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International Health Alerts 2018-1 Abstracts

Child Health / iCCM

1. *N Engl J Med* 2018; 378:1583-1592

Azithromycin to Reduce Childhood Mortality in Sub-Saharan Africa

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BACKGROUND

We hypothesized that mass distribution of a broad-spectrum antibiotic agent to preschool children would reduce mortality in areas of sub-Saharan Africa that are currently far from meeting the Sustainable Development Goals of the United Nations.

METHODS

In this cluster-randomized trial, we assigned communities in Malawi, Niger, and Tanzania to four twice-yearly mass distributions of either oral azithromycin (approximately 20 mg per kilogram of body weight) or placebo. Children 1 to 59 months of age were identified in twice-yearly censuses and were offered participation in the trial. Vital status was determined at subsequent censuses. The primary outcome was aggregate all-cause mortality; country-specific rates were assessed in pre-specified subgroup analyses.

RESULTS

A total of 1533 communities underwent randomization, 190,238 children were identified in the census at baseline, and 323,302 person-years were monitored. The mean (\pm SD) azithromycin and placebo coverage over the four twice-yearly distributions was 90.4 \pm 10.4%. The overall annual mortality rate was 14.6 deaths per 1000 person-years in communities that received azithromycin (9.1 in Malawi, 22.5 in Niger, and 5.4 in Tanzania) and 16.5 deaths per 1000 person-years in communities that received placebo (9.6 in Malawi, 27.5 in Niger, and 5.5 in Tanzania). Mortality was 13.5% lower overall (95% confidence interval [CI], 6.7 to 19.8) in communities that received azithromycin than in communities that received placebo (P <0.001); the rate was 5.7% lower in Malawi (95% CI, -9.7 to 18.9), 18.1% lower in Niger (95% CI, 10.0 to 25.5), and 3.4% lower in Tanzania (95% CI, -21.2 to 23.0). Children in the age group of 1 to 5 months had the greatest effect from azithromycin (24.9% lower mortality than that with placebo; 95% CI, 10.6 to 37.0). Serious adverse events occurring within a week after administration of the trial drug or placebo were uncommon, and the rate did not differ significantly between the groups. Evaluation of selection for antibiotic resistance is ongoing.

CONCLUSIONS

Among postneonatal, preschool children in sub-Saharan Africa, childhood mortality was lower in communities randomly assigned to mass distribution of azithromycin than in those assigned to placebo, with the largest effect seen in Niger. Any implementation of a policy of mass distribution would need to strongly consider the potential effect of such a strategy on antibiotic resistance.

2. *PLoS Med* 15(4): e1002557

PERSPECTIVE From surviving to thriving: What evidence is needed to move early child-development interventions to scale?

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Previous research has established that delivering interventions in the first 1,000 days of life improves mother-child attachment, contributes to the reduction of health inequities, has a significant impact on adult health, and is cost-effective. At the global level, the importance of the early years of a child's life is reflected in high-level World Health Organization (WHO) and United Nations Children's Fund (UNICEF) support, the Global Strategy for Women's, Children's and Adolescents' Health (with its focus on not only survival but also children's ability to thrive and progress successfully into adolescence), and the Nurturing Care Framework to be launched at the WHO World Health Assembly

in May 2018. In this week's PLOS Medicine, 2 Research Articles present findings from trials conducted in Zambia and Colombia that add to the burgeoning evidence base on the implementation of early interventions designed to improve early child development (ECD) in low- and middle-income countries (LMICs).

Child development interventions: Mechanism of impact.

Peter Rockers and colleagues assessed the impact on ECD of community-based home visiting incorporating health screening and parenting groups. The study was a 2-year follow-up of a cluster-randomised controlled trial conducted in Zambia with the caregivers of children between the ages of 6 and 12 months. The study included fortnightly home visits conducted by child development agents (CDAs) for the first year as well as parenting groups every 2 weeks for 2 years. The intervention significantly reduced stunting (odds ratio [OR] 0.45, 95% CI 0.22–0.92; $p = 0.028$) and was associated with an improvement in child language (β 0.14, 95% CI 0.01–0.27; $p = 0.039$), but there was no impact on other child-development outcomes. While Rockers and colleagues' study is important and speaks to the difficulties of improving child development in low-resource contexts, one of the key conclusions of the paper is that parenting groups may be a promising avenue for improving physical growth and child development. This of course may be true, but it is more likely that the improvements in stunting were a result of the home visits of the CDAs, and not the parenting groups, given that their visits focused on screening for infections and acute malnutrition and encouraging caregivers to attend routine health services. Without an understanding of the mechanisms involved, drawing conclusions about what component of a complex intervention is the likely agent of change is difficult.

Alison Andrew and colleagues describe the medium-term impacts of an ECD intervention in Colombia. They followed up a cohort that had previously received a psychosocial stimulation intervention integrated into a national cash transfer programme in a cluster-randomised trial that showed benefits for ECD. In the 2-year follow-up study, however, Andrew and colleagues found no impact at age 5 years on any of the outcomes assessed (cognition, language, school readiness, executive function, and behaviour). The authors hypothesise that one of the reasons for the null finding was that the original effects on child development were too small to be sustained—i.e., that they 'faded out'. The concept of fade out is of particular relevance for understanding long-term impacts of early interventions. A recent meta-analysis on childhood interventions showed a steady decline in program effect over time that was observed regardless of the duration of the intervention or when it began. As Andrew and colleagues correctly point out 'fade out' also needs to be interpreted in the light of what has come to be known as the 'resurrection effect'. That is, early effects that disappear in early or middle childhood (as well as in adolescence) may re-emerge much later in life. However, it may also be the case that early effects may disappear and that sustaining positive findings may be dependent on subsequent quality schooling and life experiences. Given the level of adversity in many LMICs, for early investments to remain productive, families and children will require subsequent access to quality environments such as day care and preschools. In contexts of high risk and adversity, the impact of early interventions may be more durable when they are built upon by interventions during later years. Finally, our understanding of pathways and mechanisms and how the dose, timing, and nature of adversity impact on outcome across the life course is limited. While early intervention is essential and foundational, it is not an inoculation against later developmental disruption. A more sophisticated understanding of mechanism of change coupled with a life-course perspective is key. With a better understanding of mechanism, pathways, and dose, we will be in a better position to determine what kinds of follow-up interventions may be necessary beyond the early years for children with significant levels of cumulative biological or psychosocial risk exposure, in order to maintain and build on early gains.

Scaling up early interventions

Despite significant current global health focus on scaling up interventions, knowledge is limited about scaling up programmes in ECD. In the Zambia study, one of the conclusions is that scale-up efforts would likely require a delivery platform integrated into existing structures. Unfortunately, in a low-resource setting such as Zambia, the intervention described by Rockers and colleagues is simply not scalable. The intensive nature of the intervention, including home visits and parenting groups, is beyond the means of all LMICs. The intervention in the Colombia study, on the other hand, was integrated from the start within a national programme. One of the explanations the authors proffer for the null results are concerns with extrapolating findings from efficacy trials (from which much of the

current evidence comes) to interventions implemented at scale. This intervention was, however, always an integrated one implemented at scale that had positive outcomes (albeit small), and any compromises were likely there from start. Having said that, the acknowledgment that it may have been worthwhile to hire local supervisors and to increase the frequency of supervision is illustrative of the urgent need for research that attempts to understand what is needed for successful scaling up—above and beyond programme content. When scaling up programmes, the ‘soft’ elements, such as recruitment, training, supervision, and accountability, are often the first to be dropped or reduced in frequency. Looking to the future, the ECD field requires rigorous implementation science research that examines the best models of recruitment, training, and supervision (in addition to programme content) to achieve impact. Finally, the high levels of poverty and developmental risk that persist across the life course in many countries make it imperative that longitudinal cohorts are established in diverse contexts in order to facilitate more informed decisions about the best mix of early and later investments.

3. [Am J Trop Med Hyg. 2018 Apr 16. doi: 10.4269/ajtmh.17-0494. \[Epub ahead of print\]](https://doi.org/10.4269/ajtmh.17-0494)

Burden of Influenza in Less Than 5-Year-Old Children Admitted to Hospital with Pneumonia in Developing and Emerging Countries: A Descriptive, Multicenter Study.

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This descriptive 4-year study reports the proportion of detection of influenza viruses in less than 5-year-old children hospitalized for pneumonia in eight developing and emerging countries and describes clinical and microbiological characteristics of influenza-related pneumonia cases. Hospitalized children presenting radiologically confirmed pneumonia aged 2–60 months were prospectively enrolled in this observational standardized study. Mean proportion of isolated influenza virus was 9.7% (95% confidence interval: 7.9–11.8%) among 888 pneumonia children analyzed, with moderate heterogeneity between countries—ranging from 6.2% in Cambodia to 18.8% in Haiti. The clinical characteristics of children with influenza-related pneumonia were not substantially different from those of other pneumonia cases. Influenza A H1N1-related pneumonia cases appeared as more severe than pneumonia cases related to other strains of influenza. *Streptococcus pneumoniae* was detected more often in blood samples from influenza-related cases than in those without detected influenza viruses (19.7% versus 9.5%, $P = 0.018$). Influenza-related pneumonia is frequent among children less than 5 years old with pneumonia, living in developing and emerging countries. Influenza might be a frequent etiologic agent responsible for pneumonia or a predisposing status factor for pneumococcal-related pneumonia in this population.

Communicable Diseases

4. [Lancet 2018;391\(10121\):700–708](https://doi.org/10.1016/S0140-6736(18)31111-1)

Evidence-based guidelines for supportive care of patients with Ebola virus disease

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The 2013–16 Ebola virus disease outbreak in west Africa was associated with unprecedented challenges in the provision of care to patients with Ebola virus disease, including absence of pre-existing isolation and treatment facilities, patients' reluctance to present for medical care, and limitations in the provision of supportive medical care. Case fatality rates in west Africa were initially greater than 70%, but decreased with improvements in supportive care. To inform optimal care in a future outbreak of Ebola virus disease, we employed the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology to develop evidence-based guidelines for the delivery of supportive care to patients admitted to Ebola treatment units. Key recommendations include administration of oral and, as necessary, intravenous hydration; systematic monitoring of vital

signs and volume status; availability of key biochemical testing; adequate staffing ratios; and availability of analgesics, including opioids, for pain relief.

From the article:

Recommendations

(1). Oral rehydration

We strongly recommend, with moderate confidence, administering oral rehydration solution in an adequate amount rather than non-standardised rehydration.

(2). Parenteral administration of fluids

We strongly recommend, with moderate confidence, parenteral administration of fluids rather than no parenteral administration for patients who are unable to drink or whose volume losses are larger than oral volume intake.

(3). Systematic monitoring and charting of vital signs and volume status

In all patients with Ebola virus disease, we strongly recommend, with low confidence, systematically monitoring and charting of vital signs and volume status rather than no systematic monitoring or charting.

(4). Serum biochemistry

We strongly recommend, with low confidence, that provision for serum biochemistry be made available, that testing be done as deemed desirable by the attending clinicians, that results be charted, and that interventions in response to the results be implemented according to clinicians' judgment.

(5). Staffing ratio

We strongly recommend, with moderate confidence, an Ebola treatment unit staffing ratio of at least one clinician to four patients, including the following considerations—patient assessment at least 3 times per day and continuous (24 h per day) monitoring of patients to allow prompt recognition of and reaction to acute changes in condition.

(6). Communication with family and friends

We conditionally suggest, with low confidence, facilitating communication with family and friends for patients admitted to the treatment unit with suspect, probable, or confirmed Ebola virus disease.

(7). Analgesic therapy

We strongly recommend, with high confidence, the use of analgesic therapy, including parenteral opioids, if necessary to reduce pain.

(8). Antibiotics

We strongly recommend, with moderate confidence, prompt administration of broad-spectrum antibiotics to patients with suspect, probable, or confirmed Ebola virus disease and high severity of illness.

Conclusion

First-hand accounts of the care that was delivered during the 2013–16 west African outbreak of Ebola virus disease provided impetus for these guidelines, which address interventions that are otherwise considered routine.

Indirectness considerably limits the quality of the evidence that informed these recommendations. One of the reasons for this dearth of evidence is that during the past 40 years, after 18 outbreaks and more than 30 000 reported cases of Ebola virus disease, clinical descriptions were mostly limited to the presenting signs and symptoms for a very small proportion of all cases (ie, this was an unrepresentative sample). Applying these recommendations could not only improve outcomes but enable data collection that will inform future practice.

5. TMIH 2018;23(2):243-250

Poor continuity of care for TB diagnosis and treatment in Zambian Prisons: a situation analysis

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Objectives. Prisons act as infectious disease reservoirs. We aimed to explore the challenges of TB control and continuity of care in prisons in Zambia.

Methods. We evaluated treatment outcomes for a cohort of inmates diagnosed with TB during a TB REACH funded screening programme initiated by the Zambia Prisons Service and the Centre for Infectious Disease Research in Zambia.

Results. Between October 2010 and September 2011, 6282 inmates from six prisons were screened for TB, of whom 374 (6.0%) were diagnosed. TB treatment was initiated in 345 of 374 (92%) inmates. Of those, 66% were cured or completed treatment, 5% died and 29% were lost to follow-up. Among those lost to follow-up, 11% were released into the community and 13% were transferred to other prisons.

Conclusions. Weak health systems within the Zambian prison service currently undermines continuity of care, despite intensive TB screening and case-finding interventions. To prevent TB transmission and the development of drug resistance, we need sufficient numbers of competent staff for health care, reliable health information systems including electronic record keeping for prison facilities, and standard operating procedures to guide surveillance, case-finding and timely treatment initiation and completion.

6. *TMIH* 2018;23(4):425–432

Impact of rotavirus vaccination on rotavirus hospitalisation rates among a resource-limited rural population in Mbita, Western Kenya

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Objectives. A two-dose oral monovalent rotavirus vaccine (RV1) was introduced into the Kenyan National Immunization Program in July 2014. We assessed trends in hospitalisation for rotavirus-specific acute gastroenteritis (AGE) and strain distribution among children <5 years in a rural, resource-limited setting in Kenya before and after the nationwide implementation of the vaccine.

Methods. Data on rotavirus AGE and strain distribution were derived from a 5-year hospital-based surveillance. We compared rotavirus-related hospitalisations and strain distribution in the 2-year post-vaccine period with the 3-year pre-vaccine baseline. Vaccine administrative data from the Unit of Vaccines and Immunization Services (UVIS) for Mbita sub-county were used to estimate rotavirus immunisation coverage in the study area.

Results. We observed a 48% (95% CI: 27–64%) overall decline in rotavirus-related hospitalisations among children aged <5 years in the post-vaccine period. Coverage with the last dose of rotavirus vaccine increased from 51% in year 1 to 72% in year 2 of the vaccine implementation. Concurrently, reductions in rotavirus hospitalisations increased from 40% in the first year to 53% in the second year of vaccine use. The reductions were most pronounced among the vaccine-eligible group, with the proportion of cases in this age group dropping to 14% in post-vaccine years from a high of 51% in the pre-vaccine period. A diversity of rotavirus strains circulated before the introduction of the vaccine with G1P[8] being the most dominant strain. G2P[4] replaced G1P[8] as the dominant strain after the vaccine was introduced.

Conclusions. Rotavirus vaccination has resulted in a notable decline in hospital admissions for rotavirus infections in a rural resource-limited population in Kenya. This provides early evidence for continued use of rotavirus vaccines in routine childhood immunisations in Kenya. Our data also underscore the need for expanding coverage on second dose so as to maximise the impact of the vaccine.

7. *International Journal of Epidemiology*, 2018, Vol.47 (2): 550 - 560

Curbing the hepatitis C virus epidemic in Pakistan: the impact of scaling up treatment and prevention for achieving elimination

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Background: The World Health Organization (WHO) has developed a global health strategy to eliminate viral hepatitis. We project the treatment and prevention requirements to achieve the WHO HCV elimination target of reducing HCV incidence by 80% and HCV-related mortality by 65% by 2030 in Pakistan, which has the second largest HCV burden worldwide.

Methods: We developed an HCV transmission model for Pakistan, and calibrated it to epidemiological data from a national survey (2007), surveys among people who inject drugs (PWID), and blood donor data. Current treatment coverage data came from expert opinion and published

reports. The model projected the HCV burden, including incidence, prevalence and deaths through 2030, and estimated the impact of varying prevention and direct-acting antiviral (DAA) treatment interventions necessary for achieving the WHO HCV elimination targets.

Results: With no further treatment (currently ~150 000 treated annually) during 2016–30, chronic HCV prevalence will increase from 3.9% to 5.1%, estimated annual incident infections will increase from 700 000 to 1 100 000, and 1 400 000 HCV-associated deaths will occur. To reach the WHO HCV elimination targets by 2030, 880 000 annual DAA treatments are required if prevention is not scaled up and no treatment prioritization occurs. By targeting treatment toward persons with cirrhosis (80% treated annually) and PWIDs (double the treatment rate of non-PWIDs), the required annual treatment number decreases to 750 000. If prevention activities also halve transmission risk, this treatment number reduces to 525 000 annually.

Conclusions: Substantial HCV prevention and treatment interventions are required to reach the WHO HCV elimination targets in Pakistan, without which Pakistan's HCV burden will increase markedly.

8. [Am J Trop Med Hyg. 2018 May;98\(5\):1397-1402. Epub 2018 Mar 8](#)

Impact of Four Years of Annual Mass Drug Administration on Prevalence and Intensity of Schistosomiasis among Primary and High School Children in Western Kenya: A Repeated Cross-Sectional Study

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Schistosomiasis remains a major public health problem in Kenya. The World Health Organization recommends preventive chemotherapy with praziquantel (PZQ) to control morbidity due to schistosomiasis. Morbidity is considered linked to intensity of infection, which along with prevalence is used to determine the frequency of mass drug administration (MDA) to school-age children. We determined the impact of annual school-based MDA on children across all primary and high school years using a repeated cross-sectional study design in five schools near Lake Victoria in western Kenya, an area endemic for *Schistosoma mansoni*. At baseline and for the following four consecutive years, between 897 and 1,440 school children in Grades 1-12 were enrolled and evaluated by Kato-Katz for *S. mansoni* and soil-transmitted helminths (STH), followed by annual MDA with PZQ and albendazole. Four annual rounds of MDA with PZQ were associated with reduced *S. mansoni* prevalence in all school children (44.7-14.0%; $P < 0.001$) and mean intensity of infection by 91% (90.4 to 8.1 eggs per gram [epg] of stool; $P < 0.001$). Prevalence of high-intensity infection (≥ 400 epg) decreased from 6.8% at baseline to 0.3% by the end of the study. Soil-transmitted helminth infections, already low at baseline, also decreased significantly over the years. In this high prevalence area, annual school-based MDA with high coverage across all Grades (1-12) resulted in rapid and progressive declines in overall prevalence and intensity of infection. This decrease was dramatic in regard to heavy infections in older school-attending children.

9. [Lancet 2018 Mar 1. pii: S0140-6736\(17\)33050-7.. \[Epub ahead of print\]](#)

Mapping the burden of cholera in sub-Saharan Africa and implications for control: an analysis of data across geographical scales

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BACKGROUND: Cholera remains a persistent health problem in sub-Saharan Africa and worldwide. Cholera can be controlled through appropriate water and sanitation, or by oral cholera vaccination, which provides transient (~3 years) protection, although vaccine supplies remain scarce. We aimed to map cholera burden in sub-Saharan Africa and assess how geographical targeting could lead to more efficient interventions. **METHODS:** We combined information on cholera incidence in sub-Saharan Africa (excluding Djibouti and Eritrea) from 2010 to 2016 from datasets from WHO, Médecins Sans Frontières, ProMED, ReliefWeb, ministries of health, and the scientific literature. We divided the study region into 20 km × 20 km grid cells and modelled annual cholera incidence in each grid cell assuming a Poisson process adjusted for covariates and spatially correlated random effects. We combined these findings with data on population distribution to estimate the number of people living

in areas of high cholera incidence (>1 case per 1000 people per year). We further estimated the reduction in cholera incidence that could be achieved by targeting cholera prevention and control interventions at areas of high cholera incidence. **FINDINGS:** We included 279 datasets covering 2283 locations in our analyses. In sub-Saharan Africa (excluding Djibouti and Eritrea), a mean of 141 918 cholera cases (95% credible interval [CrI] 141 538-146 505) were reported per year. 4.0% (95% CrI 1.7-16.8) of districts, home to 87.2 million people (95% CrI 60.3 million to 118.9 million), have high cholera incidence. By focusing on the highest incidence districts first, effective targeted interventions could eliminate 50% of the region's cholera by covering 35.3 million people (95% CrI 26.3 million to 62.0 million), which is less than 4% of the total population. **INTERPRETATION:** Although cholera occurs throughout sub-Saharan Africa, its highest incidence is concentrated in a small proportion of the continent. Prioritising high-risk areas could substantially increase the efficiency of cholera control programmes.

Emergency Medicine

10. *Reproductive Health Matters*, 25:51, 18-24 (2017)

The 2018 Inter-agency field manual on reproductive health in humanitarian settings: revising the global standards

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Since the 1990s, the Inter-agency field manual on reproductive health in humanitarian settings (IAFM) has provided authoritative guidance on reproductive health service provision during different phases of complex humanitarian emergencies. In 2018, the Inter-Agency Working Group on Reproductive Health in Crises will release a new edition of this global resource. In this article, we describe the collaborative and inter-sectoral revision process and highlight major changes in the 2018 IAFM. Key revisions to the manual include repositioning unintended pregnancy prevention within and explicitly incorporating safe abortion care into the Minimum Initial Service Package (MISP) chapter, which outlines a set of priority activities to be implemented at the outset of a humanitarian crisis; stronger guidance on the transition from the MISP to comprehensive sexual and reproductive health services; and the addition of a logistics chapter. In addition, the IAFM now places greater and more consistent emphasis on human rights principles and obligations, gender-based violence, and the linkages between maternal and newborn health, and incorporates a diverse range of field examples. We conclude this article with an outline of plans for releasing the 2018 IAFM and facilitating uptake by those working in refugee, crisis, conflict, and emergency settings.

11. *Reproductive Health Matters*, 25:51, 1-6 (2017)

Care with dignity in humanitarian crises: ensuring sexual and reproductive health and rights of displaced populations

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Each year, the number of people affected by humanitarian emergencies continues to increase, and the contexts become more complex, requiring thoughtful, intentional innovation and the creation of an evidence base that informs programme design, implementation and practice. In 2015, the numbers of people forcibly displaced from their homes hit a record high, with a 75% increase in two decades, rising from 37.3 million in 1996 to 65.3 million by the end of 2015. This translates to 24 persons being displaced from their homes every minute of every day in 2015, as a result of persecution, conflict, generalised violence or human rights violations. This trend is expected to continue. In addition, there were 19.2 million new displacements associated with natural disasters in 113 countries. The right to sexual and reproductive health (SRH) is an indispensable part of the right to health and is dependent upon a number of factors that include availability and accessibility to quality evidence-based services. While entire populations benefit from access to SRH services and rights, women and adolescent girls

face a host of particular vulnerabilities. It is estimated that around 26 million women and girls of reproductive age are living in emergency situations around the world and face increased threats to their sexual and reproductive health and rights (SRHR), requiring access to quality services. While services such as food aid, shelter, water and sanitation, security and basic health services are crucial in the early stages of a humanitarian crisis, the provision of reproductive health services has been recognised as an additional priority early in an emergency. Commendable progress has been made to make SRHR services available since the mid-90s, when a landmark report highlighted the lack of comprehensive SRH care among populations in crises. This state of affairs triggered the 1995 formation of the Inter-agency Working Group on Reproductive Health in Crises (IAWG), a network of organisations dedicated to addressing the gaps in the provision of SRH services to communities affected by conflict and disaster. For more than two decades, organisations and individuals affiliated to IAWG have made concerted efforts to advance reproductive health through advocacy, research, standard setting and guidance development. To this end, major strides have been made, although much more remains to be done.

In 2008, Reproductive Health Matters (RHM) dedicated a journal issue to the theme of conflict and crises, a well-timed issue that shed light on the devastating implications of conflict and crises on women and girls, highlighted ongoing response efforts and identified the unmet SRHR needs of populations in these fragile settings. Nearly 10 years later, with record numbers of people facing crises and displacement, it is once again time to draw attention to advances made, share best practices and discuss challenges in service implementation in crises and protracted humanitarian settings. A global evaluation conducted from 2012 to 2014 revealed that while considerable advances have been made, some of the concerns raised and gaps identified in RHM's 2008 issue still ring true today. Building on previous work, the articles published in this journal issue cover a range of complex and sensitive topics such as safe abortion care, gender-based violence, sexual violence against men and sex work among refugees. Studies also address quality improvement and training of health workers with the aim of improving practice and care for better maternal and newborn health outcomes.

Health Financing / Health Policy

12. *Lancet* 2018;391(10129):1493-512

Status and drivers of maternal, newborn, child and adolescent health in the Islamic world: a comparative analysis

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Background. The Millennium Development Goal (MDG) period saw dramatic gains in health goals MDG 4 and MDG 5 for improving child and maternal health. However, many Muslim countries in the south Asian, Middle Eastern, and African regions lagged behind. In this study, we aimed to evaluate the status of, progress in, and key determinants of reproductive, maternal, newborn, child, and adolescent health in Muslim majority countries (MMCs). The specific objectives were to understand the current status and progress in reproductive, maternal, newborn, child, and adolescent health in MMCs, and the determinants of child survival among the least developed countries among the MMCs; to explore differences in outcomes and the key contextual determinants of health between MMCs and non-MMCs; and to understand the health service coverage and contextual determinants that differ between best and poor or moderate performing MMCs.

Methods. In this country-level ecological study, we examined data from between 1990 and 2015 from multiple publicly available data repositories. We examined 47 MMCs, of which 26 were among the 75 high-burden Countdown to 2015 countries. These 26 MMCs were compared with 48 non-Muslim Countdown countries. We also examined characteristics of the eight best performing MMCs that had accelerated improvement in child survival (ie, that reached their MDG 4 targets). We estimated adolescent, maternal, under-5, and newborn mortality, and stillbirths, and the causes of death, essential interventions coverage, and contextual determinants for all MMCs and comparative groups using standardised methods. We also did a hierarchical multivariable analysis of determinants of under-5 mortality and newborn mortality in low-income and middle-income MMCs.

Findings. Despite notable reductions between 1990 and 2015, MMCs compared with a global estimate of all countries including MMCs had higher mortality rates, and MMCs relative to non-MMCs within Countdown countries also performed worse. Coverage of essential interventions across the continuum of care was on average lower among MMCs, especially for indicators of reproductive health, prenatal care, delivery, and labour, and childhood vaccines. Outcomes within MMCs for mortality and many reproductive, maternal, newborn, child, and adolescent health indicators varied considerably. Structural and contextual factors, especially state governance, conflict, and women and girl's empowerment indicators, were significantly worse in MMCs compared with non-MMCs within the high-burden Countdown countries, and were shown to be strongly associated with child and newborn mortality within low-income and middle-income MMCs. In adjusted hierarchical models, among other factors, under-5 mortality in MMCs increased with more refugees originating from a country ($\beta=23.67$, $p=0.0116$), and decreased with better political stability or absence of terrorism ($\beta=-0.99$, $p=0.0285$), greater political rights or government effectiveness ($\beta=-1.17$, $p<0.0001$), improvements in log gross national income per capita ($\beta=-4.44$, $p<0.0001$), higher total adult literacy ($\beta=-1.69$, $p<0.0001$), higher female adult literacy ($\beta=-0.97$, $p<0.0001$), and greater female to male enrolment in secondary school ($\beta=-16.1$, $p<0.0001$). The best performing MMCs were Azerbaijan, Bangladesh, Egypt, Indonesia, Kyrgyzstan, Morocco, Niger, and Senegal, which had higher coverage of family planning interventions and newborn or child vaccinations, and excelled in many of the above contextual determinants when compared with moderate or poorly performing MMCs.

Interpretation. The status and progress in reproductive, maternal, newborn, child, and adolescent health is heterogeneous among MMCs, with little indication that religion and its practice affects outcomes systemically. Some Islamic countries such as Niger and Bangladesh have made great progress, despite poverty. Key findings from this study have policy and programmatic implications that could be prioritised by national heads of state and policy makers, development partners, funders, and the Organization of the Islamic Cooperation to scale up and improve these health outcomes in Muslim countries in the post-2015 era.

13. [Lancet 2018;391\(10129\):1538-48](#)

Countdown to 2030: tracking progress towards universal coverage for reproductive, maternal, newborn, and child health

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Building upon the successes of Countdown to 2015, Countdown to 2030 aims to support the monitoring and measurement of women's, children's, and adolescents' health in the 81 countries that account for 95% of maternal and 90% of all child deaths worldwide. To achieve the Sustainable Development Goals by 2030, the rate of decline in prevalence of maternal and child mortality, stillbirths, and stunting among children younger than 5 years of age needs to accelerate considerably compared with progress since 2000. Such accelerations are only possible with a rapid scale-up of effective interventions to all population groups within countries (particularly in countries with the highest mortality and in those affected by conflict), supported by improvements in underlying socioeconomic conditions, including women's empowerment. Three main conclusions emerge from our analysis of intervention coverage, equity, and drivers of reproductive, maternal, newborn, and child health (RMNCH) in the 81 Countdown countries. First, even though strong progress was made in the coverage of many essential RMNCH interventions during the past decade, many countries are still a long way from universal coverage for most essential interventions. Furthermore, a growing body of evidence suggests that available services in many countries are of poor quality, limiting the potential effect on RMNCH outcomes. Second, within-country inequalities in intervention coverage are reducing in most countries (and are now almost non-existent in a few countries), but the pace is too slow. Third, health-sector (eg, weak country health systems) and non-health-sector drivers (eg, conflict settings) are major impediments to delivering high-quality services to all populations. Although more data for RMNCH interventions are available now, major data gaps still preclude the use of evidence to drive decision making and accountability. Countdown to 2030 is investing in improvements in measurement in several areas, such as quality of care and effective coverage, nutrition programmes, adolescent health, early childhood development, and evidence for conflict settings, and is prioritising its regional networks to enhance local analytic capacity and evidence for RMNCH.

14. TMIH 2018;23(5):570-579

Involving private practitioners in the Indian tuberculosis programme: a randomised trial

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Objectives. To assess a multicomponent intervention to improve private practitioners (PPs) involvement in referral of presumptive pulmonary TB (PTB) cases to the Revised National TB Control Programme (RNTCP) for sputum examination.

Methods. Randomised controlled trial. We randomly allocated all 189 eligible PPs in Tumkur city, South India, to intervention or control arm. The intervention, implemented between December 2014 and January 2016, included two sets of activities, one targeted at health system strengthening (building RNTCP staff capacity to collaborate with PPs, provision of feedback on referrals through SMS) and one targeted at intervention PPs (training in RNTCP, provision of referral pads and education materials and monthly visits to PPs by RNTCP staff). Crude and adjusted referral and PTB case-finding rate ratios were calculated with negative binomial regression.

Results. PPs referred 836 individuals (548 from intervention and 169 from control arm PPs) of whom 176 were diagnosed with bacteriologically confirmed PTB. The proportion (95% confidence interval) of referring PPs [0.59 (0.49, 0.68) vs. 0.42 (0.32, 0.52) in the intervention and control arm, respectively], mean referral rate per PP-year [(5.7 (3.8, 8.7) vs. 1.8 (1.2, 2.8)] and smear-positive PTB case-finding rate per PP-year [(1.5 (0.9, 2.2) vs. 0.6 (0.3, 0.9)] were significantly higher in the intervention than the control arm. Stratifying by qualification, a statistically significant difference in the above indicators remained only among GPs and internists. Overall, surgeons, paediatricians and gynaecologists referred few patients. PP referrals contributed to 20% of the sputum smear positive PTB cases detected by RNTCP in Tumkur city (14% were from intervention arm PPs).

Conclusions. We demonstrated the effectiveness of a health system-oriented intervention to improve PP's referrals of presumptive PTB cases to RNTCP.

15. Health Policy and Planning, 2018, Vol. 33 (Suppl. 1): i1–i3

Global health aid allocation in the 21st century - Editorial

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The ways multilateral agencies allocate support are idiosyncratic, include opaque judgments made with undisclosed criteria, and lead to results that are not widely disclosed. This presents deep challenges for accountability and legitimacy, and raises serious questions about how well the needs of recipient countries are assessed and addressed. The stakes are very high, and the underlying issues are very important. These include how agencies define need, determine eligibility, and decide what support to provide to whom. The governance of these processes is also crucial. However, allocation has attracted very little scrutiny. The present special issue, *Beyond Gross National Income: Innovative methods for global health aid allocation*, represents the efforts of independent academics to bring attention to allocation processes and provide ideas and insights to improve debate around it. // There are many countries for which health assistance allocation is a paramount concern. Many of these countries are in transition. Donors and agencies have used this term to describe the reduction and eventual cessation of assistance as countries become wealthier. Quite reasonably donors want to guide resources to where needed most, but virtually all allocation is still centered on GNI. The articles in this special issue show how profoundly problematic this practice has become from both technical and ethical perspectives. Our work provides the basis for countries to contest and shape these decisions by explicating current allocation practices, clarifying many of the choices surrounding them, and proposing improved alternatives. We hope to improve the legitimacy, responsiveness and efficacy of development assistance by fostering more open discussion and more transparency. However, we note with caution the limits of such a conversation if conducted by technical experts and multilaterals alone. Of all the problems in current allocation, the very low inclusion of recipient countries and citizens is the most glaring. The broader goals of advancing development and promoting more effective collaboration between countries include choices that can be made legitimate only through systematic efforts to enfranchise those who ostensibly benefit. As a step toward that, we offer these

articles to start discussion among a much broader, more inclusive audience. We look forward to the conversation.

16. Health Policy and Planning, 2018, Vol. 33 (2):192-203

How to do (or not to do)... Measuring health worker motivation in surveys in low- and middle-income countries

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A health system's ability to deliver quality health care depends on the availability of motivated health workers, which are insufficient in many low income settings. Increasing policy and researcher attention is directed towards understanding what drives health worker motivation and how different policy interventions affect motivation, as motivation is key to performance and quality of care outcomes. As a result, there is growing interest among researchers in measuring motivation within health worker surveys. However, there is currently limited guidance on how to conceptualize and approach measurement and how to validate or analyse motivation data collected from health worker surveys, resulting in inconsistent and sometimes poor quality measures. This paper begins by discussing how motivation can be conceptualized, then sets out the steps in developing questions to measure motivation within health worker surveys and in ensuring data quality through validity and reliability tests. The paper also discusses analysis of the resulting motivation measure/s. This paper aims to promote high quality research that will generate policy relevant and useful evidence.

17. Health Policy and Planning, 2018, Vol. 33 (2): 283-297

Cost-effectiveness of health systems strengthening interventions in improving maternal and child health in low- and middle-income countries: a systematic review

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Health systems strengthening (HSS) interventions are increasingly being implemented to improve maternal and child health (MCH) services in low- and middle-income countries (LMICs). This study reviews global literature on cost-effectiveness of HSS interventions in improving MCH. A systematic review was conducted. Keywords, based on World Health Organization framework on health systems and prior studies, were applied to search in bibliographic databases and on the web. Articles that estimated cost-effectiveness of HSS interventions in LMICs were included in the analysis. Each of the 24 selected studies from 15 countries was assessed in terms of quality and biases using Cochrane's criteria. Review Manager and an Excel template were used to extract data and synthesize findings. HSS interventions concentrated on the components of service delivery, health financing, human resources and quality improvement. Within each component, there existed diverse strategies to strengthen health systems. Among the 24 studies, 15 were rated as high quality, 5 as medium and 4 as low quality. A majority of studies reported cost per disability-adjusted life year (DALY) averted or cost per quality-adjusted life year (QALY) gained; other studies reported cost per life saved or life year gained. However, studies used mixed perspectives of analyses. Compared with gross domestic product per capita, interventions in studies reporting cost per DALY averted or QALY gained were all cost-effective, including performance-based financing, health insurance and quality improvement. This review shows the diversity of HSS interventions in improving MCH, and their potential cost-effectiveness. However, the different perspectives employed in the studies, costing components included in the analyses, and heterogeneous measures of effectiveness and outputs, made it challenging to compare cost-effectiveness across all studies, calling for more and standardized cost-effectiveness studies. For policy making, it is critical to examine long-term cost-effectiveness of programs and cost-effectiveness of synergistic demand- and supply-side interventions.

18. Health Policy and Planning, 2018, Vol. 33 (3): 328–334

The role of community health workers in improving HIV treatment outcomes in children: lessons learned from the ZENITH trial in Zimbabwe

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Reliance on community health workers (CHWs) for HIV care continues to increase, particularly in resource-limited settings. CHWs can improve HIV service use and adherence to treatment, but effectiveness of these programmes relies on providing an enabling work environment for CHWs, including reasonable workload, supportive supervision and adequate training and supplies. Although criteria for effective CHW programmes have been identified, these have rarely been prospectively applied to design and evaluation of new interventions. For the Zimbabwe study for Enhancing Testing and Improving Treatment of HIV in Children (ZENITH) randomized controlled trial, we based our intervention on an existing evidence-based framework for successful CHW programmes. To assess CHWs' experiences delivering the intervention, we conducted longitudinal, qualitative semi-structured interviews with all 19 CHWs at three times during implementation. The study aimed to explore CHWs' perceptions of how the intervention's structure and management affected their performance, and consider implications for the programme's future scale-up and adoption in other settings. CHWs expressed strong motivation, commitment and job satisfaction. They considered the intervention acceptable and feasible to deliver, and levels of satisfaction rose over interview rounds. Intensive supervision and mentoring emerged as critical to ensuring CHWs' long-term satisfaction. Provision of job aids, standardized manuals and refresher training were also important, as were formalized links between clinics and CHWs. Concerns raised by CHWs included poor remuneration, their reluctance to stop providing support to individual families following the requisite number of home visits, and disappointment at the lack of programme sustainability following completion of the trial. Furthermore, intensive supervision and integration with clinical services may be difficult to replicate outside a trial setting. This study shows that existing criteria for designing successful CHW programmes are useful for maximizing effectiveness, but challenges remain for ensuring long-term sustainability of 'task shifting' strategies.

19. Health Policy and Planning, 2018, Vol. 33 (3): 381-391

Sector-wide or disease-specific? Implications of trends in development assistance for health for the SDG era

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The record of the Millennium Development Goals broadly reflects the trade-offs of disease-specific financing: substantial progress in particular areas, facilitated by time-bound targets that are easy to measure and communicate, which shifted attention and resources away from other areas, masked inequalities and exacerbated fragmentation. In many ways, the Sustainable Development Goals reflect a profound shift towards a more holistic, system-wide approach. To inform responses to this shift, this article builds upon existing work on aggregate trends in donor financing, bringing together what have largely been disparate analyses of sector-wide and disease-specific financing approaches. Looking across the last 26 years, the article examines how international donors have allocated development assistance for health (DAH) between these two approaches and how attempts to bridge them have fared in practice. Since 1990, DAH has overwhelmingly favoured disease-specific earmarks over health sector support, with the latter peaking in 1998. Attempts to integrate system strengthening elements into disease-specific funding mechanisms have varied by disease, and more integrated funding platforms have failed to gain traction. Health sector support largely remains an unfulfilled promise: proportionately low amounts (albeit absolute increases) which have been inconsistently allocated, and the overall approach inconsistently applied in practice. Thus, the expansive orientation of the Sustainable Development Goals runs counter to trends over the last several decades. Financing proposals and efforts to adapt global health institutions must acknowledge and account for the persistent challenges in the financing and implementation of integrated, cross-sector policies. National and subnational experimentation may offer alternatives within and beyond the health sector.

20. *Health Policy and Planning*, 2018, Vol. 33 (3): 436-444

How to do (or not to do) ... a health financing incidence analysis

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Financing incidence analysis (FIA) assesses how the burden of health financing is distributed in relation to household ability to pay (ATP). In a progressive financing system, poorer households contribute a smaller proportion of their ATP to finance health services compared to richer households. A system is regressive when the poor contribute proportionately more. Equitable health financing is often associated with progressivity. To conduct a comprehensive FIA, detailed household survey data containing reliable information on both a cardinal measure of household ATP and variables for extracting contributions to health services via taxes, health insurance and out-of-pocket (OOP) payments are required. Further, data on health financing mix are needed to assess overall FIA. Two major approaches to conducting FIA described in this article include the structural progressivity approach that assesses how the share of ATP (e.g. income) spent on health services varies by quantiles, and the effective progressivity approach that uses indices of progressivity such as the Kakwani index. This article provides some detailed practical steps for analysts to conduct FIA. This includes the data requirements, data sources, how to extract or estimate health payments from survey data and the methods for assessing FIA. It also discusses data deficiencies that are common in many low- and middle-income countries (LMICs). The results of FIA are useful in designing policies to achieve an equitable health system.

21. *Health Policy and Planning*, 2018, Vol. 33 (4): 574-582

Donor funding for family planning: levels and trends between 2003 and 2013

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The International Conference on Population and Development in 1994 set targets for donor funding to support family planning programmes, and recent initiatives such as FP2020 have renewed focus on the need for adequate funding to rights-based family planning. Disbursements supporting family planning disaggregated by donor, recipient country and year are not available for recent years. We estimate international donor funding for family planning in 2003–13, the period covering the introduction of reproductive health targets to the Millennium Development Goals and up to the beginning of FP2020, and compare funding to unmet need for family planning in recipient countries. We used the dataset of donor disbursements to support reproductive, maternal, newborn and child health developed by the Countdown to 2015 based on the Organization for Economic Cooperation and Development Creditor Reporting System. We assessed levels and trends in disbursements supporting family planning in the period 2003–13 and compared this to unmet need for family planning. Between 2003 and 2013, disbursements supporting family planning rose from under \$400 m prior to 2008 to \$886 m in 2013. More than two thirds of disbursements came from the USA. There was substantial year-on-year variation in disbursement value to some recipient countries. Disbursements have become more concentrated among recipient countries with higher national levels of unmet need for family planning. Annual disbursements of donor funding supporting family planning are far short of projected and estimated levels necessary to address unmet need for family planning. The reimposition of the US Global Gag Rule will precipitate an even greater shortfall if other donors and recipient countries do not find substantial alternative sources of funding.

22. *International Journal of Epidemiology*, 2017, Vol.46 (6): 2036-2043

A contemporary picture of the burden of death and disability in Indian adolescents: data from the Global Burden of Disease Study

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Background: Adolescents (10–19 years old) comprise a fifth of the Indian population (253.2 million), yet there is very little published information about the burden of disease and injury for this age group. This paper aims to provide a contemporary picture of the leading causes of death and disability for Indian adolescent girls and boys for 2013, and changes in deaths and disability between 1990 and 2013.

Methods: Data from the Global Burden of Disease (GBD) study for India, for the years 1990 and 2013, were accessed. Data were categorized into two age groups: 10 to 14 years (younger adolescents) and 15 to 19 years (older adolescents) and analysed separately for girls and boys.

Results: The study shows that for both younger and older adolescent boys and for older adolescent girls, non-communicable diseases (NCDs) and injuries are responsible for a greater number of deaths and disability-adjusted life-years (DALYs) than communicable diseases. Communicable diseases are still important causes of death and disability for young adolescents. Among older adolescents there is an increasing burden of death and disability due to self-harm, road traffic injuries, fire- and heat-related injuries and mental disorders such as depressive disorders.

Conclusions: Although strategies to reduce the burden of communicable diseases among adolescents must continue to be an important focus, innovative, evidence-based strategies aimed at reducing the growing burden of NCDs and injuries must be elevated as a priority.

23. *International Journal of Epidemiology*, Vol.46 (6): 2056–2066

Impact of adding hand-washing and water disinfection promotion to oral cholera vaccination on diarrhoea-associated hospitalization in Dhaka, Bangladesh: evidence from a cluster randomized control trial

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Background: Information on the impact of hygiene interventions on severe outcomes is limited. As a pre-specified secondary outcome of a cluster-randomized controlled trial among >400 000 low-income residents in Dhaka, Bangladesh, we examined the impact of cholera vaccination plus a behaviour change intervention on diarrhoea-associated hospitalization.

Methods: Ninety neighbourhood clusters were randomly allocated into three areas: cholera-vaccine-only; vaccine-plus-behaviour-change (promotion of hand-washing with soap plus drinking water chlorination); and control. Study follow-up continued for 2 years after intervention began. We calculated cluster-adjusted diarrhoea-associated hospitalization rates using data we collected from nearby hospitals, and 6-monthly census data of all trial households.

Results: A total of 429 995 people contributed 500 700 person-years of data (average follow-up 1.13 years). Vaccine coverage was 58% at the start of analysis but continued to drop due to population migration. In the vaccine-plus-behaviour-change area, water plus soap was present at 45% of hand-washing stations; 4% of households had detectable chlorine in stored drinking water. Hospitalization rates were similar across the study areas [events/1000 person-years, 95% confidence interval (CI), cholera-vaccine-only: 9.4 (95% CI: 8.3–10.6); vaccine-plus-behaviour-change: 9.6 (95% CI: 8.3–11.1); control: 9.7 (95% CI: 8.3–11.6)]. Cholera cases accounted for 7% of total number of diarrhoea-associated hospitalizations.

Conclusions: Neither cholera vaccination alone nor cholera vaccination combined with behaviour-change intervention efforts measurably reduced diarrhoea-associated hospitalization in this highly mobile population, during a time when cholera accounted for a small fraction of diarrhoea episodes. Affordable community-level interventions that prevent infection from multiple pathogens by reliably separating faeces from the environment, food and water, with minimal behavioural demands on impoverished communities, remain an important area for research.

24. *News, BMJ* 2018;360:k560

India's antibiotic combinations thwart efforts to curb drug resistance, say researchers

Frederik Joelsing

Rising sales of antibiotic combinations in India could be undermining global efforts to limit antimicrobial resistance, says a study that found dozens of unapproved and sometimes risky formulations on the market.

India is the world's top consumer of antibiotics and a hotbed for drug evading bacteria, which are exported globally by travellers. The problem is compounded by widespread use of drug combinations that mix antimicrobials and other medicines—known as fixed dose combinations (FDCs)—because one or more of the ingredients is usually unnecessary. This fuels overuse and thus resistance, needlessly exposing patients to side effects.

“We can't blame all antimicrobial resistance on India, but they are creating a problem for themselves and everybody else with these fixed dose combinations,” said Kathleen Holloway, a retired World Health Organization staffer based at the University of Sussex, UK, who has studied drug resistance in Asia but was not involved in the new study. “There is absolutely no excuse for having all these things on the market.”

25. Feature Economic development, BMJ 2018;360:k595

Rise of a new superpower: health and China's global trade ambitions

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Massive foreign infrastructure projects are designed to increase China's economic and political influence—for example, opening up new markets to Chinese drugs and tobacco. The “belt and road initiative,” writes Flynn Murphy, the country's enigmatic policy backed by huge investment, could have profound implications for local and global health

A public hospital in copper-rich Zambia quadruples its capacity to 800 beds. A Chinese cigarette manufacturing plant near Bucharest prepares to start exporting to the Balkans. A Kazakh medical student on a scholarship to Beijing begins specialty training in neurosurgery. A Jiangsu man flies to Beijing for treatment for the yellow fever he contracted while working in Angola. These disparate events are connected by a Chinese foreign policy with profound implications for global health. China's leaders have pledged hundreds of billions of dollars—some say more than a trillion¹—in planned projects as part of the country's “belt and road initiative” (BRI). It's ostensibly a push to revive and strengthen ancient trade routes between China, Africa, and Europe—“to bring everyone, literally and physically, into China's economic orbit,” says Peter Cai, a non-resident fellow at Australia's Lowy Institute think tank and an expert on the policy. Cai says that China wants to grow its global economic and political influence using its most potent weapon: infrastructure building expertise.

Currently that means furnishing Africa, Asia, and Europe with roads, bridges, ports, high speed railways, airports, power plants, and oil and gas pipelines. Broadly, these will wind overland along a “silk road economic belt” that stretches as far as Scandinavia and Portugal, and a sea route through Asia and around the east coast of Africa along a “21st century maritime silk road.” China says at completion the initiative will connect 65% of the world's people and 35% of its finances.

26. Research, BMJ 2018;360:k817

Relaxation of the one child policy and trends in caesarean section rates and birth outcomes in China between 2012 and 2016: observational study of nearly seven million health facility births

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Introduction

China has made remarkable progress in achieving the Millennium Development Goals, but its success has come at a cost. While nearly all women now deliver in hospital, many do so by caesarean section, and many caesarean sections are thought not to be medically indicated. In 2008, 29% of births in China were by caesarean section, increasing to 35% by 2014. National averages hide huge variation however: in 2014 the caesarean section rate was as high as 62% in the north eastern province of Jilin, while it was only 4% in Tibet.

Abstract

Objective. To examine how the relaxation of the one child policy and policies to reduce caesarean section rates might have affected trends over time in caesarean section rates and perinatal and pregnancy related mortality in China.

Design. Observational study.

Setting China's National Maternal Near Miss Surveillance System (NMNMSS).

Participants 6 838 582 births at 28 completed weeks or more of gestation or birth weight ≥ 1000 g in 438 hospitals in the NMNMSS between 2012 and 2016.

Main outcome measures Obstetric risk was defined using a modified Robson classification. The main outcome measures were changes in parity and age distributions and relative frequency of each Robson group, crude and adjusted trends over time in caesarean section rates within each risk category (using Poisson regression with a robust variance estimator), and trends in perinatal and pregnancy related mortality over time.

Results. Caesarean section rates declined steadily between 2012 and 2016 (crude relative risk 0.91, 95% confidence interval 0.89 to 0.93), reaching an overall hospital based rate of 41.1% in 2016. The relaxation of the one child policy was associated with an increase in the proportion of multiparous births (from 34.1% in 2012 to 46.7% in 2016), and births in women with a uterine scar nearly doubled (from 9.8% to 17.7% of all births). Taking account of these changes, the decline in caesarean sections was amplified over time (adjusted relative risk 0.82, 95% confidence interval 0.81 to 0.84). Caesarean sections declined noticeably in nulliparous women (0.75, 0.73 to 0.77) but also declined in multiparous women without a uterine scar (0.65, 0.62 to 0.77). The decrease in caesarean section rates was most pronounced in hospitals with the highest rates in 2012, consistent with the government's policy of targeting hospitals with the highest rates. Perinatal mortality declined from 10.1 to 7.2 per 1000 births over the same period (0.87, 0.83 to 0.91), and there was no change in pregnancy related mortality over time.

Conclusions. China is the only country that has succeeded in reverting the rising trends in caesarean sections. China's success is remarkable given that the changes in obstetric risk associated with the relaxation of the one child policy would have led to an increase in the need for caesarean sections. China's experience suggests that change is possible when strategies are comprehensive and deal with the system level factors that underpin overuse as well as the various incentives at work during a clinical encounter.

27. Research, BMJ 2018;361:k1162

The health, poverty, and financial consequences of a cigarette price increase among 500 million male smokers in 13 middle income countries: compartmental model study

Global Tobacco Economics Consortium

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Introduction. On current smoking patterns where large numbers of young adults start smoking but few quit, smoking will be responsible for about one billion deaths in the 21st century. Most of these will be in low and middle income countries. At the global level, tobacco control relies on the Framework Convention on Tobacco Control and increasingly on the United Nations 2030 sustainable development goals. The latter include goals to eradicate extreme income poverty, reduce the age standardised death rates from non-communicable diseases by one third, and achieve universal health coverage so as to provide financial risk protection against the impoverishment that arises from illness. These three goals are interrelated.

Abstract.

Objective. To examine the impact of a 50% increase in market prices of cigarettes on health, poverty, and financial protection.

Design. Compartmental model study.

Setting. 13 middle income countries, totalling two billion men.

Participants. 500 million male smokers.

Main outcome measures. Life years gained, averted treatment costs, number of men avoiding catastrophic healthcare expenditures and poverty, and additional tax revenue by income group.

Results. A 50% increase in cigarette prices would lead to about 450 million years of life gained across the 13 countries from smoking cessation, with half of these in China. Across all countries, men in the bottom income group (poorest 20% of the population) would gain 6.7 times more life years than men in the top income group (richest 20% of the population; 155 v 23 million). The average life years gained from cessation for each smoker in the bottom income group was 5.1 times that of the top group (1.46 v 0.23 years). Of the \$157bn (£113bn; €127bn) in averted treatment costs, the bottom income group would avert 4.6 times more costs than the top income group (\$46bn v \$10bn). About 15.5 million men would avoid catastrophic health expenditures in a subset of seven countries without universal health coverage. As result, 8.8 million men, half of them in the bottom income group, would avoid falling below the World Bank definition of extreme poverty. These 8.8 million men constitute 2.4% of people living in extreme poverty in these countries. In contrast, the top income group would pay twice as much as the bottom income group of the \$122bn additional tax collected. Overall, the bottom income group would get 31% of the life years saved and 29% each of the averted disease costs and averted catastrophic health expenditures, while paying only 10% of the additional taxes.

Conclusions. Higher prices of cigarettes provide more health and financial gains to the poorest 20% than to the richest 20% of the population. Higher excise taxes support the targets of the sustainable development goals on non-communicable diseases and poverty, and provides financial protection against illness.

HIV / AIDS

28. *Lancet* 2018;391(10123):839–849

Efficacy, safety, and tolerability of dolutegravir-rilpivirine for the maintenance of virological suppression in adults with HIV-1: phase 3, randomised, non-inferiority SWORD-1 and SWORD-2 studies

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Background. Lifelong HIV antiretroviral therapy (ART) has prompted an interest in two-drug regimens to minimise cumulative drug exposure and toxicities. The safety, tolerability, and efficacy of dolutegravir and rilpivirine suggest potential compatibility and effectiveness as a two-drug regimen. We aimed to investigate this two-drug regimen in a phase 3 study.

Methods. We identically designed SWORD-1 and SWORD-2, which were open-label, parallel-group, multicentre, phase 3, randomised, non-inferiority studies in 12 countries evaluating efficacy and safety of once-daily dolutegravir 50 mg plus rilpivirine 25 mg versus current ART regimen (CAR). We included participants aged 18 years or older who were on first or second ART with stable plasma HIV-1 RNA (viral load <50 copies per mL) for 6 months or longer at screening. We randomly assigned participants (1:1) with stratification by third-agent class, age, and planned participation in a bone mineral density substudy. The primary endpoint was proportion of participants with viral load lower than 50 copies per mL at week 48 among those individuals who received one or more doses of study medication. Investigators monitored adverse events to assess safety. These trials are registered with ClinicalTrials.gov, numbers NCT02429791 (SWORD-1) and NCT02422797 (SWORD-2).

Findings. We screened for participants from April 14, 2015, to Oct 15, 2015, for SWORD-1 and from April 21, 2015, to Sept 25, 2015, for SWORD-2. We randomly assigned 516 participants to dolutegravir-rilpivirine and 512 to continue with CAR. At week 48 (last patient visit was Nov 22, 2016), in the pooled analysis of the intention-to-treat population, 95% of participants had viral loads lower than 50 copies per mL in each group (486 of 513 in the dolutegravir-rilpivirine group vs 485 of 511 in the CAR group), with an adjusted treatment difference of -0.2% (95% CI -3.0 to 2.5) and showed non-inferiority with a predefined margin of -8%. 395 (77%) of 513 participants in the dolutegravir-rilpivirine group and 364 (71%) of 511 participants in the CAR group reported adverse events. The most common adverse events were nasopharyngitis (49 [10%] for dolutegravir-rilpivirine

vs 50 [10%] for CAR) and headache (41 [8%] vs 23 [5%]). More participants taking dolutegravir-rilpivirine (17 [3%]) reported adverse events leading to withdrawal than did participants taking CAR (three [$<1\%$]).

Interpretation. Dolutegravir-rilpivirine was non-inferior to CAR over 48 weeks in participants with HIV suppression and showed a safety profile consistent with its components. Results support the use of this two-drug regimen to maintain HIV suppression.

29. TMIH 2018;23(2):206-220

Failure to initiate HIV treatment in patients with high CD4 counts: evidence from demographic surveillance in rural South Africa

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Objectives. To assess the relationship between CD4 count at presentation and ART uptake and assess predictors of timely treatment initiation in rural KwaZulu-Natal, South Africa.

Methods. We used Kaplan-Meier and Cox proportional hazards models to assess the association between first CD4 count and time from first CD4 to ART initiation among all adults presenting to the Hlabisa HIV Treatment and Care Programme between August 2011 and December 2012 with treatment-eligible CD4 counts (≤ 350 cells/mm³). For a subset of healthier patients ($200 < CD4 \leq 350$ cells) residing within the population surveillance of the Africa Health Research Institute, we assessed sociodemographic, economic and geographic predictors hypothesised to influence ART uptake.

Results. A total of 4739 patients presented for care with eligible CD4 counts. The proportion initiating ART within six months of diagnosis was 67% (95% CI 63, 71) in patients with $CD4 \leq 50$, 59% (0.55, 0.63) in patients with $CD4 151-200$ and 48% (95% CI 44, 51) in patients with $CD4 301-350$. The hazard of starting ART fell by 17% (95% CI 14, 20) for every 100-cell increase in baseline CD4 count. Among healthier patients under demographic surveillance ($n = 193$), observable sociodemographic, economic and geographic predictors did not add discriminatory power beyond CD4 count, age and sex to identify patients at high risk of non-initiation.

Conclusions. Individuals presenting for HIV care at higher CD4 counts were less likely to initiate ART than patients presenting at low CD4 counts. Overall, ART uptake was low. Under new guidelines that establish ART eligibility regardless of CD4 count, patients with high CD4 counts may require additional interventions to encourage treatment initiation.

30. TMIH 2018;23(3):279-294

Translating international HIV treatment guidelines into local priorities in Indonesia

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Objective. International guidelines recommend countries to expand antiretroviral therapy (ART) to all HIV-infected individuals and establish local-level priorities in relation to other treatment, prevention and mitigation interventions through fair processes. However, no practical guidance is provided for such priority-setting processes. Evidence-informed deliberative processes (EDPs) fill this gap and combine stakeholder deliberation to incorporate relevant social values with rational decision-making informed by evidence on these values. This study reports on the first-time implementation and evaluation of an EDP in HIV control, organised to support the AIDS Commission in West Java province, Indonesia, in the development of its strategic plan for 2014–2018.

Methods. Under the responsibility of the provincial AIDS Commission, an EDP was implemented to select priority interventions using six steps: (i) situational analysis; (ii) formation of a multi stakeholder Consultation Panel; (iii) selection of criteria; (iv) identification and assessment of interventions' performance; (v) deliberation; and (vi) selection of funding and implementing institutions. An independent researcher conducted in-depth interviews ($n = 21$) with panel members to evaluate the process.

Results. The Consultation Panel included 23 stakeholders. They identified 50 interventions and these were evaluated against four criteria: impact on the epidemic, stigma reduction, cost-effectiveness and

universal coverage. After a deliberative discussion, the Consultation Panel prioritised a combination of several treatment, prevention and mitigation interventions.

Conclusion. The EDP improved both stakeholder involvement and the evidence base for the strategic planning process. EDPs fill an important gap which international guidelines and current tools for strategic planning in HIV control leave unaddressed.

31. *TMIH 2018;23(3):315-326*

Treatment interruption in HIV-positive patients followed up in Cameroon's antiretroviral treatment programme: individual and health care supply-related factors (ANRS-12288 EVOLCam survey)

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Introduction. Decreasing international financial resources for HIV and increasing numbers of antiretroviral treatment (ART)-treated patients may jeopardise treatment continuity in low-income settings. Using data from the EVOLCam ANRS-12288 survey, this study aimed to document the prevalence of unplanned treatment interruption for more than 2 consecutive days (TI>2d) and investigate the associated individual and health care supply-related factors within the Cameroonian ART programme.

Methods. A cross-sectional mixed methods survey was carried out between April and December 2014 in 19 HIV services of the Centre and Littoral regions. A multilevel logistic model was estimated on 1885 ART-treated patients in these services to investigate factors of TI>2d in the past 4 weeks.

Results. Among the study population, 403 (21%) patients reported TI>2d. Patients followed up in hospitals reporting ART stock-outs were more likely to report TI>2d while those followed up in the Littoral region, in medium- or small-sized hospitals and in HIV services proposing financial support were at lower risk of TI>2d. The following individual factors were also associated with a lower risk of TI>2d: living in a couple, having children, satisfaction with attention provided by doctor, tuberculosis co-infection and not having consulted a traditional healer.

Conclusions. Besides identifying individual factors of TI>2d, our study highlighted the role of health care supply-related factors in shaping TI in Cameroon's ART programme, especially the deleterious effect of ART stock-outs. Our results also suggest that the high proportion of patients reporting TI could jeopardise progress in the fight against HIV in the country, unless effective measures are quickly implemented like ensuring the continuity of ART supply.

32. *International Journal of Epidemiology, 2018, Vol.47 (2): 537–549*

Identifying 'corridors of HIV transmission' in a severely affected rural South African population: a case for a shift toward targeted prevention strategies

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Background: In the context of a severe generalized African HIV epidemic, the value of geographically targeted prevention interventions has only recently been given serious consideration. However, to date no study has performed a population-based analysis of the micro-geographical clustering of HIV incident infections, limiting the evidential support for such a strategy.

Methods: We followed 17 984 HIV-uninfected individuals aged 15–54 in a population-based cohort in rural KwaZulu-Natal, South Africa, and observed individual HIV sero-conversions between 2004 and 2014. We geo-located all individuals to an exact homestead of residence (accuracy <2 m). We then employed a two-dimensional Gaussian kernel of radius 3 km to produce robust estimates of HIV incidence which vary across continuous geographical space. We also applied Tango's flexibly shaped spatial scan statistic to identify irregularly shaped clusters of high HIV incidence.

Results: Between 2004 and 2014, we observed a total of 2 311 HIV sero-conversions over 70 534 person-years of observation, at an overall incidence of 3.3 [95% confidence interval (CI), 3.1-3.4] per 100 person-years. Three large irregularly-shaped clusters of new HIV infections (relative risk = 1.6, 1.7 and 2.3) were identified in two adjacent peri-urban communities near the National Road (P = 0.001, 0.015) as well as in a rural node bordering a recent coal mine development (P = 0.020),

respectively. Together the clusters had a significantly higher age-sex standardized incidence of 5.1 (95% CI, 4.7-5.6) per 100 person-years compared with a standardized incidence of 3.0 per 100 person-years (95% CI, 2.9-3.2) in the remainder of the study area. Though these clusters comprise just 6.8% of the study area, they account for one out of every four sero-conversions observed over the study period.

Conclusions: Our study has revealed clear ‘corridors of transmission’ in this typical rural, hyper-endemic population. Even in a severely affected rural African population, an approach that seeks to provide preventive interventions to the most vulnerable geographies could be more effective and cost-effective in reducing the overall rate of new HIV infections. There is an urgent need to develop and test such interventions as part of an overall combination prevention approach.

33. *N Engl J Med* 2018; 378:1029-1041

HIV-Associated Cancers and Related Diseases: Review article (abridged)

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Clusters of cases of pneumocystis pneumonia and Kaposi’s sarcoma in New York and California in men who had sex with men were early harbingers of the acquired immunodeficiency syndrome (AIDS) epidemic. The syndrome was also soon noted to be associated with a high incidence of aggressive B-cell lymphomas. As the AIDS definition crystallized, Kaposi’s sarcoma, aggressive B-cell lymphomas, and invasive cervical cancer were considered to be AIDS-defining cancers when they developed in patients with human immunodeficiency virus (HIV) infection. Additional cancers are now known to be associated with HIV. The term HIV-associated cancer is used here to describe this larger group of cancers (both AIDS-defining and non-AIDS-defining cancers) that have an increased incidence among patients with HIV infection. In addition, incidental cancers also may develop in patients with HIV infection. // Although the development of ART has done much to improve overall survival and reduce the incidence of AIDS-defining cancers, other cancers have come to the forefront and have become common causes of complications and death among persons with HIV infection. As the HIV-infected population ages, a wide variety of HIV-associated cancers have become increasingly important. These cancers pose both challenges and opportunities. The National Cancer Institute sponsors a range of clinical studies in the United States and globally to prevent and treat HIV-associated cancers through the AIDS Malignancy Consortium, the Intramural Program, the Cancer Immunotherapy Trials Network, and the Bone and Marrow Transplant Clinical Trials Network. Results from previous studies support evidence-based guidelines for the treatment of several HIV-associated cancers. However, many questions remain. Addressing these questions will open new approaches for the prevention, diagnosis, and treatment of cancer among the more than 35 million people globally who are infected with HIV.

34. *PLoS Med* 15(3): e1002514

The epidemiology of adolescents living with perinatally acquired HIV: A cross-region global cohort analysis

The Collaborative Initiative for Paediatric HIV Education and Research (CIPHER) Global Cohort Collaboration, Amy L. Slogrove, et al.

Background: Globally, the population of adolescents living with perinatally acquired HIV (APHs) continues to expand. In this study, we pooled data from observational pediatric HIV cohorts and cohort networks, allowing comparisons of adolescents with perinatally acquired HIV in “real-life” settings across multiple regions. We describe the geographic and temporal characteristics and mortality outcomes of APHs across multiple regions, including South America and the Caribbean, North America, Europe, sub-Saharan Africa, and South and Southeast Asia.

Methods and findings: Through the Collaborative Initiative for Paediatric HIV Education and Research (CIPHER), individual retrospective longitudinal data from 12 cohort networks were pooled. All children infected with HIV who entered care before age 10 years, were not known to have horizontally acquired HIV, and were followed up beyond age 10 years were included in this analysis conducted from May 2016 to January 2017. Our primary analysis describes patient and treatment

characteristics of APHs at key time points, including first HIV-associated clinic visit, antiretroviral therapy (ART) start, age 10 years, and last visit, and compares these characteristics by geographic region, country income group (CIG), and birth period. Our secondary analysis describes mortality, transfer out, and lost to follow-up (LTFU) as outcomes at age 15 years, using competing risk analysis. Among the 38,187 APHs included, 51% were female, 79% were from sub-Saharan Africa and 65% lived in low-income countries. APHs from 51 countries were included (Europe: 14 countries and 3,054 APHs; North America: 1 country and 1,032 APHs; South America and the Caribbean: 4 countries and 903 APHs; South and Southeast Asia: 7 countries and 2,902 APHs; sub-Saharan Africa, 25 countries and 30,296 APHs). Observation started as early as 1982 in Europe and 1996 in sub-Saharan Africa, and continued until at least 2014 in all regions. The median (interquartile range [IQR]) duration of adolescent follow-up was 3.1 (1.5–5.2) years for the total cohort and 6.4 (3.6–8.0) years in Europe, 3.7 (2.0–5.4) years in North America, 2.5 (1.2–4.4) years in South and Southeast Asia, 5.0 (2.7–7.5) years in South America and the Caribbean, and 2.1 (0.9–3.8) years in sub-Saharan Africa. Median (IQR) age at first visit differed substantially by region, ranging from 0.7 (0.3–2.1) years in North America to 7.1 (5.3–8.6) years in sub-Saharan Africa. The median age at ART start varied from 0.9 (0.4–2.6) years in North America to 7.9 (6.0–9.3) years in sub-Saharan Africa. The cumulative incidence estimates (95% confidence interval [CI]) at age 15 years for mortality, transfers out, and LTFU for all APHs were 2.6% (2.4%–2.8%), 15.6% (15.1%–16.0%), and 11.3% (10.9%–11.8%), respectively. Mortality was lowest in Europe (0.8% [0.5%–1.1%]) and highest in South America and the Caribbean (4.4% [3.1%–6.1%]). However, LTFU was lowest in South America and the Caribbean (4.8% [3.4%–6.7%]) and highest in sub-Saharan Africa (13.2% [12.6%–13.7%]). Study limitations include the high LTFU rate in sub-Saharan Africa, which could have affected the comparison of mortality across regions; inclusion of data only for APHs receiving ART from some countries; and unavailability of data from high-burden countries such as Nigeria.

Conclusion: To our knowledge, our study represents the largest multiregional epidemiological analysis of APHs. Despite probable under-ascertained mortality, mortality in APHs remains substantially higher in sub-Saharan Africa, South and Southeast Asia, and South America and the Caribbean than in Europe. Collaborations such as CIPHER enable us to monitor current global temporal trends in outcomes over time to inform appropriate policy responses.

Malaria

35. *Am J Trop Med Hyg.* 2018 May;98(5):1382-1388. Epub 2018 Mar 15

Efficiency of a Malaria Reactive Test-and-Treat Program in Southern Zambia: A Prospective, Observational Study

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To improve malaria surveillance and achieve elimination, the Zambian National Malaria Elimination Program implemented a reactive test-and-treat program in Southern Province in 2013 in which individuals with rapid diagnostic test (RDT)-confirmed malaria are followed-up at their home within 1 week of diagnosis. Individuals present at the index case household and those residing within 140 m of the index case are tested with an RDT and treated with artemether-lumefantrine if positive. This study evaluated the efficiency of this reactive test-and-treat strategy by characterizing infected individuals missed by the RDT and the current screening radius. The radius was expanded to 250 m, and a quantitative polymerase chain reaction (qPCR) test was performed on dried blood spot specimens. From January 2015 through March 2016, 145 index cases were identified at health centers and health posts. A total of 3,333 individuals residing in 525 households were screened. Excluding index cases, the parasite prevalence was 1.1% by RDT (33 positives of 3,016 participants) and 2.4% by qPCR (73 positives of 3,016 participants). Of the qPCR-positive cases, 62% of 73 individuals tested negative by RDT. Approximately half of the infected individuals resided within the index case household (58% of RDT-positive individuals and 48% of qPCR-positive individuals). The low sensitivity of the RDT and

the high proportion of secondary cases within the index case household decreased the efficiency of this reactive test-and-treat strategy. Reactive focal drug administration in index case households would be a more efficient approach to treating infected individuals associated with a symptomatic case.

36. Am J Trop Med Hyg. 2018 May;98(5):1343-1352. Epub 2018 Mar 15

The Impact of Periodic Distribution Campaigns of Long-Lasting Insecticidal-Treated Bed Nets on Malaria Vector Dynamics and Human Exposure in Dielmo, Senegal.

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The implementation of long-lasting insecticidal-treated bed nets (LLINs) has contributed to halving the mortality rate due to malaria since 2000 in sub-Saharan Africa. These tools are highly effective against indoor-feeding malaria vectors. Thus, to achieve the World Health Assembly's new target to reduce the burden of malaria over the next 15 years by 90%, it is necessary to understand how the spatiotemporal dynamics of malaria vectors and human exposure to bites is modified in the context of scaling up global efforts to control malaria transmission. This study was conducted in Dielmo, a Senegalese village, after the introduction of LLINs and two rounds of LLINs renewals. Data analysis showed that implementation of LLINs correlated with a significant decrease in the biting densities of the main malaria vectors, *Anopheles gambiae* s.l. and *Anopheles funestus*, reducing malaria transmission. Other environment factors likely contributed to the decrease in *An. funestus*, but this trend was enhanced with the introduction of LLINs. The bulk of bites occurred during sleeping hours, but the residual vector populations of *An. gambiae* s.l. and *An. funestus* had an increased propensity to bite outdoors, so a risk of infectious bites remained for LLINs users. These results highlight the need to increase the level and correct use of LLINs and to combine this intervention with complementary control measures against residual exposure, such as spatial repellents and larval source management, to achieve the goal of eliminating malaria transmission.

37. Emerg Infect Dis. 2018 Mar;24(3):462-470

Major Threat to Malaria Control Programs by *Plasmodium falciparum* Lacking Histidine-Rich Protein 2, Eritrea

Berhane A. et al

False-negative results for *Plasmodium falciparum* histidine-rich protein (HRP) 2-based rapid diagnostic tests (RDTs) are increasing in Eritrea. We investigated HRP gene 2/3 (pfhrp2/pfhrp3) status in 50 infected patients at 2 hospitals. We showed that 80.8% (21/26) of patients at Ghindae Hospital and 41.7% (10/24) at Massawa Hospital were infected with pfhrp2-negative parasites and 92.3% (24/26) of patients at Ghindae Hospital and 70.8% (17/24) at Massawa Hospital were infected with pfhrp3-negative parasites. Parasite densities between pfhrp2-positive and pfhrp2-negative patients were comparable. All pfhrp2-negative samples had no detectable HRP2/3 antigen and showed negative results for HRP2-based RDTs. pfhrp2-negative parasites were genetically less diverse and formed 2 clusters with no close relationships to parasites from Peru. These parasites probably emerged independently by selection in Eritrea. High prevalence of pfhrp2-negative parasites caused a high rate of false-negative results for RDTs. Determining prevalence of pfhrp2-negative parasites is urgently needed in neighboring countries to assist case management policies.

38. Lancet. 2018 Apr 24. pii: S0140-6736(18)30792-X. [Epub ahead of print]

Effect of generalised access to early diagnosis and treatment and targeted mass drug administration on *Plasmodium falciparum* malaria in Eastern Myanmar: an observational study of a regional elimination programme

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BACKGROUND: Potentially untreatable *Plasmodium falciparum* malaria threatens the Greater Mekong subregion. A previous series of pilot projects in Myanmar, Laos, Cambodia, and Vietnam suggested that mass drug administration was safe, and when added to provision of early diagnosis and

treatment, could reduce the reservoir of *P falciparum* and interrupts transmission. We examined the effects of a scaled-up programme of this strategy in four townships of eastern Myanmar on the incidence of *P falciparum* malaria.

METHODS: The programme was implemented in the four townships of Myawaddy, Kawkareik, Hlaingbwe, and Hpapun in Kayin state, Myanmar. Increased access to early diagnosis and treatment of malaria was provided to all villages through community-based malaria posts equipped with rapid diagnostic tests, and treatment with artemether-lumefantrine plus single low-dose primaquine. Villages were identified as malarial hotspots (operationally defined as >40% malaria, of which 20% was *P falciparum*) with surveys using ultrasensitive quantitative PCR either randomly or targeted at villages where the incidence of clinical cases of *P falciparum* malaria remained high (ie, >100 cases per 1000 individuals per year) despite a functioning malaria post. During each survey, a 2 mL sample of venous blood was obtained from randomly selected adults. Hotspots received targeted mass drug administration with dihydroartemisinin-piperaquine plus single-dose primaquine once per month for 3 consecutive months in addition to the malaria posts. The main outcome was the change in village incidence of clinical *P falciparum* malaria, quantified using a multivariate, generalised, additive multilevel model. Malaria prevalence was measured in the hotspots 12 months after mass drug administration.

FINDINGS: Between May 1, 2014, and April 30, 2017, 1222 malarial posts were opened, providing early diagnosis and treatment to an estimated 365 000 individuals. Incidence of *P falciparum* malaria decreased by 60 to 98% in the four townships. 272 prevalence surveys were undertaken and 69 hotspot villages were identified. By April 2017, 50 hotspots were treated with mass drug administration. Hotspot villages had a three times higher incidence of *P falciparum* at malarial posts than neighbouring villages (adjusted incidence rate ratio [IRR] 2.7, 95% CI 1.8-4.4). Early diagnosis and treatment was associated with a significant decrease in *P falciparum* incidence in hotspots (IRR 0.82, 95% CI 0.76-0.88 per quarter) and in other villages (0.75, 0.73-0.78 per quarter). Mass drug administration was associated with a five-times decrease in *P falciparum* incidence within hotspot villages (IRR 0.19, 95% CI 0.13-0.26). By April, 2017, 965 villages (79%) of 1222 corresponding to 104 village tracts were free from *P falciparum* malaria for at least 6 months. The prevalence of wild-type genotype for K13 molecular markers of artemisinin resistance was stable over the three years (39%; 249/631).

INTERPRETATION: Providing early diagnosis and effective treatment substantially decreased village-level incidence of artemisinin-resistant *P falciparum* malaria in hard-to-reach, politically sensitive regions of eastern Myanmar. Targeted mass drug administration significantly reduced malaria incidence in hotspots. If these activities could proceed in all contiguous endemic areas in addition to standard control programmes already implemented, there is a possibility of subnational elimination of *P falciparum*.

Non-Communicable Diseases

39. *Am J Trop Med Hyg.* 2018 May;98(5):1419-1426. Epub 2018 Mar 29

Albendazole Treatment Improves Work Capacity in Women Smallholder Farmers Infected with Hookworm: A Double-Blind Randomized Control Trial

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An estimated 4.7 billion people live in regions exposed to soil-transmitted helminths, intestinal parasites that have significant impacts on the health of women smallholder farmers. The goal of this trial was to determine whether treatment with albendazole impacts the work capacity of these farmers. This is a prospective double-blind, randomized effectiveness trial. Participants (N = 250) were randomly selected from safe motherhood groups in the Democratic Republic of Congo. Prevalence/intensity of hookworm infection, hemoglobin, and demographics was obtained. At study (Time = 0), participants were randomized into treatment (albendazole 400 mg) and placebo (similar placebo tablet) groups. A step test was administered as a proxy metric for work capacity. Work

capacity was defined as Δ heart rate before and after 3 minutes of step testing, in beats per minute. At study (time = 7 months), the step test was repeated and work capacity remeasured. The Δ work capacity (time = 0 minus time = 7 months) was the primary outcome. Investigators/field assistants were blinded to who was enrolled in groups, hookworm status, and step test results. Regression showed highly significant interactive effects of hookworm status and treatment group relative to Δ work capacity after controlling for resting pulse rate and age ($P < 0.002$). Estimated marginal means for work capacity (WC) for each of four groups (hookworm positive plus placebo, hookworm positive plus treatment, hookworm negative plus placebo, and hookworm negative plus treatment) showed women who were hookworm positive and received treatment decreased heart rate by 9.744 (95% confidence interval [CI]: 6.42, 13.07) beats per minute (increased WC), whereas women who were hookworm positive and received placebo saw a nonsignificant decrease of 0.034 (95% CI: -3.16, 3.84) beats per minute. Treatment with albendazole was associated with improved aerobic work capacity posttreatment. Given modest costs of drug distributions, risk benefits of periodic deworming warrants further study in larger controlled trials.

Nutrition and Food

40. *Health Policy and Planning*, 2018, Vol. 33 (4): 564 -573

Designing programs to improve diets for maternal and child health: estimating costs and potential dietary impacts of nutrition-sensitive programs in Ethiopia, Nigeria, and India
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Improving maternal and child nutrition in resource-poor settings requires effective use of limited resources, but priority-setting is constrained by limited information about program costs and impacts, especially for interventions designed to improve diet quality. This study utilized a mixed methods approach to identify, describe and estimate the potential costs and impacts on child dietary intake of 12 nutrition-sensitive programs in Ethiopia, Nigeria and India. These potential interventions included conditional livestock and cash transfers, media and education, complementary food processing and sales, household production and food pricing programs. Components and costs of each program were identified through a novel participatory process of expert regional consultation followed by validation and calibration from literature searches and comparison with actual budgets. Impacts on child diets were determined by estimating of the magnitude of economic mechanisms for dietary change, comprehensive reviews of evaluations and effectiveness for similar programs, and demographic data on each country. Across the 12 programs, total cost per child reached (net present value, purchasing power parity adjusted) ranged very widely: from 0.58 to 2650 USD/year among five programs in Ethiopia; 2.62 to 1919 USD/year among four programs in Nigeria; and 27 to 586 USD/year among three programs in India. When impacts were assessed, the largest dietary improvements were for iron and zinc intakes from a complementary food production program in Ethiopia (increases of 17.7 mg iron/child/day and 7.4 mg zinc/child/day), vitamin A intake from a household animal and horticulture production program in Nigeria (335 RAE/child/day), and animal protein intake from a complementary food processing program in Nigeria (20.0 g/child/day). These results add substantial value to the limited literature on the costs and dietary impacts of nutrition-sensitive interventions targeting children in resource-limited settings, informing policy discussions and serving as critical inputs to future cost-effectiveness analyses focusing on disease outcomes.

Research Ethics

41. *N Engl J Med* 2018; 378:1374-1375

Perspective: The Blind Men and the Elephant — Aligning Efforts in Global Health

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After decades of increased funding and progress toward major goals in global health, we are entering a crucial time marked by, among other challenges, the recurring threat of pandemics, the global rise of noncommunicable diseases, and potentially catastrophic aid cuts by the Trump administration. How these challenges are met will be dictated by which motivations for global health efforts guide policy and action.

Debates over which health issues to prioritize mask fundamentally different perspectives on why global health efforts should be pursued in the first place. A diverse array of actors engage in global health initiatives — including multilateral institutions such as the World Health Organization and the World Bank, bilateral agencies such as the U.S. Agency for International Development and the U.K. Department for International Development, governmental bodies such as national ministries of health and defense departments, philanthropic entities such as the Gates and Clinton foundations, local grassroots organizations, and many others — and each one has its own reasons for doing so. Their motivations can be grouped into three overarching rationales: ensuring health security, promoting economic and political development, and achieving health equity as a universal human right. These perspectives animate different sets of actors with different areas of focus.

In the parable of the blind men and the elephant, each blind man feels only one part of the elephant — a trunk, a tusk, an ear, a tail — and is convinced he's confronting a certain sort of creature. Ultimately, they're informed that each has only a piece of the puzzle, and together they can appreciate the whole elephant. In the same way, in order to meet the challenges of the moment and move forward on strong footing, organizations engaged in global health can find pragmatic ways to bring their efforts into alignment. If they fail to do so, we will continue to fall short of the potential that is within our grasp.

Sexual and Reproductive Health

42. *Lancet* 2018;391(10119):415

FGM in Sierra Leone

Devi S

Three years after a 2014 ban against the practice of female genital mutilation in Sierra Leone, Sharmila Devi reports on the progress towards its eradication.

Campaigners against female genital mutilation (FGM) in Sierra Leone, who welcomed a ban on the practice imposed during the Ebola crisis of 2014, fear their efforts might be stalling.

Sierra Leone has reported some of the highest levels in the world of FGM or cutting (FGM/C), which refers to all procedures involving partial or total removal of the female external genitalia or other injury to the female genital organs for non-medical reasons as defined by WHO.

No recent data about FGM prevalence in Sierra Leone are available. The last national authoritative survey, the Demographic and Health Survey published in 2013, reported that 89·6% of women aged 15–49 years had been circumcised, compared with 91·3% in the 2008 survey.

During the Ebola outbreak, which claimed almost 4000 lives, the government introduced emergency health measures, including a moratorium on FGM.

“But now 3 years on, the practice has returned even though the ban is still in place”, said UN Women in a statement late last year.

Activists and campaigners continue to fight against the culturally embedded practice, including efforts towards national legislation to protect girls and women.

Female circumcision, known in Sierra Leone as Bondo Bush, is traditionally carried out during a rite of passage ceremony for girls transitioning to adulthood by women known as Soweis.

Campaigners and activists have been working with communities to inform them about the dangers of FGM as well as to support rural women with cash transfer programmes and to find alternative income sources.

43. *Lancet* 2018;391(10123):870–82

Modern contraceptive use, unmet need, and demand satisfied among women of reproductive age who are married or in a union in the focus countries of the Family Planning 2020 initiative: a systematic analysis using the Family Planning Estimation Tool

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Background. The London Summit on Family Planning in 2012 inspired the Family Planning 2020 (FP2020) initiative and the 120×20 goal of having an additional 120 million women and adolescent girls become users of modern contraceptives in 69 of the world's poorest countries by the year 2020. Working towards achieving 120 × 20 is crucial for ultimately achieving the Sustainable Development Goals of universal access and satisfying demand for reproductive health. Thus, a performance assessment is required to determine countries' progress.

Methods. An updated version of the Family Planning Estimation Tool (FPET) was used to construct estimates and projections of the modern contraceptive prevalence rate (mCPR), unmet need for, and demand satisfied with modern methods of contraception among women of reproductive age who are married or in a union in the focus countries of the FP2020 initiative. We assessed current levels of family planning indicators and changes between 2012 and 2017. A counterfactual analysis was used to assess if recent levels of mCPR exceeded pre-FP2020 expectations.

Findings. In 2017, the mCPR among women of reproductive age who are married or in a union in the FP2020 focus countries was 45.7% (95% uncertainty interval [UI] 42.4–49.1), unmet need for modern methods was 21.6% (19.7–23.9), and the demand satisfied with modern methods was 67.9% (64.4–71.1). Between 2012 and 2017 the number of women of reproductive age who are married or in a union who use modern methods increased by 28.8 million (95% UI 5.8–52.5). At the regional level, Asia has seen the mCPR among women of reproductive age who are married or in a union grow from 51.0% (95% UI 48.5–53.4) to 51.8% (47.3–56.5) between 2012 and 2017, which is slow growth, particularly when compared with a change from 23.9% (22.9–25.0) to 28.5% (26.8–30.2) across Africa. At the country level, based on a counterfactual analysis, we found that 61% of the countries that have made a commitment to FP2020 exceeded pre-FP2020 expectations for modern contraceptive use. Country success stories include rapid increases in Kenya, Mozambique, Malawi, Lesotho, Sierra Leone, Liberia, and Chad relative to what was expected in 2012.

Interpretation. Whereas the estimate of additional users up to 2017 for women of reproductive age who are married or in a union would suggest that the 120 × 20 goal for all women is overly ambitious, the aggregate outcomes mask the diversity in progress at the country level. We identified countries with accelerated progress, that provide inspiration and guidance on how to increase the use of family planning and inform future efforts, especially in countries where progress has been poor.

44. *TMIH* 2018;23(2);236-242

Prevalence, predictors and challenges of gestational diabetes mellitus screening among pregnant women in northern Tanzania

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Objectives. To determine the prevalence and predictors of gestational diabetes mellitus (GDM) as well as acceptability of returning for glucose tolerance testing among pregnant women in Moshi municipality, northern Tanzania.

Methods. Cross-sectional study from October 2015 to April 2016 among women with gestation age of 24–28 weeks of pregnancy attending at Kilimanjaro Christian Medical Centre (KCMC) referral hospital, Majengo and Pasua Health Centres. Women were interviewed and requested to return the next day (window within a month, depending on gestational age) for fasting plasma glucose (FPG) testing, followed immediately by a 75 g oral glucose tolerance test (OGTT). GDM was diagnosed using the 2013 WHO criteria. Logistic regression was conducted to reveal independent predictors for GDM.

Results. Of 433 interviewed women, 100 (23%) did not return for FPG and OGTT testing. The prevalence of GDM among the 333 screened women was 19.5%, and 3% had diabetes in pregnancy

(DIP). GDM was significantly associated with age ≥ 35 years (adjusted OR 6.75), pre-pregnancy obesity (AOR 2.22) and history of abortion (AOR 2.36).

Conclusion. Prevalence of GDM is high in Moshi. We recommend introduction of routine screening for hyperglycaemia during pregnancy along with strategies for follow-up to prevent long-term effects of GDM and DIP in women and their children.

45. TMIH 2018;23(5):541-548

Accuracy of syndromic management in targeting vaginal and cervical infections among symptomatic women of reproductive age attending primary care clinics in Dakar, Senegal

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Objective. To assess the effectiveness of the WHO syndromic algorithm in the management of vaginal discharge among women of reproductive age in Dakar

Methods. Cross-sectional study of consecutive female patients (aged 18–49 years) presenting with vaginal symptoms at six selected study sites in Dakar; of these, 276 patients were included in the analysis. Vaginal and cervical swab samples were collected and analysed to establish an aetiological diagnosis of any infection. Syndrome-based diagnosis was compared with the laboratory results to evaluate its accuracy based on sensitivity, specificity and positive and negative predictive values. The degree of agreement between the two approaches was assessed using the Cohen's kappa concordance analysis.

Results. Overall prevalence of vaginal infections was 56.9% (157/276); 5.4% (15/276) of the patients had cervical infection. Using the syndromic approach, 51% of patients were correctly managed for *Trichomonas vaginalis* (TV)/*Gardnerella vaginalis* (GV); 61% for *Candida albicans* (CA) and 54% for *Chlamydia trachomatis* (CT)/*Neisseria gonorrhoea* (NG) infections. Consequently, 31% of patients with TV/GV, 51% with CA and 53% with CT/NG infections would have missed treatment. Further, the kappa value was < 0.20 , indicating that there was no agreement or only slight agreement between the syndromic approach and laboratory-based diagnosis.

Conclusion. This study highlights the limitations of the applicability of the WHO syndromic approach in settings with low prevalence of sexually transmitted infections (STIs) and calls for affordable and accurate rapid tests for STIs.

46. PLoS Med 15(2): e1002512

Prevalence of sexually transmitted infections among young people in South Africa: A nested survey in a health and demographic surveillance site

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Background: Sexually transmitted infections (STIs) and bacterial vaginosis (BV) are associated with increased transmission of HIV, and poor reproductive and sexual health. The burden of STIs/BV among young people is unknown in many high HIV prevalence settings. We conducted an acceptability, feasibility, and prevalence study of home-based sampling for STIs/ BV among young men and women aged 15–24 years old in a health and demographic surveillance site (HDSS) in rural KwaZulu-Natal, South Africa.

Methods and findings: A total of 1,342 young people, stratified by age (15–19 and 20–24 years) and sex were selected from the HDSS sampling frame; 1,171/1,342 (87%) individuals had ≥ 1 attempted home visit between 4 October 2016 and 31 January 2017, of whom 790 (67%) were successfully contacted. Among the 645 who were contacted and eligible, 447 (69%) enrolled. Consenting/assenting participants were interviewed, and blood, self-collected urine (men), and vaginal swabs (women) were tested for herpes simplex virus type 2 (HSV-2), chlamydia, gonorrhoea, syphilis, trichomoniasis, and BV. Both men and women reported that sample collection was easy. Participants disagreed that sampling was painful; more than half of the participants disagreed that they felt anxious or embarrassed. The weighted prevalence of STIs/BV among men and women, respectively, was 5.3% and 11.2% for chlamydia, 1.5% and 1.8% for gonorrhoea, 0% and 0.4% for active syphilis, 0.6% and 4.6% for trichomoniasis, 16.8% and 28.7% for HSV-2, and 42.1% for BV (women only). Of the women with ≥ 1 curable STI, 75% reported no symptoms. Factors associated with STIs/BV included

having older age, being female, and not being in school or working. Among those who participated in the 2016 HIV serosurvey, the prevalence of HIV was 5.6% among men and 19% among women. Feasibility was impacted by the short study duration and the difficulty finding men at home.

Conclusions: A high prevalence of STIs/BV was found in this rural setting with high HIV prevalence in South Africa. Most STIs and HIV infections were asymptomatic and would not have been identified or treated under national syndromic management guidelines. A nested STI/BV survey within a HDSS proved acceptable and feasible. This is a proof of concept for population-based STI surveillance in low- and middle-income countries that could be utilised in the evaluation of STI/HIV prevention and control programmes.

47. *Am J Trop Med Hyg.* 2018 Apr;98(4):1137-1144. Epub 2018 Jan 4

Schistosomiasis and Infertility in East Africa

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Case reports and pathology series suggest associations of female genital schistosomiasis (*Schistosoma haematobium*) with infertility and ectopic pregnancy. Differential geographic distribution of infertility is not explained by analyses of known risk factors. In this cross-sectional multilevel semi-ecologic study, interpolated prevalence maps for *S. haematobium* and *Schistosoma mansoni* in East Africa were created using data from two open-access Neglected Tropical Diseases Databases. Prevalence was extracted to georeferenced survey sample points for Demographic and Health Surveys for Ethiopia, Kenya, Tanzania, and Uganda for 2000 and 2010. Exploratory spatial analyses showed that infertility was not spatially random and mapped the clustering of infertility and its co-location with schistosomiasis. Multilevel logistic regression analysis demonstrated that women living in high compared with absent *S. haematobium* locations had significantly higher odds of infertility (2000 odds ratio [OR] = 1.5 [confidence interval 95% = 1.3, 1.8]; 2010 OR = 1.2 [1.1, 1.5]). Women in high *S. haematobium* compared with high *S. mansoni* locations had significantly higher odds of infertility (2000 OR 1.4 [1.1, 1.9]; 2010 OR 1.4 [1.1, 1.8]). Living in high compared with absent *S. mansoni* locations did not affect the odds of infertility. Infertility appears to be associated spatially with *S. haematobium*.

Miscellaneous

48. *Am J Trop Med Hyg.* 2018 Feb;98(2):389-395. Epub 2017 Dec 14

Comparison of Mass Azithromycin Coverage Targets of Children in Niger: A Cluster-Randomized Trachoma Trial

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Repeated oral azithromycin distribution targeted only to children has proven effective in reducing the ocular Chlamydia that causes trachoma. Here, we assess whether an enhanced coverage target of at least 90% of children is superior to the World Health Organization recommendation of at least 80%. Twenty-four trachoma-endemic communities in Matamèye, Niger, were randomized to a single day of azithromycin distribution aiming for at least 80% coverage or up to 4 days of treatment and > 90% coverage of children under age 12. All distributions were biannual. Children < 5 years of age and adults > 15 years were monitored for ocular Chlamydia infection by polymerase chain reaction every 6 months for 36 months in children and at baseline and 36 months in adults. Ocular Chlamydia prevalence in children decreased from 24.9% (95% confidence interval [CI] 15.9-33.8%) to 4.4% (95% CI 0.6-8.2%, $P < 0.001$) at 36 months in the standard coverage arm and from 15.6% (95% CI 10.0-21.2%) to 3.3% (95% CI 1.0-5.5%; $P < 0.001$) in the enhanced coverage arm. Enhanced coverage reduced ocular Chlamydia prevalence in children more quickly over time compared with standard ($P = 0.04$). There was no difference between arms at 36 months in children (2.4% lower with enhanced coverage, 95% CI 7.7-12.5%; $P = 0.60$). No infection was detected in adults at 36 months. Increasing

antibiotic coverage among children from 80% to 90% may yield only short term improvements for trachoma control programs. Targeting treatment to children alone may be sufficient for trachoma control in this setting.

49. *Lancet* 2018 Mar 14. pii: S0140-6736(18)30460-4. [Epub ahead of print]

Delivering modern, high-quality, affordable pathology and laboratory medicine to low-income and middle-income countries: a call to action

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Modern, affordable pathology and laboratory medicine (PALM) systems are essential to achieve the 2030 Sustainable Development Goals for health in low-income and middle-income countries (LMICs). In this last in a Series of three papers about PALM in LMICs, we discuss the policy environment and emphasise three crucial high-level actions that are needed to deliver universal health coverage. First, nations need national strategic laboratory plans; second, these plans require adequate financing for implementation; and last, pathologists themselves need to take on leadership roles to advocate for the centrality of PALM to achieve the Sustainable Development Goals for health. The national strategic laboratory plan should deliver a tiered, networked laboratory system as a central element. Appropriate financing should be provided, at a level of at least 4% of health expenditure. Financing of new technologies such as molecular diagnostics is challenging for LMICs, even though many of these tests are cost-effective. Point-of-care testing can substantially reduce test-reporting time, but this benefit must be balanced with higher costs. Our research analysis highlights a considerable deficiency in advocacy for PALM; pathologists have been invisible in national and international health discourse and leadership. Embedding PALM in LMICs can only be achieved if pathologists advocate for these services, and undertake leadership roles, both nationally and internationally. We articulate eight key recommendations to address the current barriers identified in this Series and issue a call to action for all stakeholders to come together in a global alliance to ensure the effective provision of PALM services in resource-limited settings.

50. *Lancet* 2018 Mar 14. pii: S0140-6736(18)30459-8. [Epub ahead of print]

Improving pathology and laboratory medicine in low-income and middle-income countries: roadmap to solutions

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Insufficient awareness of the centrality of pathology and laboratory medicine (PALM) to a functioning health-care system at policy and governmental level, with the resultant inadequate investment, has meant that efforts to enhance PALM in low-income and middle-income countries have been local, fragmented, and mostly unsustainable. Responding to the four major barriers in PALM service delivery that were identified in the first paper of this Series (workforce, infrastructure, education and training, and quality assurance), this second paper identifies potential solutions that can be applied in low-income and middle-income countries (LMICs). Increasing and retaining a quality PALM workforce requires access to mentorship and continuing professional development, task sharing, and the development of short-term visitor programmes. Opportunities to enhance the training of pathologists and allied PALM personnel by increasing and improving education provision must be explored and implemented. PALM infrastructure must be strengthened by addressing supply chain barriers, and ensuring laboratory information systems are in place. New technologies, including telepathology and point-of-care testing, can have a substantial role in PALM service delivery, if used appropriately. We emphasise the crucial importance of maintaining PALM quality and posit that all laboratories in LMICs should participate in quality assurance and accreditation programmes. A potential role for public-private partnerships in filling PALM services gaps should also be investigated. Finally, to deliver these solutions and ensure equitable access to essential services in LMICs, we propose a PALM package focused on these countries, integrated within a nationally tiered laboratory system, as part of an overarching national laboratory strategic plan.