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1. <u>BMJ Global Health</u> 2025;10:e019345. Original research

Prevalence of undernutrition in children with cancer in low-income and middle-income countries: a systematic review Nthongase Makamo1, Sterre Schoon2 3, Nmazuo Ozuah1 4, Gertjan Kaspers2 3, Elena J Ladas5, Minke Huibers2. 1 Baylor College of Medicine Children's Foundation, Lilongwe, Malawi; 2 Prinses Máxima Center for Pediatric Oncology, Utrecht, The Netherlands; 3 Amsterdam UMC Locatie VUmc, Amsterdam, The Netherlands

2. <u>BMJ Global Health</u> 2025;10:e017866. Original research

Four-year follow-up to a home-visiting intervention to promote early childhood development and prevent family violence in rural Rwanda: the Sugira Muryango cluster randomised trial Sarah G K Jensen., et al. Developmental Medicine, Boston Children's Hospital, Boston,

Massachusetts, USA

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Singh B et al., Institute of Infection, Veterinary, and Ecological Sciences, University of Liverpool, Liverpool, UK; Brain Infections Global Intervention Study Group; Correspondence to T Solomon <tsolomon@liverpool.ac.uk>

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Cagney J et al., Institute for Health Metrics and Evaluation, University of Washington, Seattle, WA, USA; Rollins School of Public Health, Emory University, Atlanta, GA, USA Correspondence to E Gakidou gakidou@uw.edu

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Fredrika von Essen., et al; Department of Epidemiology and Global Health, Umeå University, Umea, Sweden

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Praveenkumar Aivalli et al. Corresponding author. UCD Centre for Interdisciplinary Research Education and Innovation in Health Systems (UCD IRIS Centre), School of Nursing Midwifery and Health Systems, University College Dublin, Ireland. Email: praveenkumar.aivalli@ucdconnec t.ie

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shenglan.tang@duke.edu

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Impact of an international HIV funding crisis on HIV infections and mortality in low-income and middle-income countries: a modelling study Ten Brink D et al., Burnet Institute, Melbourne, VIC, Australia <debra.tenbrink@gmail.com> Erratum in: Correction to Lancet HIV 2025; published online March 26.

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Email: tanya.doherty@mrc.ac.za

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Causes of and risk factors for postpartum haemorrhage: a systematic review and meta-analysis Yunas I et al., Department of Metabolism and Systems Science, College of Medicine and Health, University of Birmingham, Birmingham, UK Correspondence to AJ Devall a.j.devall@bham.ac.uk

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Amouzou A et al., Department of International Health, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, USA Correspondence to T Boerma ties.boerma@umanitoba.ca

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Global and regional causes of maternal deaths 2009-20: a WHO systematic analysis

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Intersectoral Collaboration Between Traditional Bonesetters and Formal Healthcare: A Systematic Review on Past Initiatives and Stakeholder Perspectives

Binnerts JJ, Thom C. C. Hendriks TCC, Hermans E et al. |Department of Surgery, Radboud University Medical Centre, Nijmegen < joost.binnerts@radboudumc.nl>

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Broad Support Among Stakeholders for Collaboration Between Traditional Bonesetters and Formal Healthcare: A Qualitative Study in a Resource-Limited Setting Binnerts J, Hendriks TCC, Edwards M, Hermans E et al., Radboud University Medical Centre, Nijmegen, The Netherlands Buzughe N, Virie Liniversiteit Medical

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Editorial The uncertain future of migrant and refugee health

IHA – International Health Alerts 2025/2

Child Health

1. BMJ Global Health 2025;10:e019345. Original research

Prevalence of undernutrition in children with cancer in low-income and middle-income countries: a systematic review

Nthongase Makamo1, Sterre Schoon2 3, Nmazuo Ozuah1 4, Gertjan Kaspers2 3, Elena J Ladas5, Minke Huibers2.

1 Baylor College of Medicine Children's Foundation, Lilongwe, Malawi; 2 Prinses Máxima Center for Pediatric Oncology, Utrecht, The Netherlands; 3 Amsterdam UMC Locatie VUmc, Amsterdam, The Netherlands

Abstract

Background Undernutrition is linked to decreased survival in childhood cancer. However, its global impact remains unclear, and childhood cancer is not recognised as a high-risk factor in WHO nutrition guidelines. This systematic review quantifies the prevalence and clinical outcomes of undernutrition among children with cancer in low-income and middle-income countries (LMICs), highlighting the global burden and impact on children with cancer.

Methods Ovid Medline, EMBASE, Cochrane and Web of Science databases were searched until September 2024. Key search terms included "developing countries", "neoplasm", "child" and "undernutrition". LMICs were classified by the World Bank data. Undernutrition was defined by the WHO and includes wasting, stunting and underweight.

Findings Data from 21 646 children across 88 studies in 23 countries revealed prevalence rates ranging from 6.1% in China to 88.4% in South Africa. Nutritional assessments predominantly relied on weight-based indicators (57.0%), with mid-upper arm circumference used in 17.0% and combined methods in 27.0%. Older children (>5 years) showed a trend towards higher undernutrition prevalence rates compared with younger children. Undernutrition was associated with deteriorating outcomes in 7 out of 11 studies (p<0.05). Interpretation Our findings show the substantial burden of undernutrition among children with cancer in LMICs. Childhood cancer should be recognised as a high-risk factor in international nutrition guidelines, in order to promote equitable care and improve survival rates. Targeted intervention studies are needed, supporting the WHO's goal of 60% survival for common and curable childhood cancer types by 2030.

2. BMJ Global Health 2025;10:e017866. Original research

Four-year follow-up to a home-visiting intervention to promote early childhood development and prevent family violence in rural Rwanda: the Sugira Muryango cluster randomised trial

Sarah G K Jensen., et al. Developmental Medicine, Boston Children's Hospital, Boston, Massachusetts, USA Abstract

Background Sugira Muryango (SM) is a home-visiting intervention designed to promote early childhood development (ECD) and prevent violence in families with young children living in extreme poverty in rural Rwanda.

Methods We present 4-year follow-up data collected in 2022 in n=1009 households (93%) from a cluster randomised trial. We compare outcomes in SM and usual care (UC) families using mixed-effect models. Results are reported as the average difference in change over time in the SM versus UC group for longitudinal outcomes and the average difference in SM versus UC groups for new outcomes.

Results Compared with UC caregivers, caregivers who participated in SM report engaging in more stimulating interaction with their children (b=0.531; 95% CI: 0.468, 0.594) and are less likely to report use of harsh discipline (b=-0.189; 95% CI: -0.292, -0.087). The SM caregivers also provide more learning materials (b=0.218; 95% CI: 0.0219, 0.414), language stimulation (b=0.159; 95% CI: 0.080, 0.240), more varied interactions (b=147; 95% CI: 0.030, 0.260), fathers are reported to be more engaged in play (b=0.253; 95% CI: 0.039, 0.467) and SM households have better hygiene practices (b=0.189; 95% CI: 0.052, 0.326) compared with UC households. We do not observe treatment effects on children's cognitive outcomes, self-regulation or behavioural problems. There is a small negative association between SM and height-for-age (b=-0.038; 95% CI: -0.062, -0.012).

Conclusions SM resulted in changes in caregivers' behaviours to support children's health and development. Despite positive caregiver effects, we did not observe effects on child development or behavioural outcomes. Programme updates may be required to support children's continued cognitive growth.

3. International Journal of Epidemiology, Vol. 54 (2), April 2025, dyaf040 Misclassification of malaria as pneumonia in children in sub-Saharan Africa Open Access Christian Bottomley et al. Corresponding author. London School of Hygiene and Tropical Medicine. Email: christian.bottomley@lshtm.ac.uk

Background: The World Health Organization (WHO) clinical case definitions for pneumonia were designed to prioritize sensitivity over specificity. In sub-Saharan Africa, the disease that is most likely to be misclassified as pneumonia is Plasmodium falciparum malaria.

Methods: By using chest X-ray positivity as an indicator for pneumonia, we estimated the extent of pneumonia misclassification due to malaria in the Pneumonia Etiology Research for Child Health (PERCH) study. Additionally, we developed a simple model to predict the proportion of pneumonia cases as defined by the WHO that could be attributed to malaria in settings with varying levels of malaria parasitaemia prevalence. Results: In the PERCH study, the prevalence of malaria parasitaemia was low (4.7% among WHO pneumonia cases and 1.4% among controls) and we estimate that only 2.5% of WHO pneumonia cases were misclassified. However, when assuming a prevalence of malaria parasitaemia of 24%, corresponding to the average for malaria-endemic areas in Africa, we estimate that 28% of WHO pneumonia cases are misclassified. Among malaria-slide-positive WHO pneumonia cases in PERCH, lower chest wall indrawing [adjusted odds ratio (aOR) =18.1, 95% confidence interval (95% CI): 1.9, 175.8, P=0.012], crackles on chest auscultation (aOR=13.1, 95% CI: 1.4, 127.4, P=0.027), and nasal flaring (aOR=5.9, 95% CI: 1.1, 32.8, P=0.041) were associated with chest X-ray positivity.

Conclusion: In settings that are typical of sub-Saharan Africa, we predict that one-quarter of WHO-defined pneumonia cases are malaria rather than pneumonia. Among children with WHO pneumonia who also test positive for malaria parasitaemia, clinical features that favour pneumonia include lower chest wall indrawing, nasal flaring, and crackles on chest auscultation.

4. International Journal of Epidemiology, Volume 54, Issue 3, June 2025, dyaf063

Commentary: Navigating symptom and diagnostic overlap in pneumonia and malaria: insights from the field from the PERCH Study

David Torres-Fernandez and Quique Bassat

Every year, severe pneumonia and malaria still cause an unacceptably high burden of disease and mortality globally. These illnesses predominantly affect children <5 years of age in low- and middle-income countries (LMICs), particularly in Southeast Asia and sub-Saharan Africa. In malaria-endemic regions, distinguishing severe pneumonia from malaria with respiratory symptoms is an almost impossible task for clinicians in the absence of accurate diagnostic tools, which are often scarcely available in these settings. The symptom overlap is frequent; in hospital-admitted paediatric patients, >40% of malaria cases have severe respiratory findings and 24% of paediatric patients fulfil World Health Organization (WHO) criteria for both diseases. The true coinfection (or dual diagnosis) proportion of severe pneumonia among paediatric patients with malaria is estimated at about one-fifth of patients. Understanding this overlapping clinical epidemiology and performing a reliable differential diagnosis between the two entities has arisen as a public health priority.

5. Lancet 2025;405(10485):1130

World Report: Warning over child deaths as aid cut Samarasekera U.

(Abbreviated)

Progress in reducing neonatal and under-5 mortality have stalled as experts call for greater investment in services.

Globally, child deaths have fallen by more than a half and stillbirths by more than a third since 2000, according to two new reports on child mortality and stillbirths by the UN Inter-agency Group for Child Mortality

Estimation (UN IGME). But the group, which includes UNICEF, WHO, and the World Bank, warns progress will be lost unless political attention and funding increases for maternal, newborn, and child survival. The call for greater investment comes as major donors, including the USA, UK, and France, have announced or signalled cuts to foreign aid. Reductions in global funding for child survival programmes are already causing healthworker shortages, clinic closures, and vaccination and treatment disruptions, says the UN IGME. Deaths in children younger than 5 years dropped from 10·1 million in 2000 to 4·8 million in 2023, whereas stillbirths fell from 3·1 million to 1·9 million over the same period, according to the UN IGME estimates. But progress has slowed in recent years.

The slow progress means 65 countries are at risk of missing the SDG target for neonatal mortality rate in 2030. In sub-Saharan Africa, 1·1 million neonatal deaths occur each year—the same number as in 1990. UN IGME members are calling on governments, donors, and public and private sector partners to increase investments, integrate services, and deliver innovations to scale access to health, nutrition, and social protection services for children and pregnant individuals.

WHO hopes a year-long campaign on maternal and newborn health starting on World Health Day on April 7, 2025, will accelerate action. Titled Healthy beginnings, hopeful futures, the campaign will urge governments and the health community to increase efforts to end preventable maternal and newborn deaths. WHO is calling for a worldwide reinvigoration of efforts to ensure access to high-quality care for women and babies, especially in low-income countries, humanitarian emergencies, and fragile settings where most maternal and newborn deaths occur.

6. Lancet Glob Health. 2025 Jun;13(6):e1043-e1056.

The aetiologies, mortality, and disability of non-traumatic coma in African children: a systematic review and meta-analysis

Stephen T J Ray et al, ...

Correction Lancet Glob Health. 2025 Apr 23:S2214-109X(25)00176-7. Online ahead of print.

Background: Non-traumatic coma in African children is a common life-threatening presentation often leading to hospital attendance. We aimed to estimate the distribution of non-traumatic coma causes and outcomes, including disease-specific outcomes, for which evidence is scarce.

Methods: We systematically reviewed MEDLINE, Embase, and Scopus databases from inception to Feb 6, 2024. We included studies recruiting children (aged 1 month to 16 years) with non-traumatic coma (Blantyre Coma Scale score ≤2, ie deep coma or comparable alternative) from any African country. Disease-specific studies were included if outcomes were reported. Primary data were requested where required. We used a DerSimonian-Laird random effects model to calculate pooled estimates for prevalence of causes, mortality, and morbidity (in-hospital and post-discharge), including analysis of mortality by temporality. This study was registered with PROSPERO (CRD4202014193).

Findings: We screened 16 666 articles. 138 studies were eligible for analysis, reporting causes, outcome data, or both from 35 027 children with non-traumatic coma in 30 African countries. 114 (89%) of 128 studies were determined to be high quality. Among the causes, cerebral malaria had highest pooled prevalence at 58% (95% CI 48-69), encephalopathy of unknown cause was associated with 23% (9-36) of cases, and acute bacterial meningitis was the cause of 10% (8-12) of cases, with all other causes representing lower proportions of cases. Pooled overall case-fatality rates were 17% (16-19) for cerebral malaria, 37% (20-55) for unknown encephalopathy, and 45% (34-55) for acute bacterial meningitis. By meta-regression, there was no significant difference in cerebral malaria (p=0.98), acute bacterial meningitis (p=0.99), or all-cause coma (p=0.081) mortality by year of study. There was no substantial difference in deaths associated with cerebral malaria inhospital compared with post-discharge (17% [16-19] vs (18% [16-20]). Mortality was higher post-discharge than in-hospital in most non-malarial comas, including acute bacterial meningitis (39% [26-52]) vs 53% [38-69]). Disability associated with cerebral malaria was 11% (9-12). Pooled disability outcomes associated with other non-malarial diseases were largely absent.

Interpretation: The prevalence and outcomes of cerebral malaria and meningitis associated with non-traumatic coma were strikingly static across five decades. Enhanced molecular and radiological diagnostics, investment, policy making, community awareness, and health service provision are all required to facilitate earlier referral to specialist centres, to drive a step-change in diagnostic yield and treatment options to improve these outcomes.

Communicable Diseases (excl. Malaria, HIV and Tuberculosis

7. Am J Trop Med Hyg . 2024 Aug 27;112(4_Suppl):109-118.

Acceptability and Feasibility of Provision of COVID-19 Services by Community Health Workers to Remote Gold Mining Communities in Suriname

Stephen Vreden 1, Marieke Heemskerk 2, Hélène Hiwat 3, Hedley Cairo 3 ...

Gold mining communities in the Amazon region typically have limited access to public health services. In Suriname, the Ministry of Health Malaria Program (MoH-MP) works with community health workers (CHWs), people from mining communities without a formal medical degree, to provide malaria diagnostic and treatment services. During the COVID-19 pandemic, the MoH-MP trained 21 of these CHWs in COVID-19 outreach and testing, using rapid antigen tests for symptomatic persons in their communities; afterward, a mixed methods research approach was used to investigate whether including COVID-19 services in the tasks of the CHWs was feasible and accepted among gold mining populations. Also, CHWs took part in active case detection missions to proactively offer COVID-19 testing to all inhabitants of specific mining areas, regardless of symptoms. In the 6 months of field implementation (May-October 2022), 1,300 persons were tested for COVID-19, among whom 28.7% were women. Eight percent tested positive. Of the 312 asymptomatic persons tested, 2.2% tested positive. Qualitative semi-structured interviews with the CHWs and quantitative pre- and postintervention surveys revealed that the communities appreciated the nearby and free COVID-19 testing opportunity. The intervention motivated individuals who otherwise would not have been tested to test for COVID-19. Twenty-nine percent of those who had tested at least once for COVID-19 reported that their most recent test was conducted through the services of the CHWs. The results suggest that integrating COVID-19 testing into other CHW services can lower health access barriers in difficult-to-reach populations in remote communities.

8. Am J Trop Med Hyg. 2025 Apr 15;112(6):1273-1279. Etiology and Outcomes of Meningitis among Adults in Three Ugandan Referral Hospitals, 2018-2023: A Prospective Cohort Study in a High-HIV Endemic Setting Timothy Mugabi et al; ...

Studies describing the global burden of meningitis often exclude HIV- or tuberculosis (TB)-related etiologies, thereby presenting a limited view of meningitis etiology in low- and middle-income countries. This study provides an updated evaluation of the etiology of meningitis and treatment outcomes in Uganda given advancements in molecular and TB diagnostics. We conducted a prospective observational cohort study from December 2018 to October 2023, for which adults with suspected meningitis were recruited from three referral hospitals in Uganda. We used a comprehensive diagnostic algorithm to determine microbiological etiologies of cases. Participants were followed through hospital discharge, and mortality was summarized by meningitis etiology. We enrolled 1,577 participants with suspected meningitis, of whom 96% (n = 1,511/1,577) had HIV infection and 51% (n = 772/1,577) were antiretroviral therapy naive. The median CD4 cell count was 39 cells/ μ L (interquartile range: 14-97 cells/ μ L). Cryptococcal meningitis was the most frequently diagnosed etiology of meningitis (62%) followed by TB meningitis (21%). Inpatient mortality was highest among participants diagnosed with possible TB meningitis (32%) followed by probable TB meningitis (29%) and bacterial meningitis (24%). Among the 4% (n = 66/1,577) of HIV-seronegative participants, TB meningitis was the most frequently (38%) diagnosed cause of meningitis. Despite improvements in access to HIV therapy, cryptococcal meningitis and tuberculous meningitis persist as the most common etiologies of meningitis in Uganda. Improved access to meningitis diagnostics and treatments is critically needed to mitigate the morbidity and mortality, particularly in the resource-limited settings of HIV and TB endemic regions.

9. BMJ Global Health 2025;10:e016249. Original research

The global economic burden of antibiotic-resistant infections and the potential impact of bacterial vaccines: a modelling study

Nichola R Naylor et al., Department of Health Services Research and Policy, The London School of Hygiene and Tropical Medicine, London, UK

Abstract

Introduction Antibiotic resistance (ABR) may increase hospital costs, utility loss and mortality risk per patient. Understanding these losses at national, regional and global scales is necessary for efficiently tackling ABR. Our aim is to estimate the global economic burden of antibiotic-resistant infections and the potential for bacterial vaccines to mitigate this burden.

Methods We take healthcare system and labour productivity perspectives. Hospital cost-per-case and lengthof-stay estimates were calculated through meta-analyses and reviewing published systematic reviews. Unit labour productivity losses were estimated through a human capital approach. Modelled estimates were used where secondary data were missing. Death and incidence data were combined with unit cost data to estimate the economic burden associated with ABR in 2019, and the potential costs averted (in 2019 US\$) based on uptake scenarios of vaccines that currently exist or are likely to be developed.

Results Multidrug-resistant tuberculosis had the highest mean hospital cost attributable to ABR per patient, the range was US\$3000 in lower-income settings to US\$41 000 in high-income settings, with carbapenem-resistant infections associated with a high cost-per-case of US\$3000–US\$7000 depending on syndrome. ABR was associated with a median value of US\$693 billion (IQR: US\$627 bn–US\$768 bn) in hospital costs globally, with US\$207 bn (IQR: US\$186 bn–US\$229 bn) potentially avertable by vaccines. Productivity losses were quantified at almost US\$194 billion, with US\$76 bn avertable by vaccines.

Conclusions The economic burden of ABR is associated with high levels of hospital bed-days occupied, hospital spending and labour productivity losses globally and should, therefore, remain high on national and international policy agendas. Vaccines against Staphylococcus aureus, Escherichia coli and Klebsiella pneumoniae would avert a substantial portion of the economic burden associated with ABR. More robust evidence, particularly in low-income countries, on the hospital costs, associated with and attributable to ABR, is needed.

10. JAMA 2025;333(5):390-399

Tenofovir and Hepatitis B Virus Transmission During Pregnancy: A Randomized Clinical Trial Calvin Q Pan CQ et al., Guangzhou Medical Research Institute of Infectious Diseases, Center for Liver Diseases, Guangzhou Eighth People's Hospital, Guangzhou Medical University, Guangzhou, China

Importance: Standard care for preventing mother-to-child transmission (MTCT) of hepatitis B virus (HBV) in highly viremic mothers consists of maternal antiviral prophylaxis beginning at gestational week 28 combined with an HBV vaccine series and HBV immune globulin (HBIG) at birth. However, HBIG is unavailable in some resource-limited areas.

Objective: To determine whether initiating tenofovir disoproxil fumarate (TDF) at gestational week 16 combined with HBV vaccinations for infants is noninferior to the standard care of TDF at gestational week 28 combined with HBV vaccinations and HBIG for infants in preventing MTCT in mothers with HBV and high levels of viremia.

Design, setting, and participants: An unblinded, 2-group, randomized, noninferiority clinical trial was conducted in 7 tertiary care hospitals in China. A total of 280 pregnant individuals (who all identified as women) with HBV DNA levels greater than 200 000 IU/mL were enrolled between June 4, 2018, and February 8, 2021. The final follow-up occurred on March 1, 2022.

Interventions: Pregnant individuals were randomly assigned to receive either TDF starting at gestational week 16 with HBV vaccinations for the infant or TDF starting at gestational week 28 with HBV vaccinations and HBIG administered to the infant.

Main outcomes and measures: The primary outcome was the MTCT rate, defined as detectable HBV DNA greater than 20 IU/mL or hepatitis B surface antigen positivity in infants at age 28 weeks. Noninferiority was established if the MTCT rate in the experimental group did not increase by more than an absolute difference of 3% compared with the standard care group, as measured by the upper limit of the 2-sided 90% CI.

Results: Among 280 pregnant individuals who enrolled in the trial (mean age, 28 years; mean gestational age at enrollment, 16 weeks), 265 (95%) completed the study. Among all live-born infants, using the last observation

carried forward, the MTCT rate was 0.76% (1/131) in the experimental group and 0% (0/142) in the standard care group. In the per-protocol analysis, the MTCT rate was 0% (0/124) in the experimental group and 0% (0/141) in the standard care group. The between-group difference was 0.76% (upper limit of the 2-sided 90% CI, 1.74%) in all live-born infants and 0% (upper limit of the 2-sided 90% CI, 1.43%) in the per-protocol analysis. Both comparisons met the criterion for noninferiority. Rates of congenital defects and malformations were 2.3% (3/131) in the experimental group and 6.3% (9/142) in the standard care group (difference, 4% [2-sided 95% CI, -8.8% to 0.7%]).

Conclusions and relevance: Among pregnant women with HBV and high levels of viremia, TDF beginning at gestational week 16 combined with HBV vaccination for infants was noninferior to the standard care of TDF beginning at gestational week 28 combined with HBIG and HBV vaccination for infants. These results support beginning TDF at gestational week 16 combined with infant HBV vaccine to prevent MTCT of HBV in geographic areas where HBIG is not available.

11. Lancet 2025;405(10482):937-50

Review

Human African trypanosomiasis

Lejon V et al., Intertryp, French National Research Institute for Sustainable Development, CIRAD, University of Montpellier, Montpellier, France <veerle.lejon@ird.fr>

Human African trypanosomiasis or sleeping sickness is caused by infection with Trypanosoma brucei gambiense or Trypanosoma brucei rhodesiense parasites, which are transmitted by tsetse flies in sub-Saharan Africa. Control of human African trypanosomiasis is based on case detection, treatment, and vector control. In the past decade, simple rapid diagnostic tests were introduced for gambiense human African trypanosomiasis, facilitating screening in primary health-care facilities. A new oral drug, fexinidazole, became the first-line treatment for gambiense human African trypanosomiasis without severe meningo-encephalitic disease, as well as for rhodesiense human African trypanosomiasis. Medical interventions, in some areas combined with tiny target-based vector control, have substantially reduced human African trypanosomiasis incidence, despite temporary disruptions to health-care systems. The elimination of human African trypanosomiasis as a public health problem has been achieved, and elimination of gambiense human African trypanosomiasis transmission is now targeted for 2030. Improved diagnostics and drugs, continued involvement of populations at risk of disease, health staff, national authorities, and partners and donors all contribute to achieve this goal.

12. Lancet 2025;405(10483):991-1003

A multifaceted intervention to improve diagnosis and early management of hospitalised patients with suspected acute brain infections in Brazil, India, and Malawi: an international multicentre intervention study Singh B et al., Institute of Infection, Veterinary, and Ecological Sciences, University of Liverpool, Liverpool, UK Brain Infections Global Intervention Study Group

Correspondence to T Solomon <tsolomon@liverpool.ac.uk>

Background: Brain infections pose substantial challenges in diagnosis and management and carry high mortality and morbidity, especially in low-income and middle-income countries. We aimed to improve the diagnosis and early management of patients admitted to hospital (adults aged 16 years and older and children aged >28 days) with suspected acute brain infections at 13 hospitals in Brazil, India, and Malawi.

Methods: With hospital stakeholders, policy makers, and patient and public representatives, we co-designed a multifaceted clinical and laboratory intervention, informed by an evaluation of routine practice. The intervention, tailored for each setting, included a diagnostic and management algorithm, a lumbar puncture pack, a testing panel, and staff training. We used multivariable logistic regression and interrupted time series analysis to compare the coprimary outcomes-the percentage of patients achieving a syndromic diagnosis and the percentage achieving a microbiological diagnosis before and after the intervention. The study was registered at ClinicalTrials.gov (NCT04190303) and is complete.

Findings: Between Jan 5, 2021, and Nov 30, 2022, we screened 10 462 patients and enrolled a total of 2233 patients at 13 hospital sites connected to the four study centres in Brazil, India, and Malawi. 1376 (62%) were

recruited before the intervention and 857 (38%) were recruited after the intervention. 2154 patients (96%) had assessment of the primary outcome (1330 [62%] patients recruited pre-intervention and 824 [38%] recruited post-intervention). The median age across centres was 23 years (IQR 6-44), with 1276 (59%) being adults aged 16 years or older and 888 (41%) children aged between 29 days and 15 years; 1264 (59%) patients were male and 890 (41%) were female. Data on race and ethnicity were not recorded. 1020 (77%) of 1320 patients received a syndromic diagnosis before the intervention, rising to 701 (86%) of 813 after the intervention (adjusted odds ratio [aOR] 1·81 [95% CI 1·40-2·34]; p<0·0001). A microbiological diagnosis was made in 294 (22%) of 1330 patients pre-intervention, increasing to 250 (30%) of 824 patients post-intervention (aOR 1·46 [95% CI 1·18-1·79]; p=0·00040). Interrupted time series analysis confirmed that these increases exceeded a modest underlying trend of improvement over time. The percentage receiving a lumbar puncture, time to appropriate therapy, and functional outcome also improved.

Interpretation: Diagnosis and management of patients with suspected acute brain infections improved following introduction of a simple intervention package across a diverse range of hospitals on three continents. The intervention is now being implemented in other settings as part of the WHO Meningitis Roadmap and encephalitis control initiatives.

13. Lancet 2025;405(10489):1555

Editorial The pandemic treaty: a milestone, but with persistent concerns

(Abbreviated)

After more than 3 years of intense negotiations, WHO member states have finally reached a consensus on a new treaty to prevent, prepare for, and respond to pandemics. Initiated in 2021, negotiations over the terms of the legally binding agreement have been substantially delayed due to several contentious issues, including over how to ensure equitable access to vaccines, treatments, and diagnostics, particularly for low-income and middle-income countries.

The treaty codifies key approaches to pandemic prevention, preparedness, and response, including One Health, strong and resilient health systems and regulatory frameworks, protection of health-care workers, and the need for equity. It also establishes several new entities to put these principles into practice.

However, shameful and unjust provisions present in earlier drafts of the treaty remain. The treaty states that manufacturers would have to share only 20% of any vaccines, therapeutics, or diagnostics. 20% is better than nothing, but it does not equate to a truly equitable and just approach.

The treaty does little to stop some countries again largely monopolising life-saving health tools and services at the expense of others.

No new pandemic funding is included in the treaty.

There is already a Pandemic Fund and development banks will likely have a role too. A Coordinating Financial Mechanism will be established to promote sustainable financing for the implementation of the agreement, but how exactly it will operate alongside existing financing instruments is unclear.

The issue of accountability is also concerning. The treaty establishes a Conference of the Parties (COP) to assess the implementation of the agreement and review its functioning every 5 years. However, the COP can only make non-binding recommendations.

Lack of independent monitoring and robust enforcement mechanisms means that there are no clear consequences for countries that fail to comply with the terms. These issues risk selective adherence, undermining the effectiveness and fairness of the agreement.

Pandemics are global by definition and a grave threat to global health, as well as societies more widely. The recent Lancet Global Health 2050 Commission estimated that there is a roughly 50% chance that a new pandemic causing 25 million or more deaths will occur between now and 2050. An international set of obligations for countries is therefore essential.

But the lack of accountability, coupled with the weak requirements on health technologies, means that the treaty will be unable to prevent repetition of one of the key failures seen during COVID-19—the voracious acquisition of key resources by a handful of powerful actors at the expense of all. When the next pandemic does arise, it will take more than the pandemic treaty to ensure a truly equitable response.

Clinical presentation and epidemiological assessment of confirmed human mpox cases in DR Congo: a surveillance-based observational study

Malembi E et al., Programme National de Lutte contre le Mpox et les Fièvres Hémorragiques, Kinshasa, Democratic Republic of the Congo

Correspondence to O Mitjà < omitja@lluita.org>

Background: Mpox, caused by the monkeypox virus, is a serious public health threat in Africa, especially in DR Congo. Previously limited to endemic areas with clade 1a, monkeypox virus has recently spread to nonendemic regions, where clade 1b has emerged. This study provides a clinical comparison of mpox cases in DR Congo regions where clade 1a and clade 1b are prevalent.

Methods: We conducted a retrospective observational study, analysing PCR-confirmed mpox cases reported from sentinel health zones in seven provinces between Oct 1, 2023, and Sept 31, 2024. Cases from the newly affected provinces (South-Kivu and Kinshasa) were described along with those from four endemic provinces (Mai-Ndombe, Tshuapa, Tshopo, South-Ubangi, and Équateur). Surveillance data, including type of exposure, demographic details, clinical presentation, complications, and outcomes were collected from national surveillance systems and local health facilities, with laboratory confirmation using quantitative PCR. All analyses were restricted to descriptive statistics.

Findings: Of 17 927 suspected cases identified, 10 986 were investigated, 5948 were PCR-positive, and 4895 met the inclusion criteria based on data completeness: 4436 in newly affected and 459 in endemic regions. In newly affected provinces, median age was 20 years (IQR 8-28), 2119 (47.8%) participants were female, and 2310 (52·1%) were male. In endemic provinces, median age was 15 years (7-26), 179 (39·0%) participants were female, and 277 (60.3%) were male. Direct or intimate human contact was reported by 1951 (44.0%) individuals in newly affected provinces versus 25 (5.4%) in endemic provinces, and zoonotic exposure in 11 (0.2%) and 99 (21.6%), respectively. The proportions of partcipants with systemic symptoms (3828 [86.3%] in newly affected provinces and 427 [93.0%] in endemic provinces) and respiratory symptoms (2450 [55.2%] and 219 [47.7%]), and median skin lesion counts (91 [IQR 37-200] and 163 [95-345]) were similar between newly affected and endemic regions. Complications included skin infections (2041 [46.0%] in newly affected provinces and 201 [43.8%] in endemic provinces), respiratory distress (82 [1.8%] and 29 [6.3%]), vision impairment (7 [0·2%] and 28 [6·1%]), and prostration (695 [15·7%] and 51 [11·1%]). The case-fatality rate was 0·7% (95% CI 0.4-1.3; 14 of 1924) in children and 0.6% (0.3-1.0; 14 of 2483) in adults in newly affected areas, compared with 5.9% (3.4-10.0; 14 of 236) in children and 2.7% (1.1-6.1; six of 222) in adults in endemic regions. Content note: this Article and its appendix contain graphic images of mpox lesions affecting various sites including the face and genitals.

Interpretation: Our study indicates concurrent mpox outbreaks in DR Congo, involving younger individuals, a higher proportion of women and girls, and distinct presentations with higher lesion counts and respiratory symptoms compared with clade 2b lineage B.1 outbreaks. The high proportion of infectious complications and case-fatality rates, especially in endemic regions, emphasise the need for timely antibiotic therapy and targeted vaccination to reduce morbidity and mortality.

15. Lancet 2025;405(10492):1865-78

Review

Trachoma

Habtamu E et al., Clinical Research Department, London School of Hygiene & Tropical Medicine, London, UK; Eyu-Ethiopia, Bahir Dar, Ethiopia; Department of Ophthalmology, College of Medicine and Health Science, Bahir Dar University, Bahir Dar, Ethiopia <esmael.ali@lshtm.ac.uk>

Trachoma, the leading infectious cause of blindness worldwide, is one of several neglected tropical diseases targeted by WHO for elimination by 2030. The disease starts in childhood with repeated episodes of conjunctival Chlamydia trachomatis infection. This infection is associated with recurrent conjunctivitis (active trachoma), which, if left untreated, leads to cicatricial trachoma characterised by scarring of the conjunctiva, and potentially in-turned eyelashes (trachomatous trichiasis) in later life. Trachoma mainly affects the poorest and most rural communities; these populations typically have limited access to water and hygiene facilities. Blinding complications are most common in women who, in many cultures, act as caregivers from a young age for infected children. To eliminate trachoma as a public health problem, programmes implement a package of

interventions known as SAFE; namely, surgery to treat trachomatous trichiasis, antibiotic mass drug administration to treat infection, facial cleanliness, and environmental improvement to limit transmission. The SAFE strategy has brought considerable success in the last two decades. As of December, 2024, 21 countries have eliminated the disease, and several others are on track to eliminate it soon. However, persistent and recrudescent active trachoma in some populations might challenge the success of the 2030 global elimination target. In such settings, novel, or more intensive, approaches must be promptly developed, tested, and scaled up to accelerate elimination.

16. Lancet Glob Health. 2025 Jun;13(6):e1091-e1100.

Safety and efficacy of praziquantel 40 mg/kg versus 80 mg/kg in preschool-aged children with intestinal schistosomiasis in Uganda: a 2 × 2 factorial, double-blind, placebo-controlled, phase 2 randomised trial Amaya L Bustinduy et al, ...

Background: Optimal dosing of praziquantel for schistosomiasis for children younger than 5 years is not established and some studies suggest this age group might need a higher dosing per kilogram. Our aim was to assess the safety and efficacy of a split dose of 80 mg/kg of praziquantel tablets given in a single day to preschool children versus the recommended single dose of 40 mg/kg for treatment of Schistosoma mansoni. Methods: We did a 2 × 2 factorial design, placebo-controlled, phase 2 randomised trial in Uganda. Children aged 12-47 months infected with Schistosoma mansoni were randomly assigned in a 1:1:1:1 ratio to receive crushed praziquantel tablets at single standard (40 mg/kg) versus double standard dosing (80 mg/kg delivered as two 40 mg/kg doses 3 hours apart) and same dose or placebo at 6 months. Coprimary outcomes were parasitological cure and egg reduction rate at 4 weeks. Secondary outcomes included antigenic cure at 4 weeks, adverse events and clinical toxicity 12 h after treatment, and key morbidity markers at 6 months and 12 months. This trial is registered with ClinicalTrials.gov (NCT03640377).

Findings: Between Feb 18 and Dec 14, 2021, 354 children were randomly assigned to either praziquantel 40 mg/kg at baseline and placebo at 6 months (n=88); 40 mg/kg at baseline and 40 mg/kg at 6 months (n=86); 80 mg/kg at baseline and placebo at 6 months (m=89); or 80 mg/kg at baseline and 80 mg/kg at 6 months (n=91). 181 (51%) of 354 participants were boys. The median age was 36 months (28-42). Cure rate at 4 weeks was 67% in the 40 mg/kg group and 90% in the 80 mg/kg group (absolute difference 23% [95% CI 14-31]; p<0·001); for egg reduction rate the difference was 2% (95% CI 1-3; p<0·001) based on geometric mean and 22% (5-59; p<0·001) based on arithmetic mean. There were no differences in adverse event rates between the trial groups. At 12 months, biannual versus annual treatment reduced prevalence of faecal occult blood and 80 mg/kg dose reduced prevalence of faecal calprotectin. No severe adverse events related to the study drug were reported.

Interpretation: Two 40 mg/kg doses given 3 hours apart are safe, well tolerated, and more effective in achieving parasitic cure than the current proposed single 40 mg/kg dose. Until a paediatric formulation of praziquantel is available in endemic areas, the use of crushed tablets with this dosing strategy can be recommended for young children living in S mansoni endemic areas. In addition, twice-a-year treatment compared with once-a-year treatment affected some intestinal morbidity markers.

17. World Health Organization, Geneva; 2025 PMID: 40393410 WHO guidelines on meningitis diagnosis, treatment and care WHO.int (download)

In line with the Defeating meningitis by 2030: a global road map, the WHO guidelines on meningitis diagnosis, treatment and care provide evidence-based recommendations for the clinical management of children and adults with community-acquired meningitis, including acute and long-term care.

Meningitis poses a significant public health threat, despite successful efforts to control the disease globally. The burden of morbidity and mortality from meningitis remains high, particularly in low- and middle-income countries and in settings experiencing large-scale, disruptive epidemics. Approximately one in five individuals affected by bacterial meningitis incurs long-term complications, which may result in disability and have a profound impact on quality of life.

The guidelines are primarily intended for health-care professionals working in first- or second-level health-care facilities, including emergency, inpatient and outpatient services. They are also directed at policy-makers,

health-care planners and programme managers, academic institutions, non-governmental and civil society organizations to inform capacity-building, teaching and research agendas.

Web annex A provides the quantitative evidence reports, Web annex B summarizes the qualitative and economic evidence and Web annex C presents the Evidence-to-Decision frameworks.

Gender/ Sexual Violence

 18. Lancet 2025;405(10486):1216-7
World Report
"Staggering" scale of sexual violence in Sudan Devi S.

(Abbreviated)

The UN has said that "horrifying, systemic sexual violence is being used as a weapon of war" in Sudan, where war broke out on April 15, 2023, after clashes between the Sudanese Armed Forces (SAF) and the paramilitary Rapid Support Forces (RSF). Since then, famine, multiple disease outbreaks, mass displacement, and sexual violence have wracked the country.

Humanitarian workers expect the situation to deteriorate even further as large cuts in aid funding take effect, at a time when the health system is on the verge of collapse. About 30 million people will need humanitarian assistance this year, during what the UN calls the largest and the most devastating humanitarian crisis in the world.

More than 12·1 million people are at risk of sexual violence, an 80% rise from last year, says UNICEF. Ingram said UNICEF's report, Sudan's Child Rape and Sexual Violence Crisis, aims to give a snapshot of the situation. Accurate data collection on such attacks, and on health indicators, is severely impeded by the conflict, the warring parties that block access for humanitarian aid, and widespread cultural stigma that prevents survivors from reporting attacks. Armed groups have also targeted human rights defenders, lawyers, journalists, and aid workers with intimidation, violence, rape, abduction, and sometimes killing. UNICEF's reporting was helped by Sudanese women-led organisations that were unnamed, as were the survivors, out of fear of reprisals. Survivors suffer severe psychological trauma. The physical consequences include sexually transmitted illnesses such as HIV, complications including miscarriages or inability to have children, injuries such as gunshot wounds, stab wounds, and broken bones, and chronic abdominal and back pains. Women and girls who have undergone female genital mutilation may require additional and complex treatment.

But there is a shortage of even basic sexual and reproductive services, which are urgently required by 5.95 million women and girls of reproductive age, including 592 000 pregnant women, said UNFPA.

With large parts of Sudan inaccessible to aid agencies, local women-led organisations are vital in delivering services, but they only receive less than 2% of total UN funding.

During the war, most of Sudan's 18 states have been simultaneously battling at least three outbreaks of disease, such as cholera, dengue, malaria, and measles, said Sahbani. More than 70% of hospitals and health facilities are no longer operational and as of mid-February, WHO had recorded nearly 150 attacks on health care. Only 34% of health-care facilities providing HIV services are functional, according to the Sudan Federal Ministry of Health, and HIV cases have risen to 48 000—the highest recorded in Sudan's history, said UNAIDS. Famine could also worsen this year, with about 25 million people facing acute hunger and more than 630 000 people facing a catastrophic, level 5 condition of hunger, according to the Integrated Food Security Phase Classification used by the UN.

19. Lancet 2025;405(10487):1313 Editorial Standing up for gender justice

A denial and distortion of the reality of gender is unfolding in the USA that will have huge consequences for health globally. President Donald Trump's actions include erasing the term gender from all documents and

recognising only two biological sexes, reinstating the global gag rule that withholds sexual and reproductive health care, rejoining the anti-abortion Geneva Consensus Declaration, and terminating all diversity, equity, and inclusion policies and initiatives. A movement that opposes the very existence of gender has been emboldened, including other leaders like Argentina's President Javier Milei. Hard-won gains towards elimination of female genital mutilation, child marriage, gender-based violence, educational attainment for girls, and political participation and workplace opportunities for women are under threat. Moreover, Trump's orders are a gross violation of human rights and a deliberate attempt to erase the entire trans and gender diverse community. Sadly, contestation and manipulation around gender are not new to global health. A new Lancet Commission on gender and global health aims to identify ways in which health practitioners, policy makers, researchers, and civil society can use more inclusive understandings of gender to improve health policies and programmes. The Commission's vision of a gender justice approach "recognises the diversity of needs and experiences, calls for the inclusion of all people, and aims to achieve both equity and equality for all". Gender is often discussed in global health but, the Commission finds, action on gender justice remains a major challenge. There is no shared understanding of gender and related terms, leading to confusion, disagreement, and misinterpretation. In research and health data systems, gender and sex are often conflated, ignoring the multiple dimensions of gender and its interactions with sex. Gender often becomes a shorthand for women and girls, excluding the needs of trans and gender diverse people, as well as boys and men. The Commission details how well-funded international networks and far-right populism have aggressively pushed a fixed male–female dichotomy of sex over the past 30 years, leading to disastrous laws against LGBTQ+ people and abortion. Meanwhile, industries exploit gender norms to promote consumption of healthharming products, such as alcohol.

Previous Series and Commissions published by The Lancet related to gender and health have shown how gender inequality is intricately linked with health inequity, but focused on specific groups—women or trans and gender diverse people—or specific dimensions, such as gender-based violence, leadership in science and medicine, or peace. The Gender and Health Commission take a broader approach that uncovers the multiple forces that drive interactions between gender and health. Its comprehensive analysis of the historical, political, social, and economic drivers in global health uncovers why the understanding of women's health is still limited to reproductive and maternal health, why boys and men are underappreciated when designing interventions to address gender-based violence, and why there is such a detrimental absence of health data for the trans and gender diverse communities.

How can actions towards achieving gender justice in global health be made more effective? First, the Commission argues that a more holistic understanding and framing of gender is needed, as well as clearer and more transparent definitions for data collection and research. Second, the Commission states that lessons can be learned from policies that have successfully applied a gender justice lens. Third, there is an urgent need for accountability mechanisms that can systematically monitor and take action on the anti-gender movement and the commercial sector, as well as innovative ways to invest in gender justice approaches.

We are at a critical inflection point as the Trump administration imposes prohibitions towards gender justice. The Lancet stands by our commitment towards advancing equity, diversity, and inclusion in science, medicine, and global health. Recommending the use of inclusive language and encouraging adherence to the Sex and Gender Equity in Research reporting guidelines remain integral to our editorial policies. These times are a test for the global health community, and society more widely, to protect and advance the gains made over recent decades in gender equality and health equity. Collectively, we must mobilise forces for resistance and activism, raising our voices for a world in which everyone can thrive, irrespective of their gender and gender identity.

20. Lancet 2025;405910487):1373-1438

Achieving gender justice for global health equity: the Lancet Commission on gender and global health Hawkes S et al, Institute for Global Health, University College London, London, UK <sarah.hawkes@globalhealth5050.org>

21. Lancet 2025;405(10492):1817-36

Prevalence of sexual violence against children and age at first exposure: a global analysis by location, age, and sex (1990-2023)

Cagney J et al., Institute for Health Metrics and Evaluation, University of Washington, Seattle, WA, USA; Rollins School of Public Health, Emory University, Atlanta, GA, USA Correspondence to E Gakidou <gakidou@uw.edu>

Background: Measuring sexual violence against children (SVAC) is vital to prevention and advocacy efforts, yet existing prevalence studies present estimates for few countries. Here we estimate the prevalence of SVAC for 204 countries by age and sex, from 1990 to 2023, and also report the age at which young survivors of lifetime sexual violence first experienced sexual violence.

Methods: We reviewed publicly available repositories for data on the prevalence of SVAC. To harmonise heterogeneity in the identified input data, we adjusted for alternative case definitions of SVAC and differential disclosure by survey mode. We then used a spatiotemporal Gaussian process regression to estimate a full time series of exposure to SVAC for each age-sex-country combination. We accounted for uncertainty in the underlying data and modelling processes. We also analysed the age at which adolescent and young adult survivors of lifetime sexual violence first experienced this type of violence by sex, data source, and world region.

Findings: We estimate that the global age-standardised prevalence of SVAC was 18.9% (95% uncertainty interval [UI] 16.0-25.2) for females and 14.8% (9.5-23.5) for males in 2023. At the super-region level, these estimates ranged from 12.2% (9.0-17.2) in southeast Asia, east Asia, and Oceania to 26.8% (21.9-32.7) in south Asia for females and from 12.3% (5.2-24.6) in central Europe, eastern Europe, and central Asia to 18.6% (9.7-32.3) in sub-Saharan Africa for males. At the country level, age-standardised estimates ranged from 6.9% (4.8-9.6) in Montenegro to 42.6% (34.4-52.1) in Solomon Islands among females and from 4.2% (1.7-9.2) in Mongolia to 28.3% (13.2-49.8) in Côte d'Ivoire among males. Globally, these estimates remained relatively stable since 1990, with slight variations at the country and regional levels. We also find that the first experience of sexual violence among adolescents and young people occurred before the age of 18 years for 67.3% of female and 71.9% of male survivors.

Interpretation: The prevalence of SVAC is extremely high for both females and males across the globe. Given data sparsity and ongoing measurement challenges, findings probably underestimate the true pervasiveness of SVAC. An overwhelmingly high proportion of survivors first experienced sexual violence during childhood, revealing a narrow yet sensitive window that should be targeted in future prevention efforts. It is a moral imperative to protect children from violence and mitigate its compounding impacts on health across the lifecourse.

22. PLoS Med 22(5): e1004592.

Sex-disaggregated data along the gendered health pathways: A review and analysis of global data on hypertension, diabetes, HIV, and AIDS

Alessandro Feraldi, et al. Danish Centre for Health Economics, University of Southern Denmark, Odense, Denmark. Mail: achang@health.sdu.dk

Background: Health data disaggregated by sex is vital for identifying the distribution of illness, and assessing risk exposures, service access, and utilization. Disaggregating data along a health pathway, i.e., the measurable continuum from risk factor exposure to final health outcome (death), and including disease prevalence and a three-step care cascade (diagnosis, treatment, and control), has the potential to provide a holistic and systematic source of information on sex- and gender-based health inequities and identify opportunities for more tailored interventions to reduce those inequities.

Methods and findings: We collected sex- and age-disaggregated data along the health pathway. We searched for papers using global datasets on the sex-disaggregated care cascade for eight major conditions and identified cascade data for only three conditions: hypertension, diabetes, and HIV and AIDS. For each condition, we collected risk factor prevalence, disease prevalence, cascade progression, and death rates. We assessed the sex difference for all steps along the pathway and interpreted inequities through a lens of gender analysis. Sex-disaggregated data on risk factors, disease prevalence, and mortality were found for all three conditions across 204 countries. Sex-disaggregated care cascades for hypertension, diabetes, and HIV and AIDS were found only for 200, 39, and 76 countries, respectively. Significant sex differences were found in each step along the pathways. In many countries, males exhibited higher disease prevalence and death rates than females, while in some countries, they also reported lower rates of healthcare seeking, diagnosis, and treatment adherence.

Smoking prevalence was higher among males in most countries, whereas prevalence of obesity and unsafe sex were higher in females in most countries.

Conclusions: Findings support the increasing need to develop strategies that encourage greater male participation in preventive and healthcare service and underscore the importance of sex-disaggregated data in understanding health inequities and guiding gender-responsive interventions at different points along the pathway. Despite limitations in data availability and completeness, this study elucidates the need for more comprehensive and harmonized datasets for these and other conditions to monitor sex differences and implement sex-/gender-responsive interventions along the health pathway.

Global health/Health Policy

23. BMJ 2025;389:r744, Editor's Choice

Why we should forgive debt for poorer countries—and medical students Kamran Abbasi, editor in chief kabbasi@bmj.com

The global conversation is locked into trade deficits. While tariffs can be temporary, as we're seeing, debt has a longer term impact. The question is, if we truly believe that people and countries should have an opportunity to flourish and prosper, how do our finance systems—that hardwire debt—support those ambitions? Debt is the deficit that requires some serious thinking and an enlightened response. Abbreviated: Extraction deficits

But we should be talking about a different type of deficit: extraction deficits. These are the reparations owed to low and middle income countries for wealth extracted through colonialism and the slave trade, as well as the costs that low and middle income countries must now incur to meet climate targets as they are urged to bypass the cheaper fossil fuel stage of their industrial and technological development. The extraction deficits run into many trillions of dollars, and the money is owed by rich countries.

A report by the National African American Reparations Commission identified at least 31 countries that are owed reparations for "transatlantic chattel slavery." The commission estimates that the US is required to pay \$26tn (£20.1tn; €23.4tn) and Britain \$24tn. ActionAid International has recently calculated that 86% of 74 low and middle income countries are at "significant risk of a debt crisis" and have external debt of \$1.45tn. Some 75% of all low and middle income countries spend more on servicing debt than on healthcare. Meanwhile, just the climate debt owed to those 74 countries is over \$250tn.

The reality is this: the rich world continues to flourish at the expense of the world's poor people. This is the central unfairness that harms global prosperity, not the unfairness to the US in trade deals. Yet the way the world order is evolving suggests that we're further than ever from holding the beneficiaries of extraction to account, from demanding that they rectify the "extraction deficit" that runs into hundreds of trillions of dollars. How do we recover from a position that feels like a point of no return? Beyond damaging the US population (doi:10.1136/bmj.r711 doi:10.1136/bmj.r726), Trump's policies legitimise other nations to deprioritise health and wellbeing, to erode human rights, and to disregard legal safeguards, bully the media, and generally silence dissent. Let's take the licence that the US's behaviour affords, for example, Israel to act with impunity against medical staff and aid workers in Gaza (doi:10.1136/bmj.r662), with barely a murmur from the international community or the United Nations.

How do we begin to pull back from the hell of a world order that ignores rights? Cancelling or forgiving debt for low and middle income countries can be a catalyst for putting the health and wellbeing of people and the planet first.

24. BMJ Global Health 2025;10:e019622. Commentary

Diaspora as partners: strengthening resilience of health systems and communities amidst aid volatility Alaa Dafallah, Sophie Witter ; Centre for Global Health Research, Nuffield Department of Medicine, University of Oxford, Oxford, UK

Summary box

Global aid volatility threatens health systems and communities in low- and middle-income countries (LMICs) and aid-dependent fragile settings, disrupting critical essential services and programmes.

Diaspora financial, human and social capital represent critical resilience capabilities for communities and health systems in LMICs and aid-dependent fragile settings.

Harnessing diaspora capabilities for resilience of health systems and communities requires recognition, integration and evidence-based action.

The shifting aid landscape necessitates a reimagining of health financing and global health partnerships, where diaspora are key partners.

25. BMJ Global Health 2025;10:e019264. Commentary

The global health workforce crisis: are task-shifting strategies sustainable?

Saeed Anwar; Community Health Sciences, Peshawar Medical College, Peshawar, Pakistan.

Summary box

The global health workforce crisis remains a major barrier to achieving Universal Health Coverage (UHC), especially in low- and middle-income countries (LMICs).

Task-shifting, or delegating clinical responsibilities to less-specialised health workers, has been widely implemented to address workforce shortages and has improved access and efficiency in many settings. Successful examples, such as Nepal's ASBA programme and task-shifting in HIV care in sub-Saharan Africa, demonstrate the potential of this strategy when supported by adequate training and infrastructure. However, concerns persist about the long-term sustainability, quality of care, and risk of reinforcing systemic weaknesses, particularly where task-shifting is used as a stopgap without addressing underlying issues. Sustainable task-shifting requires integration into national workforce planning, investment in structured training and supervision, fair remuneration, and strong regulatory frameworks to ensure quality and equity in healthcare delivery.

26. BMJ Global Health 2025;10:e015753. Original research

Do health facility governing committees improve health system performance? An ecological study of Mainland Tanzania

Fredrika von Essen., et al; Department of Epidemiology and Global Health, Umeå University, Umea, Sweden Abstract

Introduction Accountability is crucial for improved functionality of health systems and can be ensured through community participation in health governance. To engage the community in the governance of the local health system, health facility governing committees (HFGCs) have been implemented in several low-income and middle-income countries including Tanzania. However, the effect of HFGCs on health system performance is not well studied. The aim of this study was to investigate the relationship between the functionality of the HFGCs and health system performance in 180 districts of mainland Tanzania, and to assess whether this relationship varies between dispensaries, health centres and hospitals.

Methods We conducted an ecological study in which the studied outcome was health system performance. The main independent variable was functionality of HFGCs, that is, to what extent these committees reflect the concerns of and connect back to the community. Other explanatory variables included staff availability, location of the facility, gender of the manager of the facility and ownership of the facility. Data on all of the variables were retrieved from the Star Rating Assessment of 2017/2018, measured as mean proportions of all facilities in the districts. The analyses included linear regression for all facility levels combined, as well as for the levels of facility separated (dispensaries, health centres and hospitals).

Results We found a positive relationship between the functionality of the HFGCs and health system performance (β =0.53; 95% CI=0.47 to 0.60). The relationship was stronger for dispensaries (β =0.56; 95% CI=0.50 to 0.63) compared to health centres (β =0.39; 95% CI=0.33 to 0.44) and hospitals (β =0.23; 95% CI=0.15 to 0.31).

Conclusions Districts that have functional HFGCs tend to have better health system performance than others. This relationship is stronger in dispensaries compared to health centres and hospitals. Therefore, we believe the district authorities should allocate resources to strengthen the HFGCs.

27. Health Policy and Planning, Vol. 40 (6), July 2025, Pages 661-683

Power dynamics and intersectoral collaboration for health in low- and middle-income countries: a realist review

Praveenkumar Aivalli et al. Corresponding author. UCD Centre for Interdisciplinary Research Education and Innovation in Health Systems (UCD IRIS Centre), School of Nursing Midwifery and Health Systems, University College Dublin, Ireland. E-mail: praveenkumar.aivalli@ucdconnect.ie

Intersectoral collaboration (ISC) is a critical strategy in global health for addressing complex challenges requiring multi-sectoral engagement. Although studies examined ISC in low- and middle-income countries (LMICs), gaps remain in understanding how power dynamics between stakeholders influence the effectiveness of ISC in these settings. This realist synthesis examines how, why, for whom, under what context, and to what extent power dynamics shape ISC in LMIC health programmes and policies, offering insights crucial for improving health policy implementation. Five initial programme theories were developed through a scoping review, document analysis, and qualitative study. A systematic search of Medline, Embase, CINAHL, Web of Science, and grey literature (2012–23) yielded 2850 records, with 23 included after screening. This period was chosen to capture contemporary shifts in ISC, following the 2012 UN Political Declaration on NCDs and the WHO's 2013 Health in All Policies (HiAP) framework, which strengthened multi-sectoral governance in LMICs. It also builds on prior reviews, ensuring an up-to-date synthesis of power dynamics in ISC. Data were synthesized using the context-mechanism-outcome framework, generating demi-regularities to refine programme theories (PTs). Findings reveal that power imbalances frequently manifest through hierarchical governance structures, resource disparities, and historical inequities, shaping ISC outcomes. Six refined PTs highlight: (i) inclusive policy development processes mitigate power asymmetries but require intentional facilitation to prevent marginalization of less dominant sectors. (ii) Leadership commitment and shared goal alignment enhance collaboration, yet competing institutional priorities often reinforce power struggles. (iii) Equitable resource allocation acts as both a catalyst for trust and a source of conflict, with donor influence exacerbating dependency dynamics. (iv) Hierarchical communication norms in LMICs undermine transparency, though informal interpersonal networks can circumvent bureaucratic barriers. (v) Ambiguity in roles and mandates amplifies power vacuums, enabling dominant actors to disproportionately influence agendas. Additionally, a sixth PT emerged: (vi) sustained interpersonal relationships counterbalance structural power imbalances, fostering accountability and adaptive problem-solving. These findings demonstrate that power dynamics in ISC within LMICs are mediated by both structural factors (e.g. funding models and institutional hierarchies) and relational mechanisms (e.g. trust and negotiation). Successful collaboration hinges on recognizing and addressing these dual dimensions of power. This synthesis advances the theoretical and practical understanding of ISC, offering policymakers actionable insights to navigate power-related challenges in intersectoral health initiatives.

28. Lancet 2025;405(10482):897-910

Trends in the global, regional, and national burden of oral conditions from 1990 to 2021: a systematic analysis for the Global Burden of Disease Study 2021

Oral Disorders Collaborators

Correspondence to E Bernabe <e.bernabe@qmul.ac.uk>

Background: The WHO Global Oral Health Action Plan has set an overarching global target of achieving a 10% reduction in the prevalence of oral conditions by 2030. Robust and up-to-date information on the global burden of oral conditions is paramount to monitor progress towards this target. The aim of this systematic data analysis was to produce global, WHO region, and country-level estimates of the prevalence of, and disability-adjusted life-years (DALYs) attributed to, untreated caries, severe periodontitis, edentulism, other oral disorders, lip and oral cavity cancer, and orofacial clefts from 1990 to 2021.

Methods: This report is based on the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2021. Input data were extracted from epidemiological surveys, population-based registries, and vital statistics. Data were modelled with DisMod-MR 2.1, a Bayesian meta-regression modelling tool, to ensure consistency between prevalence, incidence, remission, and mortality estimates for oral conditions. DALYs were estimated as the aggregation of the years of life lost (YLLs) due to premature mortality and years lived with disability (YLDs). YLDs were calculated by multiplying prevalence estimates, the severity of the oral condition's sequelae (disability weight) and duration of the sequelae. Although all oral conditions lead to YLDs, only lip and oral cavity cancer and orofacial clefts lead to YLLs as well. 95% uncertainty intervals (UIs) were generated for every metric with the 25th and 975th ordered 1000 draw values of the posterior distribution. Findings: The combined global age-standardised prevalence of the main oral conditions (untreated caries, severe periodontitis, edentulism, and other oral disorders) was 45 900 (95% UI 42 300 to 49 800) per 100 000 population in 2021, with 3.69 billion (3.40 to 4.00) people affected globally. Untreated dental caries of permanent teeth and severe periodontitis were the most common oral conditions, with a global agestandardised prevalence of 27 500 (24 000 to 32 000) per 100 000 population and 12 500 (10 500 to 14 500) per 100 000 population, respectively. Edentulism, severe periodontitis, and lip and oral cavity cancer caused the highest burden as demonstrated by their counts of DALYs and age-standardised DALY rates. Existing trends for 1990-2021 reveal relatively small changes (upward or downward) in prevalence and burden. Increasing counts of prevalent cases and DALYs were noted for all oral conditions but untreated caries of deciduous teeth (no percentage change in prevalence or DALYs) and orofacial clefts (-68.3% [-79.3 to -46.5] decrease in DALYs). There were decreases in both age-standardised prevalence and DALY rate for untreated caries of permanent teeth and edentulism, no change in both for untreated caries of deciduous teeth and severe periodontitis, an increase in the prevalence but no change in the DALY rate for lip and oral cavity cancer, and no change in the prevalence but a decrease in the DALY rate for orofacial clefts. By WHO region, the African and Eastern Mediterranean regions showed the largest increases in prevalent cases and DALYs for most oral conditions, while the European region showed the smallest increases or no change. The European region was the only region with decreasing age-standardised prevalence of untreated caries in both deciduous (-9.88%; -12.6 to -6.71) and permanent teeth (-5.94% (-8.38 to -3.62). The prevalence and DALY rate of severe periodontitis decreased in the African region, while the prevalence and DALY rate of edentulism decreased in the African region, South-East Asia region, and Western Pacific region. Furthermore, DALY rates of lip and oral cavity cancer decreased in the European region and the region of the Americas, while DALY rates of orofacial clefts decreased in all regions.

Interpretation: The minor changes in the burden of oral conditions over the past 30 years demonstrate that past and current efforts to control oral conditions have not been successful and that different approaches are needed. Many countries now face the double challenge of controlling the occurrence of new cases of oral conditions and addressing the huge unmet need for oral health care.

29. Lancet 2025;405(10483):951 Editorial The demise of USAID: time to rethink foreign aid?

(Abbreviated)

The US Agency for International Development (USAID) is no more. Marco Rubio, the US Secretary of State, has announced that 83% of programmes funded by USAID are to be ended, with the remainder to be absorbed by the State Department. Notwithstanding legal challenges, these decisions signal the end of an organisation that has brought crucial aid to millions globally. The move confirms the worst fears of the international community, coming 6 weeks after a pause on USAID's work that saw 5200 contracts cancelled, classified documents shredded, and life-saving aid halted. The Trump Administration's dismantling of USAID is a catastrophe for global health, the consequences of which will be felt for generations.

In the 2024 fiscal year, USAID disbursed US\$32·5 billion, with Ukraine, Jordan, and Ethiopia being the top recipients. \$8·9 billion went to health programmes and \$8·6 billion to humanitarian assistance. \$2·3 billion was devoted to fighting HIV/AIDS, tuberculosis, and malaria globally, and \$290 million to vaccine development and immunisation programmes. USAID has been a key supporter of the World Bank Group, the World Food Programme, and the Global Fund to Fight AIDS, Tuberculosis, and Malaria, driving progress towards the UN Sustainable Development Goals. Without USAID, the future of many global health programmes hangs in the balance, putting countless lives at risk.

There are clear moral arguments for USAID's work, but the organisation is not a charity. Founded in 1961 by President John F Kennedy, USAID has served as an important instrument of America's soft power, providing a countervailing view of the USA in many parts of the world where the country is known primarily for its military follies and exercises of hard power. Through investments in health, education, and democracy, USAID fostered diplomatic relationships and strengthened governance and peace, positioning the USA as a leader in

international development and helping to safeguard the country's security. A vital part of what shapes the USA's global influence has been destroyed.

For years, critics have pointed to inherent flaws, arguing that aid sustains dependency instead of promoting long-term development. This dependence and influence reinforces a neocolonial dominance of the Global North. Is there, therefore, an opportunity to rethink the global aid architecture, rather than replace it? The sweeping chaotic and ill-considered unilateral halt of global health programmes is no way to institute reforms. Change should be strategic, transparent, carefully implemented, and done in a spirit of support rather than imposition. Local expertise and resources should be centred in systems that empower nations to take charge of their development and health needs. The demise of USAID leaves no choice but to reconsider the broader landscape of foreign aid itself.

30. Lancet 2025;405(10485):1167-81 Global, regional, and national burden of household air pollution, 1990-2021: a systematic analysis for the Global Burden of Disease Study 2021 GBD 2021 HAP Collaborators Correspondence to K Burkart <katburk@uw.edu>

Background: Despite a substantial reduction in the use of solid fuels for cooking worldwide, exposure to household air pollution (HAP) remains a leading global risk factor, contributing considerably to the burden of disease. We present a comprehensive analysis of spatial patterns and temporal trends in exposure and attributable disease from 1990 to 2021, featuring substantial methodological updates compared with previous iterations of the Global Burden of Diseases, Injuries, and Risk Factors Study, including improved exposure estimations accounting for specific fuel types.

Methods: We estimated HAP exposure and trends and attributable burden for cataract, chronic obstructive pulmonary disease, ischaemic heart disease, lower respiratory infections, tracheal cancer, bronchus cancer, lung cancer, stroke, type 2 diabetes, and causes mediated via adverse reproductive outcomes for 204 countries and territories from 1990 to 2021. We first estimated the mean fuel type-specific concentrations (in μ g/m3) of fine particulate matter (PM2·5) pollution to which individuals using solid fuels for cooking were exposed, categorised by fuel type, location, year, age, and sex. Using a systematic review of the epidemiological literature and a newly developed meta-regression tool (meta-regression: Bayesian, regularised, trimmed), we derived disease-specific, non-parametric exposure-response curves to estimate relative risk as a function of PM2.5 concentration. We combined our exposure estimates and relative risks to estimate population attributable fractions and attributable burden for each cause by sex, age, location, and year. Findings: In 2021, 2.67 billion (95% uncertainty interval [UI] 2.63-2.71) people, 33.8% (95% UI 33.2-34.3) of the global population, were exposed to HAP from all sources at a mean concentration of 84.2 µg/m3. Although these figures show a notable reduction in the percentage of the global population exposed in 1990 (56.7%, 56·4-57·1), in absolute terms, there has been only a decline of 0·35 billion (10%) from the 3·02 billion people exposed to HAP in 1990. In 2021, 111 million (95% UI 75.1-164) global disability-adjusted life-years (DALYs) were attributable to HAP, accounting for 3.9% (95% UI 2.6-5.7) of all DALYs. The rate of global, HAP-attributable DALYs in 2021 was 1500.3 (95% UI 1028.4-2195.6) age-standardised DALYs per 100 000 population, a decline of 63.8% since 1990, when HAP-attributable DALYs comprised 4147.7 (3101.4-5104.6) age-standardised DALYs per 100 000 population. HAP-attributable burden remained highest in sub-Saharan Africa and south Asia, with 4044·1 (3103·4-5219·7) and 3213·5 (2165·4-4409·4) age-standardised DALYs per 100 000 population, respectively. The rate of HAP-attributable DALYs was higher for males (1530.5, 1023.4-2263.6) than for females (1318.5, 866.1-1977.2). Approximately one-third of the HAP-attributable burden (518.1, 410.1-641.7) was mediated via short gestation and low birthweight. Decomposition of trends and drivers behind changes in the HAP-attributable burden highlighted that declines in exposures were counteracted by population growth in most regions of the world, especially sub-Saharan Africa.

Interpretation: Although the burden attributable to HAP has decreased considerably, HAP remains a substantial risk factor, especially in sub-Saharan Africa and south Asia. Our comprehensive estimates of HAP exposure and attributable burden offer a robust and reliable resource for health policy makers and practitioners to precisely target and tailor health interventions. Given the persistent and substantial impact of HAP in many regions and countries, it is imperative to accelerate efforts to transition under-resourced communities to cleaner

household energy sources. Such initiatives are crucial for mitigating health risks and promoting sustainable development, ultimately improving the quality of life and health outcomes for millions of people.

31. Lancet 2025;405(10490):1700-12

Review

Protecting Africa's children from extreme risk: a runway of sustainability for PEPFAR programmes Cluver L et al., Centre for Evidence-Based Social Intervention, Department of Social Policy and Intervention, University of Oxford, Oxford, UK; Department of Psychiatry and Mental Health, University of Cape Town, Cape Town, South Africa <lucie.cluver@spi.ox.ac.uk>

PEPFAR (President's Emergency Plan for AIDS Relief), a landmark US foreign health policy, is recognised for saving 26 million lives from HIV. PEPFAR investments have also had life-saving impacts for children across sub-Saharan Africa through childhood HIV prevention, care, and treatment, ensuring 7.8 million babies were born HIV-free, supporting 13 million orphaned and vulnerable children, and protecting 10.3 million girls from sexual abuse. In this Health Policy, we review data from UNAIDS, UNICEF, World Bank, Violence Against Children Surveys, SPECTRUM model data, and Population-based HIV Impact Assessments; synthesise PEPFAR reports; conduct in-depth interviews; search PubMed for programme effectiveness evidence; and review economic reports. PEPFAR support is associated with substantial collateral benefits for the USA and Africa, including a four-fold increase in export of US goods to Africa, and US\$71.6 billion in total goods trade between the USA and Africa in 2024. PEPFAR-supported countries in Africa are committed to ownership of HIV responses by 2030-overall, PEPFAR-supported countries in sub-Saharan Africa have progressively increased their co-financing of their health systems through domestic government and private expenditure from \$13.7 billion per year in 2004 to \$42.6 billion per year in 2021. The feasibility of a 5-year transition to country-led sustainability is supported by evidence of innovative cost-saving models of delivery, including through faith-based and community-based organisations, and high return-on-investment for PEPFAR programmes. There are also collateral benefits of PEPFAR for US and Africa national security and health security, for example, reducing forced migration and increasing capacity to control emerging transborder infectious disease threats. Risks in sub-Saharan Africa remain acute: one in five girls (younger than 18 years) experience rape or sexual assault; one in ten children (younger than 18 years) are orphaned; and a child (younger than 15 years) is estimated to die from AIDS every 7 min. Without continued PEPFAR programmes, models predict that by 2030, an additional 1 million children will become infected with HIV, 0.5 million additional children will die of AIDS, and 2.8 million children will additionally become orphaned by AIDS. There is now an opportunity for a transformational partnership between the USA and Africa, to accelerate domestic government co-financing, private-sector investments, and charitable foundations. A 5-year progressive runway of transition can occur through continued authorisation of PEPFAR programmes, which can lead to the end of AIDS for children and families, an historic achievement.

32. Lancet 2025;405(10492):1807-8 World Report The final 20 years of the Gates Foundation Samarasekera U.

(Abbreviated)

Bill Gates announces plans to spend nearly all his wealth over the next 20 years to tackle global health and poverty challenges.

"There are too many urgent problems to solve for me to hold onto resources that could be used to help people", wrote multibillionaire Bill Gates in a statement on the Gates Foundation's website on May 8, 2025. In an announcement that surprised many observers, the self-described impatient optimist stated that he would give away nearly all his wealth earlier than planned to help improve lives globally. Over the next 20 years, the Gates Foundation expects to spend more than US\$200 billion on health and development projects before ceasing operations on Dec 31, 2045. With this funding boost, the Microsoft co-founder and philanthropist outlined three priorities for the Foundation: reducing child and maternal mortality; fighting infectious diseases, including poliomyelitis, malaria, and measles; and reducing global poverty. "By accelerating our giving, my hope

is we can put the world on a path to ending preventable deaths of moms and babies and lifting millions of people out of poverty", Gates wrote.

Gate's announcement coincided with the 25th anniversary of the Gates Foundation. The organisation was established in 2000 by Bill and Melinda Gates, who stated on the Foundation website that "all lives have equal value" and who wanted "to use their resources to create a world where everyone has the opportunity to lead a healthy and productive life". It is now the largest private foundation in the world. Headquartered in Seattle (WA, USA), it employs more than 2000 staff globally. Over the past 25 years, it has donated more than \$100 billion to health-care and education projects, the vast majority of which have been in low-income and middle-income countries (LMICs). The Foundation played an instrumental part in creating and funding Gavi, The Vaccine Alliance, and The Global Fund to Fight AIDS, Tuberculosis, and Malaria, "resulting in large reductions in mortality from HIV and AIDS and childhood infectious diseases", says Black, Professor at the Johns Hopkins Bloomberg School of Public Health (Baltimore, MD, USA). The Foundation estimates that, combined, these organisations are estimated to have saved more than 80 million lives over the past 25 years. The Foundation has also been a key partner in reviving global efforts to eradicate poliovirus and has supported the development of a new vaccine for rotavirus, which helped reduce the number of children younger than 5 years globally who die from diarrhoea each year by 75%.

The Foundation is commended for funding a new vaccine against meningitis, and funding other health interventions, the Foundation has successfully channelled considerable attention to many intractable challenges and vulnerable populations that otherwise would be ignored, has really changed the way we think about global health and public health, helped drive down costs of essential medicines and supported life-saving innovations in other areas, like maternal and child health and has undoubtedly leveraged the political importance of global health around the world.

However, the Foundation has also been criticised over its governance and influence, and experts say these concerns remain. There are concerns about how much more power the Gates Foundation will accrue in global health and international development and about the legitimacy and accountability of such a powerful actor in global health. The Foundation does not focus on the underlying causes of poverty and inequality but continues to only treat the symptoms and consequences. The Foundation could do much more on the gendered determinants of health and has not given enough attention to sustainability and that it should support local scientists and entrepreneurs to drive innovation in countries. Experts also want to see the Foundation focus on power shifting to LMICs in its remaining years. What the Gates Foundation should do is try to build a model of philanthropy that places more power and decision making in the hands of the institutions and people that are actively facing these challenges and who, in 20 years, will have to carry on this work without the Gates Foundation at its side.

33. PLoS Med 22(4): e1004551

Progressing towards the 2030 health-related SDGs in ASEAN: A systematic analysis Yafei Si, et al. Global Health Research Center, Duke Kunshan University, Kunshan, China, Duke Global Health Institute, Duke University, Durham, North Carolina, United States of America. Mail: shenglan.tang@duke.edu

Background: The Sustainable Development Goals (SDGs) articulate an ambitious global agenda and set of targets to achieve by 2030. Among the health-related SDGs, many formidable challenges remain in settings like the Association of Southeast Asian Nations (ASEAN) which face wide-ranging social, economic and health inequalities. In advance of the 2030 horizon, charting the trajectory of the health SDGs is critical for informing policy and programmatic course corrections to advance health and well-being among ASEAN's 10 member countries with its 667 million people.

Methods and findings: We used estimates from the Global Burden of Disease (GBD) Study 2021 and surveillance data to identify 27 health-related SDG indicators. The indicators were classified into 7 thematic areas: (i) nutrition, (ii) maternal, child and reproductive health (MCH), (iii) infectious diseases, (iv) non-communicable diseases (NCDs), (v) environmental health, (vi) universal health coverage (UHC), and (vii) road injuries. We developed an attainment index ranging from 0 to 100 for each SDG indicator by referencing the SDG targets and projected their progress to 2030.

We find an overall positive progress towards the health-related SDG targets in ASEAN from 1990 to 2030. At the aggregate level by 2030, 2 member countries, Singapore and Brunei, are projected to achieve their targets

(attainment score \geq 90). At a wider regional level, ASEAN is projected to make substantial progress in nutrition, MCH, and UHC, with a majority of countries projected to come close to or achieve their targets. However, progress is projected to be slower in the areas of reducing the incidence of infectious disease (i.e., HIV and AIDs, hepatitis B, TB, and neglected tropical diseases), NCD-related mortality and its risk factors (i.e., harmful alcohol use and smoking), environment-related mortality and its risk factors (i.e., unsafe water and poor hygiene, and air pollution), and road injuries. Substantial disparities are identified in the region, with Singapore, Brunei, Malaysia and Thailand generally performing better than elsewhere.

A limitation of our study was its reliance on historical trends which may not fully capture future political, social, or technological changes.

Conclusions: As a regional bloc, ASEAN faces persistent challenges in achieving health-related SDG targets by 2030, with unequal progress between countries. Moreover, epidemiological transitions and worsening environmental threats further compound potential gains. At the country level, efforts to enhance health system financing, quality and equity will need to be coupled with wider approaches that address structural drivers of disease. Furthermore, coordinated regional efforts will be essential to effectively respond to emerging threats posed by pollution and environmental risks.

HIV/AIDS

34. JAMA 2025;Published online May 19

Viewpoint

Long-Acting HIV Treatment in Low- and Middle-Income Countries: Addressing the Public Health Need Ehrenkranz PD et al., Global Health, Gates Foundation, Seattle, Washington <peter.ehrenkranz@gatesfoundation.org>

In recent decades, the global HIV response has made extraordinary strides, particularly in Africa's highestburden countries. By 2024, an impressive 78% (range, 72%-86%) of the 20.8 million people with HIV in eastern and southern Africa had achieved viral suppression with a daily fixed-dose antiretroviral therapy (ART) regimen. Yet several million remain unsuppressed. They must deal with the lifelong commitment to daily pills due to barriers including lost wages when seeking health care, socioeconomic challenges that require frequent moves for employment, health system limitations, stigma, and treatment fatigue. Inconsistent adherence can lead to a 2- to 4-fold increase in mortality risk. Moreover, the viremia that results when people cycle on and off treatment increasingly contributes to HIV transmission.

There is an urgent need to develop new options to deliver effective care for all people with HIV. For those successfully virally suppressed with daily oral regimens, sustainability may be achieved through differentiated ART delivery requiring fewer clinical visits and leveraging both public and private channels. However, these models cannot bridge the adherence gap for everyone, a challenge heightened by the broader uncertainty facing the HIV response resulting from geopolitical realignment of global health investments. This shifting funding landscape further increases the need to ensure that high-burden countries can access biomedical innovations that sustain viral suppression and treatment access.

Fortunately, recent developments in long-acting antiretrovirals for HIV prevention and treatment offer a gamechanging solution to adherence challenges, especially if affordable and rapid access can be provided for the most at-risk populations. Positive results from recent studies highlight the potential of lenacapavir to prevent new infections, driving efforts to ensure global access to long-acting antiretrovirals for prevention.

The potential of oral or injectable long-acting antiretrovirals to improve HIV treatment and prevention outcomes is immense. To fully realize this opportunity, it is critical that originator companies support efforts to make these innovations available globally, through commitment to technology transfer, regulatory support, and partnerships with each other and with generic manufacturers—even establishing licensing agreements prior to the completion of efficacy studies.

With a WHO target product profile for long-acting antiretrovirals expected in early 2025, a phased research agenda, and extensive stakeholder engagement, the groundwork is in place to drive this transformation. The next step is to partner with originators to develop products that can be targeted at people with HIV who need

them most and can be safely delivered in settings with minimal resource requirements. Just as once-daily fixeddose oral antiretrovirals transformed HIV care in the last decade, long-acting antiretrovirals for treatment could mark the next paradigm shift, offering sustained viral suppression in a manner that can both accelerate and sustain epidemic control.

35. Lancet 2025;405(10485):1147-54

Pharmacokinetics and safety of once-yearly lenacapavir: a phase 1, open-label study Jogiraju V et al., Gilead Sciences, Foster City, CA, USA Correspondence to R Singh <renu.singh16@gilead.com>

Background: Long-acting antiretrovirals can address barriers to HIV pre-exposure prophylaxis (PrEP), such as stigma and adherence. In two phase 3 trials, twice-yearly subcutaneous lenacapavir was safe and highly efficacious for PrEP in diverse populations. Furthering long-acting PrEP efforts, this study assessed the pharmacokinetics and safety of two once-yearly intramuscular lenacapavir formulations. Methods: This phase 1, open-label study in participants aged 18-55 years without HIV evaluated the pharmacokinetics, safety, and tolerability of two lenacapavir free acid formulations administered by ventrogluteal intramuscular injection as a single 5000 mg dose (formulation 1 with 5% w/w ethanol, formulation 2 with 10% w/w ethanol). Pharmacokinetic samples were collected at prespecified timepoints up to 56 weeks. Lenacapavir plasma concentrations were measured with a validated liquid chromatographytandem mass spectrometry method and summarised with non-compartmental analysis. Pharmacokinetic parameters evaluated included the area under the concentration-time curve for the once-yearly dosing interval calculated from days 1 to 365 (AUCdays 1-365), peak plasma concentration, time to reach peak plasma concentration, and trough concentration (Ctrough). Plasma concentration data from phase 3 studies of twiceyearly subcutaneous lenacapavir (PURPOSE 1 and PURPOSE 2) were pooled for comparison with once-yearly intramuscular lenacapavir formulations. Safety and tolerability, including participant-reported pain scores, were assessed.

Findings: 20 participants received lenacapavir formulation 1 and 20 received lenacapavir formulation 2. For estimation of pharmacokinetic parameters, sample size varied over time with at least 13 participants (formulation 1) and at least 19 participants (formulation 2) due to early discontinuations for reasons unrelated to the study drug. Following administration of intramuscular lenacapavir, concentrations increased rapidly, and median time to maximum concentration was $84\cdot1$ days (IQR $56\cdot1-112\cdot0$) for formulation 1 and $69\cdot9$ days ($55\cdot3-105\cdot5$) for formulation 2. The highest median concentration of once-yearly intramuscular lenacapavir ($247\cdot0$ ng/mL [IQR $184\cdot0-346\cdot0$] for formulation 1, $336\cdot0$ ng/mL [$233\cdot5-474\cdot3$] for formulation 2) remained above the highest median twice-yearly subcutaneous lenacapavir concentration ($67\cdot3$ ng/mL [$46\cdot8-91\cdot4$]). Median Ctrough at the end of 52 weeks for formulation 1 was $57\cdot0$ ng/mL (IQR $49\cdot9-72\cdot4$) and for formulation 2 was $65\cdot6$ ng/mL ($41\cdot8-87\cdot1$), exceeding the median twice-yearly subcutaneous lenacapavir Ctrough of $23\cdot4$ ng/mL ($15\cdot7-34\cdot3$) at the end of 26 weeks. Median AUCdays 1-365 for formulation 1 was $1011\cdot1$ h*µg/mL (IQR $881\cdot0-1490\cdot2$) and for formulation 2 was $1274\cdot0$ h*µg/mL ($1177\cdot3-1704\cdot8$). Adverse events were mostly grade 1 or 2. The most common was injection-site pain (16 [80%] participants given formulation 1, 15 [75%] given formulation 2), which was generally mild, resolved within 1 week, and was substantially reduced by pretreatment with ice.

Interpretation: Following administration of once-yearly intramuscular lenacapavir, median plasma concentrations exceeded those associated with efficacy in phase 3 studies of twice-yearly subcutaneous lenacapavir for PrEP for at least 56 weeks. Both formulations were safe and well tolerated. These data show the potential for biomedical HIV prevention with a once-yearly dosing interval.

36. Lancet HIV 2025;12(5):e346-e354

Impact of an international HIV funding crisis on HIV infections and mortality in low-income and middle-income countries: a modelling study

Ten Brink D et al., Burnet Institute, Melbourne, VIC, Australia <debra.tenbrink@gmail.com> Erratum in: Correction to Lancet HIV 2025; published online March 26. Background: International funding for HIV has been crucial in reducing new HIV transmissions and deaths. Five countries providing over 90% of international HIV funding have announced reductions in international aid of between 8% and 70% between 2025 and 2026, with the US Government pausing aid with immediate effect on Jan 20, 2025. We investigated the potential impact of these funding reductions on HIV incidence and mortality through mathematical modelling.

Methods: We used 26 country-validated Optima HIV models (Albania, Armenia, Azerbaijan, Belarus, Bhutan, Cambodia, Colombia, Costa Rica, Côte d'Ivoire, Dominican Republic, Eswatini, Georgia, Kazakhstan, Kenya, Kyrgyzstan, Malawi, Malaysia, Moldova, Mongolia, Mozambique, South Africa, Sri Lanka, Tajikistan, Uganda, Uzbekistan, and Zimbabwe). HIV incidence and mortality were projected across 2025-30 for a status quo scenario (most recent HIV spending continued) and four additional scenarios capturing the effects of anticipated international aid reductions for HIV prevention and testing, plus additional effects on treatment and facility-based testing resulting from immediate discontinuation of President's Emergency Fund for AIDS Relief (PEPFAR) support. Country-specific effects were estimated using sources of country-reported HIV funding. We disaggregated outcomes for children, adults in the general population, and adults in key populations. We extrapolated the scenario outcomes to all low-income and middle-income countries (LMICs) based on the modelled proportion of globally reported international aid by source (the 26 countries representing 49% of overall aid and 54% of PEPFAR aid). Upper and lower bounds reflected different mitigation and absorption assumptions.

Findings: Across all LMICs, an anticipated 24% weighted average of international aid reductions plus discontinued PEPFAR support could cause an additional 4·43-10·75 million new HIV infections and 0·77-2·93 million HIV-related deaths between 2025 and 2030 compared with the status quo. If PEPFAR support could be reinstated or equivalently recovered, this reduced to 0·07-1·73 million additional new HIV infections and 0·005-0·061 million HIV-related deaths. The effects were greatest in countries with a higher percentage of international funding and in those with increasing incidence of HIV among key populations. Interpretation: Unmitigated funding reductions could significantly reverse progress in the HIV response by 2030, disproportionately affecting sub-Saharan African countries and key and vulnerable populations. Sustainable financing mechanisms are crucial to ensure people have continued access to HIV prevention, testing, and treatment programmes, thereby reducing new HIV infections and deaths.

37. N Engl J Med 2025;392:1344-1345

Editorial: Working at Cross-PURPOSEs to Ending HIV

Glenda E. Gray, and W.D. Francois Venter, University of the Witwatersrand.

Almost 15 years ago, the results of the Preexposure Prophylaxis Initiative (iPrEx) trial, which showed the efficacy of oral antiretroviral agents as preexposure prophylaxis (PrEP), were reported in the Journal. However, only 15% of persons who would benefit from PrEP currently receive it. The recent modest fall in the global incidence of human immunodeficiency virus (HIV) infection obscures the ongoing epidemic among key populations in high-income, middle-income, and low-income countries, including continued high infection rates among young women in southern Africa. The United Nations 2030 prevention targets will not be met unless something different is done, and soon.

The results of the PURPOSE 2 trial, reported by Kelley et al. in this issue of the Journal essentially mirror those of the PURPOSE 1 trial, which was conducted in Uganda and South Africa. The PURPOSE 1 trial showed near-total protection from HIV infection among participants who received subcutaneous lenacapavir every 6 months.

The PURPOSE 2 trial, which was conducted in the United States and six middle-income countries (Mexico, Argentina, Brazil, Thailand, Peru, and South Africa), recruited cisgender men and gender-diverse persons who were having condomless receptive anal sex with partners assigned male at birth. Recreational drug use and sexually transmitted infections (STIs) were common in the screened population.

Participants underwent randomization in a 2:1 ratio and were assigned to receive lenacapavir every 26 weeks or daily oral emtricitabine—tenofovir disoproxil fumarate (F/TDF). The incidence of HIV infection in the trial population was compared with the background incidence in the screened population.

The incidence of HIV infection was lower in the lenacapavir group than in the F/TDF group: of the 11 incident infections, 2 occurred in the lenacapavir group (0.10 per 100 person-years) and 9 occurred in the F/TDF group

(0.93 per 100 person-years). The background incidence of HIV infection in the screened population was 2.37 per 100 person-years. The adherence to oral PrEP and the efficacy of PrEP were substantially higher in the PURPOSE 2 trial than in the PURPOSE 1 trial.

The two participants in the lenacapavir group who acquired HIV infection in the current trial had active STIs. Neither participant reported symptoms of HIV infection. The participants had presumed effective lenacapavir levels, and both participants were found to have the capsid inhibitor mutation N74D, indicating that long-term resistance monitoring for breakthrough cases is warranted. This finding has potential implications for treatment options under development.

The nine HIV infections in the F/TDF group were associated with low or undetectable levels of tenofovir (in eight participants) or discontinuation of the trial drug (in one participant). Drug monitoring suggested steadily decreasing adherence over time across this group.

The near-total protection shown in the PURPOSE 1 and 2 trials is catalytic for HIV prevention. The long-acting injectable nature of lenacapavir addresses the major Achilles heel of oral PrEP: adherence. There is much to praise about these trials: the designs involved substantial community participation and used background HIV infection as the counterfactual control; recruitment was performed in populations that are disproportionately affected by HIV and have previously been underrepresented in pharmaceutical trials, and social harms were addressed at screening and throughout the trials; and the participants could continue taking lenacapavir after the trial. The safety profile appeared to be acceptable, and the PURPOSE 1 trial provides important safety data with respect to pregnancy.

But all is not well in the PrEP field. Cabotegravir, another long-acting injectable PrEP that was shown to be effective in 2020, was licensed by the Food and Drug Administration 3 years ago, but only a tiny number of people receive it globally. ViiV Healthcare, the originator, licensed the medication after a lengthy process and civil society pressure to three generic manufacturers through the Medicines Patent Pool (MPP), with scale-up only projected for late 2027. In South Africa, where almost 20% of the global population of persons with HIV live, less than 5000 people take cabotegravir PrEP, even 2 years after local registration. ViiV, the only supplier of cabotegravir, charges almost \$24,000 (in U.S. dollars) per year in wealthy countries, with an "access" price of \$180 per year for selected countries. A price of \$9 to \$15 per injection for cabotegravir is required to make the drug as cost effective as oral PrEP. Preliminary modeling suggests that lenacapavir's longer half-life and the fewer required visits would allow South Africa to attain 2030 prevention targets faster than with cabotegravir. Gilead Sciences has issued lenacapavir manufacturing licenses to only six generics companies, bypassing the MPP access process, and excluding most countries where the PURPOSE 2 trial was conducted (including the Americas), where HIV incidence is concerning; these countries are unlikely to be able to afford the price tag of \$42,000 per year. Estimates suggest that the drug can be made profitably for \$100. Gilead announced that it will supply all required lenacapavir at "no profit" until generics are available, anticipated in 2028, but gave no price. The license includes troubling and complex legal language regarding access to the active pharmaceutical ingredient, importation and packaging restrictions, and "anti-diversion" clauses with onerous reporting requirements.

A drug innovation this powerful that could change the trajectory of an epidemic should compel urgency. PrEP uptake has been so poor that immediate and creative government, agency, and donor focus is required. Injections need to be made available swiftly to inform program design so that the tens of millions of people who would benefit from PrEP can access it.

Currently, pharmaceutical companies are consigning an entire generation of people to lifelong infection and treatment, in a macabre slow dance around price and patents. They should be heroes for developing these innovations and allies in immediate access, not the villains in yet another tragic piece of HIV history.

Malaria

38. Am J Trop Med Hyg. 2025 Jun 3 Online ahead of print.

Intravenous Fluid Bolus Resuscitation Increases Mortality Risk in Malawian Children with Cerebral Malaria Meredith G Sherman et al; ...

The Fluid Expansion as Supportive Therapy (FEAST) clinical trial determined that African children with impaired perfusion receiving bolus intravenous (IV) fluids had increased mortality compared to children with impaired perfusion not receiving bolus IV fluids. Malaria was common in FEAST enrollees, but no stratified analysis for

children with cerebral malaria (CM), a common cause of febrile coma in Africa, was reported. We investigated whether bolus fluid expansion changed mortality risk in children with CM. To evaluate this association, we performed a propensity score matched retrospective cohort study with data collected from 1,674 children with CM admitted to Queen Elizabeth Central Hospital in Blantyre, Malawi from 2000 to 2018. After matching of participants by covariate balancing propensity score weighting, children who received an IV fluid bolus had increased mortality risk (odds ratio [OR]: 1.92; 95% CI: 1.36-2.71) compared with those who did not. When stratified by admission systolic blood pressure (SBP), children with an SBP greater than 100 mm Hg receiving bolus fluids had increased mortality (OR: 3.15; 95% CI: 1.81-5.48) compared with those not receiving bolus fluids. In children with an SBP ≤ 100 mm Hg at admission, receiving bolus IV fluids did not change mortality (OR: 1.44; 95% CI: 0.91-2.26). Bolus IV fluids are an ineffective therapeutic intervention in children with CM and are harmful in those with normal or elevated admission SBPs. Our results confirm the lack of efficacy and potential harm of IV bolus fluid administration in Malawian children with CM.

39. Lancet 2025;405(10483):979-90

Mapping the global prevalence, incidence, and mortality of Plasmodium falciparum and Plasmodium vivax malaria, 2000-22: a spatial and temporal modelling study

Weiss DJ et al., Curtin University, Bentley, WA, Australia; The Kids Research Institute Australia, Nedlands, WA, Australia <dan.weiss@curtin.edu.au>

Background: Malaria remains a leading cause of illness and death globally, with countries in sub-Saharan Africa bearing a disproportionate burden. Global high-resolution maps of malaria prevalence, incidence, and mortality are crucial for tracking spatially heterogeneous progress against the disease and to inform strategic malaria control efforts. We present the latest such maps, the first since 2019, which cover the years 2000-22. The maps are accompanied by administrative-level summaries and include estimated COVID-19 pandemic-related impacts on malaria burden.

Methods: We initially modelled prevalence of Plasmodium falciparum malaria infection in children aged 2-10 years in high-burden African countries using a geostatistical modelling framework. The model was trained on a large database of spatiotemporal observations of community infection prevalence; environmental and anthropogenic covariates; and modelled intervention coverages for insecticide-treated bednets, indoor residual spraying, and effective treatment with an antimalarial drug. We developed an additional model to incorporate disruptions to malaria case management caused by the COVID-19 pandemic. The resulting high-resolution maps of infection prevalence from 2000 to 2022 were subsequently translated to estimates of case incidence and malaria mortality. For other malaria-endemic countries and for Plasmodium vivax estimates, we used routine surveillance data to model annual case incidence at administrative levels. We then converted these estimates to infection prevalence and malaria mortality, and spatially disaggregated administrative-level results to produce high-resolution maps. Lastly, we combined the modelled outputs to produce global maps and summarised tables that are suitable for assessing changing malaria burden from subnational to global scales. Findings: We found an ongoing plateau in rates of malaria infection prevalence and case incidence within sub-Saharan Africa, with consistent year-on-year improvements not evident since 2015. Due to the concentration of malaria burden in sub-Saharan Africa and the region's rapid population growth relative to other endemic regions, we estimate that 2022 had 234.8 (95% uncertainty interval 179.2-299.0) million clinical cases of P falciparum malaria, the most since 2004. Despite these findings, deaths from malaria continued to decline in sub-Saharan Africa and consequently globally after 2015, except for the COVID-19-impacted years of 2020-22. Similarly, progress in reducing P falciparum and P vivax morbidity outside Africa continued despite stalled progress globally. However, a major malaria outbreak in Pakistan following intense flooding in 2022 resulted in a reversal in this improving trend and contributed heavily to the global total of 12.4 (10.7-14.8) million clinical cases of P vivax malaria. Within Africa, we found that the plateau in infection prevalence occurred earlier in more densely populated areas, whereas more sparsely populated regions have continued a trajectory of modest improvement.

Interpretation: The unprecedented investment in malaria control since the early 2000s has averted an enormous amount of malaria burden. However, case incidence rates in Africa have flattened, and with a rapidly growing population at risk, the number of P falciparum cases in Africa, and thus globally, is now comparable to levels before the surge of investment. Outside Africa progress against malaria morbidity continued after 2015, but a resurgence of P vivax cases in 2022 underscores the fragility of progress against malaria in the face of

climatic shocks. COVID-19-related disruptions led to increased malaria cases and deaths, but the impact was less severe than feared, in part because endemic countries continued to prioritise malaria control during the pandemic. Nevertheless, improved tools and strategies remain urgently needed to regain momentum against this disease.

40. Lancet Glob Health. 2025 Jun;13(6):e995-e1005.. Safety of RTS,S/AS01E malaria vaccine up to 1 year after the third dose in Ghana, Kenya, and Malawi (EPI-MAL-003): a phase 4 cohort event monitoring study Valérie Haine et al, ...

Background: RTS,S/AS01E has been successfully administered to over two million children since 2019 through the Malaria Vaccine Implementation Programme (MVIP). In this Article, we report the safety results of a study evaluating RTS,S/AS01E safety and effectiveness in real-world settings.

Methods: EPI-MAL-003 is an ongoing phase 4 disease surveillance study with prospective cohort event monitoring and hospital-based surveillance, done in the setting of routine health-care practice in Ghana, Kenya, and Malawi and fully embedded in the MVIP. The study design was dependent on the cluster-randomised vaccine implementation. In active surveillance, we enrolled children younger than 18 months from exposed (where RTS,S/AS01E was offered) and unexposed clusters. The coprimary endpoints were the occurrence of predefined adverse events of special interest and aetiology-confirmed meningitis. We report primary and secondary safety results up to 1 year after the primary vaccine schedule (three doses). The study is registered with ClinicalTrials.gov, NCT03855995.

Findings: The first participant was enrolled on March 21, 2019. The cutoff date for the current analysis was 1 year after the third RTS,S/AS01E dose for each participant. In total, 44 912 children (19 993 in Ghana, 11 990 in Kenya, and 12 929 in Malawi) were included in the analysis set for the cluster-randomised comparison: 22 508 from exposed clusters and 22 404 from unexposed clusters. Incidence rates (expressed per 100 000 personyears) for generalised convulsive seizures and intussusception were similar between vaccinated and unvaccinated children. Aetiology-confirmed meningitis was reported in two children: one case of bacterial meningitis due to Streptococcus pneumoniae in an RTS,S/AS01E-vaccinated child in the exposed clusters, and one case of viral meningitis due to human herpesvirus 6 in an unvaccinated child in the unexposed clusters. Both cases occurred within 12 months after vaccination in children in the cluster-design analysis set, leading to incidence rates of 4.1 (95% CI 0.1-23.0) per 100 000 person-years in RTS,S/AS01E-vaccinated children and 4.0 (0.1-22.6) per 100 000 person-years in unvaccinated children, and a country-adjusted incidence rate ratio (IRR) of 0.96 (95% CI 0.06-15.34; p=0.98). Cerebral malaria cases were reported for four (<0.1%) of 20 639 RTS,S/AS01E-vaccinated children in the exposed clusters and two (<0.1%) of 22 137 unvaccinated children in the unexposed clusters. These included three and two cases occurring within 12 months after the primary vaccination, in RTS,S/AS01E-vaccinated children and unvaccinated children, respectively (IRR 1.43, 95% CI 0.24-8.58, p=0.70). Incidence rates for all-cause mortality were 659.7 (95% CI 561.5-770.3) in vaccinated children versus 724.5 (622.3-838.8) in unvaccinated children, with similar incidence rates for boys and girls. Interpretation: We found no evidence of vaccination being associated with an increased risk of meningitis, cerebral malaria, or mortality among vaccinated children, and no new safety risks were identified.

41. N Engl J Med 2025;392:1320-1333

Review Article: Malaria (Abridged)

Johanna P. Daily, M.D., and Sunil Parikh, M.D. - Dr. Daily can be contacted at johanna.daily@einsteinmed.edu or at the Division of Infectious Diseases, Department of Medicine, Albert Einstein College of Medicine, Bronx, NY

Malaria is a preventable mosquito-borne illness caused by plasmodium parasites. An estimated 263 million cases of malaria and 597,000 deaths from malaria occurred worldwide in 2023. Nearly half the global population lives in regions where malaria is endemic, and outbreaks of locally acquired infection can also occur in regions where malaria is not endemic, such as the United States. Malaria therefore represents a major global public health challenge. Recent progress in the fight against malaria includes the introduction of malaria vaccines to prevent infection in children residing in regions where malaria is endemic. In addition, malaria-control efforts between 2000 and 2024 have led the World Health Organization (WHO) to certify 18 additional countries as malaria-free. However, achievements in combating malaria have been tempered by parasite and

vector adaptations. The resulting challenges include a reduction in the reliability of rapid diagnostic tests and the emergence of partial resistance to artemisinin in Plasmodium falciparum and insecticide resistance in the mosquito vectors. We review the current epidemiologic trends of malaria and the best practices, recent progress, and challenges in the prevention, diagnosis, and treatment of this deadly infection. Key Points:

Malaria remains a major threat to human health worldwide.

Malaria necessitates a prompt laboratory-based diagnosis and expedited treatment.

Microscopy and rapid diagnostic tests are the most widely used tools for the diagnosis of malaria. The accuracy of rapid diagnostic tests has decreased because of mutations in the gene encoding the target plasmodium protein.

Vaccines to prevent malaria have been approved for use in children in regions of endemicity.

Artemisinin-based combination therapy is the standard treatment for Plasmodium falciparum malaria. However, partial resistance to artemisinin has emerged in Africa.

Challenges to vector control include insecticide resistance, changes in feeding behavior, and geographic expansion of vector species.

Exciting progress has been made in the fight against malaria, with the development of vaccines and an increase in the number of countries that are now free of malaria. Yet malaria remains a formidable global health challenge. Continued investment in malaria-control programs, health care access, and research to discover new interventions may allow a future in which malaria no longer poses a threat to human health.

Non-Communicable Diseases

42. BMJ Global Health 2025;10:e017626. Commentary

Aflatoxin exposure and primary liver cancer in Ghana

Yvonne Nartey, et al., Department of Adult Health, School of Nursing & Midwifery, University of Ghana, Legon, Ghana

Introduction

Liver cancer ranks among the leading causes of cancer-related deaths globally, with over 700000 deaths reported in 2022. The incidence of liver cancer is particularly high in low- and middle-income countries (LMICs), primarily in sub-Saharan Africa and Southeast Asia. In 2022, an estimated 866136 new cases of primary liver cancer were reported worldwide, highlighting its prevalence as one of the most common cancers globally. The incidence of liver cancer and related mortality rates are projected to increase between 2020 and 2040, new cases are expected to rise by 55%, with mortality rising by 56.4%. These alarming trends underscore the need to better understand the risk factors driving the rise in liver cancer cases, particularly in regions like Ghana where multiple risk factors converge. In Ghana, an estimated 3731 people were newly diagnosed with liver cancer in 2022 and 3362 died from the disease.

Summary box

The burden of liver cancer continues to rise in Ghana.

Several factors have been linked to an increased risk of liver cancer, including aflatoxin exposure.

Ghana has a high consumption of aflatoxin-contaminated foods.

It is crucial to conduct studies to assess the contribution of aflatoxin to the rising liver cancer burden in Ghana.

43. Lancet 2025;405(10482):880-2 World Report Silicosis in India Cousins S.

(Abbreviated)

Many Indians are exposed to silica dust, but experts and patients lament the lack of information and health services related to silicosis.

Silicosis is a progressive and incurable lung disease characterised by shortness of breath, cough, and fever. It is caused by the inhalation of dust that contains free crystalline silica, which is 100 times smaller than a grain of sand and thus invisible to the naked eye. It is an occupational disease predominantly affecting workers in industries that involve direct exposure to silica dust—a mineral that makes up a large portion of the Earth's crust—such as mining, quarrying, building construction, carving, manufacturing, glass, foundry, and ceramics. The disease, which affects tens of millions of workers around the world, can present in three different forms: acute, accelerated, and chronic. Acute silicosis is the rapid development of the disease, caused by very high exposure to silica dust over a short period of time (weeks to months); accelerated silicosis involves substantial exposure over 3–10 years; and chronic silicosis is the result of long-term exposure to lower levels of silica dust. In 1995, WHO and the International Labour Organization began an awareness and prevention campaign to eliminate silicosis by 2030. In response, several high-burden countries, including Brazil, Chile, China, Indonesia, Malaysia, Thailand, and Viet Nam, developed national programmes. Meanwhile, countries such as Australia, France, and the UK have shown that it is possible to reduce the incidence of silicosis with widespread prevention and awareness programmes.

However, in many low-income and-middle income countries, the lung disease continues to be a major occupational health hazard. In India, research estimates that up to 52 million workers are employed in occupations associated with silica dust, a substantial increase from the estimated 11.5 million workers exposed in 2015.

Projections have estimated that India is home to 25% of the global workforce, 92% of whom are engaged in the informal sector. It is within this informal sector that most occupations exposing workers to silica dust are found. However, despite the huge number of workers potentially at risk, India does not have a national silicosis programme, nor is there any accurate national-level data on its prevalence, incidence, mortality, or morbidity. In interviews with The Lancet, several experts and non-government workers expressed frustration at the Government's neglect of the disease and people who underpin India's economy.

Interviews revealed the complex nature of tackling silicosis in India, including unregulated and illegal workplaces, weak worker protection laws, a lack of awareness among the public and health professionals, lack of political will, and disease-related challenges, such as tuberculosis disease.

Although the disease is notifiable, it remains severely under-reported and undiagnosed, thus the true burden of disease is unknown. For example, the 2022–23 annual report by the Ministry of Labour and Employment recorded 441 cases of silicosis between 2008 and 2022. Studies have reported varying prevalence rates of silicosis across India among different occupations, from 37% among general mine workers in the western state of Rajasthan, to up to 55% among slate pencil workers in the central state of Madhya Pradesh, and 15% among pottery workers in the state of Gujarat. Research concluded that this huge discrepancy can partly be attributed to employers' inclinations to withhold notifications from their factories to avoid legal complications and the subsequent obligation to provide compensation to affected employees.

Silicosis is entirely preventable if the correct prevention measures, such as engineering controls to control the dust levels, personal protective equipment, adequate legislation, and other work practices are implemented along with the provision of adequate health care at the workplace, including regular screening for the early detection of silicosis.

Silicosis is the second greatest risk factor for tuberculosis disease after HIV infection. In 2018, India announced its goal of eliminating tuberculosis disease by 2025, 5 years ahead of the Sustainable Development Goals' vision of 2030. Today, the country continues to have the largest share of tuberculosis cases, making up 26% of global cases. However, its incidence continues to decline, with a 17.7% decline from 237 per 100 000 population in 2015, to 195 per 100 000 population in 2023.

Workers exposed to silica dust and those who have silicosis are not only at increased risk of developing tuberculosis disease, but patients who develop the severe combination of silicotuberculosis have a far greater mortality rate compared with those with tuberculosis disease alone, along with increased risk of treatment failure and developing drug resistance. The silicotuberculosis problem is multifaceted. Many patients with silicosis are misdiagnosed or only diagnosed with tuberculosis disease. The overlapping symptoms of both diseases complicate diagnosis and treatment, along with inadequate medical equipment and a lack of awareness among health professionals.

Effects of a community-driven water, sanitation, and hygiene intervention on diarrhea, child growth, and local institutions: A cluster-randomized controlled trial in rural Democratic Republic of Congo John P. Quattrochi, et al. Department of Global Health, School of Health, Georgetown University, Washington. john.quattrochi@georgetown.edu

Background: Diarrhea and growth faltering in early childhood reduce survival and impair neurodevelopment. We assessed whether a national program combining (i) funds for latrine and water upgrades; (ii) institutional strengthening; and (iii) behavior change campaigns reduced diarrhea and stunting, and strengthened local institutions.

Methods and Findings: We collaborated with program implementers to conduct a cluster-randomized controlled trial in four provinces of the Democratic Republic of Congo (DRC). Three hundred thirty-two rural villages were grouped into 121 clusters to minimize geographic spillovers. Between 15 March and 30 June 2018, we randomly assigned, after stratifying by province and cluster size, 50 intervention and 71 control clusters. Masking of participants and interviewers was not possible. Primary outcomes were length-for-age Zscore among children under 5 years of age, caregiver-reported diarrhea in last 7 days among children under 5 years of age, and an index of community WASH institutions. The primary analysis was on an intention-to-treat basis, using a binary variable indicating whether the participant was in an intervention or control cluster. Three thousand two hundred eighty-three households were interviewed between November 2022 and April 2023, median 3.6 years post-intervention. The intervention had no effect on diarrhea (adjusted mean difference -0.01 [95% -0.05 to 0.03]). Diarrhea prevalence was high overall, at 38% in the treatment group and 42% in the control group. The intervention had no effect on length-for-age Z-scores in children (adjusted mean difference -0.01 [95% CI -0.15 to 0.12]). In the control group, the mean length-for-age Z-score was -2.18 (1.60 SD). Villages in the intervention group had a 0.40 higher score on the WASH institutions index (95% CI 0.16–0.65). The percentage of villages in the intervention group with an active water, sanitation, and hygiene (or just water) committee was 21 pp higher than the control group. Households in the intervention group were 24 pp (95% CI 12–36) more likely to report using an improved water source, 18 pp (95% CI 10–25) more likely to report using an improved sanitation facility, and reported more positive perceptions of water governance (adjusted difference 0.19 SD [95% CI 0.04–0.34]). The trial had several limitations, including incomplete (86%) adherence in the implementation group, the absence of baseline measures, and the reliance on self-reported outcomes for some measures.

Conclusions: The DRC's national rural WASH program increased access to improved water and sanitation infrastructure, and created new WASH institutions, all of which persisted for at least 3.6 years. However, these effects were not sufficient to reduce diarrhea or growth faltering. The most likely explanation for these null results is that water quality did not meaningfully improve, despite improvements to WASH institutions and both water and sanitation infrastructure.

Pharmaceuticals / Essential Drugs / Diagnostics

45. Health Policy and Planning, Vol. 40 (4), May 2025, Pages 447–458.

Can public education campaigns equitably counter the use of substandard and falsified medical products in African countries?

Janelle M Wagnild et al. Corresponding author. Department of Anthropology, Durham University, Durham, UK, E-mail: j.m.wagnild@dur.ac.uk

Substandard and falsified (SF) medical products are a serious health and economic concern that disproportionately impact low- and middle-income countries and marginalized groups. Public education campaigns are demand-side interventions that may reduce the risk of SF exposure, but the effectiveness of such campaigns, and their likelihood of benefitting everybody, is unclear. Nationwide pilot risk communication campaigns, involving multiple media, were deployed in Ghana, Nigeria, Sierra Leone, and Uganda in 2020–21. Focus group discussions (n=73 with n=611 total participants) and key informant interviews (n=80 individual interviews and n=4 group interviews with n=111 total informants) were conducted within each of the four

countries to ascertain the reach and effectiveness of the campaign. Small proportions of focus group discussants (8.0–13.9%) and key informants (12.5–31.4%) had previously encountered the campaign materials. Understandability varied: the use of English and select local languages, combined with high rates of illiteracy, meant that some were not able to understand the campaign. The capacity for people to act on the messages was extremely limited: inaccessibility, unavailability, and unaffordability of quality-assured medicines from official sources, as well as illiteracy, constrained what people could realistically do in response to the campaign. Importantly, reach, understandability, and capacity to respond were especially limited among marginalized groups, who are already at the greatest risk of exposure to SF products. These findings suggest that there may be potential for public education campaigns to help combat the issue of SF medicines through prevention, but that the impact of public education is likely to be limited and may even inadvertently widen health inequities. This indicates that public education campaigns are not a single solution; they can only be properly effective if accompanied by health system strengthening and supply-side interventions that aim to increase the effectiveness of regulation.

46. JAMA Intern Med. 2025;185(6):615-616 Viewpoint Health Care Policy and Law Warning Labels and Positive Labels for Pulse Oximeters Gerke S et al., College of Law and the European Union Center, University of Illinois Urbana-Champaign, Champaign

The criticism of pulse oximeters for underperforming in patients with darker skin has reached a new volume in the last few years. During the COVID-19 pandemic, a disproportionate number of Black patients died, some of those deaths likely leading back to the reliance on false pulse oximeter readings. However, pulse oximeters have long been known to provide less accurate results for patients with darker skin than with lighter skin. Despite this knowledge, manufacturers of pulse oximeters have not changed their design. Most pulse oximeters do not display a visible warning label for users. But there is some movement in this area. Roots Community Health (Roots) filed a complaint against major pulse oximeter manufacturers and, in October 2024, struck a victory settlement with Medtronic. Additionally, the Food and Drug Administration (FDA) published its long-awaited draft guidance on pulse oximeters for medical purposes in January 2025, proposing a positive label for devices that can demonstrate "non-disparate performance," meaning "the pulse oximeter performs comparably across groups of individuals with diverse skin pigmentation.

In this Viewpoint, we discuss Medtronic's recent settlement and the FDA's newly published draft guidance. We argue that the positive label approach taken by the FDA may help solve the problem of underperforming pulse oximeters in individuals with darker skin in ways that warning labels cannot. We also point out that many pulse oximeters sold over the counter (OTC) are not reviewed by the FDA and are not covered by the FDA's new draft guidance, flagging a problematic regulatory loophole.

47. TMIH 2025;30(4):231-4

Clinicians in low- and middle-income settings need better access to point-of-care haemoglobin tests for identifying and managing children and pregnant women with severe anaemia South A et al., MRC CTU at UCL, Institute of Clinical Trials and Methodology, UCL, London, UK

Around one in four people around the world are affected by anaemia, with 52 million person years lived with disability due to anaemia in 2021. While anaemia is common around the world, people living in sub-Saharan Africa and south Asia are most affected, with pregnant women and children bearing the brunt. Severe anaemia can be life-threatening and requires prompt diagnosis and treatment. The World Health Organization lists automated full blood counts as an essential in vitro diagnostic for use in clinical laboratories, and haemoglobinometers for use in community settings and health facilities without laboratories. In particular, haemoglobin is one of six pathology and laboratory tests that the World Health Organization recommends that all pregnant women should receive. Point-of-care (POC) haemoglobin tests can also be useful for urgent clinical care decisions in settings where there is access to laboratories, as they can provide results very quickly. However, access to these important diagnostic tests is limited.

In December 2023, the Medical Research Council Clinical Trials Unit at University College London and Global Health Network hosted a webinar titled 'Increasing access to timely haemoglobin results: unlocking the potential of point-of-care tests'. The webinar featured researchers and clinicians from Kenya, Uganda, and the United Kingdom, and was attended by more than 200 people from 93 countries. This article summarises the discussion in order to raise awareness of the need for better access to these tests and further research into how to implement these tests in low- and middle-income country (LMIC) settings, which have received little attention to date.

Conclusion

POC haemoglobin tests exist that can swiftly identify people with severe anaemia. These offer a way of providing access to diagnosis for those who are not within easy reach of laboratory services. If used for monitoring those with severe anaemia following initial diagnosis, they may also free up severely limited laboratory capacity for other tests. They can also provide additional checks in the context of insufficient laboratory quality assurance.

The current situation, where POC haemoglobin tests are not available in many primary care facilities in LMICs where they could be particularly valuable, and where laboratory capacity is so stretched, severely impacts the quality of care for children and pregnant women. It may be contributing to health inequalities for those in poor and rural communities. Research into expanding access to these tests must be a priority if we are to address the burden of severe anaemia in these settings and work towards Universal Health Coverage.

Primary (Health) Care

48. Lancet Glob Health. 2025; 13: e795-e796 Improving primary health-care services in LMIC cities Richard J Lilford et al.

Urban environments are home to more than half of the people living in low-income and middle-income countries (LMICs), and this proportion will only increase over the coming decades. Much policy discussion of health services in LMICs still relies on knowledge and models derived from rural contexts, for which a single public-sector clinic is often the only option. In contrast, contemporary evidence shows that the urban health service landscapes are made up of dense networks of competing provider clinics that constitute a market. Improvement strategies that work in non-urban contexts are therefore unlikely to be sufficient in these environments. Innovative policy approaches that leverage choice and competition to re-shape markets offer great promise.

The first paper in this Series of two describes the configuration, cost, and quality of primary-care services in LMIC cities, along with the preferences of service users for different types of service. First, we find extensive evidence that numerous facilities are available to citizens, even in low-income neighbourhoods of LMIC cities. As a result, most people can reach multiple doctor or nurse clinics within 30 min. With the exception of some hospital-based polyclinics, most facilities are not busy, with the result that clinical capacity is underused. Second, service costs vary greatly and are substantially tied to commodities such as pharmaceuticals and diagnostics. Most people report low out-of-pocket costs, but the variance is wide and asymmetrical such that a minority face catastrophic expenses. A few LMICs at higher income levels offer freely available public services or insurance, but this is not the global norm. Third, the average quality of services is generally poor; many clinicians fail to make the correct diagnosis or implement the appropriate treatment, long-term conditions are poorly managed, antibiotic stewardship is inadequate, and medicine stockouts are frequent. Fourth, despite the complexity of this environment, patients (including those who are very financially disadvantaged) exhibit considerable agency, seeking out clinics perceived to offer a higher quality care, even if they have to travel further and pay more.

These facts present a compelling new image of primary health services in LMIC cities. Facilities are omnipresent and easy to reach, but are very diverse in terms of cost, quality, and crowding. The geography of LMIC cities has resulted in what might best be described as a market in which a variety of private and public providers

compete, at least implicitly. Most providers are low cost, low quality, and not crowded—but there are important exceptions to these characteristics.

The second paper discusses the implications of these findings for policy aimed at the improvement of primary health services in these cities. The presence of primary health-care markets provides an opportunity to reshape the market through policies that change the mix of available providers. This opportunity is not available in rural areas for which choice and competition are rare (and public facilities often dominate). In this Series paper we therefore describe not only methods to improve the quality of existing providers, but also methods that take advantage of competition and choice to reshape the market. Thus, while recognising that there are no one-size-fits-all solutions, we discuss approaches in three categories: (1) shaping the market by changing the mix of available providers; (2) improving existing services (including quality and financial accessibility); and (3) facilitating effective demand for better service.

One powerful example of shaping the market is investing in public facilities, which can stimulate improvement among facilities and crowd out those that fail to improve. Likewise, judicious regulation has been shown in a recent randomised controlled trial to improve quality in the public sector, while having positive knock-on effects for the private sector. One of the best ways to invest in improving existing services is through the formation of muti-disciplinary primary care teams integrating facility care (provided by doctors and nurses) with community care (provided by community health workers). Evidence from Brazil, an early adopter of this model, suggests that these teams provide integrated and equitable, preventive, acute, and long-term care. Existing services can also be improved by well designed continuing professional development, information technology (including virtual consultations), and various forms of management support.

Many initiatives have tried to improve care by stimulating demand. Successful interventions include providing patients with information on available services, involving communities in shaping local services, and providing free access by removing user fees or providing vouchers.

There is experimental evidence for most of the previously mentioned initiatives, but judging relevance and prioritisation has been difficult because most studies evaluate compound (ie, multi-component) interventions without using a factorial design, there is little evidence beyond immediate effects, and there are few cost-effectiveness or cost-benefit analyses. In addition, there is little evidence regarding people who are homeless or unregistered and for peri-urban areas and towns.

Now is a propitious time for primary care. After many years there are signs that it is getting the recognition it deserves at a time when health investments are rising with economic growth and a renewed focus on universal health coverage. But for any increased investment to be efficacious, it needs to account for the context and environment in which it is introduced. Policies in cities offer multiple opportunities—but also multiple challenges as market interactions can lead to unintended consequences. The evidence and analysis offered in our Series is intended to provide a framework for this debate.

49. Lancet Glob Health. 2025; 13:e942-e95

Supply-side and demand-side factors affecting allopathic primary care service delivery in low-income and middle-income country cities

50. Lancet Glob Health. 2025; 13:e954-e966

Policy and service delivery proposals to improve primary care services in low-income and middle-income country cities

Sexual Reproductive Health and Rights

51. Bull World Health Organ 2025 May 12;103(6):410–412.

Perspectives: abridged

Midwifery models of care in the context of increasing caesarean delivery rates

Tanya Doherty et al. Health Systems Research Unit, South African Medical Research Council, Cape Town, South Africa. Email: tanya.doherty@mrc.ac.za

Clinicians and researchers have used the concepts of too little too late, and too much too soon for almost a decade to describe disparities in access to and levels of use of clinical procedures in maternity care worldwide. The case of caesarean delivery is the most widely debated of these procedures. In many countries, rates are below safe levels in particular geographies or population groups, indicating that mothers and babies may be experiencing adverse outcomes due to a lack of access to the operation. On the other hand, the World Health Organization (WHO) has stated that, while low caesarean delivery rates indicate poor coverage of essential maternity care, no public health benefit exists when the rate exceeds 10–15% at a population level. Most women would prefer physiological labour and birth if this is safe and well supported. Performing medically unnecessary caesarean deliveries undermines women's choices and leads to a rise in adverse outcomes for women and newborns and generates significant extra costs for health systems. Projections estimate that, by 2030, about one third of all newborns will be born surgically. Of the five countries with the highest caesarean delivery rates globally (Brazil, Cyprus, Dominican Republic, Egypt and Türkiye), four are middle-income countries and one is high-income. In some middle-income countries, both very low and very high rates are problematic. For instance, in 2020, in the southern state of Telangana in India the overall rate was 7.5 times higher than in the north-eastern Meghalaya state. Predictors of caesarean delivery included higher education, delivering in a private hospital and high socioeconomic status. Data at national levels on caesarean delivery rates within public and privately funded health sectors are scarce due to the differences in health information systems and clinical governance oversight between the two sectors. An exception is Australia, where national-level monitoring data are available showing a caesarean delivery rate of close to half among women attending private hospitals and one third among women attending public hospitals in 2022. Differences between the public and private sectors are also found in a middle-income country, South Africa, where caesarean delivery rates are 32% (284459 caesarean deliveries out of 883244 live births) in the public sector; while in the private sector, caesarean delivery rates of 77% (81103 caesarean deliveries out of 105485 live births) are among the highest in the world.

The drivers of rising caesarean delivery rates are multifaceted and include factors relating to women, society, health workers, financing arrangements and health-care organizations. Underlying these rising caesarean delivery rates is the lack of investment, commitment and advocacy for midwifery models of care. The midwifery philosophy of care promotes a person-centred approach to care; values the women–midwife relationship and partnership; optimizes physiological, biological, psychological, social and cultural processes; and uses interventions only when indicated. A recent systematic review reveals that approaches such as midwife-led continuity of care models result in higher rates of normal physiological vaginal births, reduced caesarean sections, safer outcomes, more positive birth experiences and lower costs. In October 2024, WHO published a global position paper on transitioning to midwifery models of care.

To avoid continuing health system-related harm to many women and their neonates, middle-income countries must address their alarming rates of caesarean births by shifting to more person-centred, team-based midwifery models of care. In a case study of midwife-led birth centres in four low-middle income countries (Bangladesh, Pakistan, South Africa and Uganda), four universal themes emerged that described the enabling factors influencing success of such centres: (i) an effective financing model; (ii) quality midwifery care that is recognized by the community; (iii) interdisciplinary and interfacility collaboration, coordination and functional referral systems; and (iv) supportive and enabling leadership and governance at all levels. Several countries provide examples of midwifery models of care that provide useful lessons to guide policy-makers in this health system transition. The considerations raised in this article are critical to ensure the success of such shifts, valuing the autonomy, skills and potential of midwives to transform the pregnancy, birth and postnatal care experiences for women and families, for their short and longer-term benefit.

52. Lancet 2025;405(10488):1468-80

Causes of and risk factors for postpartum haemorrhage: a systematic review and meta-analysis Yunas I et al., Department of Metabolism and Systems Science, College of Medicine and Health, University of Birmingham, Birmingham, UK

Correspondence to AJ Devall <a.j.devall@bham.ac.uk>
Background: An understanding of the causes of postpartum haemorrhage is needed to provide appropriate treatment and services. Knowledge of the risk factors for postpartum haemorrhage can help address modifiable risk factors. We did a systematic review and meta-analysis to identify and quantify the various causes and risk factors for postpartum haemorrhage.

Methods: In this systematic review and meta-analysis, we did a systematic literature search in MEDLINE, Embase, Web of Science, Cochrane Library, and Google Scholar for cohort studies of postpartum haemorrhage from Jan 1, 1960, to Nov 30, 2024 without language restrictions. At least two authors independently undertook study selection, data extraction, and quality assessment. Population-based cohort studies available in English were eligible. Rates of postpartum haemorrhage causes as well as crude and adjusted odds ratios (ORs) for risk factors were pooled using a random-effects model. Risk factors were classified as having weak, moderate, or strong association based on the pooled ORs: weak (OR >1 to 1.5), moderate (OR >1.5 to 2), and strong (OR >2). This study is registered with PROSPERO, CRD42023479686.

Findings: We synthesised data from 327 studies, including 847 413 451 women with no restriction on age, race, or ethnicity. Most studies were of high methodological quality. The pooled rates of the five commonly reported causes of postpartum haemorrhage were uterine atony (70.6% [95% CI 63.9-77.3]; n=834 707 women, 14 studies), genital tract trauma (16.9% [9.3-24.6]; n=18 449 women, six studies), retained placenta (16.4% [12.3-20.5]; n=235 021 women, nine studies), abnormal placentation (3.9% [0.1-7.6]; n=29 638 women, two studies), and coagulopathy (2.7% [0.8-4.5]; n=236 261, nine studies). The pooled rate of women with multiple postpartum haemorrhage causes was 7.8% (95% CI 4.7-10.8; n=666, two studies). Risk factors with a strong association with postpartum haemorrhage included anaemia, previous postpartum haemorrhage, caesarean birth, female genital mutilation, sepsis, no antenatal care, multiple pregnancy, placenta praevia, assisted reproductive technology use, macrosomia with a birthweight of more than 4500 g, and shoulder dystocia. Risk factors with moderate association with postpartum haemorrhage included BIMI \geq 30 kg/m2, COVID-19 infection, gestational diabetes, polyhydramnios, pre-eclampsia, and antepartum haemorrhage. Risk factors with weak association with postpartum haemorrhage included Black and Asian ethnicity, BMI 25-29.9 kg/m2, asthma, thrombocytopenia, uterine fibroids, antidepressant use, induction of labour, instrumental birth, and premature rupture of membranes.

Interpretation: The finding that uterine atony is the commonest cause of postpartum haemorrhage supports the WHO recommendation for all women giving birth to be given prophylactic uterotonics. Knowledge of risk factors with a strong association with postpartum haemorrhage can help to identify women at high risk of postpartum haemorrhage who could benefit from enhanced prophylaxis and treatment. The importance of multiple concurrent causes of postpartum haemorrhage supports the use of treatment bundles.

53. Lancet 2025;405(10488):1505-54

The 2025 report of the Lancet Countdown to 2030 for women's, children's, and adolescents' health: tracking progress on health and nutrition

Amouzou A et al., Department of International Health, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, USA

Correspondence to T Boerma < ties.boerma@umanitoba.ca>

In line with previous progress reports by Countdown to 2030 for Women's, Children's, and Adolescents' Health, this report analyses global and regional trends and inequalities in health determinants, survival, nutritional status, intervention coverage, and quality of care in reproductive, maternal, newborn, child and adolescent health (RMNCAH) and nutrition, as well as country health systems, policies, financing, and prioritisation. The focus is on low-income and middle-income countries (LMICs) where 99% of maternal deaths and 98% of child and adolescent deaths (individuals aged 0–19 years) occur, with special attention to sub-Saharan Africa and South Asia.

Recognising the urgency of reaching the Sustainable Development Goal (SDG) for health, SDG 3, and healthrelated targets by 2030, the report assesses whether the momentum needed to reach these goals has been sustained, accelerated, stagnated, or regressed in comparison with the Millennium Development Goal (MDG) period (2000–15). Although most health and health-related indicators continue to show progress, there has been a notable slowdown in the rate of improvement after 2015, falling well short of the pace needed to achieve the 2030 SDG targets. This deceleration in pace contrasts sharply with the aspired grand convergence in health, characterised by drastic reductions in mortality and RMNCAH inequalities, which was expected to occur during the SDG period based on the assumption that the spectacular progress achieved during the MDG period would continue unabated. Multiple threats, external and internal to the RMNCAH health community, must be addressed to safeguard the gains in RMNCAH and nutrition and to accelerate progress. Furthermore, a large gap between sub-Saharan Africa, especially West and Central Africa, and other parts of the world persists for many indicators, necessitating further prioritisation of this region.

Conclusions and future directions

To address slowdown in RMNCAH and nutrition progress in the first half of the SDG era, as well as variations in progress across regions and country-income groups, we hope that this report's analyses will fuel dialogue and action needed to ensure acceleration of progress in women's, children's, and adolescents' health. Our recommendations fall into five themes: Explicit focus on sub-Saharan Africa / Strengthening health systems for RMNCAH and nutrition / Safeguarding progress against crises / Monitoring and accountability / Revitalising RMNCAH and nutrition.

The challenge ahead is for the RMNCAH community to develop a persuasive framing in a changed context that would inspire unified action across all partners ranging from grassroots organisations to international actors.

54. Lancet Glob Health 2025;13(4):e626-e634

Global and regional causes of maternal deaths 2009-20: a WHO systematic analysis Cresswell JA et al., UNDP-UNFPA-UNICEF-WHO-World Bank Special Programme of Research, Development, and Research Training in Human Reproduction (HRP), Department of Sexual and Reproductive Health and Research, WHO, Geneva, Switzerland <cresswellj@who.int>

Background: Maternal mortality is not on track to meet Sustainable Development Goal (SDG) target 3.1 of a global maternal mortality ratio below 70 per 100 000 livebirths by 2030. Updated evidence on causes of death is needed to accelerate progress.

Methods: We conducted a multi-strategy systematic review to identify causes of maternal deaths occurring in 2009-20. Data sources included civil registration and vital statistics systems data from the WHO Mortality Database, reports published by Member States, and national and subnational journal articles identified via bibliographic databases. We used a Bayesian hierarchical model to estimate the maternal cause of death distribution by SDG regions and worldwide. Given the paucity of data on maternal suicide and late maternal deaths occurring beyond 42 days postpartum, additional analyses were conducted to estimate the proportion of maternal deaths from suicide and the ratio of maternal to late maternal deaths (all cause).

Findings: Globally, the most common cause of maternal death was haemorrhage (27%; 80% uncertainty interval 22-32), followed by indirect obstetric deaths (23%, 18-30), and hypertensive disorders (16%, 14-19). The proportion of haemorrhage deaths varied substantially by region and was highest in sub-Saharan Africa and Western Asia and Northern Africa. The proportion of maternal deaths from hypertensive disorders was highest in Latin America and the Caribbean. Most maternal deaths from haemorrhage and sepsis occurred during the postpartum period. Only 12 countries recorded one or more maternal suicides; of those countries, the proportion of deaths from suicide ranged from below 1% to 26% of maternal deaths. For countries reporting at least one late maternal death (ie, deaths that occur more than 42 days but less than 1 year after the termination of pregnancy), the ratio of late maternal deaths to maternal deaths up to 42 days ranged from <0.01 to 0.07.

Interpretation: Haemorrhage remains the leading cause of death, despite the existence of effective clinical interventions, emphasising the need for improved access to quality health care. The timing of most deaths in the postpartum period demands renewed commitment to improving the provision of postpartum care in addition to intrapartum care. Indirect causes of death require health system approaches to integrate obstetric and non-obstetric care.

55. Lancet Glob Health. 2025 Apr;13(4):e679-e688.

Cost-effectiveness of intrapartum azithromycin to prevent maternal infection, sepsis, or death in low-income and middle-income countries: a modelling analysis of data from a randomised, multicentre, placebo-controlled trial

Jackie K Patterson et al, ...

Background: Sepsis is one of the leading causes of maternal mortality globally. In 2023, the Azithromycin Prevention in Labor Use (A-PLUS) trial showed intrapartum azithromycin for women planning a vaginal birth reduced the risk of maternal sepsis or death and infection. We aimed to evaluate the cost-effectiveness of intrapartum azithromycin for pregnant people planning a vaginal birth in low-income and middle-income countries (LMICs) using A-PLUS trial data.

Methods: We compared the benefits and costs of intrapartum azithromycin versus standard care across 100 000 model simulations using data from the A-PLUS trial and a probabilistic decision tree model that included 24 mutually exclusive scenarios. A-PLUS was a randomised, double-blind, placebo-controlled trial that enrolled 29 278 women in labour at 28 weeks' gestation or more at eight sites in the Democratic Republic of the Congo, Kenya, Zambia, Bangladesh, India, Pakistan, and Guatemala. Women randomly assigned to azithromycin received a single intrapartum 2 g oral dose. In this cost-effectiveness analysis, we considered the cost of azithromycin treatment and its effects on a composite outcome of maternal infection, sepsis, or death and its individual components, and health-care use. Our analysis had a health-care sector perspective. We summarised results as an average and 95% CI of the model simulations. We also conducted sensitivity analyses. A-PLUS was registered at ClinicalTrials.gov, number NCT03871491.

Findings: In model simulations, intrapartum azithromycin resulted in 1592·0 (95% CI 1139·7 to 2024·1) cases of maternal infection, sepsis, or death averted per 100 000 pregnancies, yielding 248·5 (95·3 to 403·7) facility readmissions averted, 866·8 (537·8 to 1193·2) unplanned clinic visits averted, and 1816·2 (1324·5 to 2299·7) antibiotic regimens averted. Using mean health-care costs across the A-PLUS sites, intrapartum azithromycin resulted in net savings of US\$32 661 (-52 218 to 118 210) per 100 000 pregnancies and 13·2 (8·3 to 17·9) disability-adjusted life-years averted. The cost of facility readmission, cost of azithromycin, and probability of infection had the greatest impact on the incremental cost.

Interpretation: In most cases, intrapartum azithromycin is a cost-saving intervention for the prevention of maternal infection, sepsis, or death in LMICs. This evidence supports global consideration of intrapartum azithromycin as an economically efficient preventive therapy to reduce infection, sepsis, or death among women planning a vaginal birth in LMICs.

56. Lancet Glob Health. 2025 Apr;13(4):e689-e697.

Effectiveness of intrapartum azithromycin to prevent infections in planned vaginal births in low-income and middle-income countries: a post-hoc analysis of data from a multicentre, randomised, double-blind, placebo-controlled trial

Waldemar A Carlo et al, ...

57. Lancet Glob Health. 2025 May;13(5):e888-e899.

Effects and costs of a multi-component menstrual health intervention (MENISCUS) on mental health problems, educational performance, and menstrual health in Ugandan secondary schools: an open-label, school-based, cluster-randomised controlled trial Kate A Nelson et al, ...

Background: Menstrual health is a human rights issue, affecting many aspects of life including mental health, wellbeing, and education. We assessed the effectiveness and costs of a school-based, multi-component menstrual health intervention (MENISCUS) to improve mental health problems and educational performance among in-school adolescents.

Methods: We conducted a parallel-arm, cluster-randomised trial in secondary schools in Wakiso and Kalungu districts in Uganda. Schools were eligible for inclusion if they had both male and female students; senior 1-4 classes; day or mixed day and boarding students; at least minimal water, sanitation, and hygiene (WASH) facilities; and enrolments of 50-125 female Senior 1 students in Wakiso district and 40-125 female Senior 1 students in Kalungu district. Schools were randomised (1:1) to the intervention or control condition, stratified by district and baseline mean school examination score. The intervention included creating action groups, strengthening teacher-delivered puberty education, distributing menstrual kits, supporting student-led drama skits, providing pain-management strategies, and improving school water and sanitation facilities. The control condition was provision of printed government menstrual health materials. Schools, participants, and

implementors, including the study clinician who monitored adverse events, could not be masked to allocation status. Primary outcomes were mental health problems using the Strength and Difficulties Questionnaire (SDQ) Total Difficulties Score and independently assessed educational performance at individual level, assessed in all female participants at endline. We estimated cluster-intention-to-treat intervention effects using mixed-effects models accounting for school clustering and adjusted for randomisation strata and baseline school-level means of outcomes. The study was registered at the ISRCTN registry, ISRCTN45461276 and is completed. Findings: 60 randomly selected schools (44 from Wakiso and 16 from Kalungu) were randomly assigned (30 per group) to the intervention or the control group, and none withdrew. Between March 21 and July 5, 2022, 3841 female students participated in baseline assessments (89.7% of those eligible) and between June 5 and Aug 22, 2023, 3356 participated in endline assessments (1666 in the control group and 1690 in the intervention group). Female participants had a median age of 16 years (IQR 15-16). At endline, there was no evidence of a difference in mental health problems (mean SDQ score, 10.8 in the intervention group vs 10.7 in the control group; adjusted mean difference [aMD] 0.05 [95% CI -0.40 to 0.50]) nor educational performance (mean z score, 0.20 in the intervention group vs 0.12 in the control group; aMD 0.05 [95% CI -0.10 to 0.19]), despite improvements to menstrual health. The annual implementation cost was US\$85 per Senior 2 female student. One participant had a serious adverse event (severe anaemia secondary to excess vaginal bleeding), which was deemed to be possibly related to the intervention.

Interpretation: Improving multiple dimensions of menstrual health in secondary schools in Uganda is important for health and human rights but is not sufficient to improve mental health or educational performance over 1 year.

58. PLoS Med 22(2): e1004528.

Perspective: Detrimental infant and maternal outcomes of undiagnosed asymptomatic malaria in pregnancy James G. Beeson, Daniel Herbert Opi, Burnet Institute; Monash University; University of Melbourne, Melbourne, Victoria, Australia. james.beeson@burnet.edu.au

Over 40% of the world's population is at risk of malaria, yet progress in reducing the global burden has stalled since 2015. Pregnant women, in particular, are highly susceptible to both infection and disease. Malaria during pregnancy can lead to severe outcomes, including maternal anaemia and low infant birth weight, as well as pre-term birth, miscarriage and stillbirth, among others. Most malaria cases are due to the species Plasmodium falciparum and Plasmodium vivax, and clinical illness occurs during the blood-stage of infection when Plasmodium parasites infect and replicate in red blood cells (RBCs). In pregnant women, infected RBCs can accumulate in the placenta, which is a prominent feature of P. falciparum rather than P. vivax infection, contributing to negative outcomes for both the mother and developing fetus.

Malaria is typically diagnosed by testing peripheral blood using rapid diagnostic tests that can detect parasite proteins, or by microscopic examination of stained blood smears. While these tests generally perform well for diagnosis of symptomatic malaria illness with a high parasite burden, they have much lower sensitivity as screening tests for malaria infection and in asymptomatic infections in which parasitemia is typically low. Furthermore, they are less sensitive for diagnosis of P. vivax infections partly due to its different biology and low parasite densities. More sensitive nucleic acid amplification tests, such as PCR, are available, but currently they are only widely used in surveillance studies and research rather than for point-of-care diagnosis and treatment of malaria due to technical and cost limitations. So-called 'ultra-sensitive' PCR tests using highvolume concentrated blood samples have been developed that can detect very low parasitemia. Using these more sensitive tests has revealed that a large proportion of Plasmodium spp infections are not detected by standard diagnostic tests, and these are often referred to as submicroscopic infections. Studies across multiple populations show that a large proportion of Plasmodium infections in pregnancy are submicroscopic, lowdensity infections. While the negative effects of high-density and microscopically detectable infections on pregnancies are well documented, the impact of low and very low submicroscopic infections in pregnancy is less clear, especially in the Asia-Pacific region where P. vivax is often the more prevalent species and coinfections of P. falciparum and P. vivax are common.

A new study of over 4,000 pregnant women now provides important data demonstrating that even submicroscopic infections can have substantial negative impacts for both the fetus and mother. The study was conducted in a setting of low and unstable malaria transmission around the Thailand–Myanmar border, where

both P. falciparum and P. vivax are endemic, and included women attending their first antenatal clinic (median gestational age 16.5 weeks) who were followed during pregnancy. An important aspect to this study was the use of an ultra-sensitive PCR test capable of detecting as few as 22 parasites per mL of blood. The authors found that, at the first antenatal clinical visit, these submicroscopic infections were 4-times more prevalent than microscopically detectable infections. Thus, screening for infection using standard diagnostics would miss most infections in pregnancy, and even a standard PCR test using dried blood spots failed to detect 84% of infections in this study due to insufficient sensitivity. Repeated follow-up testing of samples from women during pregnancy found that most infections did not become microscopically detectable over time, underscoring the limitations of routine diagnostics in detecting these missed infections. A crucial finding of this study is the clinical sequelae associated with these low-level, asymptomatic infections: submicroscopic infections were associated with substantially lower infant birth weight, and this negative association was observed for both P. falciparum and P. vivax infections. Low birth weight is a major risk factor for infant death and can have other long-term impacts including impaired growth and development in the child. P. falciparum, but not P. vivax, infections were also associated with increased risk of maternal anaemia. The demonstration that most Plasmodium infections in pregnancy are not detected by microscopy or standard PCR, and that despite their low parasite burden, these infections have measurable negative impacts on pregnant women and infants, highlights the importance of preventing malaria in pregnancy. Moreover, these findings have important implications for malaria elimination efforts if a large proportion of infections are undetected by conventional diagnostics, and therefore remain untreated. Key questions and challenges remain about how to combat these missed submicroscopic infections. Implementing routine screening using ultrasensitive PCR, as used in this study, for all pregnant women in endemic areas is not presently feasible due to financial and technical constraints. Ongoing research around new diagnostic technologies may generate highly sensitive diagnostics in the future that are affordable and easily accessible for screening and treatment. Strengthening and investing in available malaria control and prevention measures in endemic populations remains an essential complement to development of new diagnostic tools. These include strategies to reduce mosquito exposure, such as insecticide-treated bed nets and spraying of residual insecticides; however, their efficacy is variable depending on the endemic setting. Novel approaches for vector control and prevention of exposure is an area of active research, and might generate future tools that reduce malaria and the risk for pregnant women. In settings with moderate-to-high transmission, the use of intermittent preventive treatment or chemoprophylaxis in pregnancy is recommended to clear and prevent infections, but it is generally not recommended in areas of low transmission, in part because of a less favourable balance between risks and benefits. Two new vaccines for P. falciparum have recently been approved for implementation in young children, but their potential for malaria prevention in pregnant women and in regions with low transmission is not known, and they are not effective against P. vivax. Ongoing research is focussed on developing vaccines to prevent infection and interrupt transmission of malaria. Targeted and improved control measures and effective vaccines would go a long way in reducing the huge burden of submicroscopic Plasmodium infections and the negative impacts during pregnancy.

It remains unclear how submicroscopic Plasmodium infections persist and exert their negative maternal and fetal effects during pregnancy. Further research is needed to elucidate their impact and identify strategies for detection and prevention. Parasitemia in peripheral blood may not reflect the total parasite biomass, particularly since P. falciparum can sequester in the placenta. Multi-morbidity is common among pregnant women in malaria endemic populations and low- and middle-income settings and these may contribute to negative outcomes. A better understanding of interactions between detectable and submicroscopic malaria infections and maternal co-morbidities may be valuable in preventing harmful effects and optimising pregnancy outcomes.

59. TMIH 2025;30(6):531-8

Risk stratification during antenatal care failed to identify most mothers who experienced adverse pregnancy outcomes: A prospective study from Kakamega County, Kenya

Cooper JE at al., Department of Global Health and Population, Harvard T.H. Chan School of Public Health, Boston, Massachusetts, USA

Introduction: Risk stratification of pregnancies informs clinical care globally. Yet recent research has cast doubt on the ability of currently used population-level risk measures to accurately predict poor outcomes at the individual level. We examine the assumption that existing forms of risk stratification can successfully identify women likely to develop complications during delivery in a rural setting in Kenya.

Methods: We conducted a prospective observational study of 19,653 pregnant women in Kakamega County in Western Kenya. Women were contacted three times during the perinatal period and surveyed about provideridentified risks and self-assessed concerns about pregnancy complications, delivery process outcomes, and adverse delivery outcomes. Measures of risk were derived from women's self-reporting. We compared delivery process outcomes and adverse delivery outcomes between high- and low-risk pregnancies, and between women with and without expressed concerns about delivery complications. Delivery process outcomes included intrapartum referral, unplanned caesarean section, blood transfusion, hysterectomy, or admission to an intensive care unit. Adverse delivery outcomes included stillbirth, neonatal mortality, and maternal mortality. We reported means and confidence intervals for each category, and tested for differences using bivariate linear regression.

Results: Thirty-eight percent of pregnancies had at least one risk factor consistent with a high risk pregnancy; the remaining 62% were low risk by this criteria. Rates of most adverse process outcomes and delivery outcomes were higher among pregnancies with known risks. However, 64.5% of maternal deaths and 54.8% of all deaths in the sample took place among pregnancies characterised as low risk.

Conclusions: Risk stratification using existing indicators of risk during pregnancy is inadequate to identify women at risk of adverse health outcomes in this setting.

Surgery

60. Lancet Glob Health. 2025 Apr;13(4):e635-e645.

Patient outcomes after surgery in 17 Latin American countries (LASOS): a 7 day prospective cohort study Latin American Surgical Outcomes Study (LASOS) group

Background: Access to safe surgical treatment across Latin America is limited by underfunded and fragmented health systems. Epidemiological data are required to describe surgical activity and patient outcomes. Methods: We did this 7 day prospective cohort study in 17 Latin American countries, collecting data describing inpatient surgery in adults (aged \geq 18 years). The primary outcome was in-hospital postoperative complications within 30 days after surgery. Secondary outcomes were in-hospital mortality, duration of hospital stay, and admission to critical care within 30 days after surgery. This study is registered with ClinicalTrials.gov, NCT05169164.

Findings: Between June 1, 2022, and April 30, 2023, we included 22 126 patients (mean age 49·7 years [SD 18·2]; 9260 [41·9%] male and 12 866 [58·1%] female; 10 180 [46·0%] White) from 284 hospitals. Of the 22 126 patients, 657 (3·0%) patients for the outcome of complications and 380 (1·7%) patients for mortality had missing data. Most patients were low risk (American Society of Anesthesiologists [ASA] grade I or II: 17 311 [78·7%] of 21 979 patients), undergoing non-major surgery (14 944 [68·0%] of 21 986 patients), and on an elective basis (14 837 [67·5%] of 21 988 patients). Despite this low-risk profile, 3163 (14·6%) of 21 632 patients developed postoperative complications resulting in 477 (2·2%) deaths. The most frequent complication category was infection, affecting 1795 (8·2%) patients. The high mortality from complications (failure to rescue) of 15·1% (477 deaths in 3163 patients with complications) suggests significant problems with postoperative care. 2978 (13·6%) patients were admitted to a critical unit immediately after surgery, but 180 (37·7%) of 477 patients who died never received critical care. Patients with complications. Postoperative mortality and complications were strongly associated with increasing ASA grade, urgency of surgery, and grade of surgery (intermediate and major).

Interpretation: Patients receiving inpatient surgery in Latin America experienced high mortality rates, likely relating to standards of ward care after surgery. Given the rising demand for surgical treatments, resource-efficient measures are urgently needed to improve patient outcomes after surgery across Latin America.

61. World Journal of Surgery 2025 Mar;49(3):652-663.

Intersectoral Collaboration Between Traditional Bonesetters and Formal Healthcare: A Systematic Review on Past Initiatives and Stakeholder Perspectives

Binnerts JJ, Thom C. C. Hendriks TCC, Hermans E et al. |Department of Surgery, Radboud University Medical Centre, Nijmegen, The Netherlands < joost.binnerts@radboudumc.nl>

Hussein S, Vrije Universiteit Medical Centre, Amsterdam, The Netherlands

Background: Bone fractures in low- and middle-income countries are commonly managed by traditional bonesetters (TBSs). Past studies emphasize the potential for improved fracture care through intersectoral cooperation. This review gauged support among stakeholders for intersectoral collaboration and the results of previous initiatives.

Methods: Five medical databases were reviewed. Studies focusing on stakeholder perspectives and articles detailing collabo- rative initiatives were included. Data extraction and synthesis were carried out using the Cochrane Consumers and Commu- nication Review Group's template. Additionally, all studies underwent quality assessment.

Results: Of the 3821 identified articles, 16 were included after full-text screening. Twelve articles presented stakeholder per- spectives, whereas four discussed collaborative initiatives. The overall article quality was low: articles on stakeholder per- spectives scored on average 1.42 out of 4 points, whereas articles on collaborative initiatives scored a mean 1.25 points. In total, 62% of stakeholders (75% of TBSs, 92% of hospital staff, and 52% of patients) expressed support for intersectoral collaboration. The ratio between stakeholders expressing support versus those opposing was 4.4:1. No articles presented data on governmental perspectives. The most mentioned collaborative forms were TBS training (24% of stakeholders) and an integrative model (16% of stakeholders). Interventional studies all consisted of TBS training, reporting improved clinical outcomes and increased practice integration.

Conclusion: Despite the limited and low-quality evidence on collaboration initiatives and perspectives, most stakeholders seem supportive of intersectoral collaboration, with training and integration being commonly suggested.

62. Inquiry 2025 Jan-Dec:62:469580251325031

Broad Support Among Stakeholders for Collaboration Between Traditional Bonesetters and Formal Healthcare: A Qualitative Study in a Resource-Limited Setting

Binnerts J, Hendriks TCC, Edwards M, Hermans E et al., Radboud University Medical Centre, Nijmegen, The Netherlands

Buzugbe N. Vrije Universiteit Medical Centre, Amsterdam, The Netherlands

63. World J Surg 2025;49(5):1368-76

Incidence, Impact, and Healthcare-Seeking Behavior for Extremity Fractures in Resource-Limited Settings: A Household Survey in Rural Tanzania

Binnerts JJ, Hendriks TCC, Edwards MJR, Hermans E et al., Radboud University Medical Centre, Nijmegen, The Netherlands

64. BMJ Glob Health 2025;10(5):e018423

The impact of surgical task-sharing in Sierra Leone: a nationwide longitudinal observational study on surgical workforce and volume, 2012-2023

Mali Eggen Furre # 1, Maria Svengaard # 1, Elisabeth Øvreås 1, Alex J van Duinen 1 2, Thomas Ashley 3 4, Martin P Grobusch 5, Juul Bakker 1 4, Jaap Gunneweg 4, Nobhojit Roy 6, Mustapha S Kabba # 3, Håkon Angell Bolkan # 7 2

1 Department of Public Health and Nursing, Norwegian University of Science and Technology, Trondheim, Norway.

2 Clinic of Surgery, Trondheim University Hospital St Olav's Hospital, Trondheim, Norway.

3 Ministry of Health, Freetown, Sierra Leone.

4 CapaCare, Masanga, Sierra Leone.

5 Department of Infectious Diseases, Amsterdam University Medical Centres, Amsterdam, The Netherlands.

Background: A surgical task-sharing programme was initiated by the Sierra Leonean Ministry of Health in 2011 to enhance public surgical capacity and equalise access between urban and rural populations by redistributing surgical tasks within a limited healthcare workforce.

Methods: This longitudinal nationwide study, involving all healthcare facilities with an operating theatre in Sierra Leone, analysed changes in volume and population rates of surgery and distribution of surgical resources before (2012), 5 (2017) and 10 years after (2023) the initiative was introduced.

Results: Surgical volume rates increased from 400 to 505 procedures per 100 000 population between 2012 and 2023. The public sector became the main provider, performing 56.0% of all operations in 2023, up from 39.6% in 2012. Rural surgeries increased by 77.6% over the decade, almost two times more than in urban areas. In rural areas, there was a transition from non-specialised physicians performing 46.2% of operations in 2012, to task-shared associate clinicians performing 55.1% (95% CI 49.5% to 60.7%) in 2023, making them the main surgical provider. Nationwide caesarean section rates increased from 1.4% (2012) to 5.3% (95% CI 4.6% to 6.0%) (2023). Caesarean sections were in 2023 mostly performed in public facilities (81.3%, 95% CI 80.1.0% to 82.5%) by associate clinicians (57.6%, 95% CI 53.2% to 61.9%).

Conclusions: Over the last decade, Sierra Leone has seen a shift in surgical care, with a transition from general to obstetric surgeries, from private to public institutions, and an expansion of surgical care in rural areas, with associate clinicians as the leading provider. The introduction of a nationwide surgical task-sharing initiative to strengthen the surgical workforce at district governmental hospitals in 2011 has emerged as the major contributor to the change in surgical activity and output observed in Sierra Leone over the last decade.

65. BMJ Glob Health 2025;10(5):e018512

Surgical task-sharing in Sierra Leone: barriers and enablers from provider and facilitator perspectives Jurre van Kesteren 1 2, Mirte Langeveld 2, 3, 4, Thomas Ashley 5, 6, Tairu Fofanah 6, 7, Hendrik Jaap Bonjer 8, 2, Hakon Angell Bolkan 9, 10

1 Department of Surgery, Amsterdam UMC Location VUmc, Amsterdam, Noord-Holland, Netherlands j.vankesteren@amsterdamumc.nl.;2 Global Surgery Amsterdam, Amsterdam, Netherlands.; 3 Harvard T H Chan School of Public Health, Boston, Massachusetts, USA.; 4 Department of Surgery, OLVG, Amsterdam, Netherlands.; 5 Department of Surgery, University of Sierra Leone Teaching Hospital Complex, Connaught Hospital, Freetown, Sierra Leone.; 6 CapaCare, Masanga, Sierra Leone.; 7 Office of the Chief Community Health Officer, Freetown, Sierra Leone.; 8 Department of Surgery, Amsterdam UMC Location VUmc, Amsterdam, Netherlands.; 9 Department of Public Health and Nursing, Norwegian University of Science and Technology, Trondheim, Norway; 10 Clinic of Surgery, St Olav's Hospital HF, Trondheim, Norway.

Tuberculosis

66. Lancet 2025;405(10485):1155-66

Effect of digital adherence technologies on treatment outcomes in people with drug-susceptible tuberculosis: four pragmatic, cluster-randomised trials

Degu Jerene D et al., KNCV Tuberculosis Foundation, The Hague, Netherlands <degu.dare@kncvtbc.org>

Background: The impact of digital adherence technologies on tuberculosis treatment outcomes remains poorly understood. We investigated whether smart pillboxes and medication labels can reduce poor treatment outcomes in patients with tuberculosis.

Methods: We did independent pragmatic, cluster-randomised trials in the Philippines, South Africa, Tanzania, and Ukraine. 110 clusters were randomly assigned (1:1) to standard of care versus intervention arms, which were further randomly assigned (1:1; except in Ukraine) to a smart pillbox or medication labels. We enrolled adult patients receiving treatment for drug-susceptible tuberculosis. The pillbox gave an audio-visual reminder to take medication, and when the box was opened, a signal was transmitted to the adherence platform. Those in the labels arm received medications with label attached, showing a code, which they messaged when a dose was taken; otherwise, a reminder was sent. The primary outcome was a composite poor end of treatment outcome, defined as having documented treatment failure, loss to follow-up (treatment interruption for ≥ 2 consecutive months), switched to a multidrug-resistant regimen more than 28 days after treatment start, or death. The trials are complete and registered with ISRCTN, 17706019.

Findings: Between June 21, 2021, and July 8, 2022, we enrolled 25 606 individuals (12 626 on standard of care and 12 980 on intervention) across 220 clusters in the four trials, of whom 23 483 (91·7%; 11 313 on standard of care and 12 170 on intervention) were included in the intention-to-treat population. 8208 (35·0%) of 23 483 individuals were female. 9717 (85·9%) of 11 313 individuals in the standard of care arm and 10 540 (86·6%) of 12 170 individuals in the intervention arm were analysed for the primary outcome. The risk of the primary outcome did not differ by intervention arm for all countries (Philippines adjusted odds ratio 1·13, 95% CI 0·72-1·78, p=0·59; Tanzania 1·49, 0·99-2·23; p=0·056; South Africa 1·19, 0·88-1·60; p=0·25; Ukraine adjusted risk ratio 1·15, 95% CI 0·83-1·59; p=0·38). Two incidents of social harm were reported due to inadvertent disclosure of treatment status in the pillbox arm, resulting in withdrawal of the participants.

Interpretation: Digital adherence technologies did not reduce poor treatment outcomes in the four countries investigated. The use of digital adherence technologies should be based on careful review of additional data on economic evaluation, patient and stakeholder preferences, and the effect on other important patient outcomes beyond programmatic treatment outcomes.

67. Lancet Microbe 2025; Mar 28:101085. Online ahead of print.

Performance of stool Xpert MTB/RIF Ultra for detection of Mycobacterium tuberculosis among adults living with HIV: a multicentre, prospective diagnostic study

Kasule GW 1, Sabine Hermans S 2 et al., Stool4TB Global Partnership

1 Department of Medical Microbiology, College of Health Sciences Makerere University, Kampala, Uganda; Universitat de Barcelona, Barcelona Institute for Global Health, Hospital Clínic, Barcelona, Spain; National TB Reference Laboratory, Ministry of Health, Kampala, Uganda.

2 Amsterdam UMC, location University of Amsterdam, Department of Global Health, Amsterdam Institute for Global Health and Development, Amsterdam, Netherlands; Centre for Tropical Medicine and Travel Medicine, Department of Infectious Diseases, Amsterdam UMC, location University of Amsterdam, Amsterdam Public Health-Global Health, Amsterdam Institute for Immunity and Infectious Diseases, Amsterdam, Netherlands.

Background: When people living with HIV develop pulmonary tuberculosis, it often manifests without detectable acid-fast bacilli on sputum microscopy. We aimed to assess the diagnostic accuracy of stool Xpert MTB/RIF Ultra (hereafter, Ultra) for Mycobacterium tuberculosis detection among adults with HIV. Methods: This multicentre, prospective diagnostic accuracy study was done in outpatient and inpatient health centres in Eswatini, Mozambique, and Uganda. We enrolled adults aged 15 years and older with HIV with presumptive tuberculosis. We evaluated the diagnostic accuracy of stool Ultra using the simple one-step processing method against a composite microbiological reference standard (CMRS) including three WHO-recommended tuberculosis diagnostic tests (urine tuberculosis biomarker-based lateral-flow lipoarabinomannan [TB-LAM], sputum Ultra, and sputum culture), and stratified by CD4 cell count. We compared sputum versus stool Ultra performance against a composite reference standard of TB-LAM and sputum culture (CMRS2). We also calculated the diagnostic yield among all tested. This study is registered with ClinicalTrials.gov, NCT05047315.

Findings: Between Dec 2, 2021, and Aug 14, 2024, 677 participants were enrolled (247 [36%] men and 430 [64%] women). Tuberculosis was microbiologically confirmed in 119 participants by the CMRS: 39 (33%) had a positive test with sputum Ultra, 30 (25%) had a positive test with culture, and 84 (71%) had a positive test with

urine TB-LAM. The sensitivity of stool Ultra compared with CMRS was 23·7% (28/118 [95% CI 16·4-32·4]) and the specificity was 94·0% (504/536 [91·7-95·9]). The sensitivity of stool Ultra in participants with CD4 counts less than or equal to 200 cells per µL was 45·5% (10/22 [24·4-67·8]) compared with 21·3% (17/80 [12·9-31·8]) in those with CD4 counts greater than 200 cells per µL. Against the CMRS2, we observed no differences in sensitivity between sputum and stool Ultra on the basis of CD4 cell count. Stool Ultra resulted in additional cases detected of 23% (30/133) compared with sputum Ultra, 29% (38/133) compared with sputum culture, and 33% (44/133) compared with TB-LAM. The overall diagnostic yield for all treated for stool Ultra was 9% (60/677), for TB-LAM was 12% (84/677), for sputum Ultra was 6% (39/677), and for sputum culture was 4% (30/677).

Interpretation: These results suggest stool Ultra could be used as an additional test for tuberculosis diagnosis among people with HIV, particularly among those with CD4 counts less than 200 cells per μ L.

Miscellaneous

68. Bull World Health Organ. 2025 May 3;103(6):403-409

A World Health Organization tool for assessing research ethics oversight systems Carl H Coleman et al. Seton Hall Law School, New Jersey, 07102, USA; Access to Medicines and Health Products, WHO, Geneva; Research for Health, WHO, Geneva. Email: carl.coleman@shu.edu.

Although most countries have ethical oversight systems for health-related research involving human participants, mechanisms for assessing the quality of those systems are not regularly used, particularly in lowresource settings. To address this gap, the Regulatory System Strengthening, Regulation and Safety unit and Health Ethics and Governance unit of the World Health Organization (WHO) recently released a tool for benchmarking ethics oversight of health-related research involving human participants. The tool provides a simple, easy-to-measure set of indicators for assessing the quality of research ethics oversight systems without the need to invest a great deal of resources. The tool comprises 48 indicators divided across three areas: (i) the national context; (ii) research ethics committees; and (iii) institutions that conduct health-related research involving humans, such as academic medical centres. Indicators related to the national context are intended to be evaluated in a single assessment applicable to the country as a whole, whereas indicators related to research ethics committees and research institutions are evaluated on an entity-by-entity basis. Some countries may choose to assess a representative sample of research ethics committees and institutions; alternatively, national authorities might ask research ethics committees and institutions to undertake selfassessments and report the results. Research ethics committees or institutions could also use WHO's tool on their own as part of a process of quality improvement. WHO is working with global partners to disseminate the tool and support global implementation. Widespread use of the tool is expected to enhance policy coherence in ethics oversight and facilitate multinational research.

69. Lancet 2025;405(10493):1897-8 World Report WHA adopts new strategy on traditional medicine Burki T.

(Abbreviated)

WHO is seeking ways to integrate traditional medicine—relied on by billions worldwide—into wider health systems.

On May 26, the World Health Assembly (WHA) adopted its third global strategy on traditional medicine. The strategy, which will run from 2025 to 2034, envisages "universal access to safe, effective and people-centred TCIM [traditional, complementary and integrative medicine]". Its key objectives include building the evidence base and creating appropriate regulatory mechanisms.

The 2025–34 strategy defines traditional medicine as systems "for healthcare and well-being comprising practices, skills, knowledge and philosophies originating in different historical, cultural contexts, that are distinct from and pre-date biomedicine". It adds that traditional medicine is based on experience, and emphasises holistic, nature-based remedies and personalised care.

The strategy defines complementary medicine as "additional healthcare practices that are not part of a country's mainstream medicine". Integrative medicine is characterised as "an interdisciplinary and evidence-based approach to health and well-being by using a combination of biomedical and traditional and/or complementary medical knowledge, skills and practices". The WHO strategy is part of the overarching attempt to figure out the best way to integrate TCIM into health systems around the world.

The future of the WHO Traditional, Complementary and Integrative Medicine Unit in Geneva, Switzerland is uncertain, however, with some suggestions that it might be shifted to India. WHO is facing severe financial constraints and organisational restructuring.

Around 100 countries worldwide maintain national policies and programmes for traditional and complementary medicine, with varying degrees of integration into primary, secondary, and tertiary health care. The formal and informal traditional and complementary medicine industry employs a huge number of people, some of whom are university-accredited. If properly deployed, these individuals could be used to ease the pressure on health-care systems and assist with the drive to universal health care.

Kuruvilla, Director ad interim for the WHO Global Traditional Medicine Centre (Jamnagar, India), stressed that WHO would not recommend any kind of health-care practice or treatment, regardless of its origin, unless there was robust evidence for its safety and effectiveness.

Seifert, senior physician in paediatrics and Director of the Charité Competence Center for Traditional and Integrative Medicine at the Charité–Universitätsmedizin Berlin, Germany, pointed out that researchers are incentivised to work on projects which have a good chance of being accepted by a high-impact journal and which fit with the methodology of modern research. "Indigenous people did experiments to verify their theories. Traditional medicine is backed by a system of knowledge. But there is still some resistance among editors and reviewers to accept different knowledge systems; they often regard traditional medicine as something that does not conform to the expectations of scientific research", he explained. Seifert underscored the value of randomised controlled trials in assessing single compounds—after all, 40% of pharmaceutical products are taken from the natural world. But when it comes to assessing more complicated interventions, a variety of approaches may be necessary.

"Much of traditional medicine involves complex interventions; to capture their effects, you need a complex methodology.

The second WHO Traditional Medicine Summit has been scheduled for December, 2025. The event offers an opportunity to announce new commitments for the implementation of the global strategy.

70. Lancet 2025;405(10495):2103

Editorial

The uncertain future of migrant and refugee health

(Abbreviated)

Global migration is an inescapable reality. Whether by choice or by force, 1 billion people (one in eight of the total world population) are on the move today, driven by economic, political, demographic, environmental, and sociocultural forces. In 2024, there were an estimated 304 million international migrants. Particularly alarming is the continual rise of forced displacement because of conflict, violence, persecution, human rights violations, and events that seriously disturb public order. By mid-2024, a record 122.6 million people were forcibly displaced. This number includes internally displaced people, refugees, asylum seekers, and other people in need of international protection. Furthermore, climate change is a driver of displacement. The World Bank predicts that climate change will force more than 216 million people across six continents to move within their countries by 2050.

WHO's (and the UN's) health and migration work is facing organisational restructuring and funding constraints. On April 25, Health Policy Watch reported on a "near final iteration" of WHO's reorganisation. A copy of the proposed organogram showed that migration and health has disappeared entirely. Indeed, the entire Division of Healthier Populations in which the programme sat has gone. In a statement to The Lancet, WHO said that "the final approach to the important issue of Health and migration...[is] still under consideration". The loss or weakening of WHO's dedicated Health and Migration capacity would be a major blow to global health equity, particularly at a time of rising xenophobia, policy regressions, and increasing displacement. Migrants make a huge contribution to society in terms of economic prosperity and development and enrichment of communities. Addressing migration and health is crucial for achieving the Sustainable Development Goals, including universal health coverage, protecting and promoting the health of all populations, and effectively managing health emergencies. Health is indisputably a non-negotiable human right for all. Governments have an obligation under refugee law to provide asylum for people fleeing violence and persecution. Migration demands compassionate, systemic responses, especially from high-income countries. The global health community has a key role in advancing these arguments. But a large part of the public in many countries is not swayed by these points. Many people remain sceptical of, or outrightly hostile towards, immigration. Political narratives that rely on hate and division, further fuelled by the media, are resulting in restrictive and securitised approaches to migration. This disconnect is the great challenge to making gains to protect and support refugee and migrant health. If the health community cannot find a way to change these hostile narratives, then it must find a way to operate nevertheless. Either way, the deprioritisation of migration and health in the UN system would be a damaging blow.