Center for Vaccine Ethics and Policy
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Vaccines: The Week in Review
10 August 2013
Center for Vaccine Ethics & Policy (CVEP)

This weekly summary targets news, events, announcements, articles and research in the global vaccine ethics and policy space and is aggregated from key governmental, NGO, international organization and industry sources, key peer-reviewed journals, and other media channels. This summary proceeds from the broad base of themes and issues monitored by the Center for Vaccine Ethics & Policy in its work: it is not intended to be exhaustive in its coverage. Vaccines: The Week in Review is also posted in pdf form and as a set of blog posts at http://centerforvaccineethicsandpolicy.wordpress.com/. This blog allows full-text searching of over 3,500 entries.

Comments and suggestions should be directed to
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NOTICE: *Vaccines: The Week in Review* will resume publication on 24 August 2013 following duty travel by the editor.

UNICEF said it received an emergency contribution of US$1.3 million from the Government of Japan "to procure and distribute urgently needed polio vaccines for children in Somalia." Sikander Khan, UNICEF Somalia Representative, commented, "Lack of access to routine immunization in Somalia has created the largest known reservoir of unvaccinated children in a single geographic area in the world. The total number of Somali children who had never been vaccinated between 2008 and 2012 was estimated to reach a million. The poliovirus in such a large reservoir has the potential to result in a catastrophic outbreak, the likes of which are beginning to be seen and as such constitutes an international emergency." Currently, Somalia has the second lowest coverage of polio vaccination through routine immunization in the world at 47 per cent after Equatorial Guinea. The funds will cover more than 5 million doses of oral polio vaccines for two rounds of Supplementary Immunization Activities for November and December.
http://www.unicef.org/media/media_70084.html

Update: Polio this week - *As of 7 August 2013*
Global Polio Eradication Initiative
Full report: http://www.polioeradication.org/Dataandmonitoring/Poliothisweek.aspx
[Editor's extract and bolded text]

:: **Following confirmation of 24 new cases in the Horn of Africa last week, five more cases are confirmed this week, all from Somalia.** See 'Horn of Africa' section for more.
:: In Pakistan, Federally Administered Tribal Areas (FATA) remains the major poliovirus reservoir in the country. Virus transmission in FATA is threatening progress achieved elsewhere in the country and in neighbouring Afghanistan. An analysis of vaccination status of non-polio acute flaccid paralysis (AFP) cases suggests that more than half of children in FATA remain under-immunized, with as many as 40% never having received a single dose of oral polio vaccine (OPV). See 'Pakistan' section for more.
:: In Israel, a supplementary immunization activity (SIA) with OPV is being conducted this week, targeting 200,000 children aged two months to ten years in the southern part of the country. The move follows isolation of wild poliovirus type 1 (WPV1) from sewage samples collected from 20 sampling sites since February. No cases of paralytic polio have been reported. While Israel has high vaccination coverage with inactivated polio vaccine (IPV), the objective of the OPV SIA is to boost mucosal immunity levels to rapidly interrupt virus circulation.

Nigeria

:: Two new WPV1 cases were reported in the past week (from Kano state), bringing the total number of WPV1 cases for 2013 to 42. One of the newly-reported cases is the most recent WPV1 in the country, with onset of paralysis on 14 July…
:: Following a new risk-classification of Local Government Areas (LGAs), aimed at improving the delivery of resources to areas where they are most needed, tailored approaches are being implemented in LGAs where performance has stalled, LGAs where performance has decreased and LGAs where access to populations is compromised due to insecurity.
:: Across all areas, strengthened efforts are being made to track the direct engagement and oversight by LGA Chairpersons.
:: The engagement of communities, and traditional and religious leaders, is continuing to be fostered. The Volunteer Community Mobilizer Network continues to be expanded, and social data analysis is expected to provide further understanding for children being chronically missed. Operational plans for insecure areas feature the introduction of Permanent Health Teams (PHTs), conducting wall fencing vaccinations around insecure areas, expanding transit vaccinations, implementing Short Interval Additional Dose (SIAD) campaigns and engaging non-traditional partners…

Pakistan

:: …One new cVPDV2 case was reported in the past week, bringing the total number of cVDPV2 cases for 2013 to six. It is the most recent cVDPV2 case in the country and had onset of paralysis on 30 June (from North Waziristan, FATA – the third cVDPV2 in North Waziristan).
:: Two new positive environmental samples (WPV1) were confirmed, collected in early July from Peshawar, Khyber Pakhtunkhwa (KP) and Hyderabad, Sindh. In total, 24 environmental samples have tested positive for WPV1 in 2013 from various sites across Pakistan, the bulk from Peshawar (10) and Hyderabad (6).
:: In addition to this latest cVDPV2 case, North Waziristan is also affected by WPV1. It is an area where immunization campaigns have been suspended by local leaders since last June. To minimize the risk of a major WPV1 and/or cVDPV2 outbreak in this area, it is critical that access to children is granted as quickly as possible. Immunization campaigns in neighbouring high-risk areas are being intensified, to further boost population immunity levels in those areas and minimize the risk of further spread.
:: FATA remains the major poliovirus reservoir in Pakistan, both due to WPV1 and cVDPV2. Khyber Agency is particularly affected, accounting for 13 of this year's 22 WPV1 cases in the country. Of six cVDPV2 cases in the country this year, three are from North Waziristan.

According to vaccination status of non-polio AFP cases, more than half of children in FATA are under-immunized, with as many as 40% never having received a single dose….

Horn of Africa

::Five new WPV1 cases were reported in the past week (all from Somalia), bringing the total number of WPV1 cases in the region to 110 (100 from Somalia and ten from Kenya). The most recent WPV1 case in the region had onset of paralysis on 10 July (from Somalia).

:: Two of the newly-reported cases are from Lower Shabelle, areas of which are inaccessible due to insecurity. Special strategies continue to be implemented for these areas, including increased local-level access negotiations, immunizing older age groups and setting up vaccination posts at entry/exit points of inaccessible areas…

Israel Extends Polio Vaccination Campaign

JERUSALEM | Fri Aug 9, 2013 1:33pm EDT

(Reuters) - Israel will administer the active polio vaccine to children nationwide beginning on August 18, the Health Ministry said on Friday, stepping up an inoculation campaign currently limited to the south of the country.

The decision was made after the virus was detected in sewage treatment plants in Lod and Ramle, towns close to Israel's central hub city of Tel Aviv, the ministry said in a statement.

It said it would call on parents of children born after January 2004 to bring them to publicly-funded clinics to receive oral drops of a weakened active virus vaccine between August 18 and 25.

A smaller-scale vaccination campaign has been under way since August 4 in the south, where the virus was discovered in sewage last month. The Health Ministry said 20 percent of children there had been inoculated since, and the number would increase to 50 percent within a week…
http://www.reuters.com/article/2013/08/09/us-israel-polio-idUSBRE9780UL20130809

AllAfrica **- Guest Column**

Africa: Response to Polio Outbreaks Shows Global Eradication Plan Is Working

By Helen Rees, 5 August 2013

http://allafrica.com/stories/201308052603.html?viewall=1

Just as we were seeing record-low cases of polio worldwide and coming closer than ever to eradication, 105 new cases of wild polio have been identified in Kenya and Somalia, raising new concerns about low coverage and inaccessible populations in that area. While the outbreaks are undoubtedly a setback, the Global Polio Eradication Initiative (GPEI) had anticipated that sporadic cases would occur in vulnerable settings during the final push for polio eradication, and it's noteworthy that the situation has been met with one of the quickest and most effective emergency responses to date.

Although polio has been cornered in a handful of countries, the last vestiges of the disease will be the most difficult to stop. For example, political instability and insecurity in some areas -- which in Nigeria and Pakistan culminated in the targeted murder of health care workers engaged in delivering services earlier this year -- hinder access to at-risk children and can fuel the risk of outbreaks. Fortunately, containing outbreaks, such as those in the Horn of Africa, is a crucial part of the GPEI's Polio Eradication and Endgame Strategic Plan 2013-2018.

Over the past 10 years, the GPEI has improved its outbreak response by systematically learning lessons from the more than 100 polio outbreaks that have occurred worldwide.

Since May of this year, 10 polio cases have been confirmed in Kenya and 95 in Somalia. A dozen vaccination campaigns have been conducted from May through July 24 across Somalia, Kenya, Ethiopia and Yemen that aimed to reach more than 17 million individuals, including adults in some areas. Additional campaigns will be executed in August.

The polio team is benefitting from the world's most advanced surveillance system, which detects polio cases faster and more precisely. It helped health experts quickly identify the 105 cases in the Horn of Africa - the vast majority of which occurred prior to the outbreak response activities - and subsequently guided where vaccination gaps needed to be filled. We now expect to see a drastic drop in new cases post-response. Since 2010, all but one outbreak of wild polio virus was stopped within six months.

But responding to outbreaks is only one element of the GPEI's multi-faceted eradication plan, which outlines a comprehensive series of steps all countries should take to achieve eradication by 2018. For example, to prevent outbreaks in the first place, it is essential to ensure strong immunization systems are in place and vaccination rates are high.

That is why the polio eradication plan includes significant resources for the rapid fortification of routine immunization systems. The plan commits at least half of GPEI field personnel's time to work to achieve this by the end of 2014 in endemic and high-risk countries.

Strengthening immunization has the added benefit of helping the fight against other vaccine-preventable diseases, such as rotavirus and measles.

For example, in India, the polio programme introduced a system to identify, track and immunize every newborn child in areas of the country that were at high risk for polio. These efforts helped ensure vulnerable infants were included in the routine immunization system so they would receive polio vaccines as well as others that are critical.

The global plan to eradicate polio comes with one very important caveat: it must be funded up front.

The current outbreak is just the most recent example of the risk endemic polio anywhere poses to children and polio-free countries everywhere. In 2009, a polio outbreak in Tajikistan resulted in nearly 500 polio cases and cost U.S.$10 million to end. China and the western and central parts of Africa have also seen recent outbreaks.

A fully funded plan ensures that tradeoffs are not made in emergency situations by using a meticulous modeling process to budget for future outbreaks. Full funding also gives GPEI the flexibility to effectively respond to sudden outbreaks while continuing to prioritize its intensive efforts to end transmission in the three endemic countries: Nigeria, Pakistan and Afghanistan. Earlier this year I joined with more than 400 scientists and global health experts to state my confidence in the GPEI plan. I remain a strong supporter of the plan today.

Eradicating polio is a daunting challenge, but new knowledge and innovations are leading the way. Over the last two decades, the polio program has developed highly sophisticated strategies to access the most marginalized and hard-to-reach communities by improving overall health infrastructures and increasing community trust. Applying these lessons to routine health programs will pave the way for the delivery of measles and rubella vaccines, as well as new vaccines and other health interventions, to previously unreached children.

It's a tall order to reduce costs and increase vaccine uptake - especially in communities that have low motivation to prevent diseases they do not even see and where fear and social disruption hamper progress - but this will be the challenge of the future.

The world has a plan to end polio. It's working, and we must stand behind it.

Helen Rees OBE is the executive director of the Wits Reproductive Health and HIV Institute at the University of the Witwatersrand in South Africa and honorary professor at the Department of Clinical Research at the London School of Hygiene and Tropical Medicine. She is also the

chair of the World Health Organization's Strategic Advisory Group of Experts (SAGE) on Immunization. She serves on the GAVI Alliance Board and PPC and on the South African NITAG.

MSF and GAVI issued statements addressing a new immunization initiative involving pneumococcal conjugate vaccines (PCV) for children in the Yida refugee camp in South Sudan and the larger context of pricing and availability of vaccines to the NGO community linked to GAVI purchasing volumes, current agreements with manufacturers, and resultant pricing for specific vaccines.

The MSF release of 8 August 2013 notes in part:

Global Vaccination Community Neglecting Refugee Children

"As Doctors Without Borders/Médecins Sans Frontières (MSF) begins vaccinating children against pneumonia in a refugee camp in South Sudan, the international medical humanitarian organization warned today that the global vaccination community is neglecting to provide new vaccines to crisis-affected children.

"While planning to immunize children against pneumococcal diseases in the Yida refugee camp, which is home to close to 100,000 Sudanese refugees, MSF faced multiple barriers to purchasing newer vaccines at an affordable price and struggled to navigate bureaucratic policies that exclude the needs of conflict-affected populations.

"Refugee children are incredibly vulnerable to developing vaccine-preventable diseases, so why do we keep hearing the players in the global vaccination community tell us these kids aren't their problem," asked Kate Elder, vaccines policy advisor at MSF's Access Campaign. "We should be making every effort for refugee children to benefit from the newest vaccines, instead of letting them languish in the global community's blind spot.

"Newer vaccines have primarily been introduced in poor countries with support from the Global Alliance for Vaccines and Immunization (GAVI Alliance). But GAVI does not cover vaccination in refugee and crisis-affected populations, leaving major needs unmet. Moreover, discounted prices that GAVI is able to negotiate are not systematically available to humanitarian actors working in crisis contexts…

Full text: http://www.doctorswithoutborders.org/press/release.cfm?id=6978&cat=press-release%29

GAVI's statement in response (undated) notes in part:

"The GAVI Alliance congratulates MSF on beginning to vaccinate children with pneumococcal conjugate vaccines (PCV) in the Yida refugee camp in South Sudan. We were pleased to have been able to play a facilitating role in helping MSF procure these vaccines…

"…Our focus is on expanding access to vaccines in a long-term sustainable way and that means working through the governments of the world's 73 poorest countries to strengthen and expand routine immunisation services for all children.

"South Sudan has yet to apply for GAVI support for PCV but when it does, GAVI will work with the Ministry of Health to help them roll it out sustainably to all children in the country. First, we will support South Sudan to introduce the pentavalent vaccine starting next year (2014)…

"We recognise the importance of vaccines in humanitarian emergencies and where we can add value, we have and will continue to try to help. For example, soon after we supported the introduction of PCV in Kenya, we supported the Government to provide PCV for Somali children in the Dadaab refugee camp."

Full text: http://www.gavialliance.org/library/news/statements/2013/gavi-responds-to-medecins-sans-frontieres/

The Sabin Vaccine Institute's Sustainable immunisation Financing (SIF) Program said it convened "senior officials from 17 countries to share their successes in increasing government budget allocations for national immunisation programs." Sabin noted that "greater political commitment and advocacy are building the momentum needed for countries to fully finance their immunisation programs by 2020 and achieve the goals set forth in the Global Vaccine Action Plan (GVAP)." Delegates to the two-day colloquium "participated in an open exchange of strategies and best practices that have helped their countries increase commitments to fund national immunisation programs." In panel sessions, delegates presented their legislative activities, conduct peer assessments and discuss innovations in financing, budgeting and advocacy, and were supported in preparing "short-term, country specific advocacy plans designed to make progress on sustainable immunisation financing by 2016." The 17 countries involved in the colloquium are all SIF pilot countries and included Cameroon, Cambodia, Democratic Republic of Congo, Indonesia, Kenya, Liberia, Madagascar, Mali, Mongolia, Nepal, Nigeria, Republic of Congo, Senegal, Sierra Leone, Sri Lanka, Uganda and Vietnam. SIF partners who attended include WHO, UNICEF, World Bank, GAVI Alliance and the Bill & Melinda Gates Foundation.
http://www.gavialliance.org/library/news/press-releases/2013/dakar-conference-countries-showcase-increased-efforts-to-fund-their-own-immunisation-programs/
Editor's Note: The media release on this meeting did not indicate whether or when video, transcripts or other meeting summary information will be made available.

The **Weekly Epidemiological Record (WER) for 9 August 2013,** vol. 88, 32 (pp. 337–348) includes:
:: Rubella virus nomenclature update: 2013
:: Health conditions for travellers to Saudi Arabia for the pilgrimage to Mecca (Hajj)
http://www.who.int/entity/wer/2013/wer8832.pdf

Global Immunizations News (GIN) – July 2013
http://www.who.int/entity/immunization/GIN_July_2013.pdf

CDC/MMWR Watch [to 10 August 2013]
MMWR August 9, 2013 / Vol. 62 / No. 30
No new relevant content

WHO: Global Alert and Response (GAR) – *Disease Outbreak News*
http://www.who.int/csr/don/2013_03_12/en/index.html
No new content

WHO - Humanitarian Health Action
http://www.who.int/hac/en/index.html

No new content.

UN Watch *to 10 August 2013*
Selected meetings, press releases, and press conferences relevant to immunization, vaccines, infectious diseases, global health, etc. http://www.un.org/en/unpress/
No new content.

World Bank/IMF Watch *to 10 August 2013*
Selected press releases and other selected content relevant to immunization, vaccines, infectious diseases, global health, etc. http://www.worldbank.org/en/news/all
No new content.

Reports/Research/Analysis/ Conferences/Meetings/Book Watch

Vaccines: The Week in Review has expanded its coverage of new reports, books, research and analysis published independent of the journal channel covered in Journal Watch below. Our interests span immunization and vaccines, as well as global public health, health governance, and associated themes. If you would like to suggest content to be included in this service, please contact David Curry at: david.r.curry@centerforvaccineethicsandpolicy.org

Book: *Protecting the World's Children - Immunisation policies and Practices*
Edited by Sidsel Roalkvam, Desmond McNeill, and Stuart Blume
248 pages | 234x156mm
978-0-19-966644-7 | Paperback | 09 May 2013
http://ukcatalogue.oup.com/product/9780199666447.do#.UgWJE234LxM

The strengths and limitations of global immunization programmes
By Desmond McNeill
Excerpt

"…When polio eradication was proposed as a global objective, in the late 1980s, it was vigorously debated. No one doubted the power of the polio vaccine to protect children. But experts differed in how they thought it should best be used. Some have regarded vaccination programmes as a means of strengthening primary health care, whilst others have seen them as likely to divert attention and resources from needed improvements in health services. At issue in such debates is not the immunological properties of a vaccine, but the way in which it should best be used. Taking the health care needs of children, and especially those whose health is most at risk, as the key objective, how should vaccines best be deployed?

The question is even more relevant today, as more and more new vaccines are becoming available, and huge financial resources are being deployed to promote global immunisation. These donor-funded programmes now account for a major part of the effort devoted to improving the health of children in developing countries.

Three distinctive, but interrelated, trends can be identified in international public health in recent years:
:: A growing reliance on health technologies, and on vaccines in particular;
:: A global perspective that is increasingly taken for granted;
:: Quantifiable targets, and especially the Millennium Development Goals (MDGs), play a very important role.

Health policy makers at national level are expected to implement global immunisation programmes in a standard manner and report progress according to standard indicators.

Pressures and incentives to meet the targets set are then transmitted down to the community level health worker who actually meets the parents and children to implement these programmes.

Today, despite continuing or even increased talk of 'country ownership', there are growing demands for performance accountability, reflected in demands for measurement of performance — not just outputs, but also outcomes and impacts — based on objective quantitative indicators. The MDGs have contributed to the process. One of the attractions of vaccines is precisely their measurability: both as regards specifying targets and measuring achievement. Dividing the number of vaccines distributed by the number of children of the appropriate age in the target population is made to yield two simple but powerful numbers: percentage coverage, and number of lives saved

Although we are not questioning the intentions of global actors who contribute to this situation, we do note that the effect of their actions is to strengthen the 'verticality' in the global health system. In this system money, and vaccines themselves, emanate from the global level and travel down from national to district and to village levels, accompanied by technical advice, exhortation and targets to be achieved. In return — up the chain, emanating from the most local level — come reports on performance, and measures of achievements, expressed in terms of numbers of children vaccinated. In this way, not only is the autonomy of national governments reduced, their accountability may even be reversed. Instead of being accountable 'downwards' to their citizens, they become accountable 'upwards' to global actors.

The need to show progress can create distortions and lead to the production of misleading data, and an unwillingness to report problems. Vaccines could more effectively serve children's health needs if immunisation programmes were better understood and acknowledged, and if local knowledge and realities were enabled to inform national and international health policy.

Desmond McNeill is co-editor, along with Sidsel Roalkvam and Stuart Blume, of Protecting the World's Children: Immunisation policies and Practices (2013). He is Professor, and former Director, at SUM, the Centre for Development and Environment at the University of Oslo. He heads the research area on Governance for Sustainable Development, and is Director of SUMs Research School. He has worked in over 15 developing countries in Africa, Asia and Latin America and written extensively on aid and global governance.
http://blog.oup.com/2013/08/strengths-limitations-global-immunization-programmes/#sthash.RxooNNRN.dpuf

Journal Watch

Vaccines: The Week in Review continues its weekly scanning of key peer-reviewed 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

American Journal of Infection Control

Vol 41 | No. 8 | August 2013 | Pages 667-758
http://www.ajicjournal.org/current
[Reviewed earlier]

American Journal of Public Health
Volume 103, Issue 9 (September 2013)
http://ajph.aphapublications.org/toc/ajph/current
Quadrivalent Human Papillomavirus Vaccine Uptake in Adolescent Boys and Maternal Utilization of Preventive Care and History of Sexually Transmitted Infections
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All authors are with the Department of Research and Evaluation, Kaiser Permanente Southern California, Pasadena.
http://ajph.aphapublications.org/doi/abs/10.2105/AJPH.2013.301495
Abstract
Objectives. We examined whether maternal utilization of preventive care and history of sexually transmitted infections (STIs) predicted quadrivalent human papillomavirus vaccine (HPV4) uptake among adolescent boys 1 year following the recommendation for permissive use of HPV4 for males.
Methods. We linked maternal information with electronic health records of 254 489 boys aged 9 to 17 years who enrolled in Kaiser Permanente Southern California health plan from October 21, 2009, through December 21, 2010. We used multivariable Poisson regression with robust error variance to examine whether HPV4 initiation was associated with maternal uptake of influenza vaccine, Papanicolaou (Pap) screening, and history of STIs.
Results. We identified a modest but statistically significant association between initiation of HPV4 series and maternal receipt of influenza vaccine (rate ratio [RR] = 1.16; 95% confidence interval [CI] = 1.07, 1.26) and Pap screening (RR = 1.13; 95% CI = 1.01, 1.26). Boys whose mothers had a history of genital warts were more likely to initiate HPV4 (RR = 1.47; 95% CI = 0.93, 2.34), although the association did not reach statistical significance (P = .1).
Conclusions. Maternal utilization of preventive care and history of genital warts may influence HPV4 uptake among adolescent boys. The important role of maternal health characteristics and health behaviors needs be considered in intervention efforts to increase vaccine uptake among boys.

Annals of Internal Medicine
6 August 2013, Vol. 159. No. 3
http://annals.org/issue.aspx
[No relevant content]

BMC Public Health
(Accessed 10 August 2013)
http://www.biomedcentral.com/bmcpublichealth/content
[No new relevant content]

British Medical Bulletin
Volume 106 Issue 1 June 2013
http://bmb.oxfordjournals.org/content/current
[Reviewed earlier; No relevant content]

British Medical Journal
10 August 2013 (Vol 347, Issue 7920)
http://www.bmj.com/content/347/7920
Editorial
Human to human transmission of H7N9
BMJ 2013; 347 doi: http://dx.doi.org/10.1136/bmj.f4730 (Published 6 August 2013)
Cite this as: BMJ 2013;347:f4730
http://www.bmj.com/content/347/bmj.f4730
James W Rudge, lecturer1, Richard Coker, professor12
Limited transmission between humans is not surprising

Since the new avian influenza virus, H7N9, first emerged in China, a primary concern has been whether it might spread between humans. The vast majority of the 133 confirmed cases reported so far seem to be epidemiologically unconnected, with many patients reporting a recent history of exposure to live poultry, which are suspected to be a main reservoir for the virus. Although an earlier study did report two family clusters of H7N9 cases, it was unclear whether these clusters resulted from person to person transmission or simply from exposure to a common animal source of infection.1

In the linked paper (doi:10.1136/bmj.f4752) by Qi and colleagues, a detailed investigation into one of these clusters provides the strongest evidence yet of H7N9 transmission between humans.2 The index case, a 60 year old man, was likely to have been infected at a nearby live poultry market, and subsequently developed a severe and ultimately fatal respiratory illness. His 32 year old daughter, who provided prolonged bedside care for her father before his admission to intensive care, later also became fatally infected. With no indication that the daughter was exposed to live poultry within the days before becoming sick, along with almost 100% genetic similarity between the viruses isolated from each patient, the evidence points to transmission from father to daughter.

As the authors acknowledge, there are some limitations to the study but, on balance, human to human transmission looks probable. So does this imply that H7N9 has come one step closer towards adapting fully to humans? Probably not. Crucially, there is still no evidence of sustained transmission among humans—all 43 close contacts of these two patients, including a son in law who also helped care for the father, tested negative for infection. In addition, the receptor binding sites of the viruses from the two patients are no more adapted towards humans than those of other available H7N9 isolates. In many ways, the evidence corroborates, rather than challenges, previous assertions that the transmissibility of H7N9 between humans is currently low.

Indeed, the occasional transmission event from human to human appears to be the norm rather than the exception for influenza viruses that sporadically cross the species barrier into humans. Limited human to human transmission has been reported for highly pathogenic avian influenza H5N1,3 4 which continues to cause (usually fatal) infections in humans, as well as another bird flu subtype, H7N7, which caused an outbreak of mostly mild infections in the Netherlands in 2003.5 To observe some transmission of H7N9 from human to human is

therefore not surprising, and does not necessarily indicate that the virus is on course to develop sustained transmission among humans.

Nevertheless, several traits of H7N9 are of particular concern. The linked paper2 comes close on the heels of studies showing airborne transmissibility of H7N9 between ferrets in the laboratory, a mammalian model.6 7 Also, it is now well documented that owing to its non-lethality in birds, H7N9 can spread undetected through avian populations. In addition, Chinese surveillance data suggest that the number of confirmed human cases is just the tip of the iceberg—many mild cases are likely to have passed undetected.8 The upside of this is that the actual fatality rate among H7N9 cases is likely to be substantially lower than that observed among confirmed cases.9 The flipside is that the incidence of human infections, and therefore opportunities for H7N9 to adapt to humans or to re-assort through mixed influenza infections, could be much greater than for other bird flu viruses such as H5N1.

Although the number of H7N9 cases has fallen abruptly since April 2013, with no new cases reported for several weeks, we have been warned to expect a resurgence later in the year owing to seasonal effects on transmission.10 Thus, while the paper by Qi and colleagues2 might not suggest that H7N9 is any closer to delivering the next pandemic, it does provide a timely reminder of the need to remain extremely vigilant: the threat posed by H7N9 has by no means passed.

Research

Probable person to person transmission of novel avian influenza A (H7N9) virus in Eastern China, 2013: epidemiological investigation

BMJ 2013; 347 doi: http://dx.doi.org/10.1136/bmj.f4752 (Published 6 August 2013)
Cite this as: BMJ 2013;347:f4752
http://www.bmj.com/content/347/bmj.f4752

Abstract

Objective To determine whether the novel avian influenza H7N9 virus can transmit from person to person and its efficiency.

Design Epidemiological investigations conducted after a family cluster of two patients with avian H7N9 in March 2013.

Setting Wuxi, Eastern China.

Participants Two patients, their close contacts, and relevant environments. Samples from the patients and environments were collected and tested by real time reverse transcriptase-polymerase chain reaction (rRT-PCR), viral culture, and haemagglutination inhibition assay. Any contacts who became ill had samples tested for avian H7N9 by rRT-PCR. Paired serum samples were obtained from contacts for serological testing by haemagglutination inhibition assays.

Main outcomes measures Clinical data, history of exposure before the onset of illnesses, and results of laboratory testing of pathogens and further analysis of sequences and phylogenetic tree to isolated strains.

Results The index patient became ill five to six days after his last exposure to poultry. The second patient, his daughter aged 32, who provided unprotected bedside care in the hospital, had no known exposure to poultry. She developed symptoms six days after her last contact with her father. Two strains were isolated successfully from the two patients. Genome sequence and analyses of phylogenetic trees showed that both viruses were almost genetically identical. Forty three close contacts of both patients were identified. One had mild illness but had negative results for avian H7N9 by rRT-PCR. All 43 close contacts tested negative for haemagglutination inhibition antibodies specific for avian H7N9.

Conclusions The infection of the daughter probably resulted from contact with her father (the index patient) during unprotected exposure, suggesting that in this cluster the virus was able to transmit from person to person. The transmissibility was limited and non-sustainable

Bulletin of the World Health Organization
Volume 91, Number 8, August 2013, 545-620
http://www.who.int/bulletin/volumes/91/8/en/index.html
[Reviewed earlier]

Clinical Therapeutics
Vol 35 | No. 7 | July 2013 | Pages 901-1050
http://www.clinicaltherapeutics.com/current
[Reviewed earlier]

Cost Effectiveness and Resource Allocation
(Accessed 10 August 2013)
http://www.resource-allocation.com/
Methodology
Calculating disability-adjusted-life-years lost (DALYs) in discrete-time
Larson BA Cost Effectiveness and Resource Allocation 2013, 11:18 (8 August 2013)
Open Access
http://www.resource-allocation.com/content/11/1/18/abstract
Abstract (provisional)
Disability-adjusted-life-years lost (DALYs) is a common outcome metric for cost-effectiveness analyses, and the equations used for such calculations have been presented previously by Fox-Rushby and Hanson (see, e.g., "Health Policy and Planning 16:326--331, 2001"). While the equations are clear, the logic behind them is opaque at best for a large share of public health practitioners and students. The objective of this paper is to show how to calculate DALYs using a discrete time formulation that is easy to teach to students and public health practitioners, is easy to apply for those with basic discounting skills, and is consistent with the discounting methods typically included on the costing side of cost-effectiveness analysis. A continuous-time adjustment factor is derived that can be used to ensure exact consistency between the continuous and discrete time approaches, but this level of precision is typically unnecessary for cost-effectiveness analyses. To illustrate the approach, both a new, simple example and the same example presented in Fox-Rushby and Hanson are used throughout the paper.

Current Opinion in Infectious Diseases.
August 2013 - Volume 26 - Issue 4 pp: v-vi,295-398
http://journals.lww.com/co-infectiousdiseases/pages/currenttoc.aspx
[Reviewed earlier]

Development in Practice
Volume 23, Issue 4, 2013

http://www.tandfonline.com/toc/cdip20/current
[Reviewed earlier; No relevant content]

Emerging Infectious Diseases
Volume 19, Number 8—August 2013
http://www.cdc.gov/ncidod/EID/index.htm
[Reviewed earlier]

The European Journal of Public Health
Volume 23 Issue 4 August 2013
http://eurpub.oxfordjournals.org/content/current
[Reviewed earlier]

Eurosurveillance
Volume 18, Issue 32, 08 August 2013
http://www.eurosurveillance.org/Public/Articles/Archives.aspx?PublicationId=11678
Research articles
Impact of universal two-dose vaccination on varicella epidemiology in Navarre, Spain, 2006 to 2012
by M García Cenoz, J Castilla, J Chamorro, I Martínez-Baz, V Martínez-Artola, F Irisarri, M Arriazu, C Ezpeleta, A Barricarte
[No abstract]
Surveillance and outbreak reports
International infectious disease surveillance during the London Olympic and Paralympic Games 2012: process and outcomes
J Jones [1], J Lawrence[1], L Payne Hallström[2], J Mantero[2], H Kirkbride[3], A Walsh[3], D Jermacane[4], H Simons[5], K M Hansford[6], E Bennett[6], M Catchpole[7], on behalf of the international team[8]
http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20554
Abstract
Surveillance for possible international infectious disease threats to the Olympic and Paralympic Games in London, United Kingdom, was conducted from 2 July to 12 September 2012 by a collaborative team comprising representatives from the Health Protection Agency (Public Health England since April 2013), the European Centre for Disease Prevention and Control and the National Travel Health Network and Centre. Team members enhanced their usual international surveillance activities and undertook joint risk assessments of incidents identified as relevant through an agreed set of criteria designed for the Games and using tools developed for this purpose. Although team members responded to a range of international disease incidents as part of their routine roles during this period, no incident was identified that represented a threat to the Games. Six incidents were highlighted by the team that were likely to attract media attention and hence could generate political and public concern. Responding to such concern is an important aspect of the overall public health management of mass gathering events. The lessons learned about the process and outcomes of the enhanced international surveillance will help inform planning by future hosts of similar events.

Forum for Development Studies
Volume 40, Issue 2, 2013
http://www.tandfonline.com/toc/sfds20/current
[Reviewed earlier; No relevant content]

Global Health Governance
Volume VI, Issue 1: Fall 2012
– December 31, 2012
[Reviewed earlier]

Globalization and Health
[Accessed 10 August 2013]
http://www.globalizationandhealth.com/
[No new relevant content]

Health Affairs
August 2013; Volume 32, Issue 8
http://content.healthaffairs.org/content/current
Theme: States, Health IT, Payment & Practice Reforms
[No relevant content]

Health and Human Rights
Volume 15, Issue 1
http://www.hhrjournal.org/
Theme: Realizing the Right to Health Through a Framework Convention on Global Health
[Reviewed earlier]

Health Economics, Policy and Law
Volume 8 - Issue 03 - July 2013
http://journals.cambridge.org/action/displayIssue?jid=HEP&tab=currentissue
[Reviewed earlier; No relevant content]

Health Policy and Planning
Volume 28 Issue 4 July 2013
http://heapol.oxfordjournals.org/content/current
[Reviewed earlier; No relevant content]

Human Vaccines & Immunotherapeutics (formerly Human Vaccines)
August 2013 Volume 9, Issue 8
http://www.landesbioscience.com/journals/vaccines/toc/volume/9/issue/8/

[Reviewed earlier]

Infectious Agents and Cancer
http://www.infectagentscancer.com/content
[Accessed 10 August 2013]
[No new relevant content]

Infectious Diseases of Poverty
http://www.idpjournal.com/content
[Accessed 10 August 2013]
[No new relevant content]

International Journal of Epidemiology
Volume 42 Issue 3 June 2013
http://ije.oxfordjournals.org/content/current
[Reviewed earlier]

International Journal of Infectious Diseases
Vol 17 | No. 8 | August 2013
http://www.ijidonline.com/current
[Reviewed earlier; No relevant content]

JAMA
August 7, 2013, Vol 310, No. 5
http://jama.jamanetwork.com/issue.aspx
[No relevant content]

JAMA Pediatrics
August 2013, Vol 167, No. 8
http://archpedi.jamanetwork.com/issue.aspx
[No relevant content]

Journal of Community Health
Volume 38, Issue 4, August 2013
http://link.springer.com/journal/10900/38/4/page/1
[Reviewed earlier; No relevant content]

Journal of Health Organization and Management
Volume 27 issue 5 - Latest Issue
http://www.emeraldinsight.com/journals.htm?issn=1477-7266&show=latest

[No relevant content]

Journal of Infectious Diseases
Volume 208 Issue 5 September 1, 2013
http://jid.oxfordjournals.org/content/current
[No relevant content]

Journal of Global Infectious Diseases (JGID)
April-June 2013 Volume 5 | Issue 2 Page Nos. 43-90
http://www.jgid.org/currentissue.asp?sabs=n
[Reviewed earlier; No relevant content]

Journal of Medical Ethics
August 2013, Volume 39, Issue
http://jme.bmj.com/content/current
[Reviewed earlier; No relevant content]

Journal of Medical Microbiology
August 2013; 62 (Pt 8)
http://jmm.sgmjournals.org/content/current
[Reviewed earlier; No relevant content]

Journal of the Pediatric Infectious Diseases Society (JPIDS)
Volume 2 Issue 2 June 2013
http://jpids.oxfordjournals.org/content/current
[Reviewed earlier]

Journal of Pediatrics
Vol 163 | No. 2 | August 2013 | Pages 309-612
http://www.jpeds.com/current
[Reviewed earlier]

Journal of the Royal Society – Interface
October 6, 2013; 10 (87)
http://rsif.royalsocietypublishing.org/content/current
Perspective
Making wider use of the world's most widely used vaccine: Bacille Calmette–Guérin revaccination reconsidered
Christopher Dye
J. R. Soc. Interface. 2013 10 20130365; doi:10.1098/rsif.2013.0365 (published 31 July 2013)
http://rsif.royalsocietypublishing.org/content/10/87/20130365.abstract

Abstract
Approximately 100 million newborn children receive Bacille Calmette–Guérin (BCG) annually, because vaccination is consistently protective against childhood tuberculous meningitis and miliary TB. By contrast, BCG efficacy against pulmonary TB in children and adults is highly variable, ranging from 0% to 80%, though it tends to be higher in individuals who have no detectable prior exposure to mycobacterial infections, as judged by the absence of delayed-type hypersensitivity response (a negative tuberculin skin test, TST). The duration of protection against pulmonary TB is also variable, but lasts about 10 years on average. These observations raise the possibility that BCG revaccination, following primary vaccination in infancy, could be efficacious among TST-negative adolescents as they move into adulthood, the period of highest risk for pulmonary disease. To inform continuing debate about revaccination, this paper assesses the effectiveness and cost-effectiveness of revaccinating adolescents in a setting with intense transmission—Cape Town, South Africa. For a cost of revaccination in the range US$1–10 per person, and vaccine efficacy between 10% and 80% with protection for 10 years, the incremental cost per year of healthy life recovered (disability-adjusted life years, DALY) in the vaccinated population lies between US$116 and US$9237. The intervention is about twice as cost-effective when allowing for the extra benefits of preventing transmission, with costs per DALY recovered in the range US$52–$4540. At 80% efficacy, revaccination averted 17% of cases. Under the scenarios investigated, BCG revaccination is cost-effective against international benchmarks, though not highly effective. Cost-effectiveness ratios would be more favourable if we also allow for TB cases averted by preventing transmission to HIV-positive people, for the protection of HIV-negative people who later acquire HIV infection, for the possible non-specific benefits of BCG, for the fact that some adolescents would receive BCG for the first time, and for cost sharing when BCG is integrated into an adolescent immunization programme. These findings suggest, subject to further evaluation, that BCG revaccination could be cost-effective in some settings.

Journal of Virology
August 2013, volume 87, issue 15
http://jvi.asm.org/content/current
[Reviewed earlier]

The Lancet
Aug 10, 2013 Volume 382 Number 9891 p479 - 570
http://www.thelancet.com/journals/lancet/issue/current
[No relevant content]

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Aug 2013 Volume 1 Number 2 e55 - 115
http://www.thelancet.com/journals/langlo/issue/current
[Reviewed earlier]

The Lancet Infectious Diseases
Aug 2013 Volume 13 Number 8 p639 - 724

http://www.thelancet.com/journals/laninf/issue/current
[Reviewed earlier]

Medical Decision Making (MDM)
August 2013; 33 (6)
http://mdm.sagepub.com/content/current
[Reviewed earlier; No relevant content]

The Milbank Quarterly
A Multidisciplinary Journal of Population Health and Health Policy
June 2013 Volume 91, Issue 2 Pages 219–418
http://onlinelibrary.wiley.com/doi/10.1111/milq.2013.91.issue-2/issuetoc
[Reviewed earlier; No relevant content]

Nature
Volume 500 Number 7461 pp121-248 8 August 2013
http://www.nature.com/nature/current_issue.html
Nature | Editorial
Handle with care
The possibility that H7N9 avian influenza may evolve sufficiently to cause a pandemic has scientists turning again to controversial research —they must be careful how they justify the risks taken.
07 August 2013

The H7N9 avian flu virus first reported in China in March has so far infected at least 134 people, and killed 43 of them. Thankfully, there are no signs yet that it can easily be transmitted between people — instead it is sporadically being caught by humans through contact with chickens and other fowl.

Researchers now want to make genetically engineered versions of H7N9 that are more transmissible and pathogenic in mammals. In a Correspondence published jointly this week in Nature and Science (see page 150), 22 scientists, including Ron Fouchier of the Erasmus Medical Center in Rotterdam, the Netherlands, and Yoshihiro Kawaoka of the University of Wisconsin-Madison, argue that such research can help to assess the 'pandemic potential' of H7N9. The dilemma is that should such engineered strains be accidentally or deliberately released from a lab, they could spark a flu pandemic.

The announcement is likely to prompt some replay of last year's debate over the creation by Fouchier and Kawaoka of lab strains of H5N1 that could transmit between ferrets. And it offers the first test of some of the review and oversight structures put in place for this 'gain-of-function' flu research. As this journal has said before, scientists who push for such research should be wary of over-selling the benefits to public health, at least in the short term, as a way to justify the risks taken.

A sense of perspective is crucial here. The long-term benefits of such work are clear — as long as it is done to the highest biosafety standards. It will shed light on, for example, the mechanisms of virus transmissibility and pathogenicity. But the immediate benefits to public health and our short-term ability to counter the threat of H7N9 are less clear-cut. Scientists cannot predict pandemics, so to assess the pandemic potential of viruses — and to decide

which strains warrant the manufacture of trial vaccines — comes down to judgements of relative risk.

Tests of how flu viruses behave in animal models such as ferrets can certainly provide information on the risk of transmissibility and pathogenicity, although it can be difficult to extrapolate those results to humans. A rash of papers this year has shown that H7N9 does have limited airborne transmissibility in ferrets, although the virus is not transmitting between people in the current outbreak in China.

Another way to assess pandemic potential is to monitor wild-type viruses for mutations that allow the virus more ready access to human cells. H7N9 has already acquired some of these mutations, which is why it infects humans more easily than does H5N1. But as researchers pointed out in June, there is no scientific evidence that such mutations predict the risk of a pandemic (D. M. Morens et al. N. Engl. J. Med. 368, 2345–2348; 2013). Transmissibility is more complex than that.

In creating mammalian- transmissible versions of H7N9, scientists would go a step further and hope to identify combinations of mutations that could increase virus transmissibility in ferrets or other models. Such work could yield information on the biological principles affecting transmission. But nature could well come up with combinations for transmission that are different from those obtained in experiments.

Following the H5N1 controversy, the US Department of Health and Human Services has introduced an extra layer of review that will apply to anyone seeking funding for work to make mammalian-transmissible strains of H7N9 (see page 151). The risks and benefits of the work will be assessed by a panel of experts in public health, security, risk assessment, law and ethics, and, importantly, any extra steps needed to mitigate biosafety risks will be considered. The way the review handles H7N9 will be an important test of the effectiveness and transparency of this new approach.

http://www.nature.com/news/handle-with-care-1.13505

Nature Immunology

August 2013, Volume 14 No 8 pp765-877

http://www.nature.com/ni/journal/v14/n8/index.html

[Reviewed earlier; No relevant content]

Nature Medicine

July 2013, Volume 19 No 7 pp791-945

http://www.nature.com/nm/journal/v19/n7/index.html

[Reviewed earlier]

Nature Reviews Immunology

August 2013 Vol 13 No 8

http://www.nature.com/nri/journal/v13/n8/index.html

[No relevant content]

New England Journal of Medicine

August 8, 2013 Vol. 369 No. 6

http://www.nejm.org/toc/nejm/medical-journal
[No relevant content]

OMICS: A Journal of Integrative Biology
July 2013, 17(7)
http://online.liebertpub.com/toc/omi/17/7
[Reviewed earlier; No relevant content]

Revista Panamericana de Salud Pública/Pan American Journal of Public Health (RPSP/PAJPH)
June 2013 Vol. 33, No. 6
http://www.paho.org/journal/index.php?option=com_content&task=view&id=125&Itemid=224
[Reviewed earlier]

The Pediatric Infectious Disease Journal
August 2013 - Volume 32 - Issue 8 pp: A15-A16,e314-e347,805-929
http://journals.lww.com/pidj/pages/currenttoc.aspx
[Reviewed earlier]

Pediatrics
August 2013, VOLUME 132 / ISSUE 2
http://pediatrics.aappublications.org/current.shtml
Article
Cost-Effectiveness of Using 2 vs 3 Primary Doses of 13-Valent Pneumococcal Conjugate Vaccine
Charles Stoecker, PhDa, Lee M. Hampton, MD, MSca,b, Ruth Link-Gelles, MPHa, Mark L. Messonnier, PhDa, Fangjun Zhou, PhDa, and Matthew R. Moore, MD, MPHa
+ Author Affiliations
aNational Center for Immunization and Respiratory Diseases, and
bEpidemic Intelligence Service, Centers for Disease Control and Prevention, Atlanta, Georgia
http://pediatrics.aappublications.org/content/132/2/e324.abstract
Abstract
BACKGROUND AND OBJECTIVE: Although effective in preventing pneumococcal disease, 13-valent pneumococcal conjugate vaccine (PCV13) is the most expensive vaccine on the routinely recommended pediatric schedule in the United States. We examined the cost-effectiveness of switching from 4 total doses to 3 total doses by removing the third dose in the primary series in the United States.
METHODS: We used a probabilistic model following a single birth cohort of 4.3 million to calculate societal cost savings and increased disease burden from removing the 6-month dose of PCV13. Based on modified estimates of 7-valent pneumococcal conjugate vaccine from randomized trials and observational studies, we assumed that vaccine effectiveness under the 2 schedules is identical for the first 6 months of life and largely similar after administration of the 12- to 15-month booster dose.

RESULTS: Removing the third dose of PCV13 would annually save $500 million (in 2011$) but would also result in an estimated 2.5 additional deaths among inpatients with pneumonia or invasive pneumococcal disease. Such dose removal would also result in 261 000 estimated otitis media and 12 000 estimated pneumonia cases annually. These additional illnesses could be prevented through modest increases in coverage. Overall, societal savings per additional life-year lost would be ~$6 million. When nonfatal outcomes are also considered, savings would range from $143 000 to $4 million per additional quality adjusted life-year lost, depending on the assumptions used for otitis media.
CONCLUSIONS: Sizable societal cost savings and a moderate pneumococcal disease increase could be expected from removing the PCV13 primary series' third dose.

Article

Community-Centered Education Improves Vaccination Rates in Children From Low-Income Households

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+ Author Affiliations
Department of Pediatrics, State University of New York Upstate Medical University, Syracuse, New York

http://pediatrics.aappublications.org/content/132/2/319.abstract

Abstract
OBJECTIVE: We partnered with the Salvation Army to educate resource-poor families regarding childhood immunizations in an effort to improve vaccine coverage rates.
METHODS: Eligibility for enrollment included children of families presenting at registration for our Salvation Army holiday gift program, available to families with an annual income <150% of federal poverty guidelines. Parents completed a questionnaire, were provided each child's vaccination status as documented in the New York State Immunization Information System, and interacted with the study team to address immunization-related concerns. Missed vaccines were identified and parents were directed to their child's medical home for necessary immunizations. Vaccine coverage was ascertained via the New York State Immunization Information System every 6 to 8 weeks with telephone follow-up for children who remained delayed. The McNemar test and standard 2-proportion comparison were used to determine confidence intervals when analyzing matched or independent data, respectively.
RESULTS: A total of 1531 children were enrolled; 416 (28%) of the 1477 children with accurate immunization records were vaccine complete. When we excluded influenza vaccine, 1034 (70%) of children had received all other recommended vaccines. Nine months later, vaccine completion rates increased from 28% to 45%, largely because of improvements in influenza vaccination rates, which increased by 17% (confidence interval [CI] 15.5–19.5), a significant improvement over county (8%, 95% CI 7.4–8.1) and statewide (5%, 95% CI 4.7–4.8) rates during the same period.
CONCLUSIONS: Immunization rates in poor children are suboptimal. Partnering with community-based organizations to address parental concerns, provide education, and perform follow-up was effective in improving immunization rates, particularly for influenza vaccine.

Pharmaceutics

Volume 5, Issue 3 (September 2013), Pages 371-
http://www.mdpi.com/1999-4923/5/3

[No new relevant content]

Pharmacoeconomics
Volume 31, Issue 8, August 2013
http://link.springer.com/journal/40273/31/8/page/1
[Reviewed earlier]

PLoS One
[Accessed 10 August 2013]
http://www.plosone.org/
Predictors of Three Dose On-Time Compliance with HPV4 Vaccination in a Disadvantaged, Underserved, Safety Net Population in the US Midwest
Inge Verdenius, Diane M. Harper, George D. Harris, R. Stephen Griffith, Jeffrey Wall, Laura K. Hempstead, Gerard J. Malnar, Ruud L. M. Bekkers
Research Article | published 08 Aug 2013 | PLOS ONE 10.1371/journal.pone.0071295
Abstract
Background
HPV4 is approved as a series of three timed doses expected to result in efficacy against specific HPV infections. Completion rates in the US are quite low at the same time the structure of health care delivery is changing. The aim of this study was to determine how the patient-, clinic- and systems-level characteristics facilitate or hinder the timely completion of three HPV4 doses in both adolescent and adult female populations in a high-risk safety net population.
Methods
This is a retrospective study in which patient-, clinic- and systems-level data are abstracted from the electronic medical record (EMR) for all females 10–26 years of age receiving at least one dose of HPV4 between July 1, 2006 and October 1, 2009.
Results
Adults were more likely to complete the three dose series if they had at least one health care visit in addition to their HPV4 visit, (aOR = 1.54 (95% CI:1.10, 2.15). Adults were less likely to complete the three dose series if they received their second HPV4 dose at an acute health care, preventive care or postpartum visits compared to an HPV4-only visit (aOR = 0.31 (95% CI: 0.13, 0.72), 0.12 (0.04, 0.35), 0.30 (0.14, 0.62), respectively). Hispanic adults were less likely than whites to complete the series (aOR = 0.24 (95% CI:0.10, 0.59). 39% of adolescents who completed two doses completed the series.
Conclusions
HPV4 is more likely to be effectively administered to adults in a safety net population if multiple health care needs can be met within the health care system.

PLoS Medicine
(Accessed 10 August 2013)
http://www.plosmedicine.org/
Public Engagement in Health Priority Setting in Low- and Middle-Income Countries: Current Trends and Considerations for Policy
Katarzyna Bolsewicz Alderman, David Hipgrave, Eliana Jimenez-Soto
http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.1001495
Summary Points

:: Many donors and low- and middle-income countries (LMICs) are now encouraging increased public participation in health sector priority setting (HPS).
:: Using country examples, we demonstrate that despite many attempts, affordable, appropriate, and effective engagement of the public in that context remains elusive.
:: Rather than mandating public participation in HPS, countries and donors should focus on building a policy environment that is conducive to grassroots initiatives and on strengthening the evidence for what works using small pilot studies.

PLoS Neglected Tropical Diseases
July 2013
http://www.plosntds.org/article/browseIssue.action
[No new relevant content]

PNAS - Proceedings of the National Academy of Sciences of the United States of America
(Accessed 10 August 2013)
http://www.pnas.org/content/early/recent
[No new relevant content]

Public Health Ethics
Volume 6 Issue 2 July 2013
http://phe.oxfordjournals.org/content/current
[Reviewed earlier]

Qualitative Health Research
August 2013; 23 (8)
http://qhr.sagepub.com/content/current
Special Issue: Community Care
[Reviewed earlier; No relevant content]

Risk Analysis
July 2013 Volume 33, Issue 7 Pages 1175–1381
http://onlinelibrary.wiley.com/doi/10.1111/risa.2013.33.issue-7/issuetoc
[Reviewed earlier; No relevant content]

Science
9 August 2013 vol 341, issue 6146, pages 585-688
http://www.sciencemag.org/current.dtl
Science DOI: 10.1126/science.1241800
Research Article
Protection Against Malaria by Intravenous Immunization with a Nonreplicating Sporozoite Vaccine

Robert A. Seder1,*,†, Lee-Jah Chang1,*, Mary E. Enama1, Kathryn L. Zephir1, Uzma N. Sarwar1, Ingelise J. Gordon1, LaSonji A. Holman1, Eric R. James2, Peter F. Billingsley2, Anusha Gunasekera2, Adam Richman2, Sumana Chakravarty2, Anita Manoj2, Soundarapandian Velmurugan2, MingLin Li3, Adam J. Ruben2, Tao Li2, Abraham G. Eappen2, Richard E. Stafford2,3, Sarah H. Plummer1, Cynthia S. Hendel1, Laura Novik1, Pamela J.M. Costner1, Floreliz H. Mendoza1, Jamie G. Saunders1, Martha C. Nason4, Jason H. Richardson5, Jittawadee Murphy5, Silas A. Davidson5, Thomas L. Richie6, Martha Sedegah6, Awalludin Sutamihardja6, Gary A. Fahle7, Kirsten E. Lyke8, Matthew B. Laurens8,9, Mario Roederer1, Kavita Tewari1, Judith E. Epstein6, B. Kim Lee Sim2,3, Julie E. Ledgerwood1, Barney S. Graham1,‡, Stephen L. Hoffman2,3,‡, the VRC 312 Study Team§

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http://www.sciencemag.org/content/early/2013/08/07/science.1241800.abstract

Abstract

Consistent high-level, vaccine-induced protection against human malaria has only been achieved by inoculation of Plasmodium falciparum (Pf) sporozoites (SPZ) by mosquito bites. We report that the PfSPZ vaccine, composed of attenuated, aseptic, purified, cryopreserved PfSPZ, was safe and well-tolerated when administered 4 to 6 times intravenously (IV) to 40 adults. 0/6 subjects receiving 5 doses, 3/9 subjects receiving 4 doses of 1.35 x 105 PfSPZ vaccine, and 5/6 nonvaccinated controls developed malaria following controlled human malaria infection (P = 0.015 in the 5-dose group and P = 0.028 for overall, both versus controls). PfSPZ-specific antibody and T cell responses were dose-dependent. These data indicate that there is a dose-dependent immunological threshold for establishing high-level protection against malaria that can be achieved by IV administration of a vaccine that is safe and meets regulatory standards.

Letters

Gain-of-Function Experiments on H7N9

Science 9 August 2013:
Vol. 341 no. 6146 pp. 612-613
DOI: 10.1126/science.341.6146.612
http://www.sciencemag.org/content/341/6146/612.full

The A(H7N9) virus hemagglutinin protein has several motifs that are characteristic of mammalian-adapted and human influenza viruses, including mutations that confer human-type

receptor-binding and enhanced virus replication in mammals. The pandemic risk rises exponentially should these viruses acquire the ability to transmit readily among humans.

Reports indicate that several A(H7N9) viruses from patients who were undergoing antiviral treatment acquired resistance to the primary medical countermeasure—neuraminidase inhibitors (such as oseltamivir, peramivir, and zanamivir). Acquisition of resistance to these inhibitors by A(H7N9) viruses could increase the risk of serious outcomes of A(H7N9) virus infections.

The hemagglutinin proteins of A(H7N9) viruses have a cleavage site consistent with a low-pathogenic phenotype in birds; in the past, highly pathogenic H7 variants (with basic amino acid insertions at the cleavage site that enable the spread of the virus to internal organs) have emerged from populations of low pathogenic strains circulating in domestic gallinaceous poultry.

Normally, epidemiological studies and characterization of viruses from field isolates are used to inform policy decisions regarding public health responses to a potential pandemic. However, classical epidemiological tracking does not give public health authorities the time they need to mount an effective response to mitigate the effects of a pandemic virus. To provide information that can assist surveillance activities—thus enabling appropriate public health preparations to be initiated before a pandemic—experiments that may result in GOF are critical.

Therefore, after review and approval, we propose to perform the following experiments that may result in GOF:

(i) Immunogenicity. To develop more effective vaccines and determine whether genetic changes that confer altered virulence, host range, or transmissibility also change antigenicity.

(ii) Adaptation. To assist with risk assessment of the pandemic potential of field strains and evaluate the potential of A(H7N9) viruses to become better adapted to mammals, including determining the ability of these viruses to reassort with other circulating influenza strains.

(iii) Drug resistance. To assess the potential for drug resistance to emerge in circulating viruses, evaluate the genetic stability of the mutations conferring drug resistance, evaluate the efficacy of combination therapy with antiviral therapeutics, determine whether the A(H7N9) viruses could become resistant to available antiviral drugs, and identify potential resistance mutations that should be monitored during antiviral treatment.

(iv) Transmission. To assess the pandemic potential of circulating strains and perform transmission studies to identify mutations and gene combinations that confer enhanced transmissibility in mammalian model systems (such as ferrets and/or guinea pigs).

(v) Pathogenicity. To aid risk assessment and identify mechanisms, including reassortment and changes to the hemagglutinin cleavage site, that would enable circulating A(H7N9) viruses to become more pathogenic.

All experiments proposed by influenza investigators are subject to review by institutional biosafety committees. The committees include experts in the fields of infectious disease, immunology, biosafety, molecular biology, and public health; also, members of the lay public represent views from outside the research community. Risk-mitigation plans for working with potentially dangerous influenza viruses, including 1918 virus and highly pathogenic avian H5N1 viruses, will be applied to conduct GOF experiments with A(H7N9) viruses (see supplementary text). Additional reviews may be required by the funding agencies for proposed studies of A(H7N9) viruses (see scim.ag/13BK5Hs).

The recent H5N1 virus transmission controversy focused on the balance of risks and benefits of conducting research that proved the ability of the H5N1 virus to become transmissible in mammals (see www.sciencemag.org/special/h5n1). These findings demonstrated the pandemic potential of H5N1 viruses and reinforced the need for continued optimization of pandemic preparedness measures. Key mutations associated with adaptation to mammals, included in an annotated inventory for mutations in H5N1 viruses developed by the U.S. Centers for Disease

Prevention and Control, were identified in human isolates of A(H7N9) viruses. Scientific evidence of the pandemic threat posed by A(H7N9) viruses, based on H5N1 GOF studies, factored into risk assessments by the public health officials in China, the United States, and other countries.

Since the H5N1 transmission papers were published, follow-up scientific studies have contributed to our understanding of host adaptation by influenza viruses, the development of vaccines and therapeutics, and improved surveillance.

Finally, a benefit of the H5N1 virus research controversy has been the increased dialogue regarding laboratory biosafety and dual-use research. The World Health Organization issued laboratory biosafety guidelines for conducting research on H5N1 transmission and, in the United States, additional oversight policies and risk-mitigation practices have been put in place or proposed. Some journals now encourage authors to include biosafety and biosecurity descriptions in their manuscripts, thereby raising the awareness of researchers intending to replicate experiments.

The risk of a pandemic caused by an avian influenza virus exists in nature. As members of the influenza research community, we believe that the avian A(H7N9) virus outbreak requires focused fundamental and applied research conducted by responsible investigators with appropriate facilities and risk-mitigation plans in place. To answer key questions important to public health, research that may result in GOF is necessary and should be done.

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Science Translational Medicine
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http://stm.sciencemag.org/content/current
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Vaccine
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Volume 31, Issue 38, Pages 4055-4216 (28 August 2013)

The impact of HPV vaccination delays in China: Lessons from HBV control programs
Pages 4057-4059
Danny V. Colombara, Shao-Ming Wang
[No abstract or summary]

Unequal access to vaccines in the WHO European Region during the A(H1N1) influenza pandemic in 2009
Pages 4060-4062
Pernille Jorgensen, Annemarie Wasley, Jolita Mereckiene, Suzanne Cotter, J. Todd Weber, Caroline Sarah Brown
Abstract
In a severe pandemic, rapid production and deployment of vaccines will potentially be critical in mitigating the impact on populations and essential services. We compared access to vaccines and timing of delivery relative to identification of A(H1N1)pdm09 and the geographic progression of the pandemic in the WHO European Region in order to identify gaps in provision. Information on vaccine procurement and donations was collected through a web-based survey conducted in all 53 member states of the Region. Among the 51 countries responding to the survey, the majority (84%) implemented vaccination campaigns against A(H1N1)pdm09. However, time of vaccine receipt and number of doses varied substantially across the region, with delayed access in many countries especially in those in the lowest income range. Improving access to influenza vaccines in low resource countries and solving issues of product liability should help reduce inequalities and operational challenges arising during a future public health crisis.

The state-of-the-art of approved and under-development cholera vaccines
Review Article
Pages 4069-4078
M. Pastor, J.L. Pedraz, A. Esquisabel
Abstract

Cholera remains a huge public health problem. Although in 1894, the first cholera vaccination was reported, an ideal vaccine that meets all the requirements of the WHO has not yet been produced. Among the different approaches used for cholera vaccination, attenuated vaccines represent a major category; these vaccines are beneficial in being able to induce a strong protective response after a single administration. However, they have possible negative effects on immunocompromised patient populations. Both the licensed CVD103-HgR and other vaccine approaches under development are detailed in this article, such as the Vibrio cholerae 638 vaccine candidate, Peru-15 or CholeraGarde® and the VA1.3, VA1.4, IEM 108 VCUSM2 and CVD 112 vaccine candidates. In another strategy, killed V. cholerae vaccines have been developed, including Dukoral®, mORCAX® and Sanchol™. The killed vaccines are already sold, and they have successfully demonstrated their potential to protect populations in endemic areas or after natural disasters. However, these vaccines do not fulfill all the requirements of the WHO because they fail to confer long-term protection, are not suitable for children under two years, require more than a single dose and require a distribution chain with cold storage. Lastly, other vaccine strategies under development are summarized in this review. Among these strategies, vaccine candidates based on alternative drug delivery systems that have been reported lately in the literature are discussed, such as microparticles, proteoliposomes, LPS subunits, DNA vaccines and rice seeds containing toxin subunits. Preliminary results reported by many groups working on alternative delivery systems for cholera vaccines demonstrate the importance of new technologies in addressing old problems such as cholera. Although a fully ideal vaccine has not yet been designed, promising steps have been reported in the literature resulting in hope for the fight against cholera.

Trend of human rabies prophylaxis in developing countries: Toward optimal rabies immunization

Review Article

Pages 4079-4083

Nitipong Permpalung, Supakanya Wongrakpanich, Sira Korpaisarn, Pansakorn Tanratana, Jaruboot Angsanakul

Abstract

Rabies is a fatal infectious disease. Because prevention is the key management for rabies, many vaccination regimens have been developed and used worldwide. The aims for developing rabies vaccination regimens include decreasing the number and amount of dosages, decreasing the duration and the number of clinical visits, and reducing cost. Interestingly, some intradermal (ID) regimens have proved to be as effective as the standard intramuscular (IM) regimens, and have been increasingly used in developing countries because they are less expensive. In this article, we reviewed rabies vaccines based on results obtained from clinical trials and international treatment guidelines for post-exposure prophylaxis, pre-exposure prophylaxis for the high risk group, and booster vaccination.

How do anticipated worry and regret predict seasonal influenza vaccination uptake among Chinese adults?

Original Research Article

Pages 4084-4090

Q. Liao, W.S. Wong, R. Fielding

Abstract

Objectives

To test two hypothesized models of how anticipated affect, cognitive risk estimate and vaccination intention might influence vaccination uptake against seasonal influenza.

Methods

The study collected baseline and follow-up data during the main influenza seasons (January–March) of 2009 and 2010, respectively, among 507 university students and staff of a university in Hong Kong. Following logistic regression to determine eligible variables, two mediation models of cognitive risk estimate, anticipated affect, vaccination intention and vaccination uptake against seasonal influenza were tested using structural equation modeling.
Results
Mediation analyses found that anticipated worry if not vaccinated influenced seasonal influenza vaccination uptake through its effects on either perceived probability of influenza infection (β = 0.45) or intention (β = 0.45) while anticipated regret if not vaccinated influenced vaccination uptake through its effect on intention (β = 0.45) only; anticipated regret if vaccinated impeded vaccination uptake indirectly through its effect on vaccination intention (β = −0.26) or directly (β = −0.20); perceived probability of influenza infection influenced vaccination uptake through its effect on intention (β = 0.20) or directly (β = 0.22); and finally, intention influenced vaccination uptake directly (β = 0.58).
Conclusion
The results suggest that anticipated affect seems to drive risk estimates related to seasonal influenza vaccination rather than vice versa and intention remains an important mediator of the associations of anticipated affect and cognitive risk estimate with vaccination uptake against seasonal influenza.

Rotavirus-associated hospitalization and emergency department costs and rotavirus vaccine program impact

Original Research Article
Pages 4164-4171
April Kilgore, Stephanie Donauer, Kathryn M. Edwards, Geoffrey A. Weinberg, Daniel C. Payne, Peter G. Szilagyi, Marilyn Rice, Amy Cassedy, Ismael R. Ortega-Sanchez, Umesh D. Parashar, Mary Allen Staat
Abstract
Objectives
To determine the medical costs of laboratory-confirmed rotavirus hospitalizations and emergency department (ED) visits and estimate the economic impact of the rotavirus vaccine program.
Patients and methods
During 4 rotavirus seasons (2006–2009), children <3 years of age hospitalized or seen in the ED with laboratory-confirmed rotavirus were identified through active population-based rotavirus surveillance in three US counties. Medical costs were obtained from hospital and physician billing data, and factors associated with increased costs were examined. Annual national costs were estimated using rotavirus hospitalization and ED visit rates and medical costs for rotavirus hospitalizations and ED visits from our surveillance program for pre- (2006–2007) and post-vaccine (2008–2009) time periods.
Results
Pre-vaccine, for hospitalizations, the median medical cost per child was $3581, the rotavirus hospitalization rate was 22.1/10,000, with an estimated annual national cost of $91 million. Post-vaccine, the median medical cost was $4304, the hospitalization rate was 6.3/10,000 and the estimated annual national cost was $31 million. Increased costs were associated with study site, age <3 months, underlying medical conditions and an atypical acute gastroenteritis presentation. For ED visits, the pre-vaccine median medical cost per child was $574, the ED visit rate was 291/10,000 resulting in an estimated annual national cost of $192 million. Post-

vaccine, the median medical cost was $794, the ED visit rate was 71/10,000 with an estimated annual national cost of $65 million.
Conclusions
After implementation of rotavirus immunization, the total annual medical costs decreased from $283 million to $96 million, an annual reduction of $187 million.

Vaccine
Volume 31, Issue 37, Pages 3763-4054 (20 August 2013)
http://www.sciencedirect.com/science/journal/0264410X/31/37

Hib vaccine in India: A case for universal immunization
Editorial
Pages 3763-3765
Ajay Kumar, Meenu Singh, Kiran Kumar Thumburu, Nishant Jaiswal, Harpreet Kaur, Shruti Sharma, Amit Agarwal
[No abstract or summary]

Report on the first WHO integrated meeting on development and clinical trials of influenza vaccines that induce broadly protective and long-lasting immune responses: Hong Kong SAR, China, 24–26 January 2013
Pages 3766-3771
Marc P. Girard, John S. Tam, Yuri Pervikov, Jacqueline M. Katz
Abstract
On January 24–26, 2013, the World Health Organization convened the first integrated meeting on "The development and clinical trials of vaccines that induce broadly protective and long-lasting immune responses" to review the current status of development and clinical evaluation of novel influenza vaccines as well as strategies to produce and deliver vaccines in novel ways. Special attention was given to the development of possible universal influenza vaccines. Other topics that were addressed included an update on clinical trials of pandemic and seasonal influenza vaccines in high-risk groups and vaccine safety, as well as regulatory issue.

Enhancing access to immunization services and exploiting the benefits of recent innovations in the African region
Pages 3772-3776
J.C. Okeibunor, B.D. Akanmori, G.M. Balcha, R. Mihigo, R.M. Vaz, D. Nshimirimana
Abstract
The African Regional Office of the World Health Organization (WHO AFRO) organized the annual regional conference on immunization (ARCI) from 10 to 12 December 2012 in Dar es Salaam, Tanzania, under the theme, "Innovations, access and the right of all to vaccines". The meeting reviewed the status of immunization in the region and identified all innovations, strategies and technologies available and how these could be fully utilized to enhance the access and the rights of all to vaccines. Over 50 oral presentations were made in plenary and parallel sessions of the conference which was attended by over 200 participants drawn from national immunization programs, academia, public health experts and immunization partners. In addition there were 40 poster presentations. This manuscript summarizes of the meeting, highlighting the innovations in immunization being piloted or scaled-up, their impact and suggesting ways to further improve immunization service delivery for the eradication, elimination and control of vaccine-preventable diseases in the region.

Cost-effectiveness of human papillomavirus vaccination in low and middle income countries: A systematic review

Review Article
Pages 3786-3804
Michaela Fesenfeld, Raymond Hutubessy, Mark Jit
Abstract
The World Health Organization recommends establishing that human papillomavirus vaccination is cost-effective before vaccine introduction. We searched Pubmed, Embase and the Cochrane Library to 1 April 2012 for economic evaluations of human papillomavirus vaccination in low and middle income countries. We found 25 articles, but almost all low income countries and many middle income countries lacked country-specific studies. Methods, assumptions and consequently results varied widely, even for studies conducted for the same country. Despite the heterogeneity, most studies conclude that vaccination is likely to be cost-effective and possibly even cost saving, particularly in settings without organized cervical screening programmes. However, study uncertainty could be reduced by clarity about vaccine prices and vaccine delivery costs. The review supports extending vaccination to low income settings where vaccine prices are competitive, donor funding is available, cervical cancer burden is high and screening options are limited.

Human papillomavirus (HPV) vaccine implementation in low and middle-income countries (LMICs): Health system experiences and prospects

Review Article
Pages 3811-3817
Jannah Wigle, Ernestina Coast, Deborah Watson-Jones
Abstract
Prophylactic vaccines for human papillomavirus (HPV) are being introduced in many countries for the prevention of cervical cancer, the second most important cause of cancer-related death in women globally. This is likely to have a significant impact on the future burden of cervical cancer, particularly where screening is non-existent or limited in scale. Previous research on the challenges of vaccinating girls with the HPV vaccine has focused on evidence from developed countries. We conducted a systematic search of the literature in order to describe the barriers and challenges to implementation of HPV vaccine in low- and middle-income countries. We identified literature published post-2006 to September 2012 from five major databases. We validated the findings of the literature review with evidence from qualitative key informant interviews. Three key barriers to HPV vaccine implementation were identified: sociocultural, health systems and political. A linked theme, the sustainability of HPV vaccines programmes in low- and middle-income countries, cuts across these three barriers. Delivering HPV vaccine successfully will require multiple barriers to be addressed. Earlier research in developed countries emphasised sociocultural issues as the most significant barriers for vaccine roll-out. Our evidence suggests that the range of challenges for poorer countries is significantly greater, not least the challenge of reaching girls for three doses in settings where school attendance is low and/or irregular. Financial and political barriers to HPV vaccine roll-out continue to be significant for many poorer countries. Several demonstration and pilot projects have achieved high rates of acceptability and coverage and lessons learned should be documented and shared.

Strengthening vaccination policies in Latin America: An evidence-based approach

Review Article
Pages 3826-3833
Roberto Tapia-Conyer, Miguel Betancourt-Cravioto, Rodrigo Saucedo-Martínez, Lourdes Motta-Murguía, Héctor Gallardo-Rincón
Abstract

Despite many successes in the region, Latin American vaccination policies have significant shortcomings, and further work is needed to maintain progress and prepare for the introduction of newly available vaccines. In order to address the challenges facing Latin America, the Commission for the Future of Vaccines in Latin America (COFVAL) has made recommendations for strengthening evidence-based policy-making and reducing regional inequalities in immunisation. We have conducted a comprehensive literature review to assess the feasibility of these recommendations. Standardisation of performance indicators for disease burden, vaccine coverage, epidemiological surveillance and national health resourcing can ensure comparability of the data used to assess vaccination programmes, allowing deeper analysis of how best to provide services. Regional vaccination reference schemes, as used in Europe, can be used to develop best practice models for vaccine introduction and scheduling. Successful models exist for the continuous training of vaccination providers and decision-makers, with a new Latin American diploma aiming to contribute to the successful implementation of vaccination programmes. Permanent, independent vaccine advisory committees, based on the US Advisory Committee on Immunization Practices (ACIP), could facilitate the uptake of new vaccines and support evidence-based decision-making in the administration of national immunisation programmes. Innovative financing mechanisms for the purchase of new vaccines, such as advance market commitments and cost front-loading, have shown potential for improving vaccine coverage. A common regulatory framework for vaccine approval is needed to accelerate delivery and pool human, technological and scientific resources in the region. Finally, public–private partnerships between industry, government, academia and non-profit sectors could provide new investment to stimulate vaccine development in the region, reducing prices in the long term. These reforms are now crucial, particularly as vaccines for previously neglected, developing-world diseases become available. In summary, a regionally-coordinated health policy will reduce vaccination inequality in Latin America.

Single-dose varicella vaccine effectiveness in school settings in China

Original Research Article

Pages 3834-3838

Zhe Wang, Huili Yang, Keli Li, Aihua Zhang, Zijian Feng, Jane F. Seward, Stephanie R. Bialek, Chengbin Wang

Abstract

Background

Varicella vaccine has been available in the private sector in China for a decade as a single-dose regimen, but varicella vaccine effectiveness (VE) has not been fully examined in school settings yet.

Methods

A matched case–control study was carried out in elementary schools and daycares in Tai'an prefecture, Shandong province, China. Clinical diagnosis of varicella and breakthrough disease was used for this study. Four controls were randomly selected from classmates; two from classmates of the case and two from another class of the same grade without cases. Vaccination status, date of vaccination, and vaccine product received if vaccinated were collected from home and clinic immunization records. Vaccination status of all students in schools/daycares with varicella cases from home immunization records or parental recall was used to calculate vaccination coverage.

Results

The overall varicella VE was 83.4% (95% confidence interval 71.4–90.3%). Receipt of varicella vaccine five years or more years before the outbreak was significantly associated with breakthrough varicella (odds ratio = 4.7, $P < 0.001$), while age at vaccination (<15 vs. ≥15

months) was not (odds ratio = 1.5, P = 0.62). Varicella vaccination coverage was 41% with substantial variation across schools (range of 0–93.8%).

Comparative cost-effectiveness of the quadrivalent and bivalent human papillomavirus vaccines: A transmission-dynamic modeling study

Original Research Article

Pages 3863-3871

Marc Brisson, Jean-François Laprise, Mélanie Drolet, Nicolas Van de Velde, Eduardo L. Franco, Erich V. Kliewer, Gina Ogilvie, Shelley L. Deeks, Marie-Claude Boily

Abstract

Background

The quadrivalent and bivalent human papillomavirus (HPV) vaccines are now licensed in several countries. We compared the cost-effectiveness of the HPV vaccines to provide evidence for policy decisions.

Methods

We developed HPV-ADVISE, a multi-type individual-based transmission-dynamic model of HPV infection and disease (anogenital warts, and cervical, anogenital and oropharyngeal cancers). We calibrated the model to sexual behavior and epidemiologic data from Canada, and estimated quality-adjusted life-years (QALYs) lost and costs ($CAN 2010) from the literature. Vaccine-type efficacy was based on a systematic literature review. The analysis was performed from the healthcare provider perspective, and costs and benefits were discounted at 3%. Predictions are presented using the median [10th;90th percentiles] of simulations.

Results

Under base-case assumptions (vaccinating 10-year-old girls, 80% coverage, $95/dose), using the quadrivalent and bivalent vaccines is estimated to cost $15,528 [12,056;19,140] and $20,182 [15,531;25,240] per QALY-gained, respectively. At equal price, the quadrivalent vaccine is more cost-effective than bivalent under all scenarios investigated, except when assuming longer duration of protection for the bivalent and minimal anogenital warts burden. Under base-case assumptions, the maximum additional cost per dose for the quadrivalent vaccine to remain more cost-effective than the bivalent is $32 [17;46] (using a $40,000/QALY-gained threshold). Results were most sensitive to discounting, time-horizon, differences in durations of protection and anogenital warts burden.

Conclusions

Vaccinating pre-adolescent girls against HPV is predicted to be highly cost-effective. If equally priced, the quadrivalent is the most economically desirable vaccine. However, ultimately, the most cost-effective HPV vaccine will be determined by their relative price.

Potential influence of seasonal influenza vaccination requirement versus traditional vaccine promotion strategies on unvaccinated healthcare personnel

Original Research Article

Pages 3915-3921

Mark G. Thompson, Anne F. McIntyre, Allison L. Naleway, Carla Black, Erin D. Kennedy, Sarah Ball, Deborah Klein Walker, Emily M. Henkle, Manjusha J. Gaglani

Abstract

In a prospective cohort study of 1670 healthcare personnel (HCP) providing direct patient care at Scott & White Healthcare in Texas and Kaiser Permanente Northwest in Oregon and Washington, we examined the potential impact of twelve vaccine promotion strategies on the likelihood of being vaccinated. Internet-based surveys were conducted at enrollment (Fall, 2010) and at post-season (Spring, 2011), which asked HCP whether twelve vaccination promotion strategies would make them "much less" to "much more" likely to be vaccinated next

season (on a 5-point Likert scale). Overall, 366 of 1670 HCP (22%) were unvaccinated. Half (50%) of unvaccinated HCP self-reported that a vaccination requirement would make them more likely to be vaccinated and most (62%) identified at least one strategy other than a vaccination requirement that would make them more likely to be vaccinated. In sub-groups of unvaccinated HCPs with specific barriers to vaccination, about one in three (range = 27–35%) indicated that interventions targeting specific vaccination barrier would increase the likelihood they would be vaccinated. However, in all cases, significantly more unvaccinated HCP reported that a vaccination requirement would increase the likelihood of vaccination than reported a targeted intervention would have this effect (range in difference scores = +11–23%).

Cost–effectiveness of the prophylactic HPV vaccine: An application to the Netherlands taking non-cervical cancers and cross-protection into account

Original Research Article
Pages 3922-3927
J. Luttjeboer, T.A. Westra, J.C. Wilschut, H.W. Nijman, T. Daemen, M.J. Postm

Abstract
Despite an effective screening programme, 600–700 women are still diagnosed with cervical cancer in the Netherlands each year. In 2009 a prophylactic vaccine against HPV-type 16 and 18 was implemented in the national immunisation programme to decrease the incidence of cervical cancer. There is evidence that infections with several oncogenic HPV types other than the vaccine types 16 and 18 are also prevented by vaccination, also known as cross-protection. Besides cervical cancer, HPV can also cause cancers at other sites such as the oropharynx, vulva, vagina and the anus/anal area. In this study we estimated the maximum health and economic benefits of vaccinating 12-year old girls against infection with HPV, taking cross-protection and non-cervical cancers into account. In the base-case, we found an incremental cost ratio (ICER) of €5815 per quality adjusted life year (QALY). Robustness of this result was examined in sensitivity analysis. The ICER proved to be most sensitive to vaccine price, discounting rates, costs of cervical cancer and to variation in the disutility of cervical cancer.

Cost-effectiveness of pneumococcal conjugate vaccination in immunocompromised adults

Original Research Article
Pages 3950-3956
Kenneth J. Smith, Mary Patricia Nowalk, Mahlon Raymund, Richard K. Zimmerman

Abstract
Objective
Pneumococcal disease is a significant problem in immunocompromised persons, particularly in HIV-infected individuals. The CDC recently updated pneumococcal vaccination recommendations for immunocompromised adults, adding the 13-valent pneumococcal conjugate vaccine (PCV13) to the previously recommended 23-valent pneumococcal polysaccharide vaccine (PPSV23). This analysis estimates the cost-effectiveness of pneumococcal vaccination strategies in HIV-infected individuals and in the broader immunocompromised adult group.
Design
Markov model-based cost-effectiveness analysis.
Methods
The model considered immunocompromised persons aged 19–64 years and accounted for childhood PCV13 herd immunity; in a separate analysis, an HIV-infected subgroup was considered. PCV13 effectiveness was estimated by an expert panel; PPSV23 protection was

modeled relative to PCV13 effectiveness. We assumed that both vaccines prevented invasive pneumococcal disease, but only PCV13 prevented nonbacteremic pneumonia.
Results
In all immunocompromised individuals, a single PCV13 cost $70,937 per quality adjusted life year (QALY) gained compared to no vaccination; current recommendations cost $136,724/QALY. In HIV patients, with a longer life expectancy (22.5 years), current recommendations cost $89,391/QALY compared to a single PCV13. Results were sensitive to variation of life expectancy and vaccine effectiveness. The prior recommendation was not favored in any scenario.
Conclusions
One dose of PCV13 is more cost-effective for immunocompromised individuals than previous vaccination recommendations and may be more economically reasonable than current recommendations, depending on life expectancy and vaccine effectiveness in the immunocompromised.

Dengue dynamics and vaccine cost-effectiveness in Brazil

Original Research Article
Pages 3957-3961
David P. Durham, Martial L. Ndeffo Mbah, Jan Medlock, Paula M. Luz, Lauren A. Meyers, A. David Paltiel, Alison P. Galvani
Abstract

Recent Phase 2b dengue vaccine trials have demonstrated the safety of the vaccine and estimated the vaccine efficacy with further trials underway. In anticipation of vaccine roll-out, cost-effectiveness analysis of potential vaccination policies that quantify the dynamics of disease transmission are fundamental to the optimal allocation of available doses.

We developed a dengue transmission and vaccination model and calculated, for a range of vaccination costs and willingness-to-pay thresholds, the level of vaccination coverage necessary to sustain herd-immunity, the price at which vaccination is cost-effective and is cost-saving, and the sensitivity of our results to parameter uncertainty. We compared two vaccine efficacy scenarios, one a more optimistic scenario and another based on the recent lower-than-expected efficacy from the latest clinical trials.

We found that herd-immunity may be achieved by vaccinating 82% (95% CI 58–100%) of the population at a vaccine efficacy of 70%. At this efficacy, vaccination may be cost-effective for vaccination costs up to US$ 534 (95% CI $369–1008) per vaccinated individual and cost-saving up to $204 (95% CI $39–678). At the latest clinical trial estimates of an average of 30% vaccine efficacy, vaccination may be cost-effective and cost-saving at costs of up to $237 (95% CI $159–512) and $93 (95% CI $15–368), respectively.

Our model provides an assessment of the cost-effectiveness of dengue vaccination in Brazil and incorporates the effect of herd immunity into dengue vaccination cost-effectiveness. Our results demonstrate that at the relatively low vaccine efficacy from the recent Phase 2b dengue vaccine trials, age-targeted vaccination may still be cost-effective provided the total vaccination cost is sufficiently low.

Incremental cost-effectiveness evaluation of vaccinating girls against cervical cancer pre- and post-sexual debut in Belgium

Original Research Article
Pages 3962-3971
Nadia Demarteau, Georges Van Kriekinge, Philippe Simon
Abstract
Background

Vaccination against human papillomavirus (HPV) to prevent cervical cancer (CC) primarily targets young girls before sexual debut and is cost-effective. We assessed whether vaccination with the HPV-16/18 AS04-adjuvanted vaccine added to screening remains cost-effective in females after sexual debut compared to screening alone in Belgium. The role of protection against non-HPV-16/18 was also investigated.
Methods
A published Markov cohort model was adapted to Belgium. The model replicated the natural history of HPV infection, the effects of screening, and vaccination. Vaccine efficacy (VE) included non-HPV-16/18 protection based on the PATRICIA clinical trial data. Pre- and post-HPV exposure VE were differentiated. Lifetime vaccine protection was assumed. Input data were obtained from literature review, national databases and a Delphi panel. Costing was from a healthcare payer perspective. Costs were discounted at 3% and effects at 1.5%. The incremental cost-effectiveness ratio (ICER) per quality-adjusted life-year (QALY) gained and the number of lesions prevented with vaccination from age 12 to 40 was evaluated. The specific effect of non-HPV-16/18 protection was investigated. Univariate sensitivity analysis was performed on key variables.
Results
The model estimated that vaccinating a cohort of 100,000 girls at age 12 would prevent 646 CC cases over a lifetime (102 non-HPV-16/18) with an ICER of €9171/QALY. Vaccinating at age 26 would prevent 340 CC cases (40 non-HPV-16/18) with an ICER of €17,348/QALY and vaccinating at age 40 would prevent 146 CC cases (17 non-HPV-16/18) with an ICER of €42,847/QALY. The ICER remained under the highly cost-effective threshold (1×GDP/capita) until age 33 years and under the cost-effective threshold (3×GDP/capita) beyond age 40.
Conclusion
Extending HPV vaccination to females post-sexual debut could lead to a substantial reduction in CC-related burden and would be cost-effective in Belgium.

Pregnant women's intention to take up a post-partum pertussis vaccine, and their willingness to take up the vaccine while pregnant: A cross sectional survey

Original Research Article
Pages 3972-3978
K.E. Wiley, P.D. Massey, S.C. Cooper, N. Wood, H.E. Quinn, J. Leask
Abstract
Introduction
Post-partum vaccination of new mothers is currently recommended in Australia to reduce pertussis infection in infants. Internationally, vaccination recommendations now include pregnant women in some countries. Understanding the awareness of pertussis vaccination recommendations among pregnant women, and their willingness to have the vaccine while pregnant is important for informing vaccine program implementation.
Objective
To determine awareness and intentions toward current recommendations for post-partum pertussis vaccination among Australian pregnant women, and their willingness to accept pertussis vaccine during pregnancy, should it be recommended in Australia in the future.
Design
Quantitative self-administered survey, using a non-random stratified sampling plan based on representative proportions by age, parity and region of residence.
Participants and setting
Pregnant women receiving antenatal care through three large, demographically diverse referral hospitals in metropolitan, urban and rural New South Wales, Australia.

Results
The response rate was 815/939 (87%). Most women (80%) reported willingness to have the pertussis vaccine during pregnancy, should it be recommended. Thirty four per cent of women intended to receive a pertussis vaccine post-partum, 17% had received it previously, while 45% had never heard of pertussis vaccine, had not thought about it, or were undecided about having it. Compared with those who had not received a recommendation to have the vaccine post-partum, women who had received a recommendation were 7 times more likely (95% CI 4–14) to report intention to have the vaccine.
Conclusions
Health care provider recommendation is paramount to raising awareness of pertussis vaccination recommendations among pregnant women. Women's willingness to have the vaccine while pregnant is encouraging, and indicates the potential for high pertussis vaccine coverage among pregnant women, should it be recommended in Australia.

Vaccine: Development and Therapy
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Prevention and control of influenza and dengue through vaccine development.
DP Greenberg, CA Robertson, DM Gordon - Pediatric annals, 2013
CME EDUCATIONAL OBJECTIVES 1. Review the impact of influenza infection in the pediatric population. 2. Discuss the importance of influenza B as a key cause of morbidity and review the progress on development and deployment of quadrivalent influenza ...

P5. 106 Charting the Path For Human Papillomavirus (HPV) Vaccine Introduction in Kenya: Assessing HPV Vaccine Acceptability Among Caregivers and Opinion ...
AL Friedman, E Dunne, K Onyango, M Habel, J Ford… - Sexually Transmitted …, 2013

Background Cervical cancer is the second most common cancer diagnosed, and the leading cause of cancer-related mortality among women in Kenya. Kenya's Ministry of Health has outlined new prevention strategies, including support for vaccination. Formative research ...

P3. 369 Acceptability of HPV Tetravalent Vaccine Among Males Attending the STD Clinic of Milan-The Importance of the Costs For Patients
M Cusini, S Ramoni - Sexually Transmitted Infections, 2013
Background HPV infection is usually transmitted by sexual contact and represent the most prevalent sexually transmitted infection all over the world. The clinical spectrum of HPV infection varies from the asymptomatic status to benign genital lesions to the development ...

1 5 Chronic Non-Communicable
KMV NARAYAN, D YACH - Social Injustice and Public Health, 2013
... In recent years, new private foundations have appropriately invested billions of dollars for HIV/AIDS, malaria, tuberculosis, and immunizable diseases. And international donor organizations have increased support for tobacco control. ...

The Hepatitis B Vaccine Protects Re-Exposed Healthcare Workers, but Does Not Provide Sterilizing Immunity
JM Werner, A Abdalla, N Gara, MG Ghany… - Gastroenterology, 2013
Background & Aims: Infection with hepatitis B virus (HBV) can be prevented by vaccination with HBV surface (HBs) antigen, which induces HBs-specific antibodies and T cells. However, the duration of vaccine-induced protective immunity is poorly defined for ...

Interview: An insight into cutting-edge tuberculosis vaccine research
EM Agger - Immunotherapy, 2013
Else Marie Agger speaks to Katie Lockwood, Assistant Commissioning Editor Else Marie Agger was appointed Director of the Department of Infectious Disease Immunology, Statens Serum Institut in Denmark in 2011. Prior to this, she had been heading two different ...

Media/Policy Watch

This section is intended to alert readers to substantive news, analysis and opinion from the general media on vaccines, immunization, global; public health and related themes. *Media Watch* is not intended to be exhaustive, but indicative of themes and issues CVEP is actively tracking. This section will grow from an initial base of newspapers, magazines and blog sources, and is segregated from *Journal Watch* above which scans the peer-reviewed journal ecology.

We acknowledge the Western/Northern bias in this initial selection of titles and invite suggestions for expanded coverage. We are conservative in our outlook in adding news sources which largely report on primary content we are already covering above. Many electronic media sources have tiered, fee-based subscription models for access. We will provide full-text where content is published without restriction, but most publications require registration and some subscription level.

Al Jazeera
http://www.aljazeera.com/Services/Search/?q=vaccine
Accessed 10 August 2013

[No new, unique, relevant content]

The Atlantic
http://www.theatlantic.com/magazine/
Accessed 10 August 2013
[No new, unique, relevant content]

BBC
http://www.bbc.co.uk/
Accessed 10 August 2013
[No new, unique, relevant content]

Brookings
http://www.brookings.edu/
Accessed 10 August 2013
[No new, unique, relevant content]

Council on Foreign Relations
http://www.cfr.org/
Accessed 10 August 2013
[No new, unique, relevant content]

Economist
http://www.economist.com/
Accessed 10 August 2013
[No new, unique, relevant content]

Financial Times
http://www.ft.com
Accessed 10 August 2013
[No new, unique, relevant content]

Forbes
http://www.forbes.com/
Accessed 10 August 2013
Entrepreneurs
8/06/2013
Delivering Vaccines To Where They're Needed Most
Editor's Note: In advance of the many health-related discussions to take place in September at the Clinton Global Initiative, the Social Good Summit, UN week and other such events, the Skoll World Forum asked some of the world's leading voices in global health to paint a comprehensive picture of key trends, challenges and opportunities to realizing healthcare access and treatment around the world. A new piece will be posted everyday through Friday, and you can view the entire series here.

Kevin Reilly is a senior business executive with more than 30 years' experience in the pharmaceutical and vaccine industries. During his 20 years with Wyeth Pharmaceuticals, he served in several positions covering responsibilities in Canada, Asia, and the Pacific region.

From 1999 until his retirement in 2003, he was president of Wyeth's $2 billion Vaccine and Nutrition Division.

Rahim Kanani: You bring a unique perspective to global health work, coming from a long career in the pharmaceutical and vaccine industries. What are some of the lessons you've learned or "aha" moments you've experienced in your work on broader global health and development issues?

Kevin Reilly: Personally, I've developed a deeper appreciation for the complexity involved in running successful immunization programs. From the point of view of the vaccine manufacturer, you focus on the specific activities needed to move a vaccine successfully through the stages of development, but the many challenges involved in delivering and distributing that vaccine in developing countries may be less obvious. Getting a vaccine successfully from the factory door to the arms of millions of children in low-resource settings—that's an enormously complicated task. Increasingly, I see pharmaceutical and vaccine manufacturers engaging in the dialogue about strengthening immunization and distribution systems to ensure vaccines get to where they are needed. Vaccine manufacturers were among the key partners involved in the early conversations that led to the formation of the GAVI Alliance, for example. They could see that global immunization rates were stagnating and that something needed to be done.

Similarly, I see growing awareness among global health organizations about the difficult, multiyear process required to develop vaccines and how that process influences the price. Where some organizations may once have advocated for a flat price of, say, less than $1 per dose for developing countries, now I think there is greater appreciation for the fact that new vaccines are extremely complex and expensive to develop. There are more efforts now to create a productive dialogue between manufacturers and global health organizations and to think creatively about funding structures and other mechanisms that may expand access to vaccines while also recognizing the need of manufacturers to ensure the financial health and well-being of their own corporations.

Rahim Kanani: What makes public-private partnerships between business, government, and civil society an effective way to tackle global health challenges? And what are some examples of big pharmaceutical companies partnering with other sectors?

Kevin Reilly: Vaccine manufacturers have a long history of providing vaccines at heavily discounted prices for use in the developing world, a practice that stretches back over half a century. For example, early in my career, I was involved in helping to provide polio vaccine to UNICEF for 2 cents per dose. While the prices have gone up for various reasons, this practice is still active today and is a critical factor in many vaccines reaching millions of children in the developing world.

From the standpoint of business, one of the keys to success for public-private partnerships is recognition that vaccine and pharmaceutical manufacturers have an important contribution to make but also have corporate interests that they must protect as well. So companies are striving to find that balance between using their discoveries to maximize the good they can do for people around the world and achieving a reasonable return on their investment.

I was also involved in helping bring Prevnar, the first pneumococcal conjugate vaccine, to market as president of Wyeth Pharmaceuticals' Vaccine and Nutrition Division. Wyeth and GAVI entered into a discussion early on about how the vaccine could help meet the needs of developing countries, where pneumonia is the leading cause of death in young children. Through those conversations and GAVI's innovative financing mechanism, Wyeth was able to make special arrangements for the supply of the vaccine, thus accelerating the availability of a new, complex vaccine in low-income countries.

Rahim Kanani: Is developing a vaccine the hardest part, or is it the delivery and distribution of that vaccine to the developing world?

Kevin Reilly: Both are essential for successful health outcomes—and both are immensely challenging. Developing a vaccine involves a relatively narrow set of activities driven by scientific and clinical research work. Since 2000, barely a handful of new vaccines have been developed. That's because this is complicated work dotted with setbacks and failures along the way. You try things in the lab that fail, or things don't work out clinically the way you predicted they would based on results in the lab. Prevnar was 17 years in development and went through ownership by three different corporate entities on its way to market.

On the other hand, vaccine delivery is a broad-based, multidimensional, and cross-sector activity involving many different systems and stakeholders. Ideally, you aim to bridge the two sides of this process, to develop a vaccine that is safe and effective while also being suited for efficient distribution and delivery. Sometimes, the complex biological and scientific factors involved in vaccine development limit your ability to optimize design for the distribution and delivery of the vaccine —for example, it may have special cold chain requirements that make it difficult to reach remote areas.

PATH's work on the MenAfriVac® vaccine is a good example of how vaccine development, distribution, and delivery are inextricably linked. PATH and the World Health Organization worked with dozens of global collaborators over a decade to develop the vaccine against deadly meningitis A. Simultaneously, they worked with countries across Africa's "meningitis belt" to build their capacity to integrate the vaccine into their health programs by strengthening disease surveillance, enhancing lab capacity, and reaching out to policymakers, health workers, and journalists with information and training. Recently, the vaccine became the first in Africa approved for transport and storage outside the traditional cold chain. To date, more than 100 million Africans across ten countries have received this new vaccine.

Rahim Kanani: It's clear that businesses do a tremendous amount of work in researching and developing new drugs and vaccines to fight disease and illness. What role should governments and educational institutions play in terms of investment and research, and how can they complement each other?

Kevin Reilly: Businesses primarily focus on developing products directed at specific disease targets. In many cases, they are building on the broad base of knowledge created by academic and government research facilities. A lot of this early, upstream research may not be highly visible, but it provides a crucial foundation for the specific products coming out of pharmaceutical and biotech companies. This base of knowledge is a critical asset for the progress of health and medicine, and because this approach has been most successfully applied in the US, I believe it also gives the US a significant competitive advantage. This allows business to focus on the specific development work needed to deliver a product—work that usually involves large investments and significant risk-taking associated with the success or failure of the project. I think that matching of risk capital with high-risk activity seems appropriate.

Increasingly, we are seeing drug and vaccine manufacturers coming together with global health organizations to reduce the lag time between product launches in the developed world and the developing world. This is a relatively new trend, and a welcome one. With Prevnar, for example, Wyeth was in dialogue with GAVI soon after the vaccine launched in 2000 in the US and Europe about how to accelerate the launch of the vaccine in developing countries.

Rahim Kanani: Finally, as someone with more than 30 years of experience in this space, what are some of the leadership lessons you've learned along the way when it comes to advancing global health?

Kevin Reilly: Patience and persistence. These are essential elements of success in improving health around the world. The development of drugs and vaccines is an extremely long and high-risk process. Maintaining momentum requires an unwavering faith in the final objective and an unrelenting focus on doing what it takes to get there. The same is true in other kinds of global health initiatives. Some of these programs take decades to reach fruition. Polio eradication, for example, has been a global health priority for more than 50 years. In the case of polio, it's not a matter of developing a vaccine. We've had the vaccine since the 1950s. It's overcoming the challenges of delivering the vaccine to every child in every village in every country around the world. The global health community has been pushing on this for years, knowing what a powerful payoff there will be if we are successful.

Foreign Affairs
http://www.foreignaffairs.com/
Accessed 10 August 2013
[No new, unique, relevant content]

Foreign Policy
http://www.foreignpolicy.com/
Accessed 10 August 2013
[No new, unique, relevant content]

The Guardian
http://www.guardiannews.com/
Accessed 10 August 2013
[No new, unique, relevant content]

The Huffington Post
http://www.huffingtonpost.com/
Accessed 10 August 2013
[No new, unique, relevant content]

Le Monde
http://www.lemonde.fr/
Accessed 10 August 2013
[No new, unique, relevant content]

New Yorker
http://www.newyorker.com/
Accessed 10 August 2013
[No new, unique, relevant content]

New York Times
http://www.nytimes.com/
Accessed 10 August 2013
[No new, unique, relevant content]

Reuters
http://www.reuters.com/

Accessed 10 August 2013
[see story on extension of Israël's polio immunisation campaign above]

Wall Street Journal
http://online.wsj.com/home-page
Accessed 10 August 2013
[No new, unique, relevant content]

Washington Post
http://www.washingtonpost.com/
Accessed 10 August 2013

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