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INTERNATIONAL HEALTH ALERTS 2021-2 ABSTRACTS

Child Health

1. Am J TMH 2021;104(6):2238-40

Case Report: Fulminant Infantile Beriberi: A Report of Six Cases
Samprathi M et al., Rainbow Children's Hospital, Bangalore, India

Thiamine deficiency disorders are an under-recognized public health problem in low- and middle-income countries. Infantile beriberi, the most important symptom for children, is suspected to significantly contribute to infant mortality and lifelong neurodevelopmental morbidity. Lack of awareness, varied clinical presentation, and lack of a readily available diagnostic marker lead to frequent misdiagnoses. We report six thriving infants who presented with an acute fulminant illness with varied clinical manifestations mimicking common childhood illnesses like pneumonia and sepsis. Four of them presented with the severe cardiovascular form, called Shoshin beriberi, and severe pulmonary arterial hypertension. Empirical intravenous thiamine administered to four of the six infants resulted in dramatic recovery. Awareness of the clinical definition of infantile beriberi and treatment with empirical thiamine can be lifesaving.

2. Am J TMH 2021;May 17. Online ahead of print.

Salmonella Bloodstream Infections in Hospitalized Children with Acute Febrile Illness-Uganda, 2016-2019
Appiah GD et al., Division of Foodborne, Waterborne, and Environmental Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia

Invasive Salmonella infection is a common cause of acute febrile illness (AFI) among children in sub-Saharan Africa; however, diagnosing Salmonella bacteremia is challenging in settings without blood culture. The Uganda AFI surveillance system includes blood culture-based surveillance for etiologies of bloodstream infection (BSIs) in hospitalized febrile children in Uganda. We analyzed demographic, clinical, blood culture, and antimicrobial resistance data from hospitalized children at six sentinel AFI sites from July 2016 to January 2019. A total of 47,261 children were hospitalized. Median age was 2 years (interquartile range, 1-4) and 26,695 (57%) were male. Of 7,203 blood cultures, 242 (3%) yielded bacterial pathogens including Salmonella (N = 67, 28%), Staphylococcus aureus (N = 40, 17%), Escherichia spp. (N = 25, 10%), Enterococcus spp. (N = 18, 7%), and Klebsiella pneumoniae (N = 17, 7%). Children with BSIs had longer median length of hospitalization (5 days versus 4 days), and a higher case-fatality ratio (13% versus 2%) than children without BSI (all $P < 0.001$). Children with Salmonella BSIs did not differ significantly in length of hospitalization or mortality from children with BSI resulting from other organisms. Serotype and antimicrobial susceptibility results were available for 49 Salmonella isolates, including 35 (71%) non-typhoidal serotypes and 14 Salmonella serotype Typhi (Typhi). Among Typhi isolates, 10 (71%) were multi-drug resistant and 13 (93%) had decreased ciprofloxacin susceptibility. Salmonella strains, particularly non-typhoidal serotypes and drug-resistant Typhi, were the most common cause of BSI. These data can inform regional Salmonella surveillance in East Africa and guide empiric therapy and prevention in Uganda.

3. BMJ 2021;373:n1212

Congenital cytomegalovirus infection
Pesch MH et al., Department of Pediatrics, Division of Developmental and Behavioral Pediatrics, University of Michigan, Ann Arbor, MI, USA <pesch@umich.edu>

What you need to know

- Congenital cytomegalovirus (cCMV) is common, occurring in one in every 100-200 live births
- The mainstay of prevention is prenatal education about behaviour change to reduce contact with saliva and urine of young children who may be shedding CMV
- cCMV most often presents with no visible signs at birth, yet infected infants are at increased risk for sensorineural hearing loss in childhood
- cCMV can be diagnosed shortly after birth using polymerase chain reaction to detect viral DNA in urine or saliva, or later in life by testing residual newborn dried blood spot (Guthrie card)
- All children with cCMV require close monitoring of their hearing and development

Congenital cytomegalovirus (cCMV) infection is a common congenital infection, affecting one in every 100-200 live births globally. Long term neurodevelopmental sequelae occur in a quarter of children affected. This article provides a clinical update of the literature on the prevention, diagnosis, treatment, and anticipatory management of infants and children with cCMV. Recommendations from the 2015 European Society of Paediatric Infectious Diseases (ESPID) Expert Consensus Group (largely based on expert opinion) are presented along with more recent literature relevant to the general practitioner.

What is congenital cytomegalovirus infection?

Cytomegalovirus (CMV) can cause self-limited generalised symptoms such as fatigue and lymphadenopathy in most healthy individuals, including pregnant people. cCMV infection occurs when CMV transplacentally infects a developing fetus. The virus can cause damage to the placenta, and replicate in fetal central nervous system (CNS) cells, which may result in

disrupted fetal development, miscarriage, or intrauterine fetal demise. Neonates with cCMV may experience a wide range of signs, symptoms, and long term sequelae, although most experience no recognisable signs or symptoms

4. BMJ Global Health 2021;6:e006084

Child health and the implementation of Community and District-management Empowerment for Scale-up (CODES) in Uganda: a randomised controlled trial

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Introduction. Uganda's district-level administrative units buttress the public healthcare system. In many districts, however, local capacity is incommensurate with that required to plan and implement quality health interventions. This study investigates how a district management strategy informed by local data and community dialogue influences health services.
Methods. A 3-year randomised controlled trial (RCT) comprised of 16 Ugandan districts tested a management approach, Community and District-management Empowerment for Scale-up (CODES). Eight districts were randomly selected for each of the intervention and comparison areas. The approach relies on a customised set of data-driven diagnostic tools to identify and resolve health system bottlenecks. Using a difference-in-differences approach, the authors performed an intention-to-treat analysis of protective, preventive and curative practices for malaria, pneumonia and diarrhoea among children aged 5 and younger.
Results. Intervention districts reported significant net increases in the treatment of malaria (+23%), pneumonia (+19%) and diarrhoea (+13%) and improved stool disposal (+10%). Coverage rates for immunisation and vitamin A consumption saw similar improvements. By engaging communities and district managers in a common quest to solve local bottlenecks, CODES fostered demand for health services. However, limited fiscal space-constrained district managers' ability to implement solutions identified through CODES.
Conclusion. Data-driven district management interventions can positively impact child health outcomes, with clinically significant improvements in the treatment of malaria, pneumonia and diarrhoea as well as stool disposal. The findings recommend the model's suitability for health systems strengthening in Uganda and other decentralised contexts.

5. Plos Med 18(5): e1003602

Parenting interventions to promote early child development in the first three years of life: A global systematic review and meta-analysis

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Background. Parents are the primary caregivers of young children. Responsive parent–child relationships and parental support for learning during the earliest years of life are crucial for promoting early child development (ECD). We conducted a global systematic review and meta-analysis to evaluate the effectiveness of parenting interventions on ECD and parenting outcomes.
Methods and findings. We searched MEDLINE, Embase, PsycINFO, CINAHL, Web of Science, and Global Health Library for peer-reviewed, published articles from database inception until November 15, 2020. We included randomized controlled trials (RCTs) of parenting interventions delivered during the first 3 years of life that evaluated at least 1 ECD outcome. At least 2 reviewers independently screened, extracted data, and assessed study quality from eligible studies. ECD outcomes included cognitive, language, motor, and socioemotional development, behavior problems, and attachment. Parenting outcomes included parenting knowledge, parenting practices, parent–child interactions, and parental depressive symptoms. We calculated intervention effect sizes as the standardized mean difference (SMD) and estimated pooled effect sizes for each outcome separately using robust variance estimation meta-analytic approaches. We used random-effects meta-regression models to assess potential effect modification by country-income level, child age, intervention content, duration, delivery, setting, and study quality.
Of the 11,920 articles identified, we included 111 articles representing 102 unique RCTs. Pooled effect sizes indicated positive benefits of parenting interventions on child cognitive development (SMD = 0.32, 95% CI [confidence interval]: 0.23, 0.40, $P < 0.001$), language development (SMD = 0.28, 95% CI: 0.18 to 0.37, $P < 0.001$), motor development (SMD = 0.24, 95% CI: 0.15 to 0.32, $P < 0.001$), socioemotional development (SMD = 0.19, 95% CI: 0.10 to 0.28, $P < 0.001$), and attachment (SMD = 0.29, 95% CI: 0.18 to 0.40, $P < 0.001$) and reductions in behavior problems (SMD = −0.13, 95% CI: −0.18 to −0.08, $P < 0.001$). Positive benefits were also found on parenting knowledge (SMD = 0.56, 95% CI: 0.33 to 0.79, $P < 0.001$), parenting practices (SMD = 0.33, 95% CI: 0.22 to 0.44, $P < 0.001$), and parent–child interactions (SMD = 0.39, 95% CI: 0.24 to 0.53, $P < 0.001$). However, there was no significant reduction in parental depressive symptoms (SMD = −0.07, 95% CI: −0.16 to 0.02, $P = 0.08$). Subgroup analyses revealed significantly greater effects on child cognitive, language, and motor development, and parenting practices in low- and middle-income countries compared to high-income countries; and significantly greater effects on child cognitive development, parenting knowledge, parenting practices, and parent–child interactions for programs that focused on responsive caregiving compared to those that did not. On the other hand, there was no clear evidence of effect modification by child age, intervention duration, delivery, setting, or study risk of bias. Study limitations include considerable unexplained heterogeneity, inadequate reporting of intervention content and implementation, and varying quality of evidence in terms of the conduct of trials and robustness of outcome measures used across studies.
Conclusions. Parenting interventions for children during the first 3 years of life are effective for improving ECD outcomes and enhancing parenting outcomes across low-, middle-, and high-income countries. Increasing implementation of effective

and high-quality parenting interventions is needed globally and at scale in order to support parents and enable young children to achieve their full developmental potential.

Communicable Diseases

6. Am J TMH 2021;104(6):1978-90
Epidemiology of Crimean-Congo Hemorrhagic Fever (CCHF) in Africa-Underestimated for Decades
Temur AI et al., Johns Hopkins University School of Medicine, Baltimore, Maryland

Crimean-Congo hemorrhagic fever (CCHF) is endemic in Africa, but the epidemiology remains to be defined. Using a broad database search, we reviewed the literature to better define CCHF evidence in Africa. We used a One Health approach to define the impact of CCHF by reviewing case reports, human and animal serology, and records of CCHF virus (CCHFV) isolations (1956-mid-2020). In addition, published and unpublished collection data were used to estimate the geographic distribution of Hyalomma ticks and infection vectors. We implemented a previously proposed classification scheme for organizing countries into five categories by the level of evidence. From January 1, 1956 to July 25, 2020, 494 CCHF cases (115 lethal) were reported in Africa. Since 2000, nine countries (Kenya, Mali, Mozambique, Nigeria, Senegal, Sierra Leone, South Sudan, Sudan, and Tunisia) have reported their first CCHF cases. Nineteen countries reported CCHF cases and were assigned level 1 or level 2 based on maturity of their surveillance system. Thirty countries with evidence of CCHFV circulation in the absence of CCHF cases were assigned level 3 or level 4. Twelve countries for which no data were available were assigned level 5. The goal of this review is to inform international organizations, local governments, and healthcare professionals about shortcomings in CCHF surveillance in Africa to assist in a movement toward strengthening policy to improve CCHF surveillance.

7. Am J TMH 2021;104(6):2293-7
Inaccuracies in Google's Health-Based Knowledge Panels Perpetuate Widespread Misconceptions Involving Infectious Disease Transmission
Haddow AD et al., United States Army Medical Research Institute of Infectious Diseases, Frederick, Maryland

Google health-based Knowledge Panels were designed to provide users with high-quality basic medical information on a specific condition. However, any errors contained within Knowledge Panels could result in the widespread distribution of inaccurate health information. We explored the potential for inaccuracies to exist within Google's health-based Knowledge Panels by focusing on a single well-studied pathogen, Ebola virus (EBOV). We then evaluated the accuracy of those transmission modes listed within the Google Ebola Knowledge Panel and investigated the pervasiveness of any misconceptions associated with inaccurate transmission modes among persons living in Africa. We found that the Google Ebola Knowledge Panel inaccurately listed insect bites or stings as modes of EBOV transmission. Our scoping review found 27 articles and reports that revealed that 9 of 11 countries where misconceptions regarding insect transmission of EBOV have been reported are locations of current (i.e., Democratic Republic of Congo and Guinea) or previous EBOV outbreaks. We found reports that up to 26.6% (155/582) of study respondents in Democratic Republic of Congo believed mosquito bite avoidance would prevent EBOV; in other locations of previous large-scale EBOV outbreaks (e.g., Guinea), up to 61.0% (304/498) of respondents believed insects were involved in EBOV transmission. Our findings highlight the potential for errors to exist within the health information contained in Google's health-based Knowledge Panels. Such errors could perpetuate misconceptions or misinformation, leading to mistrust of health workers and aid agencies and in turn undermining public health education or outbreak response efforts.

8. Am J TMH 2021;May 3. Online ahead of print.
Predictors and Outcomes of Dengue-Associated Acute Kidney Injury
Diptyanusa A et al., Center for Tropical Medicine, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia

Dengue viral infections present with a wide clinical spectrum ranging from asymptomatic to severe manifestations with organ involvement. The term "expanded dengue syndrome" has been commonly used to illustrate the unusual or atypical manifestations; acute kidney injury (AKI) is one of the atypical manifestations of this syndrome. The use of heterogeneous criteria to determine the presence of AKI in dengue patients due to the vast diversity in populations led to difficulties in assessing the true incidence of dengue-associated AKI. This review presents a variable, but often high, frequency of dengue-associated AKI among vastly diverse populations with various disease severities. Dengue-associated AKI is not an uncommon complication, and its importance has often been neglected during the management of dengue patients. The risk factors and certain clinical and laboratory findings commonly reported among dengue patients with AKI should be considered to support a timely diagnosis and case management. This review highlights the need for clinicians to be aware of dengue-associated AKI to reduce the morbidity and mortality associated with this common and important tropical disease.

9. BMJ Global Health 2021;6:e005332
Epidemic preparedness: Prenatal Zika virus screening during the next epidemic
Qiao L et al., Health Equity Action Lab, Department of Infectious Disease Epidemiology, London <elizabeth.brickley@lshtm.ac.uk>

Zika virus (ZIKV) is a vectorborne infectious agent of global public health significance due to its potential to cause severe teratogenic outcomes. The question of whether health systems should consider adopting screening programmes for ZIKV infections during pregnancy warrants consideration. In this analysis, we apply the Wilson-Jungner framework to appraise the potential utility of a prenatal ZIKV screening programme, outline potential screening strategies within the case-finding pathway, and consider other epidemiological factors that may influence the planning of such a screening programme. Our evaluation of a potential prenatal ZIKV screening programme highlights factors affirming its usefulness, including the importance of Congenital Zika Syndrome as a public health problem and the existence of analogous congenital prenatal screening programmes for STORCH agents (syphilis, toxoplasmosis, others (eg, human immunodeficiency virus, varicella-zoster virus, parvovirus B19), rubella, cytomegalovirus, and herpes simplex virus). However, our assessment also reveals key barriers to implementation, such as the need for more accurate diagnostic tests, effective antiviral treatments, increased social service capacity, and surveillance. Given that the reemergence of ZIKV is likely, we provide a guiding framework for policymakers and public health leaders that can be further elaborated and adapted to different contexts in order to reduce the burden of adverse ZIKV-related birth outcomes during future outbreaks.

10. EID 2021;27(9)
Multicenter Epidemiologic Study of Coronavirus Disease-Associated Mucormycosis, India
Patel A, MucoCovi Network

During September-December 2020, we conducted a multicenter retrospective study across India to compare epidemiology and outcomes among cases of coronavirus disease (COVID-19)-associated mucormycosis (CAM). Among 287 mucormycosis patients, 187 (65.2%) had CAM; CAM prevalence was 0.27% among hospitalized COVID-19 patients. We noted a 2.1-fold rise in mucormycosis during the study period compared with September-December 2019. Uncontrolled diabetes mellitus was the most common underlying disease among CAM and non-CAM patients. COVID-19 was the only underlying disease in 32.6% of CAM patients. COVID-19-related hypoxemia and improper glucocorticoid use independently were associated with CAM. The mucormycosis case-fatality rate at 12 weeks was 45.7% but was similar for CAM and non-CAM patients. Age, rhino-orbital-cerebral involvement, and intensive care unit admission were associated with increased mortality rates; sequential antifungal drug treatment improved mucormycosis survival. The COVID-19 pandemic has led to increases in mucormycosis in India, partly from inappropriate glucocorticoid use.

COVID-19

11. Lancet 2021;397(10281):1265-75
The first and second waves of the COVID-19 pandemic in Africa: a cross-sectional study
Salyer SJ et al., Africa Centres for Disease Control and Prevention, Addis Ababa, Ethiopia <stephanies@africa-union.org>

Background: Although the first wave of the COVID-19 pandemic progressed more slowly in Africa than the rest of the world, by December, 2020, the second wave appeared to be much more aggressive with many more cases. To date, the pandemic situation in all 55 African Union (AU) Member States has not been comprehensively reviewed. We aimed to evaluate reported COVID-19 epidemiology data to better understand the pandemic's progression in Africa.
Methods: We did a cross-sectional analysis between Feb 14 and Dec 31, 2020, using COVID-19 epidemiological, testing, and mitigation strategy data reported by AU Member States to assess trends and identify the response and mitigation efforts at the country, regional, and continent levels. We did descriptive analyses on the variables of interest including cumulative and weekly incidence rates, case fatality ratios (CFRs), tests per case ratios, growth rates, and public health and social measures in place.
Findings: As of Dec 31, 2020, African countries had reported 2 763 421 COVID-19 cases and 65 602 deaths, accounting for 3·4% of the 82 312 150 cases and 3·6% of the 1 798 994 deaths reported globally. Nine of the 55 countries accounted for more than 82·6% (2 283 613) of reported cases. 18 countries reported CFRs greater than the global CFR (2·2%). 17 countries reported test per case ratios less than the recommended ten to 30 tests per case ratio range. At the peak of the first wave in Africa in July, 2020, the mean daily number of new cases was 18 273. As of Dec 31, 2020, 40 (73%) countries had experienced or were experiencing their second wave of cases with the continent reporting a mean of 23 790 daily new cases for epidemiological week 53. 48 (96%) of 50 Member States had five or more stringent public health and social measures in place by April 15, 2020, but this number had decreased to 36 (72%) as of Dec 31, 2020, despite an increase in cases in the preceding month.
Interpretation: Our analysis showed that the African continent had a more severe second wave of the COVID-19 pandemic than the first, and highlights the importance of examining multiple epidemiological variables down to the regional and country levels over time. These country-specific and regional results informed the implementation of continent-wide initiatives and supported equitable distribution of supplies and technical assistance. Monitoring and analysis of these data

over time are essential for continued situational awareness, especially as Member States attempt to balance controlling COVID-19 transmission with ensuring stable economies and livelihoods.

Health Policy

12. BMJ Global Health 2021;6:e004223
Interventions to improve district-level routine health data in low-income and middle-income countries: a systematic review
Lee J et al., Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, UK <ngozierondu@gmail.com>

Background. Routine health information system(s) (RHIS) facilitate the collection of health data at all levels of the health system allowing estimates of disease prevalence, treatment and preventive intervention coverage, and risk factors to guide disease control strategies. This core health system pillar remains underdeveloped in many low-income and middle-income countries. Efforts to improve RHIS data coverage, quality and timeliness were launched over 10 years ago.
Methods. A systematic review was performed across 12 databases and literature search engines for both peer-reviewed articles and grey literature reports on RHIS interventions. Studies were analysed in three stages: (1) categorisation of RHIS intervention components and processes; (2) comparison of intervention component effectiveness and (3) whether the post-intervention outcome improved above the WHO integrated disease surveillance response framework data quality standard of 80% or above.
Results. 5294 references were screened, resulting in 56 studies. Three key performance determinants—technical, organisational and behavioural—were proposed as critical to RHIS strengthening. Seventy-seven per cent [77%] of studies identified addressed all three determinants. The most frequently implemented intervention components were 'providing training' and 'using an electronic health management information systems'. Ninety-three per cent [93%] of pre–post or controlled trial studies showed improvements in one or more data quality outputs, but after applying a standard threshold of >80% post-intervention, this number reduced to 68%. There was an observed benefit of multi-component interventions that either conducted data quality training or that addressed improvement across multiple processes and determinants of RHIS.
Conclusion. Holistic data quality interventions that address multiple determinants should be continuously practised for strengthening RHIS. Studies with clearly defined and pragmatic outcomes are required for future RHIS improvement interventions. These should be accompanied by qualitative studies and cost analyses to understand which investments are needed to sustain high-quality RHIS in low-income and middle-income countries.

13. BMJ Global Health 2021;6:e005833
Safer primary healthcare facilities are needed to protect healthcare workers and maintain essential services: lessons learned from a multicountry COVID-19 emergency response initiative
Patel LN et al., Prevent Epidemics, Resolve to Save Lives, an Initiative of Vital Strategies, New York, New York, USA. On behalf of the African Primary Health Care IPC Strengthening Community of Practice <clee@resolvetosavelives.org>

Healthcare workers (HCWs) are at increased risk of infection from SARS-CoV-2 and other disease pathogens, which take a disproportionate toll on HCWs, with substantial cost to health systems. Improved infection prevention and control (IPC) programmes can protect HCWs, especially in resource-limited settings where the health workforce is scarcest, and ensure patient safety and continuity of essential health services. In response to the COVID-19 pandemic, we collaborated with ministries of health and development partners to implement an emergency initiative for HCWs at the primary health facility level in 22 African countries. Between April 2020 and January 2021, the initiative trained 42 058 front-line HCWs from 8444 health facilities, supported longitudinal supervision and monitoring visits guided by a standardised monitoring tool, and provided resources including personal protective equipment (PPE). We documented significant short-term improvements in IPC performance, but gaps remain. Suspected HCW infections peaked at 41.5% among HCWs screened at monitored facilities in July 2020 during the first wave of the pandemic in Africa. Disease-specific emergency responses are not the optimal approach. Comprehensive, sustainable IPC programmes are needed. IPC needs to be incorporated into all HCW training programmes and combined with supportive supervision and mentorship. Strengthened data systems on IPC are needed to guide improvements at the health facility level and to inform policy development at the national level, along with investments in infrastructure and sustainable supplies of PPE. Multimodal strategies to improve IPC are critical to make health facilities safer and to protect HCWs and the communities they serve

14. BMJ Global Health 2021;6:e006504
Editorial
Global vaccine equity demands reparative justice — not charity
Harman S et al. <eugene_richardson@hms.harvard.edu>

Introduction. By late April, more than 80% of the world's COVID-19 vaccines had gone to people in wealthy countries, with just 0.3% to people in low-income countries. This reprehensible imbalance is no accident. High-income countries have used neocolonial negotiating power, global policy leverage and capital to procure enough doses to cover 245% of their citizens

while leaving few doses for poorer countries. As a result, lower-income countries may not be able to vaccinate their populations until 2023.
Such inequity is yet another example of how the interests of racial capitalism run roughshod over the golden rule of global solidarity—attend to the highest risk first. Currently, older and medically vulnerable individuals are dying from COVID-19 disproportionately in poor countries, while young, healthy individuals are getting vaccinated in wealthy ones. Vaccine apartheid is a not novel phenomenon. The notion that only certain corners of the world get to benefit from life-saving treatments is an everyday reality of a global health system driven by a capitalist, philanthropic model. But in times of crises—and as new variants threaten the vaccination plans of wealthy countries—these inequities and their solutions come to the forefront of global debate.
Policy-makers in rich nations are aware of these issues. But the solutions they have proposed so far do nothing to address the underlying structural problems. They offer charitable donations and partial, temporary fixes that are designed to deflect the substantive demands for reform that global South countries are fighting for, including challenges to unethical intellectual property (IP) regimes. This approach will not work, because it is not designed to 'work.' If we want to end vaccine apartheid, we need to target the root causes of global health inequities. We need reparative justice.
There are currently three approaches to reduce inequity in COVID-19 vaccine distribution: bilateral charity, multilateral charity and temporary waivers or suspensions of IP.
The first is the most straightforward. States that stockpile COVID-19 vaccines have committed to sharing their leftovers with low-income and middle-income countries. Norway was one of the first nations to accede to donating doses to poorer countries in parallel with its vaccine programme.....
The second is multilateral charity, best exemplified by COVAX. In 2020, COVAX emerged as an international collaboration by the World Health Organisation (WHO), United Nations Children's Fund, Gavi and the Coalition for Epidemic Preparedness Innovations to ensure equitable global access to COVID-19 vaccines. Rich countries can access doses for 10%–50% of their populations, depending on how much they have paid in, and poor countries can access doses for 20% through the scheme.....
The third approach is focused on pooling, temporary waivers, or suspension of IP. In May 2020, the WHO created the COVID-19 Technology Access Pool for companies to share IP and transfer technologies in a coordinated manner. But to date, not a single company has utilised the transfer process—likely because such forms of global IP sharing would quell profits, even if royalties are included.....

15. BMJ Global Health 2021;6:e006392
Pandemic treaty needs to start with rethinking the paradigm of global health security
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The Independent Panel on Pandemic Preparedness released on 11 May adds to the mounting calls for a new Pandemic Treaty that would address gaps in the global governance of threats to global health security. The emerging debate has quickly turned to focus on questions of structure and forms—a United Nations treaty or a framework convention under the auspices of the WHO, and verification and enforcement mechanisms—as well as on issues of process regarding who will have voice and how the negotiations will proceed. But we must not lose sight of its purpose and key objectives, and what we mean by 'global health security'. Indeed, the treaty discussions provide an opportunity and an imperative to rethink the paradigm of global health security that has shaped the current international response to the COVID-19 pandemic. The prevailing paradigm is antithetical to the core purpose of global pandemic preparedness and response for five reasons.
First, global health security needs to focus on the security of people, not national borders. The concept of 'global health security' emerged with the increasing transnational spread of disease in the late 20th century in the context of neoliberal economic globalisation, the rise in biosecurity threats, and increased migrations due to climate change, instability and armed conflicts. It led to a reframing of infectious diseases as a national security threat, bringing the language and thinking of the security sector, concerned with defending national borders, not human health. .....
Second, global health security calls for multilateral action, not go-it-alone national policies. The Panel report as well as the original call from political leaders emphasised interdependence as the rationale for multilateral action. The rapid spread of variants shows the folly, as well as immorality, of putting national interest above concerted global action. In national defence strategies, mutual interest of states is recognised but does not come first as it must in public health emergencies. The truism that 'nobody is safe until everyone is safe' means focusing on the provision of global public goods that would serve the needs of all people, universally—such as the 'people's vaccine'.
Third, institutional arrangements for global health security need to be based on fundamental human rights principles as well as the specific legally binding norms in treaties countries have already ratified. Universal access to healthcare, the essential role of public health infrastructures and ensuring substantive equality for diverse human beings' needs are core principles that underpin human rights in relation to health. .....
Fourth, the prevailing paradigm of global health security needs to be decolonised. It is built around an implicit assumption that pandemics emanate from poorer regions of the world, threatening the health and well-being of people in the more prosperous areas.....
Fifth, the geography of COVID-19 should make us question the criteria and institutions that might assess pandemic preparedness. Until the surge of cases in India starting in early 2020, global incidence and deaths from COVID-19 have been overwhelmingly concentrated in North America and Western Europe. Many commentators have observed the irony of the Johns Hopkins Index of Global Security—a 'gold standard' ranking system that resulted from a massive effort drawing on

top expertise—that placed the US first and the UK second, whereas many countries considered to be poorly prepared—such as Bhutan or Laos—have had very few COVID-19 deaths.

16. HHP 2021;36(3):239–48

How workers respond to social rewards: evidence from community health workers in Uganda

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This paper investigates the effect of a non-financial incentive—a competitive annual award—on community health workers' (CHWs) performance, an issue in the public health literature that has not been explored to its potential. Combining data on a competitive social 'Best CHW' award with the monthly performance of 4050 CHWs across Uganda, we examined if introducing social recognition awards improved the performance of CHWs. In contrast to predominant explanations about the effect of awards on motivation, our first multilevel mixed-effect models found that an award within a branch (consisting of 30 CHWs) was negatively associated with the performance of the local peers of the winning CHW. Models focused on non-winning branch offices revealed two additional findings. First, a branch showed underperformance if a CHW from any of the three neighbouring branches won an award in the previous year, with average monthly performance scores dropping by 27 percentage points. Second, this negative association was seen only in the top 50th percentile of CHWs. The bottom 50th percentile of CHWs exhibited increased performance by 13 percentage points. These counter-intuitive results suggest that the negative response from high performers might be explained by their frustration of not winning the award or by emotions such as envy and jealousy generated by negative social comparisons. Our results suggest that more fine-grained examination of data pertaining to motivators for CHWs in low-income countries is needed. Motivational incentives like awards may need to be customized for higher- and lower performing CHWs.

17. HHP 2021;36(4):572–84

Does community-based health insurance improve access to care in sub-Saharan Africa? A rapid review

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In sub-Saharan African countries, out-of-pocket payments can be a major barrier to accessing appropriate healthcare services. Community-based health insurance (CBHI) has emerged as a context-appropriate risk-pooling mechanism to provide some financial protection to populations without access to formal health insurance. The aim of this rapid review was to examine the peer-reviewed literature on the impact of CBHI on the use of healthcare services as well as its capacity to improve equity in the use of healthcare between different socio-economic groups. A systematic search of three electronic databases (Pubmed, Cochrane Library and Littérature en Santé) was performed. Data were extracted on scheme and study characteristics, as well as the impact of the schemes on relevant outcomes. Sixteen publications met the inclusion criteria, studying schemes from seven different countries. They provide strong evidence that community-based health insurance can contribute to improving access to outpatient care and weak evidence that they improve access to inpatient care. There was low evidence on their capacity to improve equity in access to healthcare among insured members. In the absence of sufficient public spending for healthcare, such schemes may be able to provide some valuable benefits for communities with limited access to primary-level care in sub-Saharan Africa. The overall high risk of bias of the studies and the wide existing variety of insurance arrangements suggest caution in generalizing these results. These findings need to be validated and further developed by rigorous studies.

18. HHP 2021;36(5):695–706

How much healthcare is wasted? A cross-sectional study of outpatient overprovision in private-for-profit and faith-based health facilities in Tanzania

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Overprovision—healthcare whose harm exceeds its benefit—is of increasing concern in low- and middle-income countries, where the growth of the private-for-profit sector may amplify incentives for providing unnecessary care, and achieving universal health coverage will require efficient resource use. Measurement of overprovision has conceptual and practical challenges. We present a framework to conceptualize and measure overprovision, comparing for-profit and not-for-profit private outpatient facilities across 18 of mainland Tanzania's 22 regions. We developed a novel conceptualization of three harms of overprovision: economic (waste of resources), public health (unnecessary use of antimicrobial agents risking development of resistant organisms) and clinical (high risk of harm to individual patients). Standardized patients (SPs) visited 227 health facilities (99 for-profit and 128 not-for-profit) between May 3 and June 12, 2018, completing 909 visits and presenting 4 cases: asthma, non-malarial febrile illness, tuberculosis and upper respiratory tract infection. Tests and treatments prescribed were categorized as necessary or unnecessary, and unnecessary care was classified by type of harm(s). Fifty-three percent of 1995 drugs prescribed and 43% of 891 tests ordered were unnecessary. At the patient-visit level, 81% of SPs received unnecessary care, 67% received care harmful to public health (prescription of unnecessary antibiotics or antimalarials) and 6% received clinically harmful care. Thirteen percent of SPs were prescribed an antibiotic defined by WHO as 'Watch' (high priority for antimicrobial stewardship). Although overprovision was common in all sectors and geographical regions, clinically harmful care was more likely in for-profit than faith-based facilities and less common in

urban than rural areas. Overprovision was widespread in both for-profit and not-for-profit facilities, suggesting considerable waste in the private sector, not solely driven by profit. Unnecessary antibiotic or antimalarial prescriptions are of concern for the development of antimicrobial resistance. Option for policymakers to address overprovision includes the use of strategic purchasing arrangements, provider training and patient education.

19. HHP 2021;36(5):707–19

The effects of polio eradication efforts on health systems: a cross-country analysis using the Develop–Distort Dilemma
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Vertical disease control programmes have enormous potential to benefit or weaken health systems, and it is critical to understand how programmes' design and implementation impact the health systems and communities in which they operate. We use the Develop–Distort Dilemma (DDD) framework to understand how the Global Polio Eradication Initiative (GPEI) distorted or developed local health systems. We include document review and 176 interviews with respondents at the global level and across seven focus countries (Afghanistan, Bangladesh, Democratic Republic of Congo, Ethiopia, India, Indonesia and Nigeria). We use DDD domains, contextual factors and transition planning to analyse interactions between the broader context, local health systems and the GPEI to identify changes. Our analysis confirms earlier research including improved health worker, laboratory and surveillance capacity, monitoring and accountability, and efforts to reach vulnerable populations, whereas distortions include shifting attention from routine health services and distorting local payment and incentives structures. New findings highlight how global-level governance structures evolved and affected national actors; issues of country ownership, including for data systems, where the polio programme is not indigenously financed; how expectations of success have affected implementation at programme and community level; and unresolved tensions around transition planning. The decoupling of polio eradication from routine immunization, in particular, plays an outsize role in these issues as it removed attention from system strengthening. In addition to drawing lessons from the GPEI experience for other efforts, we also reflect on the use of the DDD framework for assessing programmes and their system-level impacts. Future eradication efforts should be approached carefully, and new initiatives of any kind should leverage the existing health system while considering equity, inclusion and transition from the start.

20. HHP 2021;36(5):790–810

Sin taxes and their effect on consumption, revenue generation and health improvement: a systematic literature review in Latin America
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Sin or public health taxes are excise taxes imposed on the consumption of potentially harmful goods for health [sugar-sweetened beverages (SSBs), tobacco, alcohol, among others], aiming to reduce consumption, raise additional revenue and/or improve population health. This paper assesses the extent to which sin taxes (a) can reduce consumption of potentially harmful goods, (b) raise revenue for national health systems and (c) contribute to population health in Latin America. A systematic literature review was conducted on peer-reviewed and grey literature; endpoints included: impact of raising sin taxes on consumption, ability to raise revenue for health and the possibility of population health improvements. Risk of bias for each study was assessed. The synthesis of the literature on sin tax implementation showed improvements in all three endpoints across the study countries. Following the introduction of sin taxes or by simulating their potential impact, nearly all studies explicitly reported that consumption of potentially harmful goods (mainly SSBs and tobacco) declined; revenue was found to have increased in almost all countries, suggesting that there may be additional scope for further tax increase. Simulated improvements in population health have also been shown, by demonstrating a relationship between sin tax increases and reduction in prevalence of diabetes, stroke, heart attacks and associated deaths. However, sin tax effects on health would be better quantified over the long-term. Data quality and availability challenges did place some limitations on sin tax impact assessment. Sin taxes can be effective in reducing consumption of potentially harmful goods, improve population health and generate additional revenue. Promoting further research on this topic should be a priority.

21. Plos Med 18(4):e1003604

Addressing power asymmetries in global health: Imperatives in the wake of the COVID-19 pandemic
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Summary points

- The Coronavirus Disease 2019 (COVID-19) pandemic, the Black Lives Matter and Women in Global Health movements, and ongoing calls to decolonise global health have all created space for uncomfortable but important conversations that reveal serious asymmetries of power and privilege that permeate all aspects of global health.
- In this article, we, a diverse, gender-balanced group of public (global) health researchers and practitioners (most currently living in the so-called global South), outline what we see as imperatives for change in a post-pandemic world.

- At the individual level (including and especially ourselves), we emphasise the need to emancipate and decolonise our own minds (from the colonial conditionings of our education), straddle and use our privilege responsibly (to empower others and avoid elite capture), and build “Southern” networks (to affirm our ownership of global health).
- At the organisational level, we call for global health organisations to practice real diversity and inclusion (in ways that go beyond the cosmetic), to localise their funding decisions (with people on the ground in the driving seat), and to progressively self-decentralise (and so, divest themselves of financial, epistemic, and political power).
- And at both the individual and organisational level, we emphasise the need to hold ourselves, our governments, and global health organisations accountable to these goals, and especially for governance structures and processes that reflect a commitment to real change.
- By putting a spotlight on coloniality and existing inequalities, the COVID-19 pandemic inspires calls for a more equitable world and for a decolonised and decentralised approach to global health research and practice, one that moves beyond tokenistic box ticking about diversity and inclusion into real and accountable commitments to transformative change.

22. TMIH 2021;26(6):701-14
The price of quality care: cross-sectional associations between out-of-pocket payments and quality of care in six low-income countries
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Objective: To assess the relationship between out-of-pocket (OOP) payments and primary health care quality in six low-income countries: Afghanistan, the Democratic Republic of the Congo (DRC), Haiti, Nepal, Senegal and Tanzania.
Methods: We examined the association between OOP payments and quality of care during antenatal care and sick child care visits using Service Provision Assessments data. We defined four process quality outcomes from observations of clinical care: visit duration, history-taking items asked, exam items performed, and counselling items delivered. The outcome is the total amount paid for services. We used multilevel models to test the relationship between OOP payments and each quality measure in public, private non-profit and private for-profit facilities controlling for patient, provider, and facility characteristics.
Results: Across the six countries, an average of 42% of the 29 677 observed clients paid for their visit. In the adjusted models, OOP payments were positively associated with the visit duration during sick child visits, with history-taking and exam items during antenatal care visits, and with counselling in private for-profit facilities for both visit types. These associations were strong particularly in Afghanistan, the DRC and Haiti; for example, a high-quality antenatal care visit in the DRC would cost approximately USD 1.12 more than a visit with median quality.
Conclusion: Provider effort was associated with higher OOP payments for sick child and antenatal care services in the six countries studied. While many families are already spending high amounts on care, they must often spend even more to receive higher quality care.

HIV / AIDS

23. EID 2021;27(6):1553-60
Reflections on 40 Years of AIDS
De Cock KM et al.

June 2021 marks the 40th anniversary of the first description of AIDS. On the 30th anniversary, we defined priorities as improving use of existing interventions, clarifying optimal use of HIV testing and antiretroviral therapy for prevention and treatment, continuing research, and ensuring sustainability of the response. Despite scientific and programmatic progress, the end of AIDS is not in sight. Other major epidemics over the past decade have included Ebola, arbovirus infections, and coronavirus disease (COVID-19). A benchmark against which to compare other global interventions is the HIV/AIDS response in terms of funding, coordination, and solidarity. Lessons from Ebola and HIV/AIDS are pertinent to the COVID-19 response. The fifth decade of AIDS will have to position HIV/AIDS in the context of enhanced preparedness and capacity to respond to other potential pandemics and transnational health threats.

24. Lancet 2021;397(10281):1276-92
Efficacy and safety of dolutegravir with emtricitabine and tenofovir alafenamide fumarate or tenofovir disoproxil fumarate, and efavirenz, emtricitabine, and tenofovir disoproxil fumarate HIV antiretroviral therapy regimens started in pregnancy (IMPAACT 2010/VESTED): a multicentre, open-label, randomised, controlled, phase 3 trial
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Background: Antiretroviral therapy (ART) during pregnancy is important for both maternal health and prevention of perinatal HIV-1 transmission; however adequate data on the safety and efficacy of different ART regimens that are likely to be used by pregnant women are scarce. In this trial we compared the safety and efficacy of three antiretroviral regimens

started in pregnancy: dolutegravir, emtricitabine, and tenofovir alafenamide fumarate; dolutegravir, emtricitabine, and tenofovir disoproxil fumarate; and efavirenz, emtricitabine, and tenofovir disoproxil fumarate.
Methods: This multicentre, open-label, randomised controlled, phase 3 trial was done at 22 clinical research sites in nine countries (Botswana, Brazil, India, South Africa, Tanzania, Thailand, Uganda, the USA, and Zimbabwe). Pregnant women (aged ≥18 years) with confirmed HIV-1 infection and at 14-28 weeks' gestation were eligible. Women who had previously taken antiretrovirals in the past were excluded (up to 14 days of ART during the current pregnancy was permitted), as were women known to be pregnant with multiple fetuses, or those with known fetal anomaly or a history of psychiatric illness. Participants were randomly assigned (1:1:1) using a central computerised randomisation system. Randomisation was done using permuted blocks (size six) stratified by gestational age (14-18, 19-23, and 24-28 weeks' gestation) and country. Participants were randomly assigned to receive either once-daily oral dolutegravir 50 mg, and once-daily oral fixed-dose combination emtricitabine 200 mg and tenofovir alafenamide fumarate 25 mg; once-daily oral dolutegravir 50 mg, and once-daily oral fixed-dose combination emtricitabine 200 mg and tenofovir disoproxil fumarate 300 mg; or once-daily oral fixed-dose combination of efavirenz 600 mg, emtricitabine 200 mg, and tenofovir disoproxil fumarate 300 mg. The primary efficacy outcome was the proportion of participants with viral suppression, defined as an HIV-1 RNA concentration of less than 200 copies per mL, at or within 14 days of delivery, assessed in all participants with an HIV-1 RNA result available from the delivery visit, with a prespecified non-inferiority margin of -10% in the combined dolutegravir-containing groups versus the efavirenz-containing group (superiority was tested in a pre-planned secondary analysis). Primary safety outcomes, compared pairwise among treatment groups, were the occurrence of a composite adverse pregnancy outcome (ie, either preterm delivery, the infant being born small for gestational age, stillbirth, or spontaneous abortion) in all participants with a pregnancy outcome, and the occurrence of grade 3 or higher maternal and infant adverse events in all randomised participants. This trial was registered with ClinicalTrials.gov, NCT03048422.
Findings: Between Jan 19, 2018, and Feb 8, 2019, we enrolled and randomly assigned 643 pregnant women: 217 to the dolutegravir, emtricitabine, and tenofovir alafenamide fumarate group, 215 to the dolutegravir, emtricitabine, and tenofovir disoproxil fumarate group, and 211 to the efavirenz, emtricitabine, and tenofovir disoproxil fumarate group. At enrolment, median gestational age was 21·9 weeks (IQR 18·3-25·3), the median HIV-1 RNA concentration among participants was 902·5 copies per mL (152·0-5182·5; 181 [28%] of 643 participants had HIV-1 RNA concentrations of <200 copies per mL), and the median CD4 count was 466 cells per µL (308-624). HIV-1 RNA concentrations at delivery were available for 605 (94%) participants. Of these, 395 (98%) of 405 participants in the combined dolutegravir-containing groups had viral suppression at delivery compared with 182 (91%) of 200 participants in the efavirenz, emtricitabine, and tenofovir disoproxil fumarate group (estimated difference 6·5% [95% CI 2·0 to 10·7], p=0·0052; excluding the non-inferiority margin of -10%). Significantly fewer participants in the dolutegravir, emtricitabine, and tenofovir alafenamide fumarate group (52 [24%] of 216) had a composite adverse pregnancy outcome than those in the dolutegravir, emtricitabine, and tenofovir disoproxil fumarate group (70 [33%] of 213; estimated difference -8·8% [95% CI -17·3 to -0·3], p=0·043) or the efavirenz, emtricitabine, and tenofovir disoproxil fumarate group (69 [33%] of 211; -8·6% [-17·1 to -0·1], p=0·047). The proportion of participants or infants with grade 3 or higher adverse events did not differ among the three groups. The proportion of participants who had a preterm delivery was significantly lower in the dolutegravir, emtricitabine, and tenofovir alafenamide fumarate group (12 [6%] of 208) than in the efavirenz, emtricitabine, and tenofovir disoproxil fumarate group (25 [12%] of 207; -6·3% [-11·8 to -0·9], p=0·023). Neonatal mortality was significantly higher in the efavirenz, emtricitabine, and tenofovir disoproxil fumarate group (ten [5%] of 207 infants) than in the dolutegravir, emtricitabine, and tenofovir alafenamide fumarate group (two [1%] of 208; p=0·019) or the dolutegravir, emtricitabine, and tenofovir disoproxil fumarate group (three [2%] of 202; p=0·050).
Interpretation: When started in pregnancy, dolutegravir-containing regimens had superior virological efficacy at delivery compared with the efavirenz, emtricitabine, and tenofovir disoproxil fumarate regimen. The dolutegravir, emtricitabine, and tenofovir alafenamide fumarate regimen had the lowest frequency of composite adverse pregnancy outcomes and of neonatal deaths.

25. Lancet 2021;397(10281):1316-24
Review
Eliminating postnatal HIV transmission in high incidence areas: need for complementary biomedical interventions
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The rate of mother-to-child transmission (MTCT) of HIV from breastfeeding is increasing relative to other causes of MTCT. Early effective preconception and antenatal antiretroviral therapy (ART) reduces intrauterine and intrapartum MTCT, whereas maternal post-partum HIV acquisition, untreated maternal HIV, and suboptimal postnatal maternal ART adherence increase the risk of MTCT through breastfeeding. Although the absolute number of cases of MTCT acquired through breastfeeding is decreasing, the rate of decrease is less than the decrease in intrauterine and intrapartum MTCT. Unless current strategies are universally applied, they might not be sufficient to eliminate MTCT due to breastfeeding. Urgent action is needed to evaluate and implement additional preventive biomedical strategies in high HIV prevalence and incidence settings to eliminate MTCT from breastfeeding. Preventive strategies include: pre-exposure prophylaxis in breastfeeding women who have an increased risk of acquiring HIV; postnatal reinforcement strategies, such as maternal

retesting for HIV, maternal care reinforcement, and prophylaxis in infants exposed to HIV via breastmilk; and active (vaccine) or passive immunoprophylaxis with long-acting broadly neutralising antibodies.

26. Plos Med 2021;18(5):e1003630
Financial incentives and deposit contracts to promote HIV retesting in Uganda: A randomized trial
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Background. Frequent retesting for HIV among persons at increased risk of HIV infection is critical to early HIV diagnosis of persons and delivery of combination HIV prevention services. There are few evidence-based interventions for promoting frequent retesting for HIV. We sought to determine the effectiveness of financial incentives and deposit contracts in promoting quarterly HIV retesting among adults at increased risk of HIV.
Methods and findings. In peri-urban Ugandan communities from October to December 2018, we randomized HIV–negative adults with self-reported risk to 1 of 3 strategies to promote HIV retesting: (1) no incentive; (2) cash incentives (US$7) for retesting at 3 and 6 months (total US$14); or (3) deposit contracts: participants could voluntarily deposit US$6 at baseline and at 3 months that would be returned with interest (total US$7) upon retesting at 3 and 6 months (total US$14) or lost if participants failed to retest. The primary outcome was retesting for HIV at both 3 and 6 months. Of 1,482 persons screened for study eligibility following community-based recruitment, 524 participants were randomized to either no incentive (N =180), incentives (N= 172), or deposit contracts (N= 172): median age was 25 years (IQR: 22 to 30), 44% were women, and median weekly income was US$13.60 (IQR: US$8.16 to US$21.76). Among participants randomized to deposit contracts, 24/172 (14%) made a baseline deposit, and 2/172 (1%) made a 3-month deposit. In intent-to-treat analyses, HIV retesting at both 3 and 6 months was significantly higher in the incentive arm (89/172 [52%]) than either the control arm (33/180 [18%], odds ratio (OR) 4.8, 95% CI: 3.0 to 7.7, p< 0.001) or the deposit contract arm (28/172 [16%], OR 5.5, 95% CI: 3.3 to 9.1, p< 0.001). Among those in the deposit contract arm who made a baseline deposit, 20/24 (83%) retested at 3 months; 11/24 (46%) retested at both 3 and 6 months. Among 282 participants who retested for HIV during the trial, three (1%; 95%CI: 0.2 to 3%) seroconverted: one in the incentive group and two in the control group. Study limitations include measurement of retesting at the clinic where baseline enrollment occurred, only offering clinic-based (rather than community-based) HIV retesting and lack of measurement of retesting after completion of the trial to evaluate sustained retesting behavior.
Conclusions. Offering financial incentives to high-risk adults in Uganda resulted in significantly higher HIV retesting. Deposit contracts had low uptake and overall did not increase retesting. As part of efforts to increase early diagnosis of HIV among high-risk populations, strategic use of incentives to promote retesting should receive greater consideration by HIV programs.

27. Plos Med 2021;18(5):e1003646
Effects of community-based antiretroviral therapy initiation models on HIV treatment outcomes: A systematic review and meta-analysis
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Background. Antiretroviral therapy (ART) initiation in the community and outside of a traditional health facility has the potential to improve linkage to ART, decongest health facilities, and minimize structural barriers to attending HIV services among people living with HIV (PLWH). We conducted a systematic review and meta-analysis to determine the effect of offering ART initiation in the community on HIV treatment outcomes.
Methods and findings. We searched databases between 1 January 2013 and 22 February 2021 to identify randomized controlled trials (RCTs) and observational studies that compared offering ART initiation in a community setting to offering ART initiation in a traditional health facility or alternative community setting. We assessed risk of bias, reporting of implementation outcomes, and real-world relevance and used Mantel–Haenszel methods to generate pooled risk ratios (RRs) and risk differences (RDs) with 95% confidence intervals. We evaluated heterogeneity qualitatively and quantitatively and used GRADE to evaluate overall evidence certainty. Searches yielded 4,035 records, resulting in 8 included studies—4 RCTs and 4 observational studies—conducted in Lesotho, South Africa, Nigeria, Uganda, Malawi, Tanzania, and Haiti—a total of 11,196 PLWH. Five studies were conducted in general HIV populations, 2 in key populations, and 1 in adolescents. Community ART initiation strategies included community-based HIV testing coupled with ART initiation at home or at community venues; 5 studies maintained ART refills in the community, and 4 provided refills at the health facility. All studies were pragmatic, but in most cases provided additional resources. Few studies reported on implementation outcomes. All studies showed higher ART uptake in community initiation arms compared to facility initiation and refill arms (standard of care) (RR 1.73, 95% CI 1.22 to 2.45; RD 30%, 95% CI 10% to 50%; 5 studies). Retention (RR 1.43, 95% CI 1.32 to 1.54; RD 19%, 95% CI 11% to 28%; 4 studies) and viral suppression (RR 1.31, 95% CI 1.15 to 1.49; RD 15%, 95% CI 10% to 21%; 3 studies) at 12 months were also higher in the community-based ART initiation arms. Improved uptake, retention, and viral suppression with community ART initiation were seen across population subgroups—including men, adolescents, and key populations. One study reported no difference in retention and viral suppression at 2 years. There were limited data on adherence and mortality. Social harms and adverse events appeared to be minimal and similar between community ART initiation and standard of care. One study compared ART refill strategies following community ART initiation (community versus facility refills) and found no difference in viral suppression (RD −7%, 95% CI −19% to 6%) or retention at

12 months (RD −12%, 95% CI −23% to 0.3%). This systematic review was limited by few studies for inclusion, poor-quality observational data, and short-term outcomes.
Conclusions. Based on data from a limited set of studies, community ART initiation appears to result in higher ART uptake, retention, and viral suppression at 1 year compared to facility-based ART initiation. Implementation on a wider scale necessitates broader exploration of costs, logistics, and acceptability by providers and PLWH to ensure that these effects are reproducible when delivered at scale, in different contexts, and over time.

28. Plos Med 2021;18(5):e1003651
The revolving door of HIV care: Revising the service delivery cascade to achieve the UNAIDS 95-95-95 goals
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Summary points

- Antiretroviral therapy (ART) for human immunodeficiency virus (HIV) prevents illness and death from HIV disease and transmission of HIV infection. To encourage global scale-up of ART, the Joint UN Program on HIV/AIDS (UNAIDS) issued the "95-95-95" targets for the HIV "cascade of care." These targets state that by 2030, 95% of individuals living with HIV will know their HIV status, 95% of people with diagnosed HIV infection will receive ART, and 95% of those taking ART will have achieved suppression of the virus.
- While tremendous progress has been made toward achieving these targets, substantial gaps remain. The challenge of closing the final gaps requires reconsideration of the cascade itself.
- The 95-95-95 HIV care cascade depicts a linear and unidirectional continuum of care with one starting point (HIV diagnosis) and one ending point (treatment discontination or death). This simplification of the cascade oversimplifies the complex cycle of engagement, disengagement, temporary disuptions, reengagement, and transitions in care experienced by many people living with HIV (PLHIV).
- As the proportion of PLHIV who reinitiate ART after previously starting and stopping increases, we propose to update the HIV cascade of care to better reflect actual experiences of PLHIV. The new cascade makes the cycle of engaging and reengaging in HIV care both explicit and expected.

The revised cascade will inform and prioritize efforts by communities, healthcare workers, implementers, program managers, policymakers, and donors to prevent missed clinic visits, overcome barriers to care reentry, and minimize onset of advanced HIV disease. It will also emphasize that morbidity, mortality, and onward transmission can be minimized by focusing interventions on anticipating, and then reducing, the duration of gaps in care.

29. TMIH 2021;26(6):610-20
Global, regional and national disability-adjusted life years due to HIV from 1990 to 2019: findings from the Global Burden of Disease Study 2019
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Objectives: Increasing life expectancy and decreasing mortality in patients with HIV infection are well documented. However, details of how many of the years of healthy life are damaged by HIV infection vs. good health have not been understood. We conducted this study to provide a comprehensive assessment of the levels and trends of the global burden, as measured by disability-adjusted life years (DALYs), of HIV infection.
Methods: Data on HIV-related DALY were obtained from the Global Burden of Disease Study 2019. The absolute numbers and age-standardised rates of DALYs due to HIV were reported between 1990 and 2019. Estimated annual percentage changes in age-standardised rates by sex, region and nation were calculated to quantify the temporal trends in HIV burden.
Results: Global HIV infection caused 47.63 million DALYs in 2019, presenting a 1.28-fold increase from 1990 to 2019. In 2019, years of life lost contributed to most of the total DALYs, but the increases in HIV-related years lived with disability have outpaced increases in years of life lost. The age-standardised rates of HIV-related DALYs in 2019 decreased as the sociodemographic indexes increased. The highest age-standardised rates were observed in sub-Saharan Africa, and the greatest increments over time were detected in Oceania.
Conclusions: Globally, HIV continues to cause enormous healthy life loss. The first and foremost strategy for controlling the HIV burden is still the reduction of premature deaths, and much effort needs to be exerted to mitigate the harm of comorbidities.

Malaria

30. Am J TMH 2021;104(6):1955-9
World Malaria Day 2021: Commemorating 15 Years of Contribution by the United States President's Malaria Initiative
Steketee RW et al., United States President's Malaria Initiative, Centers for Disease Control and Prevention, Atlanta, Georgia

World Malaria Day 2021 coincides with the 15th anniversary of the United States President's Malaria Initiative (PMI) and follows the first anniversary of the declaration of the coronavirus disease (COVID-19) pandemic. From 2006 to the present, the PMI has led to considerable country-managed progress in malaria prevention, care, and treatment in 24 of the highest-

burden countries in sub-Saharan Africa and three countries in the Southeast Asia Greater Mekong subregion. Furthermore, it has contributed to a 29% reduction in malaria cases and a 60% reduction in the death rates in sub-Saharan Africa. In this context of progress, substantial heterogeneity persists within and between countries, such that malaria control programs can seek subnational elimination in some populations but others still experience substantial malaria disease and death. During the COVID-19 pandemic, most malaria programs have shown resilience in delivering prevention campaigns, but many experienced important disruptions in their care and treatment of malaria illness. Confronting the COVID-19 pandemic and building on the progress against malaria will require fortitude, including strengthening the quality and ensuring the safety and resiliency of the existing programs, extending services to those currently not reached, and supporting the people and partners closest to those in need.

31. Lancet Inf Dis 2021;S1473-3099(20)30997-X. Online ahead of print.
Mass drug administration for the acceleration of malaria elimination in a region of Myanmar with artemisinin-resistant falciparum malaria: a cluster-randomised trial
McLean ARD, Smithuis FM et al., Medical Action Myanmar, Yangon, Myanmar; Myanmar Oxford Clinical Research Unit, Yangon, Myanmar; Centre for Tropical Medicine and Global Health, Nuffield Department of Clinical Medicine, University of Oxford, Oxford, UK <frank.m.smithuis@gmail.com>

Background: To contain multidrug-resistant Plasmodium falciparum, malaria elimination in the Greater Mekong subregion needs to be accelerated while current antimalarials remain effective. We evaluated the safety, effectiveness, and potential resistance selection of dihydroartemisinin-piperaquine mass drug administration (MDA) in a region with artemisinin resistance in Myanmar.
Methods: We did a cluster-randomised controlled trial in rural community clusters in Kayin (Karen) state in southeast Myanmar. Malaria prevalence was assessed using ultrasensitive quantitative PCR (uPCR) in villages that were operationally suitable for MDA (villages with community willingness, no other malaria control campaigns, and a population of 50-1200). Villages were eligible to participate if the prevalence of malaria (all species) in adults was greater than 30% or P falciparum prevalence was greater than 10% (or both). Contiguous villages were combined into clusters. Eligible clusters were paired based on P falciparum prevalence (estimates within 10%) and proximity. Community health workers provided routine malaria case management and distributed long-lasting insecticidal bed-nets (LLINs) in all clusters. Randomisation of clusters (1:1) to the MDA intervention group or control group was by public coin-flip. Group allocations were not concealed. Three MDA rounds (3 days of supervised dihydroartemisinin-piperaquine [target total dose 7 mg/kg dihydroartemisinin and 55 mg/kg piperaquine] and single low-dose primaquine [target dose 0·25 mg base per kg]) were delivered to intervention clusters. Parasitaemia prevalence was assessed at 3, 5, 10, 15, 21, 27, and 33 months. The primary outcomes were P falciparum prevalence at months 3 and 10. All clusters were included in the primary analysis. Adverse events were monitored from the first MDA dose until 1 month after the final dose, or until resolution of any adverse event occurring during follow-up. This trial is registered with ClinicalTrials.gov, NCT01872702.
Findings: Baseline uPCR malaria surveys were done in January, 2015, in 43 villages that were operationally suitable for MDA (2671 individuals). 18 villages met the eligibility criteria. Three villages in close proximity were combined into one cluster because a border between them could not be defined. This gave a total of 16 clusters in eight pairs. In the intervention clusters, MDA was delivered from March 4 to March 17, from March 30 to April 10, and from April 27 to May 10, 2015. The weighted mean absolute difference in P falciparum prevalence in the MDA group relative to the control group was -10·6% (95% CI -15·1 to -6·1; p=0·0008) at month 3 and -4·5% (-10·9 to 1·9; p=0·14) at month 10. At month 3, the weighted P falciparum prevalence was 1·4% (0·6 to 3·6; 12 of 747) in the MDA group and 10·6% (7·0 to 15·6; 56 of 485) in the control group. Corresponding prevalences at month 10 were 3·2% (1·5 to 6·8; 34 of 1013) and 5·8% (2·5 to 12·9; 33 of 515). Adverse events were reported for 151 (3·6%) of 4173 treated individuals. The most common adverse events were dizziness (n=109) and rash or itching (n=20). No treatment-related deaths occurred.
Interpretation: In this low-transmission setting, the substantial reduction in P falciparum prevalence resulting from support of community case management was accelerated by MDA. In addition to supporting community health worker case management and LLIN distribution, malaria elimination programmes should consider using MDA to reduce P falciparum prevalence rapidly in foci of higher transmission.

32. Plos Med 2021;18(4):e1003494
Collection review: Towards the elimination of Plasmodium vivax malaria: Implementing the radical cure
Thriemer K et al. <lorenz@tropmedres.ac>

Summary points

- Efforts to control Plasmodium vivax malaria have been less successful than for Plasmodium falciparum, resulting in higher prevalence of P. vivax malaria in most coendemic regions. One of the key differences between the 2 species is the ability of P. vivax to form hypnozoites causing relapses which facilitate transmission. Preventing P. vivax relapses is key for the elimination of P. vivax malaria.
- The widescale use of the radical cure to clear hypnozoites has been underutilized in most endemic countries. Two breakthroughs have increased the likelihood that the radical cure will be rolled out in P. vivax endemic regions: To clear hypnozoites, primaquine can be administered in short, high-dose regimens or a single dose of the recently licensed tafenoquine is administered. Novel technologies allow measurement of glucose-6-phosphate

dehydrogenase (G6PD) activity at the point of care. Identifying patients with low G6PD activity, not eligible for these novel regimens, is a precondition for their safe administration.

- Novel approaches to P. vivax elimination such as mass drug administrations of antimalarial drugs including 8-aminoquinolines require considerable resources and carry safety risks.
- A safe and protective P. vivax vaccine would be an asset in the elimination of P. vivax malaria but is unlikely to be available in the near future.
- Case management that includes a radical cure is currently the most promising approach to P. vivax elimination. New regimens for radical cure and the possibility to minimise the risk of haemolysis through novel G6PD tests bring up operational challenges, but if deployed wisely could have sufficient impact to eliminate if not eradicate P. vivax malaria.

Other articles in this collection:
Plos Med 2021;18(4):e1003593
Perspective: Taking on Plasmodium vivax malaria: A timely and important challenge.
von Seidlein L, White NJ
Plos Med 2021;18(4):e1003560
The changing epidemiology of Plasmodium vivax: Insights from conventional and novel surveillance tools
Auburn S et al. <sarah.auburn@menzies.edu.au>
Plos Med 2021;18(4):e1003561
The prevention and treatment of Plasmodium vivax malaria.
Chu CS, White NJ <cindy@tropmedres.ac>

Mental health

33. Lancet Global Health 2021;9(3):e291-e300

The cost-effectiveness of banning highly hazardous pesticides to prevent suicides due to pesticide self-ingestion across 14 countries: an economic modelling study
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Background. Reducing suicides is a key Sustainable Development Goal target for improving global health. Highly hazardous pesticides are among the leading causes of death by suicide in low-income and middle-income countries. National bans of acutely toxic highly hazardous pesticides have led to substantial reductions in pesticide-attributable suicides across several countries. This study evaluated the cost-effectiveness of implementing national bans of highly hazardous pesticides to reduce the burden of pesticide suicides.
Methods. A Markov model was developed to examine the costs and health effects of implementing a national ban of highly hazardous pesticides to prevent suicides due to pesticide self-poisoning, compared with a null comparator. We used WHO cost-effectiveness and strategic planning (WHO-CHOICE) methods to estimate pesticide-attributable suicide rates for 100 years from 2017. Country-specific costs were obtained from the WHO-CHOICE database and denominated in 2017 international dollars (I$), discounted at a 3% annual rate, and health effects were measured in healthy life-years gained (HLYGs). We used a demographic projection model beginning with the country population in the baseline year (2017), split by 1-year age group and sex. Country-specific data on overall suicide rates were obtained for 2017 by age and sex from the Global Burden of Disease Study 2017 Data Resources. The analysis involved 14 countries spanning low-income to high-income settings, and cost-effectiveness ratios were analysed at the country-specific level and aggregated according to country income group and the proportion of suicides due to pesticides.
Findings. Banning highly hazardous pesticides across the 14 countries studied could result in about 28 000 (95% uncertainty interval [UI] 24 000–32 000) fewer suicide deaths each year at an annual cost of I$0·007 per capita (95% UI 0·006–0·008). In the population-standardised results for the base case analysis, national bans produced cost-effectiveness ratios of $94 per HLYG (95% UI 73–123) across low-income and lower-middle-income countries and $237 per HLYG (95% UI 191–303) across upper-middle-income and high-income countries. Bans were more cost-effective in countries where a high proportion of suicides are attributable to pesticide self-poisoning, reaching a cost-effectiveness ratio of $75 per HLYG (95% UI 58–99) in two countries with proportions of more than 30%.
Interpretation. National bans of highly hazardous pesticides are a potentially cost-effective and affordable intervention for reducing suicide deaths in countries with a high burden of suicides attributable to pesticides. However, our study findings are limited by imperfect data and assumptions that could be improved upon by future studies.

34. Lancet Psychiatry 2021;8(6):535-50

Review
COVID-19 mental health impact and responses in low-income and middle-income countries: reimagining global mental health
Kola L et al., Department of Psychiatry, College of Medicine, University of Ibadan, Ibadan PMB 5116, Nigeria <lola_kola2004@yahoo.com>

Most of the global population live in low-income and middle-income countries (LMICs), which have historically received a small fraction of global resources for mental health. The COVID-19 pandemic has spread rapidly in many of these countries. This Review examines the mental health implications of the COVID-19 pandemic in LMICs in four parts. First, we review the emerging literature on the impact of the pandemic on mental health, which shows high rates of psychological distress and early warning signs of an increase in mental health disorders. Second, we assess the responses in different countries, noting the swift and diverse responses to address mental health in some countries, particularly through the development of national COVID-19 response plans for mental health services, implementation of WHO guidance, and deployment of digital platforms, signifying a welcome recognition of the salience of mental health. Third, we consider the opportunity that the pandemic presents to reimagine global mental health, especially through shifting the balance of power from high-income countries to LMICs and from narrow biomedical approaches to community-oriented psychosocial perspectives, in setting priorities for interventions and research. Finally, we present a vision for the concept of building back better the mental health systems in LMICs with a focus on key strategies; notably, fully integrating mental health in plans for universal health coverage, enhancing access to psychosocial interventions through task sharing, leveraging digital technologies for various mental health tasks, eliminating coercion in mental health care, and addressing the needs of neglected populations, such as children and people with substance use disorders. Our recommendations are relevant for the mental health of populations and functioning of health systems in not only LMICs but also high-income countries impacted by the COVID-19 pandemic, with wide disparities in quality of and access to mental health care.

35. Lancet Psychiatry 2021;8(7):630-8

Motivation and methods of external organisations investing in mental health in low-income and middle-income countries: a qualitative study

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Mental disorders (including substance use disorders, dementia, and self-harm) account for a substantial burden of disease and economic costs in low-income and middle-income countries (LMICs), yet they attract little funding. External resources are urgently needed but evidence on investments is scarce. This Health Policy paper uses 35 elite interviews and documentary analyses to examine how and why external organisations have invested in mental health in LMICs over the past three decades, and how this investment has changed over time. Four levels are examined: organisations, source countries, recipient countries, and global landscape. Organisations have invested in numerous internal and external activities. Among the various factors shaping organisational decisions, actors (ie, individuals and organisations concerned with mental health) were the most salient at all four levels. To increase external organisation investments in mental health in LMICs, organisational leadership and understanding are crucial, along with increased political support in source and recipient countries, and a stronger governance structure at the global level.

Non-communicable diseases

36. BMJ Global Health 2021;6:e005222

Associations between low HDL, sex and cardiovascular risk markers are substantially different in sub-Saharan Africa and the UK: analysis of four population studies

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Introduction. Low high-density lipoprotein (HDL) is widely used as a marker of cardiovascular disease risk, although this relationship is not causal and is likely mediated through associations with other risk factors. Low HDL is extremely common in sub-Saharan African populations, and this has often been interpreted to indicate that these populations will have increased cardiovascular risk. We aimed to determine whether the association between HDL and other cardiovascular risk factors differed between populations in sub-Saharan Africa and the UK.
Methods. We compared data from adults living in Uganda and Malawi (n=26 216) and in the UK (n=8747). We examined unadjusted and adjusted levels of HDL and applied the WHO recommended cut-offs for prevalence estimates. We used spline and linear regression to assess the relationship between HDL and other cardiovascular risk factors.
Results. HDL was substantially lower in the African than in the European studies (geometric mean 0.9–1.2 mmol/L vs 1.3–1.8 mmol/L), with African prevalence of low HDL as high as 77%. Total cholesterol was also substantially lower (geometric mean 3.3–3.9 mmol/L vs 4.6–5.4 mmol/L). In comparison with European studies the relationship between HDL and adiposity (body mass index, waist to hip ratio) was greatly attenuated in African studies and the relationship with non-HDL cholesterol reversed: in African studies low HDL was associated with lower non-HDL cholesterol. The association between sex and HDL was also different; using the WHO sex-specific definitions, low HDL was substantially more common among women (69%–77%) than men (41%–59%) in Uganda/Malawi.
Conclusion. The relationship between HDL and sex, adiposity and non-HDL cholesterol in sub-Saharan Africa is different from European populations. In sub-Saharan Africans low HDL is a marker of low overall cholesterol and sex differences are markedly attenuated. Therefore low HDL in isolation is unlikely to indicate raised cardiovascular risk and the WHO sex-based cut-offs are inappropriate.

37. HPP 2021;36(4):397–406

An innovative model for management of cardiovascular disease risk factors in the low resource setting of Cambodia

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Non-communicable diseases are increasing in developing countries and control of diabetes and hypertension is needed to reduce rates of the leading causes of morbidity and mortality, stroke and ischaemic heart disease. We evaluated a programme in Cambodia, financed by a revolving drug fund, which utilizes Peer Educators to manage diabetes and hypertension in the community. We assessed clinical outcomes and retention in the programme. For all people enrolled in the programme between 2007 and 2016, the average change in blood pressure (BP) and percentage with controlled hypertension (BP < 140/<90 mmHg) or diabetes (fasting blood glucose (BG) < 7mg/dl, post-prandial BG < 130 mg/dl, or HBA1C < 7%) was calculated every 6 months from enrolment. Attrition rate in the nth year of enrolment was calculated; associations with loss to follow-up were explored using cox regression. A total of 9139 patients enrolled between January 2007 and March 2016. For all people with hypertension, mean change in systolic and diastolic BP within the first year was −15.1 mmHg (SD 23.6, *P*< 0.0001) and −8.6 mmHg (SD 14.0, *P* < 0.0001), respectively. BP control was 50.5% at year 1, peaking at 70.6% at 5.5 years. 41.3% of people with diabetes achieved blood sugar control at 6 months and 44.4% at 6.5 years. An average of 2.3 years [SD 1.9] was spent in programme. Attrition rate within year 1 of enrolment ranged from 29.8% to 61.5% with average of 44.1% [SD 10.3] across 2008–15. Patients with hypertension were more likely to leave the program compared to those with diabetes and males more likely than females. The programme shows a substantial and sustained rate of diabetes and hypertension control for those who remain in the program and could be a model for implementation in other low middle-income settings, however, further work is needed to improve patient retention.

NTDs (Neglected tropical diseases)

38. Am J TMH 2021;Apr 26. Online ahead of print.

Baseline Mapping of Neglected Tropical Diseases in Africa: The Accelerated WHO/AFRO Mapping Project

Rebollo MP et al., Expanded Special Project for Elimination of NTDs, WHO Regional Office for Africa, Brazzaville, Republic of Congo

Mapping is a prerequisite for effective implementation of interventions against neglected tropical diseases (NTDs). Before the accelerated WHO/AFRO NTD Mapping Project was initiated in 2014, mapping efforts in many countries were frequently carried out in an ad hoc and nonstandardized fashion. In 2013, there were at least 2,200 different districts (of the 4,851 districts in the WHO African region) that still required mapping, and in many of these districts, more than one disease needed to be mapped. During its 3-year duration from January 2014 through the end of 2016, the project carried out mapping surveys for one or more NTDs in at least 2,500 districts in 37 African countries. At the end of 2016, most (90%) of the 4,851 districts had completed the WHO-required mapping surveys for the five targeted Preventive Chemotherapy (PC)-NTDs, and the impact of this accelerated WHO/AFRO NTD Mapping Project proved to be much greater than just the detailed mapping results themselves. Indeed, the AFRO Mapping Project dramatically energized and empowered national NTD programs, attracted donor support for expanding these programs, and developed both a robust NTD mapping database and data portal. By clarifying the prevalence and burden of NTDs, the project provided not only the metrics and technical framework for guiding and tracking program implementation and success but also the research opportunities for developing improved diagnostic and epidemiologic sampling tools for all 5 PC-NTDs-lymphatic filariasis, onchocerciasis, schistosomiasis, soil-transmitted helminthiasis, and trachoma.

Nutrition

39. Lancet 2021;397(10282):1388-99

Revisiting maternal and child undernutrition in low-income and middle-income countries: variable progress towards an unfinished agenda

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This is the first in a Series of two papers about progress in maternal and child undernutrition.
13 years after the first Lancet Series on maternal and child undernutrition, we reviewed the progress achieved on the basis of global estimates and new analyses of 50 low-income and middle-income countries with national surveys from around 2000 and 2015. The prevalence of childhood stunting has fallen, and linear growth faltering in early life has become less pronounced over time, markedly in middle-income countries but less so in low-income countries. Stunting and wasting remain public health problems in low-income countries, where 4·7% of children are simultaneously affected by both, a condition associated with a 4·8-times increase in mortality. New evidence shows that stunting and wasting might already be present at birth, and that the incidence of both conditions peaks in the first 6 months of life. Global low birthweight prevalence declined slowly at about 1·0% a year. Knowledge has accumulated on the short-term and long-term consequences of child undernutrition and on its adverse effect on adult human capital. Existing data on vitamin A deficiency among children suggest persisting high prevalence in Africa and south Asia. Zinc deficiency affects close to half of all

children in the few countries with data. New evidence on the causes of poor growth points towards subclinical inflammation and environmental enteric dysfunction. Among women of reproductive age, the prevalence of low body-mass index has been reduced by half in middle-income countries, but trends in short stature prevalence are less evident. Both conditions are associated with poor outcomes for mothers and their children, whereas data on gestational weight gain are scarce. Data on the micronutrient status of women are conspicuously scarce, which constitutes an unacceptable data gap. Prevalence of anaemia in women remains high and unabated in many countries. Social inequalities are evident for many forms of undernutrition in women and children, suggesting a key role for poverty and low education, and reinforcing the need for multisectoral actions to accelerate progress. Despite little progress in some areas, maternal and child undernutrition remains a major global health concern, particularly as improvements since 2000 might be offset by the COVID-19 pandemic.

The second in this Series of two papers about progress in maternal and child undernutrition:
Lancet 2021;397(10282):1400-18
Mobilising evidence, data, and resources to achieve global maternal and child undernutrition targets and the Sustainable Development Goals: an agenda for action
Heidkamp RA et al., Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA <zulfiqar.bhutta@aku.edu>

Pharmaceuticals

40. BMJ Global Health 2021;6:e005405

When technology precedes regulation: the challenges and opportunities of e-pharmacy in low-income and middle-income countries
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The recent growth of medicine sales online represents a major disruption to pharmacy markets, with COVID-19 encouraging this trend further. While e-pharmacy businesses were initially the preserve of high-income countries, in the past decade they have been growing rapidly in low-income and middle-income countries (LMICs). Public health concerns associated with e-pharmacy include the sale of prescription-only medicines without a prescription and the sale of substandard and falsified medicines. There are also non-health-related risks such as consumer fraud and lack of data privacy. However, e-pharmacy may also have the potential to improve access to medicines. Drawing on existing literature and a set of key informant interviews in Kenya, Nigeria and India, we examine the e-pharmacy regulatory systems in LMICs. None of the study countries had yet enacted a regulatory framework specific to e-pharmacy. Key regulatory challenges included the lack of consensus on regulatory models, lack of regulatory capacity, regulating sales across borders and risks of over-regulation. However, e-pharmacy also presents opportunities to enhance medicine regulation—through consolidation in the sector, and the traceability and transparency that online records offer. The regulatory process needs to be adapted to keep pace with this dynamic landscape and exploit these possibilities. This will require exploration of a range of innovative regulatory options, collaboration with larger, more compliant businesses, and engagement with global regulatory bodies. A key first step must be ensuring that national regulators are equipped with the necessary awareness and technical expertise to actively oversee this e-pharmacy activity.

41. BMJ Global Health 2021;6:e005829

Why do people purchase antibiotics over-the-counter? A qualitative study with patients, clinicians and dispensers in central, eastern and western Nepal
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Introduction. Over-the-counter (OTC) use of antibiotics contributes to the burgeoning rise in antimicrobial resistance (AMR). Drawing on qualitative research methods, this article explores the characteristics of OTC sales of antibiotic in Nepal, its drivers and implications for policy.
Methods. Data were collected in and around three tertiary hospitals in eastern, western and central Nepal. Using pre-defined guides, a mix of semi-structured interviews and focus group discussions were conducted with dispensers at drug stores, patients attending a hospital and clinicians. Interviews were audio-recorded, translated and transcribed into English and coded using a combination of an inductive and deductive approach.
Results. Drug shops were the primary location where patients engaged with health services. Interactions were brief and transactional: symptoms were described or explicit requests for specific medicine made, and money was exchanged. There were economic incentives for clients and drug stores: patients were able to save money by bypassing the formal healthcare services. Clinicians described antibiotics as easily available OTC at drug shops. Dispensing included the empirical use of broad-spectrum antibiotics, often combining multiple antibiotics, without laboratory diagnostic and drug susceptibility testing. Inappropriately short regimens (2–3 days) were also offered without follow-up. Respondents viewed OTC antibiotic as a convenient alternative to formal healthcare, the access to which was influenced by distance, time and money. Respondents also described the complexities of navigating various departments in hospitals and little confidence in the

quality of formal healthcare. Clinicians and a few dispensers expressed concerns about AMR and referred to evadable policies around antibiotics use and poor enforcement of regulation.
Conclusions. The findings point to the need for clear policy guidance and rigorous implementation of prescription-only antibiotics.

42. TMIH 2021;26(5):504-17
Review
Behavioural interventions to address rational use of antibiotics in outpatient settings of low-income and lower-middle-income countries
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Objectives: To explore the current evidence on interventions to influence antibiotic prescribing behaviour of health professionals in outpatient settings in low-income and lower-middle-income countries, an underrepresented area in the literature.
Methods: The systematic review protocol for this study was registered in PROSPERO (CRD42020170504). We searched PubMed, Embase and the Cochrane Central Register of Controlled Trials (CENTRAL) for studies relating to antibiotic prescribing of health professionals in outpatient settings in low-income and lower-middle-income countries. Behavioural interventions were classified as persuasive, enabling, restrictive, structural or bundle (mix of different interventions). In total, 3,514 abstracts were screened and 42 studies were selected for full-text review, with 13 studies included in the final narrative synthesis.
Results: Of the 13 included studies, five were conducted in Vietnam, two in Sudan, two in Tanzania, two in India and two in Kenya. All studies were conducted in the outpatient or ambulatory setting: eight took place in primary health centres, two in private clinics and three in pharmacies. Our review found that enabling or educational interventions alone may not be sufficient to overcome the ingrained incentives to link revenue generation to sales of antibiotics, and hence, their inappropriate prescription or misuse. Bundle interventions appear to be very effective at changing prescription behaviour among healthcare providers, including drug sellers and pharmacists.
Conclusions: Multi-faceted bundle interventions that combine regulation enforcement with face-to-face education and peer influence may be more effective than educational interventions alone at curbing inappropriate antibiotic use.

Public Health Emergencies

43. Lancet 2021;397(10287):1856-8
Viewpoint
Problems with traffic light approaches to public health emergencies of international concern
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The declaration of a Public Health Emergency of International Concern (PHEIC) is a key mechanism within the 2005 International Health Regulations (IHR) and the governance of global health security. The declaration is made by the Director-General of WHO, upon advice of an expert Emergency Committee and is a global call for governments to prepare for a health emergency. Since this mechanism came into existence, PHEICs have been declared six times: for H1N1 influenza (2009), polio (2014), Ebola (west Africa, 2014), Zika (2016), Ebola (DR Congo, 2019), and COVID-19 (2020). Emergency Committees met but decided not to declare PHEICs for MERS-CoV (2013), yellow fever (2016), and Ebola (DR Congo, 2018). Amidst failures of international cooperation during COVID-19, there are increasing calls to reform the IHR, particularly the PHEIC mechanism, to address problems that have arisen with past emergencies and the ongoing COVID-19 pandemic. These problems include: the Director-General and Emergency Committees hesitating to advise or declare a PHEIC for fear of being accused of over-reacting, member states pressuring WHO not to declare a PHEIC in their territory because of negative effects, concern that the international community (ie, WHO member states, non-state governments, and international organisations) does not respond sufficiently even when a PHEIC is declared, and the failure of the international community to follow the temporary recommendations that accompany a PHEIC.
The described experiences show that tiered systems do not always achieve what they set out to do.
What might happen if an outbreak emerged under such a PHEIC mechanism? A tiered system would require indicators to delineate between the tiers. Early stages of outbreaks are often characterised by the absence of good data; even if such data were available, there would be a risk of reducing the PHEIC to a technical tool rather than a normative alarm, meaning that these declarations would carry less political weight, not more.
Additionally, political pressure against moving from amber to red would probably be strong. Similar to the US National Terrorism Advisory System, many outbreaks would be stuck at the middle tier, creating the perception of a stable, ongoing situation rather than one in need of close attention and preparatory or response action. This false perception would recreate the current problem (ie, states would not take the necessary preparatory or response action), and risks reducing the power of the PHEIC. At worst, the tiers could lead to even less clarity about what states should or should not be doing.
The failure of many states to adequately respond to the COVID-19 PHEIC cannot be ignored. However, introducing a tiered mechanism will not address the main problems with the PHEIC system. These problems are political: pressure not to

declare a PHEIC, inadequate response by governments upon a PHEIC declaration, non-compliance with the temporary recommendations by the Director-General following a PHEIC, and insufficient funding to finance preparedness and response domestically and internationally. These political questions are not going to be answered with a more complex, technocratic, and diffuse mechanism.
Instead, we need to understand why many states are not responding to PHEIC declarations or abiding by WHO's recommendations, and why collaboration and assistance for preparedness and response is rarely seen in practice.
Conclusion. The PHEIC mechanism is a potentially powerful and unique normative tool within the international system to spur collective action. However, PHEICs and the IHR are not perfect. The problems with PHEIC declarations are not about insufficient gradients of a health emergency. Instead, the tension within this global health security mechanism results from states' refusal to engage in collective action in response to expert advice from an international organisation, particularly when seeing action as against short-term interests: a classic problem in international relations.
Although a non-binary PHEIC might appeal, to some governments and WHO, analysing similar efforts suggests that traffic light systems might only be useful at slowing traffic. A tiered or regional system will introduce bigger problems into global health diplomacy.

Sexual and Reproductive Health

44. BMJ Global Health 2021;6:e004475

Neonatal mortality in Kenyan hospitals: a multisite, retrospective, cohort study

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Background. Most of the deaths among neonates in low-income and middle-income countries (LMICs) can be prevented through universal access to basic high-quality health services including essential facility-based inpatient care. However, poor routine data undermines data-informed efforts to monitor and promote improvements in the quality of newborn care across hospitals.
Methods. Continuously collected routine patients' data from structured paper record forms for all admissions to newborn units (NBUs) from 16 purposively selected Kenyan public hospitals that are part of a clinical information network were analysed together with data from all paediatric admissions ages 0–13 years from 14 of these hospitals. Data are used to show the proportion of all admissions and deaths in the neonatal age group and examine morbidity and mortality patterns, stratified by birth weight, and their variation across hospitals.
Findings. During the 354 hospital months study period, 90 222 patients were admitted to the 14 hospitals contributing NBU and general paediatric ward data. 46% of all the admissions were neonates (aged 0–28 days), but they accounted for 66% of the deaths in the age group 0–13 years. 41 657 inborn neonates were admitted in the NBUs across the 16 hospitals during the study period. 4266/41 657 died giving a crude mortality rate of 10.2% (95% CI 9.97% to 10.55%), with 60% of these deaths occurring on the first-day of admission. Intrapartum-related complications was the single most common diagnosis among the neonates with birth weight of 2000 g or more who died. A threefold variation in mortality across hospitals was observed for birth weight categories 1000–1499 g and 1500–1999 g.
Interpretation. The high proportion of neonatal deaths in hospitals may reflect changing patterns of childhood mortality. Majority of newborns died of preventable causes (>95%). Despite availability of high-impact low-cost interventions, hospitals have high and very variable mortality proportions after stratification by birth weight.

45. BMJ Global Health 2021;6:e005671

Trends and projections of caesarean section rates: global and regional estimates

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Background. The caesarean section (CS) rate continues to increase across high-income, middle-income and low-income countries. We present current global and regional CS rates, trends since 1990 and projections for 2030.
Methods. We obtained nationally representative data on the CS rate from countries worldwide from 1990 to 2018. We used routine health information systems reports and population-based household surveys. Using the latest available data, we calculated current regional and subregional weighted averages. We estimated trends by a piecewise analysis of CS rates at the national, regional and global levels from 1990 to 2018. We projected the CS rate and the number of CS expected in 2030 using autoregressive integrated moving-average models.
Results. Latest available data (2010–2018) from 154 countries covering 94.5% of world live births shows that 21.1% of women gave birth by caesarean worldwide, averages ranging from 5% in sub-Saharan Africa to 42.8% in Latin America and the Caribbean. CS has risen in all regions since 1990. Subregions with the greatest increases were Eastern Asia, Western Asia and Northern Africa (44.9, 34.7 and 31.5 percentage point increase, respectively) while sub-Saharan Africa and Northern America (3.6 and 9.5 percentage point increase, respectively) had the lowest rise. Projections showed that by 2030, 28.5% of women worldwide will give birth by CS (38 million caesareans of which 33.5 million in LMIC annually) ranging from 7.1% in sub-Saharan Africa to 63.4% in Eastern Asia

Conclusion. The use of CS has steadily increased worldwide and will continue increasing over the current decade where both unmet need and overuse are expected to coexist. In the absence of global effective interventions to revert the trend, Southern Asia and sub-Saharan Africa will face a complex scenario with morbidity and mortality associated with the unmet need, the unsafe provision of CS and with the concomitant overuse of the surgical procedure which drains resources and adds avoidable morbidity and mortality. If the Sustainable Development Goals are to be achieved, comprehensively addressing the CS issue is a global priority.

46. HHP 2012;36(3):260-72

Challenges in implementing emergency obstetric care (EmOC) policies: perspectives and behaviours of frontline health workers in Uganda

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Uganda is among the sub-Saharan African Countries which continue to experience high preventable maternal mortality due to obstetric emergencies. Several Emergency Obstetric Care (EmOC) policies rolled out have never achieved their intended targets to date. To explore why upstream policy expectations were not achieved at the frontline during the MDG period, we examined the implementation of EmOC policies in Uganda by; exploring the barriers frontline implementers of EmOC policies faced, their coping behaviours and the consequences for maternal health. We conducted a retrospective exploratory qualitative study between March and June 2019 in Luwero, Iganga and Masindi districts selected based on differences in maternal mortality. Data were collected using 8 in-depth interviews with doctors and 17 midwives who provided EmOC services in Uganda's public health facilities during the MDG period. We reviewed two national maternal health policy documents and interviewed two Ministry of Health Officials on referral by participants. Data analysis was guided by the theory of Street-Level Bureaucracy (SLB). Implementation of EmOC was affected by the incompatibility of policies with implementation systems. Street-level bureaucrats were expected to offer to their continuously increasing clients, sometimes presenting late, ideal EmOC services using an incomplete and unreliable package of inputs, supplies, inadequate workforce size and skills mix. To continue performing their duties and prevent services from total collapse, frontline implementers' coping behaviours oftentimes involved improvization leading to delivery of incomplete and inconsistent EmOC service packages. This resulted in unresponsive EmOC services with mothers receiving inadequate interventions sometimes after major delays across different levels of care. We suggest that SLB theory can be enriched by reflecting on the consequences of the coping behaviours of street-level bureaucrats. Future reforms should align policies to implementation contexts and resources for optimal results.

47. HHP 2021;36(3):332–40

The effects of performance-based financing on neonatal health outcomes in Burundi, Lesotho, Senegal, Zambia and Zimbabwe

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Maternal and newborn care has been a primary focus of performance-based financing (PBF) projects, which have been piloted or implemented in 21 countries in sub-Saharan Africa since 2007. Several evaluations of PBF have demonstrated improvements to facility delivery or quality of care. However, no studies have measured the impact of PBF programmes directly on neonatal health outcomes in Africa, nor compared PBF programmes against another. We assess the impact of PBF on early neonatal health outcomes and associated health care utilization and quality in Burundi, Lesotho, Senegal, Zambia and Zimbabwe. We pooled Demographic and Health Surveys and Multiple Indicator Cluster Surveys and apply difference-in-differences analysis to estimate the effect of PBF projects supported by the World Bank on early neonatal mortality and low birthweight. We also assessed the effect of PBF on intermediate outputs that are frequently explicitly incentivized in PBF projects, including facility delivery and antenatal care utilization and quality, and caesarean section. Finally, we examined the impact among births to poor or high-risk women. We found no statistically significant impact of PBF on neonatal health outcomes, health care utilization or quality in a pooled sample. PBF was also not associated with better health outcomes in each country individually, though in some countries and among poor women PBF improved facility delivery, antenatal care utilization or antenatal care quality. There was no improvement on the health outcomes among poor or high-risk women in the five countries. PBF had no impact on early neonatal health outcomes in the five African countries studied and had limited and variable effects on the utilization and quality of neonatal health care. These findings suggest that there is a need for both a deeper assessment of PBF and for other strategies to make meaningful improvements to neonatal health outcomes.

48. HHP 2021;36(5):662–72

Poor coverage and quality for poor women: Inequalities in quality antenatal care in nine East African countries

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The use of quality antenatal care (ANC) improves maternal and newborn health outcomes. Ensuring equity in access to quality maternal health services is a priority agenda in low- and middle-income countries. This study aimed to assess inequalities in the use of quality ANC in nine East African countries using the most recent Demographic and Health Surveys.

We used two outcome variables to examine ANC service adequacy: four or more ANC contacts and quality ANC. We defined quality ANC as having six of the recommended ANC components during follow-up: blood pressure measurement, urine sample test, blood sample test, provision of iron supplements, drug for intestinal parasite and tetanus toxoid injections. We used the concentration index (CCI) to examine inequalities within and across countries. We fitted a multilevel regression model to assess the predictors of inequalities in the contact and content of ANC. This study included 87 068 women; among those 54.4% (*n* = 47 387) had four or more ANC contacts, but only 21% (*n* = 15 759) reported receiving all six services. The coverage of four or more ANC and receipt of all six services was pro-rich within and across all countries. The highest inequality in four or more ANC contacts was in Ethiopia with a CCI of 0.209, while women in Burundi had the highest inequality in coverage of all six services (CCI: 0.318). Higher education levels and media exposure were predictors of service uptake, while women who had unintended pregnancies were less likely to make four or more ANC contacts and receive six services. Interventions to improve access to quality ANC require rethinking the service delivery mechanisms in all countries. Moreover, ensuring equity in access to quality ANC requires tailoring service delivery modalities to address the social determinants of service uptake.

49. Lancet 2021;397(10285):1597
Editorial
Miscarriage: worldwide reform of care is needed

Globally, an estimated 23 million miscarriages occur every year. Despite the personal toll involved, many miscarriages—defined as the loss of pregnancy before viability—are managed in relative isolation. Private grief and misconceptions—eg, the belief that miscarriage can be caused by lifting heavy objects, or that there are no effective treatments—can lead to women and their partners feeling at fault or managing alone. Similarly, in the health-care system and broader society, the continuing conviction that miscarriages are unavoidable and the requirement, enshrined in many national guidelines, that women must have recurrent miscarriages before they are eligible for investigation or intervention has created a pervasive attitude of acceptance of miscarriage, urging women to “just try again”. This mindset underestimates, and risks dismissing, the personal physical and mental consequences of a miscarriage. It has also affected the availability and quality of care that women receive after a miscarriage and does not accurately reflect the evidence on management. A new Series of 3 papers published in The Lancet reviews this evidence on miscarriage and challenges many misconceptions. The authors, Siobhan Quenby, Arri Coomarasamy, and colleagues, call for a complete rethink of the narrative around miscarriage and a comprehensive overhaul of medical care and advice offered to women who have miscarriages.

Miscarriage is common, affecting one in ten women in their lifetime. The Series sets out clear risk factors for miscarriage: increasing age (both of men and women), body-mass index, and being of Black ethnicity. Alcohol, smoking, air pollution, pesticides, persistent stress, and night shift working also have some association with miscarriage. For women who have early pregnancy bleeding and a history of miscarriages, the Series concludes that there is high-quality evidence showing vaginal micronised progesterone increases livebirth rates. Where this treatment is unsuccessful, all providers should be able to manage miscarriages expectantly, medically with mifepristone and misoprostol, and surgically with manual vacuum aspiration kits. The provision of these interventions must be made a priority in all settings, including low-income and middle-income countries, where they are often unavailable.

Although most women who have a miscarriage will go on to carry a baby to term without complications, previous miscarriage is associated with a higher risk of preterm birth, fetal growth restriction, and other obstetric complications in subsequent pregnancies. Previous miscarriage is also associated with a higher risk of long-term health problems for women, including cardiovascular disease, venous thromboembolism, and mental health complications. These associations challenge the belief that miscarriage is a single event without wider repercussions, and the Series gives a more nuanced and graduated understanding of miscarriage, which is long overdue.

The Series authors propose a graded model of care, where after one miscarriage women should have their health needs evaluated and be provided with information and guidance to support future pregnancies. If a second miscarriage occurs, women should be offered an appointment at a miscarriage clinic for a full blood count and thyroid function tests and have extra support and early scans for reassurance in any subsequent pregnancies. After three miscarriages additional tests, including genetic testing and a pelvic ultrasound, should be offered. This model represents a substantial move away from the current fragmented system of care, with barriers to access, and better reflects the significant mental and physical event that miscarriage is to many people. Reviewing the evidence on miscarriage, however, shows that the low priority afforded to miscarriage has resulted in a deficiency of high-quality epidemiology, and trials for management and prevention that should be available to guide practice and guidelines. This is especially true in low-income settings, where most miscarriages happen.

For too long miscarriage has been minimised and often dismissed. The lack of medical progress should be shocking. Instead, there is a pervasive acceptance. Not all miscarriages could be avoided, but the insidious implication that miscarriage, like other women's reproductive health issues, including menstrual pain and menopause, should be managed with minimal medical intervention is ideological, not evidence based. This Series should catalyse a major focus on miscarriage for the medical research community, for service providers, and for policy makers. The era of telling women to “just try again” is over.

Articles of this Series:
Lancet 2021;397(10285):1658-67

Miscarriage matters: the epidemiological, physical, psychological, and economic costs of early pregnancy loss
Quenby S et al.

Lancet 2021;397(10285):1668-74
Sporadic miscarriage: evidence to provide effective care
Coomarasamy A et al.

Lancet 2021;397(10285):1675-82
Recurrent miscarriage: evidence to accelerate action
Coomarasamy A et al.

50. TMIH 2021;26(5):535-45
Know-do gaps in obstetric and newborn care quality in Uganda: a cross-sectional study in rural health facilities
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Objectives: Variable and inadequate quality of maternity care is a critical factor in persistently high rates of maternal and neonatal mortality in Uganda. We investigated whether provider quality of care deviates from knowledge and the factors associated with these 'know-do gaps' in Ugandan maternity facilities.
Methods: Data were collected from 109 providers in 40 facilities. Quality was measured using direct observations of intrapartum care, and scores were based on the percentage of essential care actions provided out of a 20-item validated quality index. Knowledge was measured based on the percentage of items that providers reported knowing to do using vignette surveys. The know-do gap was the difference between knowledge and quality. Multivariable models were used to assess the association between provider- and facility-level characteristics and knowledge, quality and know-do gaps.
Results: The average quality score was 45%, with quality varying widely within and across providers. The mean knowledge score was 70%, yielding a mean know-do gap of 25%. Know-do gaps were largest for practices related to infection control, vitals monitoring, and prevention of postpartum haemorrhage. The association between quality and knowledge scores was positive but small (P = 0.08), so know-do gaps were largest for providers with the highest knowledge scores. Greater provider training was positively associated with knowledge (P = 0.005) but not with quality (P = 0.60). Having 10 or more years of work experience was associated with higher quality scores (5.3, 95%CI: 0.6 to 10.1), while higher patient volumes were associated with lower quality scores (-2.2, 95%CI: -3.7 to - 0.07). None of the factors of provider motivation, cadre, availability of essential medicines and supplies or facility staffing were associated with quality or know-do gaps.
Conclusions: Our results indicate that, in Uganda, gaps between knowledge and quality do not appear to be explained by factors such as lack of motivation, education, training or supplies. Gaps are particularly large for essential practices related to prevention of postpartum haemorrhage, a leading cause of maternal mortality in Uganda and similar settings.