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International Health Alerts 2024-4 Abstracts

Child Health

1. BMJ Global Health 2024;9:e016600
Inpatient and postdischarge mortality among children with anaemia and malaria parasitaemia in Kenya: a cohort study
Ngari M et al., KEMRI-Wellcome Trust Research Programme, Kilifi, Kenya
<mngari@kemri-wellcome.org>

Background. Anaemia and malaria are leading causes of paediatric hospitalisation and inpatient mortality in sub-Saharan Africa. However, there is limited empirical data on survival following hospital discharge. We aimed to estimate independent effects of anaemia and malaria parasitaemia on inpatient and 1 year postdischarge mortality among Kenyan children.
Methods. A retrospective cohort study among children admitted to Kilifi County Hospital (KCH) from 2010 to 2019 and followed-up for 1 year postdischarge in Kilifi Health and Demographic Surveillance System (KHDSS). The main exposures were anaemia and malaria parasitaemia at the time of hospital admission while inpatient and 1 year postdischarge mortality were the outcomes.
Results. We included 9431 admissions among 7578 children (43% girls), median (IQR) age 19 (9.9–23) months. 2069 (22%), 3893 (41%) and 1140 (12%) admissions had mild, moderate and severe anaemia, whereas 366 (3.9%), 779 (8.3%) and 224 (2.4%) had low, medium and high malaria parasitaemia, respectively. Overall, there were 381 (4.0%) inpatient deaths: 317/381 (83%) and 47/381 (12%) among children with any level of anaemia and malaria parasitaemia, respectively. Moderate and severe, but not mild anaemia, were positively associated with inpatient death. Low and high level parasitaemia were positively associated with inpatient mortality, while medium level parasitaemia was negatively associated. There were 228 (3.1%) postdischarge deaths: 32.8 (95% CI 28.8–37.3) deaths/1000 child-years. 180/228 (79%) deaths occurred within 6 months after index discharge and 99/228 (43%) occurred in the community. Overall, 180/228 (79%) and 10/228 (4.4%) postdischarge deaths occurred among children with any level of anaemia and malaria parasitaemia, respectively. Severe anaemia was positively associated with postdischarge mortality (adjusted HR 1.94 (95% CI 1.11–3.40)), while medium level parasitaemia was negatively associated.
Conclusion. Interventions to create awareness of postdischarge risks, improve uptake of existing interventions and improved discharge processes targeting high-risk groups such as children admitted with severe anaemia, need to be prioritised.

2. Lancet 2024;404(10467):2094-2116
The next 1000 days: building on early investments for the health and development of young children
Draper CE et al., South African Medical Research Council, Developmental Pathways for Health Research Unit, University of the Witwatersrand, Johannesburg, South Africa
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This is the first in a Series of two papers on early childhood development and the next 1000 days. Following the first 1000 days of life that span from conception to two years of age, the next 1000 days of a child's life from 2-5 years of age offer a window of opportunity to promote nurturing and caring environments, establish healthy behaviours, and build on early gains to sustain or improve trajectories of healthy development. This Series paper, the first of a two-paper Series on early childhood development and the next 1000 days, focuses on the transition to the next 1000 days of the life course,

describes why this developmental period matters, identifies the environments of care, risks, and protective factors that shape children's development, estimates the number of children who receive adequate nurturing care, and examines whether current interventions are meeting children's needs. Paper 2 focuses on the cost of inaction and the implications of not investing in the next 1000 days. In low-income and middle-income countries (LMICs), only 62 million children aged 3 and 4 years (25·4%) currently receive adequate nurturing care during the next 1000 days, leaving 181·9 million children exposed to risks that jeopardise their healthy development. Inputs across nurturing care dimensions of health, nutrition, protection, responsive care, and learning vary substantially across countries. In LMICs, although 86·2% of children have a healthy weight in this period, less than one in three children have access to developmental stimulation or are protected from physical punishment, and only 38·8% have access to early childhood care and education services. Intervention research in LMICs in the next 1000 days is scarce. The continuity of developmentally appropriate nurturing care, coordination across health, education, and protection sectors, and the implementation of interventions to support caregivers and improve the quality of education and care remain top priorities in this period. These sectors play key roles in promoting quality early care and education for this age group, which will help maximise developmental potential and opportunities of children globally and help progress towards the achievement of the Sustainable Development Goals.

Key messages

- Building on the foundation of the first 1000 days, the next 1000 days (from 2–5 years of age) is a crucial window of opportunity to extend nurturing care for contributing to optimal health, growth, and developmental trajectories.
- Environmental risks to health, nutrition, and development persist, including physical punishment of the child, suboptimal diets, poor caregiver mental health, exposure to pollution, and climate change.
- An estimated 8% of children younger than 5 years have a developmental disability and require targeted additional support to optimise health, wellbeing, and prevent further disadvantage.
- Protections that shape development in the next 1000 days expand from home, clinic, and community settings to include ECCE settings, but multisectoral strategies to promote and protect development are limited, especially in LMICs.
- ECCE for children in the next 1000 days is a key component of support for their learning and development, but less than 30% of children aged 3 and 4 years participate in ECCE in LMICs.
- Only 29·9% of children in LMICs receive adequate nurturing care in the next 1000 days. Poorer children, children in rural areas, and boys are less likely to receive adequate care.
- Children in LMICs who have received early learning support and responsive care are approximately two years ahead in their development, compared to children not receiving these supports.
- Interventions promoting healthy development in the next 1000 days are predominantly delivered in high-income countries; only 5% of published interventions have been implemented in LMICs.
- Despite their vulnerability, young children in LMICs are not adequately reached by a holistic set of interventions to promote development in the next 1000 days.
- Key interventions that are available (such as ECCE) warrant attention to quality, equity, and inclusion to ensure all children are reached and receiving programmes that support their development and learning, as well as an enabling policy environment that improves investment in ECCE systems and fosters demand for services.

ECCE=early childhood care and education. LMICs=low-income and middle-income countries.

Communicable Diseases

3. Am J Trop Med Hyg 2024;111(4):714-8 Print 2024 Oct 2
Urgent Response Needed: Addressing the Dengue Crisis in the Andean and Southern Cone Latin American Regions
Ortiz-Prado E et al., One Health Research Group, Faculty of Health Science, Universidad de Las Americas, Quito, Ecuador

The dengue crisis in the Latin American region is currently intensifying, exacerbated by heavy rains, widespread flooding, and the onset of the El Niño-Southern Oscillation. The indirect consequences of the COVID-19 pandemic, which weakened healthcare systems, have further compounded the situation. Comparing the first 15 weeks of 2023 with the same period in 2024, we observed a significant average increase of 600% in the number of new cases. This translates to a 536% rise in the composite rate per 100,000 inhabitants across all countries. Brazil experienced a staggering surge from 1,425,000 cases in the initial 15 weeks of 2023 to 5,177,989 cases in the corresponding period of 2024. Similarly, Paraguay witnessed a notable escalation, with cases soaring from 12,497 in 2023 to more than 240,000 thus far in 2024, marking an increase of more than 1,825%. Bolivia, however, witnessed a reduction in cases, though the cause remains unclear. Urgent action is imperative to address this escalating crisis. Strengthening surveillance systems, enhancing vector control programs, and implementing effective public health campaigns are critical. Immediate and coordinated action by regional governments and health authorities is essential to mitigate the growing dengue crisis and safeguard public health in the region.

4. BMJ Global Health 2024;9:e015245
Long Covid: a global health issue – a prospective, cohort study set in four continents
Pazukhina E et al., ISARIC Global Support Centre, Pandemic Sciences Institute, Nuffield Department of Medicine, University of Oxford, Oxford, UK

Introduction A proportion of people develop Long Covid after acute COVID-19, but with most studies concentrated in high-income countries (HICs), the global burden is largely unknown. Our study aims to characterise long-term COVID-19 sequelae in populations globally and compare the prevalence of reported symptoms in HICs and low-income and middle-income countries (LMICs).
Methods A prospective, observational study in 17 countries in Africa, Asia, Europe and South America, including adults with confirmed COVID-19 assessed at 2 to <6 and 6 to <12 months post-hospital discharge. A standardised case report form developed by International Severe Acute Respiratory and emerging Infection Consortium's Global COVID-19 Follow-up working group evaluated the frequency of fever, persistent symptoms, breathlessness (MRC dyspnoea scale), fatigue and impact on daily activities.
Results Of 11 860 participants (median age: 52 (IQR: 41–62) years; 52.1% females), 56.5% were from HICs and 43.5% were from LMICs. The proportion identified with Long Covid was significantly higher in HICs vs LMICs at both assessment time points (69.0% vs 45.3%, p<0.001; 69.7% vs 42.4%, p<0.001). Participants in HICs were more likely to report not feeling fully recovered (54.3% vs 18.0%, p<0.001; 56.8% vs 40.1%, p<0.001), fatigue (42.9% vs 27.9%, p<0.001; 41.6% vs 27.9%, p<0.001), new/persistent fever (19.6% vs 2.1%, p<0.001; 20.3% vs 2.0%, p<0.001) and have a higher prevalence of anxiety/depression and impact on usual activities compared with participants in LMICs at 2 to <6 and 6 to <12 months post-COVID-19 hospital discharge, respectively.
Conclusion Our data show that Long Covid affects populations globally, manifesting similar symptomatology and impact on functioning in both HIC and LMICs. The prevalence was higher in HICs versus LMICs. Although we identified a lower prevalence, the impact of Long Covid may be greater in LMICs if there is a lack of support systems available in HICs. Further research into the aetiology of Long Covid and the burden in LMICs is critical to implement effective, accessible treatment and support strategies to improve COVID-19 outcomes for all.

5. BMJ Global Health 2024;9:e016589
Seroprevalence of seven arboviruses of public health importance in sub-Saharan Africa: a systematic review and meta-analysis
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Background. The arboviruses continue to be a threat to public health and socioeconomic development in sub-Saharan Africa (SSA). Seroprevalence surveys can be used as a population surveillance strategy for arboviruses in the absence of treatment and vaccines for most arboviruses, guiding the public health interventions. The objective of this study was to analyse the seroprevalence of arboviruses in SSA through a systematic review and meta-analysis.
Methods. We searched PubMed/MEDLINE, Web of Science, Embase, Scopus and ScienceDirect databases for articles published between 2000 and 2022 reporting the seroprevalence of immunoglobulin G (IgG) antibodies to seven arboviruses in various human populations residing in SSA. The included studies were assessed using the checklist for assessing the risk of bias in prevalence studies, and the data were extracted using a standard form. A random effects model was used to estimate pooled seroprevalences. The potential sources of heterogeneity were explored through subgroup analyses and meta-regression. The protocol had been previously registered on International Prospective Register of Systematic Reviews with the identifier: CRD42022377946.
Results. A total of 165 studies from 27 countries, comprising 186 332 participants, were included. Of these, 141 were low-risk and 24 were moderate-risk. The pooled IgG seroprevalence was 23.7% (17.9–30.0%) for Chikungunya virus, 22.7% (17.5–28.4%) for dengue virus, 22.6% (14.1–32.5%) for West Nile virus, 16.4% (7.1–28.5%) for yellow fever virus, 13.1% (6.4–21.7%) for Zika virus, 9.2% (6.5–12.3%) for Rift Valley fever virus and 6.0% (3.1–9.7) for Crimean–Congo haemorrhagic fever virus. Subgroup and meta-regression analyses showed that seroprevalence differed considerably between countries, study populations, specific age categories, sample sizes and laboratory methods.
Conclusion. This SRMA provides information on the significant circulation of various arboviruses in SSA, which is essential for the adoption and planning of vaccines. These findings suggest the need to invest in surveillance and research activities on arbovirus in SSA countries to increase our understanding of their epidemiology to prevent and respond to future epidemics.

6. Lancet 2024;404(10458):1143-56
Review
Severe respiratory syncytial virus infection in children: burden, management, and emerging therapies
Mazur NI et al., Department of Pediatrics, Wilhelmina Children's Hospital, Utrecht, Netherlands <n.i.mazur@umcutrecht.nl>

This is the first in a Series of four papers about respiratory syncytial virus (papers 2 and 3 appear in The Lancet Respiratory Medicine). All papers in the Series are available at thelancet.com/series/https://www.thelancet.com/series/respiratory-syncytial-virus.
The global burden of respiratory syncytial virus (RSV) lower respiratory tract infection (LRTI) in young children is high. The RSV prevention strategies approved in 2023 will be essential to lowering the global disease burden. In this Series paper, we describe clinical presentation, burden of disease, hospital management, emerging therapies, and targeted prevention focusing on developments and groundbreaking publications for RSV. We conducted a systematic search for literature published in the past 15 years and used a non-systematic approach to analyse the results, prioritising important papers and the most recent reviews per subtopic. Annually, 33 million episodes of RSV LRTI occur in children younger than 5 years, resulting in 3·6 million hospitalisations and 118 200 deaths. RSV LRTI is a clinical diagnosis but a clinical case definition and universal clinical tool to predict severe disease are non-existent. The advent of molecular point-of-care testing allows rapid and accurate confirmation of RSV infection and could reduce antibiotic use. There is no evidence-based treatment of RSV, only

supportive care. Despite widespread use, evidence for high-flow nasal cannula (HFNC) therapy is insufficient and increased paediatric intensive care admissions and intubation indicate the need to remove HFNC therapy from standard care. RSV is now a vaccine-preventable disease in young children with a market-approved long-acting monoclonal antibody and a maternal vaccine targeting the RSV prefusion protein. To have a high impact on life-threatening RSV infection, infants at high risk, especially in low-income and middle-income countries, should be prioritised as an interim strategy towards universal immunisation. The implementation of RSV preventive strategies will clarify the full burden of RSV infection. Vaccine probe studies can address existing knowledge gaps including the effect of RSV prevention on transmission dynamics, antibiotic misuse, the respiratory microbiome composition, and long-term sequalae.

Other articles in the Series/about RSV:

- Lancet Respir Med 2024;12(10):810-21

Review
Early-life respiratory syncytial virus disease and long-term respiratory health
Zar HJ et al., Department of Paediatrics and Child Health, Red Cross War Memorial Children's Hospital and SA-MRC Unit on Child & Adolescent Health, University of Cape Town, Cape Town, South Africa

- Lancet Respir Med 2024;12(10):822-36

Review
Respiratory syncytial virus infections in adults: a narrative review
Wildenbeest JG et al., Department of Paediatric Infectious Diseases and Immunology, Wilhelmina Children's Hospital, University Medical Centre Utrecht, Utrecht, Netherlands.

- Lancet 2024;404(10458):1157-70

Review
Respiratory syncytial virus vaccination and immunoprophylaxis: realising the potential for protection of young children
Pecenka C et al., Center for Vaccine Innovation and Access, PATH, Seattle, WA, USA <cpecenka@path.org>

- Lancet Infect Dis 2024;24(12):e747-e761

Review
The respiratory syncytial virus vaccine and monoclonal antibody landscape: the road to global access
Terstappen J et al. Department of Paediatric Infectious Disease & Immunology, Wilhelmina Children's Hospital, University Medical Center Utrecht, Utrecht, Netherlands

7. Lancet 2024;404(10459):1182-3
World Report
"The final warning sign": XDR typhoid
Khan M.

Abbreviated
XDR typhoid is resistant to almost all of the antibiotics (ampicillin, ceftriaxone, cefixime, chloramphenicol, ciprofloxacin, and cotrimoxazole) that are supposed to treat the disease, so options are limited and death rates are higher.
Of the roughly 9 million people around the world who get sick from typhoid each year, the vast majority are infected with a drug-resistant strain. Pakistan has the highest rate of typhoid in south Asia, a problem that has only escalated since the emergence of XDR typhoid. More than 15 000 cases of XDR typhoid have been officially reported in Pakistan, and some outbreaks.
The risk of typhoid is higher where a community lacks safe water and sanitation. A neglected sewage system, for example, can contaminate water and compound the problem. In Pakistan, water is a critical issue. The country has one of the lowest rankings in the world for access to clean water near homes, and contaminated water is thought to be the cause of about 80% of diseases in the country.

Typhoid can also be prevented with a childhood vaccine. Pakistan has vaccinated more than 30 million children since 2019, but these efforts have been mostly concentrated in the south of the country, where XDR typhoid first emerged. There are more than 100 million children in Pakistan and the infection has since spread north.
Overuse of antibiotics is one of the biggest contributors to drug-resistant bacteria.
Experts in Pakistan have gone so far as to blame the Typhidot and Widal tests for driving cases of drug-resistant typhoid.
Recent studies on these rapid tests have shown that they lack sensitivity and specificity. The National Institute of Health in Pakistan has since issued a notification to discontinue their use as they are said to have little diagnostic value, but they remain widely available.
World leaders are meeting at the UN for a High-Level Meeting on antimicrobial resistance. The aim is to negotiate a political declaration for member states to curb the impact on health, the environment, and development.

8. Lancet 2024;404(10462):1493
Editorial
Cholera: a pandemic ignored

(Abbreviated)
The seventh pandemic of cholera—an easily preventable and treatable disease—has claimed millions of lives since 1961, driven by the El Tor biotype. In January, 2023, WHO classified the most recent global cholera resurgence as a grade 3 emergency—an event requiring a major to maximal response. More than 500 000 cases were subsequently reported in 2023—with the highest counts in Afghanistan, Haiti, and the Democratic Republic of the Congo—resulting in 4007 deaths, a 71% increase in deaths from the previous year. Yet the disease continues to be neglected in health agendas and on the political stage. How can such a pandemic have been left to persist for so long?
The failure to implement effective water, sanitation, and hygiene (WASH) practices lies at the core of this neglect. Despite global commitments to Sustainable Development Goal 6, which aims for universal access to sustainable water and sanitation, a world health statistics WHO report indicates that in 2020, 2 billion people lacked access to safe drinking water. Only 54% of the global population were using safely managed sanitation services. About three in ten people worldwide did not have a basic handwashing facility with water and soap at home. The benefits of sustainable WASH go beyond cholera; neglected tropical diseases, for example, disproportionately affect poor and marginalised populations, and their prevention is closely tied to access to clean water and sanitation.
There have been further failures in providing cholera vaccination and treatment to those who need it. Gavi expects that the recent prequalification of the new simplified vaccine, Euvichol-S, which offers similar efficacy to existing vaccines, will help alleviate vaccine shortage by 2025 due to its easier and cheaper production.
The resurgence of cholera presents a dire threat to health. The Global Task Force on Cholera Control aims to reduce cholera deaths by 90% from 2015 levels by 2030, a goal that is increasingly unlikely without immediate and coordinated action. Cholera's high mortality rate and devastating wider impacts have been too long neglected, most likely because of the people and countries it most affects. Technical interventions are vital, but at its heart, cholera is a disease driven by conflict, displacement, and extreme poverty. Unless we attend to those root causes, cholera will continue to thrive.

9. Lancet Glob Health 2024;12(10):e1730-e1736 Epub 2024 Sep 10
Improving Ebola virus disease outbreak control through targeted post-exposure prophylaxis
Dahl EH et al., Médecins Sans Frontières, Oslo, Norway. Correspondence to Jaspard M <marie.jaspard@coral.alima.ngo>

Ebola virus disease kills more than half of people infected. Since the disease is transmitted via close human contact, identifying individuals at the highest risk of developing the disease is possible on the

basis of the type of contact (correlated with viral exposure). Different candidates for post-exposure prophylaxis (PEP; ie, vaccines, antivirals, and monoclonal antibodies) each have their specific benefits and limitations, which we discuss in this Viewpoint. Approved monoclonal antibodies have been found to reduce mortality in people with Ebola virus disease. As monoclonal antibodies act swiftly by directly targeting the virus, they are promising candidates for targeted PEP in contacts at high risk of developing disease. This intervention could save lives, halt viral transmission, and, ultimately, help curtail outbreak propagation. We explore how a strategic integration of monoclonal antibodies and vaccines as PEP could provide both immediate and long-term protection against Ebola virus disease, highlighting ongoing clinical research that aims to refine this approach, and discuss the transformative potential of a successful PEP strategy to help control viral haemorrhagic fever outbreaks.

10. N Engl J Med 2024;391:1265-7
Perspective: The Mpox Global Health Emergency — A Time for Solidarity and Equity
Gostinet LO al., O'Neill Institute for National and Global Health Law, Georgetown University, Washington

On August 14, 2024, the director-general of the World Health Organization (WHO) declared mpox in the Democratic Republic of Congo (DRC) and neighboring countries to be a Public Health Emergency of International Concern (PHEIC) under the 2005 International Health Regulations (IHR) — the WHO's highest-level alert. The previous day, the Africa Centers for Disease Control and Prevention (Africa CDC) declared a Public Health Emergency of Continental Security (PHECS) — the organization's first-ever declaration of a regional health emergency. This regional declaration and the WHO's early response — issued without waiting for mpox to affect high-income countries — could offer a historic opportunity to mobilize lifesaving resources according to the principles of solidarity and equity.
Mpox clade I has been endemic in the DRC for more than a decade, with cases steadily increasing. In 2023, the country saw a sharp increase driven by a genetically distinct and more transmissible subtype, clade Ib. This year, the DRC has already reported more than 15,600 cases and 537 deaths. But because of insufficient surveillance, testing, and contact tracing, many more cases remain undetected. Cases have been reported throughout the DRC's 26 provinces, initially spiking in Équateur Province and then expanding into South Kivu, which has been ravaged by armed conflict and social unrest — conditions that pose major challenges for health workers. Cases have been reported in Kinshasa, a city with more than 17 million inhabitants. Overall, at least 12 African countries have reported cases, including 4 that had had no reported cases before this outbreak.
Human-to-human transmission has primarily occurred within households, in health care settings, and by means of sexual contact, with the greatest risk seen among men who have sex with men (MSM) and sex workers. Evidence suggests that clade Ib is more likely to be lethal than clade IIb — the clade that drove the global mpox outbreak in 2022, affecting primarily MSM and causing nearly 100,000 cases and 208 deaths in 116 countries. Tragically, most cases and deaths in the current mpox outbreak have occurred in children, indicating that transmission is occurring by routes other than sexual contact.
The WHO previously declared a PHEIC for the clade IIb mpox global outbreak in 2022. Yet endemic mpox has not garnered the same attention and investment — a disparity that the concurrent regional and global emergency declarations should help to rectify. The rapid international spread of a new mpox subtype is of enormous concern. Though all countries should fortify their preparedness, the priority must be coordinated action and investments focused on response efforts in Africa. In light of deeply inequitable responses to Covid-19, the WHO adopted amendments to the IHR in May 2024, the most consequential of which embedded equity in the regulations as a principle guiding pandemic response. Although the amendments won't come into effect until next year, the African mpox outbreak will put these legal obligations to their first crucial test.
There are currently two mpox vaccines recommended by the WHO's Strategic Advisory Group of Experts on Immunization. On August 9, the WHO invited mpox vaccine manufacturers to apply for an Emergency Use Listing (EUL), which African countries and supporting partners such as Gavi could rely on in deploying vaccines. The United States and other high-income countries have substantial mpox

vaccine supplies, but affected African countries have not had affordable access — an enduring indicator of inequity.

The PHEIC sets in motion binding legal obligations for international cooperation and rapid reporting of data, compliance with any relevant temporary recommendations from the WHO, and mobilization of funding for diagnostics, surveillance, and medical countermeasures. The PHECS empowers Africa CDC to coordinate the continental response. Since this is the first time that regional and international emergency declarations have been in effect concurrently, it is vital to harmonize the global mpox response and give full support to African countries and public health officials leading the response in their communities.

In our own country, the U.S. Centers for Disease Control and Prevention (CDC) has issued clinical guidance recommending further investigation in patients with suspected mpox who have recently returned from affected countries; it has also issued a level 2 travel alert. The White House has established an interagency response team, indicating heightened domestic concern. CDC modeling suggests that if clade Ib mpox seeded in the United States, household close-contact transmission would not result in a large number of cases. A separate modeling study, however, suggested that there would be an elevated risk of transmission among MSM, given relatively low uptake of the JYNNEOS mpox vaccine. Overall, low population-level orthopox immunity leaves the U.S. population vulnerable.

The IHR requires countries to avoid imposing unnecessary travel or trade restrictions and to base their response to a public health emergency on science and respect for human rights. Temporary recommendations from the WHO urge affected states to ramp up coordination, diagnostics and surveillance, risk communication, and preparatory vaccination efforts, and standing recommendations urge all countries to make countermeasures available and refrain from targeting African countries with travel-related health measures for mpox, among other advice.

Priorities for an effective global response should include major investments in health systems, including diagnostics, surveillance, and the health workforce; risk communication encouraging culturally appropriate behavior changes; equitable access to lifesaving countermeasures; and sustained financing and action in the region.

First, international financial assistance is urgently needed to support the African response on the ground and provide incentives for the development of safer and more effective countermeasures. The WHO's Contingency Fund for Emergencies recently released U.S.$1.45 million and plans further allocations under the PHEIC. Yet these funding levels are insufficient to support a robust emergency response. The WHO's regional response plan estimates that U.S.$15 million will be needed in the initial alert phase, and sustained financing will be required over time.

Second, testing and surveillance to monitor and inform our understanding of the ongoing outbreak are urgently needed. More comprehensive and accurate epidemiologic data are necessary for developing countermeasures, tailoring risk-communication strategies, and enabling a targeted response. Enhanced surveillance capacities will be especially important in border areas to prevent further international spread.

Third, international support is vital to facilitate equitable access to diagnostic kits and vaccines. When the WHO declared a PHEIC, the United States offered 50,000 vaccine doses, and the European Union and Denmark-based Bavarian Nordic agreed to distribute 200,000 doses. Yet these offers pale in comparison to Africa CDC's assessed needs of 10 million vaccine doses. African regulatory authorities should rely on the WHO's EULs to authorize vaccines that meet requisite safety and efficacy standards, and coordinate with key vaccine partners such as Gavi.

Fourth, as the epidemiology of mpox has shifted, concerns about human exposure to wild animals have been superseded by a focus on more prevalent behavioral risks among sexual partners and within households. Accurate, nonstigmatizing, and precise risk communication delivered by trusted community members will be important to mitigate further spread, especially for at-risk communities such as sex workers and MSM. Several African countries have enacted laws that criminalize same-sex sexual conduct, which can dissuade people from seeking vaccination or care.

Finally, this mpox PHEIC declaration is the third in 5 years — a clear acknowledgment of ongoing threats to health security. Each declared emergency spurs international action, which then wanes

without bringing endemic disease to an end. Bringing sustained attention and investment to the DRC and its neighbors is good for the region and good for the world.

A response with staying power that builds resilient health systems will save countless lives in the DRC and beyond. The DRC has long faced the devastating effects of colonialization, exploitation, armed conflict, and political instability. But ending this mpox epidemic is also very much in the national interests of high-income countries around the world. The August 15 report of a case in Sweden, followed by the first case in Thailand on August 22, underscores the pandemic potential of mpox. The discontinuation of routine smallpox vaccination means that much of the global population has not been exposed to orthopoxviruses. If we remain complacent, we face a real risk of a major global health event.

Dermatology

11. TMIH 2024;29(11):923-50
Systematic review of the evidence for treatment and management of common skin conditions in resource-limited settings: An update
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Introduction: The skin is the largest and most visible organ of the human body. As such, skin infections can have a significant impact on overall health, social wellbeing and self-image. In 2019, we published a systematic review of the treatment, prevention and public health control of skin infections including impetigo, scabies, crusted scabies and tinea in resource-limited settings where skin infections are endemic. This current review serves as an update to assess the evidence for treatment of these conditions as well as atopic dermatitis, molluscum contagiosum and head lice in endemic settings. The data from this systematic review have supported an update to the Australian National Healthy Skin guidelines.
Methods: A systematic review was conducted using two separate searches in MEDLINE, PubMed, Embase, CINAHL, Cochrane and Web of Science. The first search was an update of the 2018 systematic review using the same search strategy for the same skin conditions to identify emerging literature from 2018 to 2022. The second search strategy used the same key terms but with the addition of atopic dermatitis, head lice and molluscum contagiosum from 1960 to 2022. Eligible studies included Indigenous peoples and populations in resource-limited settings with a diagnosis of impetigo, scabies, crusted scabies, tinea capitis, atopic dermatitis, molluscum contagiosum or who presented with head lice. Studies conducted in high-income countries were excluded. Articles were screened for inclusion independently by one author with a second group of reviewers independently double screening. Data extraction and an in-depth quality assessment conducted by one author and checked by two others.
Results: Of 1466 original articles identified, 68 studies were included and key findings outlined for impetigo, scabies, crusted scabies, atopic dermatitis, head lice and molluscum contagiosum. Recommendations for each condition based on the available evidence are provided.
Conclusion: The importance of assessing literature relevant to the populations with heavy burden of skin infections is outlined in this systematic review. We have summarised updates to this literature, which may benefit in developing guidelines for skin infection management similar to the National Healthy Skin Guidelines for Australia.
We have summarised the available evidence for treatment of impetigo, scabies, crusted scabies, tinea, head lice, atopic dermatitis and molluscum contagiosum for clinicians working in resource limited contexts to inform Australian guidelines. All information presented in this systematic review must be considered in the context of affordability, acceptability and applicability when developing guidance for respective populations. The guidance derived from this systematic review to inform skin health care for Australian Aboriginal and Torres Strait Islander people can be found here (National Healthy Skin Guideline; telethonkids.org.au)

Gender

12. Lancet 2024;404(10456):739
Editorial
The structural roots of violence against female health workers

(Abbreviated)
Violence against female health workers is a structural problem. Underlying dynamics between genders that determine the distribution of resources and power have a crucial role in enabling violence against female health workers. Organisational and professional hierarchies facilitate the conditions for violence. Women hold just 25% of leadership roles in health and care and are over- represented in dangerous, undervalued, and underpaid front-line roles. In India, female doctors are often forced to take lower paid jobs than men in emergency settings where violence is more prevalent.
The roots of the problem run deep. In 2002, a joint task force established by the International Labour Office, the International Council of Nurses, WHO, and Public Services International recognised the need for increased equality in gender relations to prevent workplace violence in health care. But it is impossible to isolate the health-care sector from the wider society in which it is embedded. Misogynistic beliefs that women are inferior to men, which are prevalent in but by no means unique to Indian society, make women a target for aggression.
Nobody would argue that dismantling structural misogyny is simple. But ending workplace violence against female health workers must build on an appreciation of underlying gender power relations. Emerging evidence tells us what can work; one systematic review found multicomponent interventions to be effective, incorporating organisational changes and improved reporting mechanisms alongside training and education programmes. New guidelines from WHO and the International Labor Organisation provide recommendations for zero-tolerance policies and gender-responsive programmes.
Violence against female health workers is a shared problem, one that requires engagement across the entire medical community. Only by appreciating how deep the roots of the problem go, can we take effective action to protect health workers from harm.

13. Lancet Glob Health 2024;12(11):e1899-e1904
Rapid surveys on violence against women in crisis contexts: decision-making guidance based on the UN Women Rapid Gender Assessment surveys on violence against women during COVID-19
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Rapid surveys or assessments offer the possibility to collect data in contexts where classic data collection is not feasible (such as health, humanitarian, or climate crises) and when evidence-based urgent action is needed to mitigate the effects of the crisis. Until the past 5 years, rapid surveys were not widely used by practitioners, researchers, or policy makers to measure the effect of crises on violence against women due to a paucity of empirical evidence on their safety and likely utility in such contexts. In recent years, and particularly during the COVID-19 global pandemic, UN Women led the piloting and implementation of such surveys in various countries. We use our experiences from this work and other studies to offer concrete decision-making guidance-in the form of a checklist-for whether to conduct rapid surveys on violence against women in crisis contexts, with consideration of their value, risks, and the minimum safeguards needed to implement this type of work.

Global Health/Health Policy

14. BMJ Global Health 2024;9:e013816
Clinically sound and person centred: streamlining clinical decision support guidance for multiple long-term condition care
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The care of people with multiple long-term conditions (MLTCs) is complex and time-consuming, often denying them the agency to self-manage their conditions—or for the clinician they visit to provide streamlined, person-centred care. We reconfigured The Practical Approach to Care Kit, our established, evidence-based, policy-aligned clinical decision support tool for low-resource primary care settings, to provide consolidated clinical guidance for a patient journey through a primary care facility. This places the patient at the centre of that journey and shifts the screening, monitoring and health education activities of multimorbidity care more equitably among the members of the primary care team. This work forms part of a study called ENHANCE, exploring how best to streamline MLTC care in South Africa with its high burden of communicable, non-communicable and mental health conditions. This practice paper describes the four steps of codeveloping this clinical decision support tool for eleven common long-term conditions with local stakeholders (deciding the approach, constructing the content, clinical editing, and design and formatting) along with the features of the tool designed to facilitate its usability at point of care. The process highlighted tensions around prioritising one condition over another, curative over preventive treatment and pharmacological therapies over advice-giving, along with the challenges of balancing the large volume of content with a person-centred approach. If successful, the tool could augment the response to MLTC care in South Africa and other low-resource settings. In addition, our development process may contribute to scant literature around methodologies for clinical decision support development.

15. Bull World Health Organ 2024;102(10):682–682A
Editorial: A continuous improvement agenda for WHO's normative and standard-setting functions
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A foundational element of the World Health Organization's (WHO) mandate is to provide its Member States with scientific advice, normative leadership and technical support. This role is realized by developing evidence-based guidelines and other normative products that guide Member States in their public health decisions and actions, and by assisting them to implement these recommendations in their contexts. Member States reaffirmed this role by approving the Organization's General Programme of Work for 2025–2028, which has a specific focus on country-level impact. Despite this core function, at critical past junctures and in times of global crises and conflict, WHO's normative role and relevance have been questioned.
In the 2023 call for papers for this theme issue of the Bulletin of the World Health Organization, we asked for contributions that would highlight successes and failures with respect to WHO's normative function to understand where and how WHO normative guidance has been impactful, lessons learnt for future improvement, and what changes might be needed to improve WHO's standard-setting role. The papers included showcase a range of examples and experiences demonstrating the ongoing value of WHO's normative leadership. Several articles highlight the considerable effort required to adapt globally produced WHO guidance to make it fit-for-purpose for those who use it locally. Other articles suggest ways WHO's normative guidance might be improved in terms of its relevance, currency, dissemination, reach and impact. The Organization's overall mark on this core role indicates there is still room for improvement.
Important and pioneering strides have been made, including through the WHO Model list of essential medicines. Although more can be done to maximize its impact at country level, the model list has led to major advances in access to affordable essential medicines in many countries. Progress has also

been made with respect to community engagement in guideline development, as in the consolidated guideline on sexual and reproductive rights for women living with human immunodeficiency virus. Similarly, the WHO-INTEGRATE framework was designed to ensure that human rights, equity, as well as social and environmental impact are more meaningfully and explicitly considered when developing normative guidelines. Powerful examples exist of where WHO's mandate in providing global, cross-border normative guidance and leadership in otherwise regulation-free zones remains critical, such as for medical products of human origin.

Interestingly, however, many papers show how WHO's normative guidance, as currently produced, often requires significant adaptation, scale-up or other modifications before it is used in national settings. For example, many papers spanning an array of health topics point to the need for improvements in the integration of local insights, contextualization and adaptation of WHO guidelines for use in different health systems such as in countries and territories of the Caribbean, Estonia and Indonesia. In many settings, including Malawi, Nigeria and South Africa, greater local capacity and expertise are needed to develop context-specific evidence, including local health economic analyses, to ensure global guidelines are relevant.

Notably, few articles reported on research that measured or demonstrated the impact of normative guidance for its intended users. One paper that addressed this issue reports on a natural experiment assessing the uptake of voluntary versus mandatory food nutrition labels in Australia. Another documents the ways in which systematic monitoring and supported supervision in the WHO Reaching Every District (RED) approach led to increased immunization coverage in the Solomon Islands. Better methods for assessing the impact of WHO's normative work at country level are clearly needed.

Global changes will continue in the economic, demographic, environmental, technological, cultural and scientific landscape. With nearly all sustainable development goals off track halfway to 2030, progress has eroded or stagnated across many areas, including health. WHO must become more efficient, relevant and responsive to emerging global and national public health challenges. More specifically, WHO seeks to bring science further to the forefront of all its work to achieve a higher impact on people's health. To do so, WHO could develop new ways of producing, disseminating, updating and embedding the Organization's normative guidance into point-of-care systems, thereby putting evidence at the centre of everyday life. The papers in this issue demonstrate that WHO's normative leadership role in achieving health for all remains important and a core organizational mandate. We need better and more sustainable ways to support, streamline and measure the impact of WHO's normative guidance to ensure it remains trusted and timely, useful and used, and accessible and equitable for all.

16. Lancet 2024;404(10459):1199-1226

Global burden of bacterial antimicrobial resistance 1990-2021: a systematic analysis with forecasts to 2050

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Background: Antimicrobial resistance (AMR) poses an important global health challenge in the 21st century. A previous study has quantified the global and regional burden of AMR for 2019, followed with additional publications that provided more detailed estimates for several WHO regions by country. To date, there have been no studies that produce comprehensive estimates of AMR burden across locations that encompass historical trends and future forecasts.

Methods: We estimated all-age and age-specific deaths and disability-adjusted life-years (DALYs) attributable to and associated with bacterial AMR for 22 pathogens, 84 pathogen-drug combinations, and 11 infectious syndromes in 204 countries and territories from 1990 to 2021. We collected and used multiple cause of death data, hospital discharge data, microbiology data, literature studies, single drug resistance profiles, pharmaceutical sales, antibiotic use surveys, mortality surveillance, linkage data, outpatient and inpatient insurance claims data, and previously published data, covering 520 million individual records or isolates and 19 513 study-location-years. We used statistical modelling to produce estimates of AMR burden for all locations, including those with no data. Our approach

leverages the estimation of five broad component quantities: the number of deaths involving sepsis; the proportion of infectious deaths attributable to a given infectious syndrome; the proportion of infectious syndrome deaths attributable to a given pathogen; the percentage of a given pathogen resistant to an antibiotic of interest; and the excess risk of death or duration of an infection associated with this resistance. Using these components, we estimated disease burden attributable to and associated with AMR, which we define based on two counterfactuals; respectively, an alternative scenario in which all drug-resistant infections are replaced by drug-susceptible infections, and an alternative scenario in which all drug-resistant infections were replaced by no infection. Additionally, we produced global and regional forecasts of AMR burden until 2050 for three scenarios: a reference scenario that is a probabilistic forecast of the most likely future; a Gram-negative drug scenario that assumes future drug development that targets Gram-negative pathogens; and a better care scenario that assumes future improvements in health-care quality and access to appropriate antimicrobials. We present final estimates aggregated to the global, super-regional, and regional level.
Findings: In 2021, we estimated 4·71 million (95% UI 4·23-5·19) deaths were associated with bacterial AMR, including 1·14 million (1·00-1·28) deaths attributable to bacterial AMR. Trends in AMR mortality over the past 31 years varied substantially by age and location. From 1990 to 2021, deaths from AMR decreased by more than 50% among children younger than 5 years yet increased by over 80% for adults 70 years and older. AMR mortality decreased for children younger than 5 years in all super-regions, whereas AMR mortality in people 5 years and older increased in all super-regions. For both deaths associated with and deaths attributable to AMR, meticillin-resistant Staphylococcus aureus increased the most globally (from 261 000 associated deaths [95% UI 150 000-372 000] and 57 200 attributable deaths [34 100-80 300] in 1990, to 550 000 associated deaths [500 000-600 000] and 130 000 attributable deaths [113 000-146 000] in 2021). Among Gram-negative bacteria, resistance to carbapenems increased more than any other antibiotic class, rising from 619 000 associated deaths (405 000-834 000) in 1990, to 1·03 million associated deaths (909 000-1·16 million) in 2021, and from 127 000 attributable deaths (82 100-171 000) in 1990, to 216 000 (168 000-264 000) attributable deaths in 2021. There was a notable decrease in non-COVID-related infectious disease in 2020 and 2021. Our forecasts show that an estimated 1·91 million (1·56-2·26) deaths attributable to AMR and 8·22 million (6·85-9·65) deaths associated with AMR could occur globally in 2050. Super-regions with the highest all-age AMR mortality rate in 2050 are forecasted to be south Asia and Latin America and the Caribbean. Increases in deaths attributable to AMR will be largest among those 70 years and older (65·9% [61·2-69·8] of all-age deaths attributable to AMR in 2050). In stark contrast to the strong increase in number of deaths due to AMR of 69·6% (51·5-89·2) from 2022 to 2050, the number of DALYs showed a much smaller increase of 9·4% (-6·9 to 29·0) to 46·5 million (37·7 to 57·3) in 2050. Under the better care scenario, across all age groups, 92·0 million deaths (82·8-102·0) could be cumulatively averted between 2025 and 2050, through better care of severe infections and improved access to antibiotics, and under the Gram-negative drug scenario, 11·1 million AMR deaths (9·08-13·2) could be averted through the development of a Gram-negative drug pipeline to prevent AMR deaths.
Interpretation: This study presents the first comprehensive assessment of the global burden of AMR from 1990 to 2021, with results forecasted until 2050. Evaluating changing trends in AMR mortality across time and location is necessary to understand how this important global health threat is developing and prepares us to make informed decisions regarding interventions. Our findings show the importance of infection prevention, as shown by the reduction of AMR deaths in those younger than 5 years. Simultaneously, our results underscore the concerning trend of AMR burden among those older than 70 years, alongside a rapidly ageing global community. The opposing trends in the burden of AMR deaths between younger and older individuals explains the moderate future increase in global number of DALYs versus number of deaths. Given the high variability of AMR burden by location and age, it is important that interventions combine infection prevention, vaccination, minimisation of inappropriate antibiotic use in farming and humans, and research into new antibiotics to mitigate the number of AMR deaths that are forecasted for 2050.

17. Lancet 2024;404(10462):1561-1614

Review

Global health 2050: the path to halving premature death by mid-century

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In Global Health 2050, the Lancet Commission on Investing in Health concludes that dramatic improvements in human welfare are achievable by mid-century with focused health investments. By 2050, countries that choose to do so could reduce by 50% the probability of premature death in their populations—ie, the probability of dying before age 70 years—from the levels in 2019. We call this goal 50 by 50. The interventions that enable achieving the goal of 50 by 50 should also reduce morbidity and disability at all ages.

Historical experience and continued scientific advances suggest that 50 by 50 is a feasible aspiration. Seven of the 30 most populous countries have reduced their probability of premature death over the past decade at a rate that would halve the probability before 2050, including countries as diverse as Bangladesh, Ethiopia, Iran, and Türkiye. These focused gains can be achieved early on the pathway to full universal health coverage.

Conclusion

In this Commission, we have reached seven conclusions. First, dramatic improvements in human welfare are achievable everywhere by 2050 with the right health investments. Countries that choose to make these investments can halve their PPD—ie death before age 70 years—by 2050 (the 50-by-50 goal). Historical experience and continued scientific advances indicate the feasibility of achieving this goal, which is also likely to reduce morbidity and disability at all ages (in addition to reductions in premature death).

Second, rapid, sharp mortality declines and associated declines in morbidity can be achieved early on the pathway to full UHC. The 50-by-50 goal can be reached through tackling 15 priority conditions, eight related to infectious diseases and maternal health and seven related to NCDs and injuries.

Third, a modular approach to health-system strengthening supports an initial tight focus on these 15 priority conditions and a gradual broadening of effort as the priority conditions are more fully addressed. Adopting this modular approach also addresses major morbidities, such as psychiatric illness, which are not already covered by mortality-reducing interventions. Value for money can be assessed through a two-step process: assessment of technical cost-effectiveness to gauge how best to achieve module-specific goals and political assessment of trade-offs in investing in expanding module coverage.

Fourth, public financing of a few drugs and other commodities can steer health systems towards delivering high-priority health interventions. Countries should focus a substantial and increasing fraction of public resources for health on making available and affordable the specific drugs, vaccines, diagnostics, and other commodities required for control of the 15 priority conditions. The Arrow mechanism that we describe includes direct subsidising of drugs, pooled purchasing, assurance of supplies, and a long-term commitment to manufacturers to ensure availability of therapies.

Fifth, tobacco control is by far the most important intersectoral policy to help to achieve the 50-by-50 goal, in view of the number of deaths caused by tobacco and the established and improving capacity of governments to implement tobacco policy. A high level of tobacco taxation is valuable in the short-to-medium term for public finance, and should be accompanied by a package of other tobacco-control policies.

Sixth, the huge variation across countries in excess deaths during the COVID-19 pandemic, particularly before vaccines were developed, suggests that lessons can be learned from successful countries about public health basics (eg, rapid response, isolation of infected individuals, quarantine of people potentially exposed to infection, and social and financial support for people isolating or quarantining). In the next pandemic, these fundamentals will help to avert mortality while waiting for vaccine development and deployment.

These six conclusions are primarily aimed at national governments. The seventh and final conclusion is aimed at the development assistance community. We conclude that official development assistance

should focus on two broad purposes. The first is provision of direct financial and technical support to countries with the least resources to help to control diseases and develop health systems. The second is financing of global public goods, including reducing the development and spread of antimicrobial resistance, preventing and responding to pandemics, identifying and spreading best practices, and developing and deploying new health technologies. For both of these purposes, focusing efforts on the 15 priority conditions would best contribute to achieving a 50% reduction in PPD by 2050.
We acknowledge that rising geopolitical tensions, increasingly manifest climate change, growth in nationalistic populism, slowed progress towards UHC, and rising health-care costs are all having an impact on global health progress. Despite these challenges, our analysis shows that a practical pathway to halving PPD by 2050 is within reach. By focusing resources on a narrow set of conditions and scaling up financing to develop new health technologies, we believe that the global health landscape can be utterly transformed within our lifetimes.
GH2035 provided systematic evidence for the high value of mortality declines in much of the world—a value that was often a substantial fraction of GDP growth. We have updated those findings up to 2019 and reiterate the high economic value of actually experienced mortality declines. Today, the case is better than ever for the value of investing in health for reducing mortality and morbidity, alleviating poverty, and improving human welfare.

18. TMIH 2024t;29(10):849-55
Editorial
Collective knowledge exchange through regional hubs: Local expertise, global platform
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The 13th European Congress on Global Health (ECTMIH 2023) brought together around 1600 participants worldwide to explore the critical pathways needed to address global public and planetary health challenges. Aside from the in-conference sessions and abstract presentations, numerous events were included, such as global health film screenings, book clubs, colonial history walks and serious gaming in health education. It launched the ECTMIH Academy, a pre-conference activity for early career researchers and students to activate academic and creative skills and foster their network and the ECTMIH 2023 regional hubs programme. The regional hubs programme was designed as a series of activities to overcome common barriers and challenges related to physical conference attendance that are commonly overlooked by traditional conference formats. Incorporating ethical guidance and value documents drafted in the early planning stages, the regional hubs sought to operationalise the principles of diversity, equity, inclusion and sustainability. In this article, we discuss the challenges facing knowledge exchange at global scientific conferences, how a regional hubs programme can address some of these challenges and set a new model for equitable, sustainable and locally connected global conferences in the era of the planetary health crisis.

HIV/AIDS

19. JAMA 2024;Dec 1
Antiretroviral Drugs for Treatment and Prevention of HIV in Adults: 2024 Recommendations of the International Antiviral Society-USA Panel
Gandhi RT et al., Massachusetts General Hospital and Harvard Medical School, Boston

Importance: New data and new antiretroviral drugs and formulations continue to become available for the prevention and management of HIV infection.
Objective: To provide updated recommendations for HIV treatment and clinical management and HIV prevention.
Methods: A panel of volunteer expert physician scientists were appointed to provide updated consensus recommendations for 2024. Relevant evidence in the literature since the last report was identified from PubMed and Embase searches (which initially yielded 3998 unique citations, of which 249 were considered relevant); from ongoing monitoring of the literature by the panel members; from data submitted by product manufacturers; and from studies presented at peer-reviewed scientific conferences between June 2022 and October 2024.
Findings: Antiretroviral therapy continues to be recommended for all individuals with HIV. For most people with HIV, initial regimens composed of an integrase strand transfer inhibitor (InSTI), specifically bictegravir or dolutegravir, with 2 (and in some cases 1) nucleoside or nucleotide reverse transcriptase inhibitors are recommended. Recommendations are made for those with particular clinical circumstances, such as pregnancy and active opportunistic diseases, as well as for those unable to take InSTIs. Regimens may need to be changed for virologic failure, adverse effects, convenience, or cost, among other reasons. Long-acting injectable therapy is available for those who prefer not to take daily oral medications and for people struggling with adherence to daily therapy. Recommendations are provided for laboratory monitoring, management of substance use disorders and weight changes, as well as use of statins for cardiovascular disease prevention. For HIV prevention, oral (daily or intermittent) and injectable long-acting medications are effective options for people at increased likelihood of HIV exposure. Further, new tools for maintaining health and well-being among people with HIV, such as doxycycline postexposure prophylaxis to avert sexually transmitted infection, and strategies to treat substance use disorders, are recommended. Disparities in HIV acquisition and care access are discussed and solutions proposed.
Conclusions: New approaches for treating and preventing HIV offer additional tools to help end the HIV epidemic, but achieving this goal depends on addressing disparities and inequities in access to care.

20. JAMA 2024; Dec 1
Is Lenacapavir Needed for Individuals Adherent to Daily Oral PrEP?
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In 2023, roughly 1.3 million people worldwide acquired HIV—3 times more than the target set for 2025. Recently, the World Health Organization described interim results of the PURPOSE 2 trial, which evaluated long-acting injectable lenacapavir, an HIV-1 capsid inhibitor administered subcutaneously twice a year. The analysis showed that lenacapavir was 89% more effective than daily oral preexposure prophylaxis (PrEP) with emtricitabine/tenofovir disoproxil fumarate in preventing HIV among gender-diverse individuals who have sex with men. These findings are consistent with results from the PURPOSE 1 trial, which reported a 100% relative risk reduction in HIV incidence with lenacapavir among cisgender women. Together, results from PURPOSE 1 and PURPOSE 2 provide compelling evidence of lenacapavir's potential to transform HIV prevention across diverse global populations. The World Health Organization acknowledged the advantages of lenacapavir's twice-yearly injections for individuals who face challenges with adherence to daily oral PrEP, while also

emphasizing that oral PrEP remains a safe and effective option for HIV prevention when used consistently.

21. Lancet 2024;404(10468):2131
Editorial
Triumphs and threats: HIV in 2024

Abbreviated
2024 has been a year of highs and lows in the global HIV effort. More people than ever are receiving antiretroviral treatment and have viral suppression. Deaths from AIDS are at their lowest level for two decades. Yet despite this encouraging progress, the Sustainable Development Goal of ending HIV as a public health threat by 2030 is not on track. Worryingly, the pandemic continues to expand in some populations. According to the UNAIDS 2024 World AIDS Day report, nine countries have reached the 95-95-95 targets that need to be met by 2025 to end the AIDS pandemic by 2030, with the targets in reach for a further ten countries. At this pivotal moment, efforts must be intensified to bring HIV under control. A major challenge is the number of new HIV infections every year, with an estimated 1·3 million people newly infected in 2023. Prevention efforts in some regions have lost momentum and renewed focus will be needed to reverse this trajectory.
Effective HIV prevention requires a combination of behavioural, biomedical, and structural approaches, including viral suppression with antiretrovirals, condom use, needle-exchange programmes, education, and policy reform. Use of oral pre-exposure prophylaxis (PrEP) has reduced new infections in some populations but its impact has been limited in women and adolescent girls in east and southern Africa, who face a high HIV burden.
A landmark trial, published this year, showed that the HIV-1 capsid inhibitor lenacapavir, given just twice a year by subcutaneous injection, was highly effective for preventing HIV acquisition in women and girls in South Africa and Uganda (0 infections per 100 person-years vs a background incidence of 2·41 cases per 100 and 1·69 cases per 100 for daily oral emtricitabine–tenofovir disoproxil fumarate). Twice-yearly lenacapavir was similarly efficacious in a trial of cisgender men and gender-diverse people across four continents. The incredible efficacy of long-acting drugs offers an important new tool for HIV prevention.
But if long-acting preventive treatments are to make a substantial dent in new HIV infections, they must be affordable and accessible to those at greatest risk. Lenacapavir's manufacturer Gilead has signed deals with six companies—in Egypt, India, Pakistan, and the USA—to sell generic lenacapavir in 120 low-income and lower-middle-income countries. Until these deals are in place, Gilead will provide lenacapavir at no profit to 18 countries with the highest HIV burden.
For the first time, in 2023, new HIV infections in sub-Saharan Africa were outnumbered by those in the rest of the world—especially in eastern Europe, central Asia, and Latin America.
Upper-middle-income countries, such as Peru, Brazil, Mexico, and Ecuador, are not eligible to purchase generic lenacapavir and will not qualify for Global Fund aid, yet they lack the resources to pay for full-price lenacapavir (up to US$44 000 per year, although it could be mass produced for less than $100). Gilead's exclusion of many middle-income countries from the licensing deal, especially those that participated in the lenacapavir trials and where HIV is in resurgence, is a devastating decision that will cause harms.
Scientific advances alone are insufficient to end HIV as a public health threat: it is a political and financial choice. An approach grounded in human rights, combined with a biomedical, behavioural, and structural response, is needed to curtail the HIV/AIDS pandemic once and for all.

22. Lancet HIV 2024;11(12):e807-e822
Global, regional, and national burden of HIV/AIDS, 1990-2021, and forecasts to 2050, for 204 countries and territories: the Global Burden of Disease Study 2021
GBD 2021 HIV Collaborators
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Background: As set out in Sustainable Development Goal 3.3, the target date for ending the HIV epidemic as a public health threat is 2030. Therefore, there is a crucial need to evaluate current epidemiological trends and monitor global progress towards HIV incidence and mortality reduction goals. In this analysis, we assess the current burden of HIV in 204 countries and territories and forecast HIV incidence, prevalence, and mortality up to 2050 to allow countries to plan for a sustained response with an increasing number of people living with HIV globally.
Methods: We used the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2021 analytical framework to compute age-sex-specific HIV mortality, incidence, and prevalence estimates for 204 countries and territories (1990-2021). We aimed to analyse all available data sources, including data on the provision of HIV programmes reported to UNAIDS, published literature on mortality among people on antiretroviral therapy (ART) identified by a systematic review, household surveys, sentinel surveillance antenatal care clinic data, vital registration data, and country-level case report data. We calibrated a mechanistic simulation of HIV infection and natural history to available data to estimate HIV burden from 1990 to 2021 and generated forecasts to 2050 through projection of all simulation inputs into the future. Historical outcomes (1990-2021) were simulated at the 1000-draw level to support propagation of uncertainty and reporting of uncertainty intervals (UIs). Our approach to forecasting utilised the transmission rate as the basis for projection, along with new rate-of-change projections of ART coverage. Additionally, we introduced two new metrics to our reporting: prevalence of unsuppressed viraemia (PUV), which represents the proportion of the population without a suppressed level of HIV (viral load <1000 copies per mL), and period lifetime probability of HIV acquisition, which quantifies the hypothetical probability of acquiring HIV for a synthetic cohort, a simulated population that is aged from birth to death through the set of age-specific incidence rates of a given time period.
Findings: Global new HIV infections decreased by 21·9% (95% UI 13·1-28·8) between 2010 and 2021, from 2·11 million (2·02-2·25) in 2010 to 1·65 million (1·48-1·82) in 2021. HIV-related deaths decreased by 39·7% (33·7-44·5), from 1·19 million (1·07-1·37) in 2010 to 718 000 (669 000-785 000) in 2021. The largest declines in both HIV incidence and mortality were in sub-Saharan Africa and south Asia. However, super-regions including central Europe, eastern Europe, and central Asia, and north Africa and the Middle East experienced increasing HIV incidence and mortality rates. The number of people living with HIV reached 40·0 million (38·0-42·4) in 2021, an increase from 29·5 million (28·1-31·0) in 2010. The lifetime probability of HIV acquisition remains highest in the sub-Saharan Africa super-region, where it declined from its 1995 peak of 21·8% (20·1-24·2) to 8·7% (7·5-10·7) in 2021. Four of the seven GBD super-regions had a lifetime probability of less than 1% in 2021. In 2021, sub-Saharan Africa had the highest PUV of 999·9 (857·4-1154·2) per 100 000 population, but this was a 64·5% (58·8-69·4) reduction in PUV from 2003 to 2021. In the same period, PUV increased in central Europe, eastern Europe, and central Asia by 116·1% (8·0-218·2). Our forecasts predict a continued global decline in HIV incidence and mortality, with the number of people living with HIV peaking at 44·4 million (40·7-49·8) by 2039, followed by a gradual decrease. In 2025, we projected 1·43 million (1·29-1·59) new HIV infections and 615 000 (567 000-680 000) HIV-related deaths, suggesting that the interim 2025 targets for reducing these figures are unlikely to be achieved. Furthermore, our forecasted results indicate that few countries will meet the 2030 target for reducing HIV incidence and HIV-related deaths by 90% from 2010 levels.
Interpretation: Our forecasts indicate that continuation of current levels of HIV control are not likely to attain ambitious incidence and mortality reduction targets by 2030, and more than 40 million people globally will continue to require lifelong ART for decades into the future. The global community will need to show sustained and substantive efforts to make the progress needed to reach and sustain the end of AIDS as a public threat.

23. N Engl J Med 2024;391:1179-92
Twice-Yearly Lenacapavir or Daily F/TAF for HIV Prevention in Cisgender Women

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Background. There are gaps in uptake of, adherence to, and persistence in the use of preexposure prophylaxis for human immunodeficiency virus (HIV) prevention among cisgender women.
Methods. We conducted a phase 3, double-blind, randomized, controlled trial involving adolescent girls and young women in South Africa and Uganda. Participants were assigned in a 2:2:1 ratio to receive subcutaneous lenacapavir every 26 weeks, daily oral emtricitabine–tenofovir alafenamide (F/TAF), or daily oral emtricitabine–tenofovir disoproxil fumarate (F/TDF; active control); all participants also received the alternate subcutaneous or oral placebo. We assessed the efficacy of lenacapavir and F/TAF by comparing the incidence of HIV infection with the estimated background incidence in the screened population and evaluated relative efficacy as compared with F/TDF.
Results. Among 5338 participants who were initially HIV-negative, 55 incident HIV infections were observed: 0 infections among 2134 participants in the lenacapavir group (0 per 100 person-years; 95% confidence interval [CI], 0.00 to 0.19), 39 infections among 2136 participants in the F/TAF group (2.02 per 100 person-years; 95% CI, 1.44 to 2.76), and 16 infections among 1068 participants in the F/TDF group (1.69 per 100 person-years; 95% CI, 0.96 to 2.74). Background HIV incidence in the screened population (8094 participants) was 2.41 per 100 person-years (95% CI, 1.82 to 3.19). HIV incidence with lenacapavir was significantly lower than background HIV incidence (incidence rate ratio, 0.00; 95% CI, 0.00 to 0.04; P<0.001) and than HIV incidence with F/TDF (incidence rate ratio, 0.00; 95% CI, 0.00 to 0.10; P<0.001). HIV incidence with F/TAF did not differ significantly from background HIV incidence (incidence rate ratio, 0.84; 95% CI, 0.55 to 1.28; P=0.21), and no evidence of a meaningful difference in HIV incidence was observed between F/TAF and F/TDF (incidence rate ratio, 1.20; 95% CI, 0.67 to 2.14). Adherence to F/TAF and F/TDF was low. No safety concerns were found. Injection-site reactions were more common in the lenacapavir group (68.8%) than in the placebo injection group (F/TAF and F/TDF combined) (34.9%); 4 participants in the lenacapavir group (0.2%) discontinued the trial regimen owing to injection-site reactions.
Conclusions. No participants receiving twice-yearly lenacapavir acquired HIV infection. HIV incidence with lenacapavir was significantly lower than background HIV incidence and HIV incidence with F/TDF.

24. N Engl J Med 2024;391:1246-7
Editorial
The Real PURPOSE of PrEP — Effectiveness, Not Efficacy
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Given the 40 years of research and the wealth of successful tools that have been developed to prevent, diagnose, treat, and suppress human immunodeficiency virus (HIV) infection, how is it possible that in 2024 the incidence of HIV type 1 (HIV-1) infection is more than 3.5 per 100 person-years among young women in southern Africa? The efficacy of preexposure prophylaxis (PrEP) to prevent HIV infection was first shown in 2010 in the landmark Preexposure Prophylaxis Initiative (iPrEx) trial of emtricitabine–tenofovir disoproxil fumarate (F/TDF), largely in men who have sex with men (MSM). In July 2012, the time of Food and Drug Administration approval of F/TDF for HIV-1 PrEP in MSM, heated discussion ensued about whether these findings might be extrapolated to support PrEP use in other high-risk populations, such as cisgender women.
Bekker et al. now report in the Journal the results of a well-done, large, randomized, controlled trial in South Africa and Uganda of PrEP for cisgender women (PURPOSE 1). Participants were assigned in a 2:2:1 ratio to receive twice-yearly subcutaneous lenacapavir (an HIV-1 capsid inhibitor), daily oral emtricitabine–tenofovir alafenamide (F/TAF), or daily oral F/TDF (active control). Given that inclusion of a placebo group was considered to be unethical, screened persons who tested positive for HIV infection underwent further testing to assess the recency of infection; these data were used to estimate the background HIV incidence among all the persons screened.

The background HIV incidence in the screened population sadly mirrored previous estimates, at 2.41 per 100 person-years. Of the 55 incident infections among participants in the three intervention groups, there were none in the lenacapavir group, 39 in the F/TAF group, and 16 in the F/TDF group, with an incidence of 0, 2.02, and 1.69 per 100 person-years, respectively. This efficacy exceeded the predefined stopping criteria, and the trial was stopped early. Meta-analyses have previously shown a dose-responsive PrEP efficacy, depending on adherence. Although it is always challenging to fully understand a postrandomization assessment, because medication adherence and other behaviors may track together, the PURPOSE 1 trial corroborates these gradient findings. Nevertheless, adherence and active drug at the time and site of HIV-1 exposure are probably both important for effective prevention. Findings from the PURPOSE 1 trial underscore the challenges of adherence to a daily oral medication, and the incidence of HIV-1 infection was no different from background incidence when documented adherence was low. With approximately 92% attendance for the twice-yearly lenacapavir injections, the PURPOSE 1 trial exemplifies not only that women can dependably adhere to this administration schedule but also that levels of an HIV-1 capsid inhibitor can remain high enough over a period of 6 months to reliably prevent infection.

The results of the PURPOSE 1 trial will raise scientific questions. For example, how can we address the diagnostic challenges of rare acute HIV-1 infection (as shown in the cabotegravir PrEP studies also now reported in the Journal)? What are the best tactics to combat the large number of concomitant sexually transmitted infections? What is the potential for emergent viral resistance? How do these data inform potential use for other groups at high risk for HIV infection? And how can we improve contraceptive options for women at high risk for HIV infection. Given the high pregnancy rate among participants in the PURPOSE 1 trial, assessment of the safety of lenacapavir in pregnancy is a priority. Perhaps, however, the most critical question is how — more than a decade after PrEP was first approved in the United States and several years after the promising DISCOVER results among MSM — we have failed women at high risk for HIV infection for so long.

A key challenge to decreasing the incidence of HIV infection is identifying high-risk populations (especially women), engaging them, and providing them easy, low-barrier, and low-cost access to a PrEP regimen that works and to which they can adhere. Because previous PrEP regimens have proven to be highly effective when taken as prescribed, the PURPOSE 1 trial uniquely addresses only the last among these hurdles.

South Africa, the primary country of enrollment in the PURPOSE 1 trial, updated its PrEP guidelines in 2021, endorsing PrEP use for persons at greatest risk for HIV infection, including adolescent girls and young women as well as MSM, among others. Demographic data for South Africa suggest there are approximately 4.5 million adolescent girls and young women between the ages of 16 and 25 years (PURPOSE 1 enrollment criterion), and the Joint United Nations Program on HIV/AIDS estimates an additional 750,000 South Africans among PrEP-eligible key populations. With more than 5.25 million eligible South Africans, as of 2021 a mere 350,000 (<7%) had ever received a PrEP prescription; durable use is probably far lower.

Reported barriers to PrEP use among young persons in the African context include social stigma, fear of side effects, long travel or wait times for appointments, inconvenient clinical operating hours, and drug costs. To bridge the current canyon between PrEP efficacy and effectiveness, future efforts must address these challenges. To start, PrEP drugs proven to work should be financially accessible to the populations in the countries studied. F/TDF is available in South Africa for less than $50 per year. Meanwhile, lenacapavir currently costs approximately $43,000 annually in the United States, according to Red Book Online (Truven Health Analytics), and access to lenacapavir in South Africa is severely limited. But, the results of the PURPOSE 1 trial have now created a moral imperative to make lenacapavir broadly accessible and affordable as PrEP to persons who were enrolled, as well as all those who are similarly eligible and could benefit.

So now we have a PrEP product with high efficacy. That is great news for science but not (yet) great for women. Now, the imperative is to spend time, resources, and political will on access, implementation, and delivery. And that plan must include a mechanism to finance these drugs so that the women who

have borne an unacceptably high HIV infection burden and who have volunteered for decades in studies of HIV prevention can reap the PrEP benefits and remain HIV free.

Malaria

25. Am J Trop Med Hyg. 2024;111(6):1215-22 Print 2024 Dec 4
A Comprehensive Assessment of Quality of Antimalarial Medicines in Mainland Tanzania: Insights from Five Years of Postmarket Surveillance
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Sustainable access to high-quality antimalarial medicines is pivotal to achieving universal and effective malaria control. Poor-quality antimalarial medicines are prevalent in sub-Saharan Africa, impeding malaria control initiatives and claiming the lives of many children. Regular monitoring of the quality of antimalarial medicines is crucial to ensure the quality of service to the community. A cross-sectional study using a postmarket surveillance (PMS) approach was conducted from 2019 to 2023. Samples were collected from the port of entry, local manufacturers, and various distribution outlets in 15 regions of mainland Tanzania. The samples were subjected to tier 1 evaluation, comprising a product information review (PIR) and identification using the Global Pharma Health Fund-Minilab® techniques. Samples that failed the identification tests and 10% of the samples from distribution outlets that passed the tests were subjected to confirmatory testing (tier 2), which included assays, related substances, dissolution, and sterility per the pharmacopeial monographs. During five annual PMSs, 2,032 antimalarial samples were collected and subjected to quality tests. All samples complied with the standard specifications for identity, dissolution, related substances, sterility, physical evaluation, disintegration, and assay. A total of 292 (55.5%) tested samples failed the PIR evaluation, with incomplete package information in leaflets contributing to 64.7% of all deviations. Antimalarial medicines circulating in the mainland Tanzanian market meet expected quality standards. Continuous monitoring of the quality of antimalarial medicines is recommended.

26. Am J Trop Med Hyg. 2024 Oct 22 Online ahead of print
Evaluating the Implementation of Automated Malaria Rapid Diagnostic Test Readers in Health Facilities in the Democratic Republic of Congo: Process, Challenges, and Lessons Learned
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The WHO's Global Technical Strategy for malaria emphasizes the importance of reliable malaria surveillance systems to track disease burden and measure progress. A key indicator, the test positivity rate (TPR), largely depends on healthcare providers' adherence to rapid diagnostic test (RDT) results and their accurate reporting. To minimize healthcare providers' bias, this study explored the feasibility of using artificial intelligence (AI)-driven Deki Reader devices in the Democratic Republic of Congo. The devices were deployed in 144 health facilities across Haut Katanga, Kasai Central, and Sud Kivu provinces from January to December 2022. Healthcare providers performed malaria diagnostic tests using RDTs and reported the results through the routine system. In addition, they used the Deki Reader device, which automatically read, recorded, and transmitted the AI interpretation into a cloud database. The study compared TPRs from both sources to identify discrepancies. The study revealed the feasibility of using these devices but also identified several logistic and technical challenges. These included delays in device procurement due to COVID-19 pandemic and customs issues, emphasizing the need for better planning and coordination in future rollouts. Device malfunctions and the reliance on stable internet connectivity highlighted the importance of robust support systems and contingency plans. This study demonstrated both the benefits and challenges of implementing such digital health technologies in primary health facilities. Key considerations for successful deployment include careful planning, adequate training and supervision, and taking into account local infrastructure, especially internet connectivity.

27. Lancet Planet Health 2024;8(10):e804-e812

Malaria vector control in sub-Saharan Africa: complex trade-offs to combat the growing threat of insecticide resistance

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(Erratum in Lancet Planet Health. 2024 Nov;8(11):e877)

Mass distribution of insecticide-treated nets (ITNs) has been a key factor in reducing malaria cases and deaths in sub-Saharan Africa. A shortcoming has been the over-reliance on pyrethroid insecticides, with more than 2·13 billion pyrethroid ITNs (PY ITNs) distributed in the past two decades, leading to widespread pyrethroid resistance. Progressive changes are occurring, with increased deployment of more effective pyrethroid-chlorfenapyr (PY-CFP) or pyrethroid-piperonyl butoxide (PY-PBO) ITNs in areas of pyrethroid resistance. In 2023, PY-PBO ITNs accounted for 58% of all ITNs shipped to sub-Saharan Africa. PY-PBO and PY-CFP ITNs are 30-37% more expensive than standard PY ITNs, equating to an additional US$132-159 million required per year in sub-Saharan Africa to fund the shift to more effective ITNs. Several countries are withdrawing or scaling back indoor residual spraying (IRS) programmes to cover the shortfall, which is reflected by the number of structures sprayed by the US President's Malaria Initiative decreasing by 30% from 5·67 million (2021) to 3·96 million (2023). Benin, located in West Africa, is a prime example of a country that ceased IRS in 2021 after 14 years of annual spraying. Our economic evaluation indicates that IRS in Benin cost $3·50 per person protected per year, around five times more per person protected per year compared with PY-PBO ($0·73) or PY-CFP ITNs ($0·76). Although costly to implement, a major advantage of IRS is the portfolio of at least three chemical classes for prospective resistance management. With loss of synergy to PBO developing rapidly, there is the danger of over-reliance on PY-CFP ITNs. As gains in global malaria control continue to reverse each year, current WHO projections estimate that key 2030 malaria incidence milestones will be missed by a staggering 89%. This Personal View explores contemporary malaria vector control trends in sub-Saharan Africa and cost implications for improved disease control and resistance management.

Mental Health

28. Glob Ment Health (Camb) 2024; Oct 24:11:e102
Supported employment as a global mental health intervention
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The global health community has recognized that social determinants of health account for most of the inequities of health outcomes, including mental health outcomes, across and within countries. Strategies to overcome such inequities must focus on modifiable social factors. In this viewpoint, we argue for the preeminence of employment among social determinants of mental health for several reasons. People with mental health disabilities want to work, and a well-validated model of supported employment that is effective and cost-effective now exists. Employment leads to improvements in income, daily structure, self-esteem, social support, community integration and illness management, and people who are employed experience fewer emergencies and hospitalizations. Employment is empowering because people can use added income to activate their own choices regarding other social determinants. Supported employment actualizes the recovery paradigm: People who are employed in competitive jobs of their choice develop a meaningful functional life, increased self-esteem and new social supports. We provide examples of supported employment developments in diverse settings and discuss the implications of scaling up these services worldwide.

29. Glob Ment Health (Camb) 2024;11,e106,1–11
Combining a guided self-help and brief alcohol intervention to improve mental health and reduce substance use among refugee men in Uganda: a cluster-randomized feasibility trial
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Evidence on the effectiveness and implementation of mental health and psychosocial support (MHPSS) interventions for men in humanitarian settings is limited. Moreover, engagement and retention of men in such interventions has been challenging. Adaptations may therefore be required to improve the appropriateness and acceptability of these interventions for men. This study conducted formative research and examined the feasibility of combining an MHPSS intervention, Self-Help Plus, with a brief intervention to reduce harmful alcohol use among refugee men in Uganda. We conducted a cluster randomized feasibility trial comparing the combined alcohol intervention and Self-Help Plus, Self-Help Plus alone and enhanced usual care. Participants were 168 South Sudanese refugee men in Rhino Settlement who reported moderate or high levels of psychological distress. Session attendance was adequate: all sessions had at least 69% of participants present. Participant outcome measures, including symptoms of psychological distress, functional impairment, self-defined problems, depressive symptoms, post-traumatic stress symptoms, overall substance use risk, substance specific risk (alcohol, cannabis, stimulants and sedatives) and well-being, were sensitive to change. A combined approach to addressing mental health and alcohol use appears feasible among men in refugee settings, but further research is needed to examine the effectiveness of combined interventions among men.

30. Glob Ment Health (Camb) 2024 11, e109,1–18
Meta-Analysis: Prevalence of Youth Mental Disorders in Sub-Saharan Africa
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Youth in sub-Saharan Africa (SSA) face limited access to professional mental health resources. A comprehensive assessment of the prevalence of mental disorders would build an understand- ing of the scope of the need.

We conducted systematic searches in PsycInfo, Pubmed, AfriBib and Africa Journals Online to identify prevalence rates for five disorders (anxiety, depression, conduct disorder, attention problems and post-traumatic stress) among SSA youth with a mean age of less than 19 years. We calculated a random-effects pooled prevalence for each disorder and assessed possible moderators.
The meta-analysis included 63 studies with 55,071 participants. We found the following pooled prevalence rates: 12.53% post-traumatic stress disorder (PTSD), 15.27% depression, 6.55% attention-deficit hyperactivity disorder, 11.78% anxiety and 9.76% conduct disorder. We found high heterogeneity across the studies, which may have resulted from differences in samples or measurement tools. Reported prevalence rates were not explained by the sample (i.e., special or general population), but whether the psychometric tool was validated for SSA youth affected the reported prevalence of PTSD and anxiety. In a meta-regression, prevalence rates were associated with the disorder type, with a higher prevalence of depression and PTSD. We found the mean age significantly moderated the prevalence in univariate meta-regression, with increased age cor- related with greater prevalence.
Our findings suggest there is a need to explore reasons for varying prevalence rates further and to develop interventions that support youth mental health in SSA, particularly interventions for depression and PTSD. Limitations included a lack of standardization in psychometric tools and limited reporting on research methods, which influenced quality rating. Importantly, the search only considered studies published in English and was conducted 2 years ago. Although recent estimates reported slightly higher than our prevalence estimates, these reviews together highlight the prevalence and importance of youth mental health difficulties in SSA.

31. Lancet Psychiatry 2024;11(12):1012-21
Service coverage for major depressive disorder: estimated rates of minimally adequate treatment for 204 countries and territories in 2021
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(Erratum in Lancet Psychiatry. 2024 Nov 19:S2215-0366(24)00398-5)
Background: Access to effective treatment for major depressive disorder remains limited and difficult to track across place and time. We analysed the available data on minimally adequate treatment (MAT) for major depressive disorder globally with the aim of providing a useful metric against which to monitor national responses to the growing public health burden imposed by major depressive disorder.
Methods: MAT was defined as pharmacotherapy (1 month of medication, plus four visits to a medical doctor) or psychotherapy (eight visits with any professional). From existing reviews, we identified mental health surveys that assessed major depressive disorder within the general population as well as health service uptake by individuals with major depressive disorder. Data by ethnicity were not available. Estimates of MAT, antidepressant use, or use of any mental health service were extracted. The latter two estimates were adjusted to reflect likely MAT rates via a network meta-analysis. Adjusted MAT estimates were analysed via a Bayesian meta-regression using the Disease Modelling Meta-Regression (DisMod-MR 2.1) tool. This analysis estimated MAT coverage among people with major depressive disorder by age, sex, location, and year. Final MAT estimates were standardised by age and sex against the existing age and sex distribution of people with major depressive disorder globally. People with lived experience were involved in the design, preparation, interpretation, and writing of this manuscript.
Findings: The analysed dataset included 145 estimates from 32 studies, covering 31 countries, 14 regions, and six super-regions. The proportion of people with major depressive disorder receiving MAT globally in 2021 was 9·1% (95% uncertainty interval 7·2-11·6), with 10·2% (8·2-13·1) of females and 7·2% (5·7-9·3) of males with major depressive disorder receiving MAT. MAT coverage was highest in high-income locations (27·0% [21·7-34·4]), with Australasia having the highest rate (29·2% [21·4-40·8]). MAT coverage was lowest in sub-Saharan Africa (2·0% [1·5-2·6]), within which western sub-Saharan Africa (1·8% [1·4-2·5]) had the lowest coverage. Seven countries (Australia, Belgium, Canada,

Germany, the Netherlands, South Korea, and Sweden) were estimated to have MAT coverage exceeding 30%, while 90 countries were estimated to have coverage lower than 5%.
Interpretation: Despite many gaps in the available data, estimates show that, globally, most individuals with major depressive disorder do not receive MAT. Services must improve to reach a global coverage that better meets the mental health needs of those with major depressive disorder. Urgent attention should be given to the scale-up of effective intervention strategies, especially in low-income and middle-income countries, as well as further research into better quality treatment options for major depressive disorder. We present a means by which the MAT gap for major depressive disorder can be quantified, to monitor and inform action by governments and international partners.

Non-Communicable Diseases

32. Lancet 2024;404(10467):2077-93
Worldwide trends in diabetes prevalence and treatment from 1990 to 2022: a pooled analysis of 1108 population-representative studies with 141 million participants
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Background: Diabetes can be detected at the primary health-care level, and effective treatments lower the risk of complications. There are insufficient data on the coverage of treatment for diabetes and how it has changed. We estimated trends from 1990 to 2022 in diabetes prevalence and treatment for 200 countries and territories.
Methods: We used data from 1108 population-representative studies with 141 million participants aged 18 years and older with measurements of fasting glucose and glycated haemoglobin (HbA1c), and information on diabetes treatment. We defined diabetes as having a fasting plasma glucose (FPG) of 7·0 mmol/L or higher, having an HbA1c of 6·5% or higher, or taking medication for diabetes. We defined diabetes treatment as the proportion of people with diabetes who were taking medication for diabetes. We analysed the data in a Bayesian hierarchical meta-regression model to estimate diabetes prevalence and treatment.
Findings: In 2022, an estimated 828 million (95% credible interval [CrI] 757-908) adults (those aged 18 years and older) had diabetes, an increase of 630 million (554-713) from 1990. From 1990 to 2022, the age-standardised prevalence of diabetes increased in 131 countries for women and in 155 countries for men with a posterior probability of more than 0·80. The largest increases were in low-income and middle-income countries in southeast Asia (eg, Malaysia), south Asia (eg, Pakistan), the Middle East and north Africa (eg, Egypt), and Latin America and the Caribbean (eg, Jamaica, Trinidad and Tobago, and Costa Rica). Age-standardised prevalence neither increased nor decreased with a posterior probability of more than 0·80 in some countries in western and central Europe, sub-Saharan Africa, east Asia and the Pacific, Canada, and some Pacific island nations where prevalence was already high in 1990; it decreased with a posterior probability of more than 0·80 in women in Japan, Spain, and France, and in men in Nauru. The lowest prevalence in the world in 2022 was in western Europe and east Africa for both sexes, and in Japan and Canada for women, and the highest prevalence in the world in 2022 was in countries in Polynesia and Micronesia, some countries in the Caribbean and the Middle East and north Africa, as well as Pakistan and Malaysia. In 2022, 445 million (95% CrI 401-496) adults aged 30 years or older with diabetes did not receive treatment (59% of adults aged 30 years or older with diabetes), 3·5 times the number in 1990. From 1990 to 2022, diabetes treatment coverage increased in 118 countries for women and 98 countries for men with a posterior probability of more than 0·80. The largest improvement in treatment coverage was in some countries from central and western Europe and Latin America (Mexico, Colombia, Chile, and Costa Rica), Canada, South Korea, Russia, Seychelles, and Jordan. There was no increase in treatment coverage in most countries in sub-Saharan Africa; the Caribbean; Pacific island nations; and south, southeast, and central Asia. In 2022, age-standardised treatment coverage was lowest in countries in sub-Saharan Africa and south Asia, and treatment coverage was less than 10% in some African countries. Treatment coverage was 55% or higher in South Korea, many high-income western countries, and some countries in central and eastern Europe (eg, Poland, Czechia, and Russia), Latin America (eg, Costa Rica, Chile, and Mexico), and the Middle East and north Africa (eg, Jordan, Qatar, and Kuwait).
Interpretation: In most countries, especially in low-income and middle-income countries, diabetes treatment has not increased at all or has not increased sufficiently in comparison with the rise in prevalence. The burden of diabetes and untreated diabetes is increasingly borne by low-income and middle-income countries. The expansion of health insurance and primary health care should be accompanied with diabetes programmes that realign and resource health services to enhance the early detection and effective treatment of diabetes.

Ophthalmology

33. Asia-Pacific J Ophthalmol 2024;13(5):100109
Current research and future strategies for the management of vision-threatening diabetic retinopathy
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Diabetic retinopathy (DR) is a major ocular complication of diabetes and the leading cause of blindness and visual impairment, particularly among adults of working-age adults. Although the medical and economic burden of DR is significant and its global prevalence is expected to increase, particularly in low- and middle-income countries, a large portion of vision loss caused by DR remains preventable through early detection and timely intervention. This perspective reviewed the latest developments in research and innovation in three areas, first novel biomarkers (including advanced imaging modalities, serum biomarkers, and artificial intelligence technology) to predict the incidence and progression of DR, second, screening and early detection of referable DR and vision-threatening DR (VTDR), and finally, novel therapeutic strategies for VTDR, including diabetic macular oedema (DME), with the goal of reducing diabetic blindness.

Planetary Health

34. Lancet 2024;404(10463):1693-1700
Review
Climate crisis, cities, and health
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Abbreviated
Introduction
More than ever, the climate crisis is becoming a health crisis. An estimated 5 million people globally die each year because of suboptimal temperatures, with a large proportion of heat-related mortality (37%) attributable to human-induced climate change. The last few years have been the hottest on record and high temperatures claimed over 60 000 lives in Europe alone in 2022, with cities the most affected3 and temperatures in cities projected to increase.4,5 Urban heat islands that result from excessive asphalt and concrete in cities contribute to an increase in temperature and premature mortality.6 Just over half of the world's population (56%) now lives in cities and that percentage is expected to reach nearly 70% by 2050.7
The Conference of the Parties (COP) had its first health day at COP28 and over 120 countries have endorsed the COP28 UAE Declaration on Climate and Health. This historic and important event recognises and provides evidence that the climate crisis is also a health crisis and that people's health can benefit from climate action. The Declaration promotes the health arguments for climate action and health co-benefits of mitigation and discusses the strengthening climate resilience of health systems.8 Currently, the impacts of the climate crisis already lead to large health burdens and health-care costs. Therefore, climate action is also about preventing premature deaths and disease and reducing health-care costs.
In this Lecture, an overview is provided of potential climate action measures at the nexus of urban planning, environment, climate, and health to achieve climate neutral, liveable, and healthy cities. This Lecture is not a comprehensive or systematic review, but provides a brief overview of possible climate actions that cities can implement and that can improve the health of citizens.
Conclusion
Urban and transport planning practices have a large impact on greenhouse gas emissions, air pollution levels, green space availability, urban heat island effects, and disease burden. Cities therefore provide a great opportunity to address the climate crisis and promote environmental quality and health. Many climate measures are available, but what appears to be particularly lacking are political leadership, finance, and behavioural change, which are essential to making transitional changes, and of course urgency. Transitional change is difficult, but we cannot continue as we do now if we want to have a future for the next generations.
A better, more health-oriented narrative of climate action might help, particularly if immediate health benefits could be shown. But we also need a more integrated and holistic vision of what our cities should be and should look like to capture the imagination of politicians, decision makers, and citizens and change their behaviour. This vision is often still missing. A shift away from our car-centric planning and more greening are essential.
Prevention is better than cure and the medical profession should become more involved in planning in our cities to address the climate crisis and reduce the disease burden (figure 3). Innovation should not only be thought of in terms of medical care, but also of measures in our streets, neighbourhoods, and cities to improve the health of citizens. Health should be a priority in any urban planning and not be left to the medical profession.
By 2050, cities that have embraced climate action will be cleaner, greener, more resilient, and more liveable, with urban environments that prioritise sustainability and the health and wellbeing of their residents (panel). Cities that do not take decisive climate action by 2050 are likely to be characterised by environmental degradation, social inequality, economic decline, and a lower quality of life for their

residents. The contrast between cities that act and those that do not will become increasingly stark, with inaction leading to potentially irreversible consequences. 2050 is tomorrow and urgency in climate action is essential. Stop looking for excuses not to act, act now.

35. Lancet 2024;404(10465):1847-96
Review
The 2024 report of the Lancet Countdown on health and climate change: facing record-breaking threats from delayed action
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Despite the initial hope inspired by the 2015 Paris Agreement, the world is now dangerously close to breaching its target of limiting global multiyear mean heating to 1·5°C. Annual mean surface temperature reached a record high of 1·45°C above the pre-industrial baseline in 2023, and new temperature highs were recorded throughout 2024. The resulting climatic extremes are increasingly claiming lives and livelihoods worldwide.
The Lancet Countdown: tracking progress on health and climate change was established the same year the Paris Agreement entered into force, to monitor the health impacts and opportunities of the world's response to this landmark agreement.
The 2024 report of the Lancet Countdown, building on the expertise of 122 leading researchers from UN agencies and academic institutions worldwide, reveals the most concerning findings yet in the collaboration's 8 years of monitoring.
Conclusion (Abbreviated)
Data in this report show that many of the health threats and impacts of climate change are exceeding all previous records.
With current policies and actions putting the world on track to 2·7°C of heating by 2100 if maintained,11 limits to adaptation are looming closer.
The world is increasingly off-track from meeting the goals of the Paris Agreement and, despite some progress in adoption of renewable energy, many key indicators point to a world moving in the wrong direction, with many showing a reversal of progress in the last year of data.
Delays in implementing the required transformative actions mean that most countries are grossly unprepared for a healthy, net zero greenhouse gas emission future, with people in low and medium HDI countries most at risk.
Against this concerning background, an increased focus on health within UNFCCC negotiations in COP28 and the prioritisation of climate change within the WHO's GPW 14 mark important progress.
The engagement of individuals, corporations, scientists, and international organisations with climate change and health is growing (indicators 5.2, 5.3.1, 5.3.2, 5.4.2, and 5.5), raising hopes that a healthy, prosperous future could still be within reach.
However, avoiding a catastrophic increase in death, disease, and destruction will require urgent, decisive, and health-focused actions, exceeding the ambition of international commitments. Entering a new phase of activities, the Lancet Countdown will update its indicator frameworks and increase its efforts to ensure indicators are relevant to inform decision making. Such efforts will include monitoring progress towards the delivery and outcomes of those actions that have been shown to have the potential for delivering a prosperous, healthy future for all.

Pharmaceuticals and Health Policy

36. Am J Trop Med Hyg. 2024;111(6):1378-95 Print 2024 Dec 4
Relationship between Prices and Quality of Essential Medicines from Different Manufacturers Collected in Cameroon, the Democratic Republic of the Congo, and Nigeria
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Achieving universal access to affordable medicines and at the same time ensuring the quality of medicines presents a challenge, especially in low- and middle-income countries. Here, the relationship between medicine prices and medicine quality was investigated in three African countries. From different types of health facilities and medicine vendors, 711 samples of 18 different essential medicines were purchased and analyzed for quality (assay and dissolution) according to the United States Pharmacopeia. Without exception, all originator brand medicines and all SRA generics (generic medicines manufactured in countries with stringent regulatory authorities [SRAs]) complied with pharmacopeial specifications. In contrast, 21.1% of the non-SRA generics (manufactured in countries without SRAs) were substandard. The median prices of originator brands and SRA generics were three times and two times higher than those of non-SRA generics, respectively. Within the non-SRA generics, no positive correlation was observed between medicine quality and medicine price. Medicines manufactured in India, China, or African countries showed similar quality and similar prices. Only a single WHO-prequalified medicine sample was found among the 711 samples. Non-SRA generic medicines produced by manufacturers for which WHO had published Public Inspection Reports showed a significantly lower rate of substandard medicines (7.3%) and, at the same time, significantly lower prices (by 33%) than other non-SRA generics. Falsified medicines (total 2.0%) were found among all categories of medicines and had prices similar to those of non-SRA generics. Our findings indicate that adequate quality assurance does not necessarily imply an increase in medicine prices.

37. BMJ Global Health 2024;9:e015671
Understanding the barriers and facilitators related to never treatment during mass drug administration among mobile and migrant populations in Mali: a qualitative exploratory study
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Introduction Five of the neglected tropical diseases use a strategy of preventative chemotherapy distributed via mass drug administration (MDA) for all eligible people living in endemic areas. To be successful, high coverage must be sustained over multiple rounds. Therefore, it will be difficult to reach elimination as a public health problem using MDA if there remain clusters of people who have never been treated. The study aims to explore the reasons why people with high mobility report being never treated during MDA and to provide evidence to support the development of standardised questions for data collection using qualitative research tools.
Methods We conducted an exploratory study using qualitative methods among displaced people, nomads/transhumants and economic migrants who self-reported that they had never been treated during MDA in the health districts of Tominian and Kalabancoro in Mali. Data were collected through in-depth individual interviews and focus group discussions. Nvivo V.14 software was used for data management and analysis.
Results The main reasons reported for never treatment included: geographical mobility, lack of awareness/information, negative rumours, fear of side effects, conflict and insecurity and logistical difficulties faced in reaching these populations. Proposed solutions included involving communities in the MDA, increasing awareness and information campaigns, effectively managing side effects, and designing and implementing flexible and effective interventions.
Conclusion This study highlights that there are people with high mobility who may never have been treated during any round of MDA. The reasons for never treatment highlight the challenges faced when reaching particular groups during MDA activities/interventions. Suggested remedies will require

programmes to implement more flexible and tailored interventions. Customised approaches based on the context are essential to guarantee fair access to preventive chemotherapy. Effective interventions must consider the supply and demand side in crafting interventions. This research adds to the evidence base to understand never treatment, particularly among highly mobile population groups and in schistosomiasis elimination programmes.

38. BMJ Global Health 2024;9:e015790
Access to medicines among asylum seekers, refugees and undocumented migrants across the migratory cycle in Europe: a scoping review
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Introduction Access to essential medicines is a critical element of health systems and an important measure of their performance. Migrants may face barriers in accessing healthcare, including essential medicines, throughout the migration cycle, which includes the stages of departure from home or residence countries, transit through non-European or European countries, reception and settlement in a country in Europe and deportation. We aim to provide an overview of research and grey literature concerning access to essential medicines for asylum seekers, refugees and undocumented migrants in or heading to Europe (European Union, European Economic Area, Switzerland and the UK).
Methods To delineate and conceptualise access to medicines, we considered the definition of the Lancet Commission on Essential Medicines and the Pharmaceutical Management framework. These frameworks were combined to guide several critical steps in our review, including defining the search terms, data extraction, data analyses and reporting. Relevant studies and reports were identified through searches in bibliographic and grey literature databases.
Results Out of 5760 studies and 66 grey literature reports, 108 met the inclusion criteria, with 72 focusing on medicine access. Overall, medicine use and medicine expenditure were found to be lower in migrant populations compared with the host population in many European countries. Although many studies focused on the use of infectious disease and psychotropic medicines, the most frequently used medicines by migrants were analgesics, hypertension and diabetes medicines. Determinants of medicine access were legal restrictions, language and transit times, which all contributed to interruption of and inequities in access to medicines among this population. This scoping review also indicated significant gaps in the literature regarding the evidence on access to medicine at different stages of the migration cycle, specifically in departure, transit and deportation stages.
Conclusion Overall, our findings highlighted significant unmet medicine needs among migrants in or on the way to Europe and access disparities attributable to various interconnected barriers. Urgent access is needed to address such inequities, particularly legal barriers, including registration of certain medicines required for treatment. Future research should prioritise investigating medicine access during departure, transit and deportation stages. Policy discussions around migrants' access to medicines should be centred on framing healthcare as a fundamental right.

Primary Health Care

39. BMJ Global Health 2024;9:e013817
Ethiopian primary healthcare clinical guidelines 5 years on—processes and lessons learnt from scaling up a primary healthcare initiative
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Many effective health system innovations fail to reach those who need them most, falling short of the goal of universal health coverage. In the 5 years since the Federal Ministry of Health in Ethiopia localised the Practical Approach to Care Kit (PACK) programme to support primary care reforms, PACK has been scaled-up to over 90% of the country's primary care health centres. Known as the Ethiopian Primary Healthcare Clinical Guideline (EPHCG), the programme comprises a comprehensive, policy-aligned clinical decision support tool (EPHCG guide) and an implementation strategy to embed comprehensive, integrated care into every primary care consultation for individuals over 5 years of age, while addressing barriers to streamlined primary healthcare delivery. We describe the components of the EPHCG programme and the work done to establish it in Ethiopia. Yamey's framework for successful scale-up is used to examine the programme and health system factors that enabled its scale-up within a 5-year period. These included high-level ministry leadership and support, a cascade model of implementation embedded in all levels of the health system, regular EPHCG guide and training material updates and strategies to generate stakeholder buy-in from managers, health workers, patients and communities. Challenges, including stakeholder resistance, training fidelity and quality and procurement of medicines and diagnostic tests, are described, along with efforts to resolve them. Insights and learnings will be of interest to those implementing PACK programmes elsewhere, and managers and researchers responsible for design and delivery of health systems strengthening innovations at scale in low-income and middle-income countries.

40. BMJ Global Health 2024;9:e015165
A learning health systems approach to scaling up an evidence-based intervention for integrated primary mental healthcare case finding and referral in South Africa
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Despite progress in the development and evaluation of evidence-based primary mental health interventions in low-income and middle-income countries, implementation and scale-up efforts have had mixed results. Considerable gaps remain in the effective translation of research knowledge into routine health system practices, largely due to real-world contextual constraints on implementation and scale-up efforts. The Southern African Research Consortium for Mental Health Integration (S-MhINT) programme used implementation research to strengthen the implementation of an evidence-based integrated collaborative depression care model for primary healthcare (PHC) services in South Africa. To facilitate the scale-up of this model from a testing site to the whole province of KwaZulu-Natal, a capacity building programme was embedded within the Alliance for Health Policy and Systems Research (AHPSR) learning health systems (LHS) approach. The paper discusses efforts to scale up and embed case finding and referral elements of the S-MhINT package within routine PHC. Data from semistructured interviews, a focus group discussion, proceedings from participatory workshops and outputs from the application of continuous quality improvement (CQI) cycles were thematically analysed using the AHPSR LHS framework. Learning particularly occurred through information sharing at routine participatory workshops, which also offered mutual deliberation following periods of applying CQI tools to emergent problems. Individual-level, single-loop learning seemed to be particularly observable elements of the AHPSR LHS framework. Ultimately, our experience suggests that successful scale-up requires strong and sustained relationships between researchers, policy-

makers and implementers, investments into learning platforms and organisational participation across all levels to ensure ownership and acceptance of learning processes.

41. Lancet Glob Health 2024;12(10):e1693-e1705 Epub 2024 Aug 20
The state of primary health care in south Asia
Prinja S et al., Department of Community Medicine and School of Public Health, Post Graduate Institute of Medical Education and Research, Chandigarh, India p<rinja.shankar@pgimer.edu.in>

The south Asian region (SAR) is home to 1·74 billion people, corresponding to 22% of the global population. The region faces several challenges pertaining to changing epidemiology, rapid urbanisation, and social and economic concerns, which affect health outcomes. Primary health care (PHC) is a cost-effective strategy to respond to these challenges through integrated service delivery, multi-sectoral action, and empowered communities. The PHC approach has historically been an important cornerstone of health policy in SAR countries. However, the region is yet to fully reap the benefits of PHC-oriented health systems. Our introductory paper in this Lancet Series on PHC in the SAR describes the existing PHC delivery structure in five SAR nations (ie, Bangladesh, India, Nepal, Pakistan, and Sri Lanka) and critically appraises PHC performance to identify its enablers and barriers. The paper proposes investing in a shared culture of innovation and collaboration for revitalisation of PHC in the region.
Other articles of the Series:

- Lancet Glob Health 2024;12(10):e1706-e1719 Epub 2024 Aug 20

Delivering non-communicable disease services through primary health care in selected south Asian countries: are health systems prepared?
Ahmed SM et al., BRAC James P Grant School of Public Health, BRAC University, Dhaka, Bangladesh <ahmed.sm@bracu.ac.bd>

- Lancet Glob Health 2024;12(10):e1720-e1729 Epub 2024 Aug 20

Improving urban health through primary health care in south Asia
Rao KD et al, Department of International Health, Johns Hopkins University, Baltimore, MD, USA <kdrao@jhu.edu>

Sexual Reproductive Health and Rights

42. Bull World Health Organ 2024;102(11):837-9 Epub 2024 Oct 2
Inequalities in geographical access to emergency obstetric and newborn care
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(Perspective, abridged)
In 2020, an estimated 287 000 women died due to complications of pregnancy and childbirth, while 1.9 million stillbirths occurred in 2021. As many as half of maternal deaths and three in four stillbirths are preventable if women can access timely emergency care that is provided by skilled health personnel. To date, efforts of the global community to reduce maternal mortality and stillbirths have mostly focused on ensuring the availability of emergency obstetric and newborn care, minimizing financial barriers to care and, more recently, improving care quality. However, governments have given less attention to geographical accessibility and inequalities in access between and within populations. Pregnant women in low- and middle-income countries often need to seek care on their own, even in emergencies, and many face immense challenges in reaching emergency obstetric and newborn care facilities.
Here we examine the geographical accessibility to emergency obstetric and newborn care in low- and middle-income settings. We argue for the use of emerging scientific evidence and contextual understanding to better identify priority problem areas, select appropriate methods, and develop solutions and targets related to assessing geographical accessibility for emergency obstetric and newborn care.
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While countries have made progress in optimizing geographical accessibility, we argue that new thinking around this issue is needed. Geographical accessibility assessments need to better reflect realities of travel in different settings. While traditional modelling approaches may suffice in rural areas with minimal variation in travel time, navigation-enabled mobile applications should be used for urban settings to capture access variability. Strategic partnerships are necessary to ensure availability of data for these assessments, which will also require regular, government-led updates on facility functionality. We call for adopting new real-world travel time estimates combined with geospatial databases on health-seeking behaviour, care experiences and outcomes, to inform evidence-based decision-making for health system redesign. This approach will ensure cost-effective solutions, address inequities and contribute to the realization of universal health coverage. This approach will also inform context-specific and evidence-based benchmarks for geographical accessibility that reflect real-world conditions and are clinically relevant, thereby improving maternal and newborn outcomes.

43. Bull World Health Organ 2024;102(12):842–842A
Editorial: What is needed to improve sexual health and well-being
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Transformative approaches to sexual health and well-being across the life course are essential to advance comprehensive sexual and reproductive health and rights, protection of bodily autonomy and gender justice. Much of the existing evidence views this health topic reductively – focusing on maternal and reproductive health – and views sexual health as primarily about sexually transmitted infections. Sexual health is historically overlooked, and underfunded, and sexual well-being ignored. Additional efforts are therefore needed to prioritize sexual health and well-being within the broader framework of sexual and reproductive health and rights to foster more inclusive and equitable health systems for all.

This theme issue aims to spark dialogue and highlight current evidence from both health system and people-centred perspectives on sexual health and well-being.

The papers in this theme issue reiterate the message that sexual health and well-being are essential to overall health over the entire life course, including for adolescents, people of reproductive age and older people. This issue also emphasizes the importance of action from policy to practice – from the growing threats of sexually transmitted infections and the dangers of sexual exploitation during conflicts, to sexual health and well-being beyond linkages to reproduction, including understanding menstrual health as an issue of sexual justice, and preparing women for perimenopause. As global understanding of sexual health and well-being still appears to be largely disease focused, a broader, people-centred focus on sexual empowerment and social and commercial determinants of sexual health is needed. Such an evolution must also support the integration of high-quality, accessible, affordable, available and acceptable self-care options for sexual health. Self-care options can be provided through telehealth, including for underserved communities, as in a mobile health intervention for HIV prevention among female sex workers.

Further work in this area is needed to expand access to sexual health services and increase research on the range of sexual health experiences and needs in a broader, more diverse range of populations. The UNDP/UNFPA/UNICEF/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction, contained in the World Health Organization (WHO) Department of sexual and reproductive health and research, is the main instrument within the United Nations for promoting, conducting, evaluating and coordinating interdisciplinary research in sexual and reproductive health and rights. The programme has driven meaningful change over the past 50 years, and is further strengthening attention on sexual health and well-being across the life course, as evidenced by the multicountry findings on sexual health practices and experiences and addressing harmful norms in sexual health services.

Building a strong evidence base is an important tool to fight misinformation and political opposition that have long hindered progress in sexual and reproductive health and rights more broadly, and sexual health and well-being in particular, with damaging effects on societies, individuals and marginalized communities. WHO could play a vital role in establishing a global sexual and reproductive health and rights information hub, offering fact-based resources. Initiatives could include myth-busting campaigns on social media, and partnerships with schools to integrate comprehensive sexuality education. Competency-based training for health and care workers on inclusive communication methods can further support efforts to reach diverse populations. By fostering informed, open conversations around sexual health and well-being, such initiatives can build trust and dispel harmful misconceptions.

Securing the broader realization of sexual health and well-being within the sexual and reproductive health and rights framework requires an ambitious, forward-looking strategy, grounded in robust research, that prioritizes issues such as inclusivity, combats misinformation, and uses innovations such as self-care and digital health interventions. These approaches are needed to strengthen resilience in crisis settings, where health systems are often disrupted. By strengthening the sexual health and well-being aspects of sexual and reproductive health and rights, these rights can remain an accessible, integral aspect of global health, supporting the health, well-being and autonomy of all individuals. Doing so will require broad stakeholder collaboration to tackle issues such as restrictive policies and social stigma. Funding will also be required for research on diverse sexual health priorities, including for marginalized, underserved populations. With commitment and coordination, the global health community can make strides towards a future where sexual and reproductive health and rights are universally recognized, protected and celebrated.

Articles in this theme issue:

- Associations between sexual health and well-being: a systematic review. Vasconcelos P, et al.
- A risk- and needs-based strategy for HIV prevention for adolescent girls and young women, WHO African Region. Mahomed S, et al.
- Sexual health and well-being in later life. McAuliffe L, Fetherstonhaugh D.
- Mpox: an old disease poses a new threat. Bull World Health Organ. Ndembi N, et al.
- Sexual exploitation, abuse and harassment in humanitarian contexts. Westendorf JK, et al.

- Menstruation and sexual health, well-being and justice. Logie C, et al.
- Towards a more accurate global picture of perimenopause. Pyne Y, et al.
- Progress towards sustainable development goals related to sexual health. Owolabi O, et al.
- Improving measures of women's and girls' sexual empowerment. Kågesten A, et al.
- Trial of an mHealth intervention to improve HIV prophylaxis for female sex workers, United Republic of Tanzania. Mbotwa CH, et al.
- Endometriosis: disease mechanisms and health disparities. Rahmioglu N, Zondervan K.
- Cognitive testing in 19 countries to refine WHO's Sexual Health Assessment of Practices and Experiences. Hunter E, et al.

44. Lancet 2024;404(10463):1645-56
The effect of tranexamic acid on postpartum bleeding in women with moderate and severe anaemia (WOMAN-2): an international, randomised, double-blind, placebo-controlled trial
WOMAN-2 Trial Collaborators <woman2@lsthm.ac.uk>

Background: Tranexamic acid, given within 3 h of birth, reduces bleeding deaths in women with postpartum haemorrhage. We examined whether giving tranexamic acid shortly after birth can prevent postpartum haemorrhage in women with moderate or severe anaemia.
Methods: This international, randomised, double-blind, placebo-controlled trial was done in 34 hospitals across four countries (Nigeria, Pakistan, Tanzania, and Zambia). We recruited women of any age in active labour with moderate or severe anaemia (haemoglobin <100 g/L). We randomly assigned women (1:1) who had given birth vaginally to receive 1 g of tranexamic acid or matching placebo by slow intravenous injection (over 10 min) within 15 min of the umbilical cord being cut or clamped. Women were randomly assigned by selection of the lowest numbered treatment pack from a box containing 20 packs that were identical apart from the pack number. Participants, care givers, and those assessing outcomes were masked to group assignment. The primary outcome was a clinical diagnosis of primary postpartum haemorrhage, which might be an estimated blood loss of more than 500 mL or any blood loss sufficient to compromise haemodynamic stability within 24 h of randomisation, analysed on an intention-to-treat basis. Safety analyses were performed in all participants included in the intention-to-treat population. This trial was registered on ISRCTN (ISRCTN62396133), ClinicalTrials.gov (NCT03475342), and the Pan African Clinical Trial Registry (PACTR201909735842379) and is closed to recruitment.
Findings: From Aug 24, 2019, to Sept 19, 2023, 16 586 women aged 14-50 years were invited to take part and 1518 were excluded. 7580 women were randomly assigned to receive tranexamic acid and 7488 to receive placebo. Primary outcome data were unavailable for one woman in each group. The median time interval from the start of the administration of the trial treatment to the diagnosis of postpartum haemorrhage was 18·5 min (IQR 5-58); 20 min (8-64) in women with moderate anaemia and 13 min (7-44) in women with severe anaemia. 358 (35%) of 1024 with postpartum haemorrhage for whom time data were available were diagnosed before the trial treatment had been fully administered. Clinically diagnosed postpartum haemorrhage occurred in 530 (7·0%) of 7579 in the tranexamic acid group and in 497 (6·6%) of 7487 in the placebo group (risk ratio [RR] 1·05, 95% CI 0·94-1·19). There was no strong evidence against the null hypothesis of homogeneity of effects for any of the prespecified subgroup analyses: severity of anaemia (p=0·44), antepartum haemorrhage (p=0·044), birth canal trauma (p=0·37), use of pain control (p=0·37), and baseline risk of postpartum haemorrhage (p=0·31). There were no vascular occlusive events (pulmonary embolism, deep vein thrombosis, stroke, and myocardial infarction) reported in either group. There were no adverse events related to the treatment and no treatment-related deaths.
Interpretation: In women with moderate and severe anaemia, giving tranexamic acid within 15 min of the umbilical cord being clamped did not reduce the risk of clinically diagnosed postpartum haemorrhage.

45. Lancet 2024;404(10463):1657-67

Tranexamic acid for postpartum bleeding: a systematic review and individual patient data meta-analysis of randomised controlled trials
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Background: Tranexamic acid is a recommended treatment for women with a clinical diagnosis of postpartum haemorrhage, but whether it can prevent bleeding is unclear. We conducted a systematic review and individual patient data (IPD) meta-analysis of randomised controlled trials to assess the effects of tranexamic acid in women giving birth.
Methods: In this systematic review and IPD meta-analysis, we searched the WHO International Clinical Trials Registry Platform from database inception to Aug 4, 2024 for randomised trials that assessed the effects of tranexamic acid in women giving birth. Trials were eligible if they were prospectively registered, placebo-controlled, included more than 500 women, and had a low risk of bias for random sequence generation and allocation concealment. IPD were requested from the trial investigators. The primary outcomes were the numbers of women with life-threatening bleeding and thromboembolic events. We used a one-stage model to analyse the data and explored whether the effect of tranexamic acid varied by the underlying risk of life-threatening bleeding, type of birth, presence of moderate or severe anaemia, or timing of administration (before or after a diagnosis of postpartum haemorrhage). This study is registered with PROSPERO, CRD42022345775.
Findings: We analysed data on 54 404 women from five trials. We obtained IPD for 43 409 women from four trials and aggregate data on 10 995 women from one trial. All trials had a low risk of bias. Life-threatening bleeding occurred in 178 (0·65%) of 27 300 women in the tranexamic acid group versus 230 (0·85%) of 27 093 women in the placebo group (pooled odds ratio [OR] 0·77 [95% CI 0·63-0·93]; p=0·008). There was no evidence that the effect of tranexamic acid varied by the underlying risk of life-threatening bleeding, type of birth, presence of moderate or severe anaemia or timing of administration. No significant difference was identified between tranexamic acid and placebo groups with regard to thromboembolic events: 50 (0·2%) of 26 571 women in the tranexamic acid group had fatal or non-fatal thromboembolic events versus 52 (0·2%) of 26 373 women in the placebo group (pooled OR 0·96 [0·65-1·41]; p=0·82) with no significant heterogeneity identified in the subgroup analyses.
Interpretation: Tranexamic acid reduces the risk of life-threatening postpartum bleeding. We found no evidence that tranexamic acid increases the risk of thrombosis. Although we do not recommend the use of tranexamic acid in all women giving birth, consideration should be given to its use before a diagnosis of postpartum haemorrhage in women at high risk of death.

46. Lancet Glob Health. 2024 Nov;12(11):e1785-e1793 Epub 2024 Sep 24
Intimate partner violence and childhood health outcomes in 37 sub-Saharan African countries: an analysis of demographic health survey data from 2011 to 2022
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Background: Understanding the contribution of intimate partner violence (IPV) to childhood health outcomes (eg, morbidity and mortality) is crucial for improving child survival in sub-Saharan Africa. This comprehensive study aimed to explore the associations between maternal exposure to physical, sexual, or emotional violence and adverse childhood health outcomes in sub-Saharan Africa.
Methods: We analysed Demographic Health Survey datasets from 37 sub-Saharan African countries from 2011 to 2022. A generalised linear mixed model was used to examine the associations between maternal physical violence, sexual violence, or emotional violence, and early childhood health outcomes (eg, acute respiratory infection, diarrhoea, undernutrition, and child mortality). A random effects meta-analysis was used to calculate pooled odds ratios (ORs) for adverse childhood health outcomes. The odds of undernutrition and mortality were 55% and 58% higher among children younger than 5 years born to mothers who were exposed to physical and sexual violence, respectively.

Surgery

47. BMJ Global Health 2024;9:e015649
South-to-south collaboration to strengthen the health workforce: the case of paediatric cardiac surgery in Rwanda
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Paediatric cardiovascular diseases have been referred to as diseases of injustice as access to care is inequitable globally. For example, Africa only has 78 cardiac centres, with 22 located in Sub-Saharan Africa. Most of these centres rely on visiting surgical teams to provide clinical care. While visiting surgical teams provide essential care, building a sustainable and locally run cardiac workforce in Africa is critical to addressing these inequities in access to care. This paper considers the role of south-to-south partnerships in building sustainable surgical programmes using Rwanda's paediatric cardiac surgery programme as an example.

48. Lancet Glob Health 2024;12(11):e1807-e1815 Epub 2024 Sep 5
Mechanisms and causes of death after abdominal surgery in low-income and middle-income countries: a secondary analysis of the FALCON trial
NIHR Global Health Research Unit on Global Surgery

Background: Death after surgery is devasting for patients, families, and communities, but remains common in low-income and middle-income countries (LMICs). We aimed to use high-quality data from an existing global randomised trial to describe the causes and mechanisms of postoperative mortality in LMICs. To do so, we developed a novel framework, learning from both existing classification systems and emerging insights during data analysis.
Methods: This study was a preplanned secondary analysis of the FALCON trial in 54 hospitals across seven LMICs (Benin, Ghana, India, Mexico, Nigeria, Rwanda, and South Africa). FALCON was a pragmatic, 2 × 2 factorial, randomised controlled trial that compared the effectiveness of two types of interventions for skin preparation (10% aqueous povidone-iodine vs 2% alcoholic chlorhexidine) and sutures (triclosan-coated vs uncoated). Patients who did not have surgery or were lost to follow-up were excluded (n=231). The primary outcomes of the present analysis were the mechanism and cause of death within 30-days of surgery, determined using a modified verbal autopsy strategy from serious adverse event reports. Factors associated with mortality were explored in a mixed-effects Cox proportional hazards model. The FALCON trial is registered with ClinicalTrials.gov, NCT03700749.
Findings: This preplanned secondary analysis of the FALCON trial included 5558 patients who underwent abdominal surgery, of whom 4248 (76·4%) patients underwent surgery in tertiary, referral centres and 1310 (23·6%) underwent surgery in primary referral (ie, district or rural) hospitals. 3704 (66·7%) of 5558 surgeries were emergent. 306 (5·5%) of 5558 patients died within 30 days of surgery. 226 (74%) of 306 deaths were due to circulatory system failure, which included 173 (57%) deaths from sepsis and 29 (9%) deaths from hypovolaemic shock including bleeding. 47 (15%) deaths were due to respiratory failure. 60 (20%) of 306 patients died without a clear cause of death: 45 (15%) patients died with sepsis of unknown origin and 15 (5%) patients died of an unknown cause. 46 (15%) of 306 patients died within 24 h, 111 (36%) between 24 h and 72 h, 57 (19%) between >72 h and 168 h, and 92 (30%) more than 1 week after surgery. 248 (81%) of 306 patients died in hospital and 58 (19%) patients died out of hospital. The adjusted Cox regression model identified age (hazard ratio 1·01, 95% CI 1·01-1·02; p<0·0001), ASA grade III-V (4·93, 3·45-7·03; p<0·0001), presence of diabetes (1·47, 1·04-2·41; p=0·033), being an ex-smoker (1·59, 1·10-2·30; p=0·013), emergency surgery (2·08, 1·45-2·98; p<0·0001), cancer (1·98, 1·42-2·76; p<0·0001), and major surgery (3·94, 2·30-6·75; p<0·0001) as risk factors for postoperative mortality INTERPRETATION: Circulatory failure leads to most deaths after abdominal surgery, with sepsis accounting for almost two-thirds. Variability in timing of death highlights opportunities to intervene throughout the perioperative pathway, including after

hospital discharge. A high proportion of patients without a clear cause of death reflects the need to improve capacity to rescue and cure by strengthening perioperative systems.

Miscellaneous

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Review
Lead Poisoning
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Key points
Lead exposure among people in the United States has declined by more than 95% since the 1970s, but the body lead burden is still 10 to 100 times as high as the lead burden in humans who lived in preindustrial times.
• Studies conducted over the past 40 years have established that chronic, low-level lead poisoning is a major risk factor for cardiovascular disease in adults and cognitive deficits in children, even at levels previously thought to be safe or innocuous.
• Lead exposure is a risk factor for chronic kidney disease and preterm births at concentrations commonly found in people today.
• In 2019, lead exposure accounted for 5.5 million deaths from cardiovascular disease and an annual loss of 765 million IQ points in children globally.
• The steep decrease in IQ and the sharp increase in the risk of death from cardiovascular disease, even at the lowest measurable blood lead concentrations, coupled with ubiquitous exposure, indicate that population strategies are critical for eliminating lead poisoning.
Estimated Global Burden of Disease.
The global burden of disease from lead exposure is staggering. In contrast to the decline in the rate of coronary heart disease in industrialized countries, the rate has increased over the past 30 years in industrializing countries. One in three children worldwide — more than 600 mil- lion children — have lead poisoning, defined as a blood lead level exceeding 50 μg per liter; 90% of children with lead poisoning live in industrializing countries.
In 2019, a total of 5.5 million deaths from cardiovascular disease were attributed to lead exposure. Every year, lead exposure accounts for a loss of 765 million IQ points in children and 30% of the global burden of idiopathic intellectual disability, defined as an IQ of less than 70. In 2019, the economic cost of reductions in intellectual ability and increases in mortality from cardiovascular causes associated with lead poisoning was $6 trillion, equivalent to 7% of the global gross domestic product. The costs were based on the value of a statistical life (i.e., the economic benefit of avoiding a fatal out- come) with regard to mortality from cardiovascular causes and on future income loss with regard to reduced cognitive ability. Industrialized countries account for more than 90% of deaths from cardiovascular causes and intellectual dis- ability attributed to lead exposure.
Prevention of Lead Poisoning
The steep decrease in IQ and the sharp increase in the risk of death from cardiovascular disease even at the lowest measurable blood lead levels, coupled with ubiquitous exposure, indicate that government-funded population strategies are critical for eliminating lead poisoning. Surveillance to identify highly exposed populations and targeted screening for persons with high levels of exposure are important, but the solution to protecting people from lead poisoning is to identify and eliminate environmental sources of lead, wherever they are found. In the United States, that means eliminating lead acid batteries and secondary lead smelters, replacing lead service lines, banning leaded aviation fuel, reducing lead in foods, abating lead paint in older housing, and further reducing lead-contaminated soil and other legacy sources. Geoffrey Rose, a cardiovascular epidemiologist who died before lead was recognized as a risk factor for coronary heart disease, anticipated the cure: “Where exposure is collective and unavoidable, only collectively enforced control can be effective.”
The lead pandemic — the largest mass poisoning in history — is a humbling reminder that widespread exposure to an ancient metal, rarely found in high concentrations on the surface of the earth before human activity, has resulted in a staggering number of deaths and disabilities. The failure to prevent this century-long pandemic, despite early warnings, exposes an anemic regulatory system ill-suited to

protect the public from industry-orchestrated campaigns and regulatory delays. In 1925, Yandell Henderson warned, “This is probably the greatest single question in the field of public health that has ever faced the American public. It is the question whether scientific experts are to be consulted, and the action of Government guided by their advice; or whether, on the contrary, commercial interests are to be allowed to subordinate every other consideration to that of profit.”