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Communicable Diseases

1. Lancet 2014;348(9965):304

Editorial: What are affordable vaccines?

Affordability of vaccines prevents many people from accessing the benefits of immunisation, says a new report from Médecins Sans Frontières (MSF) released on Jan 20. Although the world's poorest countries are supported by GAVI, the report describes how a large group of middle-income countries, aid agencies, and GAVI-graduating countries are struggling to afford key vaccinations. For example, in 2014, 78% of low-income countries, but only 56% of middle-income countries, have introduced or intend to introduce pneumococcal conjugate vaccines.

The cost of the vaccines alone per child in the WHO immunisation schedule has increased from US$0•67 in 2001, to $32•09–45•59 in 2014, because of the inclusion of several newer, more expensive vaccines with only one or two manufacturers. These figures, based on minimum prices, underestimate the true scale of the problem for those not eligible for GAVI support since opacity surrounding vaccine pricing makes it difficult to estimate the true cost paid. Pricing opacity, the report asserts, hinders the ability of governments and aid agencies to negotiate successfully. The report also heavily criticises tiered pricing, a mechanism whereby vaccine prices should be based on economic GDP, which is supported by GAVI and numerous powerful international donors. Lack of transparency and governmental oversight, the report says, allows drug companies to implement unregulated differential pricing (Morocco and Tunisia, for example, pay higher prices than France for pneumococcal conjugate vaccines) and also acts to stifle competition by artificially lowering prices in markets where emerging market competitors are most likely to compete.

MSF calls on governments and drug companies to introduce strategies to increase transparency of vaccine prices, including provision of publicly available information on vaccine research and development costs; monitoring and accountability of vaccine prices; increased use of effective procurement strategies; and increased competition and entry of lower cost manufacturers. Ahead of the GAVI pledging conference in Berlin, Germany, on Jan 27, it is time to join the call for systematic changes to ensure long-term universal access to the benefits of vaccination.

2. TMIH 2015;20(1):98-105

Integration of diagnosis and treatment of sleeping sickness in primary healthcare facilities in the Democratic Republic of the Congo

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Background: Control of human African trypanosomiasis (HAT) in the Democratic Republic of Congo (DRC) has always been a vertical programme, although attempts at integration in general health services were made in recent years. Now that HAT prevalence is declining, the integration question becomes even more crucial. We studied the level of attainment of integration of HAT case detection and management in primary care centres in two high-prevalence districts in the province of Bandundu, DRC.

Methods: We visited all 43 first-line health centres of Mushie and Kwamouth districts, conducted structured interviews and inspected facilities using a standardised checklist. We focused on: availability of well trained staff - besides HAT, we also tested for knowledge on tuberculosis; availability of equipment, consumables and supplies; and utilisation of the services.

Results: All health centres were operating but most were poorly equipped, and attendance rates were very low. We observed a median of 14 outpatient consultations per facility (IQR 8-

21) in the week prior to our visit, that is two patients per day. The staff had good knowledge on presenting symptoms, diagnosis and treatment of both HAT and tuberculosis. Nine centres were accredited by the national programme as HAT diagnosis and treatment centres, but the most sensitive diagnostic confirmation test, the mini-anion exchange centrifugation technique (mAECT), was not present in any. Although all nine were performing the CATT screening test, only two had the required cold chain in working order.
Conclusion: In these high-prevalence districts in DRC, staff is well-acquainted with HAT but lack the tools required for an adequate diagnostic procedure. Attendance rates of these primary care centres are extremely low, making timely recognition of a resurgence of HAT unlikely in the current state of affairs.

3. Clin Infect Dis 2015 Jan 18. pii: civ004

Miltefosine for Visceral and Cutaneous Leishmaniasis: Drug Characteristics and Evidence-Based Treatment Recommendations

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Miltefosine is the only recognized oral agent with potential to treat leishmaniasis. Miltefosine had demonstrated very good cure rates for visceral leishmaniasis (VL) in India, Nepal, and Bangladesh, but high rates of clinical failures have been recently reported. Moderate efficacy has been observed for VL in East Africa, whereas data from Mediterranean countries and Latin America are scarce. Results have not been very promising for patients coinfected with VL and human immunodeficiency virus. However, miltefosine's long half-life and its oral administration could make it a good option for maintenance prophylaxis. Good evidence of efficacy has been documented in Old World cutaneous leishmaniasis (CL), and different cure rates among New World CL have been obtained depending on the geographical areas and species involved. Appropriate regimens for New World mucocutaneous leishmaniasis need to be established, although longer treatment duration seems to confer better results. Strategies to prevent the development and spread of miltefosine resistance are urgently needed.

Malaria

4. Am J TMH 2015;92(1):13-7

Artemether-Lumefantrine Compared to Atovaquone-Proguanil as a Treatment for Uncomplicated Plasmodium falciparum Malaria in Travelers

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Atovaquone-proguanil (AP) and artemether-lumefantrine (AL) are both treatments for uncomplicated Plasmodium falciparum malaria, but comparative clinical trials are lacking. We performed a retrospective analysis, comparing treatment failure and fever clearance time in non-immune travelers with uncomplicated P. falciparum malaria, treated with AP or AL. Sixty-nine patients were included during 2001-2013: 44 in the AP group and 25 in the AL group. Treatment failure was observed in 6 of 44 (13.6%) and 1 of 25 (4.0%) patients in the AP and AL groups, respectively. Six treatment failures were observed in travelers from West Africa. Fever clearance time was 44 ± 23 h in AL group versus 77 ± 28 h in AP group, ($P < 0.001$). Hospitalization time was significantly shorter in the AL group; 3.8 + 1.3 versus 5.1 + 2.8 days in the AP group ($P = 0.04$) In conclusion, travelers with uncomplicated P. falciparum

malaria recover faster on AL than on AP. The AL should probably be the drug of choice for this population.

5. Am J TMH 2015 Jan 26. pii: 14-0490

Comparing the Impact of Artemisinin-Based Combination Therapies on Malaria Transmission in Sub-Saharan Africa

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Artemisinin-based combination therapies (ACTs) are currently considered the first-line treatments for uncomplicated Plasmodium falciparum malaria. Among these, artemether-lumefantrine (AL) has been the most widely prescribed ACT in sub-Saharan Africa. Recent clinical trials conducted in sub-Saharan Africa have shown that dihydroartemisinin-piperaquine (DP), a most recent ACT, may have a longer post-treatment prophylactic period and post-treatment infection period (duration of gametocyte carriage) than AL. Using epidemiological and clinical data on the efficacy of AL and DP, we developed and parameterized a mathematical transmission model that we used to compare the population-level impact of AL and DP for reducing P. falciparum malaria transmission in sub-Saharan Africa. Our results showed that DP is likely to more effectively reduce malaria incidence of clinical episodes than AL. However in low P. falciparum transmission areas, DP and AL are likely to be equally effective in reducing malaria prevalence. The predictions of our model were shown to be robust to the empirical uncertainty summarizing the epidemiological parameters. DP should be considered as a replacement for AL as first-line treatment of uncomplicated malaria in highly endemic P. falciparum communities. To optimize the effectiveness of ACTs, it is necessary to tailor treatment policies to the transmission intensity in different settings.

6. Clin Infect Dis 2015;60(3):357-65

Efficacy and safety of the mosquitocidal drug ivermectin to prevent malaria transmission after treatment: a double-blind, randomized, clinical trial

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Background: Artemisinin combination therapy effectively clears asexual malaria parasites and immature gametocytes but does not prevent posttreatment malaria transmission. Ivermectin (IVM) may reduce malaria transmission by killing mosquitoes that take blood meals from IVM-treated humans.

Methods: In this double-blind, placebo-controlled trial, 120 asymptomatic Plasmodium falciparum parasite carriers were randomized to receive artemether-lumefantrine (AL) plus placebo or AL plus a single or repeated dose (200 µg/kg) of ivermectin (AL-IVM1 and AL-IVM2, respectively). Mosquito membrane feeding was performed 1, 3, and 7 days after initiation of treatment to determine Anopheles gambiae and Anopheles funestus survival and infection rates.
Results: The AL-IVM combination was well tolerated. IVM resulted in a 4- to 7-fold increased mortality in mosquitoes feeding 1 day after IVM ($P < .001$). Day 7 IVM plasma levels were positively associated with body mass index ($r = 0.57$, $P < .001$) and were higher in female participants ($P = .003$), for whom An. gambiae mosquito mortality was increased until 7 days after a single dose of IVM (hazard rate ratio, 1.34 [95% confidence interval, 1.07-1.69]; $P = .012$). Although we found no evidence that IVM reduced Plasmodium infection rates among surviving mosquitoes, the mosquitocidal effect of AL-IVM1 and AL-IVM2 resulted in 27% and 35% reductions, respectively, in estimated malaria transmission potential during the first week after initiation of treatment.
Conclusions: We conclude that IVM can be safely given in combination with AL and can reduce the likelihood of malaria transmission by reducing the life span of feeding mosquitoes.

Ebola

7. Lancet 2014;348(9961):e67

World Report: Sierra Leone doctors call for better Ebola care for colleagues
Miriam Shuchman

Local doctors went on strike in Sierra Leone after it emerged that they would not be able to access a specialised British-run Ebola treatment unit for health-care workers.
As Ebola rages through Sierra Leone, local health workers are among the hardest hit. Data from the US Centers of Disease Control and Prevention show that nearly 200 health staff (different cadres) were infected between May 23 and Oct 31 this year. According to media reports, 12 doctors are among the country's health worker cases, ten of whom have died. In early December, the Junior Doctors Association of Sierra Leone (JUDASIL) staged a strike, calling on authorities “to hastily facilitate the establishment of a specialised treatment centre for health workers”.
Sierra Leone already has an Ebola treatment unit designated for health-care workers, which opened last month, but local doctors are blocked from accessing it. Staffed by British Army medics, at the British-built Ebola treatment complex in Kerry Town, the 12-bed health-care workers' unit only accepts local health-care workers from UK-funded Ebola treatment facilities, according to a letter from British authorities titled “Access Criteria for Kerry Town 12-bed Facility” that The Lancet has obtained. UK Department for International Development senior press officer Angela Balakrishnan confirmed that the health-care workers' unit is available for British and Sierra Leonean health-care workers who work at “a UK-supported facility”.
Most Sierra Leonean doctors and all of the country's junior doctors work at government hospitals, so they are ineligible for admission. Junior doctor Ibrahim F Kamara who is on JUDASIL's executive told The Lancet that he thinks the British misled the country about their intentions when they described the facility they were going to build. “We're disappointed”, he said.
In late November, British Army officers met with leaders of JUDASIL and the Sierra Leone Medical and Dental Association to discuss the 12-bed unit at Kerry Town, according to

Kamara. “After much pressure, they said they will accept Sierra Leonean doctors if beds are available”, he said. The Lancet confirms that Sierra Leonean nationals are able to gain access when there is spare capacity.

8. BMJ 2014;349:g7348

Clinical Review: Ebola virus disease

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This clinical review has been developed for The BMJ in collaboration with BMJ Best Practice, based on a regularly updated web/mobile topic that supports evidence-based decision making at the point of care. To view the complete and current version, please refer to the Ebola virus infection topic on the BMJ Best Practice website.

The bottom line

- Ebola virus disease is a severe, often fatal, zoonotic infection caused by a virus of the Filoviridae family (genus Ebolavirus)
- Human to human transmission occurs through contact with body fluids from infected patients. The incubation period after infection is 1-21 days and patients are not considered infectious until they develop symptoms
- Initial stages of infection are non-specific, which makes the differential diagnosis broad. A history of exposure and clinical suspicion of infection should prompt isolation
- Management is currently focused on supportive care and infection control. Healthcare workers should familiarise themselves with local guidance
- Case fatality rates range from 30% to 90%
- Because of the high likelihood of infected people travelling, all countries should have tested and practised protocols ready for screening and managing patients

Ebola virus disease is a severe, often fatal, zoonotic filovirus infection. There are five species: Zaire ebolavirus, Sudan ebolavirus, Taï Forest ebolavirus, Bundibugyo ebolavirus, and Reston ebolavirus.

9. BMJ 2014;349:g7540

Feature The BMJ Christmas Appeal 2014: How MSF is mapping the world’s medical emergency zones

This article has a correction. Please see:Errata - December 12, 2014

Jane Feinmann, freelance journalist, London, UK jane@janefeinmann.com

A mammoth project to map the addresses of 200 million people aims to help Médecins Sans Frontières to deliver better medical care worldwide, writes Jane Feinmann. The charity has decades of experience in bringing volunteer doctors to where they are needed in emergency situations and longer term humanitarian projects. This is why The BMJ has chosen MSF for its Christmas charity appeal this year. Please give generously

“At long last, the poorest regions of the world will benefit from the lessons of 1854, when John Snow was able to trace the source of a cholera epidemic to a contaminated water pump in Soho [London] by mapping the addresses of his patients,” Kiran Jobanputra, Médecins Sans Frontières’ (MSF) adviser on non-communicable diseases, told The BMJ.

The Missing Maps project, a collaboration between MSF, the British and American Red Cross, and the Humanitarian OpenStreetMap Team, aims to create digital maps to log addresses for the “unmapped or undermapped” people of the world. These are often the

poorest and most vulnerable people living in crowded conditions in towns, cities, villages, and refugee camps, says Jobanputra, a general practitioner and deputy director of the Manson Unit, a facility attached to MSF UK in London to help the charity's volunteer doctors on the ground implement evidence based practice.
The project, launched on 7 November, aims to add an ambitious 200 million people's addresses to the maps in the next two years with the help of volunteers worldwide (box).1
Tech time: how MSF's volunteers make the maps
Mapping involves four simple steps:
Existing satellite images are loaded into OpenStreetMap software, a free world map that can be edited by multiple users (a wiki)
Volunteer amateur cartographers, many enlisted through social media (check #MissingMaps on Twitter), can log in from anywhere in the world and use an easy tool to trace the outlines of buildings, roads, parks, and rivers over the satellite image
This tracing lacks the names of streets or landmarks so local volunteers, often students or scouts, print out small sections and head out with a pencil to write down the names of streets and buildings
Once complete, the maps are scanned back into OpenStreetMap and the labels are added to the map by more volunteers. The world then has free access to a validated map forever

10. BMJ 2014; 349:g7815

News: IMF policy is blamed for contributing to Ebola epidemic

Anne Gulland London

Short term economic policies advocated by the International Monetary Fund have exacerbated the epidemic of Ebola virus disease in west Africa, a study has said.
Researchers at the London School of Hygiene and Tropical Medicine and the universities of Oxford and Cambridge looked at the fund's policies in regard to the three worst affected countries, Sierra Leone, Liberia, and Guinea. The weakness of these countries' health systems has often been highlighted as a reason for the rapid spread of the disease, and the researchers found that the IMF's policies had not allowed the three countries to invest in their health or education systems.
The fund has been providing economic support to Guinea for 21 years, Liberia for seven years, and Sierra Leone for 19 years. But researchers said that the conditions attached to the funding encouraged short term economic priorities. The conditions imposed by the IMF included reductions in government spending, prioritisation of paying back debt, and bolstering foreign exchange reserves. The IMF has incorporated "poverty-reduction expenditure" into its programmes, but all three countries failed to meet these targets in 2013, the year the first case of Ebola virus disease was recorded in Guinea.
The researchers said that the IMF often required caps on the public sector wage bill, thus affecting the recruitment of health workers. In Sierra Leone, for example, the number of community health workers was cut from 0.11 per 1000 population in 2004 to 0.02 in 2008.
The IMF also advocates decentralised health systems, which the researchers said made it "difficult to mobilise coordinated, central responses to disease outbreaks." The researchers pointed out that from the early 2000s in Guinea the IMF promoted fiscal and administrative decentralisation, but an IMF mission five years later reported "governance problems" and noted that the quality of health service delivery had deteriorated.

11. Lancet 2015;385(9962):29-35

Assessment of the potential for international dissemination of Ebola virus via commercial air travel during the 2014 west African outbreak

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Background: The WHO declared the 2014 west African Ebola epidemic a public health emergency of international concern in view of its potential for further international spread. Decision makers worldwide are in need of empirical data to inform and implement emergency response measures. Our aim was to assess the potential for Ebola virus to spread across international borders via commercial air travel and assess the relative efficiency of exit versus entry screening of travellers at commercial airports.
Methods: We analysed International Air Transport Association data for worldwide flight schedules between Sept 1, 2014, and Dec 31, 2014, and historic traveller flight itinerary data from 2013 to describe expected global population movements via commercial air travel out of Guinea, Liberia, and Sierra Leone. Coupled with Ebola virus surveillance data, we modelled the expected number of internationally exported Ebola virus infections, the potential effect of air travel restrictions, and the efficiency of airport-based traveller screening at international ports of entry and exit. We deemed individuals initiating travel from any domestic or international airport within these three countries to have possible exposure to Ebola virus. We deemed all other travellers to have no significant risk of exposure to Ebola virus.
Findings: Based on epidemic conditions and international flight restrictions to and from Guinea, Liberia, and Sierra Leone as of Sept 1, 2014 (reductions in passenger seats by 51% for Liberia, 66% for Guinea, and 85% for Sierra Leone), our model projects 2.8 travellers infected with Ebola virus departing the above three countries via commercial flights, on average, every month. 91,547 (64%) of all air travellers departing Guinea, Liberia, and Sierra Leone had expected destinations in low-income and lower-middle-income countries. Screening international travellers departing three airports would enable health assessments of all travellers at highest risk of exposure to Ebola virus infection.
Interpretation: Decision makers must carefully balance the potential harms from travel restrictions imposed on countries that have Ebola virus activity against any potential reductions in risk from Ebola virus importations. Exit screening of travellers at airports in Guinea, Liberia, and Sierra Leone would be the most efficient frontier at which to assess the health status of travellers at risk of Ebola virus exposure, however, this intervention might require international support to implement effectively.

12. Am J TMH 2015;92(2):240-1. doi: 10.4269/ajtmh.14-0803. Epub 2015 Jan 5

Ebola policies that hinder epidemic response by limiting scientific discourse

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There is an unprecedented epidemic of Ebola virus disease (EVD) in west Africa. There has been a strong response from dedicated health professionals. However, there have also been irrational and fear-based responses that have contributed to misallocation of resources, stigma, and deincentivizing volunteers to combat Ebola at its source. Recently, the State of Louisiana Department of Health and Hospitals issued a ban on those coming from affected countries wishing to attend the annual meetings of American Society of Tropical Medicine and Hygiene and the American Public Health Association, both of which were held in New Orleans. We argue against such policies, question evidence and motivations, and discuss their practical and ethical implications in hampering effective responses to EVD by the scientific

community. We aim to shed light on this issue and its implications for the future of public health interventions, reflect on the responsibility of health providers and professional societies as advocates for patients and the public health, and call for health professionals and societies to work to challenge inappropriate political responses to public health crises.

13. BMJ 2015;350:g7827

Clinical Review: WHO's crisis handling to be overhauled after slow response to Ebola

Anne Gulland London

International health leaders have voted for reorganisation at the World Health Organization in the wake of its poor initial handling of the epidemic of Ebola virus disease in west Africa.
At a special session of WHO's executive board, delegates passed a resolution to overhaul the organisation's emergency response, including the establishment of a 1500 strong global health reserve workforce and a $100m (£66m; €89m) contingency fund. Many delegates spoke of WHO's poor crisis handling capacity, with Tom Frieden, director of the US Centers for Disease Control and Prevention speaking on behalf of the US government, saying, "The WHO we have is not the one we need."
A spokesman for the charity Médecins Sans Frontières told the meeting that thousands of people had died from the disease because of "international negligence," adding, "It has become alarmingly evident that there is no functioning global response mechanism to a potential pandemic in countries with fragile health systems."

Tuberculosis

14. BMJ 2014;349:g7397

Feature Conflict and Health: Experts sound alarm as Syrian crisis fuels spread of tuberculosis

Sophie Cousins, freelance journalist, Beirut, Lebanon sophcousins@gmail.com

Tuberculosis among Syrian refugees must be treated as a health emergency say health workers as the disease numbers rise in neighbouring countries. Sophie Cousins reports
Mass movement of refugees as a result of the crisis in Syria has contributed to a rise in the number of tuberculosis cases across the region. Since the beginning of the Syrian crisis in 2011, over three million refugees have fled to neighbouring countries, including Lebanon, Turkey, and Jordan; 6.5 million have been internally displaced; and more than 100 000 have lost their lives, according to the United Nations High Commissioner for Refugees (UNHCR).
As the conflict escalated doctors and healthcare workers fled Syria, health infrastructure was destroyed, and drug supply chains were interrupted. This, in addition to poor living conditions and a sharp drop in vaccination coverage, led to outbreaks of infectious diseases, including polio, measles, hepatitis, and tuberculosis, both in Syria and in the countries that border it.
Before the crisis, the World Health Organization estimated that the prevalence of tuberculosis in Syria was 23/100 000 population, a large reduction from 85/100 000 in 1990.1 In 2013, according to the WHO's tuberculosis profile on Syria, 2816 cases of tuberculosis were identified.2
Tuberculosis care in Syria was integrated into the healthcare system with treatment facilities located in Aleppo, Homs, and other areas. However, the war has seriously affected the country's ability to diagnose, treat, and prevent the disease.

15. Clin Infect Dis 2015;60(2):188-94

Compassionate use of bedaquiline for the treatment of multidrug-resistant and extensively drug-resistant tuberculosis: interim analysis of a French cohort
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Background: Bedaquiline is a new antibiotic that was approved for the treatment of multidrug-resistant (MDR) tuberculosis. We aimed to evaluate the short-term microbiological efficacy and the tolerability profile of bedaquiline. METHODS: We performed a retrospective cohort study among patients with MDR tuberculosis receiving bedaquiline for compassionate use between January 2010 and July 2013 and evaluated at 6 months of bedaquiline treatment. **Results:** A total of 35 patients with MDR tuberculosis were included in the study. Nineteen (54%) had extensively drug-resistant (XDR) tuberculosis, and 14 (40%) had isolates resistant to fluoroquinolones (Fqs) or second-line injectables. Bedaquiline was associated with a median of 4 (range, 2-5) other drugs, including linezolid in 33 (94%) cases. At 6 months of bedaquiline treatment, culture conversion was achieved in 28 of 29 (97%) cases with culture-positive pulmonary tuberculosis at bedaquiline initiation. Median time to culture conversion was 85 days (range, 8-235 days). Variables independently associated with culture conversion were treatment with a Fq (P = .01), absence of lung cavities (P < .001), and absence of hepatitis C virus infection (P = .001). A total of 7 patients (20%) experienced a ≥60-ms increase in QT interval, leading to bedaquiline discontinuation in 2 (6%) cases. Severe liver enzyme elevation occurred in 2 patients (6%). During the study period, 1 death (3%) occurred and was reported as unrelated to tuberculosis or antituberculosis treatment. **Conclusions:** The use of bedaquiline combined with other active drugs has the potential to achieve high culture conversion rates in complicated MDR and XDR tuberculosis cases, with a reassuring safety profile at 6 months of treatment.

16. Clin Infect Dis 2015;60(4):639-45

Long-term Protection From Isoniazid Preventive Therapy for Tuberculosis in HIV-Infected Patients in a Medium-Burden Tuberculosis Setting: The TB/HIV in Rio (THRio) Study
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Background: The duration of protection against tuberculosis provided by isoniazid preventive therapy is not known for human immunodeficiency virus (HIV)-infected individuals living in settings of medium tuberculosis incidence. METHODS: We conducted an individual-level analysis of participants in a cluster-randomized, phased-implementation trial of isoniazid preventive therapy. HIV-infected patients who had positive tuberculin skin tests (TSTs) were followed until tuberculosis diagnosis, death, or administrative censoring. Nelson-Aalen cumulative hazard plots were generated and hazards were compared using the log-rank test. Cox proportional hazards models were fitted to investigate factors associated with tuberculosis diagnosis. RESULTS: Between 2003 and 2009, 1954 patients with a positive TST were studied. Among these, 1601 (82%) initiated isoniazid. Overall tuberculosis incidence was 1.39 per 100 person-years (PY); 0.53 per 100 PY in those who initiated isoniazid and 6.52 per 100 PY for those who did not (adjusted hazard ratio [aHR], 0.17; 95% confidence interval [CI], .11-.25). Receiving antiretroviral therapy at time of a positive TST was associated with a reduced risk of tuberculosis (aHR, 0.69; 95% CI, .48-1.00). Nelson-Aalen plots of tuberculosis incidence showed a constant risk, with no acceleration in 7 years of follow-up for those initiating isoniazid preventive therapy. CONCLUSIONS: Isoniazid

preventive therapy significantly reduced tuberculosis risk among HIV-infected patients with a positive TST. In a medium-prevalence setting, 6 months of isoniazid in HIV-infected patients with positive TST reduces tuberculosis risk over 7 years of follow-up, in contrast to results of studies in higher-burden settings in Africa.

HIV

17. Lancet 2015;385(9962):55-71

Global epidemiology of HIV among female sex workers: influence of structural determinants

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Female sex workers (FSWs) bear a disproportionately large burden of HIV infection worldwide. Despite decades of research and programme activity, the epidemiology of HIV and the role that structural determinants have in mitigating or potentiating HIV epidemics and access to care for FSWs is poorly understood. We reviewed available published data for HIV prevalence and incidence, condom use, and structural determinants among this group. Only 87 (43%) of 204 unique studies reviewed explicitly examined structural determinants of HIV. Most studies were from Asia, with few from areas with a heavy burden of HIV such as sub-Saharan Africa, Russia, and eastern Europe. To further explore the potential effect of structural determinants on the course of epidemics, we used a deterministic transmission model to simulate potential HIV infections averted through structural changes in regions with concentrated and generalised epidemics, and high HIV prevalence among FSWs. This modelling suggested that elimination of sexual violence alone could avert 17% of HIV infections in Kenya (95% uncertainty interval [UI] 1-31) and 20% in Canada (95% UI 3-39) through its immediate and sustained effect on non-condom use) among FSWs and their clients in the next decade. In Kenya, scaling up of access to antiretroviral therapy among FSWs and their clients to meet WHO eligibility of a CD4 cell count of less than 500 cells per μL could avert 34% (95% UI 25-42) of infections and even modest coverage of sex worker-led outreach could avert 20% (95% UI 8-36) of infections in the next decade. Decriminalisation of sex work would have the greatest effect on the course of HIV epidemics across all settings, averting 33-46% of HIV infections in the next decade. Multipronged structural and community-led interventions are crucial to increase access to prevention and treatment and to promote human rights for FSWs worldwide.

18. Clin Infect Dis 2015;60(4):612-26

The Interaction Between Sickle Cell Disease and HIV Infection: A Systematic Review

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Human immunodeficiency virus (HIV) and sickle cell disease (SCD) are regarded as endemic in overlapping geographic areas; however, for most countries only scarce data on the interaction between HIV and SCD and disease burden exist. HIV prevalence in SCD patients varies between 0% and 11.5% in published studies. SCD has been suggested to reduce disease progression of HIV into AIDS. Various interactions of antiretroviral therapy with SCD exist. Both SCD and HIV act as common risk factors for stroke, avascular necrosis, severe splenic dysfunction, pulmonary arterial hypertension, and sepsis, which may result in synergistic increase in risk of developing these diseases. No treatment guidelines regarding SCD with HIV coinfection were identified. Available evidence is mainly based on small clinical studies, thus making strong recommendations difficult. An increased effort to elucidate the precise interactions is warranted to better understand both diseases and effect more adequate treatment approaches, especially in view of their geographical coprevalence.

19. TMIH 2015;20(2):122-45

Pregnancy and HIV disease progression: a systematic review and meta-analysis

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Objective: To assess whether pregnancy accelerates HIV disease progression.
Methods: Studies comparing progression to HIV-related illness, low CD4 count, AIDS-defining illness, HIV-related death, or any death in HIV-infected pregnant and non-pregnant women were included. Relative risks (RR) for each outcome were combined using random effects meta-analysis and were stratified by antiretroviral therapy (ART) availability.
Results: 15 studies met the inclusion criteria. Pregnancy was not associated with progression to HIV-related illness [summary RR: 1.32, 95% confidence interval (CI): 0.66-2.61], AIDS-defining illness (summary RR: 0.97, 95%CI: 0.74-1.25) or mortality (summary RR: 0.97, 95%CI: 0.62-1.53), but there was an association with low CD4 counts (summary RR: 1.41, 95%CI: 0.99-2.02) and HIV-related death (summary RR: 1.65, 95%CI: 1.06-2.57). In settings where ART was available, there was no evidence that pregnancy accelerated progress to HIV/AIDS-defining illnesses, death and drop in CD4 count. In settings without ART availability, effect estimates were consistent with pregnancy increasing the risk of progression to HIV/AIDS-defining illnesses and HIV-related or all-cause mortality, but there were too few studies to draw meaningful conclusions.
Conclusions: In the absence of ART, pregnancy is associated with small but appreciable increases in the risk of several negative HIV outcomes, but the evidence is too weak to draw firm conclusions. When ART is available, the effects of pregnancy on HIV disease progression are attenuated and there is little reason to discourage healthy HIV-infected women who desire to become pregnant from doing so.

20. TMIH 2015;20(2):170-6

Mortality risk factors among HIV-exposed infants in rural and urban Cameroon

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Objectives: HIV-exposed infants, including those who do not become infected, have higher morbidity and mortality rates than HIV unexposed infants. The underlying mechanisms of this difference are largely unknown. The objective of this study was to identify the risk factors for mortality among HIV-exposed (infected as well as uninfected) infants in a prevention of mother-to-child transmission (PMTCT) programme in Cameroon.
Methods: We analysed the data from 319 mother-infant pairs included in a PMTCT programme at a rural and an urban hospital between 2004 and 2012. The programme offered free formula feeding, monthly follow-up visits and antiretroviral therapy (ART) according to national PMTCT guidelines. Mother-infant pairs were divided in three study groups, based on year of recruitment and study site: (I) rural hospital, 2004-07; (II) rural hospital, 2008-12; (III) urban hospital, 2008-12.
Results: Two hundred and eighty-five medical records were included in the final analysis. Infant mortality rates were 23.9%, 20.0% and 5.3% in group I, II and III, respectively (P = 0.02). Hazard ratios of infant mortality were 6.4 (P < 0.001) for prematurity, 4.6 (P = 0.04) for no maternal use of ARTs, 5.6 (P = 0.025) for mixed feeding, 2.7 for home deliveries (P = 0.087) and 0.4 (P = 0.138) for urban study group.
Conclusions: In this programme, prematurity, no ART use, and the practice of mixed feeding were independent predictors of infant mortality. Mixed feeding and not using ART increased the hazard of death, probably through its increased risk of HIV infection. Although mortality rates were significantly higher in the rural area, rural setting was not a risk factor for infant mortality. These findings may contribute to the development of tailor-made programmes to reduce infant mortality rates among HIV-exposed infants.

21. TMIH 2015;20(3):277-83

Repeat HIV testing during pregnancy and delivery: missed opportunities in a rural district hospital in Zambia

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Objective: To assess coverage of repeat HIV testing among women who delivered in a Zambian hospital. HIV testing of pregnant women and repeat testing every 3 months during pregnancy and breastfeeding is the recommended policy in areas of high HIV prevalence.
Methods: A prospective implementation study in a second-level hospital in rural Zambia. Included were all pregnant women who delivered in hospital during May and June 2012. Data regarding antenatal visits and HIV testing were collected by two investigators using a standardised form.
Results: Of 401 women who delivered in hospital, sufficient antenatal data could be retrieved for 322 (80.3%) women. Of these 322 women, 301 (93.5%) had attended antenatal care (ANC) at least once. At the time of discharge after delivery in hospital, 171 (53.1%) had an unclear HIV status because their negative test result was more than 3 months ago or of an unknown date, or because they had not been tested at all during pregnancy or delivery. An updated HIV status was present for 151 (46.9%) women: 25 (7.8%) were HIV positive and 126 (39.1%) had tested negative within the last 3 months. In this last group, 79 (24.5%) had been tested twice or more during pregnancy. During the study period, none of the women was tested during admission for delivery.
Conclusion: Despite high ANC coverage, opportunities for repeat HIV testing were missed in almost half of all women who delivered in this hospital in a high-prevalence HIV setting.

22. TMIH 2015;20(3):365-79

Self-transfer and mortality amongst adults lost to follow-up in ART programmes in low- and middle-income countries: systematic review and meta-analysis

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Objective: To ascertain estimates of adult patients, recorded as lost to follow-up (LTFU) within antiretroviral treatment (ART) programmes, who have self-transferred care, died or truly stopped ART in low- and middle-income countries.
Methods: PubMed, EMBASE, Web of Science, Science Direct, LILACS, IndMed and AIM databases (2003-2013) and IAS/AIDS conference abstracts (2011-2013) were searched for tracing studies reporting the proportion of traced patients found to have self-transferred, died or stopped ART. These estimates were then combined using random-effects meta-analysis. Risk of bias was assessed through subgroup and sensitivity analyses.
Results: Twenty eight studies were eligible for inclusion, reporting true outcomes for 10 806 traced patients attending approximately 258 ART facilities. None were from outside sub-Saharan Africa. Twenty three studies reported 4.5-54.4% traced LTFU patients self-transferring care, providing a pooled estimate of 18.6% (95% CI 15.8-22.0%). A significant positive association was found between rates of self-transfer and LTFU in the ART cohort. The pooled estimates for unreported deaths were 38.8% (95% CI 30.8-46.8%; 27 studies) and 28.6% (95% CI 21.9-36.0%; 20 studies) for patients stopping ART. A significant decrease in unreported deaths from 50.0% (95% CI 41.5-58.4%) to 30.0% (95% CI 21.1-38.9%) was found comparing study periods before and after 31 December 2007.
Conclusions: Substantial unaccounted for transfers and deaths amongst patients LTFU confirms that retention and mortality is underestimated where the true outcomes of LTFU patients are not ascertained.

Health Policy

23. Lancet 2014;348(9961):2256-9

Viewpoint: Improving the assessment and attribution of effects of development assistance for health

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Overseas development assistance for health (DAH) increased substantially from 2000, but has plateaued since 2010 because of the global economic crisis, with growing public demands for funders and beneficiary countries to show the effect of investments. When showing effect, donor agencies and countries need to address two challenges: first, accurate estimation of the effects of investments in different areas (eg, vaccines or health systems) on health outcomes; and second, attribution of the effects to specific investments.
We provide four suggestions to encourage agreement between donors on the principles underpinning assessment and reporting of the effect of DAH.
First, approaches to assessment and reporting should mainly respond to country needs (including national governments and end beneficiaries) and emphasise mutual accountability.
Second, approaches to assess and report the health effects of DAH should identify the contextual factors both within and outside the health system that contribute to the observed results and might affect their wider applicability.
Third, there should be greater consistency and transparency in the selection of counterfactual scenarios, taking into account potential confounding by factors such as economic growth or conversely economic shocks that can affect the determinants of health.
Fourth, approaches to assess and report the health effects of DAH should be adapted to different settings and needs. They should draw on a range of methods and designs dependent

on what inference is likely to be made from them. They should be tested in both stable and fragile states, with coordinated approaches to monitoring sector performance that foster country ownership (eg, the International Health Partnership Plus [IHP+] monitoring and evaluation framework) and reduce uncoordinated multiple donor programmes.
Improved measurement, enhanced comparability across different agencies, and strengthened transparency in assessment of the effect of DAH should give credence to the results reported by funding agencies. To advance this agenda and appraise these new approaches in more depth is crucial, in view of the large amounts of funds spent, the growing recognition of the importance of HSS interventions to achieve global health goals, and the political pressures on aid budgets at a time of economic austerity.

24. Lancet 2014;348(9961):2248-55

Viewpoint: Leaving no one behind: an agenda for equity

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Shortly before his death, Mahatma Gandhi offered a useful reflection that helps to cut through some of the complexity surrounding debates about equity. “Recall the face of the poorest and the weakest person you may have seen and ask yourself if the step you contemplate is going to be any use to them.”
It's a simple but compelling guide for policy makers concerned with combating extreme inequality. Something of the same spirit underpins the report of the High Level Panel established by the UN Secretary General to make recommendations for the post-2015 development agenda. Going beyond the identification of universal goals, the report calls for “a focus on the poorest and most marginalised” and a commitment to “leave no one behind”. This approach is in-keeping with other work on the post-2015 agenda, including the Global Sustainable Development Report. Far more than the Millennium Development Goals (MDGs)—which were largely neutral on the issue of inequality—the High Level Panel report includes a wide-ranging social justice agenda. If adopted by governments and backed by national policy commitments and a new global partnership, the Panel's agenda could put exclusion, inequality, and marginalisation at the centre of the post-2015 development framework.

25. Lancet 2014;348(9963):117-171

Global, regional, and national age–sex specific all-cause and cause-specific mortality for 240 causes of death, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013

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Background

Up-to-date evidence on levels and trends for age-sex-specific all-cause and cause-specific mortality is essential for the formation of global, regional, and national health policies. In the Global Burden of Disease Study 2013 (GBD 2013) we estimated yearly deaths for 188 countries between 1990, and 2013. We used the results to assess whether there is epidemiological convergence across countries.

Global life expectancy for both sexes increased from 65•3 years (UI 65•0–65•6) in 1990, to 71•5 years (UI 71•0–71•9) in 2013, while the number of deaths increased from 47•5 million (UI 46•8–48•2) to 54•9 million (UI 53•6–56•3) over the same interval. Global progress masked variation by age and sex: for children, average absolute differences between countries

decreased but relative differences increased. For women aged 25–39 years and older than 75 years and for men aged 20–49 years and 65 years and older, both absolute and relative differences increased. Decomposition of global and regional life expectancy showed the prominent role of reductions in age-standardised death rates for cardiovascular diseases and cancers in high-income regions, and reductions in child deaths from diarrhoea, lower respiratory infections, and neonatal causes in low-income regions. HIV/AIDS reduced life expectancy in southern sub-Saharan Africa. For most communicable causes of death both numbers of deaths and age-standardised death rates fell whereas for most non-communicable causes, demographic shifts have increased numbers of deaths but decreased age-standardised death rates. Global deaths from injury increased by 10•7%, from 4•3 million deaths in 1990 to 4•8 million in 2013; but age-standardised rates declined over the same period by 21%. For some causes of more than 100 000 deaths per year in 2013, age-standardised death rates increased between 1990 and 2013, including HIV/AIDS, pancreatic cancer, atrial fibrillation and flutter, drug use disorders, diabetes, chronic kidney disease, and sickle-cell anaemias. Diarrhoeal diseases, lower respiratory infections, neonatal causes, and malaria are still in the top five causes of death in children younger than 5 years. The most important pathogens are rotavirus for diarrhoea and pneumococcus for lower respiratory infections. Country-specific probabilities of death over three phases of life were substantially varied between and within regions.

Interpretation

For most countries, the general pattern of reductions in age-sex specific mortality has been associated with a progressive shift towards a larger share of the remaining deaths caused by non-communicable disease and injuries. Assessing epidemiological convergence across countries depends on whether an absolute or relative measure of inequality is used. Nevertheless, age-standardised death rates for seven substantial causes are increasing, suggesting the potential for reversals in some countries. Important gaps exist in the empirical data for cause of death estimates for some countries; for example, no national data for India are available for the past decade

26. Lancet 2014;348(9965):380-91

Review: Indicators linking health and sustainability in the post-2015 development agenda

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The UN-led discussion about the post-2015 sustainable development agenda provides an opportunity to develop indicators and targets that show the importance of health as a precondition for and an outcome of policies to promote sustainable development. Health as a precondition for development has received considerable attention in terms of achievement of health-related Millennium Development Goals (MDGs), addressing growing challenges of non-communicable diseases, and ensuring universal health coverage. Much less attention has been devoted to health as an outcome of sustainable development and to indicators that show both changes in exposure to health-related risks and progress towards environmental sustainability. We present a rationale and methods for the selection of health-related indicators to measure progress of post-2015 development goals in non-health sectors. The proposed indicators show the ancillary benefits to health and health equity (co-benefits) of sustainable development policies, particularly those to reduce greenhouse gas emissions and increase resilience to environmental change. We use illustrative examples from four thematic areas: cities, food and agriculture, energy, and water and sanitation. Embedding of a range of health-related indicators in the post-2015 goals can help to raise awareness of the probable

health gains from sustainable development policies, thus making them more attractive to decision makers and more likely to be implemented than before.

27. TMIH 2015;20(3):312-21

Factors influencing the decision to drop out of health insurance enrolment among urban slum dwellers in Ghana

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Objective: To identify the factors influencing dropout from Ghana's health insurance scheme among populations living in slum communities.
Methods: Cross-sectional data were collected from residents of 22 slums in the Accra Metropolitan Assembly. Cluster and systematic random sampling techniques were used to select and interview 600 individuals who had dropped out from the scheme 6 months prior to the study. Descriptive statistics and multivariate logistic regression models were computed to account for sample characteristics and reasons associated with the decision to dropout.
Results: The proportion of dropouts in the sample increased from the range of 6.8% in 2008 to 34.8% in 2012. Non-affordability of premium was the predominant reason followed by rare illness episodes, limited benefits of the scheme and poor service quality. Low-income earners and those with low education were significantly more likely to report premium non-affordability. Rare illness was a common reason among younger respondents, informal sector workers and respondents with higher education. All subgroups of age, education, occupation and income reported nominal benefits of the scheme as a reason for dropout.
Conclusion: Interventions targeted at removing bottlenecks to health insurance enrolment are salient to maximising the size of the insurance pool. Strengthening service quality and extending the premium exemption to cover low-income families in slum communities is a valuable strategy to achieve universal health coverage.

Mother and Child Health

28. BMJ 2014;349:g7509

Feature Family Planning: Why are women dying in India's sterilisation camps?

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Far from offering suitable birth control methods to men and women at different points in their lives, India's programme focuses on female tubectomy carried out in substandard camps, Priyanka Pulla reports

Two weeks after 13 women died after surgical sterilisation at a camp in the central Indian state of Chhattisgarh, the cause of their deaths remains unknown. Laboratory reports have confirmed the presence of toxins in the drugs given to these women. However, the postmortem examinations of seven of the women indicate they had septicaemia, which can result from poor hygiene during surgery, according to a fact finding mission by the non-governmental organisations Population Foundation of India, Parivar Seva Sansthan, the Family Planning Association of India, and Common Health.

Aside from the drugs, septicaemia alone "would have been enough to risk killing every woman," said Poonam Muttreja, executive director of Population Foundation of India and part of the mission.

29. TMIH 2015;20(2):177-83

Delayed cord clamping in South African neonates with expected low birthweight: a randomised controlled trial
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Objective: To evaluate safety and haematological effects of delayed cord clamping (DCC) in infants with expected low birthweight born in a resource-poor setting.
Methods: Randomised controlled trial involving pregnant women in early labour ≥18 years with intrapartum symphysal-fundal height ≤32 cm. Mothers were randomised for either early cord clamping (ECC, <30 s) or DCC (2-3 min after birth).
Results: We included 104 vigorous infants born by vaginal delivery, of whom 39% had a birthweight <2500 g. Infant haemoglobin (Hb) levels 24 h after birth were significantly higher in the DCC group (18.0 g/dl vs 16.8 g/dl, P = 0.006). Despite successful placental transfusion, hyperbilirubinemia and hyperviscosity were not observed. Two months after birth, there were no differences in Hb between groups (9.9 g/dl vs 9.8 g/dl, P = 0.60), but the infants in the DCC group had better weight gain from baseline than those with ECC (2.2 kg vs 1.9 kg, P = 0.058).
Conclusions: In this South African cohort of newborns with a subnormal distribution of birthweight delayed cord clamping was a safe procedure. Two months after birth the effect of DCC on Hb was not detectable anymore. DCC should be promoted in every singleton delivery in a resource-poor setting irrespective of the birthweight.

30. TMIH 2015;20(2):184-7
Health policy for sickle cell disease in Africa: experience from Tanzania on interventions to reduce under-five mortality
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Tanzania has made considerable progress towards reducing childhood mortality, achieving a 57% decrease between 1980 and 2011. This epidemiological transition will cause a reduction in the contribution of infectious diseases to childhood mortality and increase in contribution from non-communicable diseases (NCDs). Haemoglobinopathies are amongst the most common childhood NCDs, with sickle cell disease (SCD) being the commonest haemoglobinopathy in Africa. In Tanzania, 10 313 children with SCD under 5 years of age (U5) are estimated to die every year, contributing an estimated 7% of overall deaths in U5 children. Key policies that governments in Africa are able to implement would reduce mortality in SCD, focusing on newborn screening and comprehensive SCD care programmes. Such programmes would ensure that interventions such as prevention of infections using penicillin plus prompt diagnosis and treatment of complications are provided to all individuals with SCD.

31. TMIH 2015;20(2):230-9
The role of the private sector in the provision of antenatal care: a study of Demographic and Health Surveys from 46 low- and middle-income countries
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Objective: To examine the role of the private sector in the provision of antenatal care (ANC) across low- and middle-income countries.

Methods: Demographic and Health Survey (DHS) data from 46 countries (representing 2.6 billion people) on components of ANC given to 303 908 women aged 15-49 years for most recent birth were used. We identified 79 unique sources of care which were re-coded into home, public, private (commercial) and private (not-for-profit). Use of ANC and a quality of care index (scaled 0-1) were stratified by type of provider, region and wealth quintile. Linear regressions were used to examine the association between provider type and antenatal quality of care score.
Results: Across all countries, the main source of ANC was public (54%), followed by private commercial (36%) and home (5%), but there were large variations by region. Home-based ANC was associated with worse quality of care (0.2; 95% CI -0.2 to -0.19) relative to the public sector, while the private not-for-profit sector (0.03; 95% CI 0.02 to 0.04) was better. There were no differences in quality of care between public and private commercial providers.
Conclusions: The market for ANC varies considerably between regions. The two largest sectors - public and private commercial - perform similarly in terms of quality of care. Future research should examine the role of the private sector in other health service domains across multiple countries and test what policies and programmes can encourage private providers to contribute to increased coverage, quality and equity of maternal care.

Non Communicable Diseases

32. BMJ 2015;350:h111 Feature Multimorbidity

Why India should worry about a coepidemic of diabetes and tuberculosis

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More collaboration may be needed between largely private sector diabetes care and the public tuberculosis control programme, finds Talha Burki

Diabetes is fuelling the spread of tuberculosis warns a report published in October 2014 from the International Union Against Tuberculosis and Lung Disease and the World Diabetes Foundation.1

The report warns of a "looming co-epidemic," which could have catastrophic consequences for healthcare systems in affected countries. With the world's highest burden of tuberculosis—an estimated 65 million cases—India is especially vulnerable.2

Type 2 diabetes triples the risk of tuberculosis.1 The World Health Organization estimates that one million new cases of tuberculosis globally a year can be attributed to the condition—15% of the total burden.3 In India, this translates to about 300 000 cases of tuberculosis associated with diabetes a year. Patients with diabetes are four times more likely to relapse and twice as likely to die during treatment for tuberculosis.3 They remain infectious for longer and are less receptive to drugs.1

Interaction between drugs

"In the presence of diabetes, the pharmacokinetics of many anti-TB drugs are affected," explained Anil Kapur, former managing director of the World Diabetes Federation and now a member of its board. "Efficacy levels might go down quite substantially." All of which raises the possibility that such patients could drive a new cycle of infection and drug resistance.

"Unless you deal with diabetes, you cannot provide optimal outcomes for tuberculosis," stressed Kapur. "It is important that policymakers and those who implement the programmes on the ground are aware of this fact."

33. BMJ 2015;350:h23

Analysis: Global health agenda on non-communicable diseases: has WHO set a smart goal for physical activity?
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Philipe de Souto Barreto argues that, to reduce premature mortality, policies should focus on getting fully inactive people to do a little physical activity rather than strive for the entire population to meet current physical activity recommendations
As part of their Global Action Plan in 2013 to reduce the avoidable burden of non-communicable diseases the World Health Organization proposed a 25% relative reduction in the risk of premature mortality from cardiovascular diseases, diabetes, cancer, and chronic respiratory diseases by 2025.1 The Global Action Plan recognised the importance of four risk factors in achieving this goal—smoking, harmful use of alcohol, unhealthy diet, and physical inactivity. WHO's main goal regarding physical activity is to achieve a 10% relative reduction in the prevalence of insufficient physical activity, which is defined as <150 minutes of moderate intensity activity a week, or equivalent, for adults aged 18 or over.
WHO's policy focuses on the ideal goal of 150 minutes of moderate activity a week, but here I argue that getting inactive people to do a little bit of physical activity, even if they don't meet the recommendations, might provide greater population health gains.

Surgery

34. Lancet 2014;348(9961):2245-7
Viewpoint: Global surgery: defining an emerging global health field
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Global health is one of the defining issues of the 21st century, attracting unprecedented levels of interest and propelling health and disease from a biomedical process to a social, economic, political, and environmental concern. Surgery, however, has not been considered an integral component of global health and has remained largely absent from the discipline's discourse.1 After much inattention, surgery is now gaining recognition as a legitimate component of global health. In January, 2014, Jim Kim, President of the World Bank, urged the global health community to challenge the injustice of global inequity in surgical care, stating that "surgery is an indivisible, indispensable part of health care and of progress towards universal health coverage".

35. Lancet 2015 Feb 4. pii: S0140-6736(15)60091-5. 11
Essential surgery: key messages from Disease Control Priorities, 3rd edition
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The World Bank will publish the nine volumes of Disease Control Priorities, 3rd edition, in 2015-16. Volume 1-Essential Surgery-identifies 44 surgical procedures as essential on the basis that they address substantial needs, are cost effective, and are feasible to implement. This report summarises and critically assesses the volume's five key findings. First, provision of essential surgical procedures would avert about 1•5 million deaths a year, or 6-7% of all avertable deaths in low-income and middle-income countries. Second, essential surgical procedures rank among the most cost effective of all health interventions. The surgical

platform of the first-level hospital delivers 28 of the 44 essential procedures, making investment in this platform also highly cost effective. Third, measures to expand access to surgery, such as task sharing, have been shown to be safe and effective while countries make long-term investments in building surgical and anaesthesia workforces. Because emergency procedures constitute 23 of the 28 procedures provided at first-level hospitals, expansion of access requires that such facilities be widely geographically diffused. Fourth, substantial disparities remain in the safety of surgical care, driven by high perioperative mortality rates including anaesthesia-related deaths in low-income and middle-income countries. Feasible measures, such as WHO's Surgical Safety Checklist, have led to improvements in safety and quality. Fifth, the large burden of surgical disorders, cost-effectiveness of essential surgery, and strong public demand for surgical services suggest that universal coverage of essential surgery should be financed early on the path to universal health coverage. We point to estimates that full coverage of the component of universal coverage of essential surgery applicable to first-level hospitals would require just over US$3 billion annually of additional spending and yield a benefit-cost ratio of more than 10:1. It would efficiently and equitably provide health benefits, financial protection, and contributions to stronger health systems.