

General

Development assistance for health, 1990–2007

It is important to monitor global health resource flows to low- and middle-income countries. An assessment of development assistance for health (DAH) for 1990–2007 has been reported.

DAH was defined as all flows for health from public and private institutions whose primary purpose is to provide development assistance to low- and middle-income countries. Total DAH grew from US\$5.6 billion in 1990 to \$21.8 billion in 2007. Between 1990 and 2007 a smaller proportion of DAH came via UN agencies and development banks and a greater proportion from the Global Fund to Fight AIDS, Tuberculosis and Malaria, the Global Alliance for Vaccines and Immunisation (GAVI), and non-governmental organisations. DAH rose sharply between 2000 and 2007. Of the \$14.5 billion DAH in 2007 for which the information was available, \$5.1 billion was for HIV/AIDS, \$0.7 billion for tuberculosis, \$0.8 billion for malaria, and \$0.9 billion for health-sector support. DAH received by low- and middle-income countries was directly related to burden of disease. DAH per head was negatively related to per head gross domestic product.

Resources for health rose between 1990 and 2007.

Ravishankar N et al. Financing of global health: tracking development assistance for health from 1990 to 2007. *Lancet* 2009; 373: 2113–24; The Lancet. Who runs global health? Ibid: 2083 (editorial); Heller PS. What can be learned from data from financing of global health? Ibid: 2087–8 (comment).

Larvae for leg ulcers

Maggots have been used to treat leg ulcers for many years but the evidence for larval therapy is sparse. Now a UK trial has shown that hydrogel is as effective.

A total of 267 patients with venous or mixed venous/arterial leg ulcers were randomised to application of loose or bagged larvae of *Lucilia sericata* or hydrogel. Larval therapy significantly reduced the time to debridement but did not speed up healing, improve quality of life, or reduce bacterial load compared with hydrogel. Pain scores were increased with larval therapy.

In a cost-effectiveness analysis it was shown that, compared with hydrogel, larval therapy increased the average cost by £96.70 per patient per year. The cost

was estimated at £8826 per QALY gained and £40 per ulcer-free day.

Larval therapy is more expensive than hydrogel and causes more pain but speeds up debridement.

Dumville JC et al. Larval therapy for leg ulcers (Ven US II): randomised controlled trial. *BMJ* 2009; 338: 1047–50; Soares MO et al. Cost effectiveness analysis of larval therapy for leg ulcers. Ibid: 1050–4; Grey JE et al. How to measure success in treating chronic leg ulcers. Ibid: 1021–2 (editorial).

Information needs of seriously ill patients in Africa

Palliative care provision in sub-Saharan Africa is patchy and often poor. Now a study in South Africa and Uganda has shown that patients with life-limiting progressive disease and their caregivers are often deprived of essential information.

The study took place in four palliative care services in South Africa and one in Uganda and included 90 patients and 38 family caregivers. Among the patients, 61 had HIV infection, 28 cancer, and one motor neurone disease. Information was collected through semistructured qualitative interviews. Patients and caregivers complained of a lack of information about their disease that adversely affected their ability to cope. There was often poor communication with health-care providers, including misinformation, secrecy, and insensitivity. Paternalism, culture, and lack of time often placed barriers in the way of communication.

Recommendations for improving communication are given.

Selman L et al. Meeting information needs of patients with incurable progressive disease and their families in South Africa and Uganda: multicentre qualitative study. *BMJ* 2009; 338: 1127–31.

Tropical

Home treatment of childhood malaria in urban Uganda: little benefit

The home management of childhood malaria in Africa (treatment of febrile children using supplied pre-packaged antimalarial drugs without diagnostic testing) is advocated by WHO. A study in Kampala, Uganda, has shown little benefit from home management.

A total of 437 children aged 1–6 years from 325 households were randomised to home supply of artemether-lumefantrine for treatment of febrile illnesses or usual care. The rate of use

of antimalarial treatments was 4.7 per person-year (home management) versus 2.5 per person-year (controls).

At final assessment the rate of parasitaemia was 2% vs 10% but other clinical outcomes were similar in the two groups. One child died in each group.

These researchers suggest that home provision of artemether-lumefantrine may not be appropriate in large urban areas or in places with fairly low malaria transmission.

Staedke SG et al. Home management of malaria with artemether-lumefantrine compared with standard care in urban Ugandan children: a randomised controlled trial. *Lancet* 2009; 373: 1623–31; Källander K, Nsungwa-Sabiiti J. Home-based management of malaria in the era of urbanisation. Ibid: 1582–4.

Community involvement in dengue mosquito control

The only way of preventing transmission of dengue currently available is control of the main vector, the *Aedes aegypti* mosquito. A trial in Guantanamo, Cuba has shown that community involvement may aid vector control. A total of 32 circumscriptions (units of about 500 houses, each unit with about 2000 inhabitants) were randomised to routine *Aedes* control (controls) or routine control with a community-based environmental management approach (intervention). In the intervention group 10–20 members in each circumscription formed working groups to promote active community involvement in environmental management. *Aedes* infestation levels were similar in the two groups at baseline. At the end of the intervention levels of infestation were significantly 50–75% lower in the intervention group than in the control group.

The community-based management was effective in reducing infestation rates.

Vanlerbergh V et al. Community involvement in dengue vector control: cluster randomised trial. *BMJ* 2009; 338: 1477–80; Elder JP, Ballenger-Browning K. Community involvement in dengue vector control. Ibid: 1453–4 (editorial).

AIDS

Community plasma HIV-1 RNA concentrations and HIV-1 incidence in injecting drug users

Highly active antiretroviral therapy (HAART) reduces plasma HIV RNA concentrations. It might, therefore, reduce transmission of HIV within the community. On the other hand the availability of HAART might encourage risky behaviour

and increase HIV transmission. Now a study in Vancouver, Canada has shown a direct relationship between community plasma HIV-1 RNA concentrations among injection drug users with HIV and HIV incidence in users without HIV.

Injecting drug users were recruited into two groups between May 1996 and June 2007. Those without HIV at baseline entered the Vancouver Injection Drug Users Study (VIDUS) and those with HIV entered the Barriers to Accessing Antiretroviral Therapy (BART) study. Participants in both studies were assessed every 6 months. Data from the BART study were used to assess community plasma HIV-1 RNA concentrations every 6 months. A total of 12435 measurements of plasma HIV-1 RNA were obtained from 622 injecting drug users with HIV and among 1429 drug users without HIV there were 155 seroconversions. After adjustment for unsafe sexual behaviour and sharing used syringes the estimated community, plasma HIV-1 RNA concentration was independently associated with time to seroconversion with a hazard ratio of 3.3 per log₁₀ increase. After 1 January 1998, when the median plasma HIV RNA concentration was <20000 copies per ml, there was no longer a significant correlation between median viral load and an HIV incidence.

Community plasma HIV-1 RNA concentrations predicted HIV incidence among injecting drug users independently of high-risk sexual behaviours and sharing of used syringes. These findings could help to guide HIV prevention and treatment.

Wood E et al. Longitudinal community plasma HIV-1 RNA concentrations and incidence of HIV-1 among injecting drug users: prospective cohort study. *BMJ* 2009; 338: 1191-4.

Fortified nutritional spread for patients starting anti-retroviral therapy in Malawi

Wasting is an important determinant of outcome among patients starting anti-retroviral therapy in sub-Saharan Africa. Now a study in Malawi has shown the benefit of a read-to-use fortified nutritional spread for underweight patients.

A total of 491 adults about to start antiretroviral therapy and with a BMI <18.5 (mean 16.5) were randomised to a ready-to-use fortified spread (FS) or a corn-soy blend (C-SB, the most commonly used food supplement). Both supplements provided about 50% of the estimated daily energy requirement. FS cost about US\$16 per patient per month and C-SB,

US\$5.40. After 14 weeks the average increase in BMI was 2.2 (FS) vs 1.7 (C-SB) and in fat free body mass 2.9 vs 2.2 kg (both differences significant). Mortality was similarly high in the two groups (27% vs 26%). There were no significant differences between groups in CD4 count, HIV viral load, quality of life, or adherence to antiretroviral therapy.

Supplementary feeding with FS produced greater weight gain than with C-SB.

Ndekha MJ et al. Supplementary feeding with either ready-to-use fortified spread or corn-soy blend in wasted adults starting antiretroviral therapy in Malawi: randomised, investigator blinded, controlled trial. *BMJ* 2009; 338: 1309-12; Rollins N. Food supplements and HIV. *Ibid*: 1282-3 (editorial).

Early vs deferred anti-retroviral therapy

There is still uncertainty about the best time to start antiretroviral therapy. Now North American data have shown that starting therapy with a relatively high CD4+ count improves survival.

Two parallel analyses included a total of 17517 symptomatic, antiretroviral-naïve, HIV-positive patients in the USA and Canada in 1996-2005. Patients were stratified according to CD4+ count at the start of treatment (351-500 or >500 cells per cu μ m). In the two analyses deferred therapy (started at 351-500 cells per cu μ m) was associated with increases in risk of death of 69% and 94%.

Early antiretroviral therapy improves survival.

Kitahata MM et al. Effect of early versus deferred antiretroviral therapy for HIV on survival. *NEJM* 2009; 360: 1815-26; Sax PE, Baden LR. When to start antiretroviral therapy - ready when you are? *Ibid*: 1897-9.

Paediatrics

Consequences of sexual violence against girls in Swaziland

The prevalence of sexual violence against girls and young women in sub-Saharan Africa has been uncertain. Now a study in Swaziland has confirmed suspicions of a high rate. One-third (33.2%) of a nationally representative sample of 1244 girls and young women aged 13-24 years reported having experienced sexual violence before the age of 18 years.

The most common perpetrators in the first incident were neighbourhood men or boys, or boyfriends or husbands, most often in the girl's home. Sexual violence was associated with an increase in the

lifetime incidences of sexually transmitted diseases, pregnancy complications, unwanted pregnancy, and self-reported feelings of depression. Preventive strategies are needed.

Reza A et al. Sexual violence and its health consequences for female children in Swaziland: a cluster survey study. *Lancet* 2009; 373: 1966-72; Murray L, Burnham G. Understanding childhood sexual abuse in Africa. *Ibid*: 1924-6 (comment).

Treatment of childhood acute lymphoblastic leukaemia without cranial irradiation

Event-free survival rates at 5 years for children with acute lymphoblastic leukaemia (ALL) have been around 80% in clinical trials. Treatment-related side-effects are common. Prophylactic cranial irradiation has been routine to prevent central nervous system (CNS) relapse but the practice has been questioned and might be replaced by intrathecal and systemic therapy. The routine omission of prophylactic cranial irradiation remains, however, controversial. Now a trial in Memphis, Tennessee and Fort Worth, Texas has led to the conclusion that with appropriate chemotherapy prophylactic cranial irradiation is not necessary.

A total of 498 children with ALL were treated without prophylactic cranial irradiation and those who would previously have received such irradiation were compared with historical controls. For all 498 patients the 5-year event-free survival was 85.6% and overall 5-year survival 93.5%. The 5-year cumulative risk of isolated CNS relapse was 2.7% and of any CNS relapse 3.9%. The 71 patients who would previously have received prophylactic cranial irradiation had significantly longer continuous complete remission than 56 historical controls. The 11 patients with isolated CNS relapse remained in second remission for 0.4-5.5 years. Poorer event-free survival was associated with CNS leukaemia or traumatic lumbar puncture with blast cells at diagnosis and a high level of minimal residual disease after 6 weeks of remission induction. Risk factors for CNS relapse included CNS involvement at diagnosis, T-cell immunophenotype, and the genetic abnormality t(1;19) (TCF3-PBX1).

These researchers conclude that with effective risk-adjusted chemotherapy, prophylactic cranial irradiation can be safely omitted from the treatment of childhood ALL.

Pui C-H et al. Treating childhood acute lymphoblastic leukemia without cranial irradiation. *NEJM* 2009; 360: 2730-41.

Obs & Gyn

Universal antenatal screening for group B streptococcus

US national guidelines have recommended universal culture-based antenatal screening for group B streptococcal colonisation since 2002 with the aim of preventing early neonatal group B streptococcal disease. After the issue of these guidelines there was a 27% fall in incidence of the disease, from 0.47 cases per 1000 live births in 1999–2001 to 0.34 cases per 1000 live births afterwards. Data from 10 states for 2003–2004 have been reported.

Data were obtained for 254 births in 2003–2004 (after which the infant developed group B streptococcal disease) and 7437 control births. Data from a 1998–1999 study were used for comparison. The rate of antenatal screening for group B streptococcus was 48% in 1998–1999 and 85% in 2003–2004, and in the same periods 26.8% vs 31.7% of women were given antibiotics in labour. Antibiotic prophylaxis was given to 87% of women who had term deliveries and were group B streptococcus-positive and to 63% of women who delivered preterm and had unknown colonisation status. Early-onset group B streptococcal disease occurred in 0.73 per 1000 preterm live births and 0.26 per 1000 term live births. Nevertheless, 74.4% of cases of group B streptococcal disease were in term infants. In all, 61.4% of cases of group B streptococcal disease in term infants were in infants whose mothers had tested negative for group B streptococcus before delivery. Missed screening accounted for 34/254 (13.4%) cases of group B streptococcal disease at term.

It is concluded that improved management of preterm deliveries and improved collection, processing, and reporting of culture results could prevent more cases of early-onset group B streptococcal disease.

Van Dyke MK et al. Evaluation of universal antenatal screening for group B streptococcus. *NEJM* 2009; 360: 2626–36.

Safety of metoclopramide for pregnancy nausea and vomiting

Metoclopramide is the first-choice drug for the treatment of nausea and vomiting in pregnancy in Israel and some European countries but is little used in North America. There have, however, been few studies of the safety of first trimester

administration of metoclopramide as regards the health of the fetus. Now a study in Israel has provided reassurance.

The computerised database study included data on 81703 singleton births between January 1998 and March 2007. Of these, 3458 (4.2%) were exposed to metoclopramide in the first trimester. Exposure was not associated with significantly increased risk of major congenital malformations, low birthweight, preterm delivery, or perinatal death.

The use of metoclopramide in the first trimester does not appear to have an adverse effect on the fetus.

Matok I et al. The safety of metoclopramide use in the first trimester of pregnancy. *NEJM* 2009; 360: 2528–35.

Longer lactation reduces risk of later cardiovascular disease

Lactation increases energy expenditure, promotes postpartum weight loss, and improves glucose tolerance and lipid metabolism. It may also have long-term beneficial effects on glucose metabolism. Now data from the US Women's Health Initiative study have linked prolonged breastfeeding with lower postmenopausal cardiovascular risk.

Data were analysed from 1395681 postmenopausal women (median age 63 years) who had had at least one live birth. A lifetime history of >12 months of lactation was associated with significant reductions of 12% in hypertension, 20% in diabetes, 19% in hyperlipidaemia, and 9% in cardiovascular disease. There was no reduction in the prevalence of obesity. Over an average of 8 years of follow-up there was a significant 28% reduction in incidence of cardiovascular disease among women who had had a single live birth and breast-fed for 7–12 months compared with similar women who did not breast feed.

Prolonged breast feeding may protect against later cardiovascular disease.

Schwarz EB et al. Duration of lactation and risk factors for maternal cardiovascular disease. *Obstet Gynecol* 2009; 113: 974–82.

Cardiology

Early angioplasty after fibrinolysis for acute myocardial infarction

Patients with acute myocardial infarction who present to less well-equipped hospitals may receive fibrinolysis rather

than percutaneous coronary intervention (PCI). Now a study in Canada has shown that early transfer for PCI may be beneficial.

A total of 1059 high-risk patients with ST elevation myocardial infarction were given fibrinolytic therapy at hospitals that did not perform PCI. They were then randomised to standard treatment (including rescue PCI if required, or delayed angiography) or immediate transfer for PCI. All patients received aspirin, tenecteplase, and heparin or enoxaparin, and clopidogrel was recommended. Cardiac catheterisation was performed in 89% of patients in the standard treatment group at a median of 32.5 hours after randomisation. In the immediate transfer group catheterisation was performed on 99% of patients at a median of 2.8 hours after randomisation. The primary endpoint (death, reinfarction, recurrent ischaemia, new or worsening heart failure, or cardiogenic shock within 30 days) occurred in 11.0% (early transfer) vs 17.2% (standard care), a highly significant 36% reduction with early transfer.

Transfer for PCI within 6 hours of fibrinolysis reduced cardiac complications.

Cantor WJ et al. Routine early angioplasty after fibrinolysis for acute myocardial infarction. *NEJM* 2009; 360: 2705–18; Verheugt FWA. Routine angioplasty after fibrinolysis – how early should 'early' be? *Ibid*: 2779–81 (editorial).

Aspirin for primary prevention of vascular disease: uncertain value

Long-term antiplatelet therapy with aspirin reduces vascular event risk among people with established vascular disease. The risks of aspirin are in this case exceeded by the benefits. For primary prevention, however, the balance of risks and benefits is not so clear. Now a meta-analysis of individual participant data from 22 trials has again cast doubt on the role of aspirin in primary prevention. The analysis included six trials of primary prevention (95 000 subjects) and 16 of secondary prevention (17 000 subjects). In the primary prevention trials, aspirin was associated with a significant 12% proportional reduction in serious vascular events, mainly nonfatal myocardial infarction. There was no significant effect on risk of stroke or overall vascular mortality. Aspirin was associated with a significant increase in risk of major gastrointestinal or other extracranial bleeding (from 0.07% to 0.10% per year). The benefits of aspirin in secondary prevention were more clear-cut with greater reduc-

tions in major vascular events, including stroke.

For primary prevention the benefits of aspirin have to be weighed against the increased risk of major bleeding.

More trials are underway.

Antithrombotic Trialists' (ATT) Collaboration. Aspirin in the primary and secondary prevention of vascular disease: collaborative meta-analysis of individual participant data from randomised trials. *Lancet* 2009; 373: 1849–60; Algra A, Greving JP. Aspirin in primary prevention: sex and baseline risk matter. *Ibid*: 1821–2.

Early intervention in acute coronary syndromes

There is still debate about the best time for intervention in acute coronary syndromes. Now a large international trial has shown benefits from early intervention.

A total of 3031 patients with acute coronary syndromes were randomised to early intervention (coronary angiography 24 hours or less after randomisation) or delayed intervention (coronary angiography 36 hours or more after randomisation). The median time to intervention was 14 hours after randomisation in the early group and 50 hours in the delayed group. The rates of PCI were 59.6% (early) versus 55.1% (delayed) and of CABG, 14.8% vs 13.6%. The primary outcome (death, myocardial infarction, or stroke within 6 months) occurred in 9.6% (early) vs 11.3% (delayed), a nonsignificant 15% reduction in the early intervention group. The prespecified secondary outcome (death, myocardial infarction, or refractory ischaemia within 6 months) occurred in 9.5% vs 12.9%, a significant 28% reduction in the early intervention group. Early intervention was associated with significant 35% improvement in the primary outcome in the third of patients at highest risk but no significant improvement in the two thirds at low to intermediate risk.

Early intervention gave better results especially in higher-risk patients.

Mehta SR et al. Early versus delayed invasive intervention in acute coronary syndromes. *NEJM* 2009; 360: 2165–75; Hillis LD, Lange RA. Optimal management of acute coronary syndromes. *Ibid*: 2237–40 (editorial).

Infection

New drug for MDR tuberculosis

Multidrug-resistant (MDR) *Mycobacterium tuberculosis* (resistant to both isoniazid and rifampicin) causes, worldwide,

about 490 000 new cases of tuberculosis and 110 000 deaths each year. New drugs are needed urgently. The new drug, TMC207, is a diarylquinoline that inhibits mycobacterial ATP synthase, a new mechanism for anti-tuberculosis drugs. Preliminary in vitro, animal, and human testing has shown it to be a drug of promise for the treatment of MDR tuberculosis. Now the results of the first stage of a phase II trial in South Africa have been reported.

A total of 47 patients with newly diagnosed MDR pulmonary tuberculosis were treated with a standard five-drug (kanamycin, ofloxacin, ethionamide, pyrazinamide, and cycloserine or terizidone) regimen, and randomised to TMC207 or placebo for 8 weeks. The rates of conversion to negative sputum cultures were 48% (TMC207) vs 9% (placebo). The time to conversion was shorter in the TMC207 group (hazard ratio 11.8) and the number of colony-forming units in sputum declined more rapidly. Adverse events were usually mild but nausea occurred in 26% vs 4%. In the second stage the study will be extended to 24 weeks.

Diacon AH et al. The diarylquinoline TMC207 for multidrug-resistant tuberculosis. *NEJM* 2009; 360: 2397–405; Barry CE. Unorthodox approach to the development of a new antituberculosis therapy. *Ibid*: 2406–7 (editorial).

Anti-tuberculosis-drug resistance worldwide

The monitoring of anti-tuberculosis drug resistance worldwide has been undertaken by the Global Project on Anti-Tuberculosis Drug Resistance since 1994. A recent report has included data from 83 countries and territories from 2002–2007, including 90 726 patients.

The average prevalence of resistance to any drug in new cases was 11%. In eight countries there was no multidrug resistance (MDR) but the prevalence was 7% at two sites in China and 7–22% in nine countries of the former Soviet Union. The prevalence of MDR tuberculosis in new cases increased between 1994 and 2007 in parts of Russia but it remained constant in Estonia and Latvia and decreased (among all cases) in Hong Kong and the USA. Thirty-seven countries reported data on extensively drug resistant (XDR) tuberculosis. Five countries of the former Soviet Union reported at least 25 cases and XDR tuberculosis occurred in 7–24% of MDR tuberculosis cases. Data from Africa are sparse.

Wright A et al. Epidemiology of antituberculosis

drug resistance 2002–07: an updated analysis of the Global Project on Anti-Tuberculosis Drug Resistance Surveillance. *Lancet* 2009; 373: 1861–73; Borgdorff MW, Small PM. Scratching the surface of ignorance on MDR tuberculosis. *Ibid*: 1822–4 (comment).

Quadrivalent HPV vaccine in women aged 24–45

The highest risk of infection with human papillomavirus (HPV) is within 5–10 years of beginning sexual activity. In Columbia the 5-year cumulative risk of cervical HPV infection was 43% among women aged 15–19 and 22% among women aged 30–44. Increasing divorce rates mean that more people acquire new sexual partners later in life and women may be again at risk in their third, fourth, and fifth decades. Now a multinational study has shown the efficacy of quadrivalent HPV vaccine in women aged 24–45 years.

A total of 3819 women aged 24–45 with no history of genital warts or cervical disease were randomised at 38 centres in seven countries to quadrivalent HPV (types 6, 11, 16, and 18) vaccine or placebo at day 1 and months 2 and 6. A total of 1910 women received at least one dose of vaccine and 1907 at least one dose of placebo. In the per-protocol population, vaccine efficacy against disease or infection related to all vaccine HPV types was 90.5%. Against disease or infection related to HPV 16 or 18 efficacy was 83.1%. In the intention-to-treat population the corresponding figures were 30.9% and 22.6% because of infection and disease at baseline. By month 7, >97% of vaccinated women had seroconverted to each vaccine HPV type. There were no serious adverse events related to the vaccine.

The quadrivalent HPV vaccine is efficacious in women aged 24–45 who are not already infected with vaccine HPV types.

Munöz N et al. Safety, immunogenicity, and efficacy of quadrivalent human papillomavirus (types 6, 11, 16, and 18) recombinant vaccine in women aged 24–45 years: a randomised, double blind trial. *Lancet* 2009; 373: 1949–57; Harper DM. Preliminary HPV vaccine results for women older than 25 years. *Ibid*: 1921–2 (comment).

Psychology

Mental disorders in China

Neuropsychiatric conditions are of immense importance in all countries. It is estimated that these conditions account for around 14% of the total global bur-

den of disease and about one-third of all adult disability. About three-quarters of the global burden of disease in low- and middle-income countries is from neuropsychiatric conditions and in middle-income countries they are the leading cause of illness in adults. Efforts to provide increased resources for mental health in middle-income countries are hampered by lack of data. Now a study in China has provided such data.

A total of 96 urban and 267 rural primary sampling sites were identified in four provinces of China with a sampling frame including 12% of the country's adult population. In all, 63 004 people were screened with an expanded version of the General Health Questionnaire and psychiatrists administered a Chinese version of the Structured Clinical Interview for Diagnostic and Statistical Manual (DSM)-IV axis 1 disorders to 16 577 people. The adjusted 1-month prevalences were 17.5% (any mental disorder), 6.1% (mood disorders), 5.6% (anxiety disorders), 5.9% (substance abuse disorders), and 1.0% (psychotic disorders). Mood disorders and anxiety disorders were more prevalent in women and in people aged 40 years or older. Alcohol use disorders were 48 times more prevalent in men. Depressive disorders and alcohol dependence were more common in the country than in towns. Almost a quarter (24%) of all people with a diagnosable mental illness were moderately or severely disabled by it. Few had had professional help: 8% had ever sought such help and 5% had ever seen a mental health professional.

Low- and middle-income countries need to acquire specific data in order to assess the resources needed for mental health services. Diagnostic methodology is discussed in a comment article.

Phillips MR et al. Prevalence, treatment, and associated disability of mental disorders in four provinces of China during 2001–05: an epidemiological survey. *Lancet* 2009; 373: 2041–53; The Lancet. Ibid: 1998 (editorial); Yang LH, Link BG; Comparing diagnostic methods for mental disorders in China. Ibid: 2002–4.

Neurology

Age and neuropathology of dementia

The incidence of dementia rises with age. In earlier old age Alzheimer's disease is considered to be the main pathology but in later old age vascular and other pathologies make a greater contribution.

Now a UK study has confirmed that the pathological features of Alzheimer's disease are more common in earlier old age.

A total of 456 brains of people aged 69–103 at death were examined. With increasing age the association between the presence of moderate or severe Alzheimer's-type pathology and dementia became less marked. At age 75 the presence of neocortical neuritic plaques increased the likelihood of dementia 8.6-fold but at age 95 the increase was only 2.5-fold. By contrast, neocortical cerebral atrophy was strongly associated with dementia at both ages.

The association between the pathological features of Alzheimer's disease and dementia is less strong in very old people.

Sawa GM et al. Age, neuropathology, and dementia. *NEJM* 2009; 360: 2302–9; Ewbank DC, Arnold SE. Cool with plaques and tangles. Ibid: 2357–9.

Surgery

Rivaroxaban v enoxaparin after knee replacement

Prophylactic drug treatment against venous thromboembolism is recommended for at least 10 days after total knee arthroplasty. Oral therapy might reduce hospital stay. Rivaroxaban is a new oral drug that inhibits factor Xa. Now a multinational trial has shown oral rivaroxaban to be better than s.c. enoxaparin.

A total of 3148 patients undergoing knee arthroplasty were randomised to oral rivaroxaban 10mg daily beginning 6–8 hours after surgery or s.c. enoxaparin 30mg every 12 hours beginning 12–24 hours after surgery. Bilateral venography was performed at 11–15 days after operation. The primary efficacy outcome (deep-vein thrombosis, nonfatal pulmonary embolism, or death from any cause up to 17 days after operation) occurred in 6.9% (rivaroxaban) and 10.1% (enoxaparin), a significant difference. Two patients died in the rivaroxaban group and three in the enoxaparin group. Asymptomatic deep vein thrombosis occurred in 55/1584 (3.5%) vs 76/1564 (4.9%). Major bleeding occurred in 0.7% vs 0.3%, a nonsignificant difference.

Oral rivaroxaban gave better results than s.c. enoxaparin.

Turpie AGG et al. Rivaroxaban versus enoxaparin for thromboprophylaxis after total knee arthroplasty (RECORD4): a randomised trial. *Lancet* 2009; 373: 1673–80; Becker RC. The importance of VTE prevention after orthopaedic surgery. Ibid: 1661–2.

Cost-effectiveness of treatments for benign prostatic hypertrophy

A 2008 review of the effectiveness of various techniques for the treatment of benign prostatic hypertrophy led to the conclusion that newer technologies were effective but were associated with higher rates of retreatment compared with transurethral resection (TUR). Now a cost-effectiveness study using Markov modelling and Monte Carlo simulation has been reported.

A strategy of diathermy vaporisation followed later, if necessary, by endoscopic holmium laser enucleation had an 85% chance of being cost-effective at a willingness-to-pay value of £20 000 per QALY gained. Other strategies using diathermy vaporisation as first treatment were cheaper and more effective than TUR repeated if necessary. Potassium titanyl phosphate laser vaporisation was unlikely to be cost-effective.

The authors of this paper conclude that initial diathermy vaporisation followed by either holmium laser enucleation or TUR are cost-effective strategies. Armstrong N et al. Surgical treatments for men with benign prostatic enlargement: cost effectiveness study. *BMJ* 2009; 338: 1187–94.

Whole body CT during trauma resuscitation

The introduction of multislice CT seriously reduced scan times and made whole-body CT feasible. The use of whole-body CT during resuscitation for major trauma has increased but the effect on outcome has been unclear. Now researchers in Germany have reported improved survival.

The retrospective multicentre study included 4621 patients, 1494 (32%) of whom had whole-body CT. The mean age was 43 years, 73% were men, and mean trauma and injury severity score (TRISS) was 30. The standardised mortality ratio was 0.75 (whole-body CT) vs 1.02 (non-whole-body CT) using TRISS and 0.87 vs 1.03 using the revised injury severity classification (RISC) score (both reductions significant). Whole-body CT was a significant independent predictor of survival. The number-needed-to-scan to save 1 life was 17 based on TRISS and 32 based on RISC.

For patients with major trauma early whole-body CT may save lives.

Huber-Wagner S et al. Effect of whole-body CT during trauma resuscitation on survival: a retrospective, multicentre study. *Lancet* 2009; 373: 1455–61; Fabian TC. Whole-body CT in multiple trauma. Ibid: 1408–9 (comment).