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#### 38. BMJ Global Health

2023;8:e010306. Original research Cost-effectiveness of tuberculosis infection prevention and control interventions in South African clinics: a model-based economic evaluation informed by complexity science methods

# International Health Alerts 2023-2 Abstracts

# Child health and nutrition

# 1. Lancet 2023;401(10371):131-9 Clinical Trial

Evaluation of the safety, immunogenicity, and faecal shedding of novel oral polio vaccine type 2 in healthy newborn infants in Bangladesh: a randomised, controlled, phase 2 clinical trial Zaman K et al., International Centre for Diarrhoeal Disease Research, Chandpur, Bangladesh Background: Type 2 circulating vaccine-derived polioviruses (cVDPV2) from Sabin oral poliovirus vaccines (OPVs) are the leading cause of poliomyelitis. A novel type 2 OPV (nOPV2) has been developed to be more genetically stable with similar tolerability and immunogenicity to that of Sabin type 2 vaccines to mitigate the risk of cVDPV2. We aimed to assess these aspects of nOPV2 in poliovirus vaccine-naive newborn infants.

Methods: In this randomised, double-blind, controlled, phase 2 trial we enrolled newborn infants at the Matlab Health Research Centre, Chandpur, Bangladesh. We included infants who were healthy and were a single birth after at least 37 weeks' gestation. Infants were randomly assigned (2:1) to receive either two doses of nOPV2 or placebo, administered at age 0-3 days and at 4 weeks. Exclusion criteria included receipt of rotavirus or any other poliovirus vaccine, any infection or illness at the time of enrolment (vomiting, diarrhoea, or intolerance to liquids), diagnosis or suspicion of any immunodeficiency disorder in the infant or a close family member, or any contraindication for venipuncture.

The primary safety outcome was safety and tolerability after one and two doses of nOPV2, given 4 weeks apart in poliovirus vaccine-naive newborn infants and the primary immunogenicity outcome was the seroconversion rate for neutralising antibodies against type 2 poliovirus, measured 28 days after the first and second vaccinations with nOPV2. Study staff recorded solicited and unsolicited adverse events after each dose during daily home visits for 7 days. Poliovirus neutralising antibody responses were measured in sera drawn at birth and at age 4 weeks and 8 weeks. This study is registered on ClinicalTrials.gov, NCT04693286.

Findings: Between Sept 21, 2020, and Aug 16, 2021, we screened 334 newborn infants, of whom three (<1%) were found to be ineligible and one (<1%) was withdrawn by the parents; the remaining 330 (99%) infants were assigned to receive nOPV2 (n=220 [67%]) or placebo (n=110 [33%]). nOPV2 was well tolerated; 154 (70%) of 220 newborn infants in the nOPV2 group and 78 (71%) of 110 in the placebo group had solicited adverse events, which were all mild or moderate in severity. Severe unsolicited adverse events in 11 (5%) vaccine recipients and five (5%) placebo recipients were considered unrelated to vaccination. 306 (93%) of 330 infants had seroprotective maternal antibodies against type 2 poliovirus at birth, decreasing to 58 (56%) of 104 in the placebo group at 8 weeks. In the nOPV2 group 196 (90%) of 217 infants seroconverted by week 8 after two doses, when 214 (99%) had seroprotective antibodies.

Interpretation: nOPV2 was well tolerated and immunogenic in newborn infants, with two doses, at birth and 4 weeks, resulting in almost 99% of infants having protective neutralising antibodies.

## 2. PLoS Med 20(1): e1004166. (2023)

Essential childhood immunization in 43 low- and middle-income countries: Analysis of spatial trends and socioeconomic inequalities in vaccine coverage Anna Dimitrova, et al. Corresponding author : Scripps Institution of Oceanography, University of California, San Diego, California, USA, Mail: adimitrova@ucsd.edu

Background

Globally, access to life-saving vaccines has improved considerably in the past 5 decades. However, progress has started to slow down and even reverse in recent years. Understanding subnational heterogeneities in essential child immunization will be critical for closing the global vaccination gap. Methods and findings

We use vaccination information for over 220,000 children across 1,366 administrative regions in 43 low- and middle-income countries (LMICs) from the most recent Demographic and Health Surveys. We estimate essential immunization coverage at the national and subnational levels and quantify socioeconomic inequalities in such coverage using adjusted concentration indices. Within- and between-country variations are summarized via the Theil index. We use local indicator of spatial association (LISA) statistics to identify clusters of administrative regions with high or low values. Finally, we estimate the number of missed vaccinations among children aged 15 to 35 months across all 43 countries and the types of vaccines most often missed. We show that national-level vaccination rates can conceal wide subnational heterogeneities. Large gaps in child immunization are found across West and Central Africa and in South Asia, particularly in regions of Angola, Chad, Nigeria, Guinea, and Afghanistan, where less than 10% of children are fully immunized. Furthermore, children living in these countries consistently lack all 4 basic vaccines included in the WHO's recommended schedule for young children. Across most countries, children from poorer households are less likely to be fully immunized. The main limitations include subnational estimates based on large administrative divisions for some countries and different periods of survey data collection. Conclusions

The identified heterogeneities in essential childhood immunization, especially given that some regions consistently are underserved for all basic vaccines, can be used to inform the design and implementation of localized intervention programs aimed at eliminating child suffering and deaths from existing and novel vaccine-preventable diseases.

3. Bull World Health Organ. 2023 Mar 1; 101(3): 226–228.

Perspectives: Healthy weight in childhood

Oliver Huse, et al. Correspondence to Fiona Watson (email: fwatson@unicef.org). Abridged

Nearly one fifth of the world's children are experiencing overweight or obesity – that is, an estimated 39 million children younger than five years and 340 million children aged 5–19 years. The toll of unhealthy diets and overweight in terms of health, social and financial costs are significant, representing almost an estimated 3% of global gross domestic product – a similar economic impact to that of smoking or armed violence, war and terrorism.

Many governments in low- and middle-income countries continue to grapple with undernutrition and micronutrient deficiencies in addition to sharp increases in overweight among children. This triple burden of malnutrition has intensified as these countries face new challenges including the aftermath of the coronavirus disease 2019 pandemic, climate change and global economic recession. One consequence has been a substantial rise in the price of fresh foods which, combined with increased sales and marketing of ultra-processed foods, are driving all forms of malnutrition including overweight. Ultra-processed foods are those that contain little or no whole food, are palatable, energy-dense and low in essential nutrients, such as snacks and ready meals.

A set of promising food policies are showing positive impact in reducing the purchase and consumption of ultra-processed foods in some high- and middle-income countries, and are recommended as part of a suite of measures to address overweight and obesity by the World Health Organization (WHO). The most effective measures include the restriction of children's exposure to the marketing of food and non-alcoholic beverages based on robust nutrient profiling schemes that clearly define healthier and less healthy foods and beverages. Measures also include fiscal policies such as taxes and industry levies directed at snack foods and sugar-sweetened beverages, mandatory front of package warning labels and improving school food environments. The World Health Assembly recently endorsed a Global Acceleration Plan to Stop Obesity designed to scale up action and demonstrate impact in a set of frontrunner countries.

The United Nations Children's Fund (UNICEF) included these key policies on prevention of childhood overweight in its Strategic Plan 2018–2021, and has developed programming guidance for its regional and country offices to scale up work and support global norms and guidelines. Subsequently, the prevention of overweight was highlighted as a priority in the UNICEF Nutrition Strategy 2020–2030. United Nations agencies, including UNICEF, are important partners to national governments in designing response strategies.

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Here we bring the experience of UNICEF in stimulating government response to the growing challenge of overweight among children in low- and middle-income countries through the application of a landscape analysis tool. UNICEF in consultation with WHO developed this tool, which has been piloted in nine countries (China, Costa Rica, India, Indonesia, Mongolia, Peru, Philippines, United Republic of Tanzania and Viet Nam). The tool is designed to capture a comprehensive picture of childhood overweight and obesity by describing prevalence and trends, analysing key risk factors in early and later childhood, and assessing policies and programmes to address overweight and obesity.

# Supporting governments to act

The overall purpose of the landscape analysis is to prioritize feasible policy actions that consider the rising prevalence of overweight as well as the existing challenges of undernutrition and micronutrient deficiencies. The landscape analysis tool encourages users to consider the existence and coverage of policy and programme approaches to tackle all forms of malnutrition. Such double-duty approaches require a broad systems approach with a focus on early prevention and addressing the availability, affordability, acceptability and appeal of nutritious diets for women and children, as well as a focus on access to quality nutrition services and optimal caregiver practices.

However, additional influences that increase the risk of weight gain in children exist, and they might not be addressed in the double-duty policy approach. Examples include access to safe and attractive facilities for physical activity, and reducing time spent in sedentary behaviour. Furthermore, the tool encourages users to consider the wide range of commercial and political factors, especially linked to the products, policies and practices of the food and beverage industry, that strongly influence the drivers of obesity, the public discourse around overweight, as well as the policy and programmatic decision-making process in low- and middle-income countries related to food policies. The landscape analysis tool can help to harness political will and facilitate consensus on feasible priorities for action to address overweight and obesity.

# 4. Lancet 2023;401(10375):409 Editorial

Unveiling the predatory tactics of the formula milk industry

For decades, the commercial milk formula (CMF) industry has used underhand marketing strategies, designed to prey on parents' fears and concerns at a vulnerable time, to turn the feeding of young children into a multibillion- dollar business. The immense economic power accrued by CMF manufacturers is deployed politically to ensure the industry is under-regulated and services supporting breastfeeding are under-resourced. These are the stark findings of the 2023 Breastfeeding Series, published in The Lancet today.

The three-paper Series outlines how typical infant behaviours such as crying, fussiness, and poor nighttime sleep are portrayed by the CMF industry as pathological and framed as reasons to introduce formula, when in fact these behaviours are common and developmentally appropriate. However, manufacturers claim their products can alleviate discomfort or improve night-time sleep, and also infer that formula can enhance brain development and improve intelligence—all of which are unsubstantiated. Infant feeding is further commodified by cross-promotion of infant, follow-on, toddler, and growing-up milks using the same branding and numbered progression, which aims to build brand loyalty and is a blatant attempt to circumvent legislation that prohibits advertising of infant formula.

Breastfeeding has proven health benefits across high-income and low-income settings alike: it reduces childhood infectious diseases, mortality, and malnutrition, and the risk of later obesity; mothers who

breastfeed have decreased risk of breast and ovarian cancers, type 2 diabetes, and cardiovascular disease. However, less than 50% of babies worldwide are breastfed according to WHO recommendations, resulting in economic losses of nearly US\$350 billion each year. Meanwhile, the CMF industry generates revenues of about \$55 billion annually, with about \$3 billion spent on marketing activities every year.

The industry's dubious marketing practices are compounded by lobbying, often covertly via trade associations and front groups, against strengthening breastfeeding protection laws and challenging food standard regulations. In 1981, the World Health Assembly adopted the International Code of Marketing of Breast-milk Substitutes, a set of standards to prevent inappropriate marketing of formula. It includes prohibition of advertising of CMF to the public or promotion within health-care systems; banning provision of free samples to mothers, health-care workers, and health facilities; no promotion of formula within health services; and no sponsorship of health professionals or scientific meetings by the CMF industry. However, despite repeated calls for governments to incorporate the Code's recommendations into legislation, only 32 countries have legal measures that substantially align with the Code. A further 41 countries have legislation that moderately aligns with the Code and 50 have no legal measures at all. As a result, the Code is regularly flouted without penalty.

The prioritisation of trade interests over health was brought to the forefront in 2018, when US officials threatened to enforce trade sanctions and withdraw military aid to Ecuador unless it dropped a proposed resolution at the World Health Assembly to protect and promote breastfeeding. Some CMF lobby groups have cautioned against improved parental leave. Duration of paid maternity leave is correlated with breastfeeding prevalence and duration, and absence of, or inadequate, paid leave forces many mothers to return to work soon after childbirth. Lack of safe spaces for breastfeeding or expressing milk in workplaces, or facilities to store breastmilk, mean that breastfeeding is not a viable option for many women.

Some women choose not to breastfeed, or are unable to. Perceived pressure, or inability, to breastfeed— especially if it is at odds with a mother's wishes—can have a detrimental effect on mental health, and systems should be in place to fully support all mothers in their choices. Women and families make decisions about infant feeding based on the information they receive, and a criticism of the CMF industry's predatory marketing practices should not be interpreted as a criticism of women. All information that families receive on infant feeding must be accurate and independent of industry influence to ensure informed decision making. Marketing by the CMF industry is an interconnected, multifaceted, powerful system that knowingly exploits parents' aspirations. Under the Convention of the Rights of the Child, governments have a duty to tackle misinformation—and governments need to embrace the breastfeeding Code without further delay to ensure that manufacturers making misleading claims about their products are held to account.

Read also the next articles:

#### Lancet 2023;401(10375):472-85 Review

Breastfeeding: crucially important, but increasingly challenged in a market-driven world Pérez-Escamilla R et al., Department of Social and Behavioral Sciences, Yale School of Public Health, Yale University, New Haven, CT, USA <u>rafael.perez-escamilla@yale.edu</u>

#### Lancet 2023;401(10375):486-502 Review

Marketing of commercial milk formula: a system to capture parents, communities, science, and policy Rollins N et al.,

#### Lancet 2023;401(10375):503-24 Review

The political economy of infant and young child feeding: confronting corporate power, overcoming structural barriers, and accelerating progress Baker P et al.,

BMJ 2023;380:e071075 Research

Health and nutrition claims for infant formula: international cross sectional survey Ka Yan Cheung,

5. BMJ Global Health 2023;8:e010745. Original research

Oral iron supplementation and anaemia in children according to schedule, duration, dose and cosupplementation: a systematic review and meta-analysis of 129 randomised trials Andersen CT, Marsden DM, Duggan CP, et al

Correspondence to Dr Christopher T Andersen; chrisandersen@mail.harvard.edu Abstract

Introduction WHO guidelines on iron supplementation among children call for further research to identify the optimal schedule, duration, dose and cosupplementation regimen.

Methods A systematic review and meta-analysis of randomised controlled trials was undertaken. Randomised controlled trials providing ≥30 days of oral iron supplementation versus placebo or control to children and adolescents aged <20 years were eligible. Random-effects meta-analysis was used to summarise the potential benefits and harms of iron supplementation. Meta-regression was used to estimate iron effect heterogeneity.

Results 129 trials with 201 intervention arms randomised 34564 children. Frequent (3–7/week) and intermittent (1–2/week) iron regimens were similarly effective at decreasing anaemia, iron deficiency and iron deficiency anaemia (p heterogeneity >0.05), although serum ferritin levels and (after adjustment for baseline anaemia) haemoglobin levels increased more with frequent supplementation. Shorter (1–3 months) versus longer (7+ months) durations of supplementation generally showed similar benefits after controlling for baseline anaemia status, except for ferritin which increased more with longer duration of supplementation (p=0.04). Moderate-dose and high-dose supplements were more effective than low-dose supplements at improving haemoglobin (p=0.004), ferritin (p=0.008) and iron deficiency anaemia (p=0.02), but had similar effects to low-dose supplements for overall anaemia. Iron supplementation provided similar benefits when administered alone or in combination with zinc or vitamin A, except for an attenuated effect on overall anaemia when iron was cosupplemented with zinc (p=0.048).

Conclusions Weekly and shorter duration iron supplementation at moderate or high doses might be optimal approaches for children and adolescents at risk of deficiency.

## Communicable diseases

6. Lancet 2023;401(10373):259-60 World Report

"Unfettered flow": how ProMED-mail keeps the world alert Burki T.

The story of how Programme for Monitoring Emerging Diseases (ProMED)-mail alerted the world to the emergence of severe acute respiratory syndrome (SARS) has attained something like folklore status in global health circles. An infectious disease specialist in Maryland, USA, forwarded an email from someone who had heard rumours of unusual goings-on in China. The ProMED moderator responded as ProMED moderators usually do when they receive unverified reports of disease outbreaks. They issued a request for information to the thousands of researchers, health-care workers, veterinarians, public health officials, journalists, and members of the public who subscribe to ProMED-mail. Within 24 hours, officials from Guangdong province, for which Guangzhou is the capital, publicly acknowledged for the first time 305 cases of the atypical pneumonia that became known as SARS. The ensuing epidemic infected more than 8000 people around the world and killed 774. It was precisely the kind of scenario that Jack Woodall, Stephen Morse, and Barbara Hatch Rosenberg had in mind when they founded ProMED in 1994. SARS-CoV was a new virus spreading in human populations, yet it was not being publicised by local, national, or international authorities. It was not

until after the ProMED-mail post that WHO received its first notification of the outbreak from the Chinese Ministry of Health.

ProMED employs dozens of subject matter experts from around the world. These are specialists in fields such as virology, parasitology, epidemiology, entomology, and veterinary and plant diseases who are paid a stipend and act as moderators, screening and commenting upon reports submitted to ProMED. They also track disease outbreaks using social media and the internet, news reports, press releases, and government statements.

As ProMED approaches its 30th anniversary, the prospects for its future are uncertain. Although it only costs around US\$1 million per year to run, it has always struggled to obtain funding. Donor organisations can be reluctant to pay for salaries, stipends, and recurring costs such as those associated with informational technology, though these are the largest expense for ProMED.

7. Lancet 2023;401(10381):1039-52 Review

# Hepatitis B

Jeng WJet al., Department of Gastroenterology and Hepatology, Linkou Medical Center, Chang Gung Memorial Hospital, Taoyuan, Taiwan; College of Medicine, Chang Gung University, Taoyuan, Taiwan Hepatitis B virus (HBV) infection is a major public health problem, with an estimated 296 million people chronically infected and 820 000 deaths worldwide in 2019. Diagnosis of HBV infection requires serological testing for HBsAg and for acute infection additional testing for IgM hepatitis B core antibody (IgM anti-HBc, for the window period when neither HBsAg nor anti-HBs is detected). Assessment of HBV replication status to guide treatment decisions involves testing for HBV DNA, whereas assessment of liver disease activity and staging is mainly based on aminotransferases, platelet count, and elastography. Universal infant immunisation, including birth dose vaccination is the most effective means to prevent chronic HBV infection. Two vaccines with improved immunogenicity have recently been approved for adults in the USA and EU, with availability expected to expand. Current therapies, pegylated interferon, and nucleos(t)ide analogues can prevent development of cirrhosis and hepatocellular carcinoma, but do not eradicate the virus and rarely clear HBsAg. Treatment is recommended for patients with cirrhosis or with high HBV DNA levels and active or advanced liver disease. New antiviral and immunomodulatory therapies aiming to achieve functional cure (ie, clearance of HBsAg) are in clinical development. Improved vaccination coverage, increased screening, diagnosis and linkage to care, development of curative therapies, and removal of stigma are important in achieving WHO's goal of eliminating HBV infection by 2030.

# 8. BMJ 2023;380:p92 Feature BMJ Annual Appeal

The BMJ Appeal 2022-23: How safe burial helped end the 2022 Ebola epidemic Jane Feinmann, freelance journalist jane@janefeinmann.com Last year's Ebola epidemic in east Africa is over, in part thanks to a traditional burial process that keeps communities safe while allowing them to say goodbye in an acceptable way. Jane Feinmann reports The latest outbreak of Ebola virus disease, reported in nine districts of Uganda in September 2022, was declared officially over by the country's Ministry of Health on 11 January. A total of 142 cases and 55 deaths have been reported, contrasting with the 11000 deaths during the world's deadliest Ebola epidemic from 2014 to 2016.

The lessons learnt from the 2014-2016 epidemic in west Africa allowed the International Federation of Red Cross and Red Crescent Societies (IFRC) to develop community centred and culturally adapted public health responses that allow families to mourn their dying loved ones and say goodbye in what they regard as an acceptable way while keeping them safe from infection.

"Throughout west Africa there's a tradition of relatives washing and cleaning the body of the deceased and then using that water to cleanse their hands to signify unity," says Bronwyn Nichol.

9. BMJ 2023;380:p141 Opinion

Cholera is back but the world is looking away Petra Khoury, director of the Health and Care department To overcome this preventable disease we need to invest in failing infrastructure and tackle humanitarian crises at cholera's roots, says Petra Khoury

Once thought to be close to eradication, cholera is back—dehydrating and killing people within hours and ravaging communities across six continents. Despite the alarming numbers of cases and deaths over the past year, decision makers are averting their eyes, leaving people to die from a preventable and treatable disease.

The healthcare community should sound the alarm for immediate actions. A strong and global emergency response is urgently needed, but it is only a first step. More than ever the world must invest in water and sanitation systems and prepare communities before outbreaks occur.

Over the past 200 years, there have been seven cholera pandemics, and today's surge is the largest in a decade. In 2022, 30 countries reported cholera outbreaks, including places that had been free of the disease for decades. In Haiti, where millions of people have been displaced by violence, cholera has killed hundreds of people in just a few months. Lebanon is experiencing its first outbreak since 1993, with more than 6000 recorded cases. After devastating floods, Nigeria had a major cholera outbreak. In Malawi, the worst outbreak in decades has left 620 people dead since March. Schools are now closed in an attempt to stop the surge of infections.

The risk of cholera transmission multiplies when people live in poor or overcrowded conditions and lack access to safe water, proper sanitation, and hygiene facilities. A diarrhoeal disease caused by the Vibrio cholerae bacteria, cholera is commonly spread through contaminated food or water. Left untreated, it can cause severe dehydration and be deadly within hours.

Almost half of the world's population—approximately 3.6 billion people—live without safely managed sanitation in their home, leaving them vulnerable to cholera outbreaks. The World Health Organization reports that at least two billion people consume water from sources contaminated with faeces.

Read also:

BMJ 2023;380:p636 Feature Vaccines Cholera makes a comeback amid calls to boost vaccine production Jane Feinmann, freelance journalist jane@janefeinmann.com

## Covid-19

10. Lancet 2023;401(10371):154-68 Review

Human rights and the COVID-19 pandemic: a retrospective and prospective analysis Gostin LO et al., O'Neill Institute for National and Global Health Law, Georgetown University Law Center, Washington, DC, USA <gostin@law.georgetown.edu>

When the history of the COVID-19 pandemic is written, the failure of many states to live up to their human rights obligations should be a central narrative. The pandemic began with Wuhan officials in China suppressing information, silencing whistleblowers, and violating the freedom of expression and the right to health. Since then, COVID-19's effects have been profoundly unequal, both nationally and globally. These inequalities have emphatically highlighted how far countries are from meeting the supreme human rights command of non-discrimination, from achieving the highest attainable standard of health that is equally the right of all people everywhere, and from taking the human rights obligation of international assistance and cooperation seriously. We propose embedding human rights and equity within a transformed global health architecture as the necessary response to COVID-19's rights violations. This means vastly more funding from high-income countries to support low-income and middle-income countries in rights-based recoveries, plus implementing measures to ensure equitable distribution of COVID-19 medical technologies. We also emphasise structured approaches to funding and equitable distribution going forward, which includes embedding human rights into a new pandemic treaty. Above all, new legal instruments and mechanisms, from a right to health treaty to a fund for civil society right to health advocacy, are required so that the narratives of future health emergencies-and people's daily lives-are ones of equality and human rights.

### Health Policy

11. Bull World Health Organ. 2023 Apr 1; 101(4): 290–296.

The WHO AWaRe (Access, Watch, Reserve) antibiotic book and prevention of antimicrobial resistance Veronica Zanichelli, et al. Correspondence to Benedikt Huttner (email: bhuttner@who.int). Abstract

Guidance on the appropriate use of antibiotics for common infections is lacking in many settings. The World Health Organization (WHO) has recently released The WHO AWaRe (Access, Watch, Reserve) antibiotic book which complements the WHO Model list of essential medicines and WHO Model list of essential medicines for children. The book gives specific guidance on the empiric use of antibiotics in the model lists with a strong emphasis on the AWaRe framework, which is centred around the risk of antimicrobial resistance development associated with the use of different antibiotics.

Recommendations in the book cover 34 common infections in primary and hospital care both for children and adults. The book also includes a section on the use of the last-resort Reserve antibiotics, whose use should be restricted to very selected cases when an infection is confirmed or suspected to be caused by multidrug-resistant pathogens. The book highlights the use of first-line Access antibiotics or no antibiotic care if this is the safest approach for the patient. Here we present the background behind the development of the AWaRe book and the evidence behind its recommendations. We also outline how the book could be used in different settings to help reach the WHO target of increasing the proportion of global consumption of Access antibiotics to at least 60% of total consumption. The guidance in the book will also more broadly contribute to improving universal health coverage.

#### 12. BMJ 2023;380:p392 Editorials

The WHO Foundation and conflicts of interest

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Scrap the new foundation and strengthen WHO policies on taking private sector donations In 2021, the World Health Organization Foundation accepted a \$2.2m donation from the multinational food and drink company Nestlé to support WHO's Covid-19 Solidarity Response Fund. This caused controversy, given Nestlé's non-compliance with the International Code of Marketing of Breastmilk Substitutes. In response, the foundation redirected the donation to its own "Go Give One" vaccine campaign and announced that it would no longer accept donations from Nestlé.

WHO has a funding problem: it faces a shortfall of more than \$660m in the two years 2022-23. Only 16% of its budget is covered by member states' regular contributions. The rest is covered by voluntary donations from member states, other UN bodies, and private philanthropic organisations. These are often short term and earmarked for specific projects. Reliance on voluntary donations exposes WHO to the undue influence of contributors, impedes strategic planning, and leads to shortfalls and inflexibility.

## 13. BMJ 2023;380:p463 Editorials

The World Health Organization's pandemic treaty

Alexandra L Phelan, associate professor and senior scholar aphelan4@jhu.edu

Global equity underpins the first draft and must remain a key priority

The covid-19 pandemic showed that gross inequities in population morbidity, mortality, and access to medicines persist between nations, reflecting the colonial histories and current political status of international governance. These patterns of inequity emerge directly from colonialism's racism, violence, resource extraction, and exploitation. It is therefore welcome that "equity" underpins the World Health Organization's call to action to its member states, as they negotiate a new international instrument to advance collective action for pandemic prevention, preparedness, and response—the pandemic treaty. The treaty aims to create legally binding obligations between countries and to

establish new global mechanisms for pandemics under the auspices of WHO. On 1 February 2023, WHO released a Zero Draft of the Pandemic Treaty for its member states' consideration at the meetings of the intergovernmental negotiating body in February and April 2023. Read also:

BMJ Global Health 2023;8:e011431. Analysis

The Pandemic Treaty, the Pandemic Fund, and the Global Commons: our scepticism Evaborhene NA, Udokanma EE, Adebisi YA, et al

14. BMJ global health 2023;8:e011310. commentary

Strengthening capacity through competency-based education and training to deliver the essential public health functions: reflection on roadmap to build public health workforce

Hunter MB, Ogunlayi F, Middleton J, et al

Correspondence to Fatai Ogunlayi; fatai.ogunlayi@nhs.net Background

More than two years on from WHO's declaration of a pandemic, COVID-19 continues to expose the weaknesses in health systems and public health responses worldwide. It has highlighted the need for improved global health governance and for investment in more resilient public health systems. As the world recovers from the multisectoral impact of the pandemic, the inter-relationship between health and its social, environmental, political and economic determinants has never been more apparent. Public health requires collaboration with a diverse group of professions across health and allied sectors. While sound public health leadership can unify and guide health protection and improvement, effective public health is not the exclusive preserve of any one professional group. Multisectoral and interdisciplinary collaboration and core public health competencies are required to address the wider determinants of health and promote effective health systems.

COVID-19 pandemic has highlighted the need for improved global governance and investment in resilient public health systems.

Effective public health is not the exclusive preserve of any one professional group but requires multisectoral and interdisciplinary collaboration across a broad range of occupations.

WHO and partner organisations have published a roadmap; a five-year strategy to strengthen capacity across all countries for a multidisciplinary workforce to undertake the essential public health functions, including emergency preparedness and response.

A key action area within the roadmap is the use of competency-based education as an approach to developing the skills and abilities of diverse multidisciplinary teams, with the collective capability to deliver on the essential public health functions.

Inclusion of early career professionals in decisions about education and health policy will encourage intergenerational collaboration, bidirectional learning and serves to ensure that the future workforce has agency and is well equipped to deal with evolving health system challenges.

# 15. BMJ Global Health 2023;8:e011263. Commentary

One Health WASH: an AMR-smart integrative approach to preventing and controlling infection in farming communities

Pinto Jimenez CE, Keestra SM, Tandon P, et al

Introduction

Prevention is a critical, yet neglected, cornerstone for the response to antimicrobial resistance (AMR). The importance of a multitude of preventative measures is recognised across the One Health spectrum, with attention drawn to the issue by multilateral institutions. The 2022 World Antimicrobial Awareness Week saw the World Health Organization, the Food and Agriculture Organization, the United Nations Environment Programme and the World Organisation for Animal Health focused their campaign on the theme 'Preventing AMR together' to improve awareness and understanding of AMR and encourage best practices. While a One Health framework is now promoted for conceptualising the complex problem of AMR, the evidence base of interventions designed within this rubric is thin. Outstanding questions remain, for example, about how best to prevent and control infection across humans, animals, and the environment.

In public health, measures such as hygiene practices, biosecurity, vaccinations and other means to strengthen immunity, are commonly used to prevent and control infections. Highlighting the potential contribution of such measures to reducing AMR, the World Bank introduced the terms 'AMR-sensitive' and 'AMR-specific' to describe interventions that indirectly or directly contribute to reducing AMR, respectively. For example, measures to reduce the burden of infections in human health, such as water, sanitation, and hygiene (WASH), are recognised as essential to support AMR strategies due to their potential to indirectly combat AMR and produce co-benefits. Thus, investments in these interventions would be 'AMR-Smart.'

# Summary box

While the One Health framework is now widely accepted as a strength in understanding antimicrobial resistance (AMR), its application in intervention design to prevent and control drug-resistant infections across humans, animals, and the environment remains weak.

The potential for infection prevention and control measures to contribute to the AMR agenda is recognised in rhetoric, but evidence to guide action is patchy and uncoordinated.

While water, sanitation, and hygiene (WASH) and on-farm biosecurity interventions are key strategies for preventing and controlling infections, they are frequently implemented separately for humans and animals. We argue for integration across these sectors to improve planning for AMR control.

## 16. BMJ Global Health 2023;8:e011028. Practice

What does equitable global health research and delivery look like? Tackling Infections to Benefit Africa (TIBA) partnership as a case study

Mutapi F, Banda G, Woolhouse M

## Abstract

There is a current global push to identify and implement best practice for delivering maximum impact from development research in low-income and middle-income countries. Here, we describe a model of research and capacity building that challenges traditional approaches taken by western funders in Africa. Tackling Infections to Benefit Africa (TIBA) is a global health research and delivery partnership with a focus on strengthening health systems to combat neglected tropical diseases, malaria and emerging pathogens in Africa. Partners are academic and research institutions based in Ghana, Sudan, Rwanda, Uganda, Kenya, Tanzania, Zimbabwe, Botswana, South Africa and the UK. Fifteen other African countries have participated in TIBA activities. With a starting budget of under £7 million, and in just 4 years, TIBA has had a verified impact on knowledge, policy practice and capacity building, and on national and international COVID-19 responses in multiple African countries. TIBA's impact is shown in context-specific metrics including: strengthening the evidence base underpinning international policy on neglected tropical diseases; 77% of research publications having Africa-based first and/or last authors; postgraduate, postdoctoral and professional training; career progression for African researchers and health professionals with no net brain drain from participating countries; and supporting African institutions. Training in real-time SARS-CoV-2 viral genome sequencing provided new national capabilities and capacities that contributed to both national responses and global health security through variant detection and tracking. TIBA's experience confirms that health research for Africa thrives when the agenda and priorities are set in Africa, by Africans, and the work is done in Africa. Here, we share 10 actionable recommendations for researchers and funders from our lessons learnt.

## 17. BMJ Global Health 2023;8:e011097. Original research

Is it possible for drug shops to abide by the formal rules? The structural determinants of community medicine sales in Uganda Hutchinson E, Hansen KS, Sanyu J, et al Correspondence to Dr Eleanor Hutchinson; eleanor.hutchinson@lshtm.ac.uk Abstract The medicines retail sector is an essential element of many health systems in Africa and Asia, but it is also well known for poor practice. In the literature, it is recognised that improvements in the sector can only be made if more effective forms of governance and regulation can be identified. Recent debate suggests that interventions responsive to structural constraints that shape and underpin poor practice is a useful way forward. This paper presents data from a mixed-methods study conducted to explore regulation and the professional, economic and social constraints that shape rule breaking among drug shops in one district in Uganda. Our findings show that regulatory systems are undermined by frequent informal payments, and that although drug shops are often run by qualified staff, many are unlicensed and sell medicines beyond their legal permits. Most shops have either a small profit or a loss and rely on family and friends for additional resources as they compete in a highly saturated market. We argue that in the current context, drug shop vendors are survivalist entrepreneurs operating in a market in which it is extremely difficult to abide by policy, remain profitable and provide a service to the community. Structural changes in the medicines market, including removing unqualified sellers and making adjustments to policy are likely prerequisite if drug shops are to become places where individuals can earn a living, abide by the rules and facilitate access to medicines for people living in some of the world's poorest countries.

#### HIV/AIDS

## 18. PLoS Med 20(2): e1004088. (2023)

High PrEP uptake and objective longitudinal adherence among HIV-exposed women with personal or partner plans for pregnancy in rural Uganda: A cohort study.

Matthews LT, et al. Corresponding author: Division of Infectious Diseases, University of Alabama at Birmingham, USA. Mail: lynnmatthews@uabmc.edu

#### Background

In Uganda, fertility rates and adult HIV prevalence are high, and many women conceive with partners living with HIV. Pre-exposure prophylaxis (PrEP) reduces HIV acquisition for women and, therefore, infants. We developed the Healthy Families-PrEP intervention to support PrEP use as part of HIV prevention during periconception and pregnancy periods. We conducted a longitudinal cohort study to evaluate oral PrEP use among women participating in the intervention. Methods and findings

We enrolled HIV-negative women with plans for pregnancy with a partner living, or thought to be living, with HIV (2017 to 2020) to evaluate PrEP use among women participating in the Healthy Families-PrEP intervention. Quarterly study visits through 9 months included HIV and pregnancy testing and HIV prevention counseling. PrEP was provided in electronic pillboxes, providing the primary adherence measure ("high" adherence when pillbox was opened ≥80% of days). Enrollment questionnaires assessed factors associated with PrEP use. Plasma tenofovir (TFV) and intraerythrocytic TFV-diphosphate (TFV-DP) concentrations were determined quarterly for women who acquired HIV and a randomly selected subset of those who did not; concentrations TFV  $\geq$ 40 ng/mL and TFV-DP  $\geq$ 600 fmol/punch were categorized as "high." Women who became pregnant were initially exited from the cohort by design; from March 2019, women with incident pregnancy remained in the study with quarterly follow-up until pregnancy outcome. Primary outcomes included (1) PrEP uptake (proportion who initiated PrEP); and (2) PrEP adherence (proportion of days with pillbox openings during the first 3 months following PrEP initiation). We used univariable and multivariable-adjusted linear regression to evaluate baseline predictors selected based on our conceptual framework of mean adherence over 3 months. We also assessed mean monthly adherence over 9 months of follow-up and during pregnancy. We enrolled 131 women with mean age 28.7 years (95% CI: 27.8 to 29.5). Ninety-seven (74%) reported a partner with HIV and 79 (60%) reported condomless sex. Most women (N = 118; 90%) initiated PrEP. Mean electronic adherence during the 3 months following initiation was 87% (95% CI: 83%, 90%). No

covariates were associated with 3-month pill-taking behavior. Concentrations of plasma TFV and TFV-DP were high among 66% and 47%, 56% and 41%, and 45% and 45% at months 3, 6, and 9, respectively. We observed 53 pregnancies among 131 women (1-year cumulative incidence 53% [95% CI: 43%, 62%]) and 1 HIV-seroconversion in a non-pregnant woman. Mean pillcap adherence for PrEP users with pregnancy follow-up (N = 17) was 98% (95% CI: 97%, 99%). Study design limitations include lack of a control group.

## Conclusions

Women in Uganda with PrEP indications and planning for pregnancy chose to use PrEP. By electronic pillcap, most were able to sustain high adherence to daily oral PrEP prior to and during pregnancy. Differences in adherence measures highlight challenges with adherence assessment; serial measures of TFV-DP in whole blood suggest 41% to 47% of women took sufficient periconception PrEP to prevent HIV. These data suggest that women planning for and with pregnancy should be prioritized for PrEP implementation, particularly in settings with high fertility rates and generalized HIV epidemics. Future iterations of this work should compare the outcomes to current standard of care.

#### Malaria

#### 19. Lancet 2023;401(10375):435-46

Efficacy of pyriproxyfen-pyrethroid long-lasting insecticidal nets (LLINs) and chlorfenapyr-pyrethroid LLINs compared with pyrethroid-only LLINs for malaria control in Benin: a cluster-randomised, superiority trial

Accrombessi M et al., Faculty of Infectious and Tropical Diseases, Disease Control Department, London School of Hygiene & Tropical Medicine, London, UK <manfred.accrombessi@lshtm.ac.uk> Background: New classes of long-lasting insecticidal nets (LLINs) combining mixtures of insecticides with different modes of action could put malaria control back on track after rebounds in transmission across sub-Saharan Africa. We evaluated the relative efficacy of pyriproxyfen-pyrethroid LLINs and chlorfenapyr-pyrethroid LLINs compared with standard LLINs against malaria transmission in an area of high pyrethroid resistance in Benin.

Methods: We conducted a cluster-randomised, superiority trial in Zou Department, Benin. Clusters were villages or groups of villages with a minimum of 100 houses. We used restricted randomisation to randomly assign 60 clusters to one of three LLIN groups (1:1:1): to receive nets containing either pyriproxyfen and alpha-cypermethrin (pyrethroid), chlorfenapyr and alpha-cypermethrin, or alpha-cypermethrin only (reference). Households received one LLIN for every two people. The field team, laboratory staff, analyses team, and community members were masked to the group allocation. The primary outcome was malaria case incidence measured over 2 years after net distribution in a cohort of children aged 6 months-10 years, in the intention-to-treat population. This study is ongoing and is registered with ClinicalTrials.gov, NCT03931473.

Findings: Between May 23 and June 24, 2019, 53 854 households and 216 289 inhabitants were accounted for in the initial census and included in the study. Between March 19 and 22, 2020, 115 323 LLINs were distributed to 54 030 households in an updated census. A cross-sectional survey showed that study LLIN usage was highest at 9 months after distribution (5532 [76·8%] of 7206 participants), but decreased by 24 months (4032 [60·6%] of 6654). Mean malaria incidence over 2 years after LLIN distribution was 1·03 cases per child-year (95% CI 0·96-1·09) in the pyrethroid-only LLIN reference group, 0·84 cases per child-year (0·78-0·90) in the pyriproxyfen-pyrethroid LLIN group (hazard ratio [HR] 0·86, 95% CI 0·65-1·14; p=0·28), and 0·56 cases per child-year (0·51-0·61) in the chlorfenapyr-pyrethroid LLIN group (HR 0·54, 95% CI 0·42-0·70; p<0·0001).

Interpretation: Over 2 years, chlorfenapyr-pyrethroid LLINs provided greater protection from malaria than pyrethroid-only LLINs in an area with pyrethroid-resistant mosquitoes. Pyriproxyfen-pyrethroid LLINs conferred protection similar to pyrethroid-only LLINs. These findings provide crucial second-trial evidence to enable WHO to make policy recommendations on these new LLIN classes. This study confirms the importance of chlorfenapyr as an LLIN treatment to control malaria in areas with

pyrethroid-resistant vectors. However, an arsenal of new active ingredients is required for successful long-term resistance management, and additional innovations, including pyriproxyfen, need to be further investigated for effective vector control strategies.

# 20. PLoS Med 20(2): e1004189. (2023)

Health worker compliance with severe malaria treatment guidelines in the context of implementing pre-referral rectal artesunate in the Democratic Republic of the Congo, Nigeria, and Uganda: An operational study.

Signorell A, et al. Corresponding author : Swiss Tropical and Public Health Institute, Allschwil, Switzerland, University of Basel, Basel, Switzerland, Mail: aita.signorell@swisstph.ch Background

For a full treatment course of severe malaria, community-administered pre-referral rectal artesunate (RAS) should be completed by post-referral treatment consisting of an injectable antimalarial and oral artemisinin-based combination therapy (ACT). This study aimed to assess compliance with this treatment recommendation in children under 5 years.

Methods and findings

This observational study accompanied the implementation of RAS in the Democratic Republic of the Congo (DRC), Nigeria, and Uganda between 2018 and 2020. Antimalarial treatment was assessed during admission in included referral health facilities (RHFs) in children under 5 with a diagnosis of severe malaria. Children were either referred from a community-based provider or directly attending the RHF.

RHF data of 7,983 children was analysed for appropriateness of antimalarials; a subsample of 3,449 children was assessed additionally for dosage and method of ACT provision (treatment compliance). A parenteral antimalarial and an ACT were administered to 2.7% (28/1,051) of admitted children in Nigeria, 44.5% (1,211/2,724) in Uganda, and 50.3% (2,117/4,208) in DRC. Children receiving RAS from a community-based provider were more likely to be administered post-referral medication according to the guidelines in DRC (adjusted odds ratio (aOR) = 2.13, 95% CI 1.55 to 2.92, P < 0.001), but less likely in Uganda (aOR = 0.37, 95% CI 0.14 to 0.96, P = 0.04) adjusting for patient, provider, caregiver, and other contextual factors. While in DRC, inpatient ACT administration was common, ACTs were often prescribed at discharge in Nigeria (54.4%, 229/421) and Uganda (53.0%, 715/1,349). Study limitations include the unfeasibility to independently confirm the diagnosis of severe malaria due to the observational nature of the study.

Conclusions

Directly observed treatment was often incomplete, bearing a high risk for partial parasite clearance and disease recrudescence. Parenteral artesunate not followed up with oral ACT constitutes an artemisinin monotherapy and may favour the selection of resistant parasites. In connection with the finding that pre-referral RAS had no beneficial effect on child survival in the 3 study countries, concerns about an effective continuum of care for children with severe malaria seem justified. Stricter compliance with the WHO severe malaria treatment guidelines is critical to effectively manage this disease and further reduce child mortality.

# Mental Health

21. Lancet 2023;401(10373):257 World Report

New legislation to overhaul mental health care in Nigeria Adepoju P.

A new mental health law is hoped to transform care for patients in Nigeria. Paul Adepoju reports from Ibadan, Nigeria.

Mental health practitioners have welcomed Nigeria's new mental health law, signed by President Muhammadu Buhari on Jan 5. In a huge change to mental health care in the country, the law

establishes a National Council for Mental Health and Substance Abuse Services, which is tasked with promoting good mental health and facilitating the provision of humane care, including treatment and rehabilitation. The council has the power to set and enforce standards of care. A Mental Health Review Tribunal will be responsible for protecting patients' interests, providing guidance on minimising intrusive and irreversible treatments, such as seclusion or restraint. It will also ensure that informed consent and approval is obtained for intrusive or irreversible treatments. The law's Section 24 codifies the rights of people in need of mental health services. It provides funding for mental health care, and outlines a path for integrating mental health services into primary care at the local government level. It also prohibits discrimination and stigmatisation of individuals living with mental illnesses. The legislation is the country's first reform on mental health since independence. The old law, in place since 1916 and reviewed in 1968, was criticised for being outdated and reflective of a time when mental health was misunderstood and the treatment of those with mental health needs was inhumane and ineffective. Under the old law, attempting suicide was a criminal act punishable with imprisonment. Previous attempts at national mental health reform in 2003 and 2013 failed in Nigeria, but the National Assembly passed the National Mental Health Bill 2020 in 2021. It has taken 2 years for President Buhari to sign it into law.

Mental health in Nigeria has long been underfunded, with WHO reporting that it only represents 4.1% of total government health expenditure. Treatment for conditions such as psychosis, bipolar disorder, and depression are not included in national health insurance or reimbursement schemes. The delivery of mental health services in the country has also been affected by brain drain, with psychiatrists, psychologists, and other health practitioners leaving for careers abroad.

## Migration and health

22. Lancet 2023;401(10375):425 World Report

Health situation deteriorating in Kenyan refugee camp Devi S.

Aid agencies have sounded warnings as conflict and drought drive people to Dadaab refugee complex. Hospital admissions of children with severe malnutrition in a refugee camp in Kenya have surged as people flee Somalia to escape conflict and drought, with aid agencies warning the situation is likely to worsen amid forecasts of a record sixth consecutive year of failed rains in the region. The UN says the number of people with acute food insecurity almost doubled last year to about 22 million people in the Horn of Africa—4·3 million people in Kenya, 5·6 million in Somalia, and 12·0 million in Ethiopia and about 1·7 million have been driven from their homes by a lack of water and pasture. About 83% of those displaced across international boundaries have gone to Kenya.

Médecins Sans Frontières (MSF) says that the general malnutrition rate among children has increased by 45% between July and December, 2022, in Dagahaley, one of three refugee camps in the sprawling Dadaab refugee complex in northern Kenya. 233 000 registered refugees and more than 80 000 unregistered refugees live in the camp; more than 50 000 people arrived in 2022 alone. The first camp at Dadaab was created in 1991 when refugees fleeing civil war in Somalia went to Kenya. While successive Kenyan Governments have sought to close the complex, the new President William Ruto has spoken more about integrating refugees into communities.

The protracted nature of east Africa's crisis and donor fatigue have hit the provision of relief to people recently displaced by drought-related causes as well as the many refugees who have lived in Kenya for years, said a paper by the Migration Policy Institute.

Aid agencies such as the International insecurity Committee of the Red Cross (ICRC) have expanded their activities, including giving food, making cash transfers to pay for food and water, and expanding infrastructure projects such as water points and bore holes, Abdirahman Maalim, head of ICRC's Mombassa office, told The Lancet. "We have also arranged community engagement meetings where people say the impact of climate change is their biggest concern because of the challenges to the provision of clean water, food and livelihoods," he said.

Up to 86 million people in sub-Saharan Africa will migrate within their own countries because of climate change by 2050, according to The World Bank, with large numbers in east Africa.

## Non-communicable diseases

23. BMJ 2023;380:e071952 Research

Prevalence, awareness, treatment, and control of hypertension in China, 2004-18: findings from six rounds of a national survey

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## Abstract

Objective To assess the recent trends in prevalence and management of hypertension in China, nationally and by population subgroups.

Design Six rounds of a national survey, China.

Setting China Chronic Disease and Risk Factors Surveillance, 2004-18.

Participants 642523 community dwelling adults aged 18-69 years (30501 in 2004, 47353 in 2007, 90491 in 2010, 156836 in 2013, 162293 in 2015, and 155049 in 2018).

Main outcome measures Hypertension was defined as a blood pressure of  $\geq$ 140/90 mm Hg or taking antihypertensive drugs. The main outcome measures were hypertension prevalence and proportion of people with hypertension who were aware of their hypertension, who were treated for hypertension, and whose blood pressure was controlled below 140/90 mm Hg.

Results The standardised prevalence of hypertension in adults aged 18-69 years in China increased from 20.8% (95% confidence interval 19.0% to 22.5%) in 2004 to 29.6% (27.8% to 31.3%) in 2010, then decreased to 24.7% (23.2% to 26.1%) in 2018. During 2010-18, the absolute annual decline in prevalence of hypertension among women was more than twice that among men (-0.83 percentage points (95% confidence interval -1.13 to -0.52) v -0.40 percentage points (-0.73 to -0.07)). Despite modest improvements in the awareness, treatment, and control of hypertension since 2004, rates remained low in 2018, at 38.3% (36.3% to 40.4%), 34.6% (32.6% to 36.7%), and 12.0% (10.6% to 13.4%). Of 274 million (95% confidence interval 238 to 311 million) adults aged 18-69 years with hypertension in 2018, control was inadequate in an estimated 240 million (215 to 264 million). Across all surveys, women with low educational attainment had higher prevalence of hypertension than those with higher education, but the finding was mixed for men. The gap in hypertension control between urban and rural areas persisted, despite larger improvements in diagnosis and control in rural than in urban areas.

Conclusions The prevalence of hypertension in China has slightly declined since 2010, but treatment and control remain low. The findings highlight the need for improving detection and treatment of hypertension through the strengthening of primary care in China, especially in rural areas.

# 24. BMJ 2023;380:p717 News

Dengue and chikungunya cases surge as climate change spreads arboviral diseases to new regions Luke Taylor

Author affiliations

Arboviral diseases are causing growing concern in the Americas as chikungunya and dengue fever spread to regions that have never seen them before.

The Americas has seen a surge in dengue cases in recent years and 2023 "is showing intense dengue transmission," the World Health Organization said in a review of the epidemiological situation in the region.

Last year 2.8 million dengue cases were reported in the Americas, more than twice the 1.2 million cases reported in 2021. Deaths from dengue reached 1290 in 2022, three times the number in 2021. Major cities in Argentina and Bolivia have published health alerts in recent months as unusually large outbreaks of the mosquito borne illness has added strain on local hospitals.

#### One Health

25. Lancet 2023;401(10372):169 Editorial

One Health: a call for ecological equity

The notion that the wellbeing of an individual is directly connected to the wellbeing of the land has a long history in Indigenous societies. Nowadays, the term One Health has become an important concept in global health. The One Health High-Level Expert panel defines One Health as "an integrated, unifying approach that aims to sustainably balance and optimise the health of people, animals, and ecosystems. It recognises the health of humans, domestic and wild animals, plants, and the wider environment (including ecosystems) are closely linked and inter-dependent." On Jan 19, we published a new four-part Series online on One Health and global health security, which analyses current understanding of potential public health emergencies and explores how effective adoption of One Health could improve global health security. Although the Series focuses on pandemic preparedness, One Health goes way beyond emerging infections and novel pathogens; it is the foundation for understanding and addressing the most existential threats to societies including antimicrobial resistance, food and nutrition insecurity, and climate change.

Modern attitudes to human health take a purely anthropocentricview—thatthehumanbeingisthecentre of medical attention and concern. One Health places us in an interconnected and interdependent relationship with non-human animals and the environment. The consequences of this thinking entail a subtle but quite revolutionary shift of perspective: all life is equal, and of equal concern. This understanding is fundamental to addressing pressing health issues at the human–animal– environment interface.

The Series recommends the involvement of more environmental health organisations to better integrate environmental, wildlife, and farming issues to help address challenges relating to disease spillover.

One implication of a One Health approach is the need to reduce human pressure on the environment— an important medical intervention in itself. Take antimicrobial resistance (AMR). Driven by antimicrobial use and misuse in human, animal, and environmental sectors, and the spread of resistant bacteria and resistance genes within and between these sectors, AMR inflicts a huge global toll. An estimated 1·2 million people died in 2019 from antibiotic-resistant bacterial infections with another 4·95 million deaths associated with bacterial AMR globally. Only by applying a One Health approach can action to address AMR be achieved.

One huge concern is the risk of worsening inequalities as One Health networks are largely situated and resourced in high-income countries.

As the second paper in The Series points out, a more egalitarian approach is needed, one that is not paternalistic or colonial in telling low-income and middle-income countries what they should do. The reality is that One Health will be delivered in countries, not by concordats between multilateral organisations, but by taking a fundamentally different approach to the natural world, one in which we are as concerned about the welfare of non-human animals and the environment as we are about humans. In its truest sense, One Health is a call for ecological, not merely health, equity.

Rread also: Lancet 2023;401(10372):182-3 World report One Health in Kenya Salm-Reifferscheidt L.

Lancet 2023;401(10376):591-604 One Health 1

Advancing One human–animal–environment Health for global health security: what does the evidence say? Zinsstag J et al., Lancet 2023;401(10376):605-16 One Health 2 A global analysis of One Health Networks and the proliferation of One Health collaborations Mwatondo A et al.,

Lancet 2023;401(10377):673-87 Review / Series / One Health 3 How prepared is the world? Identifying weaknesses in existing assessment frameworks for global health security through a One Health approach Traore T et al.,

Lancet 2023;401(10377):688-704 Review / Series / One Health 4 Global and regional governance of One Health and implications for global health security Elnaiem A et al.,

Lancet 2023;401(10378):789-94 Viewpoint After 2 years of the COVID-19 pandemic, translating One Health into action is urgent Lefrançois T et al.,

## Ophthalmology

## 26. Lancet 2023;401(10374):377-89

#### Cataracts

Cicinelli MV et al., School of Medicine, Vita-Salute San Raffaele University, Milan, Italy; Department of Ophthalmology, IRCCS San Raffaele Scientific Institute, Milan, Italy.

94 million people are blind or visually impaired globally, and cataract is the most common cause of blindness worldwide. However, most cases of blindness are avoidable. Cataract is associated with decreased quality of life and reduced life expectancy. Most cases of cataract occur after birth and share ageing and oxidative stress as primary causes, although several non-modifiable and modifiable risk factors can accelerate cataract formation. In most patients, phacoemulsification with intraocular lens implantation is the preferred treatment and is highly cost-effective. There has been an increase in the use of comprehensive cataract surgical services, including diagnoses, treatment referrals, and rehabilitation. However, global inequity in surgical service quality is still a limitation. Implementation of preoperative risk assessment, risk reduction strategies, and new surgical technologies have made cataract surgery possible at an earlier stage of cataract severity with the expectation of good refractive outcomes. The main challenge is making the service that is currently available to some patients accessible to all by use of universal health coverage.

## Public Health

## 27. Health Policy and Planning, Vol. 38 (2), 2023: 261–274

The role of community health worker-based care in post-conflict settings: a systematic review Kalin Werner, et al. Corresponding author. Institute for Health and Aging, Department of Social and Behavioral Sciences, University of California, San Francisco, USA. E-mail: kalin.werner@gmail.com

Countries affected by conflict often experience the deterioration of health system infrastructure and weaken service delivery. Evidence suggests that healthcare services that leverage local community dynamics may ameliorate health system-related challenges; however, little is known about implementing these interventions in contexts where formal delivery of care is hampered subsequent to conflict. We reviewed the evidence on community health worker (CHW)-delivered healthcare in

conflict-affected settings and synthesized reported information on the effectiveness of interventions and characteristics of care delivery. We conducted a systematic review of studies in OVID MedLine, Web of Science, Embase, Scopus, The Cumulative Index to Nursing and Allied Health Literature (CINHAL) and Google Scholar databases. Included studies (1) described a context that is post-conflict, conflict-affected or impacted by war or crisis; (2) examined the delivery of healthcare by CHWs in the community; (3) reported a specific outcome connected to CHWs or community-based healthcare; (4) were available in English, Spanish or French and (5) were published between 1 January 2000 and 6 May 2021. We identified 1976 articles, of which 55 met the inclusion criteria. Nineteen countries were represented, and five categories of disease were assessed. Evidence suggests that CHW interventions not only may be effective but also efficient in circumventing the barriers associated with access to care in conflict-affected areas. CHWs may leverage their physical proximity and social connection to the community they serve to improve care by facilitating access to care, strengthening disease detection and improving adherence to care. Specifically, case management (e.g. integrated community case management) was documented to be effective in improving a wide range of health outcomes and should be considered as a strategy to reduce barrier to access in hard-to-reach areas. Furthermore, task-sharing strategies have been emphasized as a common mechanism for incorporating CHWs into health systems.

## Sexual and Reproductive Health

#### 28. TMIH 2023;28(4):335-42

Prevalence, incidence and recurrence of sexually transmitted infections in HIV-negative adult women in a rural South African setting

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Objective: Sexually transmitted infections (STIs), including syphilis, chlamydia, gonorrhoea and trichomoniasis, are of global public health concern. While STI incidence rates in sub-Saharan Africa are high, longitudinal data on incidence and recurrence of STIs are scarce, particularly in rural areas. We determined the incidence rates of curable STIs in HIV-negative women during 96 weeks in a rural South African setting.

Methods: We prospectively followed participants enrolled in a randomised controlled trial to evaluate the safety and efficacy of a dapivirine-containing vaginal ring for HIV prevention in Limpopo province, South Africa. Participants were included if they were female, aged 18-45, sexually active, not pregnant and HIV-negative. Twelve-weekly laboratory STI testing was performed during 96 weeks of follow-up. Treatment was provided based on vaginal discharge by physical examination or after a laboratory-confirmed STI.

Results: A total of 119 women were included in the study. Prevalence of one or more STIs at baseline was 35.3%. Over 182 person-years at risk (PYAR), a total of 149 incident STIs were diagnosed in 75 (65.2%) women with incidence rates of 45.6 events/PYAR for chlamydia, 27.4 events/100 PYAR for gonorrhoea and 8.2 events/100 PYAR for trichomoniasis. Forty-four women developed  $\geq 2$  incident STIs. Risk factors for incident STI were in a relationship  $\leq 3$  years (adjusted hazard ratio [aHR]: 1.86; 95% confidece interval [CI]: 1.04-2.65) and having an STI at baseline (aHR: 1.66; 95% CI: 1.17-2.96). Sensitivity and specificity of vaginal discharge for laboratory-confirmed STI were 23.6% and 87.7%, respectively.

Conclusion: This study demonstrates high STI incidence in HIV-negative women in rural South Africa. Sensitivity of vaginal discharge was poor and STI recurrence rates were high, highlighting the shortcomings of syndromic management in the face of asymptomatic STIs in this setting.

29. Lancet 2023;401(10377):632 World Report Global maternal mortality rates stagnating Zarocostas J. A new UN report shows that progress in reducing deaths of mothers plateaued between 2016 and 2020.

Progress in reducing global maternal mortality stalled from 2016 to 2020 according to the first UN report on trends during this period. Published on Feb 23, the report reveals that maternal deaths increased or stagnated in nearly all UN regions and notes that in two regions—Europe and North America, and Latin America and the Caribbean— maternal mortality increased from 2016 to 2020, by 17% and 15%, respectively. However, Australia and New Zealand, and central and southern Asia, posted significant decreases (by 35% and 16%, respectively), as did 31 countries. "More than 1 million additional maternal deaths will occur by 2030 if current trends continue", said Tedros Adhanom Ghebreyesus, WHO Director-General.

The report estimates that there were 287 000 maternal deaths globally in 2020, equivalent to almost 800 maternal deaths every day, with 70% in sub-Saharan Africa. In 2020, three countries in sub-Saharan Africa had maternal mortality ratios higher than 1000 deaths per 100 000 livebirths: South Sudan (1223), Chad (1063), and Nigeria (1047). Ten countries, all in sub-Saharan Africa except one (Afghanistan), were estimated to have maternal mortality ratios of 500–999 deaths per 100 000 livebirths.

The backsliding from successes during the Millenium Development Goals era, experts say, is partly attributed to maternal health slipping down the global political agenda, along with increases in inequities, shortfalls in resources, cutbacks in aid, and efforts in some countries by political and religious entities to limit the socioeconomic rights of women.

## 30. Thesis

Epidemiology and Etiology of Genital Fistulas in Eastern Africa Ngongo CJ.

Genital fistula poses a public health challenge in areas where women have inadequate access to quality emergency obstetric care. This retrospective records review looks back at the experiences that led to fistula development for over 6,700 women who sought fistula repair between 1994 and 2017 in Ethiopia, Kenya, Malawi, Rwanda, Tanzania, Somalia, South Sudan, Uganda, and Zambia. This large, multi-country dataset is the fruit of decades of dedicated fistula surgery and data collection by fistula surgeon Dr. Thomas Raassen and colleagues. The analysis casts light on how the causes of genital fistula vary by country and are changing over time. The project further focuses on the subset of women who developed genital fistula during childbirth to improve medical training programs, policies, and protocols related to decision-making during intrapartum care. Lastly it investigates the factors associated with women remaining married with fistula to inform policies and practices for fistula treatment and rehabilitation.

Findings include:

• Access to emergency obstetric care remained a clear challenge in South Sudan, Somalia, and Ethiopia. Access appeared higher in Uganda, Kenya, Tanzania, Malawi, Rwanda, and Zambia, signaling potential progress in obstetric fistula prevention while highlighting a need to focus on surgical safety and quality of care.

• Women who developed obstetric fistula increasingly reported having cesarean births rather than assisted vaginal births, even though most of their babies were stillborn. Training programs, policies, and protocols should reinforce evidence-based guidelines for cesarean decision-making.

• Despite the strong association between obstetric fistula and prolonged, obstructed labor, more than one quarter of women with fistula after cesarean birth had injuries due to surgical accident rather than pressure necrosis. Quality improvement measures are needed to reduce iatrogenic injuries in obstetric surgery.

• While some husbands separated from wives with fistula after childbirth, they were not the majority. If abandonment happened, it typically occurred in a woman's first two years with fistula. Communities and facilities offering fistula repair services should stress the importance of early intervention.

Healthcare providers need quality training, mentorship, accountability, and support to provide high quality care to vulnerable women. Fistula elimination will require a holistic systems approach that improves emergency obstetric care and surgical safety.

## 31. Health Policy and Planning, Vol. 38 (3), 2023: 330- 341

What is the relationship between contraceptive services and knowledge of abortion availability and legality? Evidence from a national sample of women and facilities in Ethiopia Linnea A Zimmerman, et al. Corresponding author. Department of Population, Family, and Reproductive Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, USA. E-mail: linnea.zimmerman@jh.edu

In Ethiopia, abortions are legal for minors and for rape, incest, foetal impairment or maternal disability. Knowledge of abortion legality and availability is low, and little effort has been made to disseminate this information for fear of invoking anti-abortion sentiment; instead, systems rely on health providers as information gatekeepers. This study explores how exposure to and interaction with family planning service delivery environment, specifically (1) availability of contraceptive and facility-based abortion services within 5 km of one's residence and (2) contact with a health provider in the past 12 months, relate to women's knowledge of the legality of accessing abortion services and of where to access facility-based abortion services. We used data from a nationally representative sample of 8719 women in Ethiopia and a linked health facility survey of 799 health facilities. Our outcome of interest was a categorical variable indicating if a woman had (1) knowledge of at least one legal ground for abortion, (2) knowledge of where to access abortion services, (3) knowledge of both or (4) knowledge of neither. We conducted multilevel, multinomial logistic regressions, stratified by residence. Approximately 60% of women had no knowledge of either a legal ground for abortion or a place to access services. Women who visited a health provider or who were visited by a health worker in the past 12 months were significantly more likely to know about abortion legality and availability. There were no differences based on whether women lived within 5 km of a facility that offered contraception and abortion services. We find that health workers are likely valuable sources of information; however, progress to disseminate information may be slowed if it relies on uptake of services and limited outreach. Efforts to train providers on legality and availability are critical, as is additional research on knowledge dissemination pathways.

# 32. PLoS Med 20(1): e1004143. (2023)

Regional and country-level trends in cervical cancer screening coverage in sub-Saharan Africa: A systematic analysis of population-based surveys (2000–2020)

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## Background

Sub-Saharan Africa (SSA) has the highest cervical cancer (CC) burden globally—worsened by its HIV epidemics. In 2020, the World Health Organization (WHO) introduced a CC elimination strategy with goals for vaccination, screening, and treatment. To benchmark progress, we examined temporal trends in screening coverage, percent screened at least twice by the age of 45, screening coverage among women living with HIV (WLHIV), and pre-cancer treatment coverage in SSA. Methods and findings

We conducted a systematic analysis of cross-sectional population-based surveys. It included 52 surveys from 28 countries (2000 to 2020) with information on CC screening among women aged 25 to 49 years (N = 151,338 women). We estimated lifetime and past 3-year screening coverage by age, year, country, and HIV serostatus using a Bayesian multilevel model. Post-stratification and imputations were done to obtain aggregate national, regional, and SSA-level estimates. To measure re-screening by age 45, a life table model was developed. Finally, self-reported pre-cancer treatment coverage was pooled across surveys using a Bayesian meta-analysis. Overall, an estimated 14% (95% credible intervals [95% CrI]: 11% to 21%) of women aged 30 to 49 years had ever been screened for CC in 2020, with important

regional and country-level differences. In Eastern and Western/Central Africa, regional screening coverages remained constant from 2000 to 2020 and WLHIV had greater odds of being screened compared to women without HIV. In Southern Africa, however, screening coverages increased and WLHIV had equal odds of screening. Notably this region was found to have higher screening coverage in comparison to other African regions. Rescreening rates were high among women who have already been screened; however, it was estimated that only 12% (95% CrI: 10% to 18%) of women had been screened twice or more by age 45 in 2020. Finally, treatment coverage among 4 countries with data was 84% (95% CrI: 70% to 95%). Limitations of our analyses include the paucity of data on screening modality and the few countries that had multiple surveys.

## Conclusion

Overall, CC screening coverage remains sub-optimal and did not improve much over the last 2 decades, outside of Southern Africa. Action is needed to increase screening coverage if CC elimination is to be achieved.

## 33. PLoS Med 20(2): e1004186. (2023)

Fortified balanced energy-protein supplementation during pregnancy and lactation and infant growth in rural Burkina Faso: A  $2 \times 2$  factorial individually randomized controlled trial.

Argaw A, et al. Corresponding author: Carl Lachat, Department of Food Technology, Safety and Health, Faculty of Bioscience Engineering, Ghent University, Ghent, Belgium Mail: Carl.Lachat@UGent.be Background

Optimal nutrition is crucial during the critical period of the first 1,000 days from conception to 2 years after birth. Prenatal and postnatal supplementation of mothers with multimicronutrient-fortified balanced energy–protein (BEP) supplements is a potential nutritional intervention. However, evidence on the long-term effects of BEP supplementation on child growth is inconsistent. We evaluated the efficacy of daily fortified BEP supplementation during pregnancy and lactation on infant growth in rural Burkina Faso.

# Methods and findings

A 2 × 2 factorial individually randomized controlled trial (MISAME-III) was implemented in 6 health center catchment areas in Houndé district under the Hauts-Bassins region. From October 2019 to December 2020, 1,897 pregnant women aged 15 to 40 years with gestational age <21 completed weeks were enrolled. Women were randomly assigned to the prenatal intervention arms receiving either fortified BEP supplements and iron-folic acid (IFA) tablets (i.e., intervention) or IFA alone (i.e., control), which is the standard of care during pregnancy. The same women were concurrently randomized to receive either of the postnatal intervention, which comprised fortified BEP supplementation during the first 6 months postpartum in combination with IFA for the first 6 weeks (i.e., intervention), or the postnatal control, which comprised IFA alone for 6 weeks postpartum (i.e., control). Supplements were provided by trained village-based project workers under direct observation during daily home visits. We previously reported the effect of prenatal BEP supplementation on birth outcomes. The primary postnatal study outcome was length-for-age z-score (LAZ) at 6 months of age. Secondary outcomes were anthropometric indices of growth (weight-for length and weight-for-age zscores, and arm and head circumferences) and nutritional status (prevalence rates of stunting, wasting, underweight, anemia, and hemoglobin concentration) at 6 months. Additionally, the longitudinal prevalence of common childhood morbidities, incidence of wasting, number of months of exclusive breastfeeding, and trajectories of anthropometric indices from birth to 12 months were evaluated. Prenatal BEP supplementation resulted in a significantly higher LAZ (0.11 standard deviation (SD), 95% confidence interval (CI) [0.01 to 0.21], p = 0.032) and lower stunting prevalence (-3.18 percentage points (pp), 95% CI [-5.86 to -0.51], p = 0.020) at 6 months of age, whereas the postnatal BEP supplementation did not have statistically significant effects on LAZ or stunting at 6 months. On the other hand, postnatal BEP supplementation did modestly improve the rate of monthly LAZ increment during the first 12 months postpartum (0.01 z-score/month, 95% CI [0.00 to 0.02], p = 0.030), whereas no differences in growth trajectories were detected between the prenatal study arms. Furthermore, except for the trend towards a lower prevalence of underweight found for the prenatal BEP

intervention at 6 months (-2.74 pp, 95% CI [-5.65 to 1.17], p = 0.065), no other secondary outcome was significantly affected by the pre- or postnatal BEP supplementation. Conclusions

This study provides evidence that the benefits obtained from prenatal BEP supplementation on size at birth are sustained during infancy in terms of linear growth. Maternal BEP supplementation during lactation may lead to a slightly better linear growth towards the second half of infancy. These findings suggest that BEP supplementation during pregnancy can contribute to the efforts to reduce the high burden of child growth faltering in low- and middle-income countries.

34. BMJ Global Health 2023;8:e010018. Original research

Health and economic benefits of achieving contraceptive and maternal health targets in Small Island Developing States in the Pacific and Caribbean

Kelly SL, Walsh T, Delport D, et al

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Abstract

Introduction Reducing unmet need for modern contraception and expanding access to quality maternal health (MH) services are priorities for improving women's health and economic empowerment. To support investment decisions, we estimated the additional cost and expected health and economic benefits of achieving the United Nations targets of zero unmet need for modern contraceptive choices and 95% coverage of MH services by 2030 in select Small Island Developing States.

Methods Five Pacific (Kiribati, Samoa, Solomon Islands, Tonga and Vanuatu) and four Caribbean (Barbados, Guyana, Jamaica and Saint Lucia) countries were considered based on population survey data availability. For each country, the Lives Saved Tool was used to model costs, health outcomes and economic benefits for two scenarios: business-as-usual (BAU) (coverage maintained) and coverage-targets-achieved, which scaled linearly from 2022 (following COVID-19 disruptions) coverage of evidence-based family planning and MH interventions to reach United Nations targets, including modern contraceptive methods and access to complete antenatal, delivery and emergency care. Unintended pregnancies, maternal deaths, stillbirths and newborn deaths averted by the coverage-targets-achieved scenario were converted to workforce, education and social economic benefits; and benefit–cost ratios were calculated.

Results The coverage-targets-achieved scenario required an additional US\$12.6M

(US\$10.8M–US\$15.9M) over 2020–2030 for the five Pacific countries (15% more than US\$82.4M to maintain BAU). This additional investment was estimated to avert 126000 (40%) unintended pregnancies, 2200 (28%) stillbirths and 121 (29%) maternal deaths and lead to a 15-fold economic benefit of US\$190.6M (US\$67.0M–US\$304.5M) by 2050. For the four Caribbean countries, an additional US\$17.8M (US\$15.3M–US\$22.4M) was needed to reach the targets (4% more than US\$405.4M to maintain BAU). This was estimated to avert 127000 (23%) unintended pregnancies, 3600 (23%) stillbirths and 221 (25%) maternal deaths and lead to a 24-fold economic benefit of US\$426.2M (US\$138.6M–US\$745.7M) by 2050.

Conclusion Achieving full coverage of contraceptive and MH services in the Pacific and Caribbean is likely to have a high return on investment.

# ТΒ

35. PLoS Med 20(1): e1004091. (2023)

Improving cascade outcomes for active TB: A global systematic review and meta-analysis of TB interventions.

Marley G, et al. Corresponding author: Weiming Tang, Dermatology Hospital of Southern Medical University, Guangzhou, China, University of North Carolina Project-China, Guangzhou, China, Mail: weimingtangscience@gmail.com Background To inform policy and implementation that can enhance prevention and improve tuberculosis (TB) care cascade outcomes, this review aimed to summarize the impact of various interventions on care cascade outcomes for active TB.

Methods and findings

In this systematic review and meta-analysis, we retrieved English articles with comparator arms (like randomized controlled trials (RCTs) and before and after intervention studies) that evaluated TB interventions published from January 1970 to September 30, 2022, from Embase, CINAHL, PubMed, and the Cochrane library. Commentaries, qualitative studies, conference abstracts, studies without standard of care comparator arms, and studies that did not report quantitative results for TB care cascade outcomes were excluded. Data from studies with similar comparator arms were pooled in a random effects model, and outcomes were reported as odds ratio (OR) with 95% confidence interval (CI) and number of studies (k). The quality of evidence was appraised using GRADE, and the study was registered on PROSPERO (CRD42018103331). Of 21,548 deduplicated studies, 144 eligible studies were included. Of 144 studies, 128 were from low/middle-income countries, 84 were RCTs, and 25 integrated TB and HIV care. Counselling and education was significantly associated with testing (OR = 8.82, 95% CI:1.71 to 45.43; I2 = 99.9%, k = 7), diagnosis (OR = 1.44, 95% CI:1.08 to 1.92; I2 = 97.6%, k = 9), linkage to care (OR = 3.10, 95% CI = 1.97 to 4.86; I2 = 0%, k = 1), cure (OR = 2.08, 95% CI:1.11 to 3.88; I2 = 76.7%, k = 4), treatment completion (OR = 1.48, 95% CI: 1.07 to 2.03; I2 = 73.1%, k = 8), and treatment success (OR = 3.24, 95% CI: 1.88 to 5.55; I2 = 75.9%, k = 5) outcomes compared to standardof-care. Incentives, multisector collaborations, and community-based interventions were associated with at least three TB care cascade outcomes; digital interventions and mixed interventions were associated with an increased likelihood of two cascade outcomes each. These findings remained salient when studies were limited to RCTs only. Also, our study does not cover the entire care cascade as we did not measure gaps in pre-testing, pretreatment, and post-treatment outcomes (like loss to follow-up and TB recurrence).

Conclusions

Among TB interventions, education and counseling, incentives, community-based interventions, and mixed interventions were associated with multiple active TB care cascade outcomes. However, cost-effectiveness and local-setting contexts should be considered when choosing such strategies due to their high heterogeneity.

# 36. PLoS Med 20(1): e1004030. (2023)

Mandatory, voluntary, repetitive, or one-off post-migration follow-up for tuberculosis prevention and control: A systematic review.

Wahedi K, et al. Correspondence: Kayvan Bozorgmehr, Section for Health Equity Studies & Migration, Department of General Practice & Health Services Research, Heidelberg University Hospital, Heidelberg; Department of Population Medicine and Health Services Research, School of Public Health, Bielefeld University, Germany. Mail: kayvan.bozorgmehr@uni-bielefeld.de Background

Post-migration follow-up of migrants identified to be at-risk of developing tuberculosis during the initial screening is effective, but programmes vary across countries. We aimed to review main strategies applied to design follow-up programmes and analyse the effect of key programme characteristics on reported coverage (i.e., proportion of migrants screened among those eligible for screening) or yields (i.e., proportion of active tuberculosis among those identified as eligible for follow-up screening). Methods and findings

We performed a systematic review and meta-analysis of studies reporting yields of follow-up screening programmes. Studies were included if they reported the rate of tuberculosis disease detected in international migrants through active case finding strategies and applied a post-migration follow-up (defined as one or more additional rounds of screening after finalising the initial round). For this, we retrieved all studies identified by Chan and colleagues for their systematic review (in their search until January 12, 2017) and included those reporting from active follow-up programmes. We then updated the search (from January 12, 2017 to September 30, 2022) using Medline and Embase via Ovid. Data

were extracted on reported coverage, yields, and key programme characteristics, including eligible population, mode of screening, time intervals for screening, programme providers, and legal frameworks. Differences in follow-up programmes were tabulated and synthesised narratively. Metaanalyses in random effect models and exploratory analysis of subgroups showed high heterogeneity (12 statistic > 95.0%). We hence refrained from pooling, and estimated yields and coverage with corresponding 95% confidence intervals (CIs), stratified by country, legal character (mandatory versus voluntary screening), and follow-up scheme (one-off versus repetitive screening) using forest plots for comparison and synthesis. Of 1,170 articles, 24 reports on screening programmes from 7 countries were included, with considerable variation in eligible populations, time intervals of screening, and diagnostic protocols. Coverage varied, but was higher than 60% in 15 studies, and tended to be lower in voluntary compared to compulsory programmes, and higher in studies from the United States of America, Israel, and Australia. Yield varied within and between countries and ranged between 53.05 (31.94 to 82.84) in a Dutch study and 5,927.05 (4,248.29 to 8,013.71) in a study from the United States. Of 15 estimates with narrow 95% CIs for yields, 12 were below 1,500 cases per 100,000 eligible migrants. Estimates of yields in one-off follow-up programmes tended to be higher and were surrounded by less uncertainty, compared to those in repetitive follow-up programmes. Yields in voluntary and mandatory programmes were comparable in magnitude and uncertainty. The study is limited by the heterogeneity in the design of the identified screening programmes as effectiveness, coverage and yields also depend on factors often underreported or not known, such as baseline incidence in the respective population, reactivation rate, educative and administrative processes, and consequences of not complying with obligatory measures. Conclusion

Programme characteristics of post-migration follow-up screening for prevention and control of tuberculosis as well as coverage and yield vary considerably. Voluntary programmes appear to have similar yields compared with mandatory programmes and repetitive screening apparently did not lead to higher yields compared with one-off screening. Screening strategies should consider marginal costs for each additional round of screening.

#### 37. BMJ Global Health 2023;8:e010994. Original research

Where are the missing people affected by tuberculosis? A programme review of patient-pathway and cascade of care to optimise tuberculosis case-finding, treatment and prevention in Cambodia Teo AKJ, Morishita F, Prem K, et al

#### Abstract

Background Cambodia has achieved great success in tuberculosis (TB) control in the past decade. Nevertheless, people with TB are missed by the health systems at different stages of the care pathway. This programme review corroborated the care-seeking behaviours of people with TB and TB services availability and estimated the number of people completing each step of the TB disease and TB preventive treatment (TPT) care cascade.

Methods Patient pathways and the care cascades for TB disease and TPT were constructed using data from the latest national TB prevalence survey, routine surveillance and programme, the global TB database and published studies. We also randomly selected TB survivors in the 2019 cohort to assess recurrence-free survival 1-year post-treatment. TPT care cascade was constructed for people living with HIV (PLHIV) and household contacts (children <5 years and all ages) of persons with bacteriologically-confirmed TB in 2019 and 2020.

Results Nationally, 54% of those who exhibited TB symptoms sought initial care in the private sector. Overall, 93% and 58% of people with presumptive TB did not access a facility with TB diagnostic and treatment services, respectively, at the first point of care-seeking. Approximately 56% (95% CI 52% to 57%) of the 47 000 (95% CI 31 000 to 68 000) estimated TB cases in 2019 achieved recurrence-free survival. Among the estimated PLHIV in Cambodia, <30% completed TPT. Among children <5 years, 53% (95% CI 29% to 65%) (2019) and 67% (95% CI 36% to 80%) (2020) of those eligible for TPT completed the regimen successfully. In 2019 and 2020, 23% (95% CI 22% to 25%) and 54% (95% CI

50% to 58%) of the estimated household contacts (all ages) eligible for TPT completed the regimen successfully.

Conclusion There are significant gaps in care-seeking, coverage and access to TB services and TPT in Cambodia. Action plans to improve TB response have been co-developed with local stakeholders to address the gaps throughout the care cascades.

38. BMJ Global Health 2023;8:e010306. Original research

Cost-effectiveness of tuberculosis infection prevention and control interventions in South African clinics: a model-based economic evaluation informed by complexity science methods Bozzani FM, McCreesh N, Diaconu K, et al

Correspondence to Dr Fiammetta Maria Bozzani; fiammetta.bozzani@lshtm.ac.uk Abstract

Introduction Nosocomial Mycobacterium tuberculosis (Mtb) transmission substantially impacts health workers, patients and communities. Guidelines for tuberculosis infection prevention and control (TB IPC) exist but implementation in many settings remains suboptimal. Evidence is needed on costeffective investments to prevent Mtb transmission that are feasible in routine clinic environments. Methods A set of TB IPC interventions was codesigned with local stakeholders using system dynamics modelling techniques that addressed both core activities and enabling actions to support implementation. An economic evaluation of these interventions was conducted at two clinics in KwaZulu-Natal, employing agent-based models of Mtb transmission within the clinics and in their catchment populations. Intervention costs included the costs of the enablers (eg, strengthened supervision, community sensitisation) identified by stakeholders to ensure uptake and adherence. Results All intervention scenarios modelled, inclusive of the relevant enablers, cost less than US\$200 per disability-adjusted life-year (DALY) averted and were very cost-effective in comparison to South Africa's opportunity cost-based threshold (US\$3200 per DALY averted). Two interventions, building modifications to improve ventilation and maximising use of the existing Central Chronic Medicines Dispensing and Distribution system to reduce the number of clinic attendees, were found to be cost saving over the 10-year model time horizon. Incremental cost-effectiveness ratios were sensitive to assumptions on baseline clinic ventilation rates, the prevalence of infectious TB in clinic attendees and future HIV incidence but remained highly cost-effective under all uncertainty analysis scenarios. Conclusion TB IPC interventions in clinics, including the enabling actions to ensure their feasibility, afford very good value for money and should be prioritised for implementation within the South African health system.