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

This weekly summary targets news, announcements 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 also posted in pdf form and as a set of blog posts at http://centerforvaccineethicsandpolicy.wordpress.com/. This blog allows full-text searching of some 2,500 entries..

Comments and suggestions should be directed to
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A pdf of this issue is available here: http://centerforvaccineethicsandpolicy.wordpress.com/

[Editor's Note: We provide an extended summary of the NTD announcements made in London last week, unprecedented in their scope and coordination across the public and private sectors]

Thirteen pharmaceutical companies, the governments of the U.S., U.K. and U.A.E., the Bill & Melinda Gates Foundation, the World Bank and other global health organisations "announced a new, coordinated push to accelerate progress toward eliminating or controlling 10 neglected tropical diseases (NTDs) by the end of the decade." The group said they would "sustain or expand existing drug donation programs to meet demand through 2020; share expertise and compounds to accelerate research and development of new drugs; and provide more than US$785 million to support R&D efforts and strengthen drug distribution and implementation programmes." The group also endorsed the "London Declaration on Neglected Tropical Diseases," in which they pledged new levels of collaborative effort and tracking of progress.

As part of the announcement, the Gates Foundation made a five-year, US$363 million commitment to support NTD product and operational research. Also, the WHO unveiled a new strategy, Accelerating work to overcome the global impact of neglected tropical diseases—A roadmap for implementation, that sets targets for what can be achieved by the end of the decade. Dr. Margaret Chan, Director-General of the WHO, commented, "The efforts of WHO, researchers, partners, and the contributions of industry have changed the face of NTDs. These ancient diseases are now being brought to their knees with stunning speed. With the boost to this momentum being made today, I am confident almost all of these diseases can be eliminated or controlled by the end of this decade." New commitments from these partners "will close the funding gap to eradicate Guinea worm disease and expedite progress toward the 2020 goals of elimination for lymphatic filariasis, blinding trachoma, sleeping sickness and leprosy, and control of soil-transmitted helminthes, schistosomiasis, river blindness, Chagas disease and visceral leishmaniasis."

Speaking on behalf of the CEOs of the 13 pharmaceutical companies involved, Sir Andrew Witty, CEO of GlaxoSmithKline, said, "Many companies and organisations have worked for decades to fight these horrific diseases. But no one company or organisation can do it alone. Today, we pledge to work hand-in-hand to revolutionize the way we fight these diseases now and in the future." New research and development

collaborative efforts and access agreements with 11 companies and the R&D organisation Drugs for Neglected Diseases initiative (DNDi) "are providing unprecedented access to compound libraries that could lead to new treatments. These commitments will work in parallel with other efforts to speed the development of critical NTD treatments, including WIPO Re:Search, a database of research compounds, knowledge and expertise."

SPECIFIC PARTNER COMMITMENTS ANNOUNCED INCLUDE:

Sustaining, Expanding and Extending Drug Supply:

All companies with NTD drug donation programs pledged to sustain or extend their programs to the end of the decade, and some pledged to increase their commitments. These commitments include the following:

- Sanofi, Eisai and the Bill & Melinda Gates Foundation will work together to provide 120 million DEC tablets to the WHO for its Global Lymphatic Filariasis Elimination programme. Combined with Eisai's donation commitment that will start in 2014, these new tablets will ensure a sufficient supply of DEC from 2012 through 2020.
- Bayer will double its existing donation of nifurtimox to treat Chagas disease.
- Eisai will extend its existing donation of 2.2 billion tablets of DEC for LF to 2020.
- Gilead, which announced a donation of AmBisome for visceral leishmaniasis in 2011, will continue its program to offer VL at cost and commit to investigate and invest in technologies and processes that could reduce that cost in resource-limited countries.
- GlaxoSmithKline will extend its existing donation of albendazole to treat soil-transmitted helminthes by providing 400 million tablets per year for an additional five years to 2020, as well as continuing its donation of 600 million tablets per year to combat lymphatic filariasis.
- Johnson & Johnson will extend its existing donation of mebendazole for soil-transmitted helminthes by providing 200 million tablets per year to 2020.
- MSD will continue its unlimited donation of ivermectin to combat river blindness and lymphatic filariasis (where co-endemic with river blindness), as well as discuss the use of ivermectin to combat other diseases.
- Merck KGaA will significantly increase its annual donation of praziquantel tablets from 25 million to 250 million tablets per year, extending the program indefinitely.
- Novartis will extend its commitment to provide multi-drug therapy (rifampicin, clofazimine and dapsone) to leprosy patients worldwide in a final push against the disease.
- Pfizer will continue its donation of azithromycin for blinding trachoma until at least 2020, as well as donate the drug and placebo to a study on the reduction in mortality of children treated with azithromycin.
- Sanofi will extend its existing donation of eflornithine, melarsoprol and pentamidine for sleeping sickness to 2020, as well as logistical support to ensure that the drugs continue to reach patients at the point of care cost-free.

Accelerating R&D for New Treatments:

- Product development partnerships under the coordination of DNDi with Abbott, Johnson & Johnson and Pfizer are underway to develop new drugs to treat helminth infections, notably a macrofilaricide, which kills adult worms that cause river blindness and lymphatic filariasis.
- Abbott is conducting initial drug reformulation studies and providing scientific expertise for preclinical development, with technical and supply assistance from Johnson & Johnson.

- If pre-clinical development is successful, Johnson & Johnson will co-fund clinical development, and collaborate with other partners, including technical support from Pfizer's staff scientists. J&J would obtain regulatory approval.
- Innovative licensing or collaboration agreements with DNDi by 11 companies—Abbott, AstraZeneca, Bayer, Bristol-Myers Squibb, Eisai, GlaxoSmithKline, Johnson & Johnson, MSD, Novartis, Pfizer and Sanofi—are in negotiation or underway for the sharing of compounds and knowledge in order to generate new drugs for diseases including river blindness, lymphatic filariasis, sleeping sickness, Chagas disease and visceral leishmaniasis.
- DNDi and Sanofi announced a product development collaboration to co-develop a new drug candidate for sleeping sickness, oxaborole/SCYX-7158, in addition to fexinidazole, which is already in clinical development.

Increasing funding to improve drug product and operational research, delivery and implementation programmes, including prevention, monitoring and education:

- Several partners announced US$40 million in new funding to The Carter Center that will close the gap to eradicate Guinea worm. The Gates Foundation will contribute US$23.3 million, His Highness Sheikh Khalifa bin Zayed Al Nahyan, President of the United Arab Emirates, will contribute US$10 million and the Children's Investment Fund Foundation will contribute US$6.7 million.
- This funding complements £20 million in funding from DFID, announced last week as part of a £195 million commitment through 2015, targeted at Guinea worm disease, lymphatic filariasis, river blindness and schistosomiasis, as well as developing new programmes for blinding trachoma, visceral leishmaniasis, research and integrated country approaches.
- The Gates Foundation announced a 5-year, US$363 million commitment to overcome barriers to success and address critical gaps to achieve the control and elimination of targeted NTDs by 2020.
- USAID will continue support to over 20 countries to introduce and/or scale up integrated NTD programs, including three new countries: Mozambique, Senegal and Cambodia. The U.S. Congress appropriated $89 million to USAID for NTD control in FY2012.
- At the country level, the World Bank will extend its financing and technical support to help countries build stronger community health systems that will integrate NTD elimination and control. At the regional level, the World Bank will continue fiduciary oversight of the existing trust fund that supports the fight against river blindness in Africa, and will also work with other partners to expand the trust fund to eliminate or control preventable NTDs on the continent.
- Mundo Sano contributed US$5 million to expand work in NTD control and program enhancement for selected sites in the Americas and Africa.
- The Government of Mozambique announced specific goals for NTD control and elimination in endemic areas of the country, including:
  . Reaching full geographic coverage of all endemic areas for lymphatic filariasis, soil-transmitted helminthes and schistosomiasis
  . Completely mapping and reaching full geographic coverage of trachoma by 2018
  . Building capacity for surveillance and action to sustain gains from mass drug administration programs

- The Governments of Brazil, Tanzania, Bangladesh and other NTD-endemic countries announced implementation of fully integrated or coordinated plans to control and eliminate NTDs in their countries.
- Three pharmaceutical companies—Merck KGaA, Novartis and Sanofi— will organize and provide funding to support prevention, monitoring, education and intensified disease control efforts.
- Lions Clubs International announced US$6.9 million in funding to support the Government of China in efforts to eliminate blinding trachoma by 2017.
- Coordinating and measuring NTD commitments: Industry partners pledged to work together toward the achievement of the 2020 goals. Based on the WHO roadmap, partners will follow collective progress through a scorecard that will regularly and formally track progress including whether participating organisations are meeting their supply, research, funding and implementation commitments to work toward the 2020 goals. This process will ensure accountability and transparency and identify remaining gaps.

A webcast of this event can be viewed at www.UnitingToCombatNTDs.org
http://www.gatesfoundation.org/press-releases/Pages/combating-10-neglected-tropical-diseases-120130.aspx

GAVI announced that René Karsenti has been appointed as the new Board Chair of the International Finance Facility for Immunisation (IFFIm). Dr. Karsenti joined the Board on 23 December 2011 and will take over as Chair on 24 February, replacing Alan Gillespie, who has served since IFFIm was established six years ago. Under his leadership as Chair, IFFIm has raised US$ 3.6 billion in bonds to support GAVI childhood immunisation programmes. GAVI said Dr. Karsenti, a French national, "brings to IFFIm a background both in the capital markets and in development finance. He will continue in his current role as President of the International Capital Market Association (ICMA), a self-regulatory organisation and trade body that represents some 430 member firms involved in the international capital markets. On the development side, Dr. Karsenti has served as Director General of Finance of the European Investment Bank and was the first Treasurer of the European Bank for Reconstruction and Development. He also spent more than 10 years in senior positions in the treasury organisations of the World Bank Group in Washington, including as IFC Treasurer." Dr. Karsenti said, "GAVI's mission is very important to me and I am honored to have been given the opportunity to use my capital market experience to raise money for GAVI through IFFIm and so to ensure that children in the world's poorest countries can be afforded the same vaccinations as children in richer nations. The pioneering work of Alan Gillespie has established IFFIm as a major and innovative model in development finance."
http://www.gavialliance.org/library/news/press-releases/2012/rene-karsenti-new-chair-iffim-board/

The MMWR Weekly for February 3, 2012 / Vol. 61 / No. 4 includes:
- Adult Vaccination Coverage — United States, 2010

- Progress in Global Measles Control, 2000–2010
- Recommended Adult Immunization Schedule — United States, 2012

The **Weekly Epidemiological Record (WER) for 3 February 2012**, vol. 87, 5 (pp 45–52) includes: Progress in global measles control, 2000–2010.
http://www.who.int/entity/wer/2012/wer8705.pdf

Meeting: Assessment of Studies of Health Outcomes Related to the Recommended Childhood Immunization Schedule
Sponsor: IOM (Institute of Medicine of the National Academy of Sciences)
When: February 9, 2012 (11:00 AM Eastern)
Where: The Pew Charitable Trusts • 901 E Street, NW, Washington, DC 20004
Board on Population Health and Public Health Practice
Activity Description: The IOM will conduct an independent assessment surrounding the feasibility of studying health outcomes in children who were vaccinated according to the CDC recommended schedule and those who were not (e.g. children who were unvaccinated or vaccinated with an alternate schedule). The IOM will review scientific findings and stakeholder concerns related to the safety of the recommended childhood immunization schedule. Further, the IOM will identify potential research approaches, methodologies, and study designs that could inform this question, including an assessment of the potential strengths and limitations of each approach, methodology and design, as well as the financial and ethical feasibility of doing them. A report will be issued in mid-2012 summarizing the IOM's findings and conclusions.
Registration for attending the meeting and a call-in number are posted here:
http://iom.edu/Activities/PublicHealth/ChildhoodImmunization/2012-FEB-09.aspx?utm_medium=etmail&utm_source=Institute%20of%20Medicine&utm_campaign=2.1.12+Meeting+Alert&utm_content=Meetings%20&%20Events&utm_term=Academic

Meeting: ACIP
When: February 22-23, 2012
Where: CDC, Atlanta
Draft Agenda (released 3 February 2012):
http://www.cdc.gov/vaccines/recs/acip/downloads/agenda-feb12.pdf
Further information on registration and webcast:
http://www.cdc.gov/vaccines/recs/acip/meetings.htm

Twitter Watch *[accessed 5 February 18:10]*
Items of interest from a variety of twitter feeds associated with immunization, vaccines and global public health. This capture is highly selective and is by no means intended to be exhaustive.

TropMed_IntHlth Tmih Journal
FREE Editor's Choice: #measles vaccination integrating insecticide-treated #bednets in #Madagascar. bit.ly/zUaEaU
3 Feb

IHME_UW IHME at UW
More people dying from malaria than the world thought. New study published today from IHME. bit.ly/zs1WfP #malaria
2 Feb

pahowho PAHO/WHO
Consultative Working Group to Draft New #PAHO Budget Policy - bit.ly/xj98k4

sabinvaccine Sabin Vaccine Inst.
Dr. Hotez: Neglected tropical diseases: Hot tropic | The Economist econ.st/zPzgHc
2 Feb

GAVIAlliance GAVI Alliance
1/5 of all #cancer cases r caused by chronic infections like hepatitisB & #HPV. #vaccines exist 2prevent both diseases ht.ly/8PEvB

joinRED joinred
"One of the most successful partnerships is (RED), an effort that has raised $180M for the Fund" @CerrJ @globalfundnews t.joinred.com/yat
1 Feb

gatesfoundation Gates Foundation
Why do we make media grants? Because #storytelling matters. It's critical to making progress on our issues. gates.ly/xrsIYZ
1 Feb

AnnalsofIM Annals of Int Med
Annals Clinical Guidelines: Recommended Adult Immunization Schedule: United States, 2012 bit.ly/z6Fo0v
1 Feb

PIH Partners In Health
Check out why @PIH's Paul Farmer thinks the #GlobalFund matters: ow.ly/8O8Qp via @nytimes
1 Feb

NIAIDNews NIAID News
NIAID #HIV clinical sites collaborate on pediatric #TB #vaccine study: go.usa.gov/nfJ
1 Feb

FightingMalaria Malaria Consortium
New @globalfundnews General Manager speaks to the @wsj about plans for revival on.wsj.com/zqO3UJ #globalfund #endmalaria

1 Feb

Journal Watch

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

Annals of Internal Medicine
January 17, 2012; 156 (2)
http://www.annals.org/content/current
[Reviewed earlier; No relevant content]

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

British Medical Journal
04 February 2012 (Vol 344, Issue 7842)
http://www.bmj.com/content/current
[No relevant content]

Cost Effectiveness and Resource Allocation
(Accessed 5 February 2012)
http://www.resource-allocation.com/
[No new relevant content]

Emerging Infectious Diseases
Volume 18, Number 2—February 2012
http://www.cdc.gov/ncidod/EID/index.htm
[Reviewed last week]

Global Health
Winter 2012

http://www.globalhealthmagazine.com/in_this_issue/
[Reviewed earlier]

Globalization and Health
[Accessed 5 February 2012]
http://www.globalizationandhealth.com/
[No new relevant content]

Health Affairs
January 2012; Volume 31, Issue 1
http://content.healthaffairs.org/content/current
[Reviewed earlier]

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

Health Economics, Policy and Law
Volume 7 - Special Issue 01 - January 2012
http://journals.cambridge.org/action/displayIssue?jid=HEP&tab=currentissue
[Reviewed earlier]

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

Human Vaccines & Immunotherapeutics (formerly Human Vaccines)
Volume 8, Issue 2 February 2012
http://www.landesbioscience.com/journals/vaccines/toc/volume/8/issue/1/
SHORT REPORT
Evaluation of the establishment of herd immunity in the population by means of serological surveys and vaccination coverage
Pedro Plans-Rubió
The necessary herd immunity blocking the transmission of an infectious agent in the population is established when the prevalence of protected individuals is higher than a critical value, called the herd immunity threshold. The establishment of herd immunity in the population can be determined using the vaccination coverage and seroepidemiological surveys. The vaccination coverage associated with herd immunity (Vc) can be determined from the herd immunity threshold and vaccine effectiveness. This method requires a vaccine-specific effectiveness evaluation, and it can be used only

for the herd immunity assessment of vaccinated communities in which the infectious agent is not circulating. The prevalence of positive serological results associated with herd immunity can be determined from the herd immunity threshold, in terms of prevalence of antibodies (pc) and serological test performance. The herd immunity is established when the prevalence of antibodies is higher than pc. This method can be used to assess the establishment of herd immunity in different population groups, both when the infectious agent is circulating and when it is not possible to assess vaccine effectiveness. The herd immunity assessment in Catalonia, Spain, showed that the additional vaccination coverage required to establish herd immunity was 3–6% for measles, mump and varicella and 11% poliovirus type III in schoolchildren, 17–59% for diphtheria in youth and adults and 25–46% for pertussis in schoolchildren, youth and adults.

Research Papers

National patterns in human papillomavirus vaccination: An analysis of the National survey of family growth

Gelareh Sadigh, Amanda F. Dempsey, Mack Ruffin, Ken Resnicow and Ruth C. Carlos

Human papillomavirus (HPV) vaccine has shown effectiveness for girls and young women. Despite this, there are population disparities in vaccine utilization rates. The purpose of this study was to evaluate maternal correlates of HPV vaccination among their adolescent daughters using a nationally-representative population-based sample, emphasizing race/ethnicity-specific disparities and barriers. Mothers of 9–18 y-old girls having heard of HPV vaccine and completing the HPV vaccine survey module from the 2006–2008 National Survey of Family Growth (NSFG) (n = 444) were analyzed for maternally-reported adolescent HPV vaccination and maternal intent to vaccinate her adolescent daughter if no dose had been received. Correlates of uptake and intent were examined using multivariate logistic regression. 27% of mothers (n = 98) reported that their daughters were vaccinated against HPV. Independent correlates of vaccination included African-American race (adjusted odds ratio (AOR),0.29; 95% confidence interval (CI),0.11–0.77), and living below the poverty level (AOR,4.43; 95%CI, 1.53–12.82). 46% (n = 152) of mothers of non-vaccinated daughters intended to vaccinate them. Correlates of maternal intention included maternal pelvic exam history (AOR,0.06; 95%CI, 0.007–0.51), multiple male lifetime sexual partners (AOR,3.22 ; 95% CI, 1.34–7.76), religiosity (AOR,0.37; 95% CI,0.16–0.87) and acceptability of premarital sex among 18 y-olds (AOR,2.45; 95% CI, 1.16–5.20). In conclusion, HPV vaccination initiation among adolescent daughters of mothers participating in the NSFG continues to lag among African-American participants. However, no racial/ethnic differences in maternal intent-to-vaccinate her daughter were detected. Future interventions need to address specific maternal barriers to vaccine uptake and how these may differ from vaccine intention.

The cost efficiency of HPV vaccines is significantly underestimated due to omission of conisation-associated prematurity with neonatal mortality and morbidity

Philipp Soergel, Lars Makowski, Cordula Schippert, Ismini Staboulidou, Ursula Hille and Peter Hillemanns

Introduction: Cervical intraepithelial neoplasia (CIN) represents the precursor of invasive cervical cancer and is associated with human papillomavirus infection (HPV) against which two vaccines have been approved in the last years. Standard treatments of high-grade CIN are conisation procedures, which are associated with an increased

risk of subsequent pregnancy complications like premature delivery and possible subsequent life-long disability. HPV vaccination has therefore the potential to decrease neonatal morbidity and mortality. This has not been taken into account in published cost-effectiveness models.

Material and Methods: We calculated the possible reduction rate of conisations for different vaccination strategies for Germany. Using this rate, we computed the reduction of conisation-associated preterm deliveries, life-long disability and neonatal death due to prematurity. The number of life-years saved (LYS) and gain in quality-adjusted life-years (QALYs) was estimated. The incremental costs per LYS / additional QALY were calculated.

Results: The reduction of conisation procedures was highest in scenario I (vaccination coverage 90% prior to HPV exposition) with about 50%. The costs per LYS or additional QALY were lowest in scenario I, II and III with 45,101 € or 43,505–47,855 € and rose up to 60,544 € or 58,401–64,240 € in scenario V (50% vaccinated prior to sexual activity + additional 20% catch-up at a mean age of 20 y).

Conclusion: Regarding the HPV 16 / 18 vaccines as "vaccines against conisation-related neonatal morbidity and mortality" alone, they already have the potential to be cost-effective. This effect adds up to reduction of cervical cancer cases and decreased costs of screening for CIN. Further studies on cost-effectiveness of HPV vaccination should take the significant amount of neonatal morbidity and mortality into account.

Commentaries

Perceptions of pandemic influenza vaccines

Cecile A. Marczinski

Pandemic influenza A (H1N1) (pH1N1) was first identified in North America in early 2009. The pandemic flu outbreak during the 2009–2010 influenza season demonstrated how rapidly a new strain of flu can emerge and spread. Vaccination is the most effective method to prevent influenza, and vaccination during a pandemic is critical in limiting morbidity and mortality. Unfortunately, reports of vaccination rates for pH1N1 vaccines during the 2009–2010 influenza season indicated low rates for various demographic groups, including pregnant women, health care workers, child care workers, college students, and the general public. Furthermore, when asked about perceptions of pH1N1 vaccines, respondents in a variety of studies from the pH1N1 pandemic indicated common and universal misconceptions about influenza vaccines, especially in regard to perceptions of need, efficacy and safety. Therefore, if vaccination rates are to increase, an important outcome especially during pandemics, the psychological characteristics underpinning perceptions of influenza vaccines need to be understood better.

International Journal of Infectious Diseases
Volume 16, Issue 2 pp. e75-e150 (February 2012)
http://www.sciencedirect.com/science/journal/12019712
[Reviewed earlier]

JAMA
February 1, 2012, Vol 307, No. 5, pp 431-527
http://jama.ama-assn.org/current.dtl
[No relevant content]

Journal of Infectious Diseases
Volume 205 Issue 4 February 15, 2012
http://www.journals.uchicago.edu/toc/jid/current
[Reviewed last week]

The Lancet
Feb 04, 2012 Volume 379 Number 9814 p385 – 492 e27 - 32
http://www.thelancet.com/journals/lancet/issue/current

Editorial

New estimates of malaria deaths: concern and opportunity

The Lancet

This week we publish surprising and, on the face of it, disturbing findings. According to Christopher Murray and colleagues at the Institute for Health Metrics and Evaluation (IHME) at the University of Washington in Seattle, there were 1·24 million deaths (95% uncertainty interval 0·93—1·69 million) from malaria worldwide in 2010—around twice the figure of 655 000 estimated by WHO for the same year. How should the malaria community interpret this finding? Before we answer that question, we need to look beneath the surface of this striking overall mortality figure.

First, annual malaria mortality peaked in 2004 at 1·82 million. Since then, there has been a 32% reduction in malaria deaths, driven mainly by "accelerated decreases" in sub-Saharan Africa. Second, although there has also been a substantial decrease in the number of deaths outside sub-Saharan Africa, adults now make up the major burden in these regions. In Asia and the Americas, the median proportion of deaths in those older than 15 years was 76% and 69%, respectively. Overall, the IHME data show that malaria deaths in 2010 in those aged 5 years and older were much higher than previously thought—524 000 deaths compared with 91 000 as estimated by WHO. Third, malaria accounts for many more child deaths in sub-Saharan Africa than previously estimated—24% of total child deaths, compared with the 16% previously calculated for 2008.

The reliability of these findings will certainly be the subject of much debate, as were the similarly higher estimates for India (by different methods), reported in 2010. Murray and colleagues used inputs from vital registration systems, published and unpublished verbal autopsy reports, and estimates of malaria transmission intensity to construct an array of models, which were then assessed for predictive validity. The authors will need to make their data and assumptions fully available to others who will surely wish to reproduce their calculations.

One aspect of the findings that is unlikely to raise objections is the implication that interventions scaled up since 2004 have been phenomenally successful in reducing the number of malaria deaths. Much of this success can be attributed to the work of the Global Fund To Fight AIDS, Tuberculosis and Malaria, now celebrating its tenth anniversary. The Global Fund contributes about two-thirds of the world's funding for malaria programmes, and since its inception in 2002 has dispersed 230 million insecticide-treated bednets and a similar number of doses of artemisinin-based drugs. Coverage of indoor residual insecticide spraying now stands at around 70% for the countries with the highest disease burden. With the recent and untimely resignation of

its Executive Director, Michel Kazatchkine, the Global Fund is facing an unprecedented emergency. The results we report today show how essential it is for donors to recommit to the Global Fund, as they did last summer for the Global Alliance for Vaccines and Immunisation. We therefore welcome the US$750 million promissory note announced last week by the Bill & Melinda Gates Foundation. This commitment for 2011—16 is a legally binding agreement for future payment, but also counts as cash in the bank and can thus be used to cover all grants the Global Fund has already signed off. It has thrown the Global Fund a lifeline at a time when donor support is in desperately short supply. Others should follow this lead.

We must also conclude from today's study that malaria might be a far more important cause of childhood mortality than previously thought. If correct, this finding has substantial implications for child survival programmes. It also seems clear that malaria is a greater long-term threat to adult health than we had previously imagined. Again, if correct, this finding means that malaria control and elimination programmes should be paying far greater attention to adults than is currently the case. Finally, although we can be grateful for these new estimates of malaria mortality, one important lesson from the science of estimation is that the urgency to revitalise health information systems has never been greater. We need reliable primary cause of death data to ensure that trends in malaria mortality are readily and reliably monitored—and acted upon.

What should happen now? WHO's new independent advisory body, the Malaria Policy Advisory Committee (MPAC), held its first meeting this week. But MPAC only has 15 members. We believe urgent technical and policy analyses must be initiated by WHO—involving a broader group of experts (eg, including those in child survival) and country representatives—to review these new data and their implications for malaria control programmes. This opportunity needs to be grasped with urgency and optimism.

Articles

Global malaria mortality between 1980 and 2010: a systematic analysis

Christopher JL Murray, Lisa C Rosenfeld, Stephen S Lim, Kathryn G Andrews, Kyle J Foreman, Diana Haring, Nancy Fullman, Mohsen Naghavi, Rafael Lozano, Alan D Lopez

Summary

Background

During the past decade, renewed global and national efforts to combat malaria have led to ambitious goals. We aimed to provide an accurate assessment of the levels and time trends in malaria mortality to aid assessment of progress towards these goals and the focusing of future efforts.

Methods

We systematically collected all available data for malaria mortality for the period 1980—2010, correcting for misclassification bias. We developed a range of predictive models, including ensemble models, to estimate malaria mortality with uncertainty by age, sex, country, and year. We used key predictors of malaria mortality such as Plasmodium falciparum parasite prevalence, first-line antimalarial drug resistance, and vector control. We used out-of-sample predictive validity to select the final model.

Findings

Global malaria deaths increased from 995 000 (95% uncertainty interval 711 000—1 412 000) in 1980 to a peak of 1 817 000 (1 430 000—2 366 000) in 2004, decreasing to 1 238 000 (929 000—1 685 000) in 2010. In Africa, malaria deaths increased from 493 000 (290 000—747 000) in 1980 to 1 613 000 (1 243 000—2 145 000) in 2004, decreasing by about 30% to 1 133 000 (848 000—1 591 000) in 2010. Outside of Africa,

malaria deaths have steadily decreased from 502 000 (322 000—833 000) in 1980 to 104 000 (45 000—191 000) in 2010. We estimated more deaths in individuals aged 5 years or older than has been estimated in previous studies: 435 000 (307 000—658 000) deaths in Africa and 89 000 (33 000—177 000) deaths outside of Africa in 2010.

Interpretation

Our findings show that the malaria mortality burden is larger than previously estimated, especially in adults. There has been a rapid decrease in malaria mortality in Africa because of the scaling up of control activities supported by international donors. Donor support, however, needs to be increased if malaria elimination and eradication and broader health and development goals are to be met.

Funding

The Bill & Melinda Gates Foundation.

The Lancet Infectious Disease

Feb 2012 Volume 12 Number 2 p89 - 166

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

[Reviewed last week]

Medical Decision Making (MDM)

January–February 2012; 32 (1)

http://mdm.sagepub.com/content/current

Editorials

Alan Schwartz

Measuring Health-Related Quality of Life: New Findings and New Questions

Med Decis Making January–February 2012 32: 9-10, doi:10.1177/0272989X11434207

Extract

Preference-based community valuation of health-related quality of life is a bedrock of medical decision and cost-effectiveness analysis. We want to live longer and we want to live better, and we need to know how changes in our health will affect us in order to make informed medical decisions. As a society, we need measures of preference that can help us allocate resources most beneficially. Studies advancing our understanding of preferences for life/health states and of the valuation process itself are thus a regular feature of Medical Decision Making.

Five articles in this issue of the journal focus on measurement of health-related quality of life. Two of these studies1,2 investigate properties of existing instruments for health state description (PORPUS) or quality of life measurement (WHOQOL-BREF) and provide evidence for the validity of their measurements. For PORPUS, this takes the form of …

Article

Ba' Pham, Maggie Hong Chen, Andrea C. Tricco, Andrea Anonychuk, Murray Krahn, and Chris T. Bauch

Use of a Catalytic Model to Estimate Hepatitis A Incidence in a Low-Endemicity Country: Implications for Modeling Immunization Policies

Med Decis Making January–February 2012 32: 167-175, first published on March 10, 2011 doi:10.1177/0272989X11398489

Abstract

Background. Evaluating the cost-effectiveness of vaccine programs with dynamic modeling requires accurate estimates of incidence over time. Because infectious diseases are often underreported, supplementary data and statistical analyses are required to estimate true incidence. This study estimates the true incidence of hepatitis A virus (HAV) infection in Canada using a catalytic model.

Methods. A catalytic model was used to reconcile HAV seroprevalence data with the corresponding true cumulative risk of infection estimated from incidence data.

Results. The average annual reported incidence was 6.2 cases per 100 000 from 1980 to 1989 and 7.7/100 000 from 1990 to 1999, indicating that Canada is a low-incidence country. The seroprevalence in Canadian-born individuals (n = 7 studies) was approximately 1%–8% in ages <20, 1%–11% in ages 20–29, 7%–29% in ages 30–39, and higher in older age groups. Between 1980 and 1995, the catalytic model estimated an average annual incidence of 60/100 000 (95% confidence interval, 33–524); approximately 7.73 (4.21–67.33) times the average annual reported incidence of 7.78/100 000. For a typical birth cohort of 403 434 Canadians born in 1990, the model predicted 32 750 HAV cases by age 39, with a corresponding seroprevalence of approximately 8.12% by the year 2029.

Implications. Reliable estimates of true incidence of infectious disease are required for cost-effectiveness analysis of infectious disease programs. Catalytic models enable the synthesis of dispersed data, quantification of data limitations, and reconciliation of these limitations to estimate true incidence for economic evaluations.

Nature
Volume 482 Number 7383 pp5-126 2 February 2012
http://www.nature.com/nature/current_issue.html

World View

Global health hits crisis point

The Global Fund's drive to ensure sustainability and efficiency means that it may not be able to meet its commitments to combat disease, says Laurie Garrett.

01 February 2012

Last week, Michel Kazatchkine tendered his resignation as executive director of the Global Fund to Fight AIDS, Tuberculosis and Malaria. Regardless of whether you've heard of the French AIDS scientist, or even of the fund, you should keep reading. This is a crucial, dangerous moment for global health.

Kazatchkine made clear the political struggle that forced his resignation. "The Global Fund has helped to spearhead an entirely new framework of international development partnership," he wrote in his resignation letter. But under stress during the world economic crisis, with radically declining support from donors, a battle developed. "Today, the Global Fund stands at a cross-road. In the international political economy, power-balances are shifting and new alignments of countries and decision-making institutions are emerging or will have to be developed to achieve global goals. Within the area of global health, the emergency approaches of the past decade are giving way to concerns about how to ensure long-term sustainability, while at the same time, efficiency is becoming a dominant measure of success," he wrote.

It is almost possible to hear Kazatchkine spitting out the words 'sustainability' and 'efficiency'. Since the financial crisis of November 2008, a storm has been brewing over these concepts, one that affects everything from humanitarian responses to projects

that distribute malaria bed nets. It is a fight, and on one side are those who believe that crises in general, and the AIDS pandemic and allied diseases in particular, constitute global 'emergencies' that must be tackled with full force, mistakes be damned. On the other are those who feel that AIDS is now a chronic disease that can be managed with medication and therefore requires investment in permanent infrastructure of care and treatment that can eventually be operated and funded by the countries themselves.

It is a classic battle of titans, pitting urgency against long-term sustainability. In his resignation letter, Kazatchkine essentially conceded victory to the forces for sustainability. Charitable urgency didn't stand a chance once the donor states started cinching their domestic budget belts so tightly that they had to punch new buckle holes.

The fund was established ten years ago as a unique mechanism to move billions of dollars from rich countries to poorer ones, to combat and treat three infectious diseases: HIV, malaria and tuberculosis. It acts as a granting agency, accepting applications from governments and health organizations, and convenes regular replenishment meetings to tell donors — mostly the governments of the United States, United Kingdom, France and Germany — how much money is needed for the next round.

By the end of 2009, the fund was disbursing US$2.7 billion a year, and was underwriting almost half of all HIV treatment in poor countries, about two-thirds of all malaria prevention and treatment in the world and about 65% of all tuberculosis efforts. The fund's most marked impact has been on malaria. At the end of 2011, the World Health Organization estimated that the number of malaria deaths had fallen by one-quarter between 2000 and 2010.

But Global-Fund cash has spawned dependency and expectation among its recipients. Should it disappear, or radically diminish, countries would be hard-pressed to finance malaria and tuberculosis efforts.

Indeed, the great diminishment has commenced. In October 2010, the fund asked donors for $20 billion for five years' worth of disbursements. The donors were indignant and committed just over half that. In response, the fund's flabbergasted leadership cancelled the next grant round, and it will now not distribute new grants until 2014.

"Global-fund cash has spawned dependency and expectation among its recipients." Donor scrutiny increased and a high-level independent review panel set up by the fund's governing board, which includes representatives of United Nations agencies and the World Bank, released a scathing report, citing a litany of problems, including fraud, theft and inconsistent decision-making by grant reviewers.

At a meeting in Accra, Ghana, on 21 November, the board members expressed shock at the problems identified by the high-level panel, and by reports commissioned on the situation on the ground in some countries. Some African leaders described riots and demonstrations at the lack of vital medicines, especially for HIV. The board's own investigation showed that the fund had committed assets of $10 billion for 2011–13, but had only about $4 billion in its bank accounts.

The board called for ways to stretch available resources and eliminate inefficiencies. Key to that would be the appointment of a general manager to oversee all spending, pushing Kazatchkine aside. Stepping into that position is Colombian banker Gabriel Jaramillo.

To try to give Jaramillo a running start, in Davos, Switzerland, last week, Bill Gates handed over some $750 million, redeemable by the fund in full during 2012, or spread out over time. And the Saudi Arabian government announced a $25-million donation. As generous as these millions may be, the fund needs billions just to stay alive and fulfill

country grants, let alone to grow. Right now we have no idea where that money will come from. Should the fund collapse, the consequences will be severe. Progress against tuberculosis and malaria will stall, and more than a million people living with HIV could be left without treatment.
Nature 482, 7 (02 February 2012) doi:10.1038/482007a

Nature Medicine
January 2012, Volume 18 No 1
http://www.nature.com/nm/journal/v18/n1/index.html
[Reviewed earlier; No relevant content]

Nature Reviews Immunology
February 2012 Vol 12 No 2
http://www.nature.com/nri/journal/v12/n1/index.html
[No relevant content]

New England Journal of Medicine
February 2, 2012 Vol. 366 No. 5
http://content.nejm.org/current.shtml
Perspective
Improving Childhood Vaccination Rates
D.S. Diekema
[Free Full Text]

Recently, the mother of a young child confessed to me that she didn't know any parents who were following the recommended immunization schedule for their children. She said that when she told her pediatrician she'd like to follow an alternative schedule, the physician had simply acquiesced, leading her to assume that the recommended schedule had no advantage over the one she suggested.

Despite the phenomenal success of childhood vaccination, thousands of U.S. parents refuse selected vaccines or delay their administration. Some choose not to vaccinate their children at all. These parents are not a homogeneous group: some object to immunization on religious or philosophical grounds, some are avoiding an apparently painful assault on their child, and others believe that the benefits of at least some immunizations don't justify the risks. Since parents today have little or no experience with vaccine-preventable diseases such as polio, Hemophilus influenzae type b, or measles, they can't easily appreciate the benefits of vaccination or the risks of not vaccinating.

In 2010, California reported over 9000 cases of pertussis — more than the state had seen since 1947. Of these, 89% occurred among infants younger than 6 months, a group too young to be adequately immunized and largely dependent on herd immunity for protection from infection. Ten of these infants died from their infection.

At first glance, U.S. vaccination rates appear reasonable: coverage among children entering kindergarten exceeds 90% for most recommended vaccines. A closer look, however, reveals substantial local variation. In Washington State's San Juan County, for example, 72% of kindergartners and 89% of sixth graders are either noncompliant with

or exempt from vaccination requirements for school entry. Only 52.5% of kindergartners and 4% of sixth graders were adequately immunized against pertussis for the 2010–2011 school year.[1] Not surprisingly, the county also has one of the state's highest incidence rates of pertussis.

Continued outbreaks of pertussis, measles, and H. influenzae type b indicate that U.S. vaccination levels are inadequate. Some physicians have taken matters into their own hands, refusing to see children whose parents won't allow them to be vaccinated. Others encourage alternative vaccine schedules in an effort to accommodate worried parents. Neither of these represents an adequate solution.

Because parents who oppose vaccination on the basis of personal beliefs will probably remain opposed despite the best efforts of clinicians and public health experts, the most effective way to increase vaccine coverage is to improve immunization rates among children whose parents either are open to vaccination but encounter barriers to obtaining vaccines or hesitate because of fears and concerns about safety. Health care professionals, health care organizations, and state and federal policymakers all share responsibility in this endeavor.

First, socioeconomic barriers and disincentives to vaccination should be eliminated. Even small copayments or administration fees pose substantial barriers for some families. Referral to a public health clinic is one option, but attending such clinics requires extra effort, travel, and time away from work — all disincentives to following through. Removing barriers to vaccination is an obvious first step to improving coverage. Some countries, such as Australia, have gone further, offering incentives for vaccinating children on time. Incentives can take several forms, including reduced insurance rates, tax rebates, or direct payments.

Second, school-entry requirements should be strengthened and enforced. Such requirements effectively boost immunization rates for school-age children, but they vary widely by state, in terms of both the kinds of exemptions allowed and the ease of obtaining an exemption. All states allow exemptions for medical reasons, 48 for religious reasons, and 20 for philosophical reasons. Exemption rates vary widely, from less than 0.1% among kindergarteners in Mississippi to 6.2% among those in Washington State.[2] Moreover, within Washington State, 2010–2011 exemption rates for K–12 students varied significantly by county, ranging from 1.2% to 25.4%.[1]

Although eliminating exemptions for religious and personal beliefs may seem logical, such efforts would encounter substantial resistance and probably increase antivaccinationist fervor. Some states might improve immunization rates by addressing the ease of obtaining exemptions and enforcing school-entry requirements. The exemption process should not be easier or less costly than the vaccination process. Obtaining a religious or personal-belief exemption should at least require a visit to the physician's office, including counseling on the risks posed by remaining unvaccinated; insurance should pay for such visits. States could also require that exemption requests be signed by both parents (if both possess legal decision-making authority). Although such measures wouldn't change the stance of the most resistant parents, they would eliminate many exemptions sought because of convenience rather than conviction. Finally, lax enforcement of school-entry requirements sends the message that vaccination is merely a bureaucratic requirement, rather than a prerequisite for school attendance and a mechanism for ensuring students' safety.

Third, misinformation regarding vaccines must be addressed promptly and aggressively. False or misleading information about vaccination is widely dispersed by a

few influential individuals, self-described vaccine-safety advocates, and some clinicians. Public health officials and professional organizations should respond swiftly to dishonest or unbalanced portrayals of vaccination.

Fourth, clinicians, health care organizations, and public health departments must learn to use the tools of persuasion effectively. In The Art of Rhetoric, Aristotle argued that persuasion requires not only a reasonable argument and supporting data, but also a messenger who is trustworthy and attentive to the audience and a message that engages the audience emotionally. Data and facts, no matter how strongly supportive of vaccination, will not be sufficient to compete with the opposition's emotional appeals. The use of a compelling story about a single victim of vaccine-preventable illness is far more likely than data to move an audience to action.[3]

Physicians represent the best opportunity to influence the vaccine-hesitant. Most parents trust their primary care providers and look to them for information and advice. Parents will be most receptive to considering vaccination if they believe their provider is primarily motivated by the welfare of the individual child rather than an abstract public health goal. Demonstrating a willingness to listen respectfully, encouraging questions, and acknowledging parental concerns are essential elements of this strategy. Providing accurate information about both risks and benefits is crucial to maintaining trust; interactions should include discussion of risks associated with both remaining unvaccinated and delaying certain vaccines and a reminder that vaccinations are important in part because effective treatments do not exist for most vaccine-preventable diseases.

Effective communication requires understanding parents' reasons for resisting vaccination. Physicians should approach such reluctance as they would any diagnostic challenge. “Diagnosing” the reasons for hesitancy will permit a more effective discussion and approach. Parents concerned about the number of shots at a given visit or the side effects of a single vaccine require a different strategy from parents who believe vaccines weaken the immune system, cause autism, or contain mercury. The Centers for Disease Control and Prevention, the American Academy of Pediatrics, and the American Academy of Family Physicians recently produced resources to assist clinicians in identifying communication strategies, enhancing trust, and providing reliable information (www.cdc.gov/vaccines/conversations).

Even with optimal communication strategies, some parents will remain hesitant to vaccinate their children. Maintaining the patient–provider relationship despite disagreement conveys respect, builds trust, and affords additional opportunities to discuss immunization. Asking parents who refuse to vaccinate their children to seek medical care elsewhere is counterproductive: it rarely gets a child vaccinated, it undermines trust, and it eliminates opportunities for continued dialogue about vaccination.[4]

Finally, clinicians must set an example. We're unlikely to achieve optimal vaccination rates until health care professionals comply with vaccine recommendations for themselves and their children. The unwillingness of many clinicians to submit to influenza vaccination each year is disgraceful, sets a poor example, and gives patients reason to question the safety and efficacy of vaccines. A logical place to begin increasing public confidence in vaccines is with the example we set.

Review Article

200th Anniversary Article: The Perpetual Challenge of Infectious Diseases

A.S. Fauci and D.M. Morens

[Free full text]
Extract
Among the many challenges to health, infectious diseases stand out for their ability to have a profound impact on the human species. Great pandemics and local epidemics alike have influenced the course of wars, determined the fates of nations and empires, and affected the progress of civilization, making infections compelling actors in the drama of human history.1-11 For 200 years, the Journal has captured the backdrop to this human drama in thousands of articles about infectious diseases and about biomedical research and public health efforts to understand, treat, control, and prevent them…

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

The Pediatric Infectious Disease Journal
February 2012 - Volume 31 - Issue 2 pp: A11-A12,109-214,e37-e51
http://journals.lww.com/pidj/pages/currenttoc.aspx
[Reviewed earlier]

Pediatrics
February 2012, VOLUME 129 / ISSUE 2
http://pediatrics.aappublications.org/current.shtml
Articles
Hepatitis A Vaccination Coverage Among Adolescents in the United States
Christina G. Dorell, David Yankey, Kathy K. Byrd, and Trudy V. Murphy
Pediatrics 2012; 129:213-221
Abstract
OBJECTIVE: Hepatitis A infection causes severe disease among adolescents and adults. The Advisory Committee on Immunization Practices instituted incremental recommendations for hepatitis A vaccination (HepA) at 2 years of age based on risk (1996), in selected states (1999), and universally at 1 year of age, with vaccination through 18 years of age based on risk or desire for protection (2006). We assessed adolescent HepA coverage in the United States and factors independently associated with vaccination.
METHODS: Data from the 2009 National Immunization Survey–Teen (n = 20 066) were analyzed to determine ≥1- and ≥2-dose HepA coverage among adolescents 13 to 17 years of age. We used bivariate and multivariable analyses to test associations between HepA initiation and sociodemographic characteristics stratified by state groups: group 1, universal child vaccination since 1999; group 2, consideration for child vaccination since 1999; group 3, universal child vaccination at 1 year of age since 2006.
RESULTS: In 2009, national 1-dose HepA coverage among adolescents was 42.0%. Seventy percent of vaccinees completed the 2-dose series. One-dose coverage was 74.3% among group 1 states, 54.0% for group 2 states, and 27.8% for group 3 states.

The adjusted prevalence ratios of vaccination initiation were highest for states with a vaccination requirement and for adolescents whose providers recommended HepA. CONCLUSIONS: HepA coverage was low among most adolescents in the United States in 2009 leaving a large population susceptible to hepatitis A infection maturing into adulthood.

Pharmacoeconomics
February 1, 2012 - Volume 30 - Issue 2 pp: 83-170
http://adisonline.com/pharmacoeconomics/pages/currenttoc.aspx
[Reviewed earlier]

PLoS One
[Accessed 5 February 2012]
http://www.plosone.org/article/browse.action;jsessionid=577FD8B9E1F322DAA533C413369CD6F3.ambra01?field=date
Comparing Pandemic to Seasonal Influenza Mortality: Moderate Impact Overall but High Mortality in Young Children
Cees C. van den Wijngaard, Liselotte van Asten, Marion P. G. Koopmans, Wilfrid van Pelt, Nico J. D. Nagelkerke, Cornelia C. H. Wielders, Alies van Lier, Wim van der Hoek, Adam Meijer, Gé A. Donker, Frederika Dijkstra, Carel Harmsen, Marianne A. B. van der Sande, Mirjam Kretzschmar
PLoS ONE: Research Article, published 03 Feb 2012 10.1371/journal.pone.0031197
Abstract
Background
We assessed the severity of the 2009 influenza pandemic by comparing pandemic mortality to seasonal influenza mortality. However, reported pandemic deaths were laboratory-confirmed – and thus an underestimation – whereas seasonal influenza mortality is often more inclusively estimated. For a valid comparison, our study used the same statistical methodology and data types to estimate pandemic and seasonal influenza mortality.
Methods and Findings
We used data on all-cause mortality (1999–2010, 100% coverage, 16.5 million Dutch population) and influenza-like-illness (ILI) incidence (0.8% coverage). Data was aggregated by week and age category. Using generalized estimating equation regression models, we attributed mortality to influenza by associating mortality with ILI-incidence, while adjusting for annual shifts in association. We also adjusted for respiratory syncytial virus, hot/cold weather, other seasonal factors and autocorrelation. For the 2009 pandemic season, we estimated 612 (range 266–958) influenza-attributed deaths; for seasonal influenza 1,956 (range 0–3,990). 15,845 years-of-life-lost were estimated for the pandemic; for an average seasonal epidemic 17,908. For 0–4 yrs of age the number of influenza-attributed deaths during the pandemic were higher than in any seasonal epidemic; 77 deaths (range 61–93) compared to 16 deaths (range 0–45). The ≥75 yrs of age showed a far below average number of deaths. Using pneumonia/influenza and respiratory/cardiovascular instead of all-cause deaths consistently resulted in relatively low total pandemic mortality, combined with high impact in the youngest age category.
Conclusion

The pandemic had an overall moderate impact on mortality compared to 10 preceding seasonal epidemics, with higher mortality in young children and low mortality in the elderly. This resulted in a total number of pandemic deaths far below the average for seasonal influenza, and a total number of years-of-life-lost somewhat below average. Comparing pandemic and seasonal influenza mortality as in our study will help assessing the worldwide impact of the 2009 pandemic.

PLoS Medicine
(Accessed 5 February 2012)
http://www.plosmedicine.org/article/browse.action?field=date
Hitting Hotspots: Spatial Targeting of Malaria for Control and Elimination
Teun Bousema, Jamie T. Griffin, Robert W. Sauerwein, David L. Smith, Thomas S. Churcher, Willem Takken, Azra Ghani, Chris Drakeley, Roly Gosling Policy Forum, published 31 Jan 2012
doi:10.1371/journal.pmed.1001165
Summary Points
- Heterogeneity is a common facet of infectious diseases, whereby infection and disease are concentrated in a small proportion of individuals.
- In malaria, heterogeneity is manifested as small groups of households, or hotspots, that are at a substantially increased risk of malaria transmission.
- These hotspots exist in all transmission settings but are less easily detected at high transmission intensity.
- Hotspots maintain transmission in low transmission seasons and fuel transmission in the high transmission seasons.
- Targeting hotspots is a highly efficient way to reduce malaria transmission at all levels of transmission intensity.

PNAS - Proceedings of the National Academy of Sciences of the United States of America
(Accessed 5 February 2012)
http://www.pnas.org/content/early/recent
[No new relevant content]

Science
3 February 2012 vol 335, issue 6068, pages 493-624
http://www.sciencemag.org/current.dtl
[No relevant content]

Science Translational Medicine
1 February 2012 vol 4, issue 119
http://stm.scienceag.org/content/mcurrent
[No relevant content]

Tropical Medicine & International Health
February 2012 Volume 17, Issue 2 Pages 143–261
http://onlinelibrary.wiley.com/journal/10.1111/(ISSN)1365-3156/currentissue
[Reviewed earlier]

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

Volume 30, Issue 8 pp. 1411-1528 (14 February 2012)
Introduction of human papillomavirus vaccination in Nordic countries
Review Article
Pages 1425-1433
Bente Braad Sander, Matejka Rebolj, Palle Valentiner-Branth, Elsebeth Lynge
Abstract
Introduction
Cervical screening has helped decrease the incidence of cervical cancer, but the disease remains a burden for women. Human Papillomavirus (HPV) vaccination is now a promising tool for control of cervical cancer. Nordic countries (Denmark, Finland, Greenland, Iceland, Norway and Sweden) are relatively wealthy with predominantly publicly paid health care systems. The aim of this paper was to provide an update of the current status of introduction of HPV vaccine into the childhood vaccination programs in this region.
Methods
Data on cervical cancer, cervical screening programs, childhood immunization and HPV vaccination programs for Nordic countries were searched via PubMed and various organizations. We furthermore contacted selected experts for information.
Results
The incidence of cervical cancer is highest in Greenland (25 per 100,000, age standardized, World Standard Population, ASW) and lowest in Finland (4 per 100,000 ASW) and rates in the other Nordic countries vary between 7 and 11 per 100,000 ASW. Greenland and Denmark were first to introduce HPV vaccination, followed by Norway. Vaccination programs are underway in Sweden and Iceland, while Finland has just recently recommended introduction of vaccination. HPV vaccination has been intensively debated, in particular in Denmark and Norway.
Discussion
In Nordic countries with a moderate risk of cervical cancer and a publicly paid health care system, the introduction of HPV vaccination was a priority issue. Many players became active, from the general public to health professionals, special interest groups, and the vaccine manufacturers. These seemed to prioritize different health care needs and weighed differently the uncertainty about the long-term effects of the vaccine.
Conclusion
HPV vaccination posed a pressure on public health authorities to consider the evidence for and against it, and on politicians to weigh the wish for cervical cancer protection against other pertinent health issues.
Health economics of rotavirus immunization in Vietnam: Potentials for favorable cost-effectiveness in developing countries

Original Research Article
Pages 1521-1528
Hong-Anh T. Tu, Mark H. Rozenbaum, Peter C. Coyte, Shu Chuen Li, Herman J. Woerdenbag, Maarten J. Postma
Abstract
Introduction
Rotavirus is the most common cause of severe diarrhoea worldwide. Vietnam is situated in the region of high rotavirus infection incidence and eligible for financial support to introduce rotavirus vaccines into the Expanded Program of Immunization (EPI) from the GAVI. This study was designed to assess the cost-effectiveness of rotavirus immunization in Vietnam, explicitly the use of Rotateq® and to assess the affordability of implementing universal rotavirus immunization based on GAVI-subsidized vaccine price in the context of Vietnamese healthcare system for the next 5 years.
Methodology
An age-structured cohort model was developed for the 2009 birth cohort in Vietnam. Two strategies were compared: one being the current situation without vaccination, and the other being mass universal rotavirus vaccination. The time horizon of the model was 5 years with time cycles of 1 month for children less than 1 year of age and annual analysis thereafter. Outcomes included mild, moderate, severe cases and death. Multiple outcomes per rotavirus infection are possible in the model. Monte Carlo simulations were used to examine the acceptability and affordability of the rotavirus vaccination. All costs were expressed in 2009 US$.
Results
Rotavirus vaccination would not completely protect young children against rotavirus infection due to partial nature of vaccine immunity, however, would effectively reduce severe cases of rotavirus by roughly 55% during the first 5 years of life. Under GAVI-subsidized vaccine price (US$ 0.3/dose), the vaccine cost would amount to US$ 5.5 million per annum for 3-dose of the Rotateq® vaccine. In the base-case, the incremental cost per quality-adjusted-life-year (QALY) was US$ 665 from the health system perspective, much lower than per-capita GDP of ~US$ 1150 in 2009. Affordability results showed that at the GAVI-subsidized vaccine price, rotavirus vaccination could be affordable for Vietnamese health system.
Conclusion
Rotavirus vaccination in Vietnam would be a cost-effective health intervention. Vaccination only becomes affordable if the country receives GAVI's financial support due to the current high market vaccine price. Given the high mortality rate of under-five-year children, the results showed that rotavirus immunization is the "best hope" for prevention of rotavirus-related diarrhoeal disease in Vietnam. In the next five years, Vietnam is definitely in debt to financial support from international organizations in implementing rotavirus immunization. It is recommended that new rotavirus vaccine candidates be developed at cheaper price to speed up the introduction of rotavirus immunization in the developing world in general.

Vaccine
http://www.sciencedirect.com/science/journal/0264410X
Volume 30, Issue 7 pp. 1235-1410 (8 February 2012)
The determinants of 2009 pandemic A/H1N1 influenza vaccination: A systematic review

Review Article
Pages 1255-1264
Stephanie Brien, Jeffrey C. Kwong, David L. Buckeridge
Abstract
Background
Pandemic A/H1N1 influenza vaccine coverage varied widely across countries. To understand the factors influencing pandemic influenza vaccination and to guide the development of successful vaccination programs for future influenza pandemics, we identified and summarized studies examining the determinants of vaccination during the 2009 influenza pandemic.
Methods
We performed a systematic literature review using the PubMED electronic database from June 2009 to February 2011. We included studies examining an association between a possible predictive variable and actual receipt of the pandemic A/H1N1 influenza vaccine. We excluded studies examining intention or willingness to receive the vaccine.
Results
Twenty-seven studies were identified from twelve countries. Pandemic influenza vaccine coverage varied from 4.8% to 92%. Coverage varied by population sub-group, country, and assessment method used. Most studies used questionnaires to estimate vaccine coverage, however seven (26%) used a vaccination registry. Factors that positively influenced pandemic influenza vaccination were: male sex, younger age, higher education, being a doctor, being in a priority group for which vaccination was recommended, receiving a prior seasonal influenza vaccination, believing the vaccine to be safe and/or effective, and obtaining information from official medical sources.
Conclusions
Vaccine coverage during the pandemic varied widely across countries and population sub-groups. We identified some consistent determinants of this variation that can be targeted to increase vaccination during future influenza pandemics.
The concept of vaccination failure
Review Article
Pages 1265-1268
U. Heininger, N.S. Bachtiar, P. Bahri, A. Dana, A. Dodoo, J. Gidudu, E. Matos dos Santos
Abstract
Despite remarkable success of immunization programmes on a global perspective, vaccines are neither 100% efficacious nor 100% effective. Therefore, vaccination failure, i.e. occurrence of a specific disease in an individual despite previous vaccination, may occur. Vaccination failure may be due to actual vaccine failure or failure to vaccinate appropriately.
Universally accepted concepts and definitions of vaccination failure are required to assess and compare the benefit of vaccines used in populations. Here we propose general definitions for types of vaccination failure. In the future, these should be complemented by specific definitions for specific vaccines as needed depending on public health considerations.
Characterizing providers' immunization communication practices during health supervision visits with vaccine-hesitant parents: A pilot study
Original Research Article
Pages 1269-1275

Douglas J. Opel, Jeffrey D. Robinson, John Heritage, Carolyn Korfiatis, James A. Taylor, Rita Mangione-Smith

Abstract

Objective

To determine the feasibility of using direct observation of provider–parent immunization discussions and to characterize provider communication practices with vaccine-hesitant parents.

Methods

Over a 6 month period in 2010, we videotaped immunization discussions between pediatric providers and vaccine-hesitant parents during health supervision visits involving children 2–15 months old (N = 24) in the Seattle area, Washington, USA. Videotapes were analyzed using the qualitative method of conversation analysis.

Results

We approached 96 parents seen by 9 different providers. Of those who were eligible (N = 56), we enrolled 43% (N = 24). Four videotaped visits were excluded from analysis for failure to obtain parental HIPAA authorization. Of the remaining 20 visits, there were ≥2 visits each that involved children aged 2, 4, 6, 9, 12, and 15 months, and all videotaped visits contained at least a brief immunization discussion. We identified 6 communication practices and several behavior types within each practice relevant to immunization: Practice 1, providers' initiations of the topic of vaccination; Types: participatory or presumptive format; Practice 2, parents' responses to providers' topic initiations; Types: strong or weak acceptance or resistance; Practice 3, providers' follow-ups to parent's responses; Types: no, immediate, or delayed pursuit; Practice 4, parents' vaccine-related questions or statements; Types: fact- or concern-based; Practice 5, providers' explicit solicitations of parent's questions/concerns; Types: designed to discourage or encourage discussion; and Practice 6, parents' responses to providers' solicitations of questions/concerns; Types: no question or fact- or concern-based inquiry.

Conclusion

Direct observation of immunization discussions in the primary care pediatric setting is feasible and yields insight into several provider–parent immunization communication practices that are worthy of further study to determine which are effective at improving parental acceptance of immunization.

Value in Health

January 2012, Vol. 15, No. 1

http://www.valueinhealthjournal.com/home

[Reviewed earlier]

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