.5% to 4.5%) each year. Furthermore, per-person government health spending ranged from $651 (Namibia) in 2017 purchasing power parity dollars to $4 (Central African Republic) in 2015. Good governance, national income and the share of it that is government spending were positively associated with government health spending. The results from the decomposition, however, showed that individual country characteristics made up the highest percentage of the explained variation in government health spending across sub-Saharan African countries.
Conclusion These findings highlight that a country's policy choices are important for how much the health sector receives. As the attention of the global health community focuses on ways to stimulate domestic government health spending, an understanding that individual country sociopolitical context is an important driver for success will be key.

19. Lancet 2018;392(10160):2203-12

Mortality due to low-quality health systems in the universal health coverage era: a systematic analysis of amenable deaths in 137 countries

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Background: Universal health coverage has been proposed as a strategy to improve health in low-income and middle-income countries (LMICs). However, this is contingent on the provision of good-quality health care. We estimate the excess mortality for conditions targeted in the Sustainable Development Goals (SDG) that are amenable to health care and the portion of this excess mortality due to poor-quality care in 137 LMICs, in which excess mortality refers to deaths that could have been averted in settings with strong health systems.

Methods: Using data from the 2016 Global Burden of Disease study, we calculated mortality amenable to personal health care for 61 SDG conditions by comparing case fatality between each LMIC with corresponding numbers from 23 high-income reference countries with strong health systems. We used data on health-care utilisation from population surveys to separately estimate the portion of amenable mortality attributable to non-utilisation of health care versus that attributable to receipt of poor-quality care.

Findings: 15·6 million excess deaths from 61 conditions occurred in LMICs in 2016. After excluding deaths that could be prevented through public health measures, 8·6 million excess deaths were amenable to health care of which 5·0 million were estimated to be due to receipt of poor-quality care and 3·6 million were due to non-utilisation of health care. Poor quality of health care was a major driver of excess mortality across conditions, from cardiovascular disease and injuries to neonatal and communicable disorders.

Interpretation: Universal health coverage for SDG conditions could avert 8·6 million deaths per year but only if expansion of service coverage is accompanied by investments into high-quality health systems.

Erratum in Lancet 2018 Sep 20.

20. Lancet 2018;392(10163):2426

World Report - Boosting quality diagnostics could give Africa better health

Makoni M.

The Africa Centres for Disease Control and Prevention has launched, on Nov 16, the Africa Collaborative Initiative to Advance Diagnostics (AFCAD). AFCAD's partnerships include the African Society for Laboratory Medicine, Institut de Recherche en Santé, de Surveillance Epidémiologique et de Formation, WHO-Africa, Clinton Health Access Initiative, African Field Epidemiology Network, and UNITAID.

The role of AFCAD is to support efforts to achieve equitable access of up to 80% coverage to the WHO essential package of health that includes essential diagnostics. The initiative will focus on eliminating or eradicating diseases prioritised by global health normative agencies—such as ending HIV epidemics, multiresistant tuberculosis, malaria, viral hepatitis, cervical cancer, and neglected tropical diseases; early detection and prevention of antimicrobial resistance; reduction of barriers to early detection, prevention, and management of non-communicable diseases; and institution of early warning systems to ensuring timely detection and diagnosis of epidemic-prone diseases.

The AFCAD will prioritise approaches that accelerate regulation to facilitate timely and wide access to essential diagnostics, market interventions to improve affordability, communication and dissemination of data supporting evidence-based improvement of diagnostic services, and advocacy for appropriate investment in diagnostics.

21. Lancet 2018;392(10165):2656

Editorial - Exporting or exploiting?

Here is a quiz question for you—what is Cuba's main export? As many working in global health will know, it is medical professionals. Cuba brought in US$11 billion by leasing professional medical services around the world last year, compared with the $3 billion generated by the Cuban tourist industry. Some 30 000 Cuban health personnel work around the globe.
Interesting as this fact is, the Cuban Government's removal of over 8000 health workers from Brazil in response to the newly elected Jair Bolsonaro's incendiary remarks about their presence demands more serious attention. The presence of Cuban health workers in rural areas of Brazil that might otherwise struggle for access to primary health care comprised 81% of doctors working among Brazil's indigenous population, with 1500 municipalities losing all access to health care.
Although this is, on the face of it, a disaster for the Brazilians most in need of medical care, Bolsonaro's Government has offered a typically robust response, claiming it has already filled 8000 of the rural positions with Brazilian doctors. Bolsonaro has gone further, telling reporters “we cannot allow Cuban slaves in Brazil”, a reference to the fact that the Cuban Government takes 75% of each health worker's pay. Indeed, some Cubans have so far claimed refugee status in an attempt to remain in Brazil.
It is a complex case of international medical diplomacy with no clear winners. On one side, the exercise of soft diplomacy via the export of heavily taxed professionals who are not allowed to take their families with them feels like something of an anachronism in a world where medical professionals move all over the world in search of work. Sending vast swathes of people to another country in an attempt to garner both international influence and money is a practice we should be asking harder questions about. On the other, Bolsonaro's inflammatory remarks might have caused severe damage to rural Brazil, with Brazilian mayors warning there could be as many as 30 million people facing a care crisis. Bolsonaro would be wise to temper his speech when it comes to the health of millions of his most vulnerable citizens.

22. Lancet 2019;393(10166):75-102

Universal health coverage in Indonesia: concept, progress, and challenges

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Indonesia is a rapidly growing middle-income country with 262 million inhabitants from more than 300 ethnic and 730 language groups spread over 17 744 islands, and presents unique challenges for health systems and universal health coverage (UHC). From 1960 to 2001, the centralised health system of Indonesia made gains as medical care infrastructure grew from virtually no primary health centres to 20 900 centres. Life expectancy improved from 48 to 69 years, infant mortality decreased

from 76 deaths per 1000 livebirths to 23 per 1000, and the total fertility rate decreased from 5·61 to 2·11. However, gains across the country were starkly uneven with major health gaps, such as the stagnant maternal mortality of around 300 deaths per 100 000 livebirths, and minimal change in neonatal mortality. The centralised one size fits all approach did not address the complexity and diversity in population density and dispersion across islands, diets, diseases, local living styles, health beliefs, human development, and community participation. Decentralisation of governance to 354 districts in 2001, and currently 514 districts, further increased health system heterogeneity and exacerbated equity gaps. The novel UHC system introduced in 2014 focused on accommodating diversity with flexible and adaptive implementation features and quick evidence-driven decisions based on changing needs. The UHC system grew rapidly and covers 203 million people, the largest single-payer scheme in the world, and has improved health equity and service access. With early success, challenges have emerged, such as the so-called missing-middle group, a term used to designate the smaller number of people who have enrolled in UHC in wealth quintiles Q2-Q3 than in other quintiles, and the low UHC coverage of children from birth to age 4 years. Moreover, high costs for non-communicable diseases warrant new features for prevention and promotion of healthy lifestyles, and investment in a robust integrated digital health-information system for front-line health workers is crucial for impact and sustainability. This Review describes the innovative UHC initiative of Indonesia along with the future roadmap required to meet sustainable development goals by 2030.
Comment in Lancet 2019;393(10166):2

HIV / AIDS

23. TMIH 2018;23(12):1384-93

Linkage to care and antiretroviral therapy initiation by testing modality among individuals newly diagnosed with HIV in Tanzania, 2014-2017

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Objective: To measure linkage to care and antiretroviral therapy (ART) initiation among newly diagnosed individuals with HIV in a rural Tanzanian community.
Methods: We included all new HIV diagnoses of adults made between 2014 and 2017 during community- or facility-based HIV testing and counselling (HTC) in a rural ward in northwest Tanzania. Community-based HTC included population-level HIV serological testing (sero-survey), and facility-based HTC included a stationary, voluntary HTC clinic (VCT) and an antenatal clinic (ANC) offering provider-initiated HTC (ANC-PITC). Cox regression models were used to compare linkage to care rates by testing modality and identify associated factors. Among those in care, we compared initial CD4 cell counts and ART initiation rates by testing modality.
Results: A total of 411 adults were newly diagnosed, of whom 10% (27/265 sero-survey), 18% (3/14 facility-based ANC-PITC) and 53% (68/129 facility-based VCT) linked to care within 90 days. Individuals diagnosed using facility-based VCT were seven times (95% CI: 4.5-11.0) more likely to link to care than those diagnosed in the sero-survey. We found no difference in linkage rates between those diagnosed using facility-based ANC-PITC and sero-survey (P = 0.26). Among individuals in care, 63% of those in the sero-survey had an initial CD4 count >350 cells/mm3 vs. 29% of those using

facility-based VCT (P = 0.02). The proportion who initiated ART within 1 year of linkage to care was similar for both groups (94% sero-survey vs. 85% facility-based VCT; P = 0.16).
Conclusions: Community-based sero-surveys are important for earlier diagnosis of HIV-positive individuals; however, interventions are essential to facilitate linkage to care.

Sexual and Reproductive Health

24. Am J TMH 2018 Dec;99(6):1415-18. doi: 10.4269/ajtmh.17-0957

Perinatal Outcomes in Vertically Infected Neonates During a Chikungunya Outbreak on the Island of Curaçao

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Recent outbreaks of Chikungunya virus (CHIKV) infection confirm the vulnerability of neonates after vertical transmission. In 2014, CHIKV was reported for the first time in the Americas, including the island of Curaçao. We describe the outcomes of symptomatic neonates with vertically transmitted CHIKV infection during the CHIKV epidemic, who were admitted in the Saint Elisabeth Hospital, Willemstad, Curaçao. There were three symptomatic neonates with serologically confirmed infection. Two neonates developed neurological complications, including convulsions and intracerebral bleeding. One newborn, in whom maternal infection occurred 7 weeks before delivery, had a fatal outcome after birth. Maternal-fetal transmission of CHIKV may cause severe neonatal complications. There is a need to share experiences and to implement protocols toward the management of perinatal CHIKV infection.

25. BMJ Global Health: bmjgh-2018-001167

Social return on investment of emergency obstetric care training in Kenya

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Introduction Emergency obstetric care (EmOC) training is considered a key strategy for reducing maternal and perinatal morbidity and mortality. Although generally considered effective, there is minimal evidence on the broader social impact and/or value-for-money (VfM). This study assessed the social impact and VfM of EmOC training in Kenya using social return on investment (SROI) methodology.
Methods Mixed-methods approach was used, including interviews (n=21), focus group discussions (n=18) incorporating a value game, secondary data analysis and literature review, to obtain all relevant data for the SROI analysis. Findings were incorporated into the impact map and used to estimate the SROI ratio. Sensitivity analyses were done to test assumptions.
Results Trained healthcare providers, women and their babies who received care from those providers were identified as primary beneficiaries. EmOC training led to improved knowledge and skills and improved attitudes towards patients. However, increased workload was reported as a negative outcome by some healthcare providers. Women who received care expected and experienced positive outcomes including reduced maternal and newborn morbidity and mortality. After accounting for external influences, the total social impact for 93 5-day EmOC training workshops over a 1-year period was valued at I$9.5 million, with women benefitting the most from

the intervention (73%). Total direct implementation cost was I$745 000 for 2965 healthcare providers trained. The cost per trained healthcare provider per day was I$50.23 and SROI ratio was 12.74:1. Based on multiple one-way sensitivity analyses, EmOC training guaranteed VfM in all scenarios except when trainers were paid consultancy fees and the least amount of training outcomes occurred.
Conclusion EmOC training workshops are a worthwhile investment. The implementation approach influences how much VfM is achieved. The use of volunteer facilitators, particularly those based locally, to deliver EmOC training is a critical driver in increasing social impact and achieving VfM for investments made.

26. Lancet 2019;393(10169):340-8

The frequency of intrapartum caesarean section use with the WHO partograph versus Zhang's guideline in the Labour Progression Study (LaPS): a multicentre, cluster-randomised controlled trial
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Background. There is an ongoing debate concerning which guidelines and monitoring tools are most beneficial for assessing labour progression, to help prevent use of intrapartum caesarean section (ICS). The WHO partograph has been used for decades with the assumption of a linear labour progression; however, in 2010, Zhang introduced a new guideline suggesting a more dynamic labour progression. We aimed to investigate whether the frequency of ICS use differed when adhering to the WHO partograph versus Zhang's guideline for labour progression.
Methods. We did a multicentre, cluster-randomised controlled trial at obstetric units in Norway, and each site was required to deliver more than 500 fetuses per year to be eligible for inclusion. The participants were nulliparous women who had a singleton, full-term fetus with cephalic presentation, and who entered spontaneous active labour. The obstetric units were treated as clusters, and women treated within these clusters were all given the same treatment. We stratified these clusters by size and number of previous caesarean sections. The clusters containing the obstetric units were then randomly assigned (1:1) to the control group, which adhered to the WHO partograph, or to the intervention group, which adhered to Zhang's guideline. The randomisation was computer-generated and was done in the Unit of Biostatistics and Epidemiology, Oslo University Hospital, Oslo, Norway, and investigators in this unit had no further involvement in the trial. Our study design did not enable masking of participants or health-care providers, but the investigators who were analysing the data were masked to group allocation. The primary outcome was use of ICS during active labour (cervical dilatation of 4–10 cm) in all participating women. The Labour Progression Study (LaPS) is registered with ClinicalTrials.gov, number NCT02221427.
Findings. Between Aug 1, 2014, and Sept 1, 2014, 14 clusters were enrolled in the LaPS trial, and on Sept 11, 2014, seven obstetric units were randomly assigned to the control group (adhering to the WHO partograph) and seven obstetric units were randomly assigned to the intervention group (adhering to Zhang's guideline). Between Dec 1, 2014, and Jan 31, 2017, 11 615 women were judged to be eligible for recruitment in the trial, which comprised 5421 (46·7%) women in the control group units and 6194 (53·3%) women in the intervention group units. In the control group, 2100 (38·7%) of 5421 women did not give signed consent to participate and 16 (0·3%) women abstained from participation. In the intervention group, 2181 (35·2%) of 6194 women did not give signed consent to

participate and 41 (0·7%) women abstained from participation. 7277 (62·7%) of 11 615 eligible women were therefore included in the analysis of the primary endpoint. Of these women, 3305 (45·4%) participants were in an obstetric unit that was randomly assigned to the control group (adhering to the WHO partograph) and 3972 (54·6%) participants were in an obstetric unit that was randomly assigned to the intervention group (adhering to Zhang's guideline). No women dropped out during the trial. Before the start of the trial, ICS was used in 9·5% of deliveries in the control group obstetric units and in 9·3% of intervention group obstetric units. During our trial, there were 196 (5·9%) ICS deliveries in women in the control group (WHO partograph) and 271 (6·8%) ICS deliveries in women in the intervention group (Zhang's guideline), and the frequency of ICS use did not differ between the groups (adjusted relative risk 1·17, 95% CI 0·98–1·40; p=0·08; adjusted risk difference 1·00%, 95% CI −0·1 to 2·1). We identified no maternal or neonatal deaths during our study. Interpretation. We did not find any significant difference in the frequency of ICS use between the obstetric units assigned to adhere to the WHO partograph and those assigned to adhere to Zhang's guideline. The overall decrease in ICS use that we observed relative to the previous frequency of ICS use noted in these obstetric units might be explained by the close focus on assessing labour progression more than use of the guidelines. Our results represent an important contribution to the discussion on implementation of the new guideline.

27. TMIH 2018;23(12):1332-41

Facilitators for maternity waiting home utilisation at Attat Hospital: a mixed-methods study based on 45 years of experience

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Objective: To describe facilitators for maternity waiting home (MWH) utilisation from the perspectives of MWH users and health staff.
Methods: Data collection took place over several time frames between March 2014 and January 2018 at Attat Hospital in Ethiopia, using a mixed-methods design. This included seven in-depth interviews with staff and users, three focus group discussions with 28 users and attendants, a structured questionnaire among 244 users, a 2-week observation period and review of annual facility reports. The MWH was built in 1973; consistent records were kept from 1987. Data analysis was done through content analysis, descriptive statistics and data triangulation.
Results: The MWH at Attat Hospital has become a well-established intervention for high-risk pregnant women (1987-2017: from 142 users of 777 total attended births [18.3%] to 571 of 3693 [15.5%]; range 142-832 users). From 2008, utilisation stabilised at on average 662 women annually. Between 2014 and 2017, total attended births doubled following government promotion of facility births; MWH utilisation stayed approximately the same. Perceived high quality of care at the health facility was expressed by users to be an important reason for MWH utilisation (114 of 128 MWH users who had previous experience with maternity services at Attat Hospital rated overall services as good). A strong community public health programme and continuous provision of comprehensive emergency obstetric and neonatal care (EmONC) seemed to have contributed to realising community support for the MWH. The qualitative data also revealed that awareness of pregnancy-related complications and supportive husbands (203 of 244 supported the MWH stay financially) were key facilitators. Barriers to utilisation existed (no cooking utensils at the MWH [198/244]; attendant

being away from work [190/244]), but users considered these necessary to overcome for the perceived benefit: a healthy mother and baby.
Conclusions: Facilitators for MWH utilisation according to users and staff were perceived high-quality EmONC, integrated health services, awareness of pregnancy-related complications and the husband's support in overcoming barriers. If providing high-quality EmONC and integrating health services are prioritised, MWHs have the potential to become an accepted intervention in (rural) communities. Only then can MWHs improve access to EmONC.

28. TMIH 2018;23(12):1350-63

Menstrual hygiene management and school absenteeism among adolescent students in Indonesia: evidence from a cross-sectional school-based survey

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Objective: To assess the prevalence of menstrual hygiene management (MHM) knowledge and practices among adolescent schoolgirls in Indonesia, and assess factors associated with poor MHM and school absenteeism due to menstruation.
Methods: A cross-sectional survey enrolled a representative sample of urban and rural school-going girls aged 12-19 years in four provinces of Indonesia. A semi-structured, self-administered questionnaire obtained socio-demographic characteristics, knowledge, practices and attitudes related to menstruation, MHM and school absenteeism. School water, sanitation and hygiene (WASH) facilities were also assessed. Univariate weighted population prevalence was estimated and multivariable logit regression analyses applied to explore associations.
Results: A total of 1159 adolescent girls with a mean age of 15 years (SD = 1.8) participated. Most girls (90.8%, 95% confidence interval (95% CI) = 79.7-96.1) had reached menarche. Over half (64.1%, 95% CI = 49.9-76.2) reported poor MHM practices, and 11.1% (95% CI = 8.1-15.2) had missed one or more days of school during their most recent menstrual period. Poor MHM practices were associated with rural residence (Adjusted odds ratio (AOR) = 1.73, 95% CI = 1.13-2.64), province (various AOR), lower school grade (AOR = 1.69, 95% CI = 1.05-2.74) and low knowledge of menstruation (AOR = 3.49, 95% CI = 1.61-7.58). Absenteeism was associated with living in rural areas (AOR = 3.96, 95% CI = 3.02-5.18), province (various AOR), higher school grade (AOR = 3.02, 95% CI = 2.08-4.38), believing menstruation should be kept secret (AOR = 1.47, 95% CI = 1.03-2.11), experiencing serious menstrual pain (AOR = 1.68, 95% CI = 1.06-2.68) and showed mixed associations with school WASH facilities.
Conclusions: High prevalence of poor MHM and considerable school absenteeism due to menstruation among Indonesian girls highlight the need for improved interventions that reach girls at a young age and address knowledge, shame and secrecy, acceptability of WASH infrastructure and menstrual pain management.

29. TMIH 2019;24(1):2-10

Removal of user fees and system strengthening improves access to maternity care, reducing neonatal mortality in a district hospital in Lesotho

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Objective: Lesotho has one of the highest maternal mortality rates in the world. While at primary health care (PHC) level maternity care is free, at hospital level co-payments are required from

patients. We describe service utilisation and delivery outcomes before and after removal of user fees and quality of delivery care, and associated costs, at St Joseph's Hospital (SJH) in Roma, Lesotho.
Methods: We compared utilisation of delivery services, stillbirths and maternal and neonatal mortality for the periods before (1 July 2012 to 31 December 2013) and after (1 January 2014 to 30 June 2015) user fee removal through a retrospective chart review and estimated additional costs attributed to user fee removal from provider (hospital) and patient perspectives.
Results: Of 4715 deliveries 3855 were at SJH and 860 at PHC centres. Of women delivering at SJH 684 (18.5%) were ≤19 years and 894 (23.6%) were HIV positive. After user fee removal hospital deliveries increased by 49% - from 1547 to 2308 - and neonatal mortality decreased from 4.8 to 1.3 per 1000 live births (P = 0.033). Extrapolating costs to the entire country, 1 USD per capita per year would allow user fee removal at hospital level, the provision of free transport to/from and accommodation at hospital.
Conclusion: Removing user fees for hospital delivery care in Lesotho is feasible and affordable, and has the potential to improve maternal and neonatal outcomes by removing financial barriers to skilled birth attendants and increasing coverage of institutional deliveries.

Tuberculosis

30. BMJ Global Health: bmjgh-2018-001097

Tuberculosis: treatment failure, or failure to treat? Lessons from India and South Africa
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Tuberculosis (TB) remains an enormous public health concern globally. India and South Africa rank among the top 10 high TB burden countries with the highest absolute burden of TB, and the second highest rate of TB incidence, respectively. Although the primary drivers of TB transmission vary considerably between these two countries, they do indeed share common themes. In 2017, only 64% of the global estimated incident cases of TB were reported, the remaining 36% of 'missing' cases were either undiagnosed, untreated or unreported. These 'missing TB cases' have generated much hype for the challenges they present in achieving the End TB Strategy. Although India and South Africa have indeed made significant strides in TB control, analysis of the patient cascade of care clearly suggests that these 'missed' patients are not really missing—most are actively engaging the health system—the system, however, is failing to appropriately manage them. In short, quality of TB care is suboptimal and must urgently be addressed, merely focusing on coverage of TB services is no longer sufficient. While the world awaits revolutionary vaccines, drugs and diagnostics, programmatic data indicate that much can be done to accelerate the decline of TB. In this perspective, we compare and contrast these two national epidemics, and explore barriers, with a particular focus on the role of health systems in finding the missing millions.
Summary box

- In 2017, only 64% of the global estimated incident cases of tuberculosis (TB) were reported worldwide, the remaining 36% of 'missing' cases were either undiagnosed, untreated or unreported.
- Analysis of the patient cascade of care in India and South Africa suggests that these 'missed' patients are not really missing; most are actively engaging the health system (public and private) but not adequately managed.

- National TB control programmes need to identify gaps and weaknesses along the entire patient care cascade, addressing barriers to appropriate diagnosis, linkages to treatment postdiagnosis while strengthening both public and private healthcare sectors, and bridging the gap between provider knowledge and practice.
- Integration of TB services within universal health coverage is critical for identifying and managing missing patients with TB.

31. BJM Global Health: bmjgh-2018-001323

Making the case: developing innovative adherence solutions for the treatment of tuberculosis

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Tuberculosis (TB), which claims the lives of over 3500 people every day, is the world's leading killer among infectious diseases. According to the WHO, 10 million people developed TB in 2017 with a global economic burden amounting to $12 billion annually. Furthermore, TB is the most significant pathogen in the global antimicrobial resistance (AMR) crisis. Unless radical action is taken, drug-resistant strains of TB will account for 25% of the AMR-related deaths and cost the global economy $16.7 trillion by the year 2050. TB treatment is challenging with its prolonged and frequent dosing regimen that may be associated with challenging side effects. While significant work has been done to support adherence among people living with TB who are on treatment—including direct observation of therapy and provision of socioeconomic support—there has been limited focus on translation of how the medications themselves and their administration might be altered to improve adherence.

Technologies that enable extended drug release of medication have the potential to overcome patient non-adherence to long and frequent dosing regimens. Long-acting formulations are being implemented for the reduction in the frequency of HIV treatment administration, though they require injections which can be uncomfortable for patients. Instead, a long-acting oral dosage would be very attractive and improve adherence to treatment, as the oral route of drug delivery is preferred by patients. Novel ingestible gastric-resident systems for extended controlled drug release are being developed by several groups (including the Langer and Traverso laboratories) for antimalarials and antiretrovirals.

The challenge with designing drug depot systems for TB treatment is to balance the ease and safety of administration with the accommodation of gram-level quantities of TB drugs which have low potency. Under the current regimen during the intensive phase, a 60 kg patient with TB swallows almost 100 g of antibiotics in 1 month. One potential area of development which could aid in improved delivery include inhaled or orally delivered nanocarriers which have been designed for extended release of existing TB drugs, although they have yet to be tested in large animal models. Considering that bedaquiline is the first new approved TB drug in more than 40 years and the dearth of others in the TB drug development pipeline to overcome challenges of the current drugs, nanotechnology can provide an enormous impact with design of novel and targeted delivery systems for existing drugs. Ideally, these nanomaterial-based systems would be inexpensive, easy to administer, minimise side effects and reduce the required dosing frequency to improve patient adherence.

32. BMJ Global Health: bmjgh-2018-001029

The impact of a cash transfer programme on tuberculosis treatment success rate: a quasi-experimental study in Brazil

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Background Evidence suggests that social protection policies such as Brazil's Bolsa Família Programme (BFP), a governmental conditional cash transfer, may play a role in tuberculosis (TB) elimination. However, study limitations hamper conclusions. This paper uses a quasi-experimental approach to more rigorously evaluate the effect of BFP on TB treatment success rate.
Methods Propensity scores were estimated from a complete-case logistic regression using covariates from a linked data set, including the Brazil's TB notification system (SINAN), linked to the national registry of those in poverty (CadUnico) and the BFP payroll.
Results The average effect of treatment on the treated was estimated as the difference in TB treatment success rate between matched groups (ie, the control and exposed patients, n=2167). Patients with TB receiving BFP showed a treatment success rate of 10.58 percentage points higher (95% CI 4.39 to 16.77) than patients with TB not receiving BFP. This association was robust to sensitivity analyses.
Conclusions This study further confirms a positive relationship between the provision of conditional cash transfers and TB treatment success rate. Further research is needed to understand how to enhance access to social protection so to optimise public health impact.

Miscellaneous

33. Am J TMH 2019 Jan;100(1_Suppl):9-14. doi: 10.4269/ajtmh.18-0557

Conceptual Framework of Mentoring in Low- and Middle-Income Countries to Advance Global Health

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Although mentoring is not a common practice in low- and middle-income countries (LMICs), there is a strong need for it. Conceptual frameworks provide the structure to design, study, and problem-solve complex phenomena. Following four workshops in South America, Asia, and Africa, and borrowing on theoretical models from higher education, this article proposes two conceptual frameworks of mentoring in LMICs. In the first model, we propose to focus the mentor-mentee relationship and interactions, and in the second, we look at mentoring activities from a mentees' perspective. Our models emphasize the importance of an ongoing dynamic between the mentor and mentee that is mutually beneficial. It also emphasizes the need for institutions to create enabling environments that encourage mentorship. We expect that these frameworks will help LMIC institutions to design new mentoring programs, clarify expectations, and analyze problems with existing mentoring programs. Our models, while being framed in the context of global health, have the potential for wider application geographically and across disciplines.
More articles on mentoring in same issue:
* Am J TMH 2019 Jan;100(1_Suppl):3-8. doi: 10.4269/ajtmh.18-0556. Strengthening Mentoring in Low- and Middle-Income Countries to Advance Global Health Research: An Overview.

* Am J TMH 2019 Jan;100(1_Suppl):48-53. doi: 10.4269/ajtmh.18-0563. Global Health Mentoring Toolkits: A Scoping Review Relevant for Low- and Middle-Income Country Institutions.
* Am J TMH 2019 Jan;100(1_Suppl):29-35. doi: 10.4269/ajtmh.18-0560. The Evolution of Mentorship Capacity Development in Low- and Middle-Income Countries: Case Studies from Peru, Kenya, India, and Mozambique.
* Am J TMH 2019 Jan;100(1_Suppl):20-28. doi: 10.4269/ajtmh.18-0559. Mentoring the Mentors: Implementation and Evaluation of Four Fogarty-Sponsored Mentoring Training Workshops in Low- and Middle-Income Countries.
* Am J TMH 2019 Jan;100(1_Suppl):15-19. doi: 10.4269/ajtmh.18-0558. Global Health Research Mentoring Competencies for Individuals and Institutions in Low- and Middle-Income Countries.

34. Am J TMH 2019 Jan;100(1):213-21. doi: 10.4269/ajtmh.18-0612

Evaluation of a Novel Quantitative Test for Glucose-6-Phosphate Dehydrogenase Deficiency: Bringing Quantitative Testing for Glucose-6-Phosphate Dehydrogenase Deficiency Closer to the Patient

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Glucose-6-phosphate dehydrogenase (G6PD) deficiency, a common genetic blood condition, can result in kernicterus at birth, and later in life as severe hemolysis on exposure to certain infections, foods, and drugs. The unavailability of point-of-care tests for G6PD deficiency is a barrier to routine curative treatment of Plasmodium vivax malaria with 8-aminoquinolines, such as primaquine. Two quantitative reference tests (Trinity Biotech, Bray, Ireland and Pointe Scientific, Canton, MI; Cat No. G7583) and the point-of-care STANDARD™ G6PD test (SD Biosensor, Suwon, South Korea) were evaluated. The STANDARD G6PD test was evaluated at multiple temperatures, in anticoagulated venous and capillary samples, including 79 G6PD-deficient and 66 intermediate samples and across two laboratories, one in the United States and one in Thailand. The STANDARD test performed equivalently to a reference assay for its ability to diagnose G6PD deficiency (< 30% normal) with a sensitivity of 100% (0.95 confidence interval [CI]: 95.7-100) and specificity of 97% (0.95 CI: 94.5-98.5), and could reliably identify females with less than 70% normal G6PD activity with a sensitivity of 95.5% (0.95 CI: 89.7-98.5) and specificity of 97% (0.95 CI: 94.5-98.6). The STANDARD G6PD product represents an opportunity to diagnose G6PD deficiency equally for males and females in basic clinical laboratories in high- and low-resource settings. This quantitative point-of-care diagnostic test for G6PD deficiency can provide equal access to safe radical cure of P. vivax cases in high- and low-resource settings, for males and females and may support malaria elimination, in countries where P. vivax is endemic.

35. Lancet 2018;392(10165):2736-44

Health and dignity of Palestine refugees at stake: a need for international response to sustain crucial life services at UNRWA

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The UN Sustainable Development Goals affirm equality and dignity as essential to the enjoyment of basic human rights, including the right to the highest attainable standard of physical and mental

health, which promotes global solidarity among all people, including refugees. The UN Relief and Works Agency for Palestine Refugees in the Near East (UNRWA) has provided support to Palestine refugees in Jordan, Lebanon, Syria, the Gaza Strip, and the West Bank since the 1950s. Today, however, conflict and violence, occupation, high levels of poverty, and other social determinants of health jeopardize the wellbeing of Palestine refugees. Health concerns include non-communicable diseases, mental health conditions, and access to hospital care. Additionally, UNRWA is continuing to face a severe funding crisis. Using a historical and health policy perspective, this Health Policy examines UNRWA strategies that facilitate continuous provision of health-care services for Palestine refugees. Given the increasingly volatile environment faced by this population, a multifaceted international response is needed to enable UNRWA to deliver sustainable services to Palestine refugees and avert further loss of life, dignity, and hope, pending a just and lasting solution to their plight in accordance with applicable international law and UN General Assembly resolutions.