# International Health Alerts 2017-2 Contents

# International Health Alerts 2017-1 Abstracts

## Communicable diseases

**Lessons learnt from 12 oral cholera vaccine campaigns in resource-poor settings**
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Improving water and sanitation is the preferred choice for cholera control in the long-term. Nevertheless, vaccination is an available tool that has been shown to be a cost-effective option for cholera prevention in endemic countries or during outbreaks. In 2011 the first low-cost oral cholera vaccine for international use was given prequalification by the World Health Organization (WHO). To increase and prioritize use of the vaccine, WHO created a global stockpile in 2013 from which countries may request oral cholera vaccine for reactive campaigns. WHO has issued specific guidelines for applying for the vaccine, which was previously in short supply (despite prequalification for a second oral vaccine in 2015). The addition of a third WHO-prequalified oral cholera vaccine in 2016 is expected to increase the global stockpile considerably and alleviate supply issues. However, prioritization and best use of the vaccine (e.g. how, when and where to use) will remain challenges. We describe 12 past oral cholera vaccine campaigns, conducted in settings with varying burdens of cholera. These case studies illustrate three key challenges faced in the use of the oral cholera vaccines: regulatory hurdles, cold chain logistics and vaccine coverage and uptake. To pave the way for the introduction of current and future oral cholera vaccines, we discuss operational challenges and make recommendations for future research with respect to each of these challenges.

**Infectious disease risk and international tourism demand**
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For some countries, favourable climatic conditions for tourism are often associated with favourable conditions for infectious diseases, with the ensuing development constraints on the tourist sectors of impoverished countries where tourism's economic contribution has a high potential. This paper evaluates the economic implications of eradication of Malaria, Dengue, Yellow Fever and Ebola on the affected destination countries focusing on the tourist expenditures. Methods A gravity model for international tourism flows is used to provide an estimation of the impact of each travel-related disease on international tourist arrivals. Next the potential eradication of these diseases in the affected countries is simulated and the impact on tourism expenditures is estimated. Findings The results show that, in the case of Malaria, Dengue, Yellow Fever and Ebola, the eradication of these diseases in the affected countries would result in an increase of around 10 million of tourist worldwide and a rise in the tourism expenditure of 12 billion dollars. Conclusion By analysing the economic benefits of the eradication of Dengue, Ebola, Malaria, and Yellow Fever for the tourist sector—a strategic economic sector for many of the countries where these TRD are present—this paper explores a new aspect of the quantification of health policies which should be taken into consideration in future international health assessment programmes. It is important to note that the analysis is only made of the direct impact of the diseases' eradication and consequently the potential multiplicative effects of a growth in the GDP, in terms of tourism attractiveness, are not evaluated. Consequently, the economic results can be considered to be skeleton ones.

**Patterns of infections, aetiological agents and antimicrobial resistance at a tertiary care hospital in northern Tanzania**
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**OBJECTIVE**: To determine the causative agents of infections and their antimicrobial susceptibility at a tertiary care hospital in Moshi, Tanzania, to guide optimal treatment.
**METHODS**: A total of 590 specimens (stool (56), sputum (122), blood (126) and wound swabs (286)) were collected from 575 patients admitted in the medical and surgical departments. The bacterial species were determined by conventional methods, and disc diffusion was used to determine the antimicrobial susceptibility pattern of the bacterial isolates.
**RESULTS**: A total of 249 (42.2%) specimens were culture-positive yielding a total of 377 isolates. A wide range of bacteria was isolated, the most predominant being Gram-negative bacteria: Proteus spp. (n = 48, 12.7%), Escherichia coli (n = 44, 11.7%), Pseudomonas spp. (n = 40, 10.6%) and Klebsiella spp (n = 38, 10.1%). Wound infections were characterised by multiple isolates (n = 293, 77.7%), with the most frequent being Proteus spp. (n = 44, 15%), Pseudomonas (n = 37, 12.6%), Staphylococcus (n = 29, 9.9%) and Klebsiella spp. (n = 28, 9.6%). All Staphylococcus aureus tested were resistant to penicillin (n = 22, 100%) and susceptible to vancomycin. Significant resistance to cephalosporins such as cefazolin (n = 62, 72.9%), ceftriaxone (n = 44, 51.8%) and ceftazidime (n = 40, 37.4%) was observed in Gram-negative bacteria, as well as resistance to cefoxitin (n = 6, 27.3%) in S. aureus.
**CONCLUSION**: The study has revealed a wide range of causative agents, with an alarming rate of resistance to the commonly used antimicrobial agents. Furthermore, the bacterial spectrum differs from those often observed in high-income countries. This highlights the imperative of regular generation of data on aetiological agents and their antimicrobial susceptibility patterns especially in infectious disease endemic settings. The key steps would be to ensure the diagnostic capacity at a sufficient number of sites and implement structures to routinely exchange, compare, analyse and report data. Sentinel sites (hospitals) across the country (and region) should report on a representative subset of bacterial species and their susceptibility to drugs at least annually. A central organising body should collate the data and report to relevant national and international stakeholders.

## Essential Drugs and Vaccines

**Defining pharmaceutical systems strengthening: concepts to enable measurement**
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Pharmaceutical products are indispensable for improving health outcomes. An extensive body of work on access to and use of medicines has resulted in an assortment of tools measuring various elements of pharmaceutical systems. Until now however, there has been little attempt to conceptualize a pharmaceutical system as an entity and define its strengthening in a way that allows for measuring systems strengthening. The narrow focus of available tools limits their value in ascertaining which interventions result in stronger, more resilient systems. We sought to address this shortcoming by revisiting the current definitions, frameworks and assessment tools related to pharmaceutical systems. We conducted a comprehensive literature review and consulted with select pharmaceutical experts. On the basis of our review, we propose that a pharmaceutical system consists of all structures, people, resources, processes, and their interactions within the broader health system that aim to ensure equitable and timely access to safe, effective, quality pharmaceutical products and related services that promote their appropriate and cost-effective use to improve health outcomes. We further propose that pharmaceutical systems strengthening is the process of identifying and implementing strategies and actions that achieve coordinated and sustainable improvements in the critical components of a pharmaceutical system to make it more responsive and resilient and to enhance its performance for achieving better health outcomes. Finally, we established that, in addition to system performance and resilience, seven components of the pharmaceutical system are critical for measuring pharmaceutical systems strengthening: pharmaceutical products and related services; policy, laws and governance; regulatory systems; innovation, research and development, manufacturing, and trade; financing; human resources; and information. This work adds clarity to the concept of pharmaceutical systems and their strengthening by proposing holistic definitions on the basis of systems thinking. It provides a practical starting point for measuring the progress of pharmaceutical systems strengthening.

# Health systems & Health Policy

**The impact of health insurance on maternal health care utilization: evidence from Ghana, Indonesia and Rwanda**
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While research has assessed the impact of health insurance on health care utilization, few studies have focused on the effects of health insurance on use of maternal health care. Analyzing nationally representative data from the Demographic and Health Surveys (DHS), this study estimates the impact of health insurance status on the use of maternal health services in three countries with relatively high levels of health insurance coverage—Ghana, Indonesia and Rwanda. The analysis uses propensity score matching to adjust for selection bias in health insurance uptake and to assess the effect of health insurance on four measurements of maternal health care utilization: making at least one antenatal care visit; making four or more antenatal care visits; initiating antenatal care within the first trimester and giving birth in a health facility. Although health insurance schemes in these three countries are mostly designed to focus on the poor, coverage has been highly skewed toward the rich, especially in Ghana and Rwanda. Indonesia shows less variation in coverage by wealth status. The analysis found significant positive effects of health insurance coverage on at least two of the four measures of maternal health care utilization in each of the three countries. Indonesia stands out for the most systematic effect of health insurance across all four measures. The positive impact of health insurance appears more consistent on use of facilitybased delivery than use of antenatal care. The analysis suggests that broadening health insurance to include income-sensitive premiums or exemptions for the poor and low or no copayments can increase use of maternal health care.

**Benefit incidence analysis of healthcare in Bangladesh – equity matters for universal health coverage**
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**Background**: Equity in access to and utilization of healthcare is an important goal for any health system and an essential prerequisite for achieving Universal Health Coverage for any country. Objectives: This study investigated the extent to which health benefits are distributed across socioeconomic groups; and how different types of providers contribute to inequity in health benefits of Bangladesh.
**Methodology**: The distribution of health benefits across socioeconomic groups was estimated using concentration indices. Health benefits from three types of formal providers were analysed (public, private and NGO providers), separated into rural and urban populations. Decomposition of concentration indices into types of providers quantified the relative contribution of providers to the overall distribution of benefits across socioeconomic groups. Eventually, the distribution of bene- fits was compared to the distribution of healthcare need (proxied by 'self-reported illness and symptoms') across socioeconomic groups. Data from the latest Household Income and Expenditure Survey, 2010 and WHO-CHOICE were used.
**Results**: An overall pro-rich distribution of healthcare benefits was observed (CI = 0.229, t-value = 9.50). Healthcare benefits from private providers (CI = 0.237, t-value = 9.44) largely favoured the richer socioeconomic groups. Little evidence of inequity in benefits was found in public (CI = 0.044, t-value = 2.98) and NGO (CI = 0.095, t-value = 0.54) providers. Private providers contributed by 95.9% to overall inequity. The poorest socioeconomic group with 21.8% of the need for healthcare received only 12.7% of the benefits, while the richest group with 18.0% of the need accounted for 32.8% of the health benefits.
**Conclusion**: Overall healthcare benefits in Bangladesh were pro-rich, particularly because of health benefits from private providers. Public providers were observed to contribute relatively slightly to inequity. The poorest (richest) people with largest (least) need for healthcare actually received lower

(higher) benefits. When working to achieve Universal Health Coverage in Bangladesh, particular consideration should be given to ensuring that private sector care is more equitable.

# HIV

## 7. BMJ 2017;356:j1053
**Pre-exposure prophylaxis for infants exposed to HIV through breast feeding**
Philippe Van de Perre et al., p-van_de_perre@chu-montpellier.fr

Philippe Van de Perre and colleagues say current strategies for preventing transmission of HIV infection from mother to child are inadequate and call for infants to be given pre-exposure prophylaxis The AIDS 2016 conference, held in July in Durban, South Africa, lauded pre-exposure prophylaxis (PrEP) as the way forward for substantially reducing the rate of new HIV infections worldwide. PrEP is defined as the continuous or intermittent use of an antiretroviral drug or drug combination to prevent HIV infection in people exposed to the virus. The underlying pathophysiological rationale is that impregnating uninfected cells and tissues with an antiviral drug could prevent infection by both cell-free and cell-associated HIV (cell-to-cell transfer). PrEP's tolerance and efficacy have been demonstrated in well designed clinical trials in men who have sex with men (MSM). In the Ipergay trial, 86% of HIV infections were averted in highly exposed men. PrEP has also been evaluated in other highly exposed groups such as transgender women, injecting drug users, serodiscordant heterosexual couples, and commercial sex workers.
HIV exposed children: lost in translation
Uninfected pregnant or breastfeeding women in high incidence areas have also been suggested as a potential target population for PrEP, but infants exposed to HIV through breast feeding have not been mentioned. Numerous public declarations and petitions have produced a strong advocacy for extension of the PrEP principle to all high risk populations exposed to HIV, considering access to PrEP as part of human rights. Recently, the World Health Organization recommended offering PrEP to any population in which the expected incidence of HIV infection is above 3 per 100 person-years. So why are breastfed infants born to HIV infected women, a population that often has an overall HIV acquisition rate above 3/100 person-years, not receiving this clearly beneficial preventive health measure?

## 8. PLoS Med 14(4): e1002253
RESEARCH ARTICLE **Status and methodology of publicly available national HIV care continua and 90-90-90 targets: A systematic review**
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**Background**: In 2014, the Joint United Nations Program on HIV/AIDS (UNAIDS) issued treatment goals for human immunodeficiency virus (HIV). The 90-90-90 target specifies that by 2020, 90% of individuals living with HIV will know their HIV status, 90% of people with diagnosed HIV infection will receive antiretroviral treatment (ART), and 90% of those taking ART will be virally suppressed. Consistent methods and routine reporting in the public domain will be necessary for tracking progress towards the 90-90-90 target.
**Methods and findings**: For the period 2010–2016, we searched PubMed, UNAIDS country progress reports, World Health Organization (WHO), UNAIDS reports, national surveillance and program reports, United States President's Emergency Plan for AIDS Relief (PEPFAR) Country Operational Plans, and conference presentations and/or abstracts for the latest available national HIV care continuum in the public domain. Continua of care included the number and proportion of people living with HIV (PLHIV) who are diagnosed, on ART, and virally suppressed out of the estimated number of PLHIV. We ranked the described methods for indicators to derive high-, medium-, and low-quality continuum. For 2010–2016, we identified 53 national care continua with viral suppression estimates representing 19.7 million (54%) of the 2015 global estimate of PLHIV. Of the 53, 6 (with 2% of global burden) were high quality, using standard surveillance methods to derive an overall denominator and program data from national cohorts for estimating steps in the continuum. Only nine countries in sub-Saharan Africa had care continua with viral suppression estimates. Of the 53

countries, the average proportion of the aggregate of PLHIV from all countries on ART was 48%, and the proportion of PLHIV who were virally suppressed was 40%. Seven countries (Sweden, Cambodia, United Kingdom, Switzerland, Denmark, Rwanda, and Namibia) were within 12% and 10% of achieving the 90-90-90 target for "on ART" and for "viral suppression," respectively. The limitations to consider when interpreting the results include significant variation in methods used to determine national continua and the possibility that complete continua were not available through our comprehensive search of the public domain.

**Conclusions**: Relatively few complete national continua of care are available in the public domain, and there is considerable variation in the methods for determining progress towards the 90-90-90 target. Despite bearing the highest HIV burden, national care continua from sub-Saharan Africa were less likely to be in the public domain. A standardized monitoring and evaluation approach could improve the use of scarce resources to achieve 90-90-90 through improved transparency, accountability, and efficiency.

## 9.  PLoS Med 14(4): e1002262

POLICY FORUM **Community-based strategies to strengthen men's engagement in the HIV care cascade in sub-Saharan Africa**

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Summary points
• Men in sub-Saharan Africa are less likely than women to engage in HIV services across the care cascade, resulting in poorer clinical outcomes.
• Health care facilities have achieved limited HIV testing and treatment coverage in men, with barriers including confidentiality concerns, distance to the facility, inconvenient hours, and perceptions that facilities provide women-centered services. Other barriers to male engagement include stigma, poverty, and feelings of compromised masculinity associated with seeking health care.
• Community-based HIV interventions can overcome barriers associated with facilities and increase men's engagement in care. Social and livelihood interventions can reduce stigma and poverty. • Community-based testing interventions (particularly home and mobile) have high acceptability and reach more men than health care facility-based approaches. For men testing HIV positive, providing immediate antiretroviral therapy (ART) is associated with high retention and viral suppression. This strategy of "collapsing the cascade" provides streamlined services and reduces loss to follow-up.
• Community-based interventions should be tailored to the needs of men to maximize uptake, including flexible hours, multiple follow-up visits, and convenient and private access to care. Integrating HIV testing into screening for chronic disease can reduce stigma and increase program efficiency. More research is needed on male-centered approaches to increase men's engagement in HIV services, particularly later in the cascade. Interventions targeted to men who have sex with men are urgently needed.
• The current state of evidence strongly suggests that community-based test-and-treat strategies can reduce the gender disparity in HIV testing and treatment by achieving higher levels of ART coverage and viral suppression in HIV-positive men.

## 10.  Trop Med Int Health 2017 May;22(5):516-525

**Physical function, grip strength and frailty in people living with HIV in sub-Saharan Africa: systematic review**

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**Objective**: To present the current knowledge on physical function, grip strength and frailty in HIV-infected patients living in sub-Saharan Africa, where the phenomenon is largely underestimated.
**Methods**: A systematic search was conducted on MEDLINE, Scopus and African Index Medicus. We reviewed articles on sub-Saharan African people living with HIV (PLHIV) >18 years old, published until November 2016.

**Results**: Of 537 articles, 12 were conducted in six African countries and included in this review. Five articles reported information on functional limitation and one on disability. Two of these five articles reported functional limitation (low gait speed) in PLHIV. Disability was observed in 27% and 3% of PLHIV living in rural and urban places, respectively. Two of three studies reporting grip strength reported lower grip strength (nearly 4 kg) in PLHIV in comparison with uninfected patients. One study reported that PLHIV were more likely to be frail than HIV-uninfected individuals (19.4% vs. 13.3%), whereas another reported no statistical difference.

**Conclusion**: Decline in physical function, grip strength and frailty are now part of the burden of PLHIV living in SSA countries, but current data are insufficient to characterise the real public health dimension of these impairments. Further studies are needed to depict this major public health challenge. As this is likely to contribute to a significant burden on the African healthcare systems and human resources in the near future, a holistic care approach should be developed to inform guidelines.

# Mental Health

## 11. PLoS Med 14(3): e1002271
PERSPECTIVE (abridged)
**Dementia in low-income and middle-income countries: Different realities mandate tailored solutions**

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The ageing of populations is the most significant social transformation of the 21st century and has highlighted the importance of age-related conditions such as dementia, which has been recognised across regions, countries, and cultures. The number of people living with dementia has been increasing and is estimated to reach 75 million worldwide by 2030, with the majority of these individuals living in low-income and middle-income countries (LMICs). The assessment, recognition, and care of people living with dementia in LMICs are complex issues. Dementia is often seen as part of the ageing process, and even when recognized, there still remain problems related to stigma, lack of resources for the adequate care of people with dementia (PWD), variations in the way the condition is assessed and perceived, and how it is addressed in noncommunicable disease (NCD) policies and prevention strategies.

Prevalence: Ageing across the world's populations is not a homogenous and uniform process. Over the next 15 years, the number of older people is projected to increase by 71% in Latin America and the Caribbean, 66% in Asia, 64% in Africa, 47% in Oceania, 41% in North America, and 23% in Europe. The differences in the base populations and the rates of growth and longevity mean there will be wide variations between regions. While the estimates of people living with dementia across regions and countries show a clear increase in numbers, differences in prevalence rates have been reported. A recent systematic review of the global prevalence of dementia showed that age-standardized prevalence (to the population of western Europe) varied from 2.1% in sub-Saharan Africa to 8.5% in Latin America. While true differences in population prevalence exist (attributed to differing genetic and environmental factors, life expectancy, duration with disease, and age-specific incidence), variations in prevalence data may also be due to the use of different data collection procedures (one stage/two stage), assessment schedules, diagnostic criteria, and cultural conceptions of the condition. The relative success of programmes in HICs and their replication in successful projects in LMICs do not necessarily guarantee the possibility of scaling them up or their cost-effectiveness when rolled out to larger populations. The distinctive context of care for older people in LMICs argues for a need to tailor solutions to the prevalent reality. Each country will have to find its best response within the context of its own limitations and possibilities, but it should be based on knowledge of local resources and burden of disease so that its impact can be evaluated and the most effective and sustainable response be delivered.

# Mother and Child health/Sexual Reproductive Health

**Practice: Clinical updates: Community acquired pneumonia in children**
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What you need to know
- Introduction of the pneumococcal conjugate vaccine has significantly reduced rates of community acquired pneumonia (CAP) in the developed world
- Clinical assessment requires careful evaluation of clinical features, severity, and evidence of complications
- Children with mild to moderate symptoms can be managed in the community
- Recommended empirical first line treatment is oral amoxicillin. Intravenous antibiotics are indicated in children who cannot tolerate oral medicines or have septicaemia or complications
- Patients should be reviewed 48 hours after starting treatment to monitor response and for evidence of complications

In 2015, community acquired pneumonia (CAP) accounted for 15% of deaths in children under 5 years old globally and 922 000 deaths globally in children of all ages. It is defined as a clinical diagnosis of pneumonia caused by a community acquired infection in a previously healthy child. Clinical assessment can be challenging; symptoms vary with age and can be non-specific in young children, and aetiology is often unknown at presentation.

This article will provide an update on CAP management in otherwise healthy children outside the neonatal period and summarises recommendations from the British Thoracic Society guidelines for UK practice. Similar international guidelines, including the World Health Organisation and Infectious Diseases Society of America guidelines, have some treatment variations, probably dependent on drug availability, cost, and antibiotic resistance patterns.

How common is CAP?

Around 14.4 per 10 000 children aged over 5 years and 33.8 per 10 000 under 5 years are diagnosed with CAP annually in European hospitals. CAP is more common in the developing world, estimated at 0.28 episodes per child per year and accounting for 95% of all cases. Incidence data varies and may be explained by variation in diagnostic criteria.

**The influence of customer-medicine seller transactional dynamics on childhood diarrhoea management: a qualitative study in Ghana**
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In 2004, the World Health Organization (WHO) and United Nations Children's Fund (UNICEF) jointly revised the recommended treatment for acute paediatric diarrhoea to specify supplementing reduced osmolarity oral rehydration salts (ORS) with zinc. In many countries, however, a significant knowledge-practice gap persists in appropriate diarrhoea management among private healthcare providers. For example, the United States Agency for International Development (USAID)-funded Strengthening Health Outcomes through the Private Sector (SHOPS) project recently demonstrated that over-the-counter medicine sellers (MS) in Ghana recommended inappropriate diarrhoea treatments, despite their demonstrated knowledge of appropriate treatment protocols. To explore and explain these results, we conducted 26 focus groups with MS and their customers using an indirect elicitation approach, presenting simulated drug shop transaction scenarios for each group to analyze and discuss. Through inductive and deductive data analysis, we found that the pattern of customer-MS interactions within the transactional context plays a critical role in shaping dispensing outcomes, not only in diarrhoea management but in other contexts as well. MS who engaged and negotiated with their customers were better able to introduce and promote the appropriate diarrhoea treatment protocol. Several factors hinder optimal interactions. Although MS in fact serve as frontline medical providers, they lack the perceived status of a clinician. Moreover, the need to maintain their customer

base creates a power imbalance that favours accommodating customer requests and discourages educational interaction. Finally, many MS lack a complete understanding of the recommended treatment, limiting their ability to educate and negotiate. These findings have important implications for efforts to position community-level private providers to improve outcomes across a number of health areas; the study recommends three broad approaches related to training design, marketing, and professional linkages. More generally, behaviour change initiatives should recognize the potential impact of provider interaction dynamics in facilitating or impeding desired health outcomes.

**Point-of-care assessment of C-reactive protein and white blood cell count to identify bacterial aetiologies in malaria-negative paediatric fevers in Tanzania**
Hildenwall H et al., Department of Public Health Sciences, Karolinska Institutet, Stockholm, Sweden

**OBJECTIVE**: To assess the role of point-of-care (PoC) assessment of C-reactive protein (CRP) and white blood cell (WBC) count to identify bacterial illness in Tanzanian children with non-severe non-malarial fever.
**METHODS**: From the outpatient department of a district hospital in Tanzania, 428 patients between 3 months and 5 years of age who presented with fever and a negative malaria test were enrolled. All had a physical examination and bacterial cultures from blood and urine. Haemoglobin, CRP and WBC were measured by PoC devices.
**RESULTS**: Positive blood cultures were detected in 6/428 (1.4%) children and urine cultures were positive in 24/401 (6.0%). Mean WBC was similar in children with or without bacterial illness (14.0 × 109 , 95% CI 12.0-16.0 × 109 vs. 12.0 × 109 , 95% CI 11.4-12.7 × 109), while mean CRP was higher in children with bacterial illness (41.0 mg/l, 95% CI 28.3-53.6 vs. 23.8 mg/l, 95% CI 17.8-27.8). In ROC analysis, the optimum cut-off value for CRP to identify bacterial illness was 19 mg/l but with an area under the curve of only 0.62. Negative predictive values exceeded 80%, while positive predictive values were under 40%.
**CONCLUSION**: WBC and CRP levels had limited value in identifying children with bacterial infections. The positive predictive values for both tests were too low to be used as single tools for treatment decisions.

**Beyond counting stillbirths to understanding their determinants in low- and middle-income countries: a systematic assessment of stillbirth data availability in household surveys**
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**OBJECTIVE**: To systematically map data availability for stillbirths from all countries with Demographic and Health Surveys (DHS) surveys to outline the limitations and challenges with using the data for understanding the determinants and causes of stillbirths, and for cross-country comparisons.
**METHODS**: We assessed data sources from the DHS programme website, including published DHS reports and their associated questionnaires for surveys completed between 2005 and 2015.
**RESULTS**: Between 2005 and 2015, the DHS programme completed 114 surveys across 70 low- and middle-income countries. Ninety-eight (86.0%) surveys from 66 countries collected stillbirth data adequately to calculate a stillbirth rate, while 16 surveys from 12 countries did not. The method used to count stillbirths varied; 96 (84.2%) surveys used a live birth history with a reproductive calendar, while 16 (14.0%) surveys from 12 countries did a full pregnancy history. Based on assessment of questionnaires, antenatal and delivery care information for stillbirths was only available in 15 surveys (13.2%) from 12 countries (17.1%). Data on maternal conditions/complications were captured in 17 surveys (16.0%), but only in six could these be linked to stillbirths. Data on other recognised risk factors were scarce, varying considerably across surveys. Upon further examination of data sets from surveys with maternity care data on non-live births, we found incomplete capture of these data; only two surveys had adequately and completely collected these for stillbirths.
**CONCLUSION**: Substantial variation exists in DHS surveys in the measurement of stillbirths, with limited scope to examine risk factors or causes. Without immediate improvements, our understanding

of country-specific trends and determinants for stillbirths will remain hampered, limiting the development and prioritisation of programmatic interventions to prevent these deaths.

**Determinants of morbidity associated with infant male circumcision: community-level population-based study in rural Ghana**
Gyan T et al., School of Paediatrics and Child Health, University of Western Australia, Perth, Australia

**OBJECTIVE**: Male circumcision services have expanded throughout Africa as part of a long-term HIV prevention strategy. We assessed the effect of type of service provider (formal and informal) and hygiene practices on circumcision-related morbidities in rural Ghana.
**METHODS**: Population-based, cross-sectional study conducted between May and December 2012 involving 2850 circumcised infant males aged under 12 weeks. Multivariable logistic regression models were adjusted for maternal age, maternal education, income, birthweight and site of circumcision.
**RESULTS**: A total of 2850 (90.7%) infant males were circumcised. Overall, the risk of experiencing a morbidity (defined as complications occurring during or after the circumcision procedure as reported by the primary caregiver) was 8.1% (230). Risk was not significantly increased if the circumcision was performed by informal providers (121, 7.2%) vs. formal health service providers (109, 9.8%) [adjusted odds ratio (aOR) 1.11, 95% CI 0.80-1.47, P = 0.456]. Poor hygiene practices were associated with significantly increased risk of morbidity: no handwashing [148 (11.7%)] (aOR 1.78, 95% CI 1.27-2.52, P = 0.001); not cleaning circumcision instruments [174 (10.6%)] (aOR 1.80, 95% CI 1.27-2.54, P = 0.001); and uncleaned penile area [190 (10.0%)] (aOR 1.84, 95% CI 1.25-2.70, P = 0.002).
**CONCLUSION**: The risk of morbidity after infant male circumcision in rural Ghana is high, chiefly due to poor hygiene practices. Governmental and non-governmental organisations need to improve training of circumcision providers in hygiene practices in sub-Saharan Africa.

**Inappropriate prescription of cough remedies among children hospitalised with respiratory illness over the period 2002-2015 in Kenya**
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**OBJECTIVE**: To examine trends in prescription of cough medicines over the period 2002-2015 in children aged 1 month to 12 years admitted to Kenyan hospitals with cough, difficulty breathing or diagnosed with a respiratory tract infection.
**METHODS**: We reviewed hospitalisation records of children included in four studies providing cross-sectional prevalence estimates from government hospitals for six time periods between 2002 and 2015. Children with an atopic illness were excluded. Amongst eligible children, we determined the proportion prescribed any adjuvant medication for cough. Active ingredients in these medicines were often multiple and were classified into five categories: antihistamines, antitussives, mucolytics/expectorants, decongestants and bronchodilators. From late 2006, guidelines discouraging cough medicine use have been widely disseminated and in 2009 national directives to decrease cough medicine use were issued.
**RESULTS**: Across the studies, 17 963 children were eligible. Their median age and length of hospital stay were comparable. The proportion of children who received cough medicines shrank across the surveys: approximately 6% [95% CI: 5.4, 6.6] of children had a prescription in 2015 vs. 40% [95% CI: 35.5, 45.6] in 2002. The most common active ingredients were antihistamines and bronchodilators. The relative proportion that included antihistamines has increased over time.
**CONCLUSIONS**: There has been an overall decline in the use of cough medicines among hospitalised children over time. This decline has been associated with educational, policy and mass media interventions.

**How do low-birthweight neonates fare 2 years after discharge from a low-technology neonatal care unit in a rural district hospital in Burundi?**

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**OBJECTIVES**: As neonatal care is being scaled up in economically poor settings, there is a need to know more on post-hospital discharge and longer-term outcomes. Of particular interest are mortality, prevalence of developmental impairments and malnutrition, all known to be worse in low-birthweight neonates (LBW, <2500 g). Getting a better handle on these parameters might justify and guide support interventions. Two years after hospital discharge, we thus assessed: mortality, developmental impairments and nutritional status of LBW children.
**METHODS**: Household survey of LBW neonates discharged from a neonatal special care unit in Rural Burundi between January and December 2012.
**RESULTS**: Of 146 LBW neonates, 23% could not be traced and 4% had died. Of the remaining 107 children (median age = 27 months), at least one developmental impairment was found in 27%, with 8% having at least five impairments. Main impairments included delays in motor development (17%) and in learning and speech (12%). Compared to LBW children (n = 100), very-low-birthweight (VLBW, <1500 g, n = 7) children had a significantly higher risk of impairments (intellectual - P = 0.001), needing constant supervision and creating a household burden (P = 0.009). Of all children (n-107), 18% were acutely malnourished, with a 3½ times higher risk in VLBWs (P = 0.02).
**CONCLUSIONS**: Reassuringly, most children were thriving 2 years after discharge. However, malnutrition was prevalent and one in three manifested developmental impairments (particularly VLBWs) echoing the need for support programmes. A considerable proportion of children could not be traced, and this emphasises the need for follow-up systems post-discharge.

**Determining the effective coverage of maternal and child health services in Kenya, using demographic and health survey data sets: tracking progress towards universal health coverage**

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**OBJECTIVES**: Effective coverage (EC) is a measure of health systems' performance that combines need, use and quality indicators. This study aimed to assess the extent to which the Kenyan health system provides effective and equitable maternal and child health services, as a means of tracking the country's progress towards universal health coverage.
**METHODS AND RESULTS**: The Demographic Health Surveys (2003, 2008-2009 and 2014) and Service Provision Assessment surveys (2004, 2010) were the main sources of data. Indicators of need, use and quality for eight maternal and child health interventions were aggregated across interventions and economic quintiles to compute EC. EC has increased from 26.7% in 2003 to 50.9% in 2014, but remains low for the majority of interventions. There is a reduction in economic inequalities in EC with the highest to lowest wealth quintile ratio decreasing from 2.41 in 2003 to 1.65 in 2014, but maternal health services remain highly inequitable.
**CONCLUSIONS**: Effective coverage of key maternal and child health services remains low, indicating that individuals are not receiving the maximum possible health gain from existing health services. There is an urgent need to focus on the quality and reach of maternal and child health services in Kenya to achieve the goals of universal health coverage.

**Does targeting children with hygiene promotion messages work? The effect of handwashing promotion targeted at children, on diarrhoea, soil-transmitted helminth infections and behaviour change, in low- and middle-income countries**

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**OBJECTIVES**: To synthesise evidence on the effect of handwashing promotion interventions targeting children, on diarrhoea, soil-transmitted helminth infection and handwashing behaviour, in low- and middle-income country settings.
**METHODS**: A systematic review of the literature was performed by searching eight databases, and reference lists were hand-searched for additional articles. Studies were reviewed for inclusion according to pre-defined inclusion criteria and the quality of all studies was assessed.
**RESULTS**: Eight studies were included in this review: seven cluster-randomised controlled trials and one cluster non-randomised controlled trial. All eight studies targeted children aged 5-12 attending primary school but were heterogeneous for both the type of intervention and the reported outcomes so results were synthesised qualitatively. None of the studies were of high quality and the large majority were at high risk of bias. The reported effect of child-targeted handwashing interventions on our outcomes of interest varied between studies. Of the different interventions reported, no one approach to promoting handwashing among children appeared most effective.
**CONCLUSION**: Our review found very few studies that evaluated handwashing interventions targeting children and all had various methodological limitations. It is plausible that interventions which succeed in changing children's handwashing practices will lead to significant health impacts given that much of the attributable disease burden is concentrated in that age group. The current paucity of evidence in this area, however, does not permit any recommendations to be made as to the most effective route to increasing handwashing with soap practice among children in LMIC.

# Non Communicable Diseases

### 21. BMJ 2017;356:j667
**Particulate air pollution and mortality in 38 of China's largest cities: time series analysis**

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**Introduction**
Air pollution and its negative consequences are major public health concerns in China. According to the Global Burden of Disease Study, a loss of 25 million healthy years and more than 1.2 million premature deaths in China were attributed to outdoor air pollution in 2010. In 2012 the Organisation for Economic Co-operation and Development estimated that by 2050 as many as 3.6 million people worldwide could die prematurely from air pollution each year. Most of the deaths were estimated to occur in China and India.

**Abstract**
**Objectives** To estimate the short term effect of particulate air pollution (particle diameter <10 μm, or PM10) on mortality and explore the heterogeneity of particulate air pollution effects in major cities in China.
**Design** Generalised linear models with different lag structures using time series data.
Setting 38 of the largest cities in 27 provinces of China (combined population >200 million).
Participants 350 638 deaths (200 912 in males, 149 726 in females) recorded in 38 city districts by the Disease Surveillance Point System of the Chinese Center for Disease Control and Prevention from 1 January 2010 to 29 June 2013.
Main outcome measure Daily numbers of deaths from all causes, cardiorespiratory diseases, and non-cardiorespiratory diseases and among different demographic groups were used to estimate the associations between particulate air pollution and mortality.
**Results** A 10 µg/m3 change in concurrent day PM10 concentrations was associated with a 0.44% (95% confidence interval 0.30% to 0.58%) increase in daily number of deaths. Previous day and two day lagged PM10 levels decreased in magnitude by one third and two thirds but remained statistically significantly associated with increased mortality. The estimate for the effect of PM10 on deaths from cardiorespiratory diseases was 0.62% (0.43% to 0.81%) per 10 µg/m3 compared with 0.26% (0.09% to 0.42%) for other cause mortality. Exposure to PM10 had a greater impact on females than on males. Adults aged 60 and over were more vulnerable to particulate air pollution at high levels than those aged less than 60. The PM10 effect varied across different cities and marginally decreased in cities with higher PM10 concentrations.

**Conclusion** Particulate air pollution has a greater impact on deaths from cardiorespiratory diseases than it does on other cause mortality. People aged 60 or more have a higher risk of death from particulate air pollution than people aged less than 60. The estimates of the effect varied across cities and covered a wide range of domain.

22. Health Policy and Planning 32, 2017(3);418–429
**Perceptions on diabetes care provision among health providers in rural Tanzania: a qualitative study**

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Diabetes prevalence in Tanzania was estimated at 9.1% in 2012 among adults aged 24–65 years — higher than the HIV prevalence in the general population at that time. Health systems in lower- and middle-income countries are not designed for chronic health care, yet the rising burden of no communicable diseases such as diabetes demands chronic care services. To inform policies on diabetes care, we conducted a study on the health services in place to diagnose, treat and care for diabetes patients in rural Tanzania. The study was an exploratory and descriptive study involving qualitative methods (in-depth interviews, observations and document reviews) and was conducted in a rural district in Tanzania. Fifteen health providers in four health facilities at different levels of the health care system were interviewed. The health care organization elements of the Innovative Care for Chronic Conditions (ICCC) framework were used to guide assessment of the diabetes services in the district. We found that diabetes care in this district was centralized at the referral and district facilities, with unreliable supply of necessary commodities for diabetes care and health providers who had some knowledge of what was expected of them but felt ill-prepared for diabetes care. Facility and district level guidance was lacking and the continuity of care was broken within and between facilities. The HMIS could not produce reliable data on diabetes. Support for self management to patients and their families was weak at all levels. In conclusion, the rural district we studied did not provide diabetes care close to the patients. Guidance on diabetes service provision and human resource management need strengthening and policies related to task-shifting need adjustment to improve quality of service provision for diabetes patients in rural settings.

23. Lancet 2017 Feb 25;389(10071):847-860
**The global burden of women's cancers: a grand challenge in global health**

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In this first paper of the Series on health, equity, and women's cancers, we describe the burden of breast and cervical cancer, with an emphasis on global and regional trends in incidence, mortality, and survival, and the consequences, especially in socioeconomically disadvantaged women in different settings.
Every year, more than 2 million women worldwide are diagnosed with breast or cervical cancer, yet where a woman lives, her socioeconomic status, and agency largely determines whether she will develop one of these cancers and will ultimately survive. In regions with scarce resources, fragile or fragmented health systems, cancer contributes to the cycle of poverty. Proven and cost-effective interventions are available for both these common cancers, yet for so many women access to these is beyond reach. These inequities highlight the urgent need in low-income and middle-income countries for sustainable investments in the entire continuum of cancer control, from prevention to palliative care, and in the development of high-quality population-based cancer registries.

24. Lancet 2017 Feb 25;389(10071):861-870
Interventions to close the divide for women with breast and cervical cancer between low-income and middle-income countries and high-income countries

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Breast and cervical cancers are the commonest cancers diagnosed in women living in low-income and middle-income countries (LMICs), where opportunities for prevention, early detection, or both, are few. Yet several cost-effective interventions could be used to reduce the burden of these two cancers in resource-limited environments. Population- wide vaccination against human papillomavirus (HPV) linked to cervical screening, at least once, for adult women has the potential to reduce the incidence of cervical cancer substantially. Strategies such as visual inspection with acetic acid and testing for oncogenic HPV types could make prevention of cervical cancer programmatically feasible. These two cancers need not be viewed as inevitably fatal, and can be cured, particularly if detected and treated at an early stage. Investing in the health of girls and women is an investment in the development of nations and their futures. Here we explore ways to lessen the divide between LMICs and high-income countries for breast and cervical cancers.

25.  Lancet 2017 Feb 25;389(10071):871-880
**Changing global policy to deliver safe, equitable, and affordable care for women's cancers**
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This Series paper explores the global health and public policy landscapes that intersect with women's health and global cancer control, with new approaches to bringing policy to action. Cancer is a major global social and political priority, and women's cancers are not only a tractable socioeconomic policy target in themselves, but also an important Trojan horse to drive improved cancer control and care. Breast and cervical cancer are major threats to the health of women globally, particularly in low-income and middle-income countries. Radical progress to close the global cancer divide for women requires not only evidence-based policy making, but also broad multisectoral collaboration that capitalises on recent progress in the associated domains of women's health and innovative public health approaches to cancer care and control. Such multisectoral collaboration can serve to build health systems for cancer, and more broadly for primary care, surgery, and pathology.

# Primary Health Care

26.  Health Policy and Planning 32, 2017(3);320–328
**Ethiopia's health extension workers use of work time on duty: time and motion study**
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Ethiopia implemented an innovative community-based health program, called the health extension program, to enhance access to basic health promotion, disease prevention and selected curative services by establishing health posts in every village, also called kebeles, with average of 5000 people, staffed with two health extension workers (HEWs). This time and motion study was done to estimate the amount of time that HEWs spend on various work duties and to explore differences in urban compared with rural settings and among regions. A total of 44 HEWs were observed for 21 consecutive days, and time and motion data were collected using tablet computers. On average, HEWs were on duty for 15.5 days out of the 21 days of observation period, and on average, they stayed on duty for about 6 hours per day. Out of the total observed work time, the percentages of total time spent on various activities were as follows: providing health education or services (12.8%); participating in meetings and giving trainings (9.3%); conducting community mapping and mobilization (0.8%); recordkeeping, reporting, managing family folders (13.2%); managing commodities and supplies (1.3%); receiving supervision (3.2%); receiving training (1.6%); travel between work activities (15.5%); waiting for clients in the health post (or health centre in urban settings) (24.9%); building relationships in the community (13.3%); and other activities that could not be meaningfully categorized (4%). The proportion of time spent on different activities and the total time worked varied

significantly between rural and urban areas and among the regions (at P < 0.05). Findings of this study indicate that only a minority of HEW time is spent on providing health education and services, and substantial time is spent waiting for clients. The efficiency of the HEW model may be improved by creating more demand for services or by redesigning service delivery modalities.

**Support and performance improvement for primary health care workers in low- and middle income countries: a scoping review of intervention design and methods**
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Primary health care workers (HCWs) in low- and middle-income settings (LMIC) often work in challenging conditions in remote, rural areas, in isolation from the rest of the health system and particularly specialist care. Much attention has been given to implementation of interventions to support quality and performance improvement for workers in such settings. However, little is known about the design of such initiatives and which approaches predominate, let alone those that are most effective. We aimed for a broad understanding of what distinguishes different approaches to primary HCW support and performance improvement and to clarify the existing evidence as well as gaps in evidence in order to inform decision-making and design of programs intended to support and improve the performance of health workers in these settings. We systematically searched the literature for articles addressing this topic, and undertook a comparative review to document the principal approaches to performance and quality improvement for primary HCWs in LMIC settings. We identified 40 eligible papers reporting on interventions that we categorized into five different approaches: (1) supervision and supportive supervision; (2) mentoring; (3) tools and aids; (4) quality improvement methods, and (5) coaching. The variety of study designs and quality/ performance indicators precluded a formal quantitative data synthesis. The most extensive literature was on supervision, but there was little clarity on what defines the most effective approach to the supervision activities themselves, let alone the design and implementation of supervision programs. The mentoring literature was limited, and largely focused on clinical skills building and educational strategies. Further research on how best to incorporate mentorship into pre-service clinical training, while maintaining its function within the routine health system, is needed. There is insufficient evidence to draw conclusions about coaching in this setting, however a review of the corporate and the business school literature is warranted to identify transferrable approaches. A substantial literature exists on tools, but significant variation in approaches makes comparison challenging. We found examples of effective individual projects and designs in specific settings, but there was a lack of comparative research on tools across approaches or across settings, and no systematic analysis within specific approaches to provide evidence with clear generalizability. Future research should prioritize comparative intervention trials to establish clear global standards for performance and quality improvement initiatives. Such standards will be critical to creating and sustaining a well-functioning health workforce and for global initiatives such as universal health coverage.

# Miscellaneous

**Assessment of Global Kidney Health Care Status**
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**IMPORTANCE** Kidney disease is a substantial worldwide clinical and public health problem, but information about available care is limited.
**OBJECTIVE** To collect information on the current state of readiness, capacity, and competence for the delivery of kidney care across countries and regions of the world.
DESIGN, SETTING, AND PARTICIPANTS Questionnaire survey administered from May to September 2016 by the International Society of Nephrology (ISN) to 130 ISN-affiliated countries with sampling of key stakeholders (national nephrology society leadership, policy makers, and patient

organization representatives) identified by the country and regional nephrology leadership through the ISN.

**MAIN OUTCOMES AND MEASURES** Core areas of country capacity and response for kidney care.

**RESULTS** Responses were received from 125 of 130 countries (96%), including 289 of 337 individuals (85.8%, with a median of 2 respondents [interquartile range, 1-3]), representing an estimated 93% (6.8 billion) of the world's population of 7.3 billion. There was wide variation in country readiness, capacity, and response in terms of service delivery, financing, workforce, information systems, and leadership and governance. Overall, 119 (95%), 95 (76%), and 94 (75%) countries had facilities for hemodialysis, peritoneal dialysis, and kidney transplantation, respectively. In contrast, 33 (94%), 16 (45%), and 12 (34%) countries in Africa had facilities for hemodialysis, peritoneal dialysis, and kidney transplantation, respectively. For chronic kidney disease (CKD) monitoring in primary care, serum creatinine with estimated glomerular filtration rate and proteinuria measurements were reported as always available in only 21 (18%) and 9 (8%) countries, respectively. Hemodialysis, peritoneal dialysis, and transplantation services were funded publicly and free at the point of care delivery in 50 (42%), 48 (51%), and 46 (49%) countries, respectively. The number of nephrologists was variable and was low (< 10 per million population) in Africa, the Middle East, South Asia, and Oceania and South East Asia (OSEA) regions. Health information system (renal registry) availability was limited, particularly for acute kidney injury (8 countries [7%]) and nondialysis CKD (9 countries [8%]). International acute kidney injury and CKD guidelines were reportedly accessible in 52 (45%) and 62 (52%) countries, respectively. There was relatively low capacity for clinical studies in developing nations.

**CONCLUSIONS AND RELEVANCE** This survey demonstrated significant interregional and intraregional variability in the current capacity for kidney care across the world, including important gaps in services and workforce. Assuming the responses accurately reflect the status of kidney care in the respondent countries, the findings may be useful to inform efforts to improve the quality of kidney care worldwide.

## 29. N Engl J Med 2017;376:1561-73

**Sickle Cell Disease – Review article**

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Sickle cell disease is an increasing global health problem. Estimates suggest that every year approximately 300,000 infants are born with sickle cell anemia, which is defined as homozygosity for the sickle hemoglobin (HbS) gene (i.e., for a missense mutation [Glu6Val, rs334] in the β-globin gene [HBB]) and that this number could rise to 400,000 by 2050. Although early diagnosis, penicillin prophylaxis, blood transfusion, transcranial Doppler imaging, hydroxyurea, and hematopoietic stem-cell transplantation can dramatically improve survival and quality of life for patients with sickle cell disease, our understanding of the role of genetic and nongenetic factors in explaining the remarkable phenotypic diversity of this mendelian disease is still limited. Better prediction of the severity of sickle cell disease could lead to more precise treatment and management. Beyond well-known modifiers of disease severity, such as fetal hemoglobin (HbF) levels and α-thalassemia, other genetic variants might affect specific subphenotypes. Similarly, although the influence of altitude and temperature has long been reflected in advice to patients with sickle cell disease, recent studies of nongenetic factors, including climate and air quality, suggest more complex associations between environmental factors and clinical complications. New treatments and management strategies accounting for these genetic and nongenetic factors could substantially and rapidly improve the quality of life and reduce health care costs for patients with sickle cell disease.