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International Health Alerts October 2021 Abstracts

Child Health

1. Lancet 2021;398(10297):325-39

Mortality from gastrointestinal congenital anomalies at 264 hospitals in 74 low-income, middle-income, and high-income countries: a multicentre, international, prospective cohort study
Global PaedSurg Research Collaboration, Wright NJ et al., King's Centre for Global Health and Health Partnerships, School of Population Health and Environmental Sciences, King's College London, London, UK <naomiwright@doctors.org.uk>

Background: Congenital anomalies are the fifth leading cause of mortality in children younger than 5 years globally. Many gastrointestinal congenital anomalies are fatal without timely access to neonatal surgical care, but few studies have been done on these conditions in low-income and middle-income countries (LMICs). We compared outcomes of the seven most common gastrointestinal congenital anomalies in low-income, middle-income, and high-income countries globally, and identified factors associated with mortality.
Methods: We did a multicentre, international prospective cohort study of patients younger than 16 years, presenting to hospital for the first time with oesophageal atresia, congenital diaphragmatic hernia, intestinal atresia, gastroschisis, exomphalos, anorectal malformation, and Hirschsprung's disease. Recruitment was of consecutive patients for a minimum of 1 month between October 2018, and April 2019. We collected data on patient demographics, clinical status, interventions, and outcomes using the REDCap platform. Patients were followed up for 30 days after primary intervention, or 30 days after admission if they did not receive an intervention. The primary outcome was all-cause, in-hospital mortality for all conditions combined and each condition individually, stratified by country income status. We did a complete case analysis.
Findings: We included 3849 patients with 3975 study conditions (560 with oesophageal atresia, 448 with congenital diaphragmatic hernia, 681 with intestinal atresia, 453 with gastroschisis, 325 with exomphalos, 991 with anorectal malformation, and 517 with Hirschsprung's disease) from 264 hospitals (89 in high-income countries, 166 in middle-income countries, and nine in low-income countries) in 74 countries. Of the 3849 patients, 2231 (58·0%) were male. Median gestational age at birth was 38 weeks (IQR 36-39) and median bodyweight at presentation was 2·8 kg (2·3-3·3). Mortality among all patients was 37 (39·8%) of 93 in low-income countries, 583 (20·4%) of 2860 in middle-income countries, and 50 (5·6%) of 896 in high-income countries (p<0·0001 between all

country income groups). Gastroschisis had the greatest difference in mortality between country income strata (nine [90·0%] of ten in low-income countries, 97 [31·9%] of 304 in middle-income countries, and two [1·4%] of 139 in high-income countries; p≤0·0001 between all country income groups). Factors significantly associated with higher mortality for all patients combined included country income status (low-income vs high-income countries, risk ratio 2·78 [95% CI 1·88-4·11], p<0·0001; middle-income vs high-income countries, 2·11 [1·59-2·79], p<0·0001), sepsis at presentation (1·20 [1·04-1·40], p=0·016), higher American Society of Anesthesiologists (ASA) score at primary intervention (ASA 4-5 vs ASA 1-2, 1·82 [1·40-2·35], p<0·0001; ASA 3 vs ASA 1-2, 1·58, [1·30-1·92], p<0·0001]), surgical safety checklist not used (1·39 [1·02-1·90], p=0·035), and ventilation or parenteral nutrition unavailable when needed (ventilation 1·96, [1·41-2·71], p=0·0001; parenteral nutrition 1·35, [1·05-1·74], p=0·018). Administration of parenteral nutrition (0·61, [0·47-0·79], p=0·0002) and use of a peripherally inserted central catheter (0·65 [0·50-0·86], p=0·0024) or percutaneous central line (0·69 [0·48-1·00], p=0·049) were associated with lower mortality. Interpretation: Unacceptable differences in mortality exist for gastrointestinal congenital anomalies between low-income, middle-income, and high-income countries. Improving access to quality neonatal surgical care in LMICs will be vital to achieve Sustainable Development Goal 3.2 of ending preventable deaths in neonates and children younger than 5 years by 2030.

2. Lancet 2021;398(10299):503–21

Measuring routine childhood vaccination coverage in 204 countries and territories, 1980–2019: a systematic analysis for the Global Burden of Disease Study 2020, Release 1

GBD 2020, Release 1, Vaccine Coverage Collaborators, Lim SS et al., Institute for Health Metrics and Evaluation, University of Washington, Seattle, WA, USA <stevelim@uw.edu>

Background Measuring routine childhood vaccination is crucial to inform global vaccine policies and programme implementation, and to track progress towards targets set by the Global Vaccine Action Plan (GVAP) and Immunization Agenda 2030. Robust estimates of routine vaccine coverage are needed to identify past successes and persistent vulnerabilities. Drawing from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2020, Release 1, we did a systematic analysis of global, regional, and national vaccine coverage trends using a statistical framework, by vaccine and over time.

Methods For this analysis we collated 55 326 country-specific, cohort-specific, year-specific, vaccine-specific, and dose- specific observations of routine childhood vaccination coverage between 1980 and 2019. Using spatiotemporal Gaussian process regression, we produced location-specific and year-specific estimates of 11 routine childhood vaccine coverage indicators for 204 countries and territories from 1980 to 2019, adjusting for biases in country- reported data and reflecting reported stockouts and supply disruptions. We analysed global and regional trends in coverage and numbers of zero-dose children (defined as those who never received a diphtheria-tetanus-pertussis [DTP] vaccine dose), progress towards GVAP targets, and the relationship between vaccine coverage and sociodemographic development.

Findings By 2019, global coverage of third-dose DTP (DTP3; 81·6% [95% uncertainty interval 80·4–82·7]) more than doubled from levels estimated in 1980 (39·9% [37·5–42·1]), as did global coverage of the first-dose measles- containing vaccine (MCV1; from 38·5% [35·4–41·3] in 1980 to 83·6% [82·3–84·8] in 2019). Third-dose polio vaccine (Pol3) coverage also increased, from 42·6% (41·4–44·1) in 1980 to 79·8% (78·4–81·1) in 2019, and global coverage of newer vaccines increased rapidly between 2000 and 2019. The global number of zero-dose children fell by nearly 75% between 1980 and 2019, from 56·8 million (52·6–60·9) to 14·5 million (13·4–15·9). However, over the past decade, global vaccine coverage broadly plateaued; 94 countries and territories recorded decreasing DTP3 coverage since 2010. Only 11 countries and territories were estimated to have reached the national GVAP target of at least 90% coverage for all assessed vaccines in 2019.

Interpretation After achieving large gains in childhood vaccine coverage worldwide, in much of the world this progress was stalled or reversed from 2010 to 2019. These findings underscore the

importance of revisiting routine immunisation strategies and programmatic approaches, recentring service delivery around equity and underserved populations. Strengthening vaccine data and monitoring systems is crucial to these pursuits, now and through to 2030, to ensure that all children have access to, and can benefit from, lifesaving vaccines.

3. Lancet. 2021 Aug 28;398(10302):772-785.
Global, regional, and national estimates and trends in stillbirths from 2000 to 2019: a systematic assessment.
Hug L et al., Division of Data, Analytics, Planning and Monitoring, UNICEF, New York, NY, USA. Electronic address: lhug@unicef.org.

BACKGROUND: Stillbirths are a major public health issue and a sensitive marker of the quality of care around pregnancy and birth. The UN Global Strategy for Women's, Children's and Adolescents' Health (2016-30) and the Every Newborn Action Plan (led by UNICEF and WHO) call for an end to preventable stillbirths. A first step to prevent stillbirths is obtaining standardised measurement of stillbirth rates across countries. We estimated stillbirth rates and their trends for 195 countries from 2000 to 2019 and assessed progress over time.
METHODS: For a systematic assessment, we created a dataset of 2833 country-year datapoints from 171 countries relevant to stillbirth rates, including data from registration and health information systems, household-based surveys, and population-based studies. After data quality assessment and exclusions, we used 1531 datapoints to estimate country-specific stillbirth rates for 195 countries from 2000 to 2019 using a Bayesian hierarchical temporal sparse regression model, according to a definition of stillbirth of at least 28 weeks' gestational age. Our model combined covariates with a temporal smoothing process such that estimates were informed by data for country-periods with high quality data, while being based on covariates for country-periods with little or no data on stillbirth rates. Bias and additional uncertainty associated with observations based on alternative stillbirth definitions and source types, and observations that were subject to non-sampling errors, were included in the model. We compared the estimated stillbirth rates and trends to previously reported mortality estimates in children younger than 5 years.
FINDINGS: Globally in 2019, an estimated 2·0 million babies (90% uncertainty interval [UI] 1·9-2·2) were stillborn at 28 weeks or more of gestation, with a global stillbirth rate of 13·9 stillbirths (90% UI 13·5-15·4) per 1000 total births. Stillbirth rates in 2019 varied widely across regions, from 22·8 stillbirths (19·8-27·7) per 1000 total births in west and central Africa to 2·9 (2·7-3·0) in western Europe. After west and central Africa, eastern and southern Africa and south Asia had the second and third highest stillbirth rates in 2019. The global annual rate of reduction in stillbirth rate was estimated at 2·3% (90% UI 1·7-2·7) from 2000 to 2019, which was lower than the 2·9% (2·5-3·2) annual rate of reduction in neonatal mortality rate (for neonates aged <28 days) and the 4·3% (3·8-4·7) annual rate of reduction in mortality rate among children aged 1-59 months during the same period. Based on the lower bound of the 90% UIs, 114 countries had an estimated decrease in stillbirth rate since 2000, with four countries having a decrease of at least 50·0%, 28 having a decrease of 25·0-49·9%, 50 having a decrease of 10·0-24·9%, and 32 having a decrease of less than 10·0%. For the remaining 81 countries, we found no decrease in stillbirth rate since 2000. Of these countries, 34 were in sub-Saharan Africa, 16 were in east Asia and the Pacific, and 15 were in Latin America and the Caribbean.
INTERPRETATION: Progress in reducing the rate of stillbirths has been slow compared with decreases in the mortality rate of children younger than 5 years. Accelerated improvements are most needed in the regions and countries with high stillbirth rates, particularly in sub-Saharan Africa. Future prevention of stillbirths needs increased efforts to raise public awareness, improve data collection, assess progress, and understand public health priorities locally, all of which require investment.

4. Lancet 2021;398(10303):870–905

Global, regional, and national progress towards Sustainable Development Goal 3.2 for neonatal and child health: all-cause and cause-specific mortality findings from the Global Burden of Disease Study 2019

GBD 2019 Under-5 Mortality Collaborators, Kassebaum NJ et al., Department of Health Metrics Sciences, University of Washington, Northeast Seattle, WA, USA < ickjk@uw.edu>

Background Sustainable Development Goal 3.2 has targeted elimination of preventable child mortality, reduction of neonatal death to less than 12 per 1000 livebirths, and reduction of death of children younger than 5 years to less than 25 per 1000 livebirths, for each country by 2030. To understand current rates, recent trends, and potential trajectories of child mortality for the next decade, we present the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2019 findings for all-cause mortality and cause-specific mortality in children younger than 5 years of age, with multiple scenarios for child mortality in 2030 that include the consideration of potential effects of COVID-19, and a novel framework for quantifying optimal child survival.

Methods We completed all-cause mortality and cause-specific mortality analyses from 204 countries and territories for detailed age groups separately, with aggregated mortality probabilities per 1000 livebirths computed for neonatal mortality rate (NMR) and under-5 mortality rate (U5MR). Scenarios for 2030 represent different potential trajectories, notably including potential effects of the COVID-19 pandemic and the potential impact of improvements preferentially targeting neonatal survival. Optimal child survival metrics were developed by age, sex, and cause of death across all GBD location-years. The first metric is a global optimum and is based on the lowest observed mortality, and the second is a survival potential frontier that is based on stochastic frontier analysis of observed mortality and Healthcare Access and Quality Index.

Findings Global U5MR decreased from 71·2 deaths per 1000 livebirths (95% uncertainty interval [UI] 68·3–74·0) in 2000 to 37·1 (33·2–41·7) in 2019 while global NMR correspondingly declined more slowly from 28·0 deaths per 1000 live births (26·8–29·5) in 2000 to 17·9 (16·3–19·8) in 2019. In 2019, 136 (67%) of 204 countries had a U5MR at or below the SDG 3.2 threshold and 133 (65%) had an NMR at or below the SDG 3.2 threshold, and the reference scenario suggests that by 2030, 154 (75%) of all countries could meet the U5MR targets, and 139 (68%) could meet the NMR targets. Deaths of children younger than 5 years totalled 9·65 million (95% UI 9·05–10·30) in 2000 and 5·05 million (4·27–6·02) in 2019, with the neonatal fraction of these deaths increasing from 39% (3·76 million [95% UI 3·53–4·02]) in 2000 to 48% (2·42 million; 2·06–2·86) in 2019. NMR and U5MR were generally higher in males than in females, although there was no statistically significant difference at the global level. Neonatal disorders remained the leading cause of death in children younger than 5 years in 2019, followed by lower respiratory infections, diarrhoeal diseases, congenital birth defects, and malaria. The global optimum analysis suggests NMR could be reduced to as low as 0·80 (95% UI 0·71–0·86) deaths per 1000 livebirths and U5MR to 1·44 (95% UI 1·27–1·58) deaths per 1000 livebirths, and in 2019, there were as many as 1·87 million (95% UI 1·35–2·58; 37% [95% UI 32–43]) of 5·05 million more deaths of children younger than 5 years than the survival potential frontier.

Interpretation Global child mortality declined by almost half between 2000 and 2019, but progress remains slower in neonates and 65 (32%) of 204 countries, mostly in sub-Saharan Africa and south Asia, are not on track to meet either SDG 3.2 target by 2030. Focused improvements in perinatal and newborn care, continued and expanded delivery of essential interventions such as vaccination and infection prevention, an enhanced focus on equity, continued focus on poverty reduction and education, and investment in strengthening health systems across the development spectrum have the potential to substantially improve U5MR. Given the widespread effects of COVID-19, considerable effort will be required to maintain and accelerate progress.

5. PLoS Med 2021, 18(6): e1003663.

Evaluation of a package of continuum of care interventions for improved maternal, newborn, and child health outcomes and service coverage in Ghana: A cluster-randomized trial.

Shibanuma A, et al., the Ghana EMBRACE Implementation Research Project Team (2021)

Background

In low- and middle-income countries (LMICs), the continuum of care (CoC) for maternal, newborn, and child health (MNCH) is not always complete. This study aimed to evaluate the effectiveness of an integrated package of CoC interventions on the CoC completion, morbidity, and mortality outcomes of woman–child pairs in Ghana.

Methods and findings

This cluster-randomized controlled trial (ISRCTN: 90618993) was conducted at 3 Health and Demographic Surveillance System (HDSS) sites in Ghana. The primary outcome was CoC completion by a woman–child pair, defined as receiving antenatal care (ANC) 4 times or more, delivery assistance from a skilled birth attendant (SBA), and postnatal care (PNC) 3 times or more. Other outcomes were the morbidity and mortality of women and children. Women received a package of interventions and routine services at health facilities (October 2014 to December 2015). The package comprised providing a CoC card for women, CoC orientation for health workers, and offering women with 24-hour stay at a health facility or a home visit within 48 hours after delivery. In the control arm, women received routine services only. Eligibility criteria were as follows: women who gave birth or had a stillbirth from September 1, 2012 to September 30, 2014 (before the trial period), from October 1, 2014 to December 31, 2015 (during the trial period), or from January 1, 2016 to December 31, 2016 (after the trial period). Health service and morbidity outcomes were assessed before and during the trial periods through face-to-face interviews. Mortality was assessed using demographic surveillance data for the 3 periods above. Mixed-effects logistic regression models were used to evaluate the effectiveness as difference in differences (DiD). For health service and morbidity outcomes, 2,970 woman–child pairs were assessed: 1,480 from the baseline survey and 1,490 from the follow-up survey. Additionally, 33,819 cases were assessed for perinatal mortality, 33,322 for neonatal mortality, and 39,205 for maternal mortality. The intervention arm had higher proportions of completed CoC (410/870 [47.1%]) than the control arm (246/620 [39.7%]; adjusted odds ratio [AOR] for DiD = 1.77; 95% confidence interval [CI]: 1.08 to 2.92; p = 0.024). Maternal complications that required hospitalization during pregnancy were lower in the intervention (95/870 [10.9%]) than in the control arm (83/620 [13.4%]) (AOR for DiD = 0.49; 95% CI: 0.29 to 0.83; p = 0.008). Maternal mortality was 8/6,163 live births (intervention arm) and 4/4,068 live births during the trial period (AOR for DiD = 1.60; 95% CI: 0.40 to 6.34; p = 0.507) and 1/4,626 (intervention arm) and 9/3,937 (control arm) after the trial period (AOR for DiD = 0.11; 95% CI: 0.11 to 1.00; p = 0.050). Perinatal and neonatal mortality was not significantly reduced. As this study was conducted in a real-world setting, possible limitations included differences in the type and scale of health facilities and the size of subdistricts, contamination for intervention effectiveness due to the geographic proximity of the arms, and insufficient number of cases for the mortality assessment.

Conclusions

This study found that an integrated package of CoC interventions increased CoC completion and decreased maternal complications requiring hospitalization during pregnancy and maternal mortality after the trial period. It did not find evidence of reduced perinatal and neonatal mortality.

6. PLoS Med (2021) 18(9): e1003814.

Postmortem investigations and identification of multiple causes of child deaths: An analysis of findings from the Child Health and Mortality Prevention Surveillance (CHAMPS) network.

Breiman RF, et al. Department of Global Health, Rollins School of Public Health, Emory University, Atlanta, Georgia, United States of America, Mail: rfbreiman@emory.edu

Background
The current burden of >5 million deaths yearly is the focus of the Sustainable Development Goal (SDG) to end preventable deaths of newborns and children under 5 years old by 2030. To accelerate progression toward this goal, data are needed that accurately quantify the leading causes of death, so that interventions can target the common causes. By adding postmortem pathology and microbiology studies to other available data, the Child Health and Mortality Prevention Surveillance (CHAMPS) network provides comprehensive evaluations of conditions leading to death, in contrast to standard methods that rely on data from medical records and verbal autopsy and report only a single underlying condition. We analysed CHAMPS data to characterize the value of considering multiple causes of death.
Methods and findings
We examined deaths identified from December 2016 through November 2020 from 7 CHAMPS sites (in Bangladesh, Ethiopia, Kenya, Mali, Mozambique, Sierra Leone, and South Africa), including 741 neonatal, 278 infant, and 241 child <5 years deaths for which results from Determination of Cause of Death (DeCoDe) panels were complete. DeCoDe panelists included all conditions in the causal chain according to the ICD-10 guidelines and assessed if prevention or effective management of the condition would have prevented the death. We analyzed the distribution of all conditions listed as causal, including underlying, antecedent, and immediate causes of death. Among 1,232 deaths with an underlying condition determined, we found a range of 0 to 6 (mean 1.5, IQR 0 to 2) additional conditions in the causal chain leading to death. While pathology provides very helpful clues, we cannot always be certain that conditions identified led to death or occurred in an agonal stage of death. For neonates, preterm birth complications (most commonly respiratory distress syndrome) were the most common underlying condition (n = 282, 38%); among those with preterm birth complications, 256 (91%) had additional conditions in causal chains, including 184 (65%) with a different preterm birth complication, 128 (45%) with neonatal sepsis, 69 (24%) with lower respiratory infection (LRI), 60 (21%) with meningitis, and 25 (9%) with perinatal asphyxia/hypoxia. Of the 278 infant deaths, 212 (79%) had ≥1 additional cause of death (CoD) beyond the underlying cause. The 2 most common underlying conditions in infants were malnutrition and congenital birth defects; LRI and sepsis were the most common additional conditions in causal chains, each accounting for approximately half of deaths with either underlying condition. Of the 241 child deaths, 178 (75%) had ≥1 additional condition. Among 46 child deaths with malnutrition as the underlying condition, all had ≥1 other condition in the causal chain, most commonly sepsis, followed by LRI, malaria, and diarrheal disease. Including all positions in the causal chain for neonatal deaths resulted in 19-fold and 11-fold increases in attributable roles for meningitis and LRI, respectively. For infant deaths, the proportion caused by meningitis and sepsis increased by 16-fold and 11-fold, respectively; for child deaths, sepsis and LRI are increased 12-fold and 10-fold, respectively. While comprehensive CoD determinations were done for a substantial number of deaths, there is potential for bias regarding which deaths in surveillance areas underwent minimally invasive tissue sampling (MITS), potentially reducing representativeness of findings.
Conclusions
Including conditions that appear anywhere in the causal chain, rather than considering underlying condition alone, markedly changed the proportion of deaths attributed to various diagnoses, especially LRI, sepsis, and meningitis. While CHAMPS methods cannot determine when 2 conditions cause death independently or may be synergistic, our findings suggest that considering the chain of events leading to death can better guide research and prevention priorities aimed at reducing child deaths.

7. PLoS Med (2021) 18(9): e1003787.
Gram-negative neonatal sepsis in low- and lower-middle-income countries and WHO empirical antibiotic recommendations: A systematic review and meta-analysis.
Wen SCH, et al. Centre for Clinical Research, University of Queensland, Brisbane, Queensland, Australia. Mail: Sophie.wen@health.qld.gov.au

Background
Neonatal sepsis is a significant global health issue associated with marked regional disparities in mortality. Antimicrobial resistance (AMR) is a growing concern in Gram-negative organisms, which increasingly predominate in neonatal sepsis, and existing WHO empirical antibiotic recommendations may no longer be appropriate. Previous systematic reviews have been limited to specific low- and middle-income countries. We therefore completed a systematic review and meta-analysis of available data from all low- and lower-middle-income countries (LLMICs) since 2010, with a focus on regional differences in Gram-negative infections and AMR.
Methods and findings
All studies published from 1 January 2010 to 21 April 2021 about microbiologically confirmed bloodstream infections or meningitis in neonates and AMR in LLMICs were assessed for eligibility. Small case series, studies with a small number of Gram-negative isolates (<10), and studies with a majority of isolates prior to 2010 were excluded. Main outcomes were pooled proportions of Escherichia coli, Klebsiella, Enterobacter, Pseudomonas, Acinetobacter and AMR. We included 88 studies (4 cohort studies, 3 randomised controlled studies, and 81 cross-sectional studies) comprising 10,458 Gram-negative isolates from 19 LLMICs. No studies were identified outside of Africa and Asia. The estimated pooled proportion of neonatal sepsis caused by Gram-negative organisms was 60% (95% CI 55% to 65%). Klebsiella spp. was the most common, with a pooled proportion of 38% of Gram-negative sepsis (95% CI 33% to 43%). Regional differences were observed, with higher proportions of Acinetobacter spp. in Asia and Klebsiella spp. in Africa. Resistance to aminoglycosides and third-generation cephalosporins ranged from 42% to 69% and from 59% to 84%, respectively. Study limitations include significant heterogeneity among included studies, exclusion of upper-middle-income countries, and potential sampling bias, with the majority of studies from tertiary hospital settings, which may overestimate the burden caused by Gram-negative bacteria.
Conclusions
Gram-negative bacteria are an important cause of neonatal sepsis in LLMICs and are associated with significant rates of resistance to WHO-recommended first- and second-line empirical antibiotics. AMR surveillance should underpin region-specific empirical treatment recommendations. Meanwhile, a significant global commitment to accessible and effective antimicrobials for neonates is required.

8. TMIH 2021;26(9):1088-97
Model of care, Noma Children's Hospital, northwest Nigeria
Isah S et al., Mohana Amirtharajah , Elise Farley, Adeniyi Semiyu Adetunji , Joseph Samuel , Bukola Oluyide, Karla Bil, Muhammad Shoaib, Nura Abubakar, Annette de Jong , Monique Pereboom , Annick Lenglet, Mark Sherlock
Noma Children's Hospital, Sokoto, Nigeria; Médecins Sans Frontières, Amsterdam, Netherlands; Médecins Sans Frontières, Sokoto, Nigeria; Department of Medical Microbiology, Radboud University Medical Centre, Nijmegen, The Netherlands.

The Nigerian Ministry of Health has been offering care for noma patients for many years at the Noma Children's Hospital (NCH) in Sokoto, northwest Nigeria, and Médecins Sans Frontières has supported these initiatives since 2014. The comprehensive model of care consists of four main components: acute care, care for noma sequelae, integrated hospital-based services and community-based services. The model of care is based on the limited evidence available for prevention and treatment of noma and follows WHO's protocols for acute patients and best practice guidelines for the surgical treatment of noma survivors. The model is updated continually as new evidence becomes available, including evidence generated through the operational research studies performed at NCH. By describing the model of care, we wish to share the lessons learned with other actors working in the noma and neglected tropical disease sphere in the hope of guiding programme development.

Communicable diseases

9. Am J Trop Med Hyg. 2021 Oct 11:tpmd210899. Online ahead of print.
Relative Burdens of the COVID-19, Malaria, Tuberculosis, and HIV/AIDS Epidemics in Sub-Saharan Africa.
Bell D et al., Independent Consultant, Issaquah, Washington.

COVID-19 has had considerable global impact; however, in sub-Saharan Africa, it is one of several infectious disease priorities. Prioritization is normally guided by disease burden, but the highly age-dependent nature of COVID-19 and that of other infectious diseases make comparisons challenging unless considered through metrics that incorporate life-years lost and time lived with adverse health. Therefore, we compared the 2020 mortality and disability-adjusted life-years (DALYs) lost estimates for malaria, tuberculosis, and HIV/AIDS in sub-Saharan African populations with more than 12 months of COVID-19 burden (until the end of March 2021) by applying known age-related mortality to United Nations estimates of the age structure. We further compared exacerbations of disease burden predicted from the COVID-19 public health response. Data were derived from public sources and predicted exacerbations were derived from those published by international agencies. For sub-Saharan African populations north of South Africa, the estimated recorded COVID-19 DALYs lost in 2020 were 3.7%, 2.3%, and 2.4% for tuberculosis, HIV/AIDS, and malaria, respectively. Predicted exacerbations of these diseases were greater than the estimated COVID-19 burden. Including South Africa and Lesotho, COVID-19 DALYs lost were < 12% of those for other compared diseases; furthermore, the mortality of compared diseases were dominated in all age groups younger than 65 years. This analysis suggests the relatively low impact of COVID-19. Although all four epidemics continue, tuberculosis, HIV/AIDS, and malaria remain far greater health priorities based on their disease burdens. Therefore, resource diversion to COVID-19 poses a high risk of increasing the overall disease burden and causing net harm, thereby further increasing global inequities in health and life expectancy.

10. BMJ Global Health 2021;6:e005456.Analysis
Are current preventive chemotherapy strategies for controlling and eliminating neglected tropical diseases cost-effective?
Hugo C Turner etal. hugo.turner@imperial.ac.uk

Neglected tropical diseases (NTDs) remain a significant cause of morbidity and mortality in many low-income and middle-income countries. Several NTDs, namely lymphatic filariasis, onchocerciasis, schistosomiasis, soil-transmitted helminthiases (STH) and trachoma, are predominantly controlled by preventive chemotherapy (or mass drug administration), following recommendations set by the WHO. Over one billion people are now treated for NTDs with this strategy per year. However, further investment and increased domestic healthcare spending are urgently needed to continue these programmes. Consequently, it is vital that the cost-effectiveness of preventive chemotherapy is understood. We analyse the current estimates on the cost per disability-adjusted life year (DALY) of the preventive chemotherapy strategies predominantly used for these diseases and identify key evidence gaps that require further research. Overall, the reported estimates show that preventive chemotherapy is generally cost-effective, supporting WHO recommendations. More specifically, the cost per DALY averted estimates relating to community-wide preventive chemotherapy for lymphatic filariasis and onchocerciasis were particularly favourable when compared with other public health interventions. Cost per DALY averted estimates of school-based preventive chemotherapy for schistosomiasis and STH were also generally favourable but more variable. Notably, the broader socioeconomic benefits are likely not being fully captured by the DALYs averted metric. No estimates of cost per DALY averted relating to community-wide mass antibiotic treatment for trachoma were found, highlighting the need for further research. These findings are important for informing global health policy and support the need for continuing NTD control and elimination efforts.

11. BMJ Global Health 2021;6:e006835. Commentary

Control of visceral leishmaniasis in East Africa: fragile progress, new threats.

Elin Hoffmann Dahl, et al., elin-hoffmann.dahl@oslo.msf.org

Summary box

- Significant progress has been made in reducing the global burden of visceral leishmaniasis, but new threats are on the horizon.
- Funding for elimination of visceral leishmaniasis programmes will be reduced through cuts in the UK's overseas aid budget.
- Thousands of cases may go undetected in East Africa as a result of Bio-Rad Laboratories' planned discontinuation of production of the only effective rapid test.
- A global shortage of AmBisome, a first-line treatment produced by Gilead, is looming due to COVID-19-related demand for the drug.
- The achievement of both the WHO neglected tropical diseases road map for visceral leishmaniasis by 2030 and Sustainable Development Goal 3.3 could be jeopardised.
- The UK government, Bio-Rad and Gilead must honour their commitments in order to avoid undermining decades of progress.

12. BMJ Global Health 2021;6:e005357. Original research

Unlocking the health system barriers to maximise the uptake and utilisation of molecular diagnostics in low-income and middle-income country setting.

Nyanda Elias Ntinginya et al., Correspondence to Dr Wilber Sabiiti; ws31@st-andrews.ac.uk

Background: Early access to diagnosis is crucial for effective management of any disease including tuberculosis (TB). We investigated the barriers and opportunities to maximise uptake and utilisation of molecular diagnostics in routine healthcare settings.
Methods: Using the implementation of WHO approved TB diagnostics, Xpert Mycobacterium tuberculosis/rifampicin (MTB/RIF) and Line Probe Assay (LPA) as a benchmark, we evaluated the barriers and how they could be unlocked to maximise uptake and utilisation of molecular diagnostics.
Results: Health officers representing 190 districts/counties participated in the survey across Kenya, Tanzania and Uganda. The survey findings were corroborated by 145 healthcare facility (HCF) audits and 11 policy-maker engagement workshops. Xpert MTB/RIF coverage was 66%, falling behind microscopy and clinical diagnosis by 33% and 1%, respectively. Stratified by HCF type, Xpert MTB/RIF implementation was 56%, 96% and 95% at district, regional and national referral hospital levels. LPA coverage was 4%, 3% below culture across the three countries. Out of 111 HCFs with Xpert MTB/RIF, 37 (33%) used it to full capacity, performing ≥8 tests per day of which 51% of these were level five (zonal consultant and national referral) HCFs. Likewise, 75% of LPA was available at level five HCFs. Underutilisation of Xpert MTB/RIF and LPA was mainly attributed to inadequate—utilities, 26% and human resource, 22%. Underfinancing was the main reason underlying failure to acquire molecular diagnostics. Second to underfinancing was lack of awareness with 33% healthcare administrators and 49% practitioners were unaware of LPA as TB diagnostic. Creation of a national health tax and decentralising its management was proposed by policy-makers as a booster of domestic financing needed to increase access to diagnostics.
Conclusion: Our findings suggest higher uptake and utilisation of molecular diagnostics at tertiary level HCFs contrary to the WHO recommendation. Country-led solutions are crucial for unlocking barriers to increase access to diagnostics.

13. TMIH 2021;26(10):1210-9
Review: Factors associated with pyomyositis: A systematic review and meta-analysis
Ngor C et al., School of Public Health, The University of Queensland, Brisbane, Qld, Australia

Objectives: Pyomyositis, an acute bacterial infection of skeletal muscle usually resulting in abscess formation, is well recognised in tropical regions where it can account for up to 4% of adult surgical admissions. It is increasingly being reported from high-income temperate countries. Pyomyositis occurs across all ages and in both sexes. Mortality ranges from 1% to 23%. Many risk factors have been suggested. We aimed to identify factors associated with pyomyositis.
Methods: We undertook a systematic review and meta-analysis, using PubMed, EMBASE, Scopus and the Cochrane Library and hand-searching published papers. The random-effects model meta-analysis was used to calculate pooled estimated odd ratios with the corresponding 95% confidence interval.
Results: All studies in the systematic review (n = 25) and the meta-analysis (n = 12) were hospital-based. Seven only included children. Relatively few studies have been published in the last decade, the majority of which are from high-income temperate settings. Staphylococcus aureus was the main organism isolated. Males under the age of 20 predominated, and mortality of up to 20% was reported. Factors associated with pyomyositis were HIV infection (OR = 4.82; 95% CI: 1.67-13.92) and fulfilling an AIDS surveillance definition (OR = 6.08; 95% CI: 2.79-13.23).
Conclusions: Our meta-analysis indicated significant associations between pyomyositis infection and HIV/AIDS. Major gaps in our understanding of the epidemiology, pathogenesis, clinical presentation, and outcome remain, highlighting the need for further research and more systematic studies. Pyomyositis merits consideration as a neglected tropical disease.

14. TMIH 2021;26(10):1231-9
Control of antimicrobial resistance in Cameroon: Feasibility of implementing the National Action Plan
Elvis Tajoache Amin, Amadeus Agwenam Omeichu, Divine Mamboneh Shu , Serge Raoul Ekukole Ekome, Charles Njumkeng, Marianne Antonia Bernarda van der Sande
Global Health Systems Solutions, Douala, Cameroon; Ministry of Public Health, Cameroon; Institute of Tropical Medicine, Antwerp, Belgium; Julius Centre for Health Sciences and Primary Care, Utrecht University, Utrecht, The Netherlands.

Objectives: Rising antimicrobial resistance is a major threat worldwide. WHO has developed a Global Action Plan and has urged all countries to develop and implement a National Action Plan. We analysed the implementation of the Cameroon National Action Plan by identifying the prioritised activities and assessing possible challenges which could limit implementation.
Methods: We conducted a review of national documents on the control of antimicrobial resistance, including regulations, policies and guidelines and assessed the health system structure. Publications and other supporting documents were obtained by a systematic literature search. We applied the policy analysis triangle framework and the theory of change to analyse the National Action Plan, actors involved and the process of implementation.
Results: The National Action Plan consisted of six strategic objectives, with the first five being a direct translation of the five pillars of the Global Action Plan. The related activities were to be implemented using a phased approach with allocated targets for each year. Several gaps were identified. There was no timeline of activities set per year, the chronology of activities was not consistent, there were no activities or objectives to ensure the sustainability of the National Action Plan like creating awareness on antimicrobial resistance and the indicators for impact evaluation were not included. Among the actors involved, the Ministry of Public Health had the highest interest in the implementation as the lead stakeholder to oversee the overall implementation. However, there was no clear source of funding, and stakeholders at the primary level of the various sectors responsible for implementation were not clearly defined.
Conclusion: Despite adequate multisectoral collaboration within the prioritised activities relevant to Cameroon, more is needed for effective implementation of the National Action Plan. The timeline of

the different activities, as well as the involvement of key stakeholders at the primary level, needs to be improved. The government's overall commitment to healthcare should be increased and implementation of an action plan should commence at the district or regional level, while challenges in mobilising the necessary funds need to be overcome.

Community Health

15. BMJ Global Health 2021;6:e006578.Original research

Community-based amoxicillin treatment for fast breathing pneumonia in young infants 7–59 days old: a cluster randomised trial in rural Bangladesh, Ethiopia, India and Malawi.

Enhanced Management of Pneumonia in Community (EMPIC) Study,
Yasir B Nisar. nisary@who.int

Introduction Young infants 7–59 days old with fast breathing pneumonia presented to a primary level health facility receive a 7-day course of amoxicillin as per the WHO guideline. However, community-level health workers (CLHW) are not allowed to treat these infants. This trial evaluated the community level treatment of non-hypoxaemic young infants with fast breathing pneumonia by CLHWs.
Methods This cluster-randomised, open-label, non-inferiority trial was conducted in rural areas of Bangladesh, Ethiopia, India and Malawi. We randomly allocated clusters (first-level health facility) 1:1, stratified by the population size, to an intervention group (enhanced community case management) or control group (standard community case management). Infants aged 7–59 days with a respiratory rate of ≥60 breaths/min and oxygen saturation (SpO2) ≥90% were enrolled. In the intervention clusters, these infants were treated with a 7-day course of oral amoxicillin (according to WHO weight bands) and were regularly followed up by CLHWs. In the control clusters, CLHWs continued the standard management (assess and refer after pre-referral antibiotic dose) and followed up according to the national programme guideline. The primary outcome of treatment failure was assessed in both groups by independent outcome assessors on days 6 and 14 after enrolment. Secondary outcomes (accuracy and impact of pulse oximetry) were also assessed.
Results Between September 2016 and December 2018, we enrolled 2334 infants (1168 in intervention and 1166 in control clusters) from 208 clusters (104 intervention and 104 control). Of 2334, 22 infants with fast breathing were excluded from analysis, leaving 2312 (1155 in intervention clusters and 1157 in control clusters) for intention-to-treat analysis. The proportion of treatment failure was 5.4% (63/1155) in intervention and 6.3% (73/1157) in the control clusters, including two deaths (0.2%) in each group. The adjusted risk difference for treatment failure between the two groups was −1.0% (95% CI −3.0% to 1.1%). The secondary outcome showed that CLHWs in the intervention clusters performed all recommended steps of pulse oximetry assessment in 94% (1050/1115) of enrolled patients.
Conclusions The 7-day amoxicillin treatment for 7–59 days old non-hypoxaemic infants with fast breathing pneumonia by CLHWs was non-inferior to the currently recommended referral strategy.

16. Health Research Policy and Systems, October 2021, Vol 19, Suppl.3: 130

Community Health Workers at the Dawn of a New Era: Introduction to the series

Edited by Joseph Zulu & Henry B Perry. Correspondence: hperry2@jhu.edu
Johns Hopkins Bloomberg School of Public Health, Baltimore, USA

Background
There is now rapidly growing global awareness of the potential of large-scale community health worker (CHW) programmes not only for improving population health but, even more importantly, for accelerating the achievement of universal health coverage and eliminating readily preventable child and maternal deaths. However, these programmes face many challenges that must be overcome in order for them to reach their full potential.

Findings
This editorial introduces a series of 11 articles that provide an overview highlighting a broad range of issues facing large-scale CHW programmes. The series addresses many of them: planning, coordination and partnerships; governance, financing, roles and tasks, training, supervision, incentives and remuneration; relationships with the health system and communities; and programme performance and its assessment. Above all, CHW programmes need stronger political and financial support, and this can occur only if the potential of these programmes is more broadly recognized. The authors of the papers in this series believe that these challenges can and will be overcome—but not overnight. For this reason, the series bears the title "Community Health Workers at the Dawn of a New Era". The scientific evidence regarding the ability of CHWs to improve population health is incontrovertible, and the favourable experience with these programmes at scale when they are properly designed, implemented, and supported is compelling. CHW programmes were once seen as a second-class solution to a temporary problem, meaning that once the burden of disease from maternal and child conditions and from communicable diseases in low-income countries had been appropriately reduced, there would be no further need for CHWs. That perspective no longer holds. CHW programmes are now seen as an essential component of a high-performing healthcare system even in developed countries. Their use is growing rapidly in the United States, for instance. And CHWs are also now recognized as having a critically important role in the control of noncommunicable diseases as well as in the response to pandemics of today and tomorrow in all low-, middle-, and high-income countries throughout the world.
Conclusion
The promise of CHW programmes is too great not to provide them with the support they need to achieve their full potential. This series helps to point the way for how this support can be provided. While there have been increased calls to develop and implement large-scale CHW programmes, there has been little comprehensive documentation of these challenges, including guidance on how large-scale CHW programmes can be strengthened to better contribute to meeting health goals. A notable exception was the comprehensive monograph produced in 2014 by Perry, Crigler, and Hodgins and colleagues entitled Developing and Strengthening Community Health Worker Programs at Scale: A Reference Guide and Case Studies for Program Managers and Policy Makers.
The supplement builds on this book. It is led by the same core group that led the production of the 2014 monograph: Henry Perry, Steve Hodgins, Lauren Crigler, Simon Lewin, Claire Glenton, Karen LeBan, Christopher Colvin, and Muhammad Mahmood Afzal.

Titles of contributions in the series:
1. Introduction: tensions confronting large-scale CHW programmes
2. Planning, coordination, and partnerships
3. Programme governance
4. Programme financing
5. Roles and tasks
6. Recruitment, training, and continuing education
7. Recent advances in supervision
8. Incentives and remuneration
9. CHWs' relationships with the health system and communities
10. Programme performance and its assessment
11. CHWs leading the way to "Health for All"

17. Health Policy and Planning, 2021, Vol 36 (7): 1215 - 1235
Barriers to the utilization of community-based child and newborn health services in Ethiopia: a scoping review
Nathan P Miller, et al. Corresponding author. Department of Population and Family Health, Mailman School of Public Health, Columbia University; Health Section, UNICEF, New York. E-mail: npm2102@cumc.columbia.edu

The Ethiopian Federal Ministry of Health and partners have scaled up integrated community case management (iCCM) and community-based newborn care (CBNC), allowing health extension workers (HEWs) to manage the major causes of child and newborn death at the community level. However, low service uptake remains a key challenge. We conducted a scoping review of peer-reviewed and grey literature to assess barriers to the utilization of HEW services and to explore potential solutions. The review, which was conducted to inform the Optimizing the Health Extension Program project, which aimed to increase the utilization of iCCM and CBNC services, included 24 peer-reviewed articles and 18 grey literature documents. Demand-side barriers to utilization included lack of knowledge about the signs and symptoms of childhood illnesses and danger signs; low awareness of curative services offered by HEWs; preference for home-based care, traditional care, or religious intervention; distance, lack of transportation and cost of care seeking; the need to obtain husband's permission to seek care and opposition of traditional or religious leaders. Supply-side barriers included health post closures, drug stockouts, disrespectful care and limited skill and confidence of HEWs, particularly with regard to the management of newborn illnesses. Potential solutions included community education and demand generation activities, finding ways to facilitate and subsidize transportation to health facilities, engaging family members and traditional and religious leaders, ensuring consistent availability of services at health posts and strengthening supervision and supply chain management. Both demand generation and improvement of service delivery are necessary to achieve the expected impact of iCCM and CBNC. Key steps for improving utilization would be carrying out multifaceted demand generation activities, ensuring availability of HEWs in health posts and ensuring consistent supplies of essential commodities.
The Women's Development Army has the potential to improving linkages between HEWs and communities, but this strategy needs to be strengthened to be effective.

COVID-19

18. Lancet 2021;398(10299):522–34

Estimating global and regional disruptions to routine childhood vaccine coverage during the COVID-19 pandemic in 2020: a modelling study

Causey K et al., Institute for Health Metrics and Evaluation, University of Washington, Seattle, WA, USA < jmosser@uw.edu>

Background The COVID-19 pandemic and efforts to reduce SARS-CoV-2 transmission substantially affected health services worldwide. To better understand the impact of the pandemic on childhood routine immunisation, we estimated disruptions in vaccine coverage associated with the pandemic in 2020, globally and by Global Burden of Disease (GBD) super-region.
Methods For this analysis we used a two-step hierarchical random spline modelling approach to estimate global and regional disruptions to routine immunisation using administrative data and reports from electronic immunisation systems, with mobility data as a model input. Paired with estimates of vaccine coverage expected in the absence of COVID-19, which were derived from vaccine coverage models from GBD 2020, Release 1 (GBD 2020 R1), we estimated the number of children who missed routinely delivered doses of the third-dose diphtheria-tetanus-pertussis (DTP3) vaccine and first-dose measles-containing vaccine (MCV1) in 2020.
Findings Globally, in 2020, estimated vaccine coverage was 76·7% (95% uncertainty interval 74·3–78·6) for DTP3 and 78·9% (74·8–81·9) for MCV1, representing relative reductions of 7·7% (6·0–10·1) for DTP3 and 7·9% (5·2–11·7) for MCV1, compared to expected doses delivered in the absence of the COVID-19 pandemic. From January to December 2020, we estimated that 30·0 million (27·6–33·1) children missed doses of DTP3 and 27·2 million (23·4–32·5) children missed MCV1 doses. Compared to expected gaps in coverage for eligible children in 2020, these estimates represented an additional 8·5 million (6·5–11·6) children not routinely vaccinated with DTP3 and an additional 8·9 million (5·7–13·7) children not routinely vaccinated with MCV1 attributable to the COVID-19 pandemic. Globally,

monthly disruptions were highest in April 2020, across all GBD super-regions, with 4·6 million (4·0–5·4) children missing doses of DTP3 and 4·4 million (3·7–5·2) children missing doses of MCV1. Every GBD super-region saw reductions in vaccine coverage in March and April, with the most severe annual impacts in north Africa and the Middle East, south Asia, and Latin America and the Caribbean. We estimated the lowest annual reductions in vaccine delivery in sub-Saharan Africa, where disruptions remained minimal throughout the year. For some super-regions, including southeast Asia, east Asia, and Oceania for both DTP3 and MCV1, the high-income super-region for DTP3, and south Asia for MCV1, estimates suggest that monthly doses were delivered at or above expected levels during the second half of 2020.
Interpretation Routine immunisation services faced stark challenges in 2020, with the COVID-19 pandemic causing the most widespread and largest global disruption in recent history. Although the latest coverage trajectories point towards recovery in some regions, a combination of lagging catch-up immunisation services, continued SARS-CoV-2 transmission, and persistent gaps in vaccine coverage before the pandemic still left millions of children under-vaccinated or unvaccinated against preventable diseases at the end of 2020, and these gaps are likely to extend throughout 2021. Strengthening routine immunisation data systems and efforts to target resources and outreach will be essential to minimise the risk of vaccine-preventable disease outbreaks, reach children who missed routine vaccine doses during the pandemic, and accelerate progress towards higher and more equitable vaccination coverage over the next decade.

19. Lancet 2021;398(10303):827-8
The long road ahead for COVID-19 vaccination in Africa
Jerving S

Only 2·5% of Africans are vaccinated against COVID-19. Millions more doses will be needed to meet even modest targets and experts are sceptical of success.
It was more than 2 months after the first COVID-19 vaccine was administered in the UK that the first doses from the COVID-19 Vaccines Global Access facility (COVAX) landed on the African continent—600 000 doses shipped to Ghana at the end of February 2021.
By the end of March, only 16 million doses were delivered to 28 African countries.
The vaccine scarcity began to improve in July, when African nations received more doses that month from COVAX than the entire months of April to June combined. Donated doses began to arrive in the millions, as high-income countries that had already vaccinated substantial proportions of their populations started to slightly loosen their grip on global supplies. Even so, only 2·5% of the overall population across Africa is fully vaccinated.
The Africa Centres for Disease Control and Prevention (CDC) previously aimed to vaccinate 60% of the population on the continent—780 million people— by the end of 2022, in order to reach herd immunity. But John Nkengasong, Africa CDC's director, said during a press briefing that he doubts the notion of herd immunity is relevant anymore, given the emergence of the delta variant and the fact that COVID-19 vaccines are only modestly effective at reducing transmission. He now estimates that about 70–80% of the population will need to be vaccinated.
Some African countries have secured vaccine doses of Sinopharm and Sinovac or Russia's Sputnik V on a bilateral basis, which has allowed for higher levels of vaccination.
COVAX aims to ship about 620 million doses by the end of the year to the continent, which would vaccinate almost a quarter of the population. Much of the supply is currently coming from donations, including from the USA, the UK, and EU. The facility also signed new advance purchase agreements for doses of the Sinopharm, Sinovac, Novavax, Moderna, Johnson & Johnson, and Clover vaccines since the last forecast it made on allocations.
Separately, the USA pledged 500 million Pfizer doses to low-income and lower-middle-income countries, with 200 million of these doses expected for delivery by the end of this year through COVAX and bilaterally. What proportion of these will go to African nations is still unclear.

The AU has separately secured vaccine doses for countries to purchase. It signed a deal with Johnson & Johnson for 400 million doses, partly manufactured in South Africa, for delivery over 18 months. Upfront funding to the company came from the African Export–Import Bank and the World Bank is providing financing to countries.
Production is projected to ramp up so that in January countries are expected to receive around 25 million doses per month.
Although vaccine equity advocates encourage high-income countries to donate even more vaccines, public health officials have also cautioned these countries to donate doses with at least a 3–4-month shelf life. A handful of African nations destroyed about 450 000 expired doses after they could not administer them fast enough.
The expenses of in-country roll-outs are also often overlooked. Much of the funding available for vaccine purchase and roll-out is available in loans rather than grants, which could discourage some countries from launching large- scale roll-outs.

20. TMIH 2021;26(7):716-9
Understanding varying COVID-19 mortality rates reported in Africa compared to Europe, Americas and Asia
Okonji EF et al., School of Public Health, University of the Western Cape, Cape Town, South Africa

The SARS-CoV-2 infection, which causes the COVID-19 disease, has impacted every nation on the globe, albeit disproportionately. African countries have seen lower infection and mortality rates than most countries in the Americas Europe and Asia. In this commentary, we explore some of the factors purported to be responsible for the low COVID-19 infection and case fatality rates in Africa: low testing rate, poor documentation of cause of death, younger age population, good vitamin D status as a result of exposure to sunlight, cross-immunity from other viruses including coronaviruses, and lessons learnt from other infectious diseases such as HIV and Ebola. With the advent of a new variant of COVID-19 and inadequate roll-out of vaccines, an innovative and efficient response is needed to ramp up testing, contact tracing and accurate reporting of infection rates and cause of death in order to mitigate the spread of the infection.

Development Assistance for Health

21. Lancet. 2021 Oct 9;398(10308):1317-1343. Epub 2021 Sep 22.
Tracking development assistance for health and for COVID-19: a review of development assistance, government, out-of-pocket, and other private spending on health for 204 countries and territories, 1990-2050.
Global Burden of Disease 2020 Health Financing Collaborator Network.

BACKGROUND: The rapid spread of COVID-19 renewed the focus on how health systems across the globe are financed, especially during public health emergencies. Development assistance is an important source of health financing in many low-income countries, yet little is known about how much of this funding was disbursed for COVID-19. We aimed to put development assistance for health for COVID-19 in the context of broader trends in global health financing, and to estimate total health spending from 1995 to 2050 and development assistance for COVID-19 in 2020.
METHODS: We estimated domestic health spending and development assistance for health to generate total health-sector spending estimates for 204 countries and territories. We leveraged data from the WHO Global Health Expenditure Database to produce estimates of domestic health spending. To generate estimates for development assistance for health, we relied on project-level disbursement data from the major international development agencies' online databases and annual financial statements and reports for information on income sources. To adjust our estimates for 2020 to include disbursements related to COVID-19, we extracted project data on commitments and disbursements from a broader set of databases (because not all of the data sources used to estimate

the historical series extend to 2020), including the UN Office of Humanitarian Assistance Financial Tracking Service and the International Aid Transparency Initiative. We reported all the historic and future spending estimates in inflation-adjusted 2020 US$, 2020 US$ per capita, purchasing-power parity-adjusted US$ per capita, and as a proportion of gross domestic product. We used various models to generate future health spending to 2050.
FINDINGS: In 2019, health spending globally reached $8·8 trillion (95% uncertainty interval [UI] 8·7-8·8) or $1132 (1119-1143) per person. Spending on health varied within and across income groups and geographical regions. Of this total, $40·4 billion (0·5%, 95% UI 0·5-0·5) was development assistance for health provided to low-income and middle-income countries, which made up 24·6% (UI 24·0-25·1) of total spending in low-income countries. We estimate that $54·8 billion in development assistance for health was disbursed in 2020. Of this, $13·7 billion was targeted toward the COVID-19 health response. $12·3 billion was newly committed and $1·4 billion was repurposed from existing health projects. $3·1 billion (22·4%) of the funds focused on country-level coordination and $2·4 billion (17·9%) was for supply chain and logistics. Only $714·4 million (7·7%) of COVID-19 development assistance for health went to Latin America, despite this region reporting 34·3% of total recorded COVID-19 deaths in low-income or middle-income countries in 2020. Spending on health is expected to rise to $1519 (1448-1591) per person in 2050, although spending across countries is expected to remain varied.
INTERPRETATION: Global health spending is expected to continue to grow, but remain unequally distributed between countries. We estimate that development organisations substantially increased the amount of development assistance for health provided in 2020. Continued efforts are needed to raise sufficient resources to mitigate the pandemic for the most vulnerable, and to help curtail the pandemic for all.

Essential Drugs and Vaccines

22. Lancet 2021;398(10305):1032-3
Unitaid at 15
Samarasekera U.

Founded in 2006, Unitaid has changed the treatment of major infectious diseases in low-income countries. What will the next 15 years bring?
The organisation Unitaid has now been working on access to medicines for 15 years. Officially launched on Sept 19, 2006, at the UN General Assembly, by the Governments of Brazil, Chile, France, Norway, and the UK, Unitaid's aim was to accelerate the availability of high-quality drugs and diagnostics for patients with HIV/AIDS, malaria, and tuberculosis in LMICs.
HIV co-infections were encompassed into its scope and its current strategy for 2017–21 made women and children's health an additional priority area. Now, Unitaid is developing its new strategy for 2022–26.
When Unitaid was founded, affordability was the biggest barrier for access to effective therapies, particularly antiretrovirals.
Today Unitaid has contributed to the introduction of all antiretrovirals used in Africa. Most recently, it has helped speed up access to generic versions of paediatric and adult dolutegravir. LMICs have now been able to procure dolutegravir-based regimens for less than US$70 per person per year, compared with around $20 000 per person per year in the USA.
Unitaid's main activity is providing financial grants to global health partners to accelerate access to more effective medicines, technologies, and systems.
The agency's strategy for 2017–21 set objectives to promote innovation in health products in its focus areas, catalyse equitable access to these products, and create the conditions for scale-up to reach those in need. It reports that it is on track to meet these strategic objectives and estimates more than 110 million people will have benefited from innovative health products, an additional 560

000 additional lives will have been saved, and 17 million infections averted during this strategic period.
A key focus of the organisation now is COVID-19. Unitaid is a co-convenor of the therapeutics arm and a co-lead of the diagnostics partnership of the Access to COVID-19 Tools Accelerator. Under the therapeutics pillar, the organisation has been working on increasing access to emergency oxygen and dexamethasone in LMICs.
Unitaid has been working to anticipate issues around access to future therapeutics for COVID-19 such as tocilizumab and other monoclonal antibody treatments.
As for the future, Unitaid expects to finalise its new strategy by mid-2022. Philippe Duneton, executive director of Unitaid, says it will continue to focus on HIV/AIDS, tuberculosis, and malaria, and women and children's health.

23. TMIH 2021;26(8):862-81

Meta-Analysis: Comparative assessment of the prevalence, practices and factors associated with self-medication with antibiotics in Africa
Yeika EV, Van der Sande MAB et al., Ministry of Public Health, Yaoundé, Cameroon, Global Health, Julius Center for Health Sciences and Primary Care, Utrecht University, Utrecht, The Netherlands

Objective: To evaluate and compare the prevalence, reasons, sources and factors associated with self-medication with antibiotics (SMA) within Africa.
Methods: Systematic review and meta-analysis. An electronic search of PubMed and Google Scholar databases was performed for observational studies conducted between January 2005 and February 2020. Two reviewers independently screened abstracts and full texts using the PRISMA flowchart and performed quality assessment of eligible studies. Both qualitative and quantitative syntheses were carried out.
Results: Forty studies from 19 countries were eligible for qualitative synthesis. The prevalence of SMA in Africa ranged from 12.1% to 93.9% with a median prevalence of 55.7% (IQR 41-75%). Western Africa was the sub-region with the highest reported prevalence of 70.1% (IQR 48.3-82.1%), followed by Northern Africa with 48.1% (IQR 41.1-64.3%). We identified 27 antibiotics used for self-medication from 13 different antibiotic classes. Most frequently used antibiotics were penicillins (31 studies), tetracyclines (25 studies) and fluoroquinolones (23 studies). 41% of these antibiotics belong to the WHO Watch Group. The most frequent indications for SMA were upper respiratory tract infections (27 studies), gastrointestinal tract symptoms (25 studies) and febrile illnesses (18 studies). Common sources of antibiotics used for self-medication were community pharmacies (31 studies), family/friends (20 studies), leftover antibiotics (19 studies) and patent medicine stores (18 studies). The most frequently reported factor associated with SMA was no education/low educational status (nine studies).
Conclusions: The prevalence of SMA is high in Africa and varies across sub-regions with the highest prevalence reported in Western Africa. Drivers of SMA are complex, comprising of socio-economic factors and insufficient access to health care coupled with poorly implemented policies regulating antibiotic sales.

Eye care / Opthalmology

24. 2030 In Sight

Casey C & Qureshi B, IAPB (International Agency for the Prevention of Blindness)
Caroline Casey, President of IAPB; Babar Qureshi, Chair of IAPB

2030 In Sight offers a new approach for eye health aligned with the UN's 2030 Agenda for Sustainable Development and the leave no one behind principle. At its core, it seeks to ensure that everyone has access to the eye care and rehabilitation services they need. It is an ambitious plan – but one we are well placed to achieve together.

Importantly, 2030 In Sight builds on the great work that has already been done and the major developments in the past few years including the WHO World Report on Vision, the Lancet Global Health Commission on Global Eye Health, and the recent United Nations General Assembly resolution on vision. This comes together under 3 key elements; elevate eye health as a fundamental economic, social and development issue; integrate within wider health care and activate consumer demand and market change.

Health systems, Health Systems Financing & Health Policy

25. Health Policy and Planning, 2021, Vol 36 (6): 835–847

Looking into the performance-based financing black box: evidence from an impact evaluation in the health sector in Cameroon

Damien de Walque, et al. *Corresponding author. Development Research Group, The World Bank. E-mail: ddewalque@worldbank.org

Performance-based financing (PBF) is a complex health systems intervention aimed at improving the coverage and quality of care. Several studies have shown a positive impact of PBF on health service coverage, often coupled with improvements in quality, but relatively little is known about the mechanisms driving those results. This article presents results of a randomized impact evaluation in Cameroon designed to isolate the role of specific components of the PBF approach with four study groups: (i) PBF with explicit financial incentives linked to results, (ii) direct financing with additional resources available for health providers not linked to performance, (iii) enhanced supervision and monitoring without additional resources and (iv) a control group. Overall, results indicate that, when compared with the pure control group, PBF in Cameroon led to significant increases in utilization for several services (child and maternal vaccinations, use of modern family planning), but not for others like antenatal care visits and facility-based deliveries. In terms of quality, PBF increased the availability of inputs and equipment, qualified health workers, led to a reduction in formal and informal user fees but did not affect the content of care. However, for many positively impacted outcomes, the differences between the PBF group and the group receiving additional financing not linked to performance are not significant, suggesting that additional funding rather than the explicit incentives might be driving improvements. In contrast, the intervention group offering enhanced supervision, coaching and monitoring without additional funding did not experience significant impacts compared to the control group.

26. Health Policy and Planning, 2021, Vol 36 (6): 861-868

How do healthcare providers respond to multiple funding flows? A conceptual framework and options to align them

Edwine Barasa, Inke Mathauer, et al. *Corresponding author. Department of Health Systems Governance and Financing, World Health Organization. E-mail: mathaueri@who.int

Provider payment methods are a key health policy lever because they influence healthcare provider behaviour and affect health system objectives, such as efficiency, equity, financial protection and quality. Previous research focused on analysing individual provider payment methods in isolation, or on the actions of individual purchasers. However, purchasers typically use a mix of provider payment methods to pay healthcare providers and most health systems are fragmented with multiple purchasers. From a health provider perspective, these different payments are experienced as multiple funding flows which together send a complex set of signals about where they should focus their effort. In this article, we argue that there is a need to expand the analysis of provider payment methods to include an analysis of the interactions of multiple funding flows and the combined effect of their incentives on the provision of healthcare services. The purpose of the article is to highlight the importance of multiple funding flows to health facilities and present a conceptual framework to guide their analysis. The framework hypothesizes that when healthcare providers receive multiple

funding flows, they may find certain funding flows more favourable than others based on how these funding flows compare to each other on a range of attributes. This creates a set of incentives, and consequently, healthcare providers may alter their behaviour in three ways: resource shifting, service shifting and cost shifting. We describe these behaviours and how they may affect health system objectives. Our analysis underlines the need to align the incentives generated by multiple funding flows. To achieve this, we propose three policy strategies that relate to the governance of healthcare purchasing: reducing the fragmentation of health financing arrangements to decrease the number of multiple purchaser arrangements and funding flows; harmonizing signals from multiple funding flows; and constraining providers from responding to undesirable incentives.

27. Health Policy and Planning, 2021, Vol 36 (8): 1239 - 1245

Fifteen years later: moving forward Heller's heritage on fiscal space for health

Hélène Barroy, Sanjeev Gupta, Departement for Health Systems Governance and Financing, World Health Organization. E-mail: barroyh@who.int

Economist Peter Heller, writing a seminal paper published in Health, Policy and Planning in 2006, identified five opportunities for expanding fiscal space for health: raising revenue, reprioritizing expenditure, borrowing, using seigniorage and mobilizing external grants. The development of the initial framework marked a significant conceptual advancement in health financing, by situating health reforms within a broader macro-fiscal context. Fifteen years later, fiscal space for health is not viewed simply as a question of finding additional revenues but also as a matter of improving public financial management (PFM) in the health sector, specifically for publicly funded health systems. This paper advances the concept of budgetary space for health, which explores available resources generated through greater overall public expenditure, prioritized budget allocations, and improved PFM. The paper adds a critical component, unpacking the ways through which PFM improvements can maximize budgetary space for health. The approach fits the realities of public finances in the era of the Sustainable Development Goals. The key implication is that PFM aspects should be systematically included in assessments of budgetary space to inform more effective country dialogues between the finance and health sectors.

28. Health Policy and Planning, 2021, Vol 36 (8): 1307 - 1315

Do efficiency gains really translate into more budget for health? An assessment framework and country applications

Hélène Barroy, et al. Departement for Health Systems Governance and Financing, World Health Organization. E-mail: barroyh@who.int

Efficiency has historically been considered a key mechanism to increase the amount of available revenues to the health sector, enabling countries to expand services and benefits to progress towards universal health coverage (UHC). Country experience indicates, however, that efficiency gains do not automatically translate into greater budget for health, to additional revenues for the sector. This article proposes a framework to assess whether and how efficiency interventions are likely to increase budgetary space in health systems Based on a review of the literature and country experiences, we suggest three enabling conditions that must be met in order to transform efficiency gains into budgetary gains for health. First there must be well-defined efficiency interventions that target health system inputs, implemented over a medium-term time frame. Second, efficiency interventions must generate financial gains that are quantifiable either pre- or post-intervention. Third, public financial management systems must allow those gains to be kept within the health sector and repurposed towards priority health needs. When these conditions are not met, efficiency gains do not lead to more budgetary space for health. Rather, the gains may instead result in budget cuts that can be detrimental to health systems' outputs and ultimately disincentivize further attempts to improve efficiency in the sector. The framework, when applied, offers an opportunity for policymakers to reconcile efficiency and budget expansion goals in health.

29. TMIH 2021;26(8):1002-13
Impact of Performance-Based Financing on effective coverage for curative child health services in Burkina Faso: Evidence from a quasi-experimental design
Koulidiati JL et al., Heidelberg Institute of Global Health, University Hospital and Faculty of Medicine, Heidelberg, Germany

Objective: To evaluate the impact of Performance-Based Financing (PBF) on effective coverage of child curative health services in primary healthcare facilities in Burkina Faso.
Methods: An impact evaluation of a PBF pilot programme, using an experiment nested within a quasi-experimental design, was carried out in 12 intervention and 12 comparison districts in six regions of Burkina Faso. Across the 24 districts, primary healthcare facilities (537 both at baseline and endline) and households (baseline = 7978 endline = 7898) were surveyed. Within these households, 12 350 and 15 021 under-five-year-olds caretakers were interviewed at baseline and endline respectively. Linking service quality to service utilisation, we used difference-in-differences to estimate the impact of PBF on effective coverage of curative child health services.
Results: Our study failed to detect any effect of PBF on effective coverage. Looking specifically into quality of care indicators, we detected a positive effect of PBF on structural elements of quality of care related to general service readiness, but not on the overall facility quality score, capturing both service readiness and the content of childcare.
Conclusion: The current study makes a unique contribution to PBF literature, as this is the first study assessing PBF impact on effective coverage for curative child health services in low-income settings. The absence of any significant effects of PBF on effective coverage suggests that PBF programmes require a stronger design focus on quality of care elements especially when implemented in a context of free healthcare policy.

30. TMIH 2021;26(10):1248-55
Catastrophic costs among tuberculosis-affected households in Zimbabwe: A national health facility-based survey
Timire C et al., AIDS & TB Control Programme, Ministry of Health and Child Care, Harare, Zimbabwe

Objectives: To determine the incidence and major drivers of catastrophic costs among TB-affected households in Zimbabwe.
Methods: We conducted a nationally representative health facility-based survey with random cluster sampling among consecutively enrolled drug-susceptible (DS-TB) and drug-resistant TB (DR-TB) patients. Costs incurred and income lost due to TB illness were captured using an interviewer-administered standardised questionnaire. We used multivariable logistic regression to determine the risk factors for experiencing catastrophic costs.
Results: A total of 841 patients were enrolled and were weighted to 900 during data analysis. There were 500 (56%) males and 46 (6%) DR-TB patients. Thirty-five (72%) DR-TB patients were HIV co-infected. Overall, 80% (95% CI: 77-82) of TB patients and their households experienced catastrophic costs. The major cost driver pre-TB diagnosis was direct medical costs. Nutritional supplements were the major cost driver post-TB diagnosis, with a median cost of US$360 (IQR: 240-600). Post-TB median diagnosis costs were three times higher among DR-TB (US$1,659 [653-2,787]) than drug DS-TB-affected households (US$537 [204-1,134]). Income loss was five times higher among DR-TB than DS-TB patients. In multivariable analysis, household wealth was the only covariate that remained significantly associated with catastrophic costs: The poorest households had 16 times the odds of incurring catastrophic costs versus the wealthiest households (adjusted odds ratio [aOR: 15.7 95% CI: 7.5-33.1]).
Conclusion: The majority of TB-affected households, especially those affected by DR-TB, experienced catastrophic costs. Since the major cost drivers fall outside the healthcare system, multi-sectoral approaches to TB control and linking TB patients to social protection may reduce catastrophic costs.

31. TMIH 2021;26(10):1256-75
Rising healthcare expenditure on tuberculosis: Can India achieve the End TB goal?
Yadav J et al., Department of Health Research, National Institute of Medical Statistics, New Delhi, India

Objective: To examine the out-of-pocket expenditure (OOPE), healthcare burden, catastrophic health expenditure, hardship financing and impoverishment effects of TB treatment in India.
Methods: Data of three rounds of National Statistic Surveys 60th 2004-05, 71st 2013-14 and 75th 2017-18. Descriptive statistics, bivariate estimates and multivariate models were performed to calculate the OOPE, healthcare burden, catastrophic health expenditure, hardship financing and impoverishment using standard definitions at December 2019 price values.
Results: More than two-thirds of the TB cases are seen in the economically productive age group (14-59 years). Illiterate patients had a higher healthcare burden and OOPE. The healthcare burden, hardship financing and catastrophic health expenditure are considerably higher for those utilising private hospitals. Male patients have a higher exposure to hardship financing than female patients. Impoverishment effects are higher among Hindus and illiterate populations due to utilisation of hospitalisation services.
Conclusion: The present analysis helps to understand the trends in the financial burden of TB on households over last 15 years, thus providing evidence to policymakers for more effective channelling of resources in order to achieve a TB-free India by 2025.

HIV

32. TMIH 2021;26(9):1036-46
The NSEBA Demonstration Project: implementation of a point-of-care platform for early infant diagnosis of HIV in rural Zambia
Sutcliffe CG et al., Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

Objectives: To describe the experience and resource requirements of implementing point-of-care testing for early infant diagnosis of HIV in rural Zambia.
Methods: A demonstration project was conducted using a hub-and-spoke model in 2018-2019 at five clinics in rural Zambia. Two testing hubs were established, and all HIV-exposed infants were tested with the GeneXpert system. Data on costs, turnaround times and test results were collected.
Results: Seven hundred and eighty six tests were conducted. At the hubs, results were available a median of 2.4 (IQR: 2.1, 2.8) hours after sample collection and most mothers (84%) received same-day results. At the spoke facilities, results were available a median of 9 days (IQR: 7, 12) after sample collection and provided to the mother a median of 16 days (IQR: 10, 28) after sample collection. Eleven children tested positive, and 9 (82%) started treatment a median of 13 days (IQR: 7, 21) after sample collection and on the day mothers received results. In contrast, results from matching samples sent for routine testing were available a median of 38 days (IQR: 27, 61) after sample collection and provided to the mother a median of 91 days (IQR: 47, 135) after sample collection.
Conclusions: Implementing point-of-care testing in a network of rural health centres in Zambia required significant initial and ongoing investment in infrastructure, training and supervision. However, point-of-care testing can rapidly diagnose HIV-infected infants, so they can benefit from early treatment.

Mental Health

33. Lancet Psychiatry 2021;8(8):717-31
Review: The epidemiology of psychiatric disorders in Africa: a scoping review

Greene MC et al., Program on Forced Migration and Health, Columbia University Mailman School of Public Health, New York, NY, USA

This scoping review of population-based epidemiological studies was done to provide background information on the prevalences and distribution of psychiatric disorders in Africa for calls to broaden diversity in psychiatric genetic studies. We searched PubMed, EMBASE, and Web of Science to retrieve relevant literature in English, French, and Portuguese from Jan 1, 1984, to Aug 18, 2020. In 36 studies from 12 African countries, the lifetime prevalence ranged from 3·3% to 9·8% for mood disorders, from 5·7% to 15·8% for anxiety disorders, from 3·7% to 13·3% for substance use disorders, and from 1·0% to 4·4% for psychotic disorders. Although the prevalence of mood and anxiety disorders appears to be lower than that observed in research outside the continent, we identified similar distributions by gender, although not by age or urbanicity. This review reveals gaps in epidemiological research on psychiatric disorders and opportunities to leverage existing epidemiological and genetic research within Africa to advance our understanding of psychiatric disorders. Studies that are methodologically comparable but diverse in geographical context are needed to advance psychiatric epidemiology and provide a foundation for understanding environmental risk in genetic studies of diverse populations globally.

34. Lancet Glob Health 2021;9(10):e1465-e1470

Review: Epistemic injustice in academic global health
Bhakuni H et al., Julius Global Health, Julius Center for Health Sciences and Primary Care, University Medical Center, Utrecht University, Utrecht, Netherlands; Department of Foundations and Methods of Law, Maastricht University, Maastricht, Netherlands <h.bhakuni@umcutrecht.nl>

This Viewpoint calls attention to the pervasive wrongs related to knowledge production, use, and circulation in global health, many of which are taken for granted. We argue that common practices in academic global health (eg, authorship practices, research partnerships, academic writing, editorial practices, sensemaking practices, and the choice of audience or research framing, questions, and methods) are peppered with epistemic wrongs that lead to or exacerbate epistemic injustice. We describe two forms of epistemic wrongs, credibility deficit and interpretive marginalisation, which stem from structural exclusion of marginalised producers and recipients of knowledge. We then illustrate these forms of epistemic wrongs using examples of common practices in academic global health and show how these wrongs are linked to the pose (or positionality) and the gaze (or audience) of producers of knowledge. The epistemic injustice framework shown in this Viewpoint can help to surface, detect, communicate, make sense of, avoid, and potentially undo unfair knowledge practices in global health that are inflicted upon people in their capacity as knowers, and as producers and recipients of knowledge, owing to structural prejudices in the processes involved in knowledge production, use, and circulation in global health.

35. Lancet Psychiatry 2021;8(10):919-28

Review: Burden, impact, and needs of caregivers of children living with mental health or neurodevelopmental conditions in low-income and middle-income countries: a scoping review
Temitope Ademosu T et al., Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK; Children and Families Service, London Borough of Hackney, London, UK. <temitope.ademosu@kcl.ac.uk>

This scoping review synthesises previous research on caregivers' experiences and perspectives of caring for a child with a mental health or neurodevelopmental condition while living in low-income and middle-income countries (LMICs). 35 studies done across 15 LMICs were included in this Series paper. Most studies were done in the Africa region. Child and adolescent mental health and neurodevelopmental conditions were perceived by caregivers to have both biomedical and traditional or spiritual causes and help-seeking was aligned to these explanatory beliefs. Caregivers

commonly described reduced quality of life, which they attributed to their children's mental or neurodevelopmental condition, and additional reports of family disruption, caregiver psychological distress, and financial hardship. To strengthen mental health outcomes of young people, better mental health promotion information for caregivers is required along with improved engagement with communities and increased sensitivity to caregiver wellbeing and needs when developing interventions for children and adolescents.

36. PLoS Med (2021) 18(6): e1003621.

Effectiveness of Group Problem Management Plus, a brief psychological intervention for adults affected by humanitarian disasters in Nepal: A cluster randomized controlled trial.

Jordans MJD, et al. Corresponding author: bkohrt@gwu.edu

Background

Globally, 235 million people are impacted by humanitarian emergencies worldwide, presenting increased risk of experiencing a mental disorder. Our objective was to test the effectiveness of a brief group psychological treatment delivered by trained facilitators without prior professional mental health training in a disaster-prone setting.

Methods and findings

We conducted a cluster randomized controlled trial (cRCT) from November 25, 2018 through September 30, 2019. Participants in both arms were assessed at baseline, midline (7 weeks post-baseline, which was approximately 1 week after treatment in the experimental arm), and endline (20 weeks post-baseline, which was approximately 3 months posttreatment). The intervention was Group Problem Management Plus (PM+), a psychological treatment of 5 weekly sessions, which was compared with enhanced usual care (EUC) consisting of a family psychoeducation meeting with a referral option to primary care providers trained in mental healthcare. The setting was 72 wards (geographic unit of clustering) in eastern Nepal, with 1 PM+ group per ward in the treatment arm. Wards were eligible if they were in disaster-prone regions and residents spoke Nepali. Wards were assigned to study arms based on covariate constrained randomization. Eligible participants were adult women and men 18 years of age and older who met screening criteria for psychological distress and functional impairment. Outcomes were measured at the participant level, with assessors blinded to group assignment. The primary outcome was psychological distress assessed with the General Health Questionnaire (GHQ-12). Secondary outcomes included depression symptoms, posttraumatic stress disorder (PTSD) symptoms, “heart–mind” problems, social support, somatic symptoms, and functional impairment. The hypothesized mediator was skill use aligned with the treatment’s mechanisms of action. A total of 324 participants were enrolled in the control arm (36 wards) and 319 in the Group PM+ arm (36 wards). The overall sample (N = 611) had a median age of 45 years (range 18–91 years), 82% of participants were female, 50% had recently experienced a natural disaster, and 31% had a chronic physical illness. Endline assessments were completed by 302 participants in the control arm (36 wards) and 303 participants in the Group PM+ arm (36 wards). At the midline assessment (immediately after Group PM+ in the experimental arm), mean GHQ-12 total score was 2.7 units lower in Group PM+ compared to control (95% CI: 1.7, 3.7, $p < 0.001$), with standardized mean difference (SMD) of −0.4 (95% CI: −0.5, −0.2). At 3 months posttreatment (primary endpoint), mean GHQ-12 total score was 1.4 units lower in Group PM+ compared to control (95% CI: 0.3, 2.5, $p = 0.014$), with SMD of −0.2 (95% CI: −0.4, 0.0). Among the secondary outcomes, Group PM+ was associated with endline with a larger proportion attaining more than 50% reduction in depression symptoms (29.9% of Group PM+ arm versus 17.3% of control arm, risk ratio = 1.7, 95% CI: 1.2, 2.4, $p = 0.002$). Fewer participants in the Group PM+ arm continued to have “heart–mind” problems at endline (58.8%) compared to the control arm (69.4%), risk ratio = 0.8 (95% CI, 0.7, 1.0, $p = 0.042$). Group PM+ was not associated with lower PTSD symptoms or functional impairment. Use of psychosocial skills at midline was estimated to explain 31% of the PM+ effect on endline GHQ-12 scores. Adverse events in the control arm included 1 suicide death and 1 reportable incidence of domestic violence; in the Group PM+ arm, there was 1 death due to physical illness. Study limitations

include lack of power to evaluate gender-specific effects, lack of long-term outcomes (e.g., 12 months posttreatment), and lack of cost-effectiveness information.
Conclusions
In this study, we found that a 5-session group psychological treatment delivered by nonspecialists modestly reduced psychological distress and depression symptoms in a setting prone to humanitarian emergencies. Benefits were partly explained by the degree of psychosocial skill use in daily life. To improve the treatment benefit, future implementation should focus on approaches to enhance skill use by PM+ participants.

Non Communicable Diseases

37. Lancet. 2021 Sep 11;398(10304):957-980. Epub 2021 Aug 24.
Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants.
NCD Risk Factor Collaboration (NCD-RisC). Zhou B et al.

BACKGROUND: Hypertension can be detected at the primary health-care level and low-cost treatments can effectively control hypertension. We aimed to measure the prevalence of hypertension and progress in its detection, treatment, and control from 1990 to 2019 for 200 countries and territories.
METHODS: We used data from 1990 to 2019 on people aged 30-79 years from population-representative studies with measurement of blood pressure and data on blood pressure treatment. We defined hypertension as having systolic blood pressure 140 mm Hg or greater, diastolic blood pressure 90 mm Hg or greater, or taking medication for hypertension. We applied a Bayesian hierarchical model to estimate the prevalence of hypertension and the proportion of people with hypertension who had a previous diagnosis (detection), who were taking medication for hypertension (treatment), and whose hypertension was controlled to below 140/90 mm Hg (control). The model allowed for trends over time to be non-linear and to vary by age.
FINDINGS: The number of people aged 30-79 years with hypertension doubled from 1990 to 2019, from 331 (95% credible interval 306-359) million women and 317 (292-344) million men in 1990 to 626 (584-668) million women and 652 (604-698) million men in 2019, despite stable global age-standardised prevalence. In 2019, age-standardised hypertension prevalence was lowest in Canada and Peru for both men and women; in Taiwan, South Korea, Japan, and some countries in western Europe including Switzerland, Spain, and the UK for women; and in several low-income and middle-income countries such as Eritrea, Bangladesh, Ethiopia, and Solomon Islands for men. Hypertension prevalence surpassed 50% for women in two countries and men in nine countries, in central and eastern Europe, central Asia, Oceania, and Latin America. Globally, 59% (55-62) of women and 49% (46-52) of men with hypertension reported a previous diagnosis of hypertension in 2019, and 47% (43-51) of women and 38% (35-41) of men were treated. Control rates among people with hypertension in 2019 were 23% (20-27) for women and 18% (16-21) for men. In 2019, treatment and control rates were highest in South Korea, Canada, and Iceland (treatment >70%; control >50%), followed by the USA, Costa Rica, Germany, Portugal, and Taiwan. Treatment rates were less than 25% for women and less than 20% for men in Nepal, Indonesia, and some countries in sub-Saharan Africa and Oceania. Control rates were below 10% for women and men in these countries and for men in some countries in north Africa, central and south Asia, and eastern Europe. Treatment and control rates have improved in most countries since 1990, but we found little change in most countries in sub-Saharan Africa and Oceania. Improvements were largest in high-income countries, central Europe, and some upper-middle-income and recently high-income countries including Costa Rica, Taiwan, Kazakhstan, South Africa, Brazil, Chile, Turkey, and Iran.
INTERPRETATION: Improvements in the detection, treatment, and control of hypertension have varied substantially across countries, with some middle-income countries now outperforming most high-income nations. The dual approach of reducing hypertension prevalence through primary

prevention and enhancing its treatment and control is achievable not only in high-income countries but also in low-income and middle-income settings.

38. Lancet. 2021 Jul 17;398(10296):238-248.
Body-mass index and diabetes risk in 57 low-income and middle-income countries: a cross-sectional study of nationally representative, individual-level data in 685 616 adults.
Teufel F et al., Institute of Global Health, Faculty of Medicine and University Hospital, Heidelberg University, Germany.

BACKGROUND: The prevalence of overweight, obesity, and diabetes is rising rapidly in low-income and middle-income countries (LMICs), but there are scant empirical data on the association between body-mass index (BMI) and diabetes in these settings.
METHODS: In this cross-sectional study, we pooled individual-level data from nationally representative surveys across 57 LMICs. We identified all countries in which a WHO Stepwise Approach to Surveillance (STEPS) survey had been done during a year in which the country fell into an eligible World Bank income group category. For LMICs that did not have a STEPS survey, did not have valid contact information, or declined our request for data, we did a systematic search for survey datasets. Eligible surveys were done during or after 2008; had individual-level data; were done in a low-income, lower-middle-income, or upper-middle-income country; were nationally representative; had a response rate of 50% or higher; contained a diabetes biomarker (either a blood glucose measurement or glycated haemoglobin [HbA1c]); and contained data on height and weight. Diabetes was defined biologically as a fasting plasma glucose concentration of 7·0 mmol/L (126·0 mg/dL) or higher; a random plasma glucose concentration of 11·1 mmol/L (200·0 mg/dL) or higher; or a HbA1c of 6·5% (48·0 mmol/mol) or higher, or by self-reported use of diabetes medication. We included individuals aged 25 years or older with complete data on diabetes status, BMI (defined as normal [18·5-22·9 kg/m2], upper-normal [23·0-24·9 kg/m2], overweight [25·0-29·9 kg/m2], or obese [≥30·0 kg/m2]), sex, and age. Countries were categorised into six geographical regions: Latin America and the Caribbean, Europe and central Asia, east, south, and southeast Asia, sub-Saharan Africa, Middle East and north Africa, and Oceania. We estimated the association between BMI and diabetes risk by multivariable Poisson regression and receiver operating curve analyses, stratified by sex and geographical region.
FINDINGS: Our pooled dataset from 58 nationally representative surveys in 57 LMICs included 685 616 individuals. The overall prevalence of overweight was 27·2% (95% CI 26·6-27·8), of obesity was 21·0% (19·6-22·5), and of diabetes was 9·3% (8·4-10·2). In the pooled analysis, a higher risk of diabetes was observed at a BMI of 23 kg/m2 or higher, with a 43% greater risk of diabetes for men and a 41% greater risk for women compared with a BMI of 18·5-22·9 kg/m2. Diabetes risk also increased steeply in individuals aged 35-44 years and in men aged 25-34 years in sub-Saharan Africa. In the stratified analyses, there was considerable regional variability in this association. Optimal BMI thresholds for diabetes screening ranged from 23·8 kg/m2 among men in east, south, and southeast Asia to 28·3 kg/m2 among women in the Middle East and north Africa and in Latin America and the Caribbean.
INTERPRETATION: The association between BMI and diabetes risk in LMICs is subject to substantial regional variability. Diabetes risk is greater at lower BMI thresholds and at younger ages than reflected in currently used BMI cutoffs for assessing diabetes risk. These findings offer an important insight to inform context-specific diabetes screening guidelines.

Primary Health Care

39. Health Policy and Planning, 2021, Vol 36 (7): 1163 - 1186
Modified scoping review of the enablers and barriers to implementing primary health care in the COVID-19 context

Alexandra Edelman, et al. Corresponding author: Stephanie M Topp, College of Public Health, Medical and Veterinary Sciences, James Cook University, Townsville, QLD, Australia; Nossal Institute for Global Health, University of Melbourne. E-mail: globalstopp@gmail.com

Since the Alma Ata Declaration of 1978, countries have varied in their progress towards establishing and sustaining comprehensive primary health care (PHC) and realizing its associated vision of 'Health for All'. International health emergencies such as the coronavirus-19 (COVID-19) pandemic underscore the importance of PHC in underpinning health equity, including via access to routine essential services and emergency responsiveness. This review synthesizes the current state of knowledge about PHC impacts, implementation enablers and barriers, and knowledge gaps across the three main PHC components as conceptualized in the 2018 Astana Framework. A scoping review design was adopted to summarize evidence from a diverse body of literature with a modification to accommodate four discrete phases of searching, screening and eligibility assessment: a database search in PubMed for PHC-related literature reviews and multi-country analyses (Phase 1); a website search for key global PHC synthesis reports (Phase 2); targeted searches for peer-reviewed literature relating to specific components of PHC (Phase 3) and searches for emerging insights relating to PHC in the COVID-19 context (Phase 4). Evidence from 96 included papers were analysed across deductive themes corresponding to the three main components of PHC. Findings affirm that investments in PHC improve equity and access, healthcare performance, accountability of health systems and health outcomes. Key enablers of PHC implementation include equity-informed financing models, health system and governance frameworks that differentiate multi-sectoral PHC from more discrete service-focussed primary care, and governance mechanisms that strengthen linkages between policymakers, civil society, non-governmental organizations, community-based organizations and private sector entities. Although knowledge about, and experience in, PHC implementation continues to grow, critical knowledge gaps are evident, particularly relating to country-level, context-specific governance, financing, workforce, accountability and service coordination mechanisms. An agenda to guide future country-specific PHC research is outlined.

Sexual Reproductive Health

40. BMJ Global Health 2021;6:e007226. Commentary

What's needed to improve safety and quality of abortion care: reflections from WHO/HRP Multi-Country Study on Abortion across the sub-Saharan Africa and Latin America and Caribbean regions

Hedieh Mehrtash,et al mehrtashh@who.int

Introduction

In the advent of safe methods, access to information and trained providers, abortion has become a very safe procedure; however, unsafe abortions continue to persist in many parts of the world. Unsafe abortions account for half of all abortions globally, with the majority occurring in sub-Saharan Africa and Latin America and Caribbean (LAC).1 Severe abortion-related complications arise from least safe abortions.1 Between 2008 and 2013, it was estimated that approximately 10% of maternal deaths are attributable to abortion-related causes in sub-Saharan Africa and LAC2; however, studies exploring abortion morbidity and mortality including management of these complications have been limited or varied in estimations of the complications limiting comparability as there has been a lack of standard definitions, identification criteria and measurement tools.

Summary box

Complications as a result of unsafe abortion are an important and preventable cause of maternal mortality and morbidity.

Based on indicators present at the time of facility admission, abortion-related complications were classified into five hierarchical and mutually exclusive categories based on severity: (1) severe maternal outcomes consists of mortality and near miss (3) potentially life-threatening complications, (4) moderate complications and (5) mild complications.

Across sub-Saharan Africa and Latin America and Caribbean regions, our findings illustrate that the majority of complications were moderate and mild complications, and marginally more severe complications in sub-Saharan Africa.
Women's experiences of abortion care across both regions underlined the need for effective communication and emotional support including reducing anxiety and stress during examinations.
A multi-pronged approach including self-care, clinical care, task sharing, human rights and enabling legal environment is needed to deliver high-quality abortion and postabortion care including access to contraceptives.

41. Health Policy and Planning, 2021, Vol 36 (6): 913 - 922

Midwives providing maternal health services to poor women in the private sector: is it a financially feasible model?

Zubia Mumtaz, *Corresponding author. School of Public Health, University of Alberta, Canada. E-mail: zubia.mumtaz@ualberta.ca

Governments in many low- and middle-income countries have increasingly turned to the private sector to address the gap in skilled birth attendance in rural areas. They draw on limited, but emerging evidence that the poor also seek private healthcare services. A question not addressed in this policy and strategy is: Can poor women pay the fees required for private-sector maternity care providers to financially sustain their practices? This article examined the financial viability of private-sector midwifery practices established to provide skilled birth services to Afghan refugee women in Baluchistan, Pakistan. An international non-governmental organization established 45 midwifery practices as part of a poverty alleviation project aimed at providing market-based solutions for female poverty. A retrospective micro-cost analysis was conducted on a sample of 11 practices. In-depth interviews were conducted with 33 stakeholders to explore the midwives' experiences of operating private practices, and the facilitators and barriers they experienced. The single midwife-practices saw a mean of 8.7 ANC patients (range 1–19), attended 2.9 births (range 0–10) and provided care to 1.6 postnatal patients (range 0–7). The average net income of the 11 practices in May 2014 was US$81, but the median was just US$12. To contextualize these incomes, the midwives earned, on average, 25% of Pakistan's minimum monthly living wage. The financial analysis showed only 3 out of 11 sampled practices could be considered financially viable. The qualitative data revealed that even in practices with reasonable client volumes, the patients' inability to pay was the critical factor in the midwife practices' low net incomes. The research provides empirical evidence of a potential pitfall of private funding models in resource-poor settings where providers rely on impoverished clients to pay user-fees. Such financial models essentially shift the government's responsibility to provide safe childbirth services onto providers who can least afford to offer such care.

42. Health Policy and Planning, 2021, Vol 36 (7): 1215 - 1235

A systematic review and meta-analysis of the effectiveness of maternity waiting homes in low- and middle-income countries

Daphne N McRae, et al. Corresponding author. Saskatchewan Population Health and Evaluation Research Unit, University of Saskatchewan, Canada. E-mail: daphne.mcrae@usask.ca

Maternity waiting homes (MWHs) in low- and middle-income countries (LMICs) provide women with accommodation close to a health facility to enable timely access to skilled care at birth. We examined whether MWH use and availability compared with non-use/unavailability were associated with facility birth, birth with a skilled health professional, attendance at postnatal visit(s) and/or improved maternal and newborn health, in LMICs. We included (non-)randomized controlled, interrupted time series, controlled before–after, cohort and case–control studies published since 1990. Thirteen databases were searched with no language restrictions. Included studies (1991–2020) were assessed as either moderate (n = 9) or weak (n = 10) on individual quality using the Effective Public Health

Practice Project tool. Quality was most frequently compromised by selection bias, confounding and blinding. Only moderate quality studies were analyzed; no studies examining maternal morbidity/mortality met this criterion. MWH users had less relative risk (RR) of perinatal mortality [RR 0.65, 95% confidence intervals (CIs): 0.48, 0.87] (3 studies) and low birthweight (RR 0.34, 95% CI: 0.20, 0.59) (2 studies) compared with non-users. There were no significant differences between MWH use and non-use for stillbirth (RR 0.75, 95% CI: 0.47, 1.18) (3 studies) or neonatal mortality (RR 0.51, 95% CI: 0.25, 1.02) (2 studies). Single study results demonstrated higher adjusted odds ratios (aOR) for facility birth (aOR 5.8, 95% CI: 2.6, 13.0) and attendance at all recommended postnatal visits within 6 weeks of birth (aOR 1.99, 95% CI: 1.30, 3.07) for MWH users vs. non-users. The presence vs. absence of an MWH was associated with a 19% increase in facility birth (aOR 1.19, 95% CI: 1.10, 1.29). The presence vs. absence of a hospital-affiliated MWH predicted a 47% lower perinatal mortality rate ($P < 0.01$), but at a healthcare centre-level a 13 higher perinatal mortality rate ($P < 0.01$). Currently, there remains a lack of robust evidence supporting MWH effectiveness. We outline a six-point strategy for strengthening the evidence base.

43. PLoS Med 2021, 18(6): e1003644

Direct maternal morbidity and the risk of pregnancy-related deaths, stillbirths, and neonatal deaths in South Asia and sub-Saharan Africa: A population-based prospective cohort study in 8 countries. Aftab F, Ahmed I, Ahmed S, Ali SM, Amenga-Etego S, Ariff S, et al. (2021) on behalf of The Alliance for Maternal and Newborn Health Improvement (AMANHI) maternal morbidity study group.

Background
Maternal morbidity occurs several times more frequently than mortality, yet data on morbidity burden and its effect on maternal, foetal, and newborn outcomes are limited in low- and middle-income countries. We aimed to generate prospective, reliable population-based data on the burden of major direct maternal morbidities in the antenatal, intrapartum, and postnatal periods and its association with maternal, foetal, and neonatal death in South Asia and sub-Saharan Africa.
Methods and findings
This is a prospective cohort study, conducted in 9 research sites in 8 countries of South Asia and sub-Saharan Africa. We conducted population-based surveillance of women of reproductive age (15 to 49 years) to identify pregnancies. Pregnant women who gave consent were included in the study and followed up to birth and 42 days postpartum from 2012 to 2015. We used standard operating procedures, data collection tools, and training to harmonise study implementation across sites. Three home visits during pregnancy and 2 home visits after birth were conducted to collect maternal morbidity information and maternal, foetal, and newborn outcomes. We measured blood pressure and proteinuria to define hypertensive disorders of pregnancy and woman's self-report to identify obstetric haemorrhage, pregnancy-related infection, and prolonged or obstructed labour. Enrolled women whose pregnancy lasted at least 28 weeks or those who died during pregnancy were included in the analysis. We used meta-analysis to combine site-specific estimates of burden, and regression analysis combining all data from all sites to examine associations between the maternal morbidities and adverse outcomes.
Among approximately 735,000 women of reproductive age in the study population, and 133,238 pregnancies during the study period, only 1.6% refused consent. Of these, 114,927 pregnancies had morbidity data collected at least once in both antenatal and in postnatal period, and 114,050 of them were included in the analysis. Overall, 32.7% of included pregnancies had at least one major direct maternal morbidity; South Asia had almost double the burden compared to sub-Saharan Africa (43.9%, 95% CI 27.8% to 60.0% in South Asia; 23.7%, 95% CI 19.8% to 27.6% in sub-Saharan Africa). Antepartum haemorrhage was reported in 2.2% (95% CI 1.5% to 2.9%) pregnancies and severe postpartum in 1.7% (95% CI 1.2% to 2.2%) pregnancies. Preeclampsia or eclampsia was reported in 1.4% (95% CI 0.9% to 2.0%) pregnancies, and gestational hypertension alone was reported in 7.4% (95% CI 4.6% to 10.1%) pregnancies. Prolonged or obstructed labour was reported in about 11.1% (95% CI 5.4% to 16.8%) pregnancies. Clinical features of late third trimester antepartum infection were present in 9.1% (95% CI 5.6% to 12.6%) pregnancies and those of postpartum infection in 8.6% (95% CI 4.4% to 12.8%) pregnancies. There were 187 pregnancy-related deaths per 100,000 births, 27 stillbirths per 1,000 births, and 28 neonatal deaths per 1,000 live births with variation by country and region. Direct maternal morbidities were associated with each of these outcomes.
Conclusions
Our findings imply that health programmes in sub-Saharan Africa and South Asia must intensify their efforts to identify and treat maternal morbidities, which affected about one-third of all pregnancies and to prevent associated maternal and neonatal deaths and stillbirths.

44. Lancet 2021;398(10297):341-54

Review: Pre-eclampsia

Chappell LC et al., Department of Women and Children's Health, School of Life Course Sciences, Kings' College London, London, UK <lucy.chappell@kcl.ac.uk>

Pre-eclampsia is a multisystem pregnancy disorder characterised by variable degrees of placental malperfusion, with release of soluble factors into the circulation. These factors cause maternal vascular endothelial injury, which leads to hypertension and multi-organ injury. The placental disease can cause fetal growth restriction and stillbirth. Pre-eclampsia is a major cause of maternal and perinatal mortality and morbidity, especially in low-income and middle-income countries. Prophylactic low-dose aspirin can reduce the risk of preterm pre-eclampsia, but once pre-eclampsia has been diagnosed there are no curative treatments except for delivery, and no drugs have been shown to influence disease progression. Timing of delivery is planned to optimise fetal and maternal outcomes. Clinical trials have reported diagnostic and prognostic strategies that could improve fetal and maternal outcomes and have evaluated the optimal timing of birth in women with late preterm pre-eclampsia. Ongoing studies are evaluating the efficacy, dose, and timing of aspirin and calcium to prevent pre-eclampsia and are evaluating other drugs to control hypertension or ameliorate disease progression.

Other

45. Am J Trop Med Hyg. 2021 Jul 19:tpmd210266. Online ahead of print.

The Burden of Snakebite in Rural Communities in Kenya: A Household Survey.

Ooms GI et al., Health Action International, Amsterdam, The Netherlands. And Utrecht Centre for Pharmaceutical Policy and Regulation, Division of Pharmacoepidemiology and Clinical Pharmacology, Utrecht Institute for Pharmaceutical Sciences (UIPS), Utrecht University, Utrecht, The Netherlands.

Annually, about 2.7 million snakebite envenoming's occur worldwide, primarily affecting those living in rural regions. Effective treatment exists but is scarce, and traditional treatments are commonly used. To inform context-specific policies in Kenya, this study aimed to determine the health-seeking behaviour and the health, social, and economic burden of snakebites in rural communities. Nonprobability sampling was used to survey 382 respondents from four snakebite-endemic counties, from February to August 2020, using a structured questionnaire. Descriptive statistics, Fisher's exact tests, binary logistic regressions, and Mantel-Haenszel tests were used for analysis. Life-time experience with snakebites included 13.1% of respondents who reported being personally bitten and 37.4% who reported knowing of a community member being bitten. Respondents reported death after a snakebite in 9.1% of bitten community members and in 14.6% of bitten family members. Risk of snakebite was not significantly associated with sex, educational level, or occupation. Snakebite victims were most often walking (38%) or farming (24%) when bitten. Of those bitten, 58% went to a health facility, 30% sought traditional treatment, and 12% first went to a traditional healer before visiting a facility. Significant differences existed in perceptions on the financial consequences of snakebites among those who had been personally bitten and those who had observed a snakebite. Most commonly mentioned preventive measures were wearing shoes and carrying a light in the dark. Community engagement, including engagement with traditional healers, is needed to reduce snakebites. This should be done through education and sensitization to improve used preventive measures and effective health-seeking behaviour.

46. TMIH 2021;26 (SI)

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