Vaccines: The Week in Review
16 January 2012
Center for Vaccine Ethics & Policy (CVEP)

http://centerforvaccineethicsandpolicy.wordpress.com/

A program of
- Center for Bioethics, University of Pennsylvania http://www.bioethics.upenn.edu/
- The Wistar Institute Vaccine Center http://www.wistar.org/vaccinecenter/default.html
- Children's Hospital of Philadelphia, Vaccine Education Center http://www.chop.edu/service/vaccine-education-center/home.html

This weekly summary targets news and events in global vaccines ethics and policy gathered from key governmental, NGO and industry sources, key journals and other sources. This summary supports ongoing initiatives of the Center for Vaccine Ethics & Policy, and is not intended to be exhaustive in its coverage. Vaccines: The Week in Review is now also posted in pdf form and as a set of blog posts at http://centerforvaccineethicsandpolicy.wordpress.com/. This blog allows full-texting searching of some 2,000 content items.

Comments and suggestions should be directed to
David R. Curry, MS
Editor and
Executive Director
Center for Vaccine Ethics & Policy
david.r.curry@centerforvaccineethicsandpolicy.org

India recorded a full year without new polio cases. A WHO report noted that India "appears to have interrupted wild poliovirus transmission, completing one year without polio since its last case, in a 2-year-old girl in the state of West Bengal, on 13 January 2011." WHO noted that India was once recognized as the world's epicentre of polio. If all pending laboratory investigations return negative, in the coming weeks India will officially be deemed to have stopped indigenous transmission of wild poliovirus. The number of polio-endemic countries, those which have never stopped indigenous wild poliovirus transmission, will then be reduced to a historical low of three: Afghanistan, Nigeria and Pakistan.

The WHO announcement noted that "global health leaders paid tribute to the Government of India for its leadership and financial commitment to the polio eradication effort, and to the millions of vaccinators, community mobilizers, Rotarians, parents and caregivers who have supported polio eradication for more than a decade. The scale of the eradication effort in India is mind-boggling: each year, more than 170 million children under the age of 5 are vaccinated in two national immunization campaigns, with up to 70 million children in the highest-risk areas vaccinated multiple times in additional special campaigns; the whole effort requires nearly a billion doses of oral polio vaccine annually."

WHO Director-General Margaret Chan said, "India's success is arguably its greatest public health achievement and has provided a global opportunity to push for the end of polio. The Global Polio Eradication Initiative is in full emergency mode and focused on using this momentum to close this crippling disease down. Stopping polio in India required creativity, perseverance and professionalism – many of the innovations in polio eradication were sparked by the challenges in India. The lessons from India must now be adapted and implemented through emergency actions to finish polio everywhere." India is described as one of the largest donors to polio eradication, largely self-financing its immunization efforts. By 2013, India will have contributed US$2 billion for its polio campaigns.
http://www.who.int/mediacentre/news/releases/2012/polio_20120113/en/index.html

The Global Network for Neglected Tropical Diseases, an initiative of the Sabin Vaccine Institute, launched the END7 Campaign, "dedicated to eliminating seven major neglected tropical diseases (NTDs) as a public health threat to poor communities by the end of 2020." The campaign noted that NTDs infect one in six people worldwide, including 500 million children, carry a higher health burden than malaria and tuberculosis, and that treatment for NTDs is one of the most cost-effective health programs available today. Pills to treat the seven leading NTDs are donated by pharmaceutical companies and many programs use existing infrastructure, such as schools and community centers, to administer the treatments. The END7 campaign "raises the public awareness and funding required to cover the costs of distributing medicine and setting up treatment programs in impoverished communities." The annual cost works out to approximately 50 cents to treat and protect one person for a whole year against all seven diseases. The announcement said that the UK and U.S. governments, as well as major pharmaceutical companies, have already made significant contributions. END7 works with global partners such as the World Health Organization and the Bill & Melinda Gates Foundation. The campaign will be managed through a Facebook hub "to promote campaign videos, photographs, success stories and other content —including a real-time donation ticker."
http://www.prnewswire.com/news-releases/major-campaign-launched-to-eliminate-seven-diseases-by-2020-136999458.html

WHO's Strategic Advisory Group of Experts (SAGE) on immunization published the report of its November 2011 meeting. The announcement noted that SAGE "recommended…that to eradicate polio there must be accountability and consequences at all levels for individuals, institutions and governments who fail to deliver on their mandates. SAGE stated unequivocally that the risk of failure to finish global polio eradication constitutes a programmatic emergency of global proportions for public health and is not acceptable under any circumstances. Moreover, the country reports produced by the Global Polio Eradication Initiative Independent Monitoring Board must identify the root causes why some infected countries are failing to interrupt transmission and hold appropriate individuals, agencies and authorities responsible. Failure, SAGE warned, would lead to a resurgence of the disease and would be seen as the most expensive public health failure in history.

"SAGE welcomed the Decade of Vaccines collaboration as a new initiative to create a global coalition to fully realize the potential of immunization in saving lives. SAGE reviewed the draft Decade of Vaccines global action plan and although the expert group supported the overall direction, it was agreed that the plan needed to be more exciting and innovative, extending the benefits of immunization beyond childhood. SAGE requested the planning teams to identify a few major "game-changers" which if implemented would have a significant impact.

"Other topics were also discussed during the meeting such as: the negotiations around the legally binding instrument on mercury and thiomersal containing vaccines; monitoring national immunization coverage and reinforcing surveillance; optimizing

immunization schedules for conjugate pneumococcal vaccines; use of hepatitis A vaccines; and progress of tuberculosis vaccine candidate trials."
Full report of the SAGE November 2011 meetingpdf, 869kb
Background documents and presentations
Agenda, list of participants and declarations of interests
http://www.who.int/immunization/newsroom/newsstory_sage_nov_2011_report/en/index.html

The Decade of Vaccines Collaboration (DoVC) initiated an online consultation capability seeking feedback on the draft Global Vaccine Action Plan (GVAP) via its website. The consultation, which complements ongoing meetings with a range of civil society organizations, governments and other stakeholders, runs 16 January – 1 February 2012. Participants are invited to register for the consultation at http://www.dovcollaboration.org/consultation/?login which leads to a password-protected area of the website where the GVAP draft is made available and an online survey is provided. The survey is focused to four questions about the GVAP draft:
- Do you feel the Global Vaccine Action Plan accurately reflects what is needed over the next decade? If not, can you provide suggestions to improve the document?
- What are the top five most transformational changes you could see in the next 10 years that would truly be "game changing?" Are they captured in the document?
- Do you feel that your stakeholder group is sufficiently and appropriately represented in the document? If not, can you provide suggestions to improve the document?
- Do you have any other comments or suggestions?
The GVAP draft will continue to evolve and will be submitted in March 2012 for World Health Assembly action when WHA meets in May, 2012.

The Pharmaceutical Research and Manufacturers of America (PhRMA), in a new report, said that **America's biopharmaceutical companies are researching 282 medicines currently in clinical trials or under review by the FDA "to help meet the unique health care needs of children and adolescents."** The reviews these medicines noting:
- 54 for cancer which, despite significant progress, is still the leading cause of death by disease among American children,
- 49 for infectious diseases, resulting in more than 164 million missed school days annually in American public schools due to the spread of infectious diseases,
- 48 for genetic disorders, including medicines for cystic fibrosis, which affects 30,000 American children and adults,
- 25 for neurologic disorders, including medicines for epilepsy, which affects more than 300,000 school children under age 14 in the United States.
The report is available here: http://bit.ly/xRAVhd
http://www.phrma.org/media/releases/nearly-300-medicines-development-meet-unique-needs-children

Twitter Watch

Items of interest from a variety of twitter feeds associated with immunization, vaccines and global public health. This capture is highly selective and is by no means intended to be exhaustive.

GAVIAlliance GAVI Alliance
Learn more about #GAVI 's pneumococcal AMC! Step by step guide to the method behind the AMC mechanism- ht.ly/8u1St #globalhealth
2 hours ago

UNDP UN Development
Be involved: @WorldBank asks for input on Global Partnership For Enhanced Social Accountability on.undp.org/wcH7h5
3 hours ago

MSF_USA Doctors w/o Borders
Two years after the EQ, the health care system in Port-au-Prince and surrounding areas is still in disarray. bit.ly/xeDXMZ #Haiti
5 hours ago

GAVIAlliance GAVI Alliance
Rigorous monitoring and the bivalent oral #polio vaccine are main factors in India's 1 year Polio-free success -http://ht.ly/8tsS5 @Rotary
14 Jan

historyvaccines History of Vaccines
Dr. Hotez gives Hilleman Lecture at CHOP: Innovations in neglected tropical diseases bit.ly/wgsVPj #vaccine #NTD
12 Jan

globalfundnews The Global Fund
We're reading: 'French Government Defends Global AIDS Fund' bit.ly/zTUb8B
13 Jan

WHO WHO
Congratulations to #India for 12 months without #polio - a remarkable milestone bit.ly/wV2c06
12 Jan

GAVIAlliance GAVI Alliance
Good news in the fight against measles! China's #measles incidence hits record low in 2011- ht.ly/8q7sr #globalhealth
11 Jan

NIAIDNews NIAID News
Healthy volunteers needed for NIAID #clinicaltrials testing #vaccines to prevent #malaria, #HIV and more go.usa.gov/RXz

11 Jan

sabinvaccine Sabin Vaccine Inst.
Water and sanitation is a human right- Dr Roses @pahowho #StopCholera
11 Jan

Journal Watch

Vaccines: The Week in Review continues its weekly scanning of key journals to identify and cite articles, commentary and editorials, books reviews and other content supporting our focus on vaccine ethics and policy. ***Journal Watch*** **is not intended to be exhaustive, but indicative of themes and issues the Center is actively tracking.** We selectively provide full text of some editorial and comment articles that are specifically relevant to our work. Successful access to some of the links provided may require subscription or other access arrangement unique to the publisher. If you would like to suggest other journal titles to include in this service, please contact David Curry at: david.r.curry@centerforvaccineethicsandpolicy.org

Annals of Internal Medicine
January 3, 2012; 156 (1 Part 1)
http://www.annals.org/content/current
[Reviewed last week]

British Medical Bulletin
Volume 100 Issue 1 December 2011
http://bmb.oxfordjournals.org/content/current
[Reviewed earlier; No relevant content]

British Medical Journal
14 January 2012 (Vol 344, Issue 7839)
http://www.bmj.com/content/current
[No relevant content]

Cost Effectiveness and Resource Allocation
(Accessed 15 January 2012)
http://www.resource-allocation.com/
[No new relevant content]

Emerging Infectious Diseases
Volume 18, Number 1—January 2012
http://www.cdc.gov/ncidod/EID/index.htm

[Reviewed earlier]

Global Health
Winter 2012
http://www.globalhealthmagazine.com/in_this_issue/
[Reviewed earlier]

Globalization and Health
[Accessed 15 January 2012]
http://www.globalizationandhealth.com/
Research
Descriptive Review and Evaluation of the Functioning of the International Health Regulations (IHR) Annex 2
Anema A, Druyts E, Hollmeyer HG, Hardiman MC and Wilson K Globalization and Health 2012, 8:1 (10 January 2012)
Open Access
Abstract (provisional)
Background
The International Health Regulations (IHRs) (2005) was developed with the aim of governing international responses to public health risks and emergencies. The document requires all 194 World Health Organization (WHO) Member States to detect, assess, notify and report any potential public health emergency of international concern (PHEIC) under specific timelines. Annex 2 of the IHR outlines decision-making criteria for State-appointed National Focal Points (NFP) to report potential PHEICs to the WHO, and is a critical component to the effective functioning of the IHRs.
Methods
The aim of the study was to review and evaluate the functioning of Annex 2 across WHO-reporting States Parties. Specific objectives were to ascertain NFP awareness and knowledge of Annex 2, practical use of the tool, activities taken to implement it, its perceived usefulness and user-friendliness. Qualitative telephone interviews, followed by a quantitative online survey, were administered to NFPs between October, 2009 and February, 2010.
Results
A total of 29 and 133 NFPs participated in the qualitative and quantitative studies, respectively. Qualitative interviews found most NFPs had a strong working knowledge of Annex 2; perceived the tool to be relevant and useful for guiding decisions; and had institutionalized management, legislation and communication systems to support it. NFPs also perceived Annex 2 as human and disease-centric, and emphasized its reduced applicability to potential PHEICs involving bioterrorist attacks, infectious diseases among animals, radio-nuclear and chemical spills, and water- or food-borne contamination. Among quantitative survey respondents, 88% reported having excellent/good knowledge of Annex 2; 77% reported always/usually using Annex 2 for assessing potential PHEICs; 76% indicated their country had some legal, regulatory or administrative provisions for using Annex 2; 95% indicated Annex 2 was always/usually useful for facilitating decisions regarding notifiability of potential PHEICs.
Conclusion

This evaluation, including a large sample of WHO-reporting States Parties, found that the IHR's Annex 2 is perceived as useful for guiding decisions about notifiability of potential PHEICs. There is scope for the WHO to expand training and guidance on application of the IHR's Annex 2 to specific contexts. Continued monitoring and evaluation of the functioning of the IHR is imperative to promoting global health security.

Health Affairs
January 2012; Volume 31, Issue 1
http://content.healthaffairs.org/content/current
Issue Theme: Confronting The Growing Diabetes Crisis [23 articles covering a range of issue relevant to this theme]
Overview Of The Crisis
Confronting The Urgent Challenge Of Diabetes: An Overview
Judith E. Fradkin
Health Aff January 2012 31:12-19; doi:10.1377/hlthaff.2011.1150
Abstract
The rising tide of diabetes has an unacceptable human and societal toll. Rates of all major forms of diabetes are increasing at enormous individual and societal cost: 8.3 percent of the US population is afflicted today, and financial costs reached $174 billion for 2007. A major cause of blindness, renal failure, amputation, and cardiovascular disease, diabetes also increases the risk of cancer and dementia and more than doubles individual health care costs. Control of glucose, blood pressure, and lipids improves outcomes. Yet diabetes management is nonetheless suboptimal, particularly in disproportionately affected poor and minority populations. Safer, less burdensome, and more personalized approaches to therapy are needed. People at high risk for type 2 diabetes must be identified if society is to realize the benefits of therapies proven to delay or prevent the disease. We have many of the tools we need to address this challenge, and we must apply them now.
Web first
Use Of 13 Disease Registries In 5 Countries Demonstrates The Potential To Use Outcome Data To Improve Health Care's Value
Stefan Larsson, Peter Lawyer, Göran Garellick, Bertil Lindahl, and Mats Lundström
Health Aff January 2012 31:220-227; published ahead of print December 7, 2011, doi:10.1377/hlthaff.2011.0762
Abstract
As health care systems worldwide struggle with rising costs, a consensus is emerging to refocus reform efforts on value, as determined by the evaluation of patient outcomes relative to costs. One method of using outcome data to improve health care value is the disease registry. An international study of thirteen registries in five countries (Australia, Denmark, Sweden, the United Kingdom, and the United States) suggests that by making outcome data transparent to both practitioners and the public, well-managed registries enable medical professionals to engage in continuous learning and to identify and share best clinical practices. The apparent result: improved health outcomes, often at lower cost. For example, we calculate that if the United States had a registry for hip replacement surgery comparable to one in Sweden that enabled reductions in the rates at which these surgeries are performed a second time to replace or repair hip

prostheses, the United States would avoid $2 billion of an expected $24 billion in total costs for these surgeries in 2015.

The Global Financial Crisis Has Led To A Slowdown In Growth Of Funding To Improve Health In Many Developing Countries

Katherine Leach-Kemon, David P. Chou, Matthew T. Schneider, Annette Tardif, Joseph L. Dieleman, Benjamin P.C. Brooks, Michael Hanlon, and Christopher J.L. Murray
Health Aff January 2012 31:228-235; published ahead of print December 14, 2011, doi:10.1377/hlthaff.2011.1154

Abstract

How has funding to developing countries for health improvement changed in the wake of the global financial crisis? The question is vital for policy making, planning, and advocacy purposes in donor and recipient countries alike. We measured the total amount of financial and in-kind assistance that flowed from both public and private channels to improve health in developing countries during the period 1990–2011. The data for the years 1990–2009 reflect disbursements, while the numbers for 2010 and 2011 are preliminary estimates. Development assistance for health continued to grow in 2011, but the rate of growth was low. We estimate that assistance for health grew by 4 percent each year from 2009 to 2011, reaching a total of $27.73 billion. This growth was largely driven by the World Bank's International Bank for Reconstruction and Development and appeared to be a deliberate strategy in response to the global economic crisis. Assistance for health from bilateral agencies grew by only 4 percent, or $444.08 million, largely because the United States slowed its development assistance for health. Health funding through UN agencies stagnated, and the Global Fund to Fight AIDS, Tuberculosis, and Malaria announced that it would make no new grants for the next two years because of declines in funding. Given the international community's focus on meeting the Millennium Development Goals by 2015 and persistent economic hardship in donor countries, continued measurement of development assistance for health is essential for policy making.

Health and Human Rights

Vol 13, No 2 (2011)
http://hhrjournal.org/index.php/hhr
[Reviewed earlier]

Health Economics, Policy and Law

Volume 7 - Special Issue 01 - January 2012
http://journals.cambridge.org/action/displayIssue?jid=HEP&tab=currentissue
[Reviewed last week]

Health Policy and Planning

Volume 27 Issue 1 January 2012
http://heapol.oxfordjournals.org/content/current
[Reviewed earlier]

Human Vaccines & Immunotherapeutics (formerly Human Vaccines)
Volume 8, Issue 1 January 2012
http://www.landesbioscience.com/journals/vaccines/toc/volume/8/issue/1/
[Reviewed last week]

International Journal of Infectious Diseases
Volume 16, Issue 1 pp. e1-e74 (January 2012)
http://www.sciencedirect.com/science/journal/12019712
[No relevant content]

JAMA
January 11, 2012, Vol 307, No. 2, pp 115-213
http://jama.ama-assn.org/current.dtl
[No relevant content]

Journal of Infectious Diseases
Volume 205 Issue 3 February 1, 2012
http://www.journals.uchicago.edu/toc/jid/current
Editorial Commentaries
Carlos G. Grijalva and Marie R. Griffin
Unveiling the Burden of Influenza-Associated Pneumococcal Pneumonia
J Infect Dis. (2012) 205(3): 355-357 doi:10.1093/infdis/jir753
Extract
In the United States alone, seasonal (interpandemic) influenza is responsible for an average of 226 000 hospitalizations and >23 000 deaths per year [1, 2]. Although all age groups are susceptible to influenza virus infections, children experience the highest disease incidence, whereas older adults suffer the most serious disease-related complications and mortality. Many of these events are secondary bacterial pneumonias, most of which are thought to be caused by Streptococcus pneumoniae (the pneumococcus). Although several observations have suggested that influenza plays an important role in the pneumococcal pneumonia incidence, its contribution has been difficult to appreciate. In this issue of the Journal, Weinberger and colleagues present an elegant assessment that helps to clarify the contribution of influenza virus infections to pneumococcal pneumonia hospitalizations during the 2009 influenza pandemic [3]. Several lines of evidence indirectly support an interaction between influenza virus and the pneumococcus: First, pneumococcal nasopharyngeal acquisition patterns mirror the seasonal patterns of influenza outbreaks [4]. Second, increases in pneumococcal pneumonias during previous influenza pandemics have been documented [5, 6]. Third, concurrent influenza infections and pneumococcal pneumonias have been described [7, 8], and prevention of these pneumonias has been demonstrated in an efficacy trial of a 9-valent pneumococcal conjugate vaccine in South African children. In that randomized study, vaccination with pneumococcal conjugate vaccine reduced the incidence of influenza-associated pneumonia (ie, pneumococcal pneumonia with concurrent influenza infection) by 45% compared with controls [9]. This decline, however, was seen only in human immunodeficiency virus–infected children, and significant reductions were also

observed for concurrent infections with parainfluenza viruses and human metapneumovirus [9 ...

VIRUSES

Daniel M. Weinberger, Lone Simonsen, Richard Jordan, Claudia Steiner, Mark Miller, and Cécile Viboud

Impact of the 2009 Influenza Pandemic on Pneumococcal Pneumonia Hospitalizations in the United States

J Infect Dis. (2012) 205(3): 458-465 doi:10.1093/infdis/jir749

Abstract

Background. Infection with influenza virus increases the risk for developing pneumococcal disease. The A/H1N1 influenza pandemic in autumn 2009 provided a unique opportunity to evaluate this relationship.

Methods. Using weekly age-, state-, and cause-specific hospitalizations from the US State Inpatient Databases of the Healthcare Cost and Utilization Project 2003–2009, we quantified the increase in pneumococcal pneumonia hospitalization rates above a seasonal baseline during the pandemic period.

Results. We found a significant increase in pneumococcal hospitalizations from late August to mid-December 2009, which corresponded to the timing of highest pandemic influenza activity. Individuals aged 5–19 years, who have a low baseline level of pneumococcal disease, experienced the largest relative increase in pneumococcal hospitalizations (ratio, 1.6 [95% confidence interval {CI}, 1.4–1.7]), whereas the largest absolute increase was observed among individuals aged 40–64 years. In contrast, there was no excess disease in the elderly. Geographical variation in the timing of excess pneumococcal hospitalizations matched geographical patterns for the fall pandemic influenza wave.

Conclusions. The 2009 influenza pandemic had a significant impact on the rate of pneumococcal pneumonia hospitalizations, with the magnitude of this effect varying between age groups and states, mirroring observed variations in influenza activity.

The Lancet

Jan 14, 2012 Volume 379 Number 9811 p93 – 192 e5 - 11
http://www.thelancet.com/journals/lancet/issue/current

Editorial

WHO and Margaret Chan: the next 5 years

The Lancet

WHO is in the process of appointing a Director-General whose tenure will run from June, 2012, to June, 2017. Margaret Chan, the current incumbent, is the only candidate standing. WHO's Executive Board will consider her appointment when they meet later this month, and the World Health Assembly will ratify the Board's decision in May. It is certain that Dr Chan will win a second term.

Her renewed appointment comes at a perilous moment for WHO. As a letter we publish online this week from Oxfam reveals, WHO is in crisis. Rescue is needed. But is this predicament a fair reflection of the Director-General's performance? No, it is not. When Dr Chan was elected she made a promise—namely, that she wanted her term to be judged by progress on health for Africa and for women. WHO's leadership of Every Woman, Every Child, the UN Secretary-General's Global Strategy on Women's and Children's Health, has been her great success these past 5 years. Add to that the

remarkable achievement in September, 2011, of a political declaration on non-communicable diseases, together with her refashioning of a failing health systems agenda around universal coverage, and you have a record that is a surprising success for an agency in the vortex of a financial emergency.

One cannot judge Dr Chan's legacy without recalling that her first priority 5 years ago was to deliver the initiatives begun by her predecessor, Dr Lee Jong-wook, who tragically died during his first term as Director-General. The most important project left unfinished was the Commission on Social Determinants of Health. Initially sceptical, Dr Chan not only saw this important report through to completion, but also became a significant champion of the social determinants agenda. Also recall that Dr Chan deftly led communications with the media and public during the 2009 influenza A H1N1 pandemic.

None of this is to say that there have not been disappointments. Her leadership team has not been a success. Only recently have the right people been selected for crucial portfolios. Several regional offices of WHO remain lacklustre backwaters. And sometimes one wishes for a sharper message, a stronger articulation of what WHO is for in the 21st century. These matters can be addressed during a second term. But that term will depend on proper financing of WHO by its donors. And here Dr Chan faces her greatest test of all.

Online First

Correspondence

Jan 13, 2012

Action to preserve WHO's core functions cannot wait for organisational reform

Mohga M Kamal-Yanni

Preview

While WHO undergoes a wide-ranging reform sparked by a US$300 million budget shortfall, the agency is facing an exodus of qualified staff that is affecting its ability to work.1 The Executive Board is due to meet on Jan 16 to agree long-term principles and priorities for the organisation; it must ensure, in particular, that core functions are accorded the priority they merit. Oxfam is especially concerned that inadequate funding will severely diminish the WHO Essential Medicines Department, which for more than three decades has had an indispensable role in enabling developing countries to access affordable medicines.

Health Policy

Building of the global movement for health equity: from Santiago to Rio and beyond

Michael Marmot, Jessica Allen, Ruth Bell, Peter Goldblatt

Summary

Health inequalities are present throughout the world, both within and between countries. The Commission on Social Determinants of Health drew attention to dramatic social gradients in health within most countries and made proposals for action. These inequalities are not inevitable. The purpose of this article is to report on activity that has taken place worldwide after the report by the Commission on Social Determinants of Health. First, we summarise the global situation. Second, we summarise an interim report of the emerging findings from an independent review of social determinants and the health divide, which was commissioned by the WHO European region. The world conference on social determinants of health will be held in Rio de Janeiro, Brazil, in

October, 2011. This summit provides an opportunity to galvanise support, prioritise action, and respond to the call by the Commission on Social Determinants of Health for social justice as a route to a fair distribution of health.

The Lancet Infectious Disease
Jan 2012 Volume 12 Number 1 p1 - 88
http://www.thelancet.com/journals/laninf/issue/current
[Reviewed earlier]

Medical Decision Making (MDM)
November/December 2011; 31 (6)
http://mdm.sagepub.com/content/current
[No relevant content]

Nature
Volume 481 Number 7380 pp113-230 12 January 2012
http://www.nature.com/nature/current_issue.html
World View
Don't censor life-saving science
Controlling who is allowed access to information about mutations in the H5N1 bird flu virus is unacceptable, says Peter Palese.
11 January 2012

The recent arguments over the creation of a transmissible form of the bird flu virus (H5N1) feel very familiar. My colleagues and I were at the centre of a similar controversy in 2005, when we reconstructed the 1918 flu virus, which had killed up to 50 million people worldwide. News stories around the globe debated the merits of our research and television pundits argued opposing viewpoints. Naturally, the US government was concerned — as it is now. Yet our research was published in full. So why are similar concerns being used now to demand unacceptable censorship of the H5N1 scientific papers?

I have spent my career studying potentially dangerous pathogens — 20 years ago, my lab developed the technique that has enabled the H5N1 researchers to insert the mutations that render the virus more easily transmissible. In the 1990s, researchers discovered degraded samples of the 1918 virus in lung tissue from US soldiers who had died from the 'Spanish flu'. Using polymerase chain reaction technology, they amplified and sequenced the virus's RNA. We then took an existing influenza virus and, one by one, swapped its genes with those from the 1918 virus, eventually recreating a live version.

As we prepared our results for publication, the US government convened the National Science Advisory Board for Biosecurity (NSABB), which advises the community about research using agents that pose threats to national security or public health. Our experiments had made some people nervous.

During our discussions with members of the NSABB, we explained the importance of bringing such a deadly pathogen back to life. Although these experiments may seem dangerously foolhardy, they are actually the exact opposite. They gave us the

opportunity to make the world safer, allowing us to learn what makes the virus dangerous and how it can be disabled. Thankfully, the discussions were largely constructive — within a week, the NSABB recommended that we continue to study the virus under biocontainment conditions, and publish the results so that other scientists could participate in the research. After we published our full paper in 2005 (T. M. Tumpey et al. Science 310, 77–80; 2005), researchers poured into the field who probably would not otherwise have done, leading to hundreds of papers about the 1918 virus. As a result, we now know that the virus is sensitive to the seasonal flu vaccine, as well as to the common flu drugs amantadine (Symmetrel) and oseltamivir (Tamiflu). Had we not reconstructed the virus and shared our results with the community, we would still be in fear that a nefarious scientist would recreate the Spanish flu and release it on an unprotected world. We now know such a worst-case scenario is no longer possible.

This experience has made the NSABB's latest recommendation — that the H5N1 researchers not reveal the mutations behind the virus's transmissibility — all the more frustrating. I make the same argument today that we made in 2005 — publishing those experiments without the details is akin to censorship, and counter to science, progress and public health. Why did the (different) members of the committee come to a different conclusion in this case? I can only hope that they take a more sensible stance and change their minds, or that the scientific community at large convinces them to do so. Certainly, the authors of the papers, as well as the journals considering them for publication (including this one), should resist the committee's unworkable compromise that the full information should be released only to approved experts, and insist on full disclosure.

Giving the full details to vetted scientists is neither practical nor sufficient. Once 20–30 laboratories with postdoctoral fellows and students have such information available, it will be impossible to keep the details secret. Even more troublesome, however, is the question of who should decide which scientists are allowed to have the information. We need more people to study this potentially dangerous pathogen, but who will want to enter a field in which you can't publish your most scientifically interesting results?

"Who will want to enter a field in which you can't publish your most scientifically interesting results?"

Knowing which mutations render the virus more dangerous could help on a public-health level — if an outbreak of bird flu occurs in Taiwan, for instance, and researchers sequence the virus and see those mutations, we would know to ramp up the production of appropriate vaccines and antiviral drugs.

Incidentally, I believe that the risk of future outbreaks in humans is low: H5N1 has had the opportunity to cause widespread pandemics for many, many decades, yet it has not done so. Although we know the virus is transmissible between ferrets, little is known about how it will behave in other animals, including humans.

The more danger a pathogen poses, the more important it is to study it (under appropriate containment conditions), and to share the results with the scientific community. Slowing down the scientific enterprise will not 'protect' the public — it only makes us more vulnerable.

Nature Medicine
January 2012, Volume 18 No 1
http://www.nature.com/nm/journal/v18/n1/index.html

[No relevant content]

Nature Reviews Immunology
January 2012 Vol 12 No 1
http://www.nature.com/nri/journal/v12/n1/index.html
[Reviewed earlier]

New England Journal of Medicine
January 12, 2012 Vol. 366 No. 2
http://content.nejm.org/current.shtml
[No relevant content]

OMICS: A Journal of Integrative Biology
http://www.liebertonline.com/toc/omi/15/11
Volume 15, Number 12
[No relevant content]

The Pediatric Infectious Disease Journal
January 2012 - Volume 31 - Issue 1 pp: A11-A12,1-9,e1-e36
http://journals.lww.com/pidj/pages/currenttoc.aspx
[reviewed last week]

Pediatrics
January 2012, VOLUME 129 / ISSUE 1
http://pediatrics.aappublications.org/current.shtml
[Reviewed earlier]

Pharmacoeconomics
January 1, 2012 - Volume 30 - Issue 1 pp: 1-81
http://adisonline.com/pharmacoeconomics/pages/currenttoc.aspx
[Reviewed earlier]

PLoS One
[Accessed 15 January 2012]
http://www.plosone.org/article/browse.action;jsessionid=577FD8B9E1F322DAA533C413369CD6F3.ambra01?field=date
Effect of Vaccines and Antivirals during the Major 2009 A(H1N1) Pandemic Wave in Norway – And the Influence of Vaccination Timing
Birgitte Freiesleben de Blasio, Bjørn G. Iversen, Gianpaolo Scalia Tomba
PLoS ONE: Research Article, published 10 Jan 2012 10.1371/journal.pone.0030018
Abstract

To evaluate the impact of mass vaccination with adjuvanted vaccines (eventually 40% population coverage) and antivirals during the 2009 influenza pandemic in Norway, we fitted an age-structured SEIR model using data on vaccinations and sales of antivirals in 2009/10 in Norway to Norwegian ILI surveillance data from 5 October 2009 to 4 January 2010. We estimate a clinical attack rate of approximately 30% (28.7–29.8%), with highest disease rates among children 0–14 years (43–44%). Vaccination started in week 43 and came too late to have a strong influence on the pandemic in Norway. Our results indicate that the countermeasures prevented approximately 11–12% of potential cases relative to an unmitigated pandemic. Vaccination was found responsible for roughly 3 in 4 of the avoided infections. An estimated 50% reduction in the clinical attack rate would have resulted from vaccination alone, had the campaign started 6 weeks earlier. Had vaccination been prioritized for children first, the intervention should have commenced approximately 5 weeks earlier in order to achieve the same 50% reduction. In comparison, we estimate that a non-adjuvanted vaccination program should have started 8 weeks earlier to lower the clinical attack rate by 50%.
In conclusion, vaccination timing was a critical factor in relation to the spread of the 2009 A(H1N1) influenza. Our results also corroborate the central role of children for the transmission of A(H1N1) pandemic influenza.

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Trends in Compulsory Licensing of Pharmaceuticals Since the Doha Declaration: A Database Analysis
Reed Beall, Randall Kuhn
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Abstract
Background
It is now a decade since the World Trade Organization (WTO) adopted the "Declaration on the TRIPS Agreement and Public Health" at its 4th Ministerial Conference in Doha. Many anticipated that these actions would lead nations to claim compulsory licenses (CLs) for pharmaceutical products with greater regularity. A CL is the use of a patented innovation that has been licensed by a state without the permission of the patent title holder. Skeptics doubted that many CLs would occur, given political pressure against CL activity and continued health system weakness in poor countries. The subsequent decade has seen little systematic assessment of the Doha Declaration's impact.
Methods and Findings
We assembled a database of all episodes in which a CL was publically entertained or announced by a WTO member state since 1995. Broad searches of CL activity were conducted using media, academic, and legal databases, yielding 34 potential CL episodes in 26 countries. Country- and product-specific searches were used to verify government participation, resulting in a final database of 24 verified CLs in 17 nations. We coded CL episodes in terms of outcome, national income, and disease group over three distinct periods of CL activity. Most CL episodes occurred between 2003 and 2005, involved drugs for HIV/AIDS, and occurred in upper-middle-income countries (UMICs).

Aside from HIV/AIDS, few CL episodes involved communicable disease, and none occurred in least-developed or low-income countries.
Conclusions
Given skepticism about the Doha Declaration's likely impact, we note the relatively high occurrence of CLs, yet CL activity has diminished markedly since 2006. While UMICs have high CL activity and strong incentives to use CLs compared to other countries, we note considerable countervailing pressures against CL use even in UMICs. We conclude that there is a low probability of continued CL activity. We highlight the need for further systematic evaluation of global health governance actions.
Editors' Summary
Background
The development of a new drug is a time-consuming and expensive process. To stimulate investment in drug development, the creators of new drugs (including the pharmaceutical companies that undertake the development and testing that is needed before any drug can be used in patients) can apply for "intellectual property rights" (a patent). Intellectual property rights protect the investments made by companies during drug development by preventing other companies from making the new drug for a fixed period of time and by providing a means by which creators of new drugs can negotiate payment from other companies for the use of their creation. Until recently, the extent and enforcement of intellectual property rights varied widely around the world. Then, in 1995, the World Trade Organization (WTO) was established. By providing a set of ground rules for trade among nations, the WTO aims to ensure that trade flows as smoothly, predictably, and freely as possible around the world. One of the founding documents of the WTO is the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement), which attempts to bring the protection of intellectual property rights (including patents) under common international rules.
Why Was This Study Done?
Unfortunately, patent protection for drugs (pharmaceuticals) means that many medicines are too expensive for use in developing countries. While maintaining incentives for drug development, the TRIPS Agreement allows governments to license the use of patented inventions to someone else without the consent of the patent owner. Such "compulsory licensing" normally occurs only after negotiations for a voluntary license have failed, and the patent owner still receives an appropriate payment. It soon became clear that some governments were unsure of their right to use compulsory licensing and other flexibilities in the TRIPS Agreement, a situation likely to affect public health in poor countries by hindering universal access to medicines. Consequently, the WTO issued the "Declaration on the TRIPS Agreement and Public Health" at its 4th Ministerial Conference in Doha in November 2001. Reaction to the Doha Declaration, which reaffirms that the "TRIPS Agreement does not and should not prevent members from taking measures to protect public health," has been mixed. Some experts predicted that it would increase compulsory licensing of pharmaceuticals, but others suggested that political pressure against compulsory licensing and health system weaknesses in poor countries would limit claims for compulsory licenses. In this database analysis, the researchers systematically assess the impact of the Doha Declaration on the compulsory licensing of pharmaceuticals.
What Did the Researchers Do and Find?
By systematically searching media archives for reports of WTO member states considering or announcing compulsory licensing of pharmaceuticals, the researchers

identified 24 verified compulsory licensing episodes in 17 nations that occurred between January 1995 and June 2011. Half of these episodes ended with an announcement of a compulsory license, and the majority ended in a price reduction for a specific pharmaceutical product for the potential issuing nation through a compulsory license, a voluntary license, or a negotiated discount. Sixteen of the compulsory licensing episodes involved drugs for HIV/AIDS, four involved drugs for other communicable diseases, and four involved drugs for non-communicable diseases such as cancer. More than half the compulsory licensing episodes occurred in upper-middle-income countries (including Brazil and Thailand). Finally, most compulsory licensing episodes occurred between 2003 and 2005. There was a smaller peak of activity in the months leading up to the Doha conference, but after 2006 activity declined substantially.

What Do These Findings Mean?

Given these findings, the researchers suggest that the Doha Declaration is unlikely to have an important long-term impact on the use of compulsory licensing or on access to pharmaceuticals for communicable diseases other than HIV/AIDS in developing and low-income countries. Most notably, the researchers found no evidence of a spike in compulsory licensing episodes immediately after the Doha Declaration, and they note that the lagged spike that occurred between 2003 and 2005 could have resulted in large part from the global antiretroviral advocacy campaign. Moreover, compulsory licensing activity has diminished greatly since 2006. Thus, the researchers conclude, health advocates who pushed for the Doha Declaration reforms have had little success in engaging trade as a positive, proactive force for addressing health gaps.

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