Vaccines: The Week in Review
3 October 2011
Center for Vaccine Ethics & Policy (CVEP)
http://centerforvaccineethicsandpolicy.wordpress.com/
A program of
- Center for Bioethics, University of Pennsylvania
http://www.bioethics.upenn.edu/
- The Wistar Institute Vaccine Center
http://www.wistar.org/vaccinecenter/default.html
- Children's Hospital of Philadelphia, Vaccine Education Center
http://www.chop.edu/consumer/jsp/microsite/microsite.jsp

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

Comments and suggestions should be directed to
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The GAVI Alliance announced it will provide funding for 16 more developing countries to introduce rotavirus vaccines and 18 more countries to introduce pneumococcal vaccines, noting that the roll out of rotavirus vaccines across Africa has already begun in Sudan. GAVI CEO Seth Berkley M.D. said, "Thanks to our donors and partners, the GAVI Alliance is now delivering on its promise to protect more children across the developing world against rotavirus, pneumococcal disease and other life-threatening yet preventable diseases. The death toll of rotavirus and pneumococcal infections in Africa is particularly devastating, and this is where these vaccines will make the most significant impact, not only in lives saved, but also in terms of healthy lives lived. Immunisation enables good health and healthy people are more productive and ultimately fuel economic growth." GAVI also approved applications from five countries for pentavalent vaccine, and 12 for other types of vaccines (see detailed list of approved countries).
http://www.who.int/immunization/newsroom/press/vaccines_to_reach_37_more_countries/en/index.html

J.P. Morgan, the World Bank and the International Finance Facility for Immunisation (IFFIm) announced the issuance of US$169.4 million (equivalent) of IFFIm "vaccine bonds" in Japan. The proceeds will support GAVI Alliance programs. Alan Gillespie, IFFIm Board Chair, said, "The investment by the Japanese people in IFFIm is a testament to their commitment to GAVI's life-saving work. We also greatly appreciate J.P. Morgan and our three Japanese distributors for their role in placing IFFIm's AAA-rated bonds."
http://www.iffim.org/library/news/press-releases/2011/new-iffim-vaccine-bonds-issued-to-support-life-saving-immunisation-in-poorest-countries/

A Thomson Reuters-NPR Health Poll in the U.S. found that 26.6 percent of respondents expressed concern over the safety of vaccines. Households with children under the age of 18 demonstrated the greatest level of concern (30.8%). The lowest level of concern (18.5%) was found in respondents 65 years old and up. Thomson Reuters and NPR conduct a monthly poll to gauge attitudes and opinions on a wide range of health issues.
The poll found that, among those with concerns, 47.3 percent attributed their fear of vaccines to future long-term impact on health and 46.0 percent said they were worried about side effects. Nearly one in five said they have questioned or refused a vaccine for themselves or their children -- with a higher rate among those under 35 (28.1 percent) and a lower rate among those 65 and older (12.7 percent). When asked about specific safety concerns, 21.4 percent of respondents said they believe vaccines can cause of autism, 9.2 percent said they believe vaccines can be linked to cancer, 6.9 percent believe they play a role in diabetes, and 5.9 percent cite a connection between vaccines and heart disease. Overall, 24 percent of respondents said their opinions of vaccines have changed in the past five years. Of those, 59 percent say their views on vaccines have become less favorable. Poll survey results:
http://healthcare.thomsonreuters.com/npr/assets/NPR_report_vaccines.pdf
http://www.prnewswire.com/news-releases/thomson-reuters-npr-health-poll-finds-one-in-four-americans-believe-vaccines-are-unsafe-130837193.html

The Board of the Global Fund announced adoption of recommendations "for major reforms made by an independent panel of distinguished individuals" designed to help the Global Fund evolve from an organization responding to an emergency into an even more effective one delivering a sustainable response." Global Fund Chair Simon Bland commented, "We are determined to carry out these changes quickly to ensure that donors and implementing countries maintain absolute confidence that the Global Fund is an efficient and effective funding channel that delivers value for money. Following the Board meeting we now have a clear way forward to make these changes." The Board's governance is being overhauled "to provide comprehensive oversight" with its four standing committees being reduced to three: one to focus on strategy and investment, a second one to concentrate on finance and operational performance, and a third committee -- with a majority of independent members -- dealing with audits and ethics.

http://www.theglobalfund.org/en/mediacenter/pressreleases/2011-09-27_Global_Fund_Board_adopts_Panel_recommendations_calling_for_urgent_reform/

The **MMWR Weekly for September 30, 2011** / Vol. 60 / No. 38 includes:
- Severe Illness from 2009 Pandemic Influenza A (H1N1) --- Utah, 2009--10 Influenza Season
- Progress in Implementing Measles Mortality Reduction Strategies --- India, 2010--2011

The **Weekly Epidemiological Record (WER) for 30 September 2011**, vol. 86, 40 includes: Confirmed international spread of wild poliovirus from Pakistan; Progress in implementing measles mortality reduction strategies, India 2010–2011
http://www.who.int/entity/wer/2011/wer8640.pdf

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

ArthurCaplan Arthur Caplan
flu mandates for hcws taking off in usa! bit.ly/qLIjSe

gatespolio Gates Polio
by EndPolioNow
@billgates and Busuyi Onabolu, PolioPlus Chairman in Nigeria: ending polio is #morethanagoal @FCBarcelona @rotary gates.ly/qAPxUS

PIH Partners In Health
RT @seaif: Paul Farmer explains why global health has to first focus on #poverty: http://ow.ly/6JWgt via @TheHumanosphere #CGI2011 @PIH

PublicHealth APHA
State & local public health officials should decide where & how to store antibiotics against anthrax attack, says IOM: goo.gl/jlLJq

UNICEF UNICEF
bit.ly/rqP0Pv -- Video report on how bednets are saving lives in #Mozambique -- #Malaria -- @Malaria_Envoy -- @MalariaNoMore

AIDSvaccine IAVI
Economists panel w 3 Nobel Laureates finds #HIV vaccine R&D shld be a top priority as part of comp response to pandemic bit.ly/oHr5Y8

GAVIAlliance GAVI Alliance
Check out the latest blog from @OrinLevine - Progress That Demands Performance http://ht.ly/6IoOp

WHOnews WHO
It's World Rabies Day. Worldwide, more than 55,000 people die of #rabies every year bit.ly/puYDRM #globalhealth
28 Sep

unfoundation UN Foundation
RT @gatespolio: Great news: Saudi Arabia gives $30 million toward #polio eradication gates.ly/oM5kFO @unfoundation @rotary
28 Sep

GAVISeth Seth Berkley
@GAVIAlliance delivers on the promise, approving an unprecedented 37 countries for #vaccines support: ht.ly/6Gbcb
28 Sep

Journal Watch

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

Annals of Internal Medicine
September 20, 2011; 155 (6)
http://www.annals.org/content/current
[Reviewed earlier; No relevant content]

British Medical Bulletin
Volume 99 Issue 1 September 2011
http://bmb.oxfordjournals.org/content/current
[Reviewed earlier; No relevant content]

British Medical Journal
1 October 2011 Volume 343, Issue 7825
http://www.bmj.com/content/current

Editor's Choice

Why don't we know how much vaccines cost?

Fiona Godlee, editor, BMJ

[Free full-text]

The Global Alliance on Vaccines and Immunisation can be proud of what it has achieved. As Sophie Arie reports, it has prevented more than five million premature deaths since it started in 2000 (doi:10.1136/bmj.d5182). It has also attracted huge amounts of funding, reflecting the confidence of major donors, so it's well set to meet its target of saving a further four million lives by 2015.

But GAVI has prominent critics, raising challenges for its incoming chief executive officer, Seth Berkley, who is interviewed this week by Rebecca Coombes (bmj.com/podcasts). At issue is GAVI's current strategy. Could it use its vast resources more effectively? Is it right to focus on access to new vaccines against rotavirus and pneumonia for children in countries that can afford to contribute financially? Or should it help the very poorest countries building health systems so their children can get basic vaccines against diphtheria, tetanus, and pertussis? Most vexed of all, is GAVI paying too much for vaccines? Could it vaccinate even more children with the funds it has been given if it negotiated a better deal from the industry?

Most of the vaccines acquired by GAVI and then bought by Unicef and other agencies come from the major vaccine manufacturers; GSK, Pfizer, and Merck. But as Arie explains, there is growing competition from emerging markets, notably India and China, where manufacturers can in some cases produce vaccines for less than half the standard price. This is in spite of GAVI getting vaccine manufacturers to agree to charge substantially less if they are paid in advance.

The major manufacturers have the important advantage of being able to provide rapid and reliable supplies. GAVI is clear that delays in supply cost lives. But one thing has introduced more competitive edge. Against fierce resistance from the major manufacturers, Unicef started publishing the prices for the drugs and vaccines it buys. This revealed substantial profits, in one case of around 180%.

So what about western governments' decisions to buy vaccines? The UK must shortly decide which vaccine to buy if it is to continue its vaccination programme against human papilloma virus. The programme has been a success, according to René Verheijen (doi:10.1136/bmj.d5720). Coverage is on target at around 80% and the evidence on efficacy and safety is strong. But which is the most cost effective vaccine? In 2008 the UK chose the bivalent vaccine Cervarix. Compared with the quadrivalent vaccine Gardasil it provides greater protection against cervical cancer, but no protection against anogenital warts. As Mark Jit and colleagues reported in their modelling study in 2008 (BMJ 2008;337:a769) and again in an updated study this week (doi:10.1136/bmj.d5775), the bivalent vaccine is only cost effective if it is substantially cheaper. However, as Verhiejen says, because the price of the vaccines is confidential we don't know whether the right decision has been made. "In the end then, the key determinant of cost effectiveness is the only factor that cannot be evaluated."

Unicef's brave decision to publish the price of the drugs and vaccines it buys has changed the conversation on global health. Why don't governments, purchasing drugs and vaccines on our behalf, show equal courage

International Health : How should GAVI build on its success?

Sophie Arie

BMJ 2011;343:doi:10.1136/bmj.d5182 (Published 8 September 2011)

Extract

Immunisation programmes supported by GAVI have prevented more than five million deaths in a decade, but critics argue that the alliance could do more to bring prices down and help the most vulnerable countries. Sophie Arie reports

There are not many development organisations these days that can say they have raised the full amount of funding they need to meet their goals. But GAVI, the Global Alliance for Vaccines and Immunisation, is in that happy position only 10 years after it was created.

At GAVI's first pledging conference in June this year, public and private donors pledged $4.3bn (£2.7bn; €3bn), bringing the alliance's funds for 2011-15 to a total of $7.6bn. With that, the organisation says, it can achieve its aim of immunising more than 250 million of the world's poorest children against life threatening diseases, thus preventing more than four million premature deaths by 2015. 1

Geneva based GAVI, which brings together governments of developing and donor countries, UN agencies, the World Bank, major philanthropists, and the drug industry, has prevented more than five million deaths since it began work in 2000, according to its 2011 progress report. 2

But can donors be sure that the money pledged will be spent in the best possible way? Could GAVI be vaccinating more children and saving even more lives if it did things differently?

Price concerns

Everyone agrees GAVI has made huge achievements and that vaccination is a highly efficient form of development aid. The knock on effects on the economies of recipient countries are huge in terms of children being able to attend school and become productive adults and their parents being able to work rather than care for sick and dying children.

The UK Department for International Development's assessment of multilateral development organisations showed that GAVI was the best value in …

Research

Comparing bivalent and quadrivalent human papillomavirus vaccines: economic evaluation based on transmission model

Mark Jit, Ruth Chapman, Owain Hughes, Yoon Hong Choi

BMJ 2011;343:doi:10.1136/bmj.d5775 (Published 27 September 2011)

Abstract (Free full-text: http://www.bmj.com/content/343/bmj.d5775.full)

Objectives To compare the effect and cost effectiveness of bivalent and quadrivalent human papillomavirus (HPV) vaccination, taking into account differences in licensure indications, protection against non-vaccine type disease, protection against disease related to HPV types 6 and 11, and reported long term immunogenicity.

Design A model of HPV transmission and disease previously used to inform UK vaccination policy, updated with recent evidence and expanded to include scenarios where the two vaccines differ in duration of protection, cross protection, and end points prevented.

Setting United Kingdom.

Population Males and females aged 12–75 years.

Main outcome measure Incremental cost effectiveness ratios for both vaccines and additional cost per dose for the quadrivalent vaccine to be equally cost effective as the bivalent vaccine.

Results The bivalent vaccine needs to be cheaper than the quadrivalent vaccine to be equally cost effective, mainly because of its lack of protection against anogenital warts. The price difference per dose ranges from a median of £19 (interquartile range £12–£27) to £35 (£27–£44) across scenarios about vaccine duration, cross protection, and end points prevented (assuming one quality adjusted life year (QALY) is valued at £30 000 and both vaccines can prevent all types of HPV related cancers).

Conclusions The quadrivalent vaccine may have an advantage over the bivalent vaccine in reducing healthcare costs and QALYs lost. The bivalent vaccine may have an advantage in preventing death due to cancer. However, considerable uncertainty remains about the differential benefit of the two vaccines.

Cost Effectiveness and Resource Allocation
(accessed 2 October 2011)
http://www.resource-allocation.com/
[No new relevant content]

Emerging Infectious Diseases
Volume 17, Number 10—October 2011
http://www.cdc.gov/ncidod/EID/index.htm
[No relevant content]

Health Affairs
September 2011; Volume 30, Issue 9
The New Urgency To Lower Costs
http://content.healthaffairs.org/content/current
[Reviewed earlier; No relevant content]

Health Economics, Policy and Law
Volume 6 - Issue 04 - 01 October 2011
http://journals.cambridge.org/action/displayIssue?jid=HEP&tab=currentissue
[Reviewed earlier]

Human Vaccines
Volume 7, Issue 9 September 2011
http://www.landesbioscience.com/journals/vaccines/toc/7/9/
[Reviewed earlier]

International Journal of Infectious Diseases
Volume 15, Issue 10 pp. e655-e730 (October 2011)
http://www.sciencedirect.com/science/journal/12019712
Correspondence

Pneumococcal vaccination and Hajj
Page e730
Philippe Gautret, Marie Bauge, Fabrice Simon, Samir Benkouiten, Philippe Parola, Philippe Brouqui

JAMA
September 28, 2011, Vol 306, No. 12, pp 1289-1395
http://jama.ama-assn.org/current.dtl
Health Agencies Update
Toddler Flu Vaccinations
Bridget M. Kuehn
JAMA. 2011;306(12):1315.doi:10.1001/jama.2011.1376

Combining administration of intranasal and injectable influenza vaccines during the course of an infant or toddler's vaccinations appears to be a safe and effective approach, according to a study funded by the National Institute of Allergy and Infectious Diseases.

The researchers compared the effects of 3 vaccination regimens—the injectable formulation only, the intranasal formulation only, or some combination of the 2—in 65 children aged 6 months to 36 months (Hoft DF et al. J Infect Dis. 2011;204[6]:845-853). Use of a single formulation for the prime dose and boost doses and the use of different formulations were comparable. However, only those regimens that included a dose of the intranasal formulation triggered the development of a wide array of T cells. These findings suggest that use of the intranasal vaccine in this age group may be more likely to provide cross-protection against influenza strains not included in the vaccine.

Journal of Infectious Diseases
Volume 204 Issue 9 November 1, 2011
http://www.journals.uchicago.edu/toc/jid/current
VIRUSES
Natasha Larke, Sara L. Thomas, Isabel dos Santos Silva, and Helen A. Weiss
Male Circumcision and Human Papillomavirus Infection in Men: A Systematic Review and Meta-Analysis
J Infect Dis. (2011) 204(9): 1375-1390 doi:10.1093/infdis/jir523
Abstract
Background. We systematically reviewed the evidence for an association between male circumcision and Human Papillomavirus (HPV) infection and genital warts in men.
Methods. PubMed and Embase were searched to 15 September 2010. The measure of effect was the adjusted odds ratio (OR) or rate ratio (RR) when present and the crude estimate otherwise. Random effects meta-analyses were used to calculate summary measures of effect.
Results. We identified 23 papers about the association between circumcision and HPV DNA. Circumcised men were less likely to have prevalent genital HPV infection than uncircumcised men (summary OR, 0.57, 95% confidence interval [CI], 0.45–0.71) with between-study heterogeneity (P-heterogeneity = 0.006; I2 = 50.5%; 19 studies). Similar summary associations were seen in clinical and methodological subgroups. The effect of circumcision was stronger at the glans/corona (OR, 0.47; 95% CI, 0.37–0.60)

and urethra (OR, 0.35; 95% CI, 0.12–1.05) compared with sites more distal to the foreskin. There was weak evidence that circumcision was associated with decreased HPV incidence (summary RR, 0.75, 95% CI, 0.57–0.99; 3 studies) and increased HPV clearance (summary RR, 1.33; 95% CI, 0.89–1.98; 3 studies) but no evidence of an association with prevalent genital warts (OR, 0.93, 95% CI, 0.65–1.33; 15 studies). Conclusions. Several countries are expanding access to voluntary medical male circumcision to reduce HIV prevalence. This could provide additional benefit in reducing HPV prevalence.

The Lancet
Oct 01, 2011 Volume 378 Number 9798 p1197 - 1274
http://www.thelancet.com/journals/lancet/issue/current

Editorial

Five reasons to fund the Global Fund

The Lancet

The Global Fund to Fight AIDS, Tuberculosis and Malaria is at a crossroads. Last week saw the release of the final report of the high-level independent review panel on fiduciary controls and oversight mechanisms at the Fund. The panel was set up in March to look at the way in which the Fund operates following allegations of grant fraud in several recipient countries. The panel's report makes six broad recommendations. It calls for the Fund to move from an emergency to sustainable response, strengthen internal governance, streamline its grant approval process, develop and adopt a new risk-management framework, empower middle management's decision making, and focus on results. Under each theme, the panel lists practical steps to be taken—eg, develop basic standards in the rules of fiduciary documentation and ethical behaviour.

The changes needed at the Fund are clearly substantial. However, as the report notes, there is "nothing that cannot be fixed by appropriate reform". Whether governments in this era of austerity will stick by the Fund as it evolves is now a major concern. But there are good reasons for donors to keep funding the Global Fund. First, it saves lives. Programmes supported by the Fund have provided antiretroviral drugs to 3 million people, detected and treated 7·7 million cases of tuberculosis, and distributed 160 million insecticide-treated bednets, saving an estimated 6·5 million lives since 2002. Second, the Fund gives the largest and broadest return on investment than any other financing mechanism in global health. Third, without continued and increased support, progress on the Millennium Development Goals will be curtailed, and even reversed. Fourth, it, like no other multilateral organisation, is transparent about corruption allegations, making them public and taking swift measures to investigate. Fifth, it is responsive to criticism and committed to continuous improvement. In response to the panel's report, the Fund plans to accelerate organisational reforms, which will make it a more effective and efficient funding agency.

The case for continued support of the Fund is strong. As the panel's report puts it: "Failure of the Global Fund would be a global health catastrophe." It is a disaster that the global health community must not allow to happen.

The Lancet Infectious Disease
Oct 2011 Volume 11 Number 10 p721 - 800

http://www.thelancet.com/journals/laninf/issue/current

Editorial

Innovation for polio eradication

The Lancet Infectious Diseases

In 2010, WHO's Director General, Margaret Chan, formed an independent monitoring board to assess progress towards achievement of the milestones of the Global Polio Eradication Initiative strategic plan 2010—12. The board's report in April this year showed that the number of poliomyelitis cases has decreased from 350 000 in 1988 to 1294 in 2010. Endemic transmission of wild poliovirus types 1 and 3 continued only in Afghanistan, India, Nigeria, and Pakistan, the four countries in which poliovirus transmission has never been stopped. Wild poliovirus type 2 was eradicated in 1999.

Although in 2010 the number of polio cases fell by more than 90% in Nigeria and India and by 34% in Afghanistan, the situation in Pakistan was disappointing—the number of confirmed cases rose from 89 in 2009 to 144 in 2010, an increase of 62%. Pakistan has had 77 cases of poliomyelitis so far in 2011. In the first 3 months of 2011, the number of infections with wild poliovirus in Chad, the Democratic Republic of the Congo, and Pakistan was higher than was reported for the same period in 2010. The report noted that a funding gap of US$665 million exists from the $1·2 billion needed for the 2010—12 plan and concluded that the achievement of global eradication by the end of 2012 is at risk.

Poliomyelitis is an acute viral infection that affects mainly children younger than 5 years and leads to paralysis. It is not curable and can only be prevented by immunisation. In poliomyelitis-endemic countries, poliovirus types 1 and 3 both circulate. Prevention is typically through use of the oral polio vaccine (OPV). Introduction of effective immunisation strategies, such as the marking of either the front doors of houses visited by vaccinators or the fingers of children once they have been immunised, have improved the coverage of populations in poliomyelitis-endemic countries. The success of these strategies can be seen in western Uttar Pradesh, India, where, in a dense and constantly changing population, no cases of type 1 poliomyelitis have been registered for more than a year.

So what are the major challenges for the four remaining poliomyelitis-endemic countries? First, OPV might not be effective in the last phase of eradication. In Pakistan, 44% of 144 individuals with poliomyelitis reported in 2010 were given more than one dose of OPV, indicating that some pockets of the population remain unprotected after immunisation. Moreover, monovalent and trivalent vaccine is not effective against vaccine-derived type 2 poliovirus that emerged in the past 6 years in Nigeria. Vaccination studies that combine inactivated poliomyelitis vaccine and OPV result in fewer children failing to seroconvert than those that use either vaccine alone, suggesting an innovative solution to vaccination failures.

However, the issues afflicting Pakistan and other countries in the fight against poliomyelitis are largely social. Children in these countries miss out on vaccination for several reasons, including lack of information and poor community mobilisation. Vaccine campaigns have been dogged by mistaken beliefs, such as that OPV causes infertility and illness—parental doubts about the motivation and need for vaccination campaigns also create a barrier. Members of isolated communities might be unwilling to accept vaccines from people who come from outside their community. Moreover, some parents are not aware that their children can be vaccinated with OPV and as a consequence do not seek routine vaccination. One of the greatest challenges in India and Pakistan is to

reach the high risk and most vulnerable populations—those in the most remote villages with the poorest access to health care and those in Federally Administered Tribal Areas (a semi-autonomous tribal region in the northwest of Pakistan), which have been completely disrupted by conflicts. The motivation of health workers is essential for the eradication of poliomyelitis, as is communication with the people delivering vaccines to ensure they have the skills to support local needs. Health workers should work together with community mobilisation networks to increase house-to-house visits at the community and subdistrict level and build a stronger demand. And special training is needed for health workers to access the most vulnerable and isolated populations and to work with community health workers.

2012 is the landmark year for global poliomyelitis eradication. Although progress towards eradication was substantial in 2010, data from the end of 2010 and the first quarter of 2011 indicate that urgent action needs to be taken. Better commitment from both poliomyelitis eradication partners and national and local governments of affected countries will be of strategic importance to address the real social barriers and to search for more creative and innovative solutions.

Comment

Efficacy of RTS,S malaria vaccine given with EPI vaccines

Alassane Dicko, Ogobara Doumbo

Assessing the effect of pneumococcal conjugate vaccines: what is the value of routinely collected surveillance data?

Carlos G Grijalva, Matthew R Moore, Marie R Griffin

Articles

Safety and efficacy of the RTS,S/AS01E candidate malaria vaccine given with expanded-programme-on-immunisation vaccines: 19 month follow-up of a randomised, open-label, phase 2 trial

Kwaku Poku Asante, Salim Abdulla, Selidji Agnandji, John Lyimo, Johan Vekemans, Solange Soulanoudjingar, Ruth Owusu, Mwanajaa Shomari, Amanda Leach, Erik Jongert, Nahya Salim, Jose F Fernandes, David Dosoo, Maria Chikawe, Saadou Issifou, Kingsley Osei-Kwakye, Marc Lievens, Maria Paricek, Tina Möller, Stephen Apanga, Grace Mwangoka, Marie-Claude Dubois, Tigani Madi, Evans Kwara, Rose Minja, Aurore B Hounkpatin, Owusu Boahen, Kingsley Kayan, George Adjei, Daniel Chandramohan, Terrell Carter, Preeti Vansadia, Marla Sillman, Barbara Savarese, Christian Loucq, Didier Lapierre, Brian Greenwood, Joe Cohen, Peter Kremsner, Seth Owusu-Agyei, Marcel Tanner, Bertrand Lell

Summary

Background

The RTS,S/AS01E candidate malaria vaccine is being developed for immunisation of infants in Africa through the expanded programme on immunisation (EPI). 8 month follow-up data have been reported for safety and immunogenicity of RTS,S/AS01E when integrated into the EPI. We report extended follow-up to 19 months, including efficacy results.

Methods

We did a randomised, open-label, phase 2 trial of safety and efficacy of the RTS,S/AS01E candidate malaria vaccine given with EPI vaccines between April 30, 2007, and Oct 7, 2009, in Ghana, Tanzania, and Gabon. Eligible children were 6—10 weeks of age at first vaccination, without serious acute or chronic illness. All children received the EPI diphtheria, tetanus, pertussis (inactivated whole-cell), and hepatitis-B vaccines,

Haemophilus influenzae type b vaccine, and oral polio vaccine at study months 0, 1, and 2, and measles vaccine and yellow fever vaccines at study month 7. Participants were randomly assigned (1:1:1) to receive three doses of RTS,S/AS01E at 6, 10, and 14 weeks (0, 1, 2 month schedule) or at 6 weeks, 10 weeks, and 9 months (0, 2, 7 month schedule) or placebo. Randomisation was according to a predefined block list with a computer-generated randomisation code. Detection of serious adverse events and malaria was by passive case detection. Antibodies against Plasmodium falciparum circumsporozoite protein and HBsAg were monitored for 19 months. This study is registered with ClinicalTrials.gov, number NCT00436007.

Findings

511 children were enrolled. Serious adverse events occurred in 57 participants in the RTS,S/AS01E 0, 1, 2 month group (34%, 95% CI 27—41), 47 in the 0, 1, 7 month group (28%, 21—35), and 49 (29%, 22—36) in the control group; none were judged to be related to study vaccination. At month 19, anticircumsporozoite immune responses were significantly higher in the RTS,S/AS01E groups than in the control group. Vaccine efficacy for the 0, 1, 2 month schedule (2 weeks after dose three to month 19, site-adjusted according-to-protocol analysis) was 53% (95% CI 26—70; p=0·0012) against first malaria episodes and 59% (36—74; p=0·0001) against all malaria episodes. For the entire study period, (total vaccinated cohort) vaccine efficacy against all malaria episodes was higher with the 0, 1, 2 month schedule (57%, 95% CI 33—73; p=0·0002) than with the 0, 1, 7 month schedule (32% CI 16—45; p=0·0003). 1 year after dose three, vaccine efficacy against first malaria episodes was similar for both schedules (0, 1, 2 month group, 61·6% [95% CI 35·6—77·1], p<0·001; 0, 1, 7 month group, 63·8% [40·4—78·0], p<0·001, according-to-protocol cohort).

Interpretation

Vaccine efficacy was consistent with the target put forward by the WHO-sponsored malaria vaccine technology roadmap for a first-generation malaria vaccine. The 0, 1, 2 month vaccine schedule has been selected for phase 3 candidate vaccine assessment.

Funding

Program for Appropriate Technology in Health Malaria Vaccine Initiative; GlaxoSmithKline Biologicals.

Herd immunity and serotype replacement 4 years after seven-valent pneumococcal conjugate vaccination in England and Wales: an observational cohort study

Elizabeth Miller, Nicholas J Andrews, Pauline A Waight, Mary PE Slack, Robert C George

Preview

Despite much serotype replacement, a substantial reduction in invasive pneumococcal disease in young children can be achieved with PCV7 vaccination, with some indirect benefit in older age groups. Further reductions should be achievable by use of higher valency vaccines. Robust surveillance data are needed to properly assess the *epidemiological effect of multivalent pneumococcal disease vaccines.*

Historical Review

Determinants of mortality in naval units during the 1918–19 influenza pandemic

G Dennis Shanks, Michael Waller, Alison MacKenzie, John F Brundage

Preview

In 1918, two waves of epidemic influenza arose with very different clinical phenotypes. During the first wave, infection rates were high but mortality was low. During the

second wave, high numbers of deaths occurred and mortality differed 30–100 times among seemingly similar groups of affected adults, but the reason for this variation is unclear. In 1918, the crews of most warships and some island populations were affected by influenza during both waves of infection and had no or very few deaths during the second wave.

Medical Decision Making (MDM)
September/October 2011; 31 (5)
http://mdm.sagepub.com/content/current
[Reviewed earlier]

Nature
Volume 477 Number 7366 pp509-626 29 September 2011
http://www.nature.com/nature/current_issue.html
[No relevant content]

Nature Medicine
September 2011, Volume 17 No 9
http://www.nature.com/nm/index.html
[Reviewed earlier]

New England Journal of Medicine
September 29, 2011 Vol. 365 No. 13
http://content.nejm.org/current.shtml
[No relevant content]

The Pediatric Infectious Disease Journal
October 2011 - Volume 30 - Issue 10 pp: A7-A8,821-918,e179-e202
http://journals.lww.com/pidj/pages/currenttoc.aspx
[Reviewed earlier]

Pediatrics
October 2011, VOLUME 128 / ISSUE 4
http://pediatrics.aappublications.org/current.shtml
[No relevant content]

Pharmacoeconomics
October 1, 2011 - Volume 29 - Issue 10 pp: 823-911
http://adisonline.com/pharmacoeconomics/pages/currenttoc.aspx
[Reviewed earlier]

PLoS One
[Accessed 2 October 2011]
http://www.plosone.org/article/browse.action;jsessionid=577FD8B9E1F322DAA533C413369CD6F3.ambra01?field=date
[No new relevant content]

PLoS Medicine
(Accessed 2 October 2011)
http://www.plosmedicine.org/article/browse.action?field=date
Editorial
Why Drug Safety Should Not Take a Back Seat to Efficacy
The PLoS Medicine Editors Editorial, published 27 Sep 2011
doi:10.1371/journal.pmed.1001097
Setting Research Priorities to Reduce Global Mortality from Childhood Pneumonia by 2015
Igor Rudan, Shams El Arifeen, Zulfiqar A. Bhutta, Robert E. Black, Abdullah Brooks, Kit Yee Chan, Mickey Chopra, Trevor Duke, David Marsh, Antonio Pio, Eric A.F. Simoes, Giorgio Tamburlini, Evropi Theodoratou, Martin W. Weber, Cynthia G. Whitney, Harry Campbell, Shamim A. Qazi, and the WHO/CHNRI Expert Group on Childhood Pneumonia Guidelines and Guidance, published 27 Sep 2011
doi:10.1371/journal.pmed.1001099
Summary Points
- This paper aims to identify health research priorities that could assist the rate of progress in childhood pneumonia mortality reduction globally, as set out in the United Nation's Millennium Development Goal 4.
- The authors applied the Child Health and Nutrition Research Initiative methodology for setting priorities in health research investments. The process was coordinated by the World Health Organization.
- Forty-five leading childhood pneumonia researchers suggested more than 500 research ideas, which were merged into 158 research questions that spanned the broad spectrum of epidemiological research, health policy and systems research, improvement of existing interventions, and development of new interventions.
- Within the short time frame in which gains were expected globally, the research priorities were dominated by health systems and policy research topics (e.g., studying barriers to health care seeking and access, as well as barriers to increased coverage with available vaccines; and evaluating the potential to safely scale up antibiotic treatment through community health workers).
- These were followed by epidemiological questions to identify the main gaps in knowledge (e.g., predictors of severe pneumonia that requires hospitalisation); priorities for improvement of the existing interventions (e.g., training of community health workers to recognise danger signs, refer, and treat sick children); and identifying cost reduction mechanisms for the available conjugate vaccines.
- Among the new interventions, the greatest support was shown for the development of low-cost conjugate vaccines and cross-protective common protein vaccines against the pneumococcus.

Proceedings of the National Academy of Sciences of the United States of America
(Accessed 2 October 2011)
http://www.pnas.org/content/early/recent
[No new relevant content]

Science
30 September 2011 vol 333, issue 6051, pages 1785-1924
http://www.sciencemag.org/current.dtl
[No relevant content]

Science Translational Medicine
28 September 2011 vol 3, issue 102
http://stm.sciencemag.org/content/current
Commentary
Policy
Disclosure of Clinical Trial Results When Product Development Is Abandoned
Michael A. Rogawski and Howard J. Federoff
28 September 2011: 102cm29
Abstract
Currently, sponsors are not required to report the outcomes of clinical research on drugs or devices that do not lead to an approved product. Consequently, the public cannot benefit from scientific information derived from all failed or abandoned drugs and devices. Provisions in the U.S. Food and Drug Administration Amendments Act of 2007 provide an opportunity for the Department of Health and Human Services to rectify this situation. By reporting the results of clinical trials of abandoned products in a publicly accessible database and in the peer-reviewed journal literature, sponsors would satisfy a core ethical obligation of clinical research and enhance translational science.

Tropical Medicine & International Health
October 2011 Volume 16, Issue 10 Pages 1191–1352
http://onlinelibrary.wiley.com/journal/10.1111/(ISSN)1365-3156/currentissue
[Reviewed earlier]

Vaccine
http://www.sciencedirect.com/science/journal/0264410X
Volume 29, Issue pp. 7285-7576 (6 October 2011)
Special Section - Universal Influenza Vaccination of Children: Food for Thought [see articles summary below]

Short Communications

Hospital-based surveillance of rotavirus gastroenteritis in the era of limited vaccine uptake through the private sector

Pages 7292-7295

Georgios Trimis, Ioanna Koutsoumbari, Christine Kottaridi, Nikoletta Palaiologou, Efstathia Assimakopoulou, Aris Spathis, Evaggelia Lebessi, Andreas Konstantopoulos, Dimitris Kafetzis, Petros Karakitsos, Vassiliki Papaevangelou

Abstract

To investigate possible impact of limited vaccine uptake by the private sector since 2007, a prospective observational study included all children <5 years hospitalized for acute gastroenteritis (AGE) in a Tertiary Care Hospital between 09/2006 and 08/2010. Rotavirus (RV) antigen was detected in stools by a rapid immunochromatographic test and genotype analysis was performed on positive samples by RT-PCR. Compared to 2006–2008, the likelihood of rotavirus infection was significantly reduced among children hospitalized for AGE in 2008–2010 (OR 0.64; 95%CI: 0.49–0.84, $p < 0.001$). This was mainly due to the reduction of RVGE cases in infants 0–11 months ($p = 0.035$). Moreover, RVGE cases as well as the rate of RVGE/10,000 hospitalized children significantly decreased ($p = 0.009$ and $p = 0.010$ respectively). No children with rotavirus gastroenteritis (RVGE) had received any vaccine dose. G4P was the most common genotype (64/90). In conclusion, this study indicates that even low RV vaccination coverage may have significant effect.

Regular Papers

Vaccine counseling: A content analysis of patient–physician discussions regarding human papilloma virus vaccine

Pages 7343-7349

Sarah L. Goff, Kathleen M. Mazor, Shawn J. Gagne, Kristin C. Corey, Diane R. Blake

Abstract

Objectives

(1) Describe content and character of patient–physician human papilloma virus (HPV) vaccine discussions; (2) explore the relationship between selected characteristics and vaccine uptake.

Methods

Content analyses were conducted on 184 transcripts of audio-taped patient encounters with 11–26 year old female patients that occurred from August 2008 to March 2009 and contained mention of the HPV vaccine. Directed qualitative content analysis sought to identify key themes with a focus on elements related to communication. Quantitative content analysis included determination of associations between selected factors (e.g., physician specialty, communication variables, patient age) and vaccination rates.

Results

Communication themes identified though qualitative content analysis demonstrated potential opportunities for improvement in vaccine communication were identified. Quantitative content analysis showed twenty-eight percent of eligible patients received HPV vaccine and on average these patients were younger (17.0 vs. 19.6 years). The youngest and oldest patients were vaccinated less frequently.

Conclusions

Targeting age groups with lower vaccination rates may increase overall vaccine uptake. Additional quantitative analyses of patient–physician discussions about vaccine may generate further recommendations regarding optimal communication strategies for HPV vaccine counseling.

Attitudes to HPV vaccination among mothers in the British Jewish community: Reasons for accepting or declining the vaccine

Pages 7350-7356

Daniel Gordon, Jo Waller, Laura A.V. Marlo

Abstract

Objective

This study aimed to explore attitudes to human papillomavirus (HPV) vaccination and reasons for accepting or declining the vaccine in the British Jewish community.

Methods

A qualitative approach was used to explore maternal attitudes towards HPV vaccination. Participants were mothers of girls who had been offered HPV vaccination and were purposively sampled through Jewish secondary schools. Face-to-face interviews were conducted with vaccine-accepting (n = 10) and vaccine-declining (n = 10) mothers. Interviews were transcribed verbatim and analysed using a framework approach.

Results

HPV and cervical cancer knowledge varied, with poor knowledge attributed to lack of contact with the disease. Although mothers thought HPV vaccination was a good idea in general, many did not perceive it as necessary for their daughter, citing Jewish religious laws governing family purity and abstinence until marriage as reasons for daughter's low susceptibility. These beliefs combined with concerns about the novelty of the vaccination were the main reasons given for declining the vaccine. Mothers who accepted the vaccine generally did so to protect their daughters health and because they felt unable to predict their daughters future behaviour and HPV susceptibility. Many mothers expressed a wish to wait until their daughter was older and the vaccine was more established before consenting. Among some mothers there was disappointment in the information they had received and a feeling that the concerns and questions of the Jewish community had not been addressed.

Conclusion

Attitudes to HPV vaccine in religious communities may lead to reduced vaccine coverage. The development of community-specific information about the importance of the vaccine may help address concern

Seasonal influenza vaccination predicts pandemic H1N1 vaccination uptake among healthcare workers in three countries

Pages 7364-7369

Josette S.Y. Chor, Surinder K. Pada, Iain Stephenson, William B. Goggins, Paul A. Tambyah, Tristan William Clarke, Mariejo Medina, Nelson Lee, Ting Fun Leung, Karry L.K. Ngai, Shu Kei Law, Timothy H. Rainer, Sian Griffiths, Paul K.S. Chan

Abstract

The aim of this study was to identify the common barriers and facilitators for acceptance of pandemic influenza vaccination across different countries. This study utilized a standardized, anonymous, self-completed questionnaire-based survey recording the demographics and professional practice, previous experience and perceived risk and severity of influenza, infection control practices, information of H1N1 vaccination, acceptance of the H1N1 vaccination and reasons of their choices and opinions on mandatory vaccination. Hospital-based doctors, nurses and allied healthcare workers in Hong Kong (HK), Singapore (SG) and Leicester, United Kingdom (UK) were recruited. A total of 6318 (HK: 5743, SG: 300, UK: 275) questionnaires were distributed, with response rates of 27.1% (HK), 94.7% (SG) and 94.5% (UK). The uptake rates for

monovalent 2009 pandemic H1N1 vaccine were 13.5% (HK), 36.2% (SG) and 41.3% (UK). The single common factor associated with vaccine acceptance across all sites was having seasonal influenza vaccination in 2009. In UK and HK, overestimation of side effect reduced vaccination acceptance; and fear of side effect was a significant barrier in all sites. In HK, healthcare workers with more patient contact were more reluctant to accept vaccination. Drivers for vaccination in UK and HK were concern about catching the infection and following advice from health authority. Only a small proportion of respondents agreed with mandatory pandemic influenza vaccination (HK: 25% and UK: 42%), except in Singapore where 75.3% were in agreement. Few respondents (<5%) chose scientific publications as their primary source of information, but this group was more likely to receive vaccination.
The acceptance of pandemic vaccine among healthcare workers was poor (13–41% of respondents). Breaking barriers to accept seasonal influenza vaccination should be part of the influenza pandemic preparedness plan. Mandatory vaccination even during pandemic is likely to arouse substantial discontent.

Cost-effectiveness of universal rotavirus vaccination in reducing rotavirus gastroenteritis in Ireland

Pages 7463-7473

L. Tilson, M. Jit, S. Schmitz, C. Walsh, P. Garvey, P. McKeown, M. Barry

Abstract

We evaluated the cost-effectiveness of universal infant rotavirus (RV) vaccination compared to current standard of care of "no vaccination". Two RV vaccines are currently licensed in Ireland: Rotarix™ and RotaTeq™.

A cohort model used in several European countries was adapted using Irish epidemiological, resource utilisation and cost data. The base case model considers the impact of Rotarix vaccination on health-related quality of life of children under five years old from a healthcare payer perspective. Other scenarios explored the use of RotaTeq, impact on one caregiver, on societal costs and on cases that do not seek medical attention. Cost was varied between the vaccine list price (€100/course) in the base case and an assumed tender price (€70/course). One-way and probabilistic sensitivity analyses were conducted.

Implementing universal RV vaccination may prevent around 1970 GP visits, 3280 A&E attendances and 2490 hospitalisations. A vaccination programme was estimated to cost approximately €6.54 million per year but €4.65 million of this would be offset by reducing healthcare resource use. The baseline ICER was €112,048/QALY and €72,736/QALY from the healthcare payer and societal perspective, respectively, falling to €68,896 and €43,916/QALY, respectively, if the impact on one caregiver was considered. If the price fell to €70 per course, universal RV vaccination would be cost saving under all scenarios. Results were sensitive to vaccination costs, incidence of RV infection and direct medical costs.

Universal RV vaccination would not be cost-effective under base case assumptions. However, it could be cost-effective at a lower vaccine price or from a wider societal perspective.

Vaccine

http://www.sciencedirect.com/science/journal/0264410X

Volume 29, Issue pp. 7285-7576 (6 October 2011)

Special Section: Universal influenza vaccination of children: Food for thought

Value in Health
September 2011, Vol. 14, No. 6
http://www.valueinhealthjournal.com/home
[No relevant content]