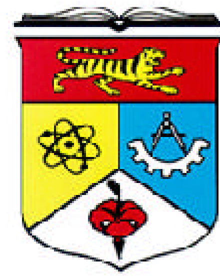
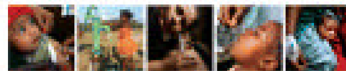


abstract of Lancet

Volume 371, Number 9620 & 9621 - April 12 & 19, 2008

THE LANCET

Countdown to 2015 for maternal, newborn, and child survival:
"Rapid progress is possible, but much more can and must be done."



THE LANCET

"A strategy of combining D-dimer and multislice CT is a safe and effective means of excluding pulmonary embolism."

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SERIES. Cronic Cough

Prevalence, pathogenesis, and causes of chronic cough.
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WORLD REPORTS

Fraser, B. (2008). Peru makes progress on maternal health. *Lancet, 371 (9620), 1233-1234.*
Peru has reduced maternal deaths by adapting health facilities to accommodate the cultural preferences of its rural population. But although this move has saved lives, many mothers are still dying because of critical problems facing health care in the country. Barbara Fraser reports. Sunday is the busiest day of the week in the tiny health centre in Quiquijana, high in the Andes Mountains of Peru. The town square fills with vendors from surrounding communities, and the health centre's dimly lit, sparsely furnished waiting room fills with women wearing the fringed, embroidered hats typical of this part of the Cusco region, many with babies slung in woven blankets on their backs. Some are pregnant, and Ninoska Mora and her staff bustle from person to person, measuring the dilation of one patient and checking the histories of others.

Kohn, D. (2008). Community involvement saves new born infants in India. *Lancet, 371 (9620), 1235-1236.*
In a rural village in India, newborn deaths have been halved not by neonatologists or high-tech interventions but by local villagers trained in simple life-saving practices. Some experts, however, are sceptical about whether this strategy can work everywhere. David Kohn reports. 4 million newborn babies die every year around the world—almost all in poor countries. Most infant mortality experts have argued that the answer is more specialised medical care. This solution, of course, is too costly for the developing world, and so in some countries little progress has been made in improving infant survival. But now some experts think that with a little training, local villagers can prevent many of these neonatal deaths themselves, with simple, inexpensive methods. This idea is controversial, though, because it shifts responsibility for infant health from doctors to poor, uneducated people with no training in neonatology.

Solberg, K.E. (2008).Health crisis amid the Maoist insurgency in India. *Lancet, 371 (9621), 1059-1060.*
The ongoing conflict between India's Maoist rebels and the government across states in the east and centre of the country has displaced thousands of people. Refugees living in camps and settlements face a multitude of health problems. Kristin Elisabeth Solberg reports. In the intense Indian midday heat, a 3-year-old barefoot refugee stumbles towards his father. Madivi Gangar's stomach is bloated, and his thin arms are dotted with the scaly patches of ringworm. With tired eyes he looks up at his father—a skinny man queuing up for basic medicines being handed out by a visiting non-governmental organisation (NGO). "We don't have anything to eat. My wife died from starvation last year", Moodivi Ramesh says as he receives a pack of painkillers. The family is among several hundred thousand caught up in an armed Maoist insurgency in the heart of India. The violent conflict, which analysts say will escalate in the coming years, has already had a devastating effect on the physical and mental health of people in affected areas, which are largely poor and rural. Malaria, diarrhoea, and skin infections flourish in the conflict zone.

Wilkinson, E. (2008). Can you pay people to be healthy? *Lancet, 371 (9621), 1325-1326.*
Several countries have used financial incentives to encourage people to adopt healthier lifestyles with encouraging results. Now this approach has been suggested in a number of UK policy documents. But what is the evidence that it works? Emma Wilkinson asks the experts. For the UK's National Health Service (NHS) to be sustainable, individuals need to take greater responsibility for their health. That was the message laid out by a major, independent review of health-care funding in the UK, published in 2002. It was followed by a government White Paper, which detailed how the NHS and other sectors could make healthy choices easier for people. Some of the proposals in Choosing Health have, 4 years later, become reality—including increased limitations on advertising of junk food to children and a smoking ban in public places.

ARTICLES

Countdown Coverage Writing Group. (2008). Count down to 2015 for maternal, newborn, and child survival: the 2008 report on tracking coverage of interventions. *Lancet, 371 (9620), 1247-1258.*
The Countdown to 2015 for Maternal, Newborn, and Child Survival initiative monitors coverage of priority interventions to achieve the Millennium Development Goals (MDG) for reduction of maternal and child mortality. We aimed to report on 68 countries which have 97% of maternal and child deaths worldwide, and on 22 interventions that have been proven to improve maternal, newborn, and child survival. We selected countries with high rates of maternal and child deaths, and interventions with the most potential to avert such deaths. We analysed country-specific data for maternal and child mortality and coverage of selected interventions. We also tracked cause-of-death profiles; indicators of nutritional status; the presence of supportive policies; financial flows to maternal, newborn, and child health; and equity in coverage of interventions. Of the 68 priority countries, 16 were on track to meet MDG 4. Of these, seven had been on track in 2005 when the Countdown initiative was launched, three (including China) moved into the on-track category in 2008, and six were included in the Countdown process for the first time in 2008. Trends in maternal mortality that would indicate progress towards MDG 5 were not available, but in most (56 of 68) countries, maternal mortality was high or very high. Coverage of different

interventions varied widely both between and within countries. Interventions that can be routinely scheduled, such as immunisation and antenatal care, had much higher coverage than those that rely on functional health systems and 24-hour availability of clinical services, such as skilled or emergency care at birth and care of ill newborn babies and children. Data for postnatal care were either unavailable or showed poor coverage in almost all 68 countries. The most rapid increases in coverage were seen for immunisation, which also received significant investment during this period. Rapid progress is possible, but much more can and must be done. Focused efforts will be needed to improve coverage, especially for priorities such as contraceptive services, care in childbirth, postnatal care, and clinical case management of illnesses in newborn babies and children. Bill & Melinda Gates Foundation, UK Department for International Development, Norwegian Agency for Development Cooperation, Partnership for Maternal, Newborn and Child Health, Save the Children US and UK, United Nations Children's Fund, United Nations Population Fund, and World Health Organization.

Countdown 2008 Equity Analysis Group. (2008). Mind the gap: equity and trends in coverage of maternal, newborn, and child health ser vices in 54 Countdown countries. *Lancet, 371 (9620), 1259-1267.*

Increasing the coverage of key maternal, newborn, and child health interventions is essential if Millennium Development Goals (MDG) 4 and 5 are to be reached. We have assessed equity and trends in coverage rates of a key set of interventions through a summary index, to provide overall insight into past performance and progress perspectives. Data from household surveys from 54 countries in the Countdown to 2015 for Maternal, Newborn and Child Survival initiative during 1990–2006 were used to compute an aggregate coverage index based on four intervention areas: family planning, maternal and newborn care, immunisation, and treatment of sick children. The four areas were given equal weight in the computation of the index. Standard measures were applied to assess current levels and trends in the coverage gap measure by wealth quintile. The overall size of the coverage gap ranged from less than 20% in Tajikistan and Peru to over 70% in Ethiopia and Chad, with a mean of 43% for the most recent surveys in the 54 countries. Large intracountry differences were noted, with a country mean coverage gap of 54% for the poorest quintiles of the population and 29% for the wealthiest. Differences between the poorest and the wealthiest were largest for the maternal and newborn health intervention area and smallest for immunisation. In 40 countries with more than one survey, the coverage gap had decreased by an average of 0.9 percentage points per year since the early 1990s. Declines greater than 2 percentage points per year were seen in only three countries after 1995: Cambodia, Mozambique, and Nepal. Country inequity patterns were remarkably persistant over time, with only gradual changes from top inequity (disproportionately smaller gap for the wealthiest) in countries with coverage gaps exceeding 40%, to linear patterns and bottom inequity (disproportionately greater gap for the poorest) in surveys with gaps below 40%. Despite most Countdown countries having made gradual progress since 1990, coverage gaps for key interventions remain wide and, in most such countries, the pace of decline needs to be more than doubled to reach levels of coverage of these and other interventions needed in the context of MDG 4 and 5. In general, in-country patterns of inequality are consistant and change only gradually if at all, which has implications for the targeting of interventions.

Greco, G., Timothy Powell-Jackson, Josephine Borgi and Anne Mills. (2008). Countdown to 2015: assessment of donor assistance to maternal, newborn, and child health between 2003 and 2006. *Lancet, 371 (9620), 1268-1275.*

To track donor assistance to maternal, newborn, and child health-related activities is necessary to assess progress towards Millennium Development Goals 4 and 5 and to foster donor accountability. Our aim was to analyse aid flows to maternal, newborn, and child health for 2005 and 2006 and trends between 2003 and 2006. We analysed and coded the complete aid activities database for 2005 and 2006 with methods that we developed previously to track official development assistance. For the 68 Countdown priority countries, we report two indicators for use in monitoring donor disbursements: official development assistance to child health per child and official development assistance to maternal and neonatal health per livebirth. Donor disbursements increased from US$2119 million in 2003 to $3482 million in 2006; funding for child health increased by 63% and that for maternal and newborn health increased by 66%. In the 68 priority countries, child-related disbursements increased from a mean of $4 per child in 2003 to $7 per child in 2006; disbursements for maternal and neonatal health increased from $7 per livebirth in 2003 to $12 per livebirth in 2006. Nonetheless, disbursements fell in some countries. After adjustment for other determinants, countries with higher under-5 mortality received more official development assistance per child, but official development assistance to maternal and newborn health did not seem to be well targeted towards countries with the greatest maternal health needs. Donor resource tracking should be continued to help hold donors accountable and encourage targeting of resources to countries with greatest needs.

Masanja, H., Don de Savigny, Paul Smithson, Joanna Schellenberg, Theopista John, Conrad Mbuya, Gabriel Upunda, Ties Boerma, Cesar Victora, Tom Smith and Hassan Mshinda. (2008). Child survival gains in Tanzania: analysis of data from demographic and health surveys. *Lan cet, 371 (9620), 1276-1283.*

A recent national survey in Tanzania reported that mortality in children younger than 5 years dropped by 24% over the 5 years between 2000 and 2004. We aimed to investigate yearly changes to identify what might have contributed to this reduction and to investigate the prospects for meeting the Millennium Development Goal for child survival (MDG 4).We analysed data from the four demographic and health surveys done in Tanzania since 1990 to generate estimates of mortality in children younger than 5 years for every 1-year period before each survey back to 1990. We estimated trends in mortality between 1990 and 2004 by fitting Lowess regression, and forecasted trends in mortality in 2005 to 2015. We aimed to investigate contextual factors, whether part of Tanzania's health system or not, that could have affected child mortality. Disaggregated estimates of mortality showed a sharp acceleration in the reduction in mortality in children younger than 5 years in Tanzania between 2000 and 2004. In 1990, the point estimate of mortality was 141·5 (95% CI 141·5–141·5) deaths per 1000 livebirths. This was reduced by 40%, to reach a point estimate of 83·2 (95% CI 70·1–96·3) deaths per 1000 livebirths in 2004. The change in absolute risk was 58·4 (95% CI 32·7–83·8; p<0·0001).

Papp, K., R Bissonnette, L Rosoph, N Wasel, CW Lynde, G Searles, NH Shear, RB Huizinga and WP Maksymowych. (2008).Efficacy of ISA247 in plaque psoriasis: a randomised, multicentre, double-blind, placebo-controlled phase III study. *Lancet, 371 (9621), 1337-1342.*

The use of systemic calcineurin inhibitors for the treatment of patients with psoriasis is limited by toxicity, particularly nephrotoxicity. ISA247, a novel inhibitor, was effective and well tolerated in a phase II study of patients with plaque psoriasis. Therefore its efficacy was assessed in this phase III study. 451 patients aged 18–65 years with plaque psoriasis involving at least 10% of the body surface area were randomly assigned in equal proportions to receive placebo or ISA247 at 0·2 mg/kg, 0·3 mg/kg, or 0·4 mg/kg orally twice a day in dermatology clinics. The primary endpoint was a 75% reduction in the psoriasis area and severity index (PASI 75) score at week 12. Treatment allocation was concealed from patient and physicians doing the assessments by use of sealed envelopes. The method of analysis was by modified intention to treat. The trial is registered at ClinicalTrials.gov, number NCT00244842. 107, 113, and 116 patients were assigned to the ISA247 0·2 mg/kg, 0·3 mg/kg, and 0·4 mg/kg groups, respectively, and 115 to the placebo group. At week 12, PASI 75 scores were achieved in the ISA247 0·2 mg/kg, 0·3 mg/kg, and 0·4 mg/kg groups by 14 (16%; 95% CI 9–24) of 105, 26 (25%; 17–24) of 111, and 44 (47%; 27–57) of 113 patients, respectively, and in the placebo group by 4 (4%; 0–8) of 113 patients. Efficacy was maintained during 24 weeks. Mild to moderate glomerular filtration rate reductions were noted in seven patients in the ISA247 0·4 mg/kg group and in one in the ISA247 0·3 mg/kg group. ISA247 blood concentrations showed a strong correlation with mean percentage reduction in PASI. ISA247 was safe and effective in the treatment of patients with moderate to severe psoriasis during 24 weeks, with the highest dose providing the best efficacy. The strong correlation between ISA247 concentrations and efficacy might allow for accurate dosing of patients compared with existing calcineurin inhibitors.

Righini, M., Grégoire Le Gal, Drahomir Aujesky, Pierre-Marie Roy, Olivier Sanchez, Franck Verschuren, Olivier Rutschmann, Michel Nonent, Jacques Cornuz, Frédéric Thys, Cédric Petit Le Manach, Marie-Pierre Revel, Pierre-Alexandre Poletti, Guy Meyer, Dominique Mottier, Thomas Perneger, and Henri Bounameaux. (2008). Diagnosis of pulmonary embolism by multidetector CT alone or combined with venous ultrasonography of the leg: a randomised non-inferiority trial. *Lancet, 371 (9621), 1343-1352.*

Multislice CT (MSCT) combined with D-dimer measurement can safely exclude pulmonary embolism in patients with a low or intermediate clinical probability of this disease. We compared this combination with a strategy in which both a negative venous ultrasonography of the leg and MSCT were needed to exclude pulmonary embolism. We included 1819 consecutive outpatients with clinically suspected pulmonary embolism in a multicentre non-inferiority randomised controlled trial comparing two strategies: clinical probability assessment and either D-dimer measurement and MSCT (DD-CT strategy [n=903]) or D-dimer measurement, venous compression ultrasonography of the leg, and MSCT (DD-US-CT strategy [n=916]). Randomisation was by computer-generated blocks with stratification according to centre. Patients with a high clinical probability according to the revised Geneva score and a negative work-up for pulmonary embolism were further investigated in both groups. The primary outcome was the 3-month thromboembolic risk in patients who were left untreated on the basis of the exclusion of pulmonary embolism by diagnostic strategy. Clinicians assessing outcome were blinded to group assignment. Analysis was per protocol. This study is registered with ClinicalTrials.gov, number NCT00117169. The prevalence of pulmonary embolism was 20·6% in both groups (189 cases in DD-US-CT group and 186 in DD-CT group). We analysed 855 patients in the DD-US-CT group and 838 in the DD-CT group per protocol. The 3-month thromboembolic risk was 0·3% (95% CI 0·1–1·1) in the

DD-US-CT group and 0·3% (0·1–1·2) in the DD-CT group (difference 0·0% [-0·9 to 0·8]). In the DD-US-CT group, ultrasonography showed a deep-venous thrombosis in 53 (9% [7–12]) of 574 patients, and thus MSCT was not undertaken. The strategy combining D-dimer and MSCT is as safe as the strategy using D-dimer followed by venous compression ultrasonography of the leg and MSCT for exclusion of pulmonary embolism. An ultrasound could be of use in patients with a contraindication to CT. Swiss National Research Foundation, Projets Hospitaliers de Recherche Clinique (France), Pneumologie Développement (France).

Wiviott, S., D., Eugene Braunwald, Carolyn H McCabe, Ivan Horvath, Matyas Keltai, Jean-Paul R Herrman, Frans Van de Werf, William E Downey, Benjamin M Scirica, Sabina A Murphy, and Elliott M Antman. (2008).In tensive oral antiplatelet therapy for reduc tion of ischaemic events including stent thrombosis in patients with acute coronary syndromes treated with percutaneous coro nary intervention and stenting in the TRI TON-TIMI 38 trial: a subanalysis of a randomised trial. *Lancet, 371 (9621), 1353-1363.*

Intracoronary stenting can improve procedural success and reduce restenosis compared with balloon angioplasty in patients with acute coronary syndromes, but can also increase the rate of thrombotic complications including stent thrombosis. The TRITON–TIMI 38 trial has shown that prasugrel—a novel, potent thienopyridine—can reduce ischaemic events compared with standard clopidogrel therapy. We assessed the rate, outcomes, and prevention of ischaemic events in patients treated with prasugrel or clopidogrel with stents in the TRITON–TIMI 38 study. Patients with moderate-risk to high-risk acute coronary syndromes were included in our analysis if they had received at least one coronary stent at the time of the index procedure following randomisation in TRITON-TIMI 38, and were further subdivided by type of stent received. Patients were randomly assigned in a 1 to 1 fashion to receive a loading dose of study drug (prasugrel 60 mg or clopidogrel 300 mg) as soon as possible after randomisation, followed by daily maintenance therapy (prasugrel 10 mg or clopidogrel 75 mg). All patients were to receive aspirin therapy. Treatment was to be continued for a minimum of 6 months and a maximum of 15 months. Randomisation was not stratified by stents used or stent type. The primary endpoint was the composite of cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke. Stent thrombosis was assessed using Academic Research Consortium definitions, and analysis was by intention to treat. TRITON-TIMI 38 is registered with ClinicalTrials.gov, number NCT00097591. 120844 patients received at least one coronary stent; 5743 received only drug-eluting stents, and 6461 received only bare-metal stents. Prasugrel compared with clopidogrel reduced the primary endpoint (9·7 vs 11·9%, HR 0·81, p=0·0001) in the stented cohort, in patients with only drug-eluting stents (9·0 vs 11·1%, HR 0·82, p=0·019), and in patients with only bare-metal stents (10·0 vs 12·2%, HR 0·80, p=0·003). Stent thrombosis was associated with death or myocardial infarction in 89% (186/210) of patients. Stent thrombosis was reduced with prasugrel overall (1·13 vs 2·35%, HR 0·48, p<0·0001), in patients with drug-eluting stents only (0·84 vs 2·31%, HR 0·36, p<0·0001), and in those with bare-metal stents only (1·27 vs 2·41%, HR 0·52, p=0·0009). Intensive antiplatelet therapy with prasugrel resulted in fewer ischaemic outcomes including stent thrombosis than with standard clopidogrel. These findings were statistically robust irrespective of stent type, and the data affirm the importance of intensive platelet inhibition in patients with intracoronary stents.

HEALTH POLICY

Countdown Working Group on Health Policy and Health Systems. (2008). Assessment of the health system and policy environment as a critical complement to tracking intervention coverage for maternal, newborn, and child health. *Lancet, 371 (9620), 1284-1293.*

In 2008, the Countdown to 2015 initiative identified 68 priority countries for action on maternal, newborn, and child health. Much attention was paid to monitoring country-level progress in achieving high and equitable coverage with interventions effective in reducing mortality of mothers, newborn infants, and children up to 5 years of age. To have a broader understanding of the environment in which health services are delivered and health outcomes are produced is essential to increase intervention coverage. Programmes to address MNCH rely on health systems to generate information needed for effective decisions and to achieve the expected outcomes. Governance and leadership are needed throughout the process not only to create policies and implement them but also to assure quality and efficiency of care, to finance health services sufficiently and in an equitable way, and to manage the health workforce. We present a systematic approach to assess the wider health system and policy environment needed to achieve positive outcomes for maternal, newborn, and child health. We report on results from 13 indicators and show gaps in policy adoption as well as weaknesses in other health system building blocks. We identify areas for future action in measurement of key indicators and their use to support decision making. We hope that this information will provide an additional dimension to the discussions on feasible and sustainable solutions to accelerate progress towards Millennium Development Goals 4 and 5, both at the global level but most importantly in individual countries.

SERIES. Cronic Cough

Chung, K.F. (2008). Prevalence, pathogenesis, and causes of chronic cough. *Lancet, 371 (9621), 1364-1374.*

Cough is a reflex action of the respiratory tract that is used to clear the upper airways. Chronic cough lasting for more than 8 weeks is common in the community. The causes include cigarette smoking, exposure to cigarette smoke, and exposure to environmental pollution, especially particulates. Diseases causing chronic cough include asthma, eosinophilic bronchitis, gastro-oesophageal reflux disease, postnasal drip syndrome or rhinosinusitis, chronic obstructive pulmonary disease, pulmonary fibrosis, and bronchiectasis. Doctors should always work towards a clear diagnosis, considering common and rare illnesses. In some patients, no cause is identified, leading to the diagnosis of idiopathic cough. Chronic cough is often associated with an increased response to tussive agents such as capsaicin. Plastic changes in intrinsic and synaptic excitability in the brainstem, spine, or airway nerves can enhance the cough reflex, and can persist in the absence of the initiating cough event. Structural and inflammatory airway mucosal changes in non-asthmatic chronic cough could represent the cause or the traumatic response to repetitive coughing. Effective control of cough requires not only controlling the disease causing the cough but also desensitisation of cough pathways.