International Health Alerts 2017-3 Contents

International Health Alerts 2017-3 Abstracts

Child Health / iCCM

1. BMJ 2017;358:j3423 Research

A growth reference for mid upper arm circumference for age among school age children and adolescents, and validation for mortality: growth curve construction and longitudinal cohort study

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Objectives: To construct growth curves for mid-upper-arm circumference (MUAC)-for-age z score for 5-19 year olds that accord with the World Health Organization growth standards, and to evaluate their discriminatory performance for subsequent mortality.
Design: Growth curve construction and longitudinal cohort study.
Setting: United States and international growth data, and cohorts in Kenya, Uganda, and Zimbabwe.
Participants: The Health Examination Survey (HES)/National Health and Nutrition Examination Survey (NHANES) US population datasets (age 5-25 years), which were used to construct the 2007 WHO growth reference for body mass index in this age group, were merged with an imputed dataset matching the distribution of the WHO 2006 growth standards age 2-6 years. Validation data were from 685 HIV infected children aged 5-17 years participating in the Antiretroviral Research for Watoto (ARROW) trial in Uganda and Zimbabwe; and 1741 children aged 5-13 years discharged from a rural Kenyan hospital (3.8% HIV infected). Both cohorts were followed-up for survival during one year.
Main outcome measures: Concordance with WHO 2006 growth standards at age 60 months and survival during one year according to MUAC-for-age and body mass index-for-age z scores.
Results. The new growth curves transitioned smoothly with WHO growth standards at age 5 years. MUAC-for-age z scores of −2 to −3 and less than−3, compared with −2 or more, was associated with hazard ratios for death within one year of 3.63 (95% confidence interval 0.90 to 14.7; P=0.07) and 11.1 (3.40 to 36.0; P<0.001), respectively, among ARROW trial participants; and 2.22 (1.01 to 4.9; P=0.04) and 5.15 (2.49 to 10.7; P<0.001), respectively, among Kenyan children after discharge from hospital. The AUCs for MUAC-for-age and body mass index-for-age z scores for discriminating subsequent mortality were 0.81 (95% confidence interval 0.70 to 0.92) and 0.75 (0.63 to 0.86) in the ARROW trial (absolute difference 0.06, 95% confidence interval −0.032 to 0.16; P=0.2) and 0.73 (0.65 to 0.80) and 0.58 (0.49 to 0.67), respectively, in Kenya (absolute difference in AUC 0.15, 0.07 to 0.23; P=0.0002).
Conclusions: The MUAC-for-age z score is at least as effective as the body mass index-for-age z score for assessing mortality risks associated with undernutrition among African school aged children and adolescents. MUAC can provide simplified screening and diagnosis within nutrition and HIV programmes, and in research.

2. IJE 2017; 817–26

Child and Infant Health Facility distance and child mortality: a multicountry study of health facility access, service utilization, and child health outcomes

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Background: Access to health facilities remains limited in many resource-poor settings, and women and their children often have to travel far to seek care. However, data on distance are scarce, and it is unclear whether distance is associated with worse child health outcomes. We estimate the relationships between distance to facility, service utilization and child mortality in low- and middle-income countries.

Methods: Population-representative data are pooled from 29 demographic and health surveys across 21 low- and middle-income countries. Multivariable logistic models and meta-analysis regressions are used to estimate associations between facility distance, child mortality, and health care utilization in the pooled sample as well as for each survey.
Results: Compared with children who live within 1 km of a facility, children living within 2 km, 3 km, and 5 km of a facility have a 7.7% [95% confidence interval (CI): 0.927 – 1.251], 16.3% (95% CI: 1.020 – 1.327) and 25% (95% CI: 1.087 – 1.439) higher odds of neonatal mortality, respectively; children living farther than 10 km have a 26.6% (95% CI: 1.108 – 1.445) higher odds of neonatal mortality. Women living farther than 10 km from a facility have a 55.3% lower odds of in-facility delivery compared with women who live within 1 km [odds ratio (OR): 0.447; 95% CI: 0.394 – 0.508].
Conclusions: Even relatively small distances from health facilities are associated with substantial mortality penalties for children. Policies that reduce travel distances and travel times are likely to increase utilization of health services and reduce neonatal mortality.

Communicable Diseases

3. Am J TMH 2017;96(6):1468-71

Evaluation of a Mobile Phone-Based Microscope for Screening of Schistosoma haematobium Infection in Rural Ghana

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Schistosomiasis affects over 170 million people in Africa. Here we compare a novel, low-cost mobile phone microscope to a conventional light microscope for the label-free diagnosis of Schistosoma haematobium infections in a rural Ghanaian school setting. We tested the performance of our handheld microscope using 60 slides that were randomly chosen from an ongoing epidemiologic study in school-aged children. The mobile phone microscope had a sensitivity of 72.1% (95% confidence interval [CI]: 56.1-84.2), specificity of 100% (95% CI: 75.9-100), positive predictive value of 100% (95% CI: 86.3-100), and a negative predictive value of 57.1% (95% CI: 37.4-75.0). With its modest sensitivity and high specificity, this handheld and cost-effective mobile phone-based microscope is a stepping-stone toward developing a powerful tool in clinical and public health settings where there is limited access to conventional laboratory diagnostic support.

4. Am J TMH 2017;Jul 10

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

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

with high specificity and acceptable sensitivity, the latter being dependent on the limit of detection of RDTs. Furthermore, CHWs showed excellent adherence to test results and treatment guidelines, suggesting they can be deployed for screen and treat approaches of malaria in pregnancy.

5. Am J TMH 2017;97(1):97-108

Experience with a Multinational, Secondary School Education Module with a Focus on Prevention of Virus Infections

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Worldwide, virus infections are responsible for many diseases in terms of morbidity and mortality. Vaccinations and therapies are only available for relatively few virus infections and not always where they are needed. However, knowledge of transmission routes can prevent virus infection. In the context of this study, we measured the effects of a secondary school education module, named Viruskenner, on knowledge, attitude, and risk behavior as these relate to virus infections. A nonrandomized intervention study was conducted between April and August 2015 to assess the effect of this 2-month education module on knowledge, attitude, and behavior of 684 secondary school students in the Netherlands, Suriname, and Indonesia. For the Netherlands, a control group of a further 184 students was added. Factor analysis was performed on questions pertaining to attitude and behavior. Comparative analyses between pre- and posttest per country were done using multiple linear regression, independent sample T-tests, and one-way analysis of variance. These showed a significant increase in knowledge about virus infections and the prevention of infectious diseases among the Dutch and Surinamese groups, whereas a trend of increased knowledge was evident among the Indonesian participants. The Dutch control group showed an overall decrease in knowledge. Regression analyses showed that there was a significant interaction effect between participation and time on knowledge, attitude, and awareness and behavior and risk infection. Attitudes improved significantly in the intervention group. Pearson correlation coefficients between knowledge, attitude, and behavior were found to be positive.

6. Lancet 2017;Mar10.pii:S0140-6736(17)30559-7

Cholera

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Cholera is an acute, watery diarrhoeal disease caused by Vibrio cholerae of the O1 or O139 serogroups. In the past two centuries, cholera has emerged and spread from the Ganges Delta six times and from Indonesia once to cause global pandemics. Rational approaches to the case management of cholera with oral and intravenous rehydration therapy have reduced the case fatality of cholera from more than 50% to much less than 1%. Despite improvements in water quality, sanitation, and hygiene, as well as in the clinical treatment of cholera, the disease is still estimated to cause about 100 000 deaths every year. Most deaths occur in cholera-endemic settings, and virtually all deaths occur in developing countries. Contemporary understanding of immune protection against cholera, which results from local intestinal immunity, has yielded safe and protective orally administered cholera vaccines that are now globally stockpiled for use in the control of both epidemic and endemic cholera.

7. Lancet 2017;Jun30.pii:S0140-6736(17)31510-6

Human African trypanosomiasis

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Human African trypanosomiasis (sleeping sickness) is a parasitic infection that almost invariably progresses to death unless treated. Human African trypanosomiasis caused devastating epidemics during the 20th century. Thanks to sustained and coordinated efforts over the past 15 years, the number of reported cases has fallen to a historically low level. Fewer than 3000 cases were reported in 2015, and the disease is targeted for elimination by WHO. Despite these recent successes, the disease is still endemic in parts of sub-Saharan Africa, where it is a considerable burden on rural communities, most notably in central Africa. Since patients are also reported from non-endemic countries, human African trypanosomiasis should be considered in differential diagnosis for travellers, tourists, migrants, and expatriates who have visited or lived in endemic areas. In the absence of a vaccine, disease control relies on case detection and treatment, and vector control. Available drugs are suboptimal, but ongoing clinical trials provide hope for safer and simpler treatments.

8. Lancet 2017;Sep4.pii:S0140-6736(17)31930-X

Soil-transmitted helminth infections

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More than a quarter of the world's population is at risk of infection with the soil-transmitted helminths Ascaris lumbricoides, hookworm (Ancylostoma duodenaleand Necator americanus), Trichuris trichiura, and Strongyloides stercoralis. Infected children and adults present with a range of medical and surgical conditions, and clinicians should consider the possibility of infection in individuals living in, or returning from, endemic regions. Although safe and effective drugs are donated free to endemic countries, only half of at-risk children received treatment in 2016. This Seminar describes the epidemiology, lifecycles, pathophysiology, clinical diagnosis, management, and public health control of soil-transmitted helminths. Previous work has questioned the effect of population-level deworming; however, it remains beyond doubt that treatment reduces the severe consequences of soil-transmitted helminthiasis. We highlight the need for refined diagnostic tools and effective control options to scale up public health interventions and improve clinical detection and management of these infections.

9. NEJM 2017;377(5): 414-17

Perspective (Abridged): Recognizing Sepsis as a Global Health Priority — A WHO Resolution

Reinhart K et al., The authors constitute the Executive Board of the Global Sepsis Alliance

“Some very important clinical issues, some of them affecting life and death, stay largely in a backwater which is inhabited by academics and professionals and enthusiasts, dealt with very well at the clinical and scientific level but not visible to the public, political leaders, leaders of healthcare systems. . . . The public and political space is the space in which [sepsis] needs to be in order for things to change.” So said Sir Liam Donaldson, the former chief medical officer for England and the current World Health Organization (WHO) envoy for patient safety, on May 24, 2017. Two days later, the World Health Assembly (WHA), the WHO’s decision-making body, adopted a resolution on improving the prevention, diagnosis, and management of sepsis.

The true burden of disease arising from sepsis remains unknown. The current estimates of 30 million episodes and 6 million deaths per year come from a systematic review that extrapolated from published national or local population estimates to the global population. The likelihood that the result was a significant underestimate was recognized by the authors, who could find no data from the low- and middle-income countries (LMICs) where 87% of the world’s population lives.

Ensuring greater awareness on the part of both the public and health care workers is a crucial step in reducing the global burden of sepsis. Approximately 70% of sepsis cases are community-acquired, and since treatment with appropriate antibiotics must begin early to be effective, educating people about seeking treatment without delay is key to preventing unnecessary deaths and disability. The progression from infection to sepsis can be insidious and is unpredictable. Although populations such as the very young, the very old, and the immunosuppressed are known to be at high risk and should be

targeted for education, sepsis can affect anyone at any time, which means that national public awareness programs are needed.
The WHA resolution, with its implicit recognition of sepsis as a major threat to patient safety and global health, has the potential to save millions of lives. To realize this potential, the actions proposed in the resolution need to be taken. These actions require coordinated efforts by politicians, policymakers, health care administrators, researchers, and clinicians working with people of all ages in all health care settings and in the community. Actions will vary by region and country and must acknowledge the unique challenges faced by LMICs.

10. TMIH 2017;22(8):960-70

Dengue data and surveillance in Tanzania: a systematic literature review

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Objective: Although there is evidence that dengue virus is circulating in Tanzania, the country lacks a dengue surveillance system. Consequently, the true estimate of dengue seroprevalence, as well as the incidence in the population, the frequency and magnitude of outbreaks is unknown. This study therefore sought to systematically review available dengue data from Tanzania.
Methods: The systematic review was conducted and reported using the PRISMA tool. Five databases (PubMed, Embase, Web of Science, WHOLIS and Google Scholar) were searched for articles using various keywords on the illness, data and geographical location. Identified articles were assessed for inclusion based on predefined eligibility criteria. Data were extracted from included articles, analysed and reported.
Results: Based on the 10 seroprevalence studies in defined populations with estimates of acute confirmed infections that were included in the review, the estimated seroprevalence of past dengue infection in Tanzania ranged from 50.6% in a health facility-based study to 11% in a population-based study. Acute confirmed infections of dengue were estimated to be as high as 38.2% of suspected cases. Only one study reported on an outbreak.
Conclusions: It is evident that dengue needs to become part of regular disease surveillance in Tanzania. Control measures need to be instituted with a focus on building human resource capacity and integrating dengue control measures in ongoing health programmes, for both preventive and curative interventions. Systematic reviews are valuable in assessing health issues when surveillance data are not available.

11. TMIH 2017;22(9):1072-80

Utility of the urine reagent strip leucocyte esterase assay for the diagnosis of meningitis in resource-limited settings: meta-analysis

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Objective: Diagnosis of bacterial meningitis often requires cytometry, chemistry and/or microbiologic culture capabilities. Unfortunately, laboratory resources in low-resource settings (LRS) often lack the capacity to perform these studies. We sought to determine whether the presence of white blood cells in CSF detected by commercially available urine reagent strips could aid in the diagnosis of bacterial meningitis.
Methods: We searched PubMed for studies published between 1980 and 2016 that investigated the use of urine reagent strips to identify cerebrospinal fluid (CSF) pleocytosis. We assessed studies in any language that enrolled subjects who underwent lumbar puncture and had cerebrospinal fluid testing by both standard laboratory assays and urine reagent strips. We abstracted true-positive, false-negative, false-positive and true-negative counts for each study using a diagnostic threshold of ≥10 white blood cells per microlitre for suspected bacterial meningitis and performed mixed regression modelling with random effects to estimate pooled diagnostic accuracy across studies.
Results: Our search returned 13 studies including 2235 participants. Urine reagent strips detected CSF pleocytosis with a pooled sensitivity of 92% (95% CI: 84-96), a pooled specificity of 98% (95% CI: 94-99) and a negative predictive value of 99% when the bacterial meningitis prevalence is 10%.

Conclusions: Urine reagent strips could provide a rapid and accurate tool to detect CSF pleocytosis, which, if negative, can be used to exclude diagnosis of bacterial meningitis in settings without laboratory infrastructure. Further investigation of the diagnostic value of using protein, glucose and bacteria components of these strips is warranted.

Global Burden of Diseases

12. Lancet 2017;389(10082):1907-18

Estimates and 25-year trends of the global burden of disease attributable to ambient air pollution: an analysis of data from the Global Burden of Diseases Study 2015

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Background: Exposure to ambient air pollution increases morbidity and mortality, and is a leading contributor to global disease burden. We explored spatial and temporal trends in mortality and burden of disease attributable to ambient air pollution from 1990 to 2015 at global, regional, and country levels.
Methods: We estimated global population-weighted mean concentrations of particle mass with aerodynamic diameter less than 2·5 μm (PM2·5) and ozone at an approximate 11 km × 11 km resolution with satellite-based estimates, chemical transport models, and ground-level measurements. Using integrated exposure-response functions for each cause of death, we estimated the relative risk of mortality from ischaemic heart disease, cerebrovascular disease, chronic obstructive pulmonary disease, lung cancer, and lower respiratory infections from epidemiological studies using non-linear exposure-response functions spanning the global range of exposure.
Findings: Ambient PM2·5 was the fifth-ranking mortality risk factor in 2015. Exposure to PM2·5 caused 4·2 million (95% uncertainty interval [UI] 3·7 million to 4·8 million) deaths and 103·1 million (90·8 million 115·1 million) disability-adjusted life-years (DALYs) in 2015, representing 7·6% of total global deaths and 4·2% of global DALYs, 59% of these in east and south Asia. Deaths attributable to ambient PM2·5 increased from 3·5 million (95% UI 3·0 million to 4·0 million) in 1990 to 4·2 million (3·7 million to 4·8 million) in 2015. Exposure to ozone caused an additional 254 000 (95% UI 97 000-422 000) deaths and a loss of 4·1 million (1·6 million to 6·8 million) DALYs from chronic obstructive pulmonary disease in 2015.
Interpretation: Ambient air pollution contributed substantially to the global burden of disease in 2015, which increased over the past 25 years, due to population ageing, changes in non-communicable disease rates, and increasing air pollution in low-income and middle-income countries. Modest reductions in burden will occur in the most polluted countries unless PM2·5 values are decreased substantially, but there is potential for substantial health benefits from exposure reduction.

13. NEJM 2017;377:80-81

Editorial: Global Health Effects of Overweight and Obesity

Gregg EW et al.

The Global Burden of Disease (GBD) study that is now reported in the Journal*) offers a discouraging reminder that the global obesity epidemic is worsening in most parts of the world and that its implications regarding both physical health and economic health remain ominous. The study, in which researchers assembled data from 195 countries to model trends in overweight and obesity and related morbidity and mortality, showed that the prevalence of obesity has more than doubled since 1980 and is now 5% in children and 12% in adults — findings that mirror similar global trends in type 2 diabetes. Apart from a possible recent plateau in the prevalence of obesity in high income countries, the prevalence has increased in all other sociodemographic strata. On the encouraging side, despite this increase in prevalence, the effect of high body-mass index (BMI) on population-level age-adjusted rates of death and disability has not grown, which suggests that obese persons are healthier and live longer now than in previous decades because of better care and risk-factor management. Unfortunately, even this success brings a new burden, since the mix of increased prevalence and

decreased mortality leads to more years spent with obesity and more time for the damaging coexisting illnesses, such as type 2 diabetes and chronic kidney disease, to develop. The most worrisome finding is the approximate tripling of obesity seen in youth and young adults of developing, middle-income countries such as China, Brazil, and Indonesia. An early onset of obesity is likely to translate into a high cumulative incidence of type 2 diabetes, hypertension, and chronic kidney disease. These findings come on the heels of reports from the United States that the incidence of type 2 diabetes in youth has increased substantially in minority populations, and when type 2 diabetes occurs in youth, it brings a much higher prevalence of complications than does type 1 diabetes. Since reductions in diabetes complications have been dominated by improvements among older adults, an increased incidence of diabetes among children may shift a proportionately greater load of morbidity into middle age and spread the burden of chronic disease more fully across the entire age distribution, even as populations continue to age. The findings of the GBD investigators are an impressive and essential effort to provide policymakers with both global and country-specific estimates that most countries alone lack. However, some of the modeling assumptions in the current report might obscure important variation in both the threats and the successes underlying the obesity epidemic. First, the assumption that the risk of outcomes at any given level of obesity is uniform across populations could skew morbidity estimates. For example, at any given level of BMI, Asians have been shown to have a higher absolute risk of diabetes and hypertension and African Americans to have a lower risk of cardiovascular disease than other groups. Once chronic conditions such as diabetes and cardiovascular disease develop, the associated relative risk of death may vary according to location — as was recently seen in Mexico, where the relative risk of death associated with diabetes far exceeds that in the United States and Europe. Second, there may be important, missed variation in the high end of the BMI distribution, which disproportionately drives the development of type 2 diabetes and other coexisting illnesses.

In some regions, the high prevalence of severe obesity may persist even when levels of overweight and obesity appear to plateau. Finally, global findings only hint at some of the actual successes in prevention that may finally be under way. In the United States, the past decade has brought an apparent peak and plateau in the prevalence of obesity and diagnosed diabetes, decreases in the intake of overall calories and of sugared beverages, and increasing levels of physical activity. Similarly, more communities in the United States now report reductions in the incidence of childhood obesity and adult type 2 diabetes. Gaps in available data have forced the GBD researchers to make the best of a checkerboard of periodic and suboptimal data to provide a global picture. However, the magnitude of obesity related morbidity and the demands for effective public health decision making point to the need for improvements in at least three types of data: efficient, continuous surveillance systems to assess risk factors, prevalence, care, and outcomes of chronic diseases; cohorts in more diverse populations to capture variation in progression to outcomes; and platforms for natural experimental studies to determine which of the interventions are working locally and why. Although obesity and diabetes have become a shared global burden requiring a strong response from governments, their determinants and effects — and particularly their solutions — also depend on the specific environment in which people live. Better data systems would permit policymakers in the hardest hit areas of the world to respond more quickly and to shorten the long learning period that is typically required to overcome chronic diseases.

*) NEJM 2017;377:13-27

Health Effects of Overweight and Obesity in 195 Countries over 25 Years

The GBD 2015 Obesity Collaborators <cjlm@uw.edu>

Health Financing / Health Policy

14. BMJ Series, Published 31 August 2017

* BMJ 2017; 358 :j3339

World Bank’s financing, priorities, and lending structures for global health

* BMJ 2017; 358 :j3347

Universal health coverage, health systems strengthening, and the World Bank

* BMJ 2017; 358 :j3394
Earmarking for global health: benefits and perils of the World Bank's trust fund model

* BMJ 2017; 358 :j3397
Health as a "global public good": creating a market for pandemic risk

* BMJ 2017; 358 :j3395
World Bank and the Global Financing Facility

15. Lancet 2017;390(10090):191-202
Levers for addressing medical underuse and overuse: achieving high-value health care
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The 3 preceding papers *) in this Series (name: Right care) have outlined how underuse and overuse of health-care services occur within a complex system of health-care production, with a multiplicity of causes. Because poor care is ubiquitous and has considerable consequences for the health and wellbeing of billions of people around the world, remedying this problem is a morally and politically urgent task. Universal health coverage is a key step towards achieving the right care. Therefore, full consideration of potential levers of change must include an upstream perspective-ie, an understanding of the system-level factors that drive overuse and underuse, as well as the various incentives at work during a clinical encounter. One example of a system-level factor is the allocation of resources (eg, hospital beds and clinicians) to meet the needs of a local population to minimise underuse or overuse. Another example is priority setting using tools such as health technology assessment to guide the optimum diffusion of safe, effective, and cost-effective health-care services. In this Series paper we investigate a range of levers for eliminating medical underuse and overuse. Some levers could operate effectively (and be politically viable) across many different health and political systems (eg, increase patient activation with decision support) whereas other levers must be tailored to local contexts (eg, basing coverage decisions on a particular cost-effectiveness ratio). Ideally, policies must move beyond the purely incremental; that is, policies that merely tinker at the policy edges after underuse or overuse arises. In this regard, efforts to increase public awareness, mobilisation, and empowerment hold promise as universal methods to reset all other contexts and thereby enhance all other efforts to promote the right care.

*) Right care 1: Lancet. 2017 Jul 8;390(10090):169-77
Evidence for underuse of effective medical services around the world
Glasziou P et al., Centre for Research in Evidence-Based Practice, Bond University, Robina, QLD, Australia <paul_glasziou@bond.edu.au>

*) Right care 2: Lancet. 2017 Jul 8;390(10090):156-68
Evidence for overuse of medical services around the world
Brownlee S et al., Lown Institute, Brookline, MA, USA <sbrownlee@lownistitute.org>

*) Right care 3: Lancet 2017 Jul 8;390(10090):178-90
Drivers of poor medical care
Saini Vet al., Lown Institute, Brookline, MA, USA <vsaini@lowninstitute.org>

16. Lancet 2017;390(10091):324-32
Who pays for cooperation in global health? A comparative analysis of WHO, the World Bank, the Global Fund to Fight HIV/AIDS, Tuberculosis and Malaria, and Gavi, the Vaccine Alliance
Clinton C et al., Mailman School of Public Health, Columbia University, New York, NY, USA <devi.sridhar@ed.ac.uk>

In this report we assess who pays for cooperation in global health through an analysis of the financial flows of WHO, the World Bank, the Global Fund to Fight HIV/AIDS, TB and Malaria, and Gavi, the Vaccine Alliance.
Key messages:
1. Three major trends in global health governance over the past two decades have been: towards more discretionary funding and away from core or longer-term funding; towards multi-stakeholder governance and away from traditional government-centred representation and decision making; and towards narrower mandates or problem-focused vertical initiatives and away from broader systemic goals sought through multilateral cooperation.
2. These shifts are reflected in the creation of partnerships such as the Global Fund to Fight HIV/AIDS, TB and Malaria and Gavi, the Vaccine Alliance, as well as in the increased voluntary contributions to WHO and the World Bank. These mechanisms allow donors to finance and deliver assistance in ways that they can more closely control and monitor at every stage.
3. WHO's volatile financial state is a reflection of a lack of donors' trust in the agency. Reform should focus on improving the agency's relationship to monitoring and accountability through addressing membership, including voting rights for non-state actors, and transparency to the public and member states.
4. The past few decades have seen the consolidation of influence across three of our four case study institutions in the roles the USA, the UK, and the Bill & Melinda Gates Foundation have all had in financing. Despite a proliferation of initiatives in global health, much of the financing for global cooperation comes from a few powerful donors.

HIV / AIDS

17. Lancet 2017;Jul21.pii:S0140-6736(17)31917-7
Long-acting intramuscular cabotegravir and rilpivirine in adults with HIV-1 infection (LATTE-2): 96-week results of a randomised, open-label, phase 2b, non-inferiority trial
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Background: Cabotegravir and rilpivirine are antiretroviral drugs in development as long-acting injectable formulations. The LATTE-2 study evaluated long-acting cabotegravir plus rilpivirine for maintenance of HIV-1 viral suppression through 96 weeks.
Methods: In this randomised, phase 2b, open-label study, treatment-naive adults infected with HIV-1 initially received oral cabotegravir 30 mg plus abacavir-lamivudine 600-300 mg once daily. The objective of this study was to select an intramuscular dosing regimen based on a comparison of the antiviral activity, tolerability, and safety of the two intramuscular dosing regimens relative to oral cabotegravir plus abacavir-lamivudine. After a 20-week induction period on oral cabotegravir plus abacavir-lamivudine, patients with viral suppression (plasma HIV-1 RNA <50 copies per mL) were randomly assigned (2:2:1) to intramuscular long-acting cabotegravir plus rilpivirine at 4-week intervals (long-acting cabotegravir 400 mg plus rilpivirine 600 mg; two 2 mL injections) or 8-week intervals (long-acting cabotegravir 600 mg plus rilpivirine 900 mg; two 3 mL injections) or continued oral cabotegravir plus abacavir-lamivudine. Randomisation was computer-generated with stratification by HIV-1 RNA (<50 copies per mL, yes or no) during the first 12 weeks of the induction period. The primary endpoints were the proportion of patients with viral suppression at week 32 (as defined by the US Food and Drug Administration snapshot algorithm), protocol-defined virological failures, and safety events through 96 weeks. All randomly assigned patients who received at least one dose of study drug during the maintenance period were included in the primary efficacy and safety analyses. The primary analysis used a Bayesian approach to evaluate the hypothesis that the proportion with viral suppression for each long-acting regimen is not worse than the oral regimen proportion by more than 10% (denoted comparable) according to a prespecified decision rule (ie, posterior probability for comparability >90%). Difference in proportions and associated 95% CIs were supportive to the primary analysis. The trial is registered at ClinicalTrials.gov, number NCT02120352.

Findings: Among 309 enrolled patients, 286 were randomly assigned to the maintenance period (115 to each of the 4-week and 8-week groups and 56 to the oral treatment group). This study is currently ongoing. At 32 weeks following randomisation, both long-acting regimens met primary criteria for comparability in viral suppression relative to the oral comparator group. Viral suppression was maintained at 32 weeks in 51 (91%) of 56 patients in the oral treatment group, 108 (94%) of 115 patients in the 4-week group (difference 2·8% [95% CI -5·8 to 11·5] vs oral treatment), and 109 (95%) of 115 patients in the 8-week group (difference 3·7% [-4·8 to 12·2] vs oral treatment). At week 96, viral suppression was maintained in 47 (84%) of 56 patients receiving oral treatment, 100 (87%) of 115 patients in the 4-week group, and 108 (94%) of 115 patients in the 8-week group. Three patients (1%) experienced protocol-defined virological failure (two in the 8-week group; one in the oral treatment group). Injection-site reactions were mild (3648 [84%] of 4360 injections) or moderate (673 [15%] of 4360 injections) in intensity and rarely resulted in discontinuation (two [<1%] of 230 patients); injection-site pain was reported most frequently. Serious adverse events during maintenance were reported in 22 (10%) of 230 patients in the intramuscular groups (4-week and 8-week groups) and seven (13%) of 56 patients in the oral treatment group; none were drug related.
Interpretation: The two-drug combination of all-injectable, long-acting cabotegravir plus rilpivirine every 4 weeks or every 8 weeks was as effective as daily three-drug oral therapy at maintaining HIV-1 viral suppression through 96 weeks and was well accepted and tolerated.

18. NEJM 2017;377: 283-4

Editorial: The Enduring Challenge of Advanced HIV Infection

Ford N et al.

Until recently, progress in the fight against human immunodeficiency virus (HIV) infection was primarily measured in terms of the number of patients who were started on antiretroviral therapy (ART). Major efforts to increase access to ART in the low- and middle-income countries that are most affected by HIV infection began in 2000, and over the following 15 years, an estimated 8 million HIV-related deaths were averted. In countries with a high burden of disease, this decline translated into important increases in life expectancy. Notwithstanding these gains, the decrease in HIV-associated deaths appears to have plateaued in recent years. HIV still causes more than 1 million deaths per year worldwide and remains a leading cause of death and complications in subSaharan Africa. A key explanation for this enduring high mortality is that despite an evolution toward offering treatment earlier in the course of the disease, HIV continues to be identified in a substantial number of patients with advanced infection (which is defined by the World Health Organization [WHO] as a CD4+ count of fewer than 200 cells per cubic millimeter). A recent study of trends across 55 countries showed that more than a third (37%) of the patients who initiated ART in 2015 already had advanced HIV infection. Such patients are at high risk for death, even after starting ART (which can increase the inflammatory response), and the risk increases with a decreasing CD4+ count. A worrisome new trend that has been observed in countries with long-standing HIV treatment programs is an increase in the number of patients who present for care with advanced HIV infection after a period of treatment interruption. A report on the REALITY trial, published in this issue of the Journal *), describes a prophylaxis package that was aimed at reducing the risk of death among patients who presented with advanced HIV infection in four African countries: Uganda, Zimbabwe, Malawi, and Kenya. The package, which includes fluconazole (100 mg daily for 12 weeks), azithromycin (5 days), albendazole (single dose), and a fixed-dose combination tablet of trimethoprim–sulfamethoxazole, isoniazid, and pyridoxine, is designed to provide protection against leading infectious causes of hospitalization and death — in particular, tuberculosis, cryptococcal infection, and severe bacterial infections6 — among patients with advanced HIV infection. In this trial, at the 24-week cutoff for the primary outcome, patients who had started the enhanced-prophylaxis package at the time of ART initiation had a 27% lower rate of death than those who received standard prophylaxis with trimethoprim–sulfamethoxazole alone (8.9% vs. 12.2% by Kaplan–Meier analysis). The incidence of new cases of tuberculosis was significantly lower with enhanced prophylaxis than with standard prophylaxis (7.1% vs. 10.2%), as was the incidence of cryptococcal infection (1.0% vs. 2.6%), candidiasis (1.1% vs. 2.6%), and new hospitalization (17.0% vs. 20.7%). The package of drugs had an acceptable side-effect profile; the

levels of adherence were high, and there was no discernable effect on adherence to ART, despite the additional pill burden. Although the investigators did not find a between-group difference in mortality due to severe bacterial infections, it is plausible that a proportion of the unexplained causes of death (which made up 40% of all deaths and were significantly less common in the enhanced-prophylaxis group) included bacterial infections that are more challenging to diagnose with certainty. This prophylaxis package is particularly relevant in centers with limited access to laboratory investigations such as cryptococcal antigen testing, tuberculosis diagnostics, and bacterial culture. In such locations, this approach is practical for reducing illness and death from the most common causes, which can occur rapidly. (Most of the deaths in the REALITY trial occurred within the first 3 weeks after ART initiation.) Nevertheless, there are some concerns with this approach that merit careful assessment — notably, the potential risk of microbial resistance to fluconazole and azithromycin and the cost-effectiveness of blanket prophylaxis in locations in which diagnostic tests are available. These issues were taken into consideration during a recent consultation held by the WHO to define a minimum package of diagnostic, prophylactic, and therapeutic interventions that should be made available to support the management of advanced HIV infection within a public health framework. In the REALITY trial, almost half the patients with a CD4+ count of fewer than 100 cells per cubic millimeter (the cutoff value for participation in the trial) had mild or no symptoms (WHO clinical stage 1 or 2 disease). This observation serves to highlight the limits of relying on clinical assessment alone to identify HIV-positive patients at high risk for severe disease and death. It also reinforces the importance of maintaining the capacity to measure CD4+ cells. In locations in which viral-load testing is available, the CD4+ count is no longer required in order to determine a patient's eligibility for antiretroviral therapy or to track the response to treatment, yet measurement of the CD4+ count remains essential for assessing the risk of severe disease, both in patients who newly present for care and in those who return for care after a period of treatment interruption. With the advent of new treatment options, HIV infection has evolved from a probable death sentence to a chronic disease. If patients start ART early, they can expect a near-normal life expectancy. Early treatment also reduces the risk of HIV transmission, and much of the focus today is on reducing the spread of new infections to achieve epidemic control. Nevertheless, the relatively consistent proportion of patients who newly present for care with a low CD4+ count, together with an additional number of seriously ill patients who return for care after a period of treatment interruption, calls for a renewed focus to respond to the needs of patients with advanced HIV infection who are at high risk for illness and death.
*) NEJM 2017;377:233-45
Enhanced Prophylaxis plus Antiretroviral Therapy for Advanced HIV Infection in Africa
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19. TMIH 2017;22(7):797-806

Behavioural disinhibition in the general population during the antiretroviral therapy roll-out in Sub-Saharan Africa: systematic review and meta-analysis

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Objectives: Improved life expectancy and reduced transmission probabilities due to ART may result in behavioural disinhibition - that is an increase in sexual risk behaviour in response to a perceived lower risk of HIV. We examined trends in sexual risk behaviour in the general population of sub-Saharan African countries 1999-2015.
Methods: We systematically reviewed scientific literature of sexual behaviour and reviewed trends in Demographic and Health Surveys. A meta-analysis on four indicators of sexual risk behaviour was performed: unprotected sex, multiple sexual partners, commercial sex and prevalence of sexually transmitted infections.
Results: Only two peer-reviewed studies met our inclusion criteria, while our review of DHS data spanned 18 countries and 16 years (1999-2015). We found conflicting trends in sexual risk behaviour. Reported unprotected sex decreased consistently across the 18 countries, for both sexes. In contrast, reporting multiple partners was decreasing over the period 1999 to the mid-2000s, yet has been

consistently increasing thereafter. Similar trends were found for reported sexually transmitted infections and commercial sex (men only).
Conclusions: In conclusion, we found no clear evidence of behavioural disinhibition due to expanded access to ART in sub-Saharan Africa. Substantial increases in condom use coincided with increases in reported multiple partners, commercial sex and sexually transmitted infections, especially during the period of ART scale-up. Further research is needed into how these changes might affect HIV transmission.

Malaria

20. Am J TMH 2017;96(6):1430-40
The Economic Value of Long-Lasting Insecticidal Nets and Indoor Residual Spraying Implementation in Mozambique
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Malaria-endemic countries have to decide how much of their limited resources for vector control to allocate toward implementing long-lasting insecticidal nets (LLINs) versus indoor residual spraying (IRS). To help the Mozambique Ministry of Health use an evidence-based approach to determine funding allocation toward various malaria control strategies, the Global Fund convened the Mozambique Modeling Working Group which then used JANUS, a software platform that includes integrated computational economic, operational, and clinical outcome models that can link with different transmission models (in this case, OpenMalaria) to determine the economic value of vector control strategies. Any increase in LLINs (from 80% baseline coverage) or IRS (from 80% baseline coverage) would be cost-effective (incremental cost-effectiveness ratios ≤ $114/disability-adjusted life year averted). However, LLIN coverage increases tend to be more cost-effective than similar IRS coverage increases, except where both pyrethroid resistance is high and LLIN usage is low. In high-transmission northern regions, increasing LLIN coverage would be more cost-effective than increasing IRS coverage. In medium-transmission central regions, changing from LLINs to IRS would be more costly and less effective. In low-transmission southern regions, LLINs were more costly and less effective than IRS, due to low LLIN usage. In regions where LLINs are more cost-effective than IRS, it is worth considering prioritizing LLIN coverage and use. However, IRS may have an important role in insecticide resistance management and epidemic control. Malaria intervention campaigns are not a one-size-fits-all solution, and tailored approaches are necessary to account for the heterogeneity of malaria epidemiology.

21. EID 2017;23(5):758-64
Insecticide-Treated Nets and Protection against Insecticide-Resistant Malaria Vectors in Western Kenya
Ochomo E et al.

Insecticide resistance might reduce the efficacy of malaria vector control. In 2013 and 2014, malaria vectors from 50 villages, of varying pyrethroid resistance, in western Kenya were assayed for resistance to deltamethrin. Long-lasting insecticide-treated nets (LLIN) were distributed to households at universal coverage. Children were recruited into 2 cohorts, cleared of malaria-causing parasites, and tested every 2 weeks for reinfection. Infection incidence rates for the 2 cohorts were 2.2 (95% CI 1.9-2.5) infections/person-year and 2.8 (95% CI 2.5-3.0) infections/person-year. LLIN users had lower infection rates than non-LLIN users in both low-resistance (rate ratio 0.61, 95% CI 0.42-0.88) and high-resistance (rate ratio 0.55, 95% CI 0.35-0.87) villages (p = 0.63). The association between insecticide resistance and infection incidence was not significant (p = 0.99). Although the incidence of infection was high among net users, LLINs provided significant protection (p = 0.01) against infection with malaria parasite regardless of vector insecticide resistance.

Non-Communicable Diseases

22. Lancet 2017;90(10091):311-23
Seminar: Sickle cell disease
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Sickle cell disease is a common and life-threatening haematological disorder that affects millions of people worldwide. Abnormal sickle-shaped erythrocytes disrupt blood flow in small vessels, and this vaso-occlusion leads to distal tissue ischaemia and inflammation, with symptoms defining the acute painful sickle-cell crisis. Repeated sickling and ongoing haemolytic anaemia, even when subclinical, lead to parenchymal injury and chronic organ damage, causing substantial morbidity and early mortality. Currently available treatments are limited to transfusions and hydroxycarbamide, although stem cell transplantation might be a potentially curative therapy. Several new therapeutic options are in development, including gene therapy and gene editing. Recent advances include systematic universal screening for stroke risk, improved management of iron overload using oral chelators and non-invasive MRI measurements, and point-of-care diagnostic devices. Controversies include the role of haemolysis in sickle cell disease pathophysiology, optimal management of pregnancy, and strategies to prevent cerebrovascular disease.

Mental Health

23. BMJ 2017;357:j2738 News
Five minutes with . . . Lynne Jones
Kmietowicz Z

The humanitarian psychiatrist talks about working in war and disaster zones
“I did not plan a career as a humanitarian psychiatrist; I sort of blundered into it. It began more than 25 years ago in Guatemala while I was doing research. I was asked by a woman friend to come and see her brother. After a long walk up into the mountains I was introduced to a young man who could not speak or move. The history his sister gave me made it clear he was depressed and catatonic. He had had antidepressants in the past, which had helped, but the nearest psychiatrist was three days by bus and they had no money. All I could do was give them money to get this young man to hospital. But I suddenly realised that this was what I wanted to do: work with mentally ill people with no access to psychiatric care.
“Then I was lucky enough to have a training supervisor who sanctioned my requests for unpaid leave to work for various humanitarian agencies in the Balkans during the conflict there and actively encouraged me to do research.
“I soon learnt that integrating mental healthcare into primary healthcare clinics was the best way to establish a psychiatric service, because it does not stigmatise mental illness and allows those with psychiatric problems to be identified.
“Many people assume that the main problem in emergencies is post-traumatic stress disorder, but that is not the case. Of course, there are cases of PTSD, but most people in acute situations are suffering grief, loss, acute stress, and anxiety. These are all normal reactions to horrifying situations, and if they are dealt with effectively most people won’t develop mental illnesses.
“The basic approach to helping people after terrifying events is similar whether it is an earthquake in Haiti or a terrorist attack in London. Firstly, make people feel safe, comfort them, offer them immediate care for their wounds, provide them with food, water, and shelter, and connect them with those they love. If they want to talk, be able to listen. Any member of the public can do these things, and it’s impressive how many have been offering this kind of support in the attacks here in the UK. In the weeks that follow, some people may not recover in the normal way and may need more help.
“My particular concern in war and disaster settings is for a group that gets forgotten: those people who have severe or chronic psychiatric conditions, particularly psychosis. If they have chronic conditions

their treatment can be interrupted and they can lose the support that was helping them cope. In Port-au-Prince the asylum was partly destroyed by the earthquake. Patients had no food, no running water, no bedding or clean clothes, and no medication. In that situation we have to address patients' basic needs first and then get them treatment.

24. HPP 2017;32(5):699–709

Strengthening mental health system governance in six low- and middle-income countries in Africa and South Asia: challenges, needs and potential strategies

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Poor governance has been identified as a barrier to effective integration of mental health care in low- and middle-income countries. Governance includes providing the necessary policy and legislative framework to promote and protect the mental health of a population, as well as health system design and quality assurance to ensure optimal policy implementation. The aim of this study was to identify key governance challenges, needs and potential strategies that could facilitate adequate integration of mental health into primary health care settings in low- and middle-income countries. Key informant qualitative interviews were held with 141 participants across six countries participating in the Emerging mental health systems in low- and middle-income countries (Emerald) research program: Ethiopia, India, Nepal, Nigeria, South Africa, and Uganda. Data were transcribed (and where necessary, translated into English) and analysed thematically using framework analysis, first at the country level, then synthesized at a cross-country level. While all the countries fared well with respect to strategic vision in the form of the development of national mental health policies, key governance strategies identified to address challenges included: strengthening capacity of managers at sub-national levels to develop and implement integrated plans; strengthening key aspects of the essential health system building blocks to promote responsiveness, efficiency and effectiveness; developing workable mechanisms for inter-sectoral collaboration, as well as community and service user engagement; and developing innovative approaches to improving mental health literacy and stigma reduction. Inadequate financing emerged as the biggest challenge for good governance. In addition to the need for overall good governance of a health care system, this study identifies a number of specific strategies to improve governance for integrated mental health care in low- and middle-income countries.

Research Ethics

25. HPP 2017;32(6):890–910

Ethics of health policy and systems research: a scoping review of the literature

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Health policy and systems research (HPSR) is increasingly funded and undertaken as part of health system strengthening efforts worldwide. HPSR ethics is also a relatively new and emerging field, with numerous normative and descriptive questions that have largely not been considered. Normative questions include what ethical principles and values should guide HPSR. Descriptive questions include what ethical concerns arise when conducting HPSR. A small but growing body of scholarly work characterizes the various ethics issues inherent in HPSR. Towards informing the future development of ethics guidance for HPSR, a scoping review was undertaken to: (1) identify the range of ethics issues relevant to the conduct of HPSR—with a deliberate (though not exclusive) focus on low- and middle-income country settings and (2) describe existing guidance on key ethics issues relevant to HPSR. Using the Cochrane methods as a basis, the review identified formal and informal literature on HPSR ethics by searching the following databases: PubMed's Medline, Embase, Global Health, Scopus, WHO Global Health Regional Libraries, LILACs, OpenDOAR and Bielefeld Academic Search Engine. In total, 11 062 documents were identified from the formal (10 519) and

informal (543) literature. One hundred and seven of these documents (formal 99 and informal 8) met at least one inclusion criterion and underwent thematic analysis. Ethical issues in four main categories were identified: upholding autonomy, identifying and balancing risks and benefits, justice and determination of ethical review requirements. The review indicated that the ethical values behind HPSR place an emphasis on its contributing to the reduction of health disparities. Unsurprisingly then, numerous ethical concerns relating to justice arise in HPSR. However, the majority of existing guidance focuses on obtaining or waiving informed consent and, thus, appears to be insufficient for HPSR. A list of priority ethics issues in HPSR in need of guidance development is provided.

Sexual and Reproductive Health

26. HPP 2017;32(6):769–80

Barriers and facilitators for institutional delivery among poor Mesoamerican women: a cross-sectional study

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Professional skilled care has shown to be one of the most promising strategies to reduce maternal mortality, and in-facility deliveries are a cost-effective way to ensure safe births. Countries in Mesoamerica have emphasized in-facility delivery care by professionally skilled attendants, but access to good-quality delivery care is still lacking for many women. We examined the characteristics of women who had a delivery in a health facility and determinants of the decision to bypass a closer facility and travel to a distant one. We used baseline information from the Salud Mesoamerica Initiative (SMI). Data were collected from a large household and facilities sample in the poorest quintile of the population in Guatemala, Honduras and Nicaragua. The analysis included 1592 deliveries. After controlling for characteristics of women and health facilities, being primiparous (RR = 1.15, 95% CI 1.10, 1.21), being literate (RR = 1.24, 95% CI 1.04, 1.48), having antenatal care (RR = 1.68, 95% CI 1.24, 2.27), being informed of the need for having a C-section (RR = 1.07, 95% CI 1.02, 1.11) and travel time to the closest facility totaling 1–2 h vs under 30 min (RR = 0.88, 95% CI 0.77, 0.99) were associated with in-health facility deliveries. In Guatemala, increased availability of medications and equipment at a distant facility was strongly associated with bypassing the closest facility in favor of a distant one for delivery (RR = 2.10, 95% CI 1.08, 4.07). Our study showed a strong correlation between well-equipped facilities and delivery attendance in poor areas of Mesoamerica. Indeed, women were more likely to travel to more distant facilities if the facilities were of higher level, which scored higher on our capacity score. Our findings call for improving the capacity of health facilities, quality of care and addressing cultural and accessibility barriers to increase institutional delivery among the poor population in Mesoamerica.

27. IJE 2017;662–75

Women's Health: Child marriage and intimate partner violence: a comparative study of 34 countries

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Background: Studies in South Asia suggest that child marriage is a strong risk factor for intimate partner violence (IPV), but evidence outside the region is lacking.
Methods: This study uses standardized data from demographic and health surveys in 34 countries to test the hypothesis that young women (age 20–24) who married as children are at increased risk of past year physical and/or sexual IPV as compared with those women who married as adults.
Results: Globally, 9% of respondents were married before they turned 15; another 25% were married between the ages of 15 and 17. Past year physical and/or sexual IPV was higher among women who married as children (29%) compared with those who married as adults (20%). This difference persisted in logistic regression models that adjust for sociodemographic characteristics [odds ratio (OR) 1.41 (1.30–1.52) for marriage before 15, and 1.42 (1.35–1.50) for marriage at 15–17]. However,

there was considerable heterogeneity between countries: marriage before age 15 was associated with a combined measure of past year physical and/or sexual IPV in nine countries; women married between 15 and 17 were at increased risk of physical and/or sexual IPV in 19 countries. This heterogeneity was most evident in sub-Saharan Africa, and warrants further investigation in so far as it may help identify protective policies and norms.
Conclusion: Substantial reductions in IPV will likely require interventions to combat child marriage itself and to protect women from IPV within child marriages.

28. Lancet 2017;Jul7.pii:S0140-6736(17)31449-6

Effectiveness of a group B outer membrane vesicle meningococcal vaccine against gonorrhoea in New Zealand: a retrospective case-control study

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Background: Gonorrhoea is a major global public health problem that is exacerbated by drug resistance. Effective vaccine development has been unsuccessful, but surveillance data suggest that outer membrane vesicle meningococcal group B vaccines affect the incidence of gonorrhoea. We assessed vaccine effectiveness of the outer membrane vesicle meningococcal B vaccine (MeNZB) against gonorrhoea in young adults aged 15-30 years in New Zealand.
Methods: We did a retrospective case-control study of patients at sexual health clinics aged 15-30 years who were born between Jan 1, 1984, and Dec 31, 1998, eligible to receive MeNZB, and diagnosed with gonorrhoea or chlamydia, or both. Demographic data, sexual health clinic data, and National Immunisation Register data were linked via patients' unique personal identifier. For primary analysis, cases were confirmed by laboratory isolation or detection of Neisseria gonorrhoeae only from a clinical specimen, and controls were individuals with a positive chlamydia test only. We estimated odds ratios (ORs) comparing disease outcomes in vaccinated versus unvaccinated participants via multivariable logistic regression. Vaccine effectiveness was calculated as 100×(1-OR).
Findings: 11 of 24 clinics nationally provided records. There were 14 730 cases and controls for analyses: 1241 incidences of gonorrhoea, 12 487 incidences of chlamydia, and 1002 incidences of co-infection. Vaccinated individuals were significantly less likely to be cases than controls (511 [41%] vs 6424 [51%]; adjusted OR 0·69 [95% CI 0·61-0·79]; p<0·0001). Estimate vaccine effectiveness of MeNZB against gonorrhoea after adjustment for ethnicity, deprivation, geographical area, and sex was 31% (95% CI 21-39).
Interpretation: Exposure to MeNZB was associated with reduced rates of gonorrhoea diagnosis, the first time a vaccine has shown any protection against gonorrhoea. These results provide a proof of principle that can inform prospective vaccine development not only for gonorrhoea but also for meningococcal vaccines.

29. Lancet 2017;390(0091):204

Editorial: Curbing the rise in gonococcal AMR

At the start of the G20 summit and ahead of the Sexually Transmitted Infections (STI) & HIV World Congress, on July 9–12, WHO released new data on antimicrobial resistance (AMR) in gonococci. 70 (97%) of 72 countries surveyed from 2009 to 2014 reported finding resistant Neisseria gonorrhoeae isolates. Continued and increased resistance to primary antibiotics was observed and 51 (66%) of 77 countries surveyed reported some resistance to last-resort antibiotics.
In an accompanying paper, WHO's Global Antibiotic Research and Development Partnership outlined a plan, which requires donor support, to develop a new clinical treatment by 2023: introduction of a new molecule, identification of combinations among existing antibiotics, formulation of new fixed-drug combinations, and establishment of a stewardship framework for the distribution and use of the treatments. Only three antibiotics against N gonorrhoeae are currently being developed.
Although the plan did not describe a role for vaccines to combat gonococcal AMR, WHO put out a call to action on STI vaccines at the world congress. Currently, no effective vaccine against this

disease exists, but a study published online in The Lancet on July 10 might offer an avenue for gonorrhoea control. A 31% decrease in the incidence of new gonorrhoea infections was found among 14 000 adults in New Zealand who had been immunised with a meningococcal group B vaccine. Meanwhile, promotion of safe sexual behaviours remains the most effective method of preventing gonorrhoea transmission. However, as highlighted in the new STI Commission published in The Lancet Infectious Diseases, a worrying unintentional consequence of increased use of antiviral prophylaxis to prevent HIV acquisition is a decline in condom use among key at-risk populations. For gonococcal AMR to be curbed, a comprehensive policy is needed, which involves effective prevention advocacy, investment in infrastructure for research and surveillance, and development of, and better access to, point-of-care testing. The focus needs to shift from treatment to control of the global burden, and the role of vaccines needs to be further explored.

30. Lancet 2017;390(10095):669-80

Foley catheterisation versus oral misoprostol for induction of labour in hypertensive women in India (INFORM): a multicentre, open-label, randomised controlled trial

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Background: Between 62 000 and 77 000 women die annually from pre-eclampsia and eclampsia. Prompt delivery, preferably by the vaginal route, is vital for good maternal and neonatal outcomes. Two low-cost interventions-low-dose oral misoprostol tablets and transcervical Foley catheterisation-are already used in low-resource settings. We aimed to compare the relative risks and benefits of these interventions.

Methods: We undertook this multicentre, open-label, randomised controlled trial in two public hospitals in Nagpur, India. Women (aged ≥18 years) who were at 20 weeks' gestation or later with a live fetus and required delivery as a result of pre-eclampsia or hypertension were randomly assigned (1:1), via computer-generated block randomisation (block sizes of four, six, and eight) with concealment by use of opaque, sequentially numbered, sealed envelopes, to receive labour induction with either oral misoprostol 25 μg every 2 h (maximum of 12 doses) or a transcervical Foley catheter (silicone, size 18 F with 30 mL balloon). Randomisation was stratified by study centre. The catheter remained in place until active labour started, the catheter fell out, or 12 h had elapsed. If the catheter did not fall out within 12 h, induction continued with artificial membrane rupture and oxytocin, administered through a micro-drip gravity infusion set. Fetal monitoring was by intermittent auscultation. The primary outcome was vaginal birth within 24 h. Due to the nature of the interventions, masking of participants, study investigators, and care providers to group allocation was not possible. We analysed by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT01801410.

Findings: Between Dec 20, 2013, and June 29, 2015, we randomly assigned 602 women to induction with misoprostol (n=302) or the Foley catheter (n=300; intention-to-treat population). Vaginal birth within 24 h was more common in women in the misoprostol group than in the Foley catheter group (172 [57·0%] vs 141 [47·0%] women; absolute risk difference 10·0%, 95% CI 2·0-17·9; p=0·0136). Rates of uterine hyperstimulation were low in both the misoprostol and Foley catheter groups (two [0·7%] vs one [0·3%] cases; absolute risk difference 0·3%, 95% CI -0·8 to 1·5; p=0·566) and neonatal deaths did not differ significantly between groups (six [2·0%] vs three [1·0%] neonatal deaths; 1·0, -1·04 to 2·97; p=0·322). 17 serious adverse events (3%) were reported during the study: one case of intrapartum convulsion and one case of disseminated intravascular coagulation (both in the Foley group); ten perinatal deaths, including two stillbirths (both in the Foley catheter group) and eight neonatal deaths (n=5 in the misoprostol group and n=3 in the Foley catheter group); and five of neonatal morbidity, comprising birth asphyxia (n=3), septicaemia (n=1), and neonatal convulsion (n=1).

Interpretation: Oral misoprostol was more effective than transcervical Foley catheterisation for induction of labour in women with pre-eclampsia or hypertension. Future studies are required to assess whether oxytocin augmentation following misoprostol can be replaced by regular doses of oral misoprostol tablets.

31. TMIH 2017;22(8):938-59

Barriers to obstetric fistula treatment in low-income countries: a systematic review

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Objective: To identify the barriers faced by women living with obstetric fistula in low-income countries that prevent them from seeking care, reaching medical centres and receiving appropriate care.
Methods: Bibliographic databases, grey literature, journals, and network and organisation websites were searched in English and French from June to July 2014 and again from August to November 2016 using key search terms and specific inclusion and exclusion criteria for discussion of barriers to fistula treatment. Experts provided recommendations for additional sources.
Results: Of 5829 articles screened, 139 were included in the review. Nine groups of barriers to treatment were identified: psychosocial, cultural, awareness, social, financial, transportation, facility shortages, quality of care and political leadership. Interventions to address barriers primarily focused on awareness, facility shortages, transportation, financial and social barriers. At present, outcome data, though promising, are sparse and the success of interventions in providing long-term alleviation of barriers is unclear.
Conclusion: Results from the review indicate that there are many barriers to fistula treatment, which operate at the individual, community and national levels. The successful treatment of obstetric fistula may thus require targeting several barriers, including depression, stigma and shame, lack of community-based referral mechanisms, financial cost of the procedure, transportation difficulties, gender power imbalances, the availability of facilities that offer fistula repair, community reintegration and the competing priorities of political leadership.

32. TMIH 2017;22(9):1081-98

Who delivers where? The effect of obstetric risk on facility delivery in East Africa

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Objectives: Skilled attendance at birth is key for the survival of pregnant women. This study investigates whether women at increased risk of maternal and newborn complications in four East African countries are more likely to deliver in a health facility than those at lower risk.
Methods: Demographic and Health Survey data for Kenya 2014, Rwanda 2014-15, Tanzania 2015-16 and Uganda 2011 were used to study women with a live birth in the three years preceding the survey. A three-level obstetric risk index was created using known risk factors. Generalised linear Poisson regression was used to investigate the association between obstetric risk and facility delivery.
Results: We analysed data from 13 119 women across the four countries of whom 42-45% were considered at medium risk and 12-17% at high risk, and the remainder were at low risk. In Rwanda, 93% of all women delivered in facilities but this was lower (59-66%) in the other three countries. There was no association between a woman's obstetric risk level and her place of delivery in any country; greater wealth and more education were, however, independently strongly associated with facility delivery.
Conclusions: In four East African countries, women at higher obstetric risk were not more likely to deliver in a facility than those with lower risk. This calls for a renewed focus on antenatal risk screening and improved communication on birth planning to ensure women with an increased chance of maternal and newborn complications are supported to deliver in facilities with skilled care.

Tuberculosis

33. TMIH 2017;22(6):734-43

Microscopic observation drug-susceptibility assay vs. Xpert® MTB/RIF for the diagnosis of tuberculosis in a rural African setting: a cost-utility analysis

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Objective: To compare the cost-utility of microscopic observation drug-susceptibility assay (MODS) and Xpert® MTB/RIF implementation for tuberculosis (TB) diagnosis in rural northern Mozambique.
Methods: Stochastic transmission compartmental TB model from the healthcare provider perspective with parameter input from direct measurements, systematic literature reviews and expert opinion. MODS and Xpert® MTB/RIF were evaluated as replacement test of smear microscopy (SM) or as an add-on test after a negative SM. Costs were calculated in 2013 USD, effects in disability-adjusted life years (DALY). Willingness to pay threshold (WPT) was established at once the per capita Gross National Income of Mozambique.
Results: MODS as an add-on test to negative SM produced an incremental cost-effectiveness ratio (ICER) of 5647.89USD/DALY averted. MODS as a substitute for SM yielded an ICER of 5374.58USD/DALY averted. Xpert® MTB/RIF as an add-on test to negative SM yielded ICER of 345.71USD/DALY averted. Xpert® MTB/RIF as a substitute for SM obtained an ICER of 122.13USD/DALY averted. TB prevalence and risk of infection were the main factors impacting MODS and Xpert® MTB/RIF ICER in the one-way sensitivity analysis. In the probabilistic sensitivity analysis, Xpert® MTB/RIF was most likely to have an ICER below the WPT, whereas MODS was not.
Conclusion: Our cost-utility analysis favours the implementation of Xpert® MTB/RIF as a replacement of SM for all TB suspects in this rural high TB/HIV prevalence African setting.

Miscellaneous

34. HPP 2017;32(7):1049–71
Understanding the linkages between social safety nets and childhood violence: a review of the evidence from low- and middle-income countries
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As many as one billion children experience violence every year, and household- and community level poverty are among the risk factors for child protection violations. Social safety nets (SSNs) are a main policy tool to address poverty and vulnerability, and there is substantial evidence demonstrating positive effects on children's health and human capital. This paper reviews evidence and develops a framework to understand linkages between non-contributory SSNs and the experience of childhood emotional, physical and sexual violence in low- and middle-income countries. We catalogue 14 rigorous impact evaluations, 11 of which are completed, analysing 57 unique impacts on diverse violence indicators. Among these impacts, approximately one in five represent statistically significant protective effects on childhood violence. Promising evidence relates to sexual violence among female adolescents in Africa, while there is less clear evidence of significant impacts in other parts of the developing world, and on young child measures, including violent discipline. Further, few studies are set up to meaningfully unpack mechanisms between SSNs and childhood violence; however, those most commonly hypothesized operate at the household level (through increases in economic security and reductions in poverty-related stress), the interpersonal level (improved parental behaviours, caregiving practices, improved psychosocial well-being) and at the child-level (protective education and decreases in problem or risky behaviours). It is important to emphasize that traditional SSNs are never designed with violence prevention as primary objectives, and thus should not be considered as standalone interventions to reduce risks for childhood violence. However, SSNs, particularly within integrated protection systems, appear to have potential to reduce violence risk. Linkages between SSNs and childhood violence are understudied, and investments should be made to close this evidence gap.

35. Lancet 2017;June 8
Series: Health in Humanitarian Crises

Executive Summary Large-scale humanitarian crises are ongoing in Syria, Afghanistan, Central African Republic, DR Congo, Iraq, Libya, Nigeria, Somalia, South Sudan, and Yemen among others.

This Lancet Series of four papers and accompanying Comments *) assesses the evidence base for health interventions in humanitarian crises and finds significant variations in the quantity and quality of evidence. It brings together lessons learned from recent failures in humanitarian crises to provide recommendations to improve a broken system. It calls for action to put the protection of humanitarian workers front and centre, to align humanitarian interventions with development programmes, to improve leadership and coordination, to ensure timely and robust health information, and to make interventions more efficient, effective, and sustainable.

*) Improving evidence for health in humanitarian crises
Samarasekera U & Horton R

*) Where is the science in humanitarian health?
Waldman RJ & Toole MJ

*) Humanitarian medicine is more than a technical exercise
Hawkins V & Pérache AH

*) Research ethics and evidence for humanitarian health
O'Mathúna D & Siriwardhana C

*) Moses Massaquoi: health leader in humanitarian crises
Lane R

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

*) Public health information in crisis-affected populations: a review of methods and their use for advocacy and action
Checchi F et al.

*) Recurrent failings of medical humanitarianism: intractable, ignored, or just exaggerated?
Colombo S et al.

*) The humanitarian system is not just broke, but broken: recommendations for future humanitarian action
Spiegel PB

*) Attacks against health care in Syria, 2015–16: results from a real-time reporting tool
Elamein M et al.

36. TMIH 2017;22(6):708-15
Scarification in sub-Saharan Africa: social skin, remedy and medical import
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Various forms of body modification may be observed in sub-Saharan Africa. Hypotheses and theories of scarification and tribal marking in sub-Saharan Africa are described, plus the procedure of scarification, examples from several African countries, assumed effects in prevention and treatment of diseases, and the medical risks resulting from unsterile manipulation.

37. TMIH 2017;22(9):1054-62
Treatment strategies for chronic osteomyelitis in low- and middle-income countries: systematic review

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Objectives: To identify a standard treatment regime or highly successful procedure for chronic osteomyelitis in low- and middle-income countries.
Methods: Systematic review following PRISMA guidelines.
Results: The initial search resulted in 102 studies of which nine met the inclusion criteria and were analysed qualitatively. The included studies involved 1173 patients from Africa and Asia. All patients were diagnosed with chronic osteomyelitis. Surgical and antibiotic treatment regimens differed substantially. No better judgement than moderate risk of selection bias could be made due to the study designs.
Conclusions: The evidence is not sufficiently robust to identify the most effective treatment, or to even allow a recommendation of the best suitable treatment of chronic osteomyelitis in low-income countries.