

Preparing for PrEP An advisory committee of the US Food and Drug Administration (FDA) has recommended approval of combined tenofovir-emtricitabine for HIV-1 pre-exposure prophylaxis (PrEP) in high-risk populations, including for serodiscordant couples and men who have sex with men. A final decision from the FDA is expected on June 15.



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Dignified death The Argentine Senate has passed a law that allows patients with incurable illnesses or injuries to refuse treatment. If patients are unable to communicate, their relatives or legal representatives can act on their behalf. Politicians stress that this legislation does not allow euthanasia, but aims to give patients and their families input into end-of-life decisions.

Too risky to publish? The UK cabinet and Health Secretary Andrew Lansley have vetoed the publication of an internal Department of Health report assessing the risks involved in the government's reform of the National Health Service. Critics are concerned that the government is preventing publication to cover up substantial criticisms of the reforms.

Initiatives to spur R&D The International Federation of Pharmaceutical Manufacturers and Associations has released a review of initiatives to boost research and development (R&D) for HIV, tuberculosis, malaria, and neglected tropical diseases. The study encourages optimisation of various steps in the R&D process and mechanisms that effectively address its complexities.

African maternal deaths South Africa's Minister of Health has launched the African Union Commission's Campaign for Accelerated Reduction of Maternal Mortality in Africa, which is supported by the UN and other organisations. The initiative aims to reduce the high number of pregnancy-related deaths in Africa, and as a result to improve the health of children younger than 5 years.

Granting hope The UK's Royal College of Paediatrics and Child Health has won a £2 million grant aimed at reducing mortality in African children younger than 5 years. The college will work with six hospitals in Kenya, Rwanda, and Uganda, providing practical support, training, and mentorship. A volunteer placement scheme will also allow UK and African medics to swap locations for up to a year.

New drugs from old The US National Institutes of Health are to partner with drug manufacturers to research new uses for drug compounds that proved ineffective for their originally intended purpose. Companies will supply research groups with drug compounds and retain ownership, but the academic groups will hold intellectual property rights over anything developed.

For the UK Government's announcement about its review of the risk of NHS reform see <http://www.dh.gov.uk/health/2012/05/transition-register/>

For the report on initiatives to boost R&D on neglected diseases see http://www.ifpma.org/fileadmin/content/Publication/2012/Assembling_the_RD_puzzle_FINAL.pdf

For South Africa's launch of the Campaign for Accelerated Reduction of Maternal Mortality in Africa see <http://www.info.gov.za/speech/DynamicAction?pageid=461&sid=27013&tid=66231>

For the US report on overseas aid in times of austerity see http://www.cgdev.org/files/1426170_file_Norris_Veillette_austerity.pdf

For more on the Royal College of Paediatrics and Child Health grant award see <http://www.rcpch.ac.uk/news/royal-college-paediatrics-and-child-health-wins-%C2%A32-million-grant-reduce-under-five-mortality-af>

For more on the NIH initiative on discovering new therapeutic uses for existing molecules see <http://www.nih.gov/news/health/may2012/od-03.htm>

For the "Believe It, Do It" campaign see <http://www.unaids.org/believeitdoit/>



Reuters

Russia adopts disabled rights Russia has ratified the UN Convention on the Rights of Persons with Disabilities and committed itself to harmonising its laws with the Convention within 2 years. More than 13 million Russians, including 500 000 children, have disabilities, yet only 2% of schools have inclusive education for children with disabilities. This is scheduled to increase to 50% by 2015.

Nepal fights malaria The Government of Nepal has launched a plan to reduce the spread of malaria in the country. Last year saw 3000 infections, although there has not been a death from malaria in Nepal since 2009. The Government aims to distribute antimalarial drugs to 500 000 people in the southern parts of the country, which are most affected by the disease.

Feeling the pinch Representatives from the Center for American Progress and Center for Global Development have recommended a new bipartisan approach to overseas aid. The report urges a focus on countries that are more likely to embrace reform, acceleration of cost sharing with middle-income countries, and a switch to locally purchased food aid.

Human flesh pills Almost 17 500 pills smuggled from China have been seized by South Korean health officials. The pills, which supposedly boost stamina and health, have been found to contain the powdered flesh of babies and fetuses. The pills, first reported in a documentary in 2010, also contain large numbers of multidrug-resistant bacteria and present a health risk, officials warn.

HIV-free generation On May 8 UNAIDS launched a new campaign "Believe it. Do it" to raise awareness and promote action on the goal of ending new HIV infections in children by 2015, and ensuring HIV-infected mothers remain healthy. The campaign encourages everyone to "get the facts, send a message, and support a mother".



UNAIDS

Chronic disease management in ageing populations

The world's population is ageing owing to increasing life expectancy and declining fertility. The populations of low-income and middle-income countries are now joining those of high-income countries in facing an increasing burden of chronic diseases. A report, *Shades of gray: a cross-country study of health and well-being of the old populations in SAGE countries, 2007–2011*, jointly published on May 9 by the US Census Bureau and WHO, aims to improve documentation of health outcomes in such populations. The report focuses on six countries—China, Ghana, India, Mexico, Russia, and South Africa—which hosted 42% of the world's 1.4 billion people aged 50 years and older in 2010. The report concludes that chronic diseases are the leading cause of mortality in older people in these countries and that consequently such diseases are "certain to have a remarkable impact on the world's overall disease burden and healthcare".

The report's analyses are based on self-reported responses. Respondents were asked if they had ever been diagnosed with a chronic disease—arthritis, stroke, angina, diabetes, chronic lung disease, asthma, hypertension, or cataracts. Hypertension was the most commonly reported disorder for people aged 50 years and older, except in India, where it was the second most commonly reported disorder after arthritis. In the six countries, the health score—based on self-reported health in eight domains covering affect/emotions, cognition, interpersonal activities and relationships, mobility, pain, self-care, sleep/energy, and vision—for those with a chronic disease was lower than for those without that disease. China had the highest mean health score of 68.1 (on a scale of 0–100) for both sexes combined, with the lowest score of 54.1 in India. On the basis of the report's results, different approaches for population-based risk reduction, as well as tackling risk factors for chronic diseases, are needed.

In a Comment in today's *Lancet*, Jan De Maeseneer and colleagues argue that integrated primary care is the key to tackling non-communicable diseases (NCDs), and should go beyond case finding for disease-oriented (vertical) programmes to provide "a source of comprehensive care that integrates and coordinates care for all health problems and engages individuals, families, and the community". In linked Correspondence, Robert Beaglehole and colleagues express reservations about

such a "short-sighted" approach. NCDs require much more than a medical response. Yet community-oriented primary care, De Maeseneer and colleagues insist, could be the foundation for a health system that also addresses the social and political determinants that are so fundamental to the perpetuation of NCDs. Strengthening of people-centred and integrated primary health care to deal with all common disorders, irrespective of cause, was recognised in the political statement from the UN High-Level meeting on NCDs last September, and it is indeed an essential component of the management of older people, who might well have more than one of these chronic disorders.

Cancer was also recognised as one of the NCDs to tackle in the global agenda by the High-Level Meeting of the General Assembly of the UN. There were an estimated 12.7 million new cases of cancer globally in 2008, with about two-thirds of cancer deaths in less developed countries. In a recent article published in *The Lancet Oncology*, Catherine de Martel and colleagues provided an updated systematic analysis of the proportion of cancer cases attributable to infections globally and by region in 2008. Compared with earlier reports, the annual absolute number of cancer cases due to infection increased by about half a million since 1990, whereas the proportion of cancer cases on the basis of infection remained stable at about 16–18%. For the four main infections together, the relative contribution of human papillomavirus to cancer burden is similar in developed countries and developing countries. The contribution of *Helicobacter pylori* is proportionally larger in more developed countries, and that of hepatitis B and C virus is large in less developed countries. Most of the cases attributable to infection occurred in less developed countries and were due to preventable and treatable infections. Improved vaccination programmes could be implemented at a national level.

It is important to establish a detailed understanding of health outcomes and access to health care by older populations, especially in low-income and middle-income countries. Improving the quality and quantity of health information and measurement techniques in chronic diseases is essential for prioritising preventive programmes for ageing populations and monitoring their effectiveness in all countries, rich and poor. ■ *The Lancet*



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For *Shades of gray: a cross-country study of health and well-being of the old populations in SAGE countries, 2007–2011* see <http://www.census.gov/prod/2012pubs/p95-12-01.pdf>

Genomics and world health: a decade on

In May, 2002, under the auspices of its Advisory Committee on Health Research, WHO released *Genomics and World Health*,¹ a report that assessed genomics research and its future possibilities. The report addressed issues of equitable sharing of benefits between low-income and high-income countries, ethical concerns, and integration into delivery of health services, and gave recommendations to ameliorate the problems identified.² What progress has been made since release of the report?

The past decade has been marked by unprecedented advances in the technologies associated with genomic science, as exemplified by the dramatic increase in speed, and reduction in cost, of genome sequencing. This technology has made possible large-scale genome-wide association studies that aim to identify genes for susceptibility to chronic diseases, such as cardiovascular disease and diabetes, and hence learn more about their cause and prevention. Genomic biobanks, repositories of human DNA linked to clinical and other patient data, promise more incisive analysis of genetic risk factors.

The cautious tone of *Genomics and World Health* seems to have been justified, however. The completion of the Human Genome Project in 2003 was accompanied by predictions that its fruits would transform medical practice within 20 years. Yet, so far, applications of genomics for medical research and practice have had limited clinical benefits.³ This moderate progress partly reflects the complexity that has emerged in subsequent studies of the regulation of our genomes. Currently, it is unclear whether advances will come from the complex mathematical approaches of systems biology or by focusing on the genetic regulation of individual cells.⁴ Given these uncertainties, and the added complexity of the biology of ageing and common diseases, it is not surprising that progress has been slow. However, there is undoubtedly light on the horizon.

The application of genomics to diagnosis and prenatal detection of monogenic diseases, exemplified by the inherited disorders of haemoglobin that affect thousands of children in low-income countries, has already had a role in the control of these disorders.⁵ This progress owes much to the development of North/

South partnerships, which were strongly recommended in the WHO report. In addition, studies of the genetic variation that underlies resistance or susceptibility to common infectious agents in tropical climates are beginning to raise considerable possibilities for their more effective control. Meanwhile, work on the molecular basis of cancer, for example by the Wellcome Trust Sanger Institute's Cancer Genome Project, despite revealing underlying genetic complexity,⁶ has already provided valuable diagnostic agents following the early lead on the discovery of the *BRCA* genes and their relation to breast and ovarian cancer.⁷ This work has also anticipated the era of personalised medicine and pharmacogenomics by identifying the genetic susceptibility of particular tumours to anti-cancer therapy, in the treatment of leukaemia for example.⁸

For infectious diseases, advances in genomics research have led to the rapid identification of emerging and re-emerging pathogens, the most recent example being the identification of a new bunyavirus in China associated with severe fever with thrombocytopenia syndrome.⁹ Increasingly large databases of genome sequences of human and animal pathogens mean that early identification has been accompanied, critically, by the ability to develop rapid diagnostic tests to aid in surveillance and implementation of public health containment measures, for example, the recent discovery of the major genome region underlying artemisinin resistance in malaria.¹⁰ Future benefits are expected in therapeutics, drug discovery, and vaccine development.¹¹ The Malaria Genomic Epidemiology Network was established in 2008 to bring together researchers from 21 countries in a consortium that hopes to better understand genetic variation as an aid to eliminating malaria.¹² Although the lack of therapeutic results from similar approaches to other major infectious diseases is disappointing, it is inevitable that the development of drugs or vaccines from such research is a slow process.

Concerns about equity that were expressed in *Genomics and World Health* have been partially addressed by the creation of biobanks in such countries as China (Chinese Kadoorie Study of Chronic Disease) and Mexico (Mexico City Prospective Study). This is part of an overall desire to ensure that people worldwide benefit from advances in



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genomics research by including diverse ethnic groups in large population-scale genetic studies and not just those of European descent.^{13,14} Indeed, China has become a major player in genomics through the Beijing Genomics Institute, for example.¹⁵

Despite the important scientific advances, some ethical, legal, and social concerns remain. There are ethical, privacy, and security concerns associated with direct-to-consumer genetic testing and the establishment of biobanks, which relate mainly to interaction with patients and the problems of confidentiality, as well as continuing concerns about the potential misuse of technology itself—for example, the controversy around publication of the genetic sequence of a mutated H5N1 influenza virus created in the laboratory.¹⁶

Progress in the future will depend on the scientific community, industry, government, patient groups, and civil society organisations working together to realise the potential of genomics research. Although the technology of genetic profiling continues to improve¹⁷ there is still insufficient detailed analysis of clinical features and heterogeneity of the diseases under investigation. The rediscovery of phenomics,¹⁸ which in a clinical context comprises detailed analysis of every aspect of the diseases that are being studied, is therefore encouraging. Progress in this area will require much closer collaboration between clinicians and geneticists. Finally, genomics must not continue to neglect rare diseases, lessons learned from which have often had implications for the better understanding of common disease;¹⁹ a fact conveyed in a letter written to a colleague in 1657 by William Harvey. As evidenced by William Harvey's discoveries, revolutions in the biological sciences often take a long time to yield practical applications. Genomics, although still in its infancy, promises a great deal for the future.

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Pazopanib and the treatment palette for soft-tissue sarcoma

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Development of new therapeutics for adults with metastatic soft-tissue sarcoma has been frustratingly slow, with few effective drugs identified in the past 30 years. Despite their common mesenchymal origin, soft-tissue sarcomas are heterogeneous and increasing knowledge of their molecular biology will drive future drug development.¹ Effective targeting of *KIT* mutations by imatinib² for gastrointestinal stromal

tumours has been a notable success story in modern sarcoma therapy. Unfortunately, similar successes for other soft-tissue sarcomas have been rare, since tumour growth is usually driven by complex molecular alterations.

In *The Lancet*, Winette van der Graaf and colleagues³ report results of the PALETTE study, assessing pazopanib—an oral multitargeted angiogenesis

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