Center for Vaccine Ethics and Policy
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**Vaccines and Global Health: The Week in Review**
**28 March 2015**
**Center for Vaccine Ethics & Policy (CVEP)**

*This weekly summary targets news, events, announcements, articles and research in the vaccine and global health ethics and policy space and is aggregated from key governmental, NGO, international organization and industry sources, key peer-reviewed journals, and other media channels. This summary proceeds from the broad base of themes and issues monitored by the Center for Vaccine Ethics & Policy in its work: it is not intended to be exhaustive in its coverage.*

*Vaccines and Global Health: The Week in Review is also **posted in pdf form** and as a set of blog posts at http://centerforvaccineethicsandpolicy.wordpress.com/. This blog allows full-text searching of over 6,500 entries.*

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***Request an email version:** Vaccines and Global Health: The Week in Review is published as a single email summary, scheduled for release each Saturday evening before midnight (EDT in the U.S.). If you would like to receive the email version, please send your request to david.r.curry@centerforvaccineethicsandpolicy.org.*

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**POLIO** [to 28 March 2015]
*Public Health Emergency of International Concern (PHEIC)*

**GPEI Update: Polio this week - *As of 25 March 2015***
Global Polio Eradication Initiative
*[Editor's Excerpt and text bolding]*
Full report: http://www.polioeradication.org/Dataandmonitoring/Poliothisweek.aspx
:: Inactivated polio vaccine (IPV) was launched this week in Bangladesh, as part of global efforts to introduce the vaccine globally by end-2015, ahead of the planned switch from trivalent OPV to bivalent OPV in early 2016. "Together with GPEI, Gavi is supporting an unprecedented push to introduce IPV into most countries by the end of 2015. Strong routine immunization is an essential factor to interrupt and maintain zero polio transmission," commented Dr Seth Berkley, CEO of Gavi, the Vaccine Alliance. More.

:: The GPEI is currently accepting applications from students and recent graduates interested in summer 2015 internships at the World Health Organization. More information is available here.

*[Selected country-level report content]*

***Pakistan***

:: One new WPV1 case was reported in the past week, from Quetta, Balochistan, with onset of paralysis on 20 February. This brings the total number of WPV1 cases for 2015 to 20 (and 2014 remains 306). The most recent case had onset of paralysis on 24 February (from Khyber, Federally Administered Tribal Areas - FATA).

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**EBOLA/EVD** [to 28 March 2015]

*Public Health Emergency of International Concern (PHEIC); "Threat to international peace and security" (UN Security Council)*

**Ebola Situation Report - 25 March 2015**

*Incorporating the WHO Activity Report*

*[Excerpts]*

SUMMARY

:: A total of 79 new confirmed cases of Ebola virus disease (EVD) were reported in the week to 22 March: the lowest weekly total in 2015. There were 45 new confirmed cases reported from Guinea. Having reported no cases for 3 consecutive weeks, a new confirmed case was reported from Liberia on 20 March. Sierra Leone reported 33 new confirmed cases in the week to 22 March…

:: In the context of falling case incidence and a receding zone of transmission, treatment capacity now far exceeds demand in both Liberia and Sierra Leone. Accordingly, and with technical guidance from WHO, national authorities in both countries have begun to implement plans for the phased safe decommissioning of surplus facilities. Each country will retain a core capacity of high-quality Ebola treatment centres, strategically located to ensure complete geographic coverage, with additional rapid-response capacity held in reserve…

:: There have been almost 25 000 reported confirmed, probable, and suspected cases of EVD in Guinea, Liberia and Sierra Leone (table 1), with over 10 000 reported deaths (outcomes for many cases are unknown). A total of 45 new confirmed cases were reported in Guinea, 1 in Liberia, and 33 in Sierra Leone in the 7 days to 22 March…

**WHO: Ebola diaries**

27 March 2015 -- Starting from the initial detection of the Ebola outbreak, to the arrival of the first responders, to the overwhelming spread of cases in West Africa — The Ebola Diaries is a series of first-person accounts describing what it has been like working on the front lines of a global health crisis of unprecedented proportion…

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**First Ebola vaccine to be tested in affected communities one year into outbreak**

Guinea WHO Country Office

*Ring vaccination starts in Coyah, Guinea*

Conakry, 25 March, 2015 – The Guinean Government with the World Health Organization (WHO) initiated the very first efficacy trial of an Ebola vaccine this week in an affected community of the Basse-Guinée, one of the areas where most Ebola cases are found in the country. Ring vaccination tests of VSV-EBOV, a lead Ebola vaccine developed by the Public Health Agency of Canada, received an excellent response from the community in a small village in the Coyah prefecture, where the trial team arrived on 23 March.

"This landmark operation gives hope to all of us, in Guinea and in the world, that we might soon have an effective public health tool against Ebola, should the vaccine prove to be safe and effective," stated the WHO Representative in Guinea, Dr. Jean-Marie Dangou. "The start of ring vaccination clinical testing today in Guinea is therefore one of the most important milestones we have achieved in seeking a modern line of defense against Ebola."

Trained medical staff, vaccines and other essential equipment were dispatched from Conakry to Coyah to vaccinate contacts of recently infected people who have given consent in a village of the Coyah prefecture. Vaccinations for now will include only adults, who are most at risk of infection, with the exception of pregnant women.

"We are committed to ending this epidemic," said Dr. Sakoba Keita, National Coordinator of the Fight against Ebola in Guinea. "Combined with control measures that we are putting in place with our partners, a safe and effective vaccine will allow us to close this trying chapter and start rebuilding our country."

The ring vaccination strategy consists in identifying recently infected patients and vaccinating all their contacts, thereby creating a 'ring of immunity' around them to stop the virus from spreading.

"This very same strategy was a key contribution to eradicating smallpox in the 1970's, and allows us to vaccinate all those at greatest risk," explained WHO Coordinator for the Guinea Vaccine Trial, Dr. Ana Maria Henao Restrepo.

Dr. Bertrand Draguez, Medical Director for the Non-governmental Organization Médecins sans Frontières (MSF) stressed that: "The trial is organized on a voluntary basis, and participation is confidential, free and non-remunerated."

The Guinean Government is fully committed to the success of the vaccine clinical trial. In a 20 March official letter addressed to all the Mayors, Prefects and local Health Officials in Guinea, the Head of the National Coordination Against Ebola in Guinea, Dr Sakoba Keita, asked all local public actors for their full cooperation and support.

A total of around 10,000 people are planned to be vaccinated in 190 rings within a six-eight week period. Volunteers will be followed for three months. Results could be available as early as July 2015.

*Note to editors*

About the vaccine and the vaccination strategy:

VSV-EBOV Vaccine was developed by the Public Health Agency of Canada. The vaccine was licensed to NewLink Genetics, and on November 24, 2014, NewLink Genetics and Merck

announced their collaboration on the vaccine.

The concept of ring vaccination applied to the Guinea Ebola vaccine clinical trial is based on vaccinating the "rings" (group of contacts of a newly diagnosed Ebola "index case") either immediately after confirmation of the Ebola diagnosis of the "index case", or three weeks later (delayed vaccination). This strategy allows all the known contacts to be vaccinated within a short period of time, and it constitutes an excellent alternative to the use of a placebo. The ring vaccination trial design was developed by an international group of experts from Canada, France, Guinea, Norway, Switzerland, United Kingdom, United States, and WHO. This group included Professor Donald A. Henderson, who led the WHO smallpox eradication effort.

About the partners:

The Guinea Ebola vaccine trial is a coordinated effort among numerous international partners. The trial is implemented under the responsibility of the Guinean government. The World Health Organization (WHO) is the sponsor of the study. The Government of Guinea, Doctors without Borders / Medecins sans Frontières (MSF), Epicentre, the Norwegian Institute of Public Health and WHO are coordinating its implementation. The trial is funded by MSF; the Research Council of Norway through the Norwegian Institute of Public Health; the Canadian government through the Public Health Agency of Canada, Canadian Institutes of Health Research, International Development Research Centre and Department of Foreign Affairs, Trade and Development; and WHO, with support from the Wellcome Trust, United Kingdom.

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**NIH Watch** [to 28 March 2015]
http://www.nih.gov/news/index.html
:: **Ebola test vaccines appear safe in Phase 2 Liberian clinical trial**
*Liberia-U.S. partnership planning Phase 3 trial and study of Ebola survivors.*
March 26, 2015 —
Two experimental Ebola vaccines appear to be safe based on evaluation in more than 600 people in Liberia who participated in the first stage of the Partnership for Research on Ebola Vaccines in Liberia (PREVAIL) Phase 2/3 clinical trial, according to interim findings from an independent Data and Safety Monitoring Board review. Based on these findings, the study, which is sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, may now advance to Phase 3 testing.

"We are grateful to the Liberian people who volunteered for this important clinical trial and encouraged by the study results seen with the two investigational Ebola vaccine candidates," said NIAID Director Anthony S. Fauci, M.D. "Now we must move forward to adapt and expand the study so that ultimately we can determine whether these experimental vaccines can protect against Ebola virus disease and therefore be used in future Ebola outbreaks."

The PREVAIL trial, which began on Feb. 2, 2015 in Monrovia, Liberia, is testing the safety and efficacy of the cAd3-EBOZ candidate vaccine co-developed by NIAID scientists and GlaxoSmithKline, and the VSV-ZEBOV candidate vaccine developed by the Public Health Agency of Canada and licensed to NewLink Genetics Corporation and Merck. Volunteers are assigned at random to receive a single injection of the NIAID/GSK (cAd3-EBOZ) vaccine, the VSV-ZEBOV vaccine, or a placebo (saline) injection. The trial is also double-blinded, meaning that neither study subjects nor staff know whether a vaccine or placebo was administered. A randomized, double-blind, placebo-controlled trial is considered the "gold standard" in clinical research.

While the initial enrollment goal in the Phase 2 study has been met and the vaccines proven safe, the researchers are continuing Phase 2 study enrollment at Redemption Hospital in Monrovia, Liberia, through late April 2015. This would boost enrollment in the Phase 2 portion of the trial to approximately 1,500 people and would be done, in part, to increase the percentage of women (currently, about 16 percent) in the study for a more robust data set overall. The study follow-up period would be at least one year, and two additional blood samples would be obtained from all volunteers at six and 12 months post-vaccination to determine the durability of the immune responses. These proposed changes will be discussed with the U.S. Food and Drug Administration and are under review by the institutional review boards in Liberia and the United States.

Investigators planned to enroll 27,000 people in Liberia at risk of Ebola infection in the Phase 3 portion of the trial. However, there has been only one new confirmed case of Ebola infection in the country since Feb. 19, 2015. Given this decline in Ebola infection incidence, the trial leaders — H. Clif ford Lane, M.D., NIAID deputy director for clinical research, and Liberian co-principal investigators Stephen Kennedy, M.D., and Fatorma Bolay, Ph.D. — have determined that it is scientifically appropriate to expand the trial to additional sites in other West African countries. Discussions are underway to explore that possibility.

The Liberia–U.S. research team also plans to launch a separate natural history study of Ebola survivors to better understand the after-effects of Ebola virus disease. Four sites in Monrovia, Liberia and locations in the United States may begin enrollment into this study in the coming months, pending regulatory review and approval. More information on this study will be provided when the trial launches

:: **NIH study finds no evidence of accelerated Ebola virus evolution in West Africa**
March 26, 2015 — *The study compares virus sequencing data from patient samples.*
The Ebola virus circulating in humans in West Africa is undergoing relatively few mutations, none of which suggest that it is becoming more severe or transmissible, according to a National Institutes of Health study in Science. The study compares virus sequencing data from samples taken from patients in Guinea (March 2014), Sierra Leone (June 2014) and Mali (November 2014).

"The Ebola virus in the ongoing West African outbreak appears to be stable—that is, it does not appear to be mutating more rapidly than viruses in previous Ebola outbreaks, and that is reassuring," said Anthony S. Fauci, director of the National Institute of Allergy and Infectious Diseases (NIAID), part of NIH. "We look forward to additional information to validate this finding, because understanding and tracking Ebola virus evolution are critical to ensuring that our scientific and public health response keeps pace."

Obtaining virus samples for analysis was challenging for researchers during the outbreak. The NIAID study published today relies on data from the Guinea and Sierra Leone cases as well as samples from two case clusters in Mali obtained from the International Center for Excellence in Research (ICER) located in Bamako. NIAID and the Malian government have been partners in the ICER since 2002. The Mali case clusters originated from people who became infected in Guinea and traveled to Mali, where they were diagnosed.

Today's study, from NIAID's Rocky Mountain Laboratories, finds that there appear to be no genetic changes that would increase the virulence or change the transmissibility of the circulating Ebola virus, and that despite extensive human-to-human transmission during the outbreak, the virus is not mutating at a rate beyond what is expected. Further, they say, based on their data it is unlikely that the types of genetic changes thus far observed would impair diagnostic measures, or affect the efficacy of candidate vaccines or potential virus-specific treatments.

:: **Update on clinical status of patient with Ebola virus disease at the NIH Clinical Center**
March 26, 2015 — Status changes from critical to serious condition.

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**UNMEER** [to 28 March 2015]
https://ebolaresponse.un.org/un-mission-ebola-emergency-response-unmeer

***Press Releases***
26 Mar 2015
Bank mission led by Vice-President Wardell pays visit to Ebola-affected countries of Liberia and Sierra Leone

24 Mar 2015
The African Development Bank participates in the Mano River Union Technical and Ministerial Meeting on Post-Ebola Recovery Strategy

***UN Mission Situation Reports***
- 27 Mar 2015
- 26 Mar 2015
- 25 Mar 2015
- 24 Mar 2015
- 23 Mar 2015

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**Report: Pushed to the Limit and Beyond -- A year into the largest ever Ebola outbreak**
MSF, March 2015 :: 22 pages
Pdf: http://www.msf.org.uk/sites/uk/files/ebola_-_pushed_to_the_limit_and_beyond.pdf
*Press Release*
Pushed to the Limit and Beyond: MSF on the global Ebola response one year into the deadliest outbreak in history
March 23, 2015
One year ago today, an outbreak of Ebola in the West African country of Guinea was announced. Since then, nearly 10,000 people have died of the disease, and it has not yet been defeated. Médecins Sans Frontières/Doctors Without Borders (MSF) today released a critical analysis of the Ebola epidemic over the past year, revealing the shortcomings of the global

response to the crisis and warning that the outbreak, despite an overall decline in cases, is not yet over.

The report, *Pushed to the Limit and Beyond,* is based on interviews with dozens of MSF staff involved in the organization's Ebola intervention. It describes MSF's early warnings one year ago about cases of Ebola spreading in Guinea, the initial denial by governments of the affected countries, and the unprecedented steps that MSF was forced to take in the face of global inaction as the outbreak engulfed neighbouring states.

*Exposing inefficiencies in aid and health systems*

"Today we share our initial reflections and take a critical look at both MSF's response and the wider global response to the deadliest Ebola outbreak in history," says Dr. Joanne Liu, MSF international president. "The Ebola epidemic proved to be an exceptional event that exposed the reality of how inefficient and slow health and aid systems are to respond to emergencies."

The report details the effects of the several months-long "global coalition of inaction," during which the virus spread wildly, leading MSF to issue a rare call for the mobilization of international civilian and military medical assets with biohazard capacity. By the end of August, MSF's ELWA3 centre in Monrovia was overwhelmed with patients. Staff were forced to turn away visibly ill people from the front gate, in the full knowledge that they would likely return to their communities and infect others.

"The Ebola outbreak has often been described as a perfect storm: a cross-border epidemic in countries with weak public health systems that had never seen Ebola before," says Christopher Stokes, MSF's general director. "Yet this is too convenient an explanation. For the Ebola outbreak to spiral this far out of control required many institutions to fail. And they did, with tragic and avoidable consequences."…

**PLoS Medicine**

(Accessed 28 March 2015)

http://www.plosmedicine.org/

*Policy Forum*

**Strengthening the Detection of and Early Response to Public Health Emergencies: Lessons from the West African Ebola Epidemic**

Mark J. Siedner, Lawrence O. Gostin, Hilarie H. Cranmer, John D. Kraemer

Published: March 24, 2015

DOI: 10.1371/journal.pmed.1001804

*Summary Points*

:: The international response to the West African Ebola virus disease epidemic has exemplified the great potential of the global public health community. However, the protracted early response also revealed critical gaps, which likely resulted in exacerbation of the epidemic.

:: It is incumbent on international health partners to learn from missteps that occurred in the early stages of the epidemic and strengthen our public health capacity to better respond to future public health emergencies.

:: Strategies to consider include development of a more precise system to risk stratify geographic settings susceptible to disease outbreaks, reconsideration of the 2005 International Health Regulations Criteria to allow for earlier responses to localized epidemics before they reach epidemic proportions, increasing the flexibility of the World Health Organization director general to characterize epidemics with more granularity, development of guidelines for best practices to promote partnership with local stakeholders and identify locally acceptable

response strategies, and, most importantly, making good on international commitments to establish a fund for public health emergency preparedness and response.
:: The recent success of the global action to stem the Ebola virus disease epidemic is laudable but should not encourage complacency in our efforts to improve the global public health infrastructure.

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**IVI Watch** [to 28 March 2015]
http://www.ivi.org/web/www/home
:: **160 000 people targeted with oral cholera vaccine in Nsanje** [Malawi]
*Written by Martin Chiwanda*

Nsanje, Malawi March 25: The Ministry of Health is expected to embark on an Oral Cholera Vaccine campaign targeting 160,000 people in the flood hit Nsanje district.

Ministry of Health Epidemiologist Settie Kanyanda disclosed the development in an interview Tuesday on the sidelines of a District Executive Committee meeting in Nsanje.

He said the ministry had targeted Nsanje because it was prone to the cholera outbreak.

"Nsanje district is experiencing more cases of cholera as compared to other districts. We feel that the Oral vaccine is a preventive measure to the attacks," he stated.

Kanyada assured communities in Nsanje that the vaccine would make a difference in the fight against cholera as it works for five years.

"The Shanchol vaccine which will be given in two doses with interval between 2 to 6 weeks is one of the oral cholera vaccine prequalified by World Health Organisation (WHO) in September 2011 for use by member countries. It is a bivalent whole cell killed oral cholera vaccine with an efficacy of 65percent for five years," he explained.

With the limited resources available to the ministry, Kanyanda said the exercise will only be administered in Nsanje targeting 160,000 people which is half the district's population projected at 280, 000.

"The vaccine will be administered to all 100,000 to 160,000 people in the district with ages from one year and above living in camps and surrounding communities. We cannot afford to provide the vaccine to the whole population because of limited resources."

"This exercise has been supported by the World Health Organization and the International Vaccine Institute of Korea. However, we are appealing to other partners to come in and assist in the course," added Kanyanda.

He also challenged people in the lower shire district to continue exercising good hygiene practices if they were to be safe from typhoid and other diarrhea diseases.

"World Health Organization recommends that vaccination should be used as a tool to control cholera however provision of clean water and adequate sanitation remain the mainstays of cholera control," clarified Kanyanda.

As of Monday, 23rd March, 2015, Nsanje district had recorded 137 cases of cholera with two deaths, according to District Medical Officer, Dr. Yamikani Mastala.

The Oral vaccine exercise first dose will commence on March 31 and ends on April 4, 2014.

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**WHO & Regionals** [to 28 March 2015]

:: **Millions of Syrians endure deteriorating health crisis: WHO calls for increased funding**

March 2015 – It is estimated that there are more than 1.3 million people in need of health assistance in Aleppo. Ahead of next week's third International Humanitarian Pledging Conference for Syria in Kuwait, the WHO appeals for US$ 124 million to continue its support to health services in the Syrian Arab Republic.

:: **Cyclone Pam delivers a devastating blow to health services in Vanuatu**

25 March 2015 --WHO is responding to the health needs of those affected by Tropical Cyclone Pam – a storm which has been described as the strongest cyclone in the Pacific in more than a decade. To be able to respond to these crisis and provide emergency medical supplies and support to re-establishment of the health system WHO is requesting US$ 3 Million.

- WHO donor alert for Cyclone Pam

:: **Global Alert and Response (GAR): Disease Outbreak News (DONs)**

- 26 March 2015 Middle East respiratory syndrome coronavirus (MERS-CoV) – Saudi Arabia

:: The **Weekly Epidemiological Record (WER) 27 March 2015,** vol. 90, 12 (pp. 109–120) includes:

- Reducing mortality from emerging diseases
- Meningococcal disease control in countries of the African meningitis belt, 2014

**:: WHO Regional Offices**

**WHO African Region AFRO**

:: First Ebola Vaccine to Be Tested in Affected Communities One Year into Outbreak Ring Vaccination Starts in Coyah, Guinea 25 March 2015

:: Central African Republic: health emergency at a crossroads 25 March 2015

:: Message of the Regional Director on the occasion of World Tuberculosis Day 2015 Infographic: Gear Up to end TB [jpg, 759kb]

**WHO Region of the Americas PAHO**

:: PAHO/WHO urges better detection and treatment of tuberculosis to "End TB" in the Americas (03/23/2015)

**WHO South-East Asia Region SEARO**

:: One year of polio-free certification 27 March 2015

:: World Water Day 2015: Water and Sustainable Development 22 March 2015

**WHO European Region EURO**

:: Europe leading the way in plain packaging legislation for tobacco products 26-03-2015

:: New WHO report shows that transparency and cooperation help to reduce high prices for new medicines 26-03-2015

:: Using price policies to promote healthier diets 23-03-2015

**WHO Eastern Mediterranean Region EMRO**

:: Millions of Syrians endure deteriorating health crisis: WHO calls for increased funding

Aleppo, Syria, 27 March, 2015 – Ahead of next week's third International Humanitarian Pledging Conference for Syria in Kuwait, WHO appeals for US$ 124 million to continue its support to health services in the Syrian Arab Republic…

:: WHO and health partners respond to increased health needs as a result of conflict in Yemen 26 March 2015

**WHO Western Pacific Region**

:: Brunei Darussalam, Cambodia, Japan verified as achieving measles elimination

MANILA, 27 March 2015 – Brunei Darussalam, Cambodia and Japan have been verified as having achieved measles elimination by the Measles Regional Verification Commission. The three countries join Australia, Macao SAR (China), Mongolia and the Republic of Korea as countries and areas in the Western Pacific Region that have successfully eliminated measles

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**CDC/MMWR/ACIP Watch** [to 28 March 2015]
http://www.cdc.gov/media/index.html
:: **ACIP Presentation Slides: February 2015 Meeting**
February 26, 2015

:: **MMWR Weekly March 27, 2015 / Vol. 64 / No. 11**
- Use of 9-Valent Human Papillomavirus (HPV) Vaccine: Updated HPV Vaccination Recommendations of the Advisory Committee on Immunization Practices
- Updated Recommendations for the Use of Typhoid Vaccine — Advisory Committee on Immunization Practices, United States, 2015

**Sabin Vaccine Institute Watch** [to 28 March 2015]
http://www.sabin.org/updates/pressreleases
**Dr. Gary Michelson Receives Albert B. Sabin Humanitarian Award**

WASHINGTON, D.C. — March 25, 2015 — The Sabin Vaccine Institute (Sabin) will present the Albert B. Sabin Humanitarian Award to Gary Michelson, MD, a distinguished orthopedic spinal surgeon and inventor, in recognition of his extraordinary philanthropy and commitment toward the control and elimination of neglected tropical diseases (NTDs) through high-level advocacy and vaccine research and development. He will be honored today at a private event with Sabin's executive leadership, Board of Trustees and key members of the scientific community in Houston, Texas.

**European Medicines Agency Watch** [to 28 March 2015]
http://www.ema.europa.eu/ema/
27/03/2015
Gardasil 9 offers wider protection against cancers caused by human papillomavirus (HPV)
*Vaccine covers five more types of HPV than previously approved Gardasil vaccine*

The European Medicines Agency (EMA) has recommended Gardasil 9 (human papillomavirus vaccine) for the prevention of diseases caused by nine types of human papillomavirus (HPV). This means that Gardasil 9 covers five more HPV types than Gardasil, one of two HPV vaccines available in the European Union (EU)…

…Gardasil 9 is recommended for use in boys and girls from nine years of age to protect against cervical cancer and pre-malignant cervical lesions, vulvar and vaginal cancers and pre-malignant vulvar and vaginal lesions, pre-malignant anal lesions and anal cancers and external genital warts covered by HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58…

…The safety of Gardasil 9 was evaluated in more than 23,000 people in seven clinical trials. The assessment also took into account experience from the use of Gardasil, which has been authorised in the EU since 2006. The most commonly reported adverse reactions were injection site pain, swelling, redness, and headaches.

Gardasil 9 is administered in three separate injections, with the initial dose followed by additional injections given two and six months later. All three doses should be given within a one-year period.

The company received scientific advice from the Committee for Medicinal Products for Human Use (CHMP) which pertained to clinical aspects of the company's application.

The opinion adopted by the CHMP at its March 2015 meeting is an intermediary step on Gardasil 9's path to patient access. The CHMP opinion will now be sent to the European Commission for the adoption of a decision on EU-wide marketing authorisation. Once a marketing authorisation has been granted, a decision about price and reimbursement will then take place at the level of each Member State considering the potential role/use of this vaccine in the context of the national health system of that country.

27/03/2015
Meeting highlights from the Committee for Medicinal Products for Human Use (CHMP) 23-26 March 2015
*Five new medicines, including one orphan, recommended for approval*
…One recommendation on extension of therapeutic indication
The Committee recommended an extension of indication for Tamiflu to include the treatment of influenza in infants below one year of age.

27/03/2015
Regulatory information - EU recommendations for 2015/2016 seasonal flu vaccine composition
*EMA annual recommendations are based on WHO observations*

The European Medicines Agency has issued the European Union (EU) recommendations for the influenza virus strains that vaccine manufacturers should include in vaccines for the prevention of seasonal influenza from autumn 2015.

Trivalent vaccines for the 2015/2016 season should contain these three virus strains:
:: an A/California/7/2009 (H1N1)pdm09-like virus
:: an A/Switzerland/9715293/2013 (H3N2)-like virus
:: a B/Phuket/3073/2013-like virus

For quadrivalent vaccines with two influenza B viruses, a B/Brisbane/60/2008-like virus in addition to the strains mentioned above is considered appropriate.

Detailed recommendations including the specific virus strains recommended are available in a report from the Biologics Working Party (BWP) ad-hoc Influenza Working Group…

**Industry Watch** [to 28 March 2015]

:: **Sanofi Pasteur Announces FDA Approval of Quadracel DTaP-IPV Combination Vaccine for Children Aged 4-6**

March 26, 2015

*Approval allows children to receive a combination of two recommended vaccinations*

SWIFTWATER, Pa., March 25, 2015 /PRNewswire/ -- Sanofi Pasteur, the vaccines division of Sanofi, announced today that the U.S. Food and Drug Administration (FDA) has approved use of Quadracel™ (Diphtheria and Tetanus Toxoids and Acellular Pertussis Absorbed and Inactivated Poliovirus; DTaP-IPV) vaccine for active immunization against diphtheria, tetanus, pertussis and poliomyelitis in children 4 through 6 years of age.

"The FDA approval of Quadracel vaccine provides health care providers with a new combination vaccine, potentially reducing the number of vaccine injections children aged 4 through 6 would need," said David P. Greenberg, M.D., Vice President, U.S. Scientific and Medical Affairs, Sanofi Pasteur. "Our goal is to help remove barriers to timely immunization and we think this combination vaccine could help ensure children are getting vaccinated in line with current recommendations."…

…This FDA approval is based on data from a pivotal multicenter, randomized, controlled, Phase III study designed to compare the safety and immunogenicity of Quadracel vaccine (DTaP-IPV) with DAPTACEL (DTaP) and IPOL (IPV) vaccines in children 4 through 6 years of age who were previously vaccinated with DAPTACEL and/or Pentacel (DTaP-IPV/Hib) vaccines. Results show Quadracel vaccine has similar safety and immunogenicity profiles as compared to those of separately administered DAPTACEL and IPOL vaccines…

**UNICEF Watch** [to 28 March 2015]

:: **Easier access to the most reliable and up-to-date stats on children through UNICEF's revamped data websites**

NEW YORK, 23 March 2015 – UNICEF has made all its data on health, nutrition, education, water and sanitation, child protection, and HIV/AIDS publicly available, in an easily searchable format which includes redesigned country profiles and a new data visualisation tool for the creation of charts, maps and graphs: UNICEF DATA AND ANALYTICS. All of which make UNICEF the most reliable and up-to-date source of statistics on women and children.

Problems that go unmeasured often go unsolved. Consistent, credible data about children, their families and their communities are critical to the improvement of children's lives and indispensable to the realisation of their rights.

UNICEF's data provide a fuller picture than ever before of the situation of children across the globe. The data tells intricate and detailed stories about where and how children are born and cared for, how they grow, learn, work and connect with others, and how they make their way in the world.

**U.S. White House: Our Plan to Combat and Prevent Antibiotic-Resistant Bacteria**

Secretary Sylvia Mathews Burwell, Secretary Tom Vilsack, Secretary Ash Carter
March 27, 2015

Antibiotics save millions of lives every year. Today, however, the emergence of drug resistance in bacteria is undermining the effectiveness of current antibiotics and our ability to treat and prevent disease. The Centers for Disease Control and Prevention (CDC) estimates that drug-resistant bacteria cause two million illnesses and approximately 23,000 deaths each year in the United States alone. Antibiotic resistance also limits our ability to perform a range of modern medical procedures, such as chemotherapy, surgery, and organ transplants. That's why fighting antibiotic resistance is a national priority.

Over the past year, the Administration has taken important steps to address the threat of antibiotic resistance. In September 2014, the President issued Executive Order (EO) 13676: Combating Antibiotic-Resistant Bacteria, which outlines steps for implementing the National Strategy on Combating Antibiotic-Resistant Bacteria and addressing the policy recommendations of the President's Council of Advisors on Science and Technology (PCAST)'s report on Combating Antibiotic Resistance. Furthermore, the President's FY 2016 Budget released earlier this year proposed nearly doubling the amount of Federal funding for combating and preventing antibiotic resistance to more than $1.2 billion.

Combating and preventing antibiotic resistance, however, will be a long-term effort. That's why, today, the Administration is releasing the National Action Plan for Combating Antibiotic Resistant Bacteria (NAP).

The NAP outlines a whole-of-government approach over the next five years targeted at addressing this threat:

*1. Slow the emergence of resistant bacteria and prevent the spread of resistant infections*

The judicious use of antibiotics in health care and agriculture settings is essential to combating the rise in antibiotic resistance. We can help slow the emergence of resistant bacteria by being smarter about prescribing practices across all human and animal health care settings, and by continuing to eliminate the use of medically-important antibiotics for growth promotion in animals.

*2. Strengthen national "One-Health" surveillance efforts*

A "One-Health" approach to disease surveillance will improve detection and control of antibiotic resistance by integrating data from multiple monitoring networks, and by providing high-quality information, such as detailed genomic data, necessary to tracking resistant bacteria in diverse settings in a timely fashion.

*3. Advance development and use of rapid and innovative diagnostic tests*

The development of rapid "point-of-need" diagnostic tests could significantly reduce unnecessary antibiotic use by allowing health care providers to distinguish between viral and bacterial infections, and identify bacterial drug susceptibilities during a single health care visit making it easier for providers to recommend appropriate, targeted treatment.

*4. Accelerate basic and applied research and development*

New antibiotics and alternative treatments for both humans and animals are critical to maintaining our capacity to treat and prevent disease. This involves supporting and streamlining the drug development process, as well as increasing the number of candidate drugs at all

stages of the development pipeline. Additionally, boosting basic research to better understand the ecology of antibiotic resistance will help us develop effective mitigation strategies.

*5. Improve international collaboration and capacities*
Antibiotic resistance is a global problem that requires global solutions. The United States will engage with foreign ministries and institutions to strengthen national and international capacities to detect, monitor, analyze, and report antibiotic resistance; provide resources and incentives to spur the development of therapeutics and diagnostics for use in humans and animals; and strengthen regional networks and global partnerships that help prevent and control the emergence and spread of resistance.

The NAP is a comprehensive effort that will require the coordinated and complementary efforts of individuals and groups around the world, including public- and private-sector partners, health care providers, health care leaders, veterinarians, agriculture industry leaders, manufacturers, policymakers, and patients. Working together, we can turn the tide against the rise in antibiotic resistance and make the world a healthier and safer place for the next generation.

National Action Plan for Combating Antibiotic Resistant Bacteria (NAP)
The White House, Washington
March 2015 :: 63 pages
Pdf:
https://www.whitehouse.gov/sites/default/files/docs/national_action_plan_for_combating_antibiotic-resistant_bacteria.pdf
*Vision:* The United States will work domestically and internationally to prevent, detect, and control illness and death related to infections caused by antibiotic-resistant bacteria by implementing measures to mitigate the emergence and spread of antibiotic-resistance and ensuring the continued availability of therapeutics for the treatment of bacterial infections.

**Global Fund** [to 28 March 2015]
25 March 2015
Doing the Right Thing: Human Rights for Those Affected by TB

23 March 2015
Global Steering Committee Advances Efforts for Quality Assurance

**::::::**

**GAVI** [to 28 March 2015]
http://www.gavialliance.org/library/news/press-releases/
*No new digest content identified.*

**European Vaccine Initiative Watch** [to 28 March 2015]
http://www.euvaccine.eu/news-events
*No new digest content identified.*

**PATH** [to 28 March 2015]
http://www.path.org/news/index.php

*No new digest content identified.*

**BMGF (Gates Foundation)** [to 28 March 2015]
http://www.gatesfoundation.org/Media-Center/Press-Releases
*No new digest content identified.*

**FDA Watch** [to 28 March 2015]
http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/default.htm
*No new digest content identified.*

**DCVMN / PhRMA / EFPIA / IFPMA / BIO Watch** [to 28 March 2015]
*No new digest content identified.*

## ***Reports/Research/Analysis/Commentary/Conferences/Meetings/Book Watch/Tenders***

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

### New look for the NITAG Resource Center

*National Immunization Technical Advisory Groups*

The vamped website for the NITAG Resource Center (www.nitag-resource.org) went live on March 18. The Resource Centre was devised by AMP's Health Policy and Institutional Development unit, which is a WHO Collaborating Center for evidence-informed immunization policy-making.

The site…aims to provide information, tools and training materials for National Immunization Technical Advisory Groups (NITAGs) and the international immunization community as a way of improving evidence-based decision-making at national level. The site has been completely redesigned and restructured to make it as practical and user-friendly as possible in an effort to meet the stated objective of all partners: to make it the sole platform for collaboration between NITAGs.

Technological innovations for easier searching

The new site features a streamlined and intuitive multi-criteria search engine to give more accurate searching of the document database, which includes (amongst other things) the recommendations from all existing NITAGs, reference documents and generic tools developed by all partners. The site has also been revamped to adapt automatically to the screen width on any device – PCs, tablets and smartphones – the goal being, once more, to improve readability.

A dedicated space for easy collaboration

There are several new sections on the site covering latest events, news and topics subject to review by the NITAGs and worldwide technical partners in the coming years, the goal being to promote knowledge sharing in the global NITAG and wider international immunization community.

Last but not least, the biggest innovation on the new site is an interactive world map that shows the status of NITAGs. Users can now have immediate access to the operating

indicators defined by WHO for each NITAG. In addition, clicking on a particular country opens a country fact sheet that gives more information on the relevant NITAG.

**NFID: 18th Annual Conference on Vaccine Research**
National Foundation for Infectious Diseases
April 13-15, 2015
Bethesda, MD
*Overview:*
The Annual Conference on Vaccine Research (ACVR) provides high-quality, current reports of scientific progress and best practices featured in both invited presentations and submitted oral abstracts and posters. The ACVR brings together the diverse disciplines involved in the research and development of vaccines and associated technologies for disease control through immunization. By drawing upon an international audience of scientists and researchers, healthcare professionals and trainees, veterinarians, vaccine manufacturers, and public health officials, the conference is designed to encourage the exchange of ideas across a broad range of disciplines.

**Bioethics Commission: Ebola Teaches Us Public Health Preparedness Requires Ethics Preparedness**
*Commission calls for accountable integration of ethics into emergency public health response*
February 26, 2015

WASHINGTON, D.C. – Today the Presidential Commission for the Study of Bioethical Issues (Bioethics Commission) reported that the federal government has both a prudential and a moral responsibility to actively participate in coordinated global responses to public health emergencies wherever they arise.

"The Ebola epidemic in western Africa overwhelmed fragile health systems, killed thousands of people, and highlighted major inadequacies in our ability to respond to global public health emergencies," Commission Chair Amy Gutmann, Ph.D., said. "It demonstrated the dire need to prepare before the next epidemic. A failure to prepare and a failure to follow good science — for example, by not developing vaccines and not supporting health care providers — will lead to needless deaths."

Explaining why the Bioethics Commission chose to take on the topic, Gutmann said: "Both justice and prudence demand that we do our part in combating such devastating outbreaks. Once we recognize our humanitarian obligations and the ability of infectious diseases to travel in our interconnected world, we cannot choose between the ethical and the prudential. Ethics and enlightened interest converge in calling for our country to address epidemics at their source."

In its brief, Ethics and Ebola: Public Health Planning and Response, the Bioethics Commission argues that the United States must strengthen health infrastructure and emergency response capabilities, improve health communications, and integrate ethics expertise at every level of public health emergency planning and response.

"Public health preparedness requires ethics preparedness," Gutmann said. "We need to be prepared, for example, to communicate early and often during an Ebola epidemic — drawing upon the best scientific evidence — why not to quarantine asymptomatic individuals. Needlessly restricting the freedom of expert and caring health care workers is both morally wrong and counterproductive; it will do more to lose than to save lives."

The Bioethics Commission's seven recommendations offer targeted policy and research design suggestions. For example, the Bioethics Commission recommended that the United States strengthen key elements of its domestic and global health emergency response capabilities. These include:
:: Strengthening the capacity of the World Health Organization to respond to global health emergencies through the provision of increased funding and collaboration with other international, national, and non-governmental public health organizations;
:: Identifying and empowering a single U.S. health official accountable for all federal domestic and international public health emergency response activities; and
:: Strengthening the deployment capabilities of the U.S. Public Health Service, including by streamlining command structure for deployment and providing appropriate resources to train and maintain skills needed for emergency response.

In addition, the Bioethics Commission recommended that ethical principles be integrated into timely and agile public health decision making processes employed in response to rapidly unfolding epidemics. It called for qualified public health ethics expertise to be readily available to identify ethical considerations relevant to public health emergencies and responses in light of real-time available evidence. Specifically, it recommends that a single U.S. health official should be accountable for ethics integration.

On the contentious issue of quarantine and other policies related to movement restrictions, the Bioethics Commission recommended that governments and public health organizations employ the least restrictive means necessary—based on the best available scientific evidence—when implementing restrictive public health measures.

"Governments and public health organizations should be prepared to clearly communicate the rationale for such measures and provide ongoing updates to the public about their implementation, with particular attention to the needs of those most directly affected," the Bioethics Commission wrote in its brief…

## ***Journal Watch***

*Vaccines and Global Health: The Week in Review* continues its weekly scanning of key peer-reviewed journals to identify and cite articles, commentary and editorials, books reviews and other content supporting our focus on vaccine ethics and policy. ***Journal Watch*** **is not intended to be exhaustive, but indicative of themes and issues the Center is actively tracking.** We selectively provide full text of some editorial and comment articles that are specifically relevant to our work. Successful access to some of the links provided may require subscription or other access arrangement unique to the publisher.

*If you would like to suggest other journal titles to include in this service, please contact David Curry at: david.r.curry@centerforvaccineethicsandpolicy.org*

**The American Journal of Bioethics**
Volume 15, Issue 3, 2015
http://www.tandfonline.com/toc/uajb20/current
[No relevant content identified]

**American Journal of Infection Control**

March 2015 Volume 43, Issue 3, p199-312
http://www.ajicjournal.org/current
[Reviewed earlier]

**American Journal of Preventive Medicine**
March 2015 Volume 48, Issue 3, p241-364, e1-e4
http://www.ajpmonline.org/current
[Reviewed earlier]

**American Journal of Public Health**
Volume 105, Issue S2 (April 2015)
http://ajph.aphapublications.org/toc/ajph/current
*Editor's Choice*
**A New Era for Population Health: Government, Academia, and Community Moving Upstream Together**
Bechair Choucair, Jay D. Bhatt
American Journal of Public Health: April 2015, Vol. 105, No. S2: S144–S144.
[No abstract]
*Editorials*
**Improving Population Health by Learning From Systems and Services**
Glen P. Mays, F. Douglas Scutchfield
American Journal of Public Health: April 2015, Vol. 105, No. S2: S145–S147.
[No abstract]
**The Value of the "System" in Public Health Services and Systems Research**
Craig W. Thomas, Liza Corso, Judith A. Monroe
American Journal of Public Health: April 2015, Vol. 105, No. S2: S147–S149
[No abstract]
**Building a Culture of Health: A Critical Role for Public Health Services and Systems Research**
Alonzo L. Plough
American Journal of Public Health: April 2015, Vol. 105, No. S2: S150–S152.
[No abstract]

**American Journal of Tropical Medicine and Hygiene**
March 2015; 92 (3)
http://www.ajtmh.org/content/current
[Reviewed earlier]

**Annals of Internal Medicine**
17 March 2015, Vol. 162. No. 6
http://annals.org/issue.aspx
[Reviewed earlier]

**BMC Health Services Research**
http://www.biomedcentral.com/bmchealthservres/content
(Accessed 28 March 2015)
*Research article*
## Inefficiency, heterogeneity and spillover effects in maternal care in India: a spatial stochastic frontier analysis
Yohannes Kinfu[1]* and Monika Sawhney[2]
Author Affiliations
BMC Health Services Research 2015, 15:118 doi:10.1186/s12913-015-0763-x
Published: 25 March 2015
*Abstract* (provisional)
Background
Institutional delivery is one of the key and proven strategies to reduce maternal deaths. Since the 1990s, the government of India has made substantial investment on maternal care to reduce the huge burden of maternal deaths in the country. However, despite the effort access to institutional delivery in India remains below the global average. In addition, even in places where health investments have been comparable, inter- and intra-state difference in access to maternal care services remain wide and substantial. This raises a fundamental question on whether the sub-national units themselves differ in terms of the efficiency with which they use available resources, and if so, why?
Methods
Data obtained from round 3 of the country's District Level Health and Facility Survey was analyzed to measure the level and determinants of inefficiency of institutional delivery in the country. Analysis was conducted using spatial stochastic frontier models that correct for heterogeneity and spatial interactions between sub-national units. Results Inefficiency differences in maternal care services between and within states are substantial. The top one third of districts in the country has a mean efficiency score of 90 per cent or more, while the bottom 10 per cent of districts exhibit mean inefficiency score of as high as over 75 per cent or more. Overall mean inefficiency is about 30 per cent. The result also reveals the existence of both heterogeneity and spatial correlation in institutional delivery in the country.
Conclusions
Given the high level of inefficiency in the system, further progress in improving coverage of institutional delivery in the country should focus both on improving the efficiency of resource utilization—especially where inefficiency levels are extremely high—and on bringing new resources in to the system. The additional investment should specifically focus on those parts of the country where coverage rates are still low but efficiency levels are already at a high level. In addition, given that inefficiency was also associated inversely with literacy and urbanization and positively related with proportion of households belonging to poor households, investment in these areas can also improve coverage of institutional delivery in the country.
*Research article*
## Integrating an infectious disease programme into the primary health care service: a retrospective analysis of Chagas disease community-based surveillance in Honduras
Ken Hashimoto[12]*, Concepción Zúniga[3], Jiro Nakamura[24] and Kyo Hanada[56]
Author Affiliations
BMC Health Services Research 2015, 15:116 doi:10.1186/s12913-015-0785-4
Published: 24 March 2015
*Abstract* (provisional)
Background

Integration of disease-specific programmes into the primary health care (PHC) service has been attempted mostly in patient-centred disease control such as HIV/AIDS and tuberculosis but rarely in vector control. Chagas disease is controlled principally by interventions against the triatomine vector. In Honduras, after successful reduction of household infestation by vertical approach, the Ministry of Health implemented community-based vector surveillance at the PHC services (health centres) to prevent the resurgence of infection. This paper retrospectively analyses the effects and process of integrating a Chagas disease vector surveillance system into health centres.

Methods

We evaluated the effects of integration at six pilot sites in western Honduras during 2008–2011 on; surveillance performance; knowledge, attitude and practice in schoolchildren; reports of triatomine bug infestation and institutional response; and seroprevalence among children under 15 years of age. The process of integration of the surveillance system was analysed using the PRECEDE-PROCEED model for health programme planning. The model was employed to systematically determine influential and interactive factors which facilitated the integration process at different levels of the Ministry of Health and the community.

Results

Overall surveillance performance improved from 46 to 84 on a 100 point-scale. Schoolchildren's attitude (risk awareness) score significantly increased from 77 to 83 points. Seroprevalence declined from 3.4% to 0.4%. Health centres responded to the community bug reports by insecticide spraying. As key factors, the health centres had potential management capacity and influence over the inhabitants' behaviours and living environment directly and through community health volunteers. The National Chagas Programme played an essential role in facilitating changes with adequate distribution of responsibilities, participatory modelling, training and evaluation.

Conclusions

We found that Chagas disease vector surveillance can be integrated into the PHC service. Health centres demonstrated capacity to manage vector surveillance and improve performance, children's awareness, vector report-response and seroprevalence, once tasks were simplified to be performed by trained non-specialists and distributed among the stakeholders. Health systems integration requires health workers to perform beyond their usual responsibilities and acquire management skills. Integration of non-patient-centred vector control is feasible and can contribute to strengthening the preventive capacity of the PHC service.

**BMC Infectious Diseases**

http://www.biomedcentral.com/bmcinfectdis/content

(Accessed 28 March 2015)

*Research article*

## A national cross-sectional study for poliovirus seroprevalence in the Republic of Korea in 2012: implication for deficiency in immunity to polio among middle-aged people

Hye-Jin Kim[13], Seoyeon Hwang[1], Somin Lee[1], Yunhyung Kwon[24], Kwangsook Park[2], Young Joon Park[2], Geun-Ryang Bae[2], Sang Won Lee[1], Yong-Seok Jeong[3] and Ji-Yeon Hyeon[1]*

Author Affiliations

BMC Infectious Diseases 2015, 15:164 doi:10.1186/s12879-015-0894-z

Hye-Jin Kim and Seoyeon Hwang contributed equally to this work.

Published: 28 March 2015

*Abstract* (provisional)

Background

A worldwide poliomyelitis eradication program was initiated in 1988; however, strains of wild poliovirus (WPV) are still endemic in some countries. Until WPV transmission is eradicated globally, importation and outbreaks of WPV are alarming possibilities. This study is the first report to document the polio immunity after 2004, when an inactivated polio vaccine (IPV) was introduced in the Republic of Korea.

Methods

A total of 745 serum samples from randomly selected patients ranging from 6 to 84 years of age were used for neutralization tests, performed in the World Health Organization polio national reference laboratory.

Results

Among the 745 tested sera, 439 (58.9%) were seropositive and 19 (2.6%) were seronegative to all PV serotypes. In all age groups, PV3 showed the lowest level of seroprevalence, at 509 cases (68.3%), compared to 616 (82.7%) for PV1 and 685 (91.9%) for PV2. In the 6–10-year age group, which included IPV-immunized children, the highest seropositive rate was observed and the difference in seroprevalence between PV3 and other serotypes was the lowest compared to the other age groups immunized with oral PV vaccines (OPV). In addition, the seronegative rates of all three PV types in children aged 6–10 in this study were found to be lower than those in OPV-immunized children reported in a previous study from the Republic of Korea. Meanwhile, middle-aged subjects (41–60 years) had the lowest seroprevalence and geometric mean titer.

Conclusions

This study indicates a deficiency in immunity to PV in middle-aged individuals, and low seroprevalence to PV3 in all age groups. In addition, due to the ongoing risk of importing PV, middle-aged people should consider PV vaccination before visiting a PV-endemic country. Our findings provide data to assist those involved in deciding future national polio vaccination strategies for the maintenance of a polio-free status in Korea.

*Research article*

**The long-term immunogenicity of recombinant hepatitis B virus (HBV) vaccine: contribution of universal HBV vaccination in Italy**

Nicola Coppola, Anna Corvino, Stefania De Pascalis, Giuseppe Signoriello, Eliana Di Fiore, Albert Nienhaus, Evangelista Sagnelli, Monica Lamberti BMC Infectious Diseases 2015, 15:149 (25 March 2015)

*Abstract*

Background

Universal hepatitis B virus (HBV) vaccination of newborn babies was introduced in Italy in 1991 and was extended to 12-years-old children for the first 12 years of application so as to cover in a dozen years the Italian population aged 0-24 years. The aim of this study was to identify factors associated with long-term immunogenicity against HBV 17 years after primary vaccination in students attending medical schools in Naples, Italy.

Methods

1,704 students attending the school of medicine, schools of the healthcare professions, or postgraduate medical schools of the Second University of Naples, Italy, from September 2012 to December 2013 were enrolled in this study. Of these, 588 had been vaccinated against HBV in infancy and 1,116 when 12 years old. Multivariate logistic regression analysis was used to identify factors associated with the level of long-term immunogenicity.

Results

All vaccinated subjects were HBsAg/anti-HBc negative: 270 (15.8%) had an anti-HBs titer between 1 and 9 IU/L, 987 (57.9%) between 10 and 400 IU/L, and 447 (26.3%) over 400 IU/L. When compared with the latter two subgroups, those with anti-HBs titers lower than 10 IU/L were younger (24 plus/minus 5.2 years vs. 26 plus/minus 4.9 years, p<0.000), more frequently students attending a healthcare school (59% vs. 47%, p<0.001), and more frequently had been vaccinated in infancy (50% vs. 31.5%, p<0.0001). Multivariate logistic regression identified age at vaccination as the only factor independently associated with an anti-HBs titer <10 IU/L (OR: 2.43; C.I. 95%: 1.57–3.76, p=0.001).
Conclusions
Universal HBV vaccination in Italy has been more effective in generating a prolonged protective response in subjects vaccinated at adolescence than in infancy. Students with a low anti-HBs titer should be considered for a booster dose because most will be exposed to the risk of acquiring HBV for decades.

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**BMC Medical Ethics**
http://www.biomedcentral.com/bmcmedethics/content
(Accessed 28 March 2015)
[No new relevant content]

**BMC Pregnancy and Childbirth**
http://www.biomedcentral.com/bmcpregnancychildbirth/content
(Accessed 28 March 2015)
[No new relevant content]

**BMC Public Health**
http://www.biomedcentral.com/bmcpublichealth/content
(Accessed 28 March 2015)
[No new relevant content]

**BMC Research Notes**
http://www.biomedcentral.com/bmcresnotes/content
(Accessed 28 March 2015)
[No new relevant content]

**BMJ Open**
2015, Volume 5, Issue 3
http://bmjopen.bmj.com/content/current
[Reviewed earlier]

**British Medical Journal**
28 March 2015(vol 350, issue 8001)
http://www.bmj.com/content/350/8001

***Feature***

# Commentary: Will 20th century patient safeguards be reversed in the 21st century?

BMJ 2015; 350 doi: http://dx.doi.org/10.1136/bmj.h1500 (Published 25 March 2015) Cite this as: BMJ 2015;350:h1500

Gregg Gonsalves, lecturer in law, Yale University, New Haven, CT, USA,
Diana Zuckerman, president, National Center for Health Research, Washington, DC, USA

Most physicians and patients assume that medications are proved safe and effective. This hasn't always been the case. The US Food and Drug Administration was born out of a series of 20th century tragedies: contamination of vaccines at the turn of that century; dangerous substances found in commonly sold medicines in the 1900s; deaths of over 100 children and adults in 1937 from a sulfa drug dissolved in diethylene glycol (antifreeze); extensive birth defects caused by thalidomide in the early 1960s; and infertility and deaths caused by the Dalkon Shield intrauterine device in the 1970s.1 Those tragedies all inspired laws that strengthened the criteria used to allow medical products on the market.

Subsequently, the first effective challenge to the FDA's growing authority came from an unlikely source: people with HIV/AIDS. In the 1980s, as people with AIDS faced certain death, they criticized the FDA's drug approval process as too slow and unresponsive to their needs. AIDS activists pressed for expedited drug approval and making experimental therapies widely available, demonstrating at FDA headquarters, and speaking out to FDA officials, the media, and Congress. They were remarkably successful, helping shape FDA reforms, including pathways for accelerated drug approval and expanded access programs for experimental medicines.

AIDS activists quickly learnt, however, that speedier approval and wider access had risks as well as benefits. They had assumed that any drug would be better than nothing, and that new drugs would be better than old ones, so they were greatly disappointed when the first generation of antiretroviral agents were less effective than expected. In fact, research did not confirm long term clinical benefit of these medicines; conflicting trial results and inconclusive studies piled up in the early 1990s. The activists realised that access alone does not necessarily provide answers, which now were in short supply.2 Much of this debate, however, became moot after a new generation of AIDS drugs, protease inhibitors, were used in combination with the older medicines. These new combinations had transformative clinical benefits, with dramatic reductions in AIDS related morbidity and mortality, raising patients from their deathbeds in what was called the Lazarus effect.3

The arrival of the AIDS epidemic in the US coincided with conservative presidential leadership and a growing conservatism among Congressional Republicans. Together, they sought to limit the size of the federal government and the scope of its powers. Although they had far different politics, AIDS activists had helped grease the wheels for a deregulatory agenda at the FDA. Starting in the early 1990s, a series of initiatives supported by conservative think tanks and drug industry lobbyists sought to further weaken the FDA's authority and mandate, often invoking the legacy of AIDS activists and the rights of patients. AIDS activists balked at the appropriation of their work for these purposes, and in another unexpected turn of events, now defended the agency. But this time their protests went unheeded.4

In the 1990s, Congress began to gradually erode the standards used for drug approval and the safeguards for patients: reducing the number of studies required to get new drugs on the market from at least two to one and reducing restrictions on the advertising and promotion of medical products. With AIDS, the FDA had shown it could expedite drug approval and access to experimental agents without new legislation, and many questioned the need for these new legislative initiatives.5

Despite numerous changes in White House and Congressional leadership, the 21st century has seen a steady escalation of legislation chipping away at the FDA. In response to legislative and political pressure, the FDA has offered numerous concessions to industry and its lobbyists. It now offers four pathways to speed the approval process for many drugs and biologics6 as well as an easier approval pathway for drugs for orphan diseases (those affecting fewer than 200,000 patients in the US).7 Though all drugs are supposed to meet "appropriate standards" for safety and effectiveness, the standards for most drugs approved through expedited pathways are clearly lower, with smaller and shorter term studies than are otherwise required. For example, in 2008, an average of about 100 patients were tested with new drugs that were approved through expedited pathways, compared with almost 600 for standard approvals.8 As a result, patients relied on drugs for which safety and effectiveness were not always confirmed when they were first on the market. Instead of requiring clear proof of safety or effectiveness before approval, most evidence is not required until afterwards. Sadly, "required" postmarketing studies are often delayed for years,9 and when problems are discovered, corrective action doesn't happen swiftly. It takes on average 11 years after approval for the FDA to institute new black box warnings, rescind approval, or require new risk information or contraindications be made public.8

Medical devices are subject to even weaker approval criteria, with only 1% of devices reviewed through a process that requires clinical trials.10 Most of the thousands of medical devices not subject to clinical trials every year do not even get "approved" by the FDA, but are rather "cleared" for market—90% of them within 90 days.11 Nevertheless, the FDA has responded to political pressure by proposing a new expedited pathway for devices.12, 13 Now, Congress is proposing new legislation to further speed the drug approval process while further weakening the standards for safety and efficacy. It's a trade-off with potentially deadly consequences. The 21st Century Cures draft legislation released by Republicans on the House health committee in January 2015 is sweeping and would jettison the phase III testing requirements for new drugs and largely dismantle the key components of the drug approval process in place since the thalidomide tragedy.14 Unsurprisingly, its proponents say the reforms are needed to meet patients' needs. But patients need knowledge—answers about the drugs they put in their bodies—not just access.

If passed, this bill and other 2015 legislative proposals will radically alter the nature of drug, device, and biologics approval in the US, roll back patient safeguards, and leave an FDA that looks more like the one that existed in the mid-20th century, not one worthy of the 21st.

References at http://www.bmj.com/content/350/bmj.h1500

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Volume 93, Number 3, March 2015, 133-208
http://www.who.int/bulletin/volumes/93/3/en/
[Reviewed earlier]

**Clinical Infectious Diseases** (CID)
Volume 60 Issue 8 April 15, 2015
http://cid.oxfordjournals.org/content/current
[New issue; No relevant content]

**Clinical Therapeutics**
February 2015 Volume 37, Issue 2, p243-480
http://www.clinicaltherapeutics.com/current
[Reviewed earlier]

**Complexity**
March/April 2015 Volume 20, Issue 4 Pages C1–C1, 1–80
http://onlinelibrary.wiley.com/doi/10.1002/cplx.v20.4/issuetoc
[Reviewed earlier]

**Conflict and Health**
[Accessed 28 March 2015]
http://www.conflictandhealth.com/
[No new relevant content]

**Contemporary Clinical Trials**
Volume 42, In Progress (May 2015)
http://www.sciencedirect.com/science/journal/15517144/42
[Reviewed earlier]

**Cost Effectiveness and Resource Allocation**
http://www.resource-allocation.com/
(Accessed 28 March 2015)
[No new relevant content]

**Current Opinion in Infectious Diseases**
April 2015 - Volume 28 - Issue 2 pp: v-v,117-198
http://journals.lww.com/co-infectiousdiseases/pages/currenttoc.aspx
[Reviewed earlier]

**Developing World Bioethics**
April 2015 Volume 15, Issue 1 Pages ii–iii, 1–57
http://onlinelibrary.wiley.com/doi/10.1111/dewb.2015.15.issue-1/issuetoc
[Reviewed earlier]

**Development in Practice**
Volume 25, Issue 2, 2015
http://www.tandfonline.com/toc/cdip20/current
[Reviewed earlier]

**Emerging Infectious Diseases**
Volume 21, Number 4—April 2015
http://wwwnc.cdc.gov/eid/
*Perspective*
## Reappearance of Chikungunya, Formerly Called Dengue, in the Americas
Scott B. Halstead
Author affiliation: Uniformed Services University of the Health Sciences, Bethesda, Maryland, USA
*Abstract*
After an absence of ≈200 years, chikungunya returned to the American tropics in 2013. The virus is maintained in a complex African zoonotic cycle but escapes into an urban cycle at 40- to 50-year intervals, causing global pandemics. In 1823, classical chikungunya, a viral exanthem in humans, occurred on Zanzibar, and in 1827, it arrived in the Caribbean and spread to North and South America. In Zanzibar, the disease was known as kidenga pepo, Swahili for a sudden cramp-like seizure caused by an evil spirit; in Cuba, it was known as dengue, a Spanish homonym of denga. During the eighteenth century, dengue (present-day chikungunya) was distinguished from breakbone fever (present-day dengue), another febrile exanthem. In the twentieth century, experiments resulted in the recovery and naming of present-day dengue viruses. In 1952, chikungunya virus was recovered during an outbreak in Tanzania, but by then, the virus had lost its original name to present-day dengue viruses.
*Synopsis*
## Evolution of Ebola Virus Disease from Exotic Infection to Global Health Priority, Liberia, Mid-2014
M. Allison Arwady✉ , Luke Bawo, Jennifer C. Hunter, Moses Massaquoi, Almea Matanock, Bernice Dahn, Patrick Ayscue, Tolbert Nyenswah, Joseph D. Forrester, Lisa E. Hensley, Benjamin Monroe, Randal J. Schoepp, Tai-Ho Chen, Kurt E. Schaecher, Thomas George, Edward Rouse, Ilana J. Schafer, Satish K. Pillai, and Kevin M. De Cock

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*Abstract*
Over the span of a few weeks during July and August 2014, events in West Africa changed perceptions of Ebola virus disease (EVD) from an exotic tropical disease to a priority for global health security. We describe observations during that time of a field team from the Centers for Disease Control and Prevention and personnel of the Liberian Ministry of Health and Social Welfare. We outline the early epidemiology of EVD within Liberia, including the practical limitations on surveillance and the effect on the country's health care system, such as infections among health care workers. During this time, priorities included strengthening EVD surveillance; establishing safe settings for EVD patient care (and considering alternative isolation and care models when Ebola Treatment Units were overwhelmed); improving infection control practices; establishing an incident management system; and working with Liberian airport authorities to implement EVD screening of departing passengers.

**Epidemics**

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http://www.sciencedirect.com/science/journal/17554365
[Reviewed earlier]

**Epidemiology and Infection**
Volume 143 - Issue 06 - April 2015
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**The European Journal of Public Health**
Volume 25, Issue 2, 01 April 2015
http://eurpub.oxfordjournals.org/content/25/suppl_1
*Commentaries*
**The Ebola crisis: perspectives from European Public Health**
Aura Timen , Marc Sprenger , Michael Edelstein , Jose Martin-Moreno , Martin McKee
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*Extract*

As of 26 November 2014, 15 935 cases of Ebola had been reported to the World Health Organization (WHO), of whom 5689 have died.1 It is widely believed that these figures are underreported and the actual number of cases and deaths is higher.2 Six cases and one death were reported outside West Africa.3 This unprecedented outbreak took professionals and policy makers by surprise as it occurred where it was not expected and developed on a scale that could not have been predicted. Or at least, that has been the accepted view. A consideration of the population affected and the weak health infrastructure of the countries most affected should have led to a recognition that, once a contagious disease such as Ebola developed in this setting, the scope for rapid spread was great, given the high population density and degree of connectivity among the people of the region.4 Unlike previous outbreaks that occurred in remote rural areas of central Africa,5 this developed in a densely populated area and, very quickly, outbreaks occurred in the capitals of the main affected countries (Guinea, Sierra Leone and Liberia). Rapid initial spread was facilitated by lack …

**Ebola's media outbreak: lessons for the future**
José Joaquín Mira , Susana Lorenzo , María Teresa Gea , Jesús Aranaz , Carlos Aibar
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*Extract*

On 8 August 2014, the World Health Organization (WHO's) Emergency Committee declared the Ebola virus disease (EVD or 'Ebola') outbreak a Public Health Emergency of International Concern. On 6 October 2014, the first case of EVD contracted in Europe was diagnosed.1 A healthcare worker was infected, after providing treatment to an Ebola patient in Spain. This secondary case, like those that occurred in Dallas, tested both the responsiveness of the healthcare system, and the attitudes and skills of the population, the health professionals and the media.

Virulence and infectivity are epidemiological characteristics that define the magnitude and significance of an infectious disease. EVD virulence is evident as shown by its lethality. The number of cases this time exceeded past outbreaks suggesting people that infectivity was greater.2 These factors coalesced to generate social alarm.

Unlike EVD, transmitted by direct contact with an infected patient or contaminated material, virus fear can spread in…

**Immigrants' health and health inequality by type of integration policies in European countries**

Davide Malmusi

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*Abstract*

Background: Recent efforts to characterize integration policy towards immigrants and to compare immigrants' health across countries have rarely been combined so far. This study explores the relationship of country-level integration policy with immigrants' health status in Europe.

Methods: Cross-sectional study with data from the 2011 European Union Survey on Income and Living Conditions. Fourteen countries were grouped according to a typology of integration policies based on the Migrant Integration Policy Index: 'multicultural' (highest scores: UK, Italy, Spain, Netherlands, Sweden, Belgium, Portugal, Norway, Finland), 'exclusionist' (lowest scores: Austria, Denmark) and 'assimilationist' (high or low depending on the dimension: France, Switzerland, Luxembourg). People born in the country (natives, n = 177 300) or outside the European Union with >10 years of residence (immigrants, n = 7088) were included. Prevalence ratios (PR) of fair/poor self-rated health between immigrants in each country cluster, and for immigrants versus natives within each, were computed adjusting by age, education, occupation and socio-economic conditions.

Results: Compared with multicultural countries, immigrants report worse health in exclusionist countries (age-adjusted PR, 95% CI: men 1.78, 1.49–2.12; women 1.58, 1.37–1.82; fully adjusted, men 1.78, 1.50–2.11; women 1.47, 1.26–1.70) and assimilationist countries (age-adjusted, men 1.21, 1.03–1.41; women 1.21, 1.06–1.39; fully adjusted, men 1.19, 1.02–1.40; women 1.22, 1.07–1.40). Health inequalities between immigrants and natives were also highest in exclusionist countries, where they persisted even after adjusting for differences in socio-economic situation.

Conclusion: Immigrants in 'exclusionist' countries experience poorer socio-economic and health outcomes. Future studies should confirm whether and how integration policy models could make a difference on migrants' health.

**Eurosurveillance**

Volume 20, Issue 12, 26 March 2015

http://www.eurosurveillance.org/Public/Articles/Archives.aspx?PublicationId=11678

***Editorials***

**The tail of the epidemic and the challenge of tracing the very last Ebola case**

by K Kaasik-Aaslav, D Coulombier

***Rapid communications***

**Ebola response missions: To go or not to go? Cross-sectional study on the motivation of European public health experts, December 2014**

by U Rexroth, M Diercke, E Peron, C Winter, M an der Heiden, A Gilsdorf

**Australian Hajj pilgrims' knowledge, attitude and perception about Ebola, November 2014 to February 2015**

by AS Alqahtani, KE Wiley, HW Willaby, NF BinDhim, M Tashani, AE Heywood, R Booy, H Rashid

***Research articles***

**Evaluation of a point-of-care blood test for identification of Ebola virus disease at Ebola holding units, Western Area, Sierra Leone, January to February 2015**
by NF Walker, CS Brown, D Youkee, P Baker, N Williams, A Kalawa, K Russell, AF Samba, N Bentley, F Koroma, MB King, BE Parker, M Thompson, T Boyles, B Healey, B Kargbo, D Bash-Taqi, AJ Simpson, A Kamara, TB Kamara, M Lado, O Johnson, T Brooks
**Wild bird surveillance around outbreaks of highly pathogenic avian influenza A(H5N8) virus in the Netherlands, 2014, within the context of global flyways**
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by C Fähnrich, K Denecke, OO Adeoye, J Benzler, H Claus, G Kirchner, S Mall, R Richter, MP Schapranow, N Schwarz, D Tom-Aba, M Uflacker, G Poggensee, G Krause

**Global Health: Science and Practice (GHSP)**
March 2015 | Volume 3 | Issue 1
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Volume 11, Issue 1, 2015
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*Special issue: Digital methods in epidemiology*

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**JAMA**
March 24/31, 2015, Vol 313, No. 12
http://jama.jamanetwork.com/issue.aspx
*Editorial* | March 24/31, 2015
**Emergency Treatment for Exposure to Ebola Virus: The Need to Fast-track Promising Vaccines** FREE
Thomas W. Geisbert, PhD1,2
[+] Author Affiliations
JAMA. 2015;313(12):1221-1222. doi:10.1001/jama.2015.2057.
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Ebola virus is among the most deadly pathogens, with case fatality rates of up to 90%.1 Ebola virus is categorized as a tier 1 pathogen by the US government because of its potential for deliberate misuse with significant potential for mass casualties. The current outbreak of Ebola virus in West Africa with more than 23 000 cases and 9000 deaths2 also demonstrates the long-underestimated public health threat that Ebola virus poses as a natural human pathogen. There are no licensed vaccines or postexposure treatments for combating Ebola virus. However, substantial progress has been made in developing vaccines and antivirals that can protect laboratory animals against lethal disease.1,3 Advancing these interventions for human use is a matter of utmost urgency.

In this issue of JAMA, Lai et al4 report the use of a first-generation recombinant vesicular stomatitis virus–based Ebola vaccine (VSVΔG-ZEBOV)5 to treat a physician who experienced a needlestick in an Ebola treatment unit in Sierra Leone during the current Ebola virus outbreak. A single dose of the VSVΔG-ZEBOV vaccine was administered approximately 43 hours after the potential exposure. The patient experienced a transient febrile syndrome after vaccination. Importantly, no evidence of Ebola virus infection was detected, and the vaccine elicited strong innate and Ebola virus–specific adaptive immune responses. Most significantly, the vaccine, which expresses the surface glycoprotein of Ebola virus, was able to induce an IgG antibody response against the Ebola virus glycoprotein at a level that has been associated with protection of nonhuman primates.5

It is difficult to draw any definitive conclusions from a single case report. The inability to detect evidence of Ebola virus infection most likely is because there was not an actual exposure;

however, it cannot be completely ruled out that the intervention was effective in controlling Ebola virus replication. Even though this patient experienced some adverse events after vaccination, the patient reported having traveler's diarrhea prior to receiving the VSVΔG-ZEBOV vaccine; therefore, it is also not possible to draw any strong conclusions regarding any adverse events from this case in regard to the safety of the vaccine. This is the second time that the VSVΔG-ZEBOV vaccine has been used to treat a potential exposure to Ebola virus. The initial use occurred in 2009 for a laboratory worker in Germany[6] and also involved a needlestick injury. The results of that incident were nearly identical; however, the severity of adverse events following vaccination was less notable in the German case compared with the patient in the case report by Lai et al.[4]

The 2 incidents involving the use of the VSVΔG-ZEBOV vaccine for the treatment of high-risk Ebola virus exposures further reinforce the need for public health approaches that prevent and control outbreaks. Efforts to develop effective vaccines and treatments against Ebola virus began soon after its discovery in 1976. However, advances were slow until the decade of the 2000s when at least 10 different preventive vaccines were developed that conferred complete protection in the criterion standard nonhuman primate models.[1] Postexposure treatments and therapies that can protect nonhuman primates against Ebola virus have been much more difficult to develop.

Similar to the rabies vaccine, the VSVΔG-ZEBOV vaccine can be used both as a conventional preventive vaccine and as a postexposure treatment. When used as a treatment, the VSVΔG-ZEBOV vaccine protected 50% of nonhuman primates against lethal Ebola virus (Zaire species) infection when given shortly after exposure.[7]

Only 2 potential therapies, ZMapp[8] and TKM-Ebola,[9] have been shown to completely protect 100% of nonhuman primates from a lethal Ebola virus (Zaire species) infection when administered after exposure. Both drugs have been administered under compassionate use during the current outbreak to treat a number of patients repatriated to Europe and the United States. Even though these patients have had very high survival rates, the role of ZMapp and TKM-Ebola in the outcome is unknown because in many cases they received multiple types of experimental therapies, including convalescent serum, and also likely benefited from the advanced supportive medical care in specialized facilities. Other treatments such as brincidofovir and favipiravir also have been used to treat patients infected with Ebola virus during the current outbreak; however, their benefit is even more difficult to measure because neither treatment has been associated with strong protection of nonhuman primates against Ebola virus.

An important point noted in the report by Lai et al[4] is that the patient declined other experimental drugs in lieu of the VSVΔG-ZEBOV vaccine. This also raises issues regarding patient consent and the use of experimental therapies. This is an important consideration because ultimately the patient or a representative of the patient makes the decision and should be informed of all options, available data, and risks. It is unknown what other drugs were offered to the patient in the report by Lai et al.[4] Shortages of ZMapp during the current Ebola virus outbreak have been reported, and it is clear that even though promising antivirals have been developed, they have yet to be produced at levels sufficient for the large numbers of cases associated with an outbreak of this magnitude.

The need for antiviral treatments for Ebola virus infection is unquestionable, and stockpiles of ZMapp and TKM-Ebola are critically needed. However, the most effective way to prevent and control outbreaks and to protect high-risk personnel, including medical staff and laboratory workers, is through the use of preventive vaccines along with use of appropriate personal protective equipment. Historically, there has been a small global market for developing an Ebola virus vaccine and there was no financial interest for large pharmaceutical companies to become involved. The current epidemic has spurred substantial scientific activity to develop vaccines.

Companies, including GlaxoSmithKline, Merck, and Johnson & Johnson, are attempting to fast-track the licensure of several Ebola virus vaccines. Phase 1 trials have been initiated, and studies at some test sites have been completed for the GlaxoSmithKline chimpanzee adenovirus-based Ebola virus vaccine and the first-generation Merck-acquired VSVΔG-ZEBOV vaccine. It is encouraging that these large pharmaceutical companies have joined the campaign to address Ebola virus, but small biotech firms also have made important contributions.

Moreover, much of the progress during the last decade is a direct result of basic research and early-stage product development funded by the US government, including the Department of Defense, the National Institute of Allergy and Infectious Diseases, and the National Institutes of Health, in particular the Partnerships for Biodefense Program, which has been instrumental in the development of many of the lead candidate interventions.

Reports to date suggest that some adverse events could be associated with the VSVΔG-ZEBOV vaccine, which is not unusual because this vaccine uses a replication-competent virus. Profectus Biosciences has developed a novel next-generation vesicular stomatitis virus–based Ebola virus vaccine that has been engineered for enhanced safety and has been shown to confer complete protection of nonhuman primates against Ebola virus.[10] Phase 1 trials are also expected soon with the newer Profectus vaccine and it may prove to be safer than the first-generation vaccine candidate.

In addition to Profectus, other companies, including Novavax, are moving forward with Ebola virus vaccine candidates. Having a variety of competing vaccines should mitigate risk and ensure that in the near future an effective licensed Ebola virus vaccine will be available for human use. Even though vaccination of large populations in endemic areas in Africa may not be practical, vaccination of medical staff and first responders will be of value, particularly because medical staff have been at high risk for infection in the current Ebola virus outbreak. In addition, ring vaccination strategies can be valuable in controlling outbreaks, particularly if rapid-acting single-injection vaccines, such as the vesicular stomatitis virus–based Ebola virus vaccines, are available.

Although it is not possible to know with absolute certainty whether the first-generation VSVΔG-ZEBOV vaccine used to treat the potential high-risk exposure had any influence on survival of the exposed patient in the report by Lai et al,[4] this incident serves as an example of how important it is to have safe and effective countermeasures available in sufficient quantities that can be rapidly deployed for emergency use for both medical workers and affected populations.

*Preliminary Communication*
**Emergency Postexposure Vaccination With Vesicular Stomatitis Virus–Vectored Ebola Vaccine After Needlestick** FREE

Lilin Lai, MD; Richard Davey, MD; Allison Beck, MPAS; Yongxian Xu, MD; Anthony F. Suffredini, MD; Tara Palmore, MD; Sarah Kabbani, MD; Susan Rogers, RPh; Gary Kobinger, PhD; Judie Alimonti, PhD; Charles J. Link Jr, MD; Lewis Rubinson, MD; Ute Ströher, PhD; Mark Wolcott, PhD; William Dorman, BS; Timothy M. Uyeki, MD; Heinz Feldmann, MD, PhD; H. Clifford Lane, MD; Mark J. Mulligan, MD
Includes: Supplemental Content, Author Video Interviews, JAMA Report Video, Author Interview

**JAMA Pediatrics**
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**Journal of Community Health**
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**Journal of Global Ethics**
Volume 10, Issue 3, 2014
http://www.tandfonline.com/toc/rjge20/.U2V-Elf4L0I#.VAJEj2N4WF8
*Tenth Anniversary Forum: The Future of Global Ethics*
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http://www.jgid.org/currentissue.asp?sabs=n
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**Journal of Immigrant and Minority Health**
Volume 17, Issue 2, April 2015

http://link.springer.com/journal/10903/17/2/page/1
***Special Focus: Food, Diet, and Nutrition***
- *39 articles covering these themes in different ethic and nationals contexts*

**Journal of Immigrant & Refugee Studies**
Volume 13, Issue 1, 2015
http://www.tandfonline.com/toc/wimm20/current#.VQS0KOFnBhW
[Reviewed earlier]

**Journal of Infectious Diseases**
Volume 211 Issue 8 April 15, 2015
http://jid.oxfordjournals.org/content/current
**Weighing the Risk of Drug Resistance With the Benefits of HIV Preexposure Prophylaxis**
Robert M. Grant1,2,3 and Teri Liegler2
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(See the major article by Lehman et al on pages 1211–8.)
*Extract*
The threat of drug resistance deserves careful attention from clinicians and public health officials advocating antiretroviral use as a way to control the human immunodeficiency virus (HIV) epidemic. Such antiretroviral use includes early treatment and preexposure prophylaxis (PrEP) and postexposure prophylaxis (PEP). Concerns about drug resistance were raised before rolling out widespread antiretroviral therapy in Africa, based on the assumption that adherence to therapy would be poor and drug resistance would become prevalent. Defying expectations, the benefits of antiretroviral therapy for improving health, averting death, and preventing transmission were subsequently proven to outweigh the risks of drug resistance, and adherence to therapy in African populations is often outstanding [1]…
**Large-scale Convalescent Blood and Plasma Transfusion Therapy for Ebola Virus Disease**
Robert L. Colebunders1,2 and Robert O. Cannon2
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1Department of Clinical Sciences, Institute of Tropical Medicine
2Epidemiology and Social Medicine, University of Antwerp, Belgium
(See the major article by Gutfraind and Meyers on pages 1262–7.)
*Extract*
An effective therapy for Ebola virus disease (EVD) not only will lower the case-fatality rate but also will provide an incentive for patients to seek treatment, thereby enhancing primary and secondary prevention efforts. While several experimental drugs are being considered, the World Health Organization (WHO) has prioritized Ebola convalescent whole blood (CWB) and convalescent plasma (CP) transfusion for evaluation because this can be done relatively quickly and, if proven to be safe and effective, could be implemented without delay [1]. The use of blood from recuperated individuals has a long history of use for treatment of other serious infectious diseases and, with appropriate precautions, is generally considered safe [2].

However, the WHO has indicated that this intervention must be considered as experimental for EVD and, therefore, that initial studies should be conducted within a clinical trial framework [1].

In this issue of The Journal of Infectious Diseases, Gutfraind and Meyers [3] extend an Ebola virus transmission model published by the Centers for Disease Control and Prevention (CDC) [4] to include large-scale hospital-based convalescent donations and transfusions. Using epidemiological estimates for Ebola in Liberia and assuming that convalescent transfusions reduce the case-fatality rate to 12.5% [5], they calculated that, under a 30% hospitalization rate, CWB and CP transfusions are estimated to reduce the number of deaths in Liberia by 65 (0.37%; 95% confidence interval [CI], .07%–2.6%) and 151 (0.9%; 95% CI, .21%–11%), respectively. They conclude that transfusion therapy for Ebola is a low-cost measure that can potentially save many lives in Liberia but will not measurably influence incidence.

There are, however, at least 8 major issues to consider in determining the advisability of implementing a large-scale CWB…

**The Journal of Law, Medicine & Ethics**
Winter 2014 Volume 42, Issue 4 Pages 408–602
http://onlinelibrary.wiley.com/doi/10.1111/jlme.2014.42.issue-4/issuetoc
*Special Issue: SYMPOSIUM: The Buying and Selling of Health Care*
[Reviewed earlier]

**Journal of Medical Ethics**
April 2015, Volume 41, Issue 4
http://jme.bmj.com/content/current
*Research ethics*
*Paper*
**Results of a self-assessment tool to assess the operational characteristics of research ethics committees in low- and middle-income countries**
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7Johns Hopkins School of Medicine, Baltimore, Maryland, USA
Published Online First 19 April 2014
*Abstract*
Purpose
Many research ethics committees (RECs) have been established in low- and middle-income countries (LMICs) in response to increased research in these countries. How well these RECs are functioning remains largely unknown. Our objective was to assess the usefulness of a self-assessment tool in obtaining benchmarking data on the extent to which RECs are in compliance with recognised international standards.
Methods

REC chairs from several LMICs (Egypt, South Africa and India) were asked to complete an online self-assessment tool for RECs with a maximum score of 200. Individual responses were collected anonymously.
Results
The aggregate mean score was 137.4±35.8 (~70% of maximum score); mean scores were significantly associated with the presence of a budget ($p<0.001$), but not with duration of existence, frequency of meetings, or the presence of national guidelines. As a group, RECs achieved more than 80% of the maximum score for the following domains: submission processes and documents received, recording of meeting minutes, criteria for ethical review and criteria for informed consent. RECs achieved less than 80% of the maximum score for the following domains: institutional commitment, policies and procedures of the REC, membership composition and training, policies and procedures for protocol review, elements of a decision letter and criteria for continuing review.
Conclusions
This study highlights areas where RECs from LMICs can improve to be in compliance with recommended international standards for RECs. The self-assessment tool provides valuable benchmarking data for RECs and can serve as a quality improvement method to help RECs enhance their operations.

**Journal of Medical Internet Research**
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http://www.jmir.org/2015/3
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**Journal of Medical Microbiology**
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**Journal of Virology**
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http://jvi.asm.org/content/current
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**The Lancet**
Mar 28, 2015 Volume 385 Number 9974 p1151-1260
http://www.thelancet.com/journals/lancet/issue/current
*Editorial*
**Dementia: turning fine aspirations into measurable progress**
The Lancet
*Summary*
"I look young, but I am actually quite old", pronounced WHO Director-General Margaret Chan at the first Ministerial Conference on Global Action Against Dementia, hosted by WHO, the Organisation for Economic Co-operation and Development (OECD), and the UK Department of Health in Geneva on March 16–17. Dr Chan continued, with great clarity and sincerity, to describe her own desire to grow old gracefully and with dignity, contrasting her own aspirations with the plight of 47 million people worldwide who struggle to cope with the debilitating effect of dementia, a disorder that is expected to double in prevalence over the next two decades, and that comes with an estimated health bill worldwide in excess of US$600 billion.
*Editorial*
**1 year on—lessons from the Ebola outbreak for WHO**
*The Lancet*
*Summary*
This week has seen what is likely to be the beginning of an onslaught of criticism levelled against WHO for its handling of the Ebola outbreak in west Africa. First, ahead of the 1-year anniversary of the outbreak's start, an article by the Associated Press (AP) reported that WHO deliberately delayed declaring the Ebola epidemic as an emergency in early June, 2014, waiting instead until Aug 8 to finally make the announcement. AP obtained internal emails and documents suggesting that senior WHO officials were not only told of the desperate situation, but also received anguished pleas for help. Instead of taking urgent and decisive action, the article said WHO decided that managing the political repercussions in countries would outweigh the benefits that declaring an emergency would bring. It "could be seen as a hostile act", said one memo. Downplaying the epidemic may have cost lives, said AP. In response, WHO insisted that the spread of the virus was unprecedented, and the lack of resources and intelligence on the ground hindered its ability to act.

Second, Médecins Sans Frontières (MSF), who did more than any other organisation to bring the world's attention to Ebola and who led the operational response against the outbreak, published their searingly critical report—Pushed to the limit and beyond—this week. Despite

early warnings about the severity of the outbreak and urgent calls for help, MSF were ignored by governments and WHO. They dubbed the response a "global coalition of inaction". MSF described the horrors of having to turn patients away because their health centres and staff were simply overwhelmed.

This year will see at least three further international, independent investigations into WHO's conduct in the Ebola response. Regrettably, it is likely that WHO's reputation is going to suffer more wounds in the coming months. The Lancet's focus will be to try and draw larger lessons from the Ebola outbreak. In early May, we will be publishing a collection of essays on global health security, together with one of the first analyses of the deeper consequences of Ebola.

*Series*

**Health-system reform and universal health coverage in Latin America**

Prof Rifat Atun, FRCP, Prof Luiz Odorico Monteiro de Andrade, PhD, Gisele Almeida, PhD, Daniel Cotlear, DPhil, T Dmytraczenko, PhD, Patricia Frenz, PhD, Prof Patrícia Garcia, PhD, Octavio Gómez-Dantés, MPH, Felicia M Knaul, PhD, Prof Carles Muntaner, PhD, Juliana Braga de Paula, MSc, Felix Rígoli, MD, Prof Pastor Castell-Florit Serrate, PhD, Adam Wagstaff, PhD

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*Summary*

Starting in the late 1980s, many Latin American countries began social sector reforms to alleviate poverty, reduce socioeconomic inequalities, improve health outcomes, and provide financial risk protection. In particular, starting in the 1990s, reforms aimed at strengthening health systems to reduce inequalities in health access and outcomes focused on expansion of universal health coverage, especially for poor citizens. In Latin America, health-system reforms have produced a distinct approach to universal health coverage, underpinned by the principles of equity, solidarity, and collective action to overcome social inequalities. In most of the countries studied, government financing enabled the introduction of supply-side interventions to expand insurance coverage for uninsured citizens—with defined and enlarged benefits packages—and to scale up delivery of health services. Countries such as Brazil and Cuba introduced tax-financed universal health systems. These changes were combined with demand-side interventions aimed at alleviating poverty (targeting many social determinants of health) and improving access of the most disadvantaged populations. Hence, the distinguishing features of health-system strengthening for universal health coverage and lessons from the Latin American experience are relevant for countries advancing universal health coverage.

*Series*

**Overcoming social segregation in health care in Latin America**

Dr Daniel Cotlear, DPhil, Octavio Gómez-Dantés, MD, Felicia Knaul, PhD, Prof Rifat Atun, FRCP, Ivana C H C Barreto, PhD, Prof Oscar Cetrángolo, MPhil, Prof Marcos Cueto, PhD, Prof Pedro Francke, MSc, Patricia Frenz, MD, Ramiro Guerrero, MSc, Prof Rafael Lozano, MD, Robert Marten, MPH, Prof Rocío Sáenz, MD

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*Summary*

Latin America continues to segregate different social groups into separate health-system segments, including two separate public sector blocks: a well resourced social security for salaried workers and their families and a Ministry of Health serving poor and vulnerable people with low standards of quality and needing a frequently impoverishing payment at point of service. This segregation shows Latin America's longstanding economic and social inequality, cemented by an economic framework that predicted that economic growth would lead to rapid

formalisation of the economy. Today, the institutional setup that organises the social segregation in health care is perceived, despite improved life expectancy and other advances, as a barrier to fulfilling the right to health, embodied in the legislation of many Latin American countries. This Series paper outlines four phases in the history of Latin American countries that explain the roots of segmentation in health care and describe three paths taken by countries seeking to overcome it: unification of the funds used to finance both social security and Ministry of Health services (one public payer); free choice of provider or insurer; and expansion of services to poor people and the non-salaried population by making explicit the health-care benefits to which all citizens are entitled.

**The Lancet Global Health**
Apr 2015 Volume 3 Number 4 e178-e239
http://www.thelancet.com/journals/langlo/issue/current
[Reviewed earlier]

**The Lancet Infectious Diseases**
Apr 2015 Volume 15 Number 4 p361-486
http://www.thelancet.com/journals/laninf/issue/current
*Editorial*
**Comprehensive approach to better malaria control**
The Lancet Infectious Diseases
DOI: http://dx.doi.org/10.1016/S1473-3099(15)70113-1
Malaria is a complex and deadly disease but is also treatable and preventable. In 2000, an estimated 350 million to 500 million malaria cases led to the death of 1 million people, mostly African children. Since then, the establishment of the Millennium Development Goals for reducing global malaria incidence and mortality, have driven greater awareness and progress towards malaria control, and more than 4 million lives have been saved.

With the aim of accelerating progress toward malaria elimination, the Roll Back Malaria (RBM) partnership has coordinated the development of the Global Malaria Action Plan 2 (GMAP2), Towards a Malaria-Free World: A Global Case for Investment and Action 2016–2030—the second generation of an RBM consensus document that provides a practical, multisectoral, action-oriented guide toward better control of malaria transmission. The draft of the English version of the document was under review until March 18, allowing interested partners and individuals to contribute. Representatives from more than 90 countries participated in the development of the consensus document. The approach is extremely collaborative and involves academia, the private sector, research bodies, and governments. The consensus document will be accompanied by a second document, the Global Technical Strategy (GTS) for Malaria 2016–2030, which will be presented to the World Health Assembly in May, 2015.

The five chapters of GMAP2 provide a comprehensive overview of how resources should be mobilised. Its strategy sets out how to reduce malaria case incidence globally by 90% in 2030 compared with 2015, and how to eliminate malaria from at least 35 countries by 2030 in which malaria was transmitted in 2015. Crucial to reaching global malaria targets is adequate funding, and GMAP2 estimates that US$8 billion of investment will be needed annually between 2026 and 2030 to reach its goals, as well as an additional annual $673 million to fund malaria

research and development. If achieved, this will lead to 12 million lives saved and 2·9 billion cases averted. The report highlights that if the 2030 targets are not met, the costs will be catastrophic. If the coverage of malaria interventions were to revert to the 2007 level, there would be an additional 2 billion malaria cases and 4·9 million deaths, leading to $5·8 billion in direct costs to health systems and households. Returns on investment in malaria control, according to the report, will be higher than expected: $4·6 trillion in economic benefits in 2030.

Small investments can bring major returns. The report highlights the case of Neema Gunda, a widow and head of a household in rural Tanzania—thanks to the bednets and instruction on their correct use she and her family get sick less often. Although small investments can make enormous differences to individual lives, substantial investments will have worldwide benefits for billions of people. But to have the greatest effect worldwide, investments will need to be channelled into locally tailored interventions sensitive to the needs of specific nations, regions, and villages.

The report also focuses on how environmental, social, cultural, and biological factors are all interconnected elements in the control of the disease. Biological factors, such as the growing problem of resistance to antimalarial drugs and insecticides, represent one of the biggest threats to reaching the 2030 goal. Agriculture, education, housing, water and sanitation, and tourism are also all important, as well as the interfaces between land use, climate change, and environmental policy. Stakeholders in all these areas need to intensify their engagement.

Despite progress, as of today, about 3 billion people are at risk in 109 countries. Ongoing advances in the fight against malaria will contribute to the realisation of the Sustainable Development Goals (SDG), and progress towards the SDGs will support the continued reduction and elimination of malaria. Tackling malaria is essential if sustainable changes are to be made for people living in areas where it is endemic. For example, it creates healthier, more productive workforces which can help attract trade and commerce, it makes a substantial contribution to improvements in child health, and protects households from lost earnings and the costs of seeking care. The SDGs provide an unprecedented opportunity to widen the circle of engagement and intensify multisectoral action and cross-country collaboration to defeat malaria. The comprehensive approach of GMAP2 will help ensure this opportunity will be taken and will guide us, we hope, towards a brighter future of malaria control.

*Comment*

**Applied public health research on the frontline**

Arto A Palmu, Helena Käyhty

Published Online: 17 February 2015
DOI: http://dx.doi.org/10.1016/S1473-3099(15)70052-6

*Summary*

Prevention of pneumococcal disease in resource-poor countries, including many Asian countries, is desperately needed. The implementation of pneumococcal conjugate vaccines (PCVs) has been slow due to scarce funding, but also because the burden of pneumococcal disease is poorly known. However, with the financial assistance of the GAVI Alliance, the introduction of PCVs has been accelerated.1

*Comment*

**Rotavirus vaccines roll-out in resource-deprived regions**

Miguel L O'Ryan, Ralf Clemens

Published Online: 28 January 2015

Open Access
DOI: http://dx.doi.org/10.1016/S1473-3099(14)71089-8
Tables and Figures
References

Rotaviruses cause 30–50% of severe diarrhoea cases in children younger than 5 years, leading to about 450 000 deaths every year.[1] Infections during the first months of life are protective against symptomatic reinfections later on, setting the stage for vaccine development.[2], [3] The existence of four major genotypes—G1[P8], G2[P4], G3[P8], and G4[P8]—created a great challenge because in-vitro studies suggested that antibodies to a specific type neutralised only that type, raising the question of whether it would be necessary for a vaccine to include all common genotypes.

During the 1990s the first licensed vaccine, Rotashield (Wyeth Laboratories, Collegeville, PA, USA), which contained an attenuated simian and three simian–human reassortant strains of the virus, showed that 70–90% of cases of severe rotavirus disease could potentially be prevented in lower-middle-income and high-income countries with vaccination.[4] However, intestinal intussusception was induced in about one in 11 000 children who received the vaccine, leading to its withdrawal and posing a large challenge for new candidate vaccines because future trials needed to include 60 000 children to reasonably assure safety.[5], [6] Post-licensure studies of the second-generation vaccines Rotarix (GlaxoSmithKline, Brentford, UK), which contains a single human attenuated strain, and RotaTeq (Merck, Kenilworth, NJ, USA) based on five human-bovine reassortant strains, suggest an acceptable class effect risk for intestinal intussusception of somewhere between one in 20 000 and one in 100 000 individuals.[7] Importantly, both vaccines showed high efficacy (more than 80%) against severe rotavirus disease in prelicensure studies[5], [6] and against several predominating genotypes. As trials were progressively done in various regions worldwide, it became clear that protective efficacy for both vaccines was lower in resource-deprived countries than in high-income countries[8] and that efficacy might not be the same among serotypes and genotypes, especially against G2[P4].[5], [9]

First licensed in 2006, these vaccines have been progressively introduced worldwide and dozens of effectiveness trials, done mostly in high or middle-high income countries, have confirmed efficacy rates reported in prelicensure trials. A major unanswered question is how effective these vaccines will be in real-world scenarios in the poorest regions of the world (where diarrhoea mortality is at its highest) and in the presence of varied circulating types. Children might be infected in their first months of life in these regions (where a first infection is not as protective as in higher-income regions) such that children develop several severe episodes of rotavirus disease throughout their first years.[3], [10] Vaccine effectiveness could be substantially lower in these regions, and, thus, meticulous prospective studies are essential for policy decisions and for the potential design and assessment of new vaccine strategies.

In The Lancet Infectious Diseases, Naor Bar-Zeev and colleagues[11] report results of the second effectiveness study to be done in Africa (Blantyre, Malawi). In the first study, Michelle Groome and colleagues[12] showed 57% (95% CI 40–68) effectiveness against rotavirus diarrhoea that required a minimum of overnight hospital admission in children in South Africa younger than 2 years who were vaccinated at 6 and 14 weeks of life. Bar-Zeev and colleagues[11] report 64% (24–83) effectiveness for reduction of emergency room visits (compared with rotavirus test-negative controls) for rotavirus in children younger than 5 years (94% of samples tested from children younger than 2 years) using an accelerated 6 and 10 week of age schedule with the

monovalent human rotavirus vaccine. Early effect was documented with roughly 10% reductions every year in rotavirus detection rates in infants during their first and second years of age, and an overall rate reduction of near 15% after 2 years for all children younger than 5 years. Genotype G2[P4] was the most commonly detected (25% of samples tested), but the vaccine had a lower non-significant effectiveness point estimate of 53% (95% CI −28 to 83) for G2[P4] than it did for G1[P8] (82%, 42–95), strongly suggesting lower effectiveness against this genotype.

That data for vaccine effectiveness in Malawi are similar to, if not better than, those for other efficacy trials is good news and findings can probably be extrapolated to regions with similar socioeconomic conditions. Differential serotype and genotype effectiveness will have to be continuously monitored and the search for even better vaccines and strategies must continue. Although, the natural history of rotavirus infection and disease in low-resource regions[10] suggests that oral vaccines that mimic protection conferred by natural infections might have reached their maximum effectiveness, this figure is still substantial and vaccines could potentially prevent nearly 300 000 deaths of infants and children every year.

*Articles*

**Comparison of two-dose priming plus 9-month booster with a standard three-dose priming schedule for a ten-valent pneumococcal conjugate vaccine in Nepalese infants: a randomised, controlled, open-label, non-inferiority trial**

Mainga Hamaluba, Rama Kandasamy, Shyam R Upreti, Giri R Subedi, Shrijana Shrestha, Shiva Bhattarai, Meeru Gurung, Rahul Pradhan, Merryn Voysey, Santosh Gurung, Shachi Pradhan, Anushil K Thapa, Rakesh Maharjan, Usha Kiran, Simon A Kerridge, Jason Hinds, Fiona van der Klis, Matthew D Snape, David R Murdoch, Sarah Kelly, Dominic F Kelly, Neelam Adhikari, Stephen Thorson, Andrew J Pollard

**Effectiveness of a monovalent rotavirus vaccine in infants in Malawi after programmatic roll-out: an observational and case-control study**

Naor Bar-Zeev, Lester Kapanda, Jacqueline E Tate, Khuzwayo C Jere, Miren Iturriza-Gomara, Osamu Nakagomi, Charles Mwansambo, Anthony Costello, Umesh D Parashar, Robert S Heyderman, Neil French, Nigel A Cunliffe, for the VacSurv Consortium

*Open Access*

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Volume 19, Issue 4, April 2015

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[Reviewed earlier]

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[Reviewed earlier]

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March 2015 Vol 15 No 3
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[Reviewed earlier]

**New England Journal of Medicine**
March 26, 2015 Vol. 372 No. 13
http://www.nejm.org/toc/nejm/medical-journal
*Review Article*
**Chikungunya Virus and the Global Spread of a Mosquito-Borne Disease**
Scott C. Weaver, Ph.D., and Marc Lecuit, M.D., Ph.D.
N Engl J Med 2015; 372:1231-1239 March 26, 2015 DOI: 10.1056/NEJMra1406035
Chikungunya virus infection is a rapid-onset, febrile disease with intense asthenia, arthralgia, myalgia, headache, and rash. This mosquito-borne alphavirus has spread throughout the Caribbean and into much of Central America. Further spread in the Americas seems likely.
*Correspondence*
**Ebola Virus Disease among Children in West Africa**
N Engl J Med 2015; 372:1274-1277 March 26, 2015 DOI: 10.1056/NEJMc1415318
*To the Editor:*
The epidemic of Ebola virus disease (EVD) in West Africa has caused clinical illness and deaths among persons with reported ages ranging from less than 1 year to more than 100 years. Most published estimates of key epidemiologic parameters have been based on patients of all ages[1,2] and have thus been dominated by cases in which patients are 16 years of age or older, and as of January 5, 2015, these cases accounted for 79% of the confirmed and probable cases for which age has been reported.

Here we investigate the progression and outcome of EVD in confirmed and probable pediatric cases reported from Guinea, Liberia, and Sierra Leone, stratified according to age. The absolute and per capita case incidence of EVD among children younger than 16 years of age has been significantly and consistently lower than the incidence among adults in all three countries

(Figure 1A, 1B, and 1CFigure 1Age-Group–Specific Incidence of Ebola Virus Disease in West Africa, Incubation Period, Intervals from Onset to Death and Onset to Hospitalization, and Case Fatality Rate.). This pattern is similar to that observed in past EVD outbreaks.3,4 However, because the current epidemic is so large, it provides an opportunity to explore the ways in which epidemiologic and clinical parameters vary according to age. Although the age distribution of confirmed, probable, and suspected cases is similar in all three countries (Fig. S3 in the Supplementary Appendix, available with the full text of this letter at NEJM.org), the proportion of pediatric cases (those younger than 16 years of age) among all cases increased over the course of 2014 (Figure 1C, and Fig. S4 in the Supplementary Appendix).

The mean incubation period (the average time from infection until symptom onset) was shortest, on average, in the youngest children, with means ranging from 6.9 days (95% confidence interval [CI], 5.1 to 9.5) in 14 children younger than 1 year of age to 9.8 days (95% CI, 8.7 to 11.1) in 184 children 10 to 15 years of age (Figure 1D, and Table S1 and Fig. S5 in the Supplementary Appendix). Younger children also had shorter times from symptom onset to hospitalization and from symptom onset to death (Figure 1D, and Fig. S6 and S7 and Tables S2 and S3 in the Supplementary Appendix). There was no clear evidence that age affected the distribution of the intervals between symptom onset and hospital discharge, between hospitalization and death, between hospitalization and hospital discharge, or between symptom onset and onward transmission (Fig. S8 to S11 and Tables S4 to S7 in the Supplementary Appendix).

Almost all children with EVD who were younger than 1 year of age had fever (92%) before clinical presentation, and children younger than 16 years of age were more likely than adults to present with fever ($P<0.001$) (Table S8 and Fig. S13 in the Supplementary Appendix). Children were less likely than adults (i.e., persons 16 years of age or older) to report pain in the abdomen, chest, joints, or muscles, difficulty breathing or swallowing, and hiccups between symptom onset and clinical presentation ($P<0.001$); however, this finding may reflect the difficulty young children have in reporting such symptoms rather than a different symptom profile (Table S8 and Fig. S12 in the Supplementary Appendix). The case fatality rate (CFR) was lowest among children between 10 and 15 years of age and highest among those 4 years of age or younger (Figure 1E, and Fig. S14 and S15 and Table S9 in the Supplementary Appendix). The CFR for persons younger than 45 years of age (most of whom are 5 to 44 years of age) was lower than that among those 45 years of age or older (Figure 1E), a finding that is in line with that of an earlier report.5

The shorter incubation period in children, the relatively high risk of death among children younger than 5 years of age (as compared with older children), and the more rapid progression to death highlight the importance of including children among case contacts for follow-up, of examining children for early signs of disease during active case finding, and of explaining the risk of EVD to parents, guardians, and caregivers. All persons in whom EVD is suspected, but especially children, need the earliest possible referral for diagnostic testing, and children need age-appropriate treatment. The causes of the relatively rapid disease progression and relatively high CFR in the youngest children requires further investigation.

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*Editorial*
**Testing and Treating the Missing Millions with Tuberculosis**
Madhukar Pai, Puneet Dewan
Published: March 24, 2015
DOI: 10.1371/journal.pmed.1001805
[No abstract]
*Policy Forum*
**Strengthening the Detection of and Early Response to Public Health Emergencies: Lessons from the West African Ebola Epidemic**
Mark J. Siedner, Lawrence O. Gostin, Hilarie H. Cranmer, John D. Kraemer
Published: March 24, 2015
DOI: 10.1371/journal.pmed.1001804
*Summary Points*
:: The international response to the West African Ebola virus disease epidemic has exemplified the great potential of the global public health community. However, the protracted early response also revealed critical gaps, which likely resulted in exacerbation of the epidemic.
:: It is incumbent on international health partners to learn from missteps that occurred in the early stages of the epidemic and strengthen our public health capacity to better respond to future public health emergencies.
:: Strategies to consider include development of a more precise system to risk stratify geographic settings susceptible to disease outbreaks, reconsideration of the 2005 International Health Regulations Criteria to allow for earlier responses to localized epidemics before they reach epidemic proportions, increasing the flexibility of the World Health Organization director

general to characterize epidemics with more granularity, development of guidelines for best practices to promote partnership with local stakeholders and identify locally acceptable response strategies, and, most importantly, making good on international commitments to establish a fund for public health emergency preparedness and response.
:: The recent success of the global action to stem the Ebola virus disease epidemic is laudable but should not encourage complacency in our efforts to improve the global public health infrastructure.

**PLoS Neglected Tropical Diseases**
http://www.plosntds.org/
(Accessed 28 March 2015)
**Geographic Distribution and Mortality Risk Factors during the Cholera Outbreak in a Rural Region of Haiti, 2010-2011**
Anne-Laure Page, Iza Ciglenecki, Ernest Robert Jasmin, Laurence Desvignes, Francesco Grandesso, Jonathan Polonsky, Sarala Nicholas, Kathryn P. Alberti, Klaudia Porten, Francisco J. Luquero
Research Article | published 26 Mar 2015 | PLOS Neglected Tropical Diseases
10.1371/journal.pntd.0003605
*Abstract*
Background
In 2010 and 2011, Haiti was heavily affected by a large cholera outbreak that spread throughout the country. Although national health structure-based cholera surveillance was rapidly initiated, a substantial number of community cases might have been missed, particularly in remote areas. We conducted a community-based survey in a large rural, mountainous area across four districts of the Nord department including areas with good versus poor accessibility by road, and rapid versus delayed response to the outbreak to document the true cholera burden and assess geographic distribution and risk factors for cholera mortality.
Methodology/Principal Findings
A two-stage, household-based cluster survey was conducted in 138 clusters of 23 households in four districts of the Nord Department from April 22nd to May 13th 2011. A total of 3,187 households and 16,900 individuals were included in the survey, of whom 2,034 (12.0%) reported at least one episode of watery diarrhea since the beginning of the outbreak. The two more remote districts, Borgne and Pilate were most affected with attack rates up to 16.2%, and case fatality rates up to 15.2% as compared to the two more accessible districts. Care seeking was also less frequent in the more remote areas with as low as 61.6% of reported patients seeking care. Living in remote areas was found as a risk factor for mortality together with older age, greater severity of illness and not seeking care.
Conclusions/Significance
These results highlight important geographical disparities and demonstrate that the epidemic caused the highest burden both in terms of cases and deaths in the most remote areas, where up to 5% of the population may have died during the first months of the epidemic. Adapted strategies are needed to rapidly provide treatment as well as prevention measures in remote communities.
*Author Summary*
In October 2010, a large cholera outbreak was declared in Haiti and rapidly spread throughout the country, quickly overwhelming the existing health system. Specialized treatment structures were opened rapidly, generally in cities or large villages, and decentralized treatment units or

rehydration points were gradually opened later on. To gain insight into the true burden of the cholera outbreak in the community and on potential geographical differences due to accessibility, we conducted a survey in April–May 2011 in a large rural area across four mountainous districts in the Nord department. We interviewed 3,187 households, corresponding to 16,900 individuals, of whom 2,034 (12%) had had diarrhea, probably cholera, since the beginning of the outbreak. The two most remote districts showed higher proportions of population affected by the disease, up to 16.2%, and higher proportions of deaths among patients with probable cholera, up to 15.2%, than the two districts with better accessibility. Remote populations, older patients, severe cases and those not seeking care were at increased risk of dying of the disease. These results show the very high burden of the cholera outbreak in remote areas, emphasizing the need to develop strategies to rapidly provide treatment and prevention measures in remote communities.

**PLoS One**
[Accessed 28 March 2015]
http://www.plosone.org/
**Homologous and heterologous protection of nonhuman primates by ebola and Sudan virus-like particles**
Warfield KL1, Dye JM2, Wells JB2, Unfer RC1, Holtsberg FW1, Shulenin S1, Vu H1, Swenson DL2, Bavari S2, Aman MJ1.
Author information
2015 Mar 20;10(3):e0118881. doi: 10.1371/journal.pone.0118881. eCollection 2015.
*Abstract*
Filoviruses cause hemorrhagic fever resulting in significant morbidity and mortality in humans. Several vaccine platforms that include multiple virus-vectored approaches and virus-like particles (VLPs) have shown efficacy in nonhuman primates. Previous studies have shown protection of cynomolgus macaques against homologous infection for Ebola virus (EBOV) and Marburg virus (MARV) following a three-dose vaccine regimen of EBOV or MARV VLPs, as well as heterologous protection against Ravn Virus (RAVV) following vaccination with MARV VLPs. The objectives of the current studies were to determine the minimum number of vaccine doses required for protection (using EBOV as the test system) and then demonstrate protection against Sudan virus (SUDV) and Taï Forest virus (TAFV). Using the EBOV nonhuman primate model, we show that one or two doses of VLP vaccine can confer protection from lethal infection. VLPs containing the SUDV glycoprotein, nucleoprotein and VP40 matrix protein provide complete protection against lethal SUDV infection in macaques. Finally, we demonstrate protective efficacy mediated by EBOV, but not SUDV, VLPs against TAFV; this is the first demonstration of complete cross-filovirus protection using a single component heterologous vaccine within the Ebolavirus genus. Along with our previous results, this observation provides strong evidence that it will be possible to develop and administer a broad-spectrum VLP-based vaccine that will protect against multiple filoviruses by combining only three EBOV, SUDV and MARV components.
*Research Article*
**Linking Human Health and Livestock Health: A "One-Health" Platform for Integrated Analysis of Human Health, Livestock Health, and Economic Welfare in Livestock Dependent Communities**

S. M. Thumbi, M. Kariuki Njenga, Thomas L. Marsh, Susan Noh, Elkanah Otiang, Peninah Munyua, Linus Ochieng, Eric Ogola, Jonathan Yoder, Allan Audi, Joel M. Montgomery, Godfrey Bigogo, Robert F. Breiman, Guy H. Palmer, Terry F. McElwain
Published: March 23, 2015
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*Abstract*

Background

For most rural households in sub-Saharan Africa, healthy livestock play a key role in averting the burden associated with zoonotic diseases, and in meeting household nutritional and socio-economic needs. However, there is limited understanding of the complex nutritional, socio-economic, and zoonotic pathways that link livestock health to human health and welfare. Here we describe a platform for integrated human health, animal health and economic welfare analysis designed to address this challenge. We provide baseline epidemiological data on disease syndromes in humans and the animals they keep, and provide examples of relationships between human health, animal health and household socio-economic status.

Method

We designed a study to obtain syndromic disease data in animals along with economic and behavioral information for 1500 rural households in Western Kenya already participating in a human syndromic disease surveillance study. Data collection started in February 2013, and each household is visited bi-weekly and data on four human syndromes (fever, jaundice, diarrhea and respiratory illness) and nine animal syndromes (death, respiratory, reproductive, musculoskeletal, nervous, urogenital, digestive, udder disorders, and skin disorders in cattle, sheep, goats and chickens) are collected. Additionally, data from a comprehensive socio-economic survey is collected every 3 months in each of the study households.

Findings

Data from the first year of study showed 93% of the households owned at least one form of livestock (55%, 19%, 41% and 88% own cattle, sheep, goats and chickens respectively). Digestive disorders, mainly diarrhea episodes, were the most common syndromes observed in cattle, goats and sheep, accounting for 56% of all livestock syndromes, followed by respiratory illnesses (18%). In humans, respiratory illnesses accounted for 54% of all illnesses reported, followed by acute febrile illnesses (40%) and diarrhea illnesses (5%). While controlling for household size, the incidence of human illness increased 1.31-fold for every 10 cases of animal illness or death observed (95% CI 1.16–1.49). Access and utilization of animal source foods such as milk and eggs were positively associated with the number of cattle and chickens owned by the household. Additionally, health care seeking was correlated with household incomes and wealth, which were in turn correlated with livestock herd size.

Conclusion

This study platform provides a unique longitudinal dataset that allows for the determination and quantification of linkages between human and animal health, including the impact of healthy animals on human disease averted, malnutrition, household educational attainment, and income levels.

**PLoS Pathogens**

http://journals.plos.org/plospathogens/

(Accessed 28 March 2015)

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Vol 6 (2015)
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[No relevant content]

**Public Health Ethics**
Volume 8 Issue 1 April 2015
http://phe.oxfordjournals.org/content/current
**Public Health: Beyond the Role of the State**
Angus Dawson*
University of Birmingham, UK
Marcel Verweij
Wageningen University, The Netherlands
*Extract*

Most of the papers in this issue of Public Health Ethics—more generally a large part of academic work in our field—are concerned with ethical problems of disease prevention and health promotion activities within nation states. Such discussions often involve reflection on the exact obligations of governments and public health officials acting on behalf of the state while pursuing these ends. In liberal approaches to such discussions, it is common to see a minimal role for the state and a focus on promoting the freedom and responsibility of individual citizens. Indeed, some choose to see public health ethics as being centrally about the conflict between individuals and the state (Holland, 2007; Nuffield Council on Bioethics 2007; Krebs 2008). In various places we have argued that public health ethics should not be conceptualized as being centred on conflicts between individual liberty and the responsibility of the state to protect health (Dawson 2010; Dawson 2011; Verweij & Dawson 2013, Verweij 2014). In this editorial, we suggest that we can see another problem that arises from the individual-vs-state way of structuring such discussions. Public health as an activity goes beyond the role of the state.

Some may argue that public health necessarily involves state action (Rothstein, 2002). This makes some sense, as it is certainly true that many interventions to protect health involve the exertion of power over citizens or even coercive policies, through, for example, the enforcement of legislation. In a previous paper, we have taken and argued for a broader view of public health, legitimate public health activity and public health ethics (Verweij and Dawson, 2007).

There we argued that public health ought to be seen as involving collective interventions to protect and promote population health…

**Qualitative Health Research**
April 2015; 25 (4)
http://qhr.sagepub.com/content/current
*Special Issue: Perceptions of Caregivers*
[Reviewed earlier]

**Revista Panamericana de Salud Pública/Pan American Journal of Public Health (RPSP/PAJPH)**
December 2014 Vol. 36, No. 6
http://www.paho.org/journal/index.php?option=com_content&view=article&id=151&Itemid=266&lang=en
[Reviewed earlier]

**Risk Analysis**
February 2015 Volume 35, Issue 2 Pages 179–344
http://onlinelibrary.wiley.com/doi/10.1111/risa.2015.35.issue-2/issuetoc
[Reviewed earlier]

**Science**
27 March 2015 vol 347, issue 6229, pages 1389-1512
http://www.sciencemag.org/current.dtl
*In Depth*
*Infectious Diseases*
**A reassuring snapshot of Ebola**
Gretchen Vogel
*Summary*
As Ebola has taken its horrific toll across West Africa, passing from person to person in its longest known chains of human infections, researchers worried the virus might mutate to become even more threatening. New viral genome data from Mali suggest a glimmer of good news: The Ebola virus that infected eight people there in October and November had not changed significantly from the one that infected people at the beginning of the known outbreak, back in March 2014. Diagnostic tests, experimental antibody-based treatments, and potential vaccines for Ebola are all developed based on the virus's recent sequence. If it were to change too much, cases could go unrecognized, and treatments and vaccines could become ineffective. Mutations might even lead to more dramatic symptoms or allow the virus to pass from person to person more easily. But genome sequences of four recent Ebola virus samples suggest that the virus, so far, has remained fairly stable.

**Social Science & Medicine**
Volume 131, In Progress (April 2015)

http://www.sciencedirect.com/science/journal/02779536/131
[Reviewed earlier]

**Tropical Medicine and Health**
Vol. 43(2015) No. 1
https://www.jstage.jst.go.jp/browse/tmh/43/0/_contents
[Reviewed earlier]

**Tropical Medicine & International Health**
March 2015 Volume 20, Issue 3 Pages 251–406
http://onlinelibrary.wiley.com/doi/10.1111/tmi.2014.20.issue-1/issuetoc
[Reviewed earlier]

**Vaccine**
Volume 33, Issue 16, Pages 1897-1998 (15 April 2015)
http://www.sciencedirect.com/science/journal/0264410X/33/16
*Brief Report*
**Immunogenicity and safety of 3-dose primary vaccination with combined DTPa-HBV-IPV/Hib vaccine in Canadian Aboriginal and non-Aboriginal infants**
Pages 1897-1900
David W. Scheifele, Murdo Ferguson, Gerald Predy, Meena Dawar, Deepak Assudani, Sherine Kuriyakose, Olivier Van Der Meeren, Htay-Htay Han
*Abstract*
This study compared immune responses of healthy Aboriginal and non-Aboriginal infants to Haemophilus influenzae type b (Hib) and hepatitis B virus (HBV) components of a DTaP-HBV-IPV/Hib combination vaccine, 1 month after completing dosing at 2, 4 and 6 months of age. Of 112 infants enrolled in each group, 94 Aboriginal and 107 non-Aboriginal infants qualified for the immunogenicity analysis. Anti-PRP concentrations exceeded the protective minimum (≥0.15 μg/ml) in ≥97% of infants in both groups but geometric mean concentrations (GMCs) were higher in Aboriginal infants (6.12 μg/ml versus 3.51 μg/ml). All subjects were seroprotected (anti-HBs ≥10 mIU/mL) against HBV, with groups having similar GMCs (1797.9 versus 1544.4 mIU/mL, Aboriginal versus non-Aboriginal, respectively). No safety concerns were identified. We conclude that 3-dose primary vaccination with DTaP-HBV-IPV/Hib combination vaccine elicited immune responses to Hib and HBV components that were at least as high in Aboriginal as in non-Aboriginal Canadian infants.
Clinical Trial Registration NCT00753649.
**Post-licensure surveillance of quadrivalent live attenuated influenza vaccine United States, Vaccine Adverse Event Reporting System (VAERS), July 2013–June 2014**
Original Research Article
Pages 1987-1992
Penina Haber, Pedro L. Moro, Maria Cano, Paige Lewis, Brock Stewart, Tom T. Shimabukuro
*Abstract*
Background

Quadrivalent live attenuated influenza vaccine (LAIV4) was approved in 2012 for healthy persons aged 2–49 years. Beginning with the 2013–2014 influenza season, LAIV4 replaced trivalent live attenuated influenza vaccine (LAIV3).
Methods
We analyzed LAIV4 reports to VAERS, a national spontaneous reporting system. LAIV4 reports in 2013–2014 were compared to LAIV3 reports from the previous three influenza seasons. Medical records were reviewed for non-manufacturer serious reports (i.e., death, hospitalization, prolonged hospitalization, life-threatening illness, permanent disability) and reports of selected conditions of interest. We conducted Empirical Bayesian data mining to identify disproportional reporting for LAIV4.
Results
In 2013–2014, 12.7 million doses of LAIV4 were distributed and VAERS received 779 reports in individuals aged 2–49 years; 95% were non-serious. Expired drug administered (42%), fever (13%) and cough (8%) were most commonly reported in children aged 2–17 years when LAIV4 was administered alone, while headache (18%), expired drug administered (15%) and exposure during pregnancy (12%) were most common in adults aged 18–49 years. We identified one death report in a child who died from complications of cerebellar vascular tumors. Among non-death serious reports, neurologic conditions were common in children and adults. In children, seizures (3) and Guillain-Barré syndrome (2) were the most common serious neurologic outcomes. We identified three serious reports of asthma/wheezing following LAIV4 in children. Data mining detected disproportional reporting for vaccine administration errors and for influenza illness in children.
Conclusions
Our analysis of VAERS reports for LAIV4 did not identify any concerning patterns. The data mining finding for reports of influenza illness is consistent with low LAIV4 vaccine effectiveness observed for influenza A disease in children in 2013–2014. Reports of LAIV4 administration to persons in whom the vaccine is not recommended (e.g., pregnant women) indicate the need for education, training and screening regarding indications.

**Determinants of influenza vaccination among young Taiwanese childr**en

Original Research Article
Pages 1993-1998
Chang-Hsun Chen, Po-Ju Chiu, Yi-Chien Chih, Gwo-Liang Yeh
*Abstract*
Objective
According to the Health Belief Model (HBM), individual perceptions of susceptibility, severity, benefit, barrier, self-efficacy, and cues to action are associated with health actions. In this study, we investigated the perceptions and social factors that influence the intention to vaccinate children against influenza among parents of young Taiwanese children.
Methods
A nationwide survey was performed using stratified random sampling to explore the beliefs, attitudes, and intentions of parents/main caregivers with regard to vaccinating children aged 6 months to 3 years against influenza. A questionnaire was developed based on the HBM and multivariate logistic regression analyses of 1300 eligible participants were used to identify significant predictors of the intention to vaccinate.
Results
Greater perceived benefit, cues to action, and self-efficacy of childhood vaccination against influenza were positively associated with the intention to vaccinate. Children's experience of influenza vaccinations in the past year was also a positive predictor. However, perceived

susceptibility, perceived severity regarding influenza and perceived barriers to vaccination were not predictive of the intention to vaccinate.
Conclusion
In addition to perceived benefits and cues to action, self-efficacy of parents/main caregivers was significantly predictive of their intention to accept influenza vaccination for their young children. These components of the HBM could be used in formulating strategies aimed at promoting the use of influenza vaccine.

**Vaccine**
Volume 33, Issue 15, Pages 1757-1896 (8 April 2015)
http://www.sciencedirect.com/science/journal/0264410X/33/15

**Rubella susceptibility in pregnant women and results of a postpartum immunization strategy in Catalonia, Spain**

Original Research Article
Pages 1767-1772
Alba Vilajeliu, Alberto L. García-Basteiro, Salomé Valencia, Saul Barreales, Laura Oliveras, Valentín Calvente, Anna Goncé, José M. Bayas
*Abstract*
Background
Elimination of congenital rubella syndrome depends not only on effective childhood immunization but also on the identification and immunization of rubella susceptible women. We assessed rubella susceptibility among pregnant women and evaluated the adherence and response to postpartum immunization with measles, mumps and rubella (MMR) vaccine.
Methods
Cross-sectional study of women who gave birth at the Hospital Clinic de Barcelona (Spain) between January 2008 and December 2013. Antenatal serological screening for rubella was performed in all women during pregnancy. In rubella-susceptible women, two doses of MMR vaccine were recommended following birth. We evaluated rubella serological response to MMR vaccination in mothers who complied with the recommendations.
Results
A total of 22,681 pregnant women were included in the study. The mean age was 32.3 years (SD 5.6), and 73.6% were primipara. The proportion of immigrants ranged from 43.4% in 2010 to 38.5% in 2012. The proportion of women susceptible to rubella was 5.9% (1328). Susceptibility to rubella declined with increasing maternal age. Immigrant pregnant women were more susceptible to rubella (7.6%) than women born in Spain (4.6%). Multivariate analyses showed that younger age (≤19 years) aOR 1.7 (95% CI 1.1–2.5), primiparas aOR 1.3 (95% CI 1.1–1.5) and immigrant women aOR 1.6 (95% CI 1.4–1.8) were more likely to be susceptible. The second dose of MMR vaccine was received by 57.2% (718/1256) of rubella-susceptible women, with the highest proportion being immigrant women compared with women born in Spain. After vaccination, all women showed rubella immunity.
Conclusions
The higher rubella susceptibility found in the three youngest age groups and in immigrant women highlights the relevance of antenatal screening, in order to ensure identification and postpartum immunization. The postpartum immunization strategy is an opportunity to protect women of childbearing age and consequently prevent occurrence of CRS, and to increase vaccination coverage against rubella and other vaccine-preventable diseases.

**Acceptability of using standing orders to deliver human papillomavirus vaccines in the outpatient obstetrician/gynecologist setting**

Original Research Article
Pages 1773-1779
Amanda F. Dempsey, Jennifer Pyrzanowski, Sarah Brewer, Juliana Barnard, Carter Sevick, Sean T. O'Leary
*Abstract*
Objective
Standing orders, an effective method for increasing vaccination, are not widely used for HPV vaccine. This is especially so among obstetrician/gynecologists (Ob/Gyns) – the specialty many women use as their primary care provider. We sought to understand the acceptability of using standing orders for HPV vaccination among a sample of women attending outpatient Ob/Gyn clinics.
Study design
From February to April 2014, an on-line survey was administered to a convenience sample of 400 women aged 15–26 recruited from 9 Ob/Gyn practices in Colorado. The survey identified attitudes about standing orders for HPV vaccination, demographics and prior experience with HPV vaccines.
Results
The response rate was 44%. Receipt of prior HPV vaccine doses was reported by 67% of respondents. Approximately half (53%) were comfortable with the idea of standing orders for HPV vaccination at Ob/Gyn clinics among women generally, but only 40% of the 154 women not initially opposed to HPV vaccination indicated they would personally feel comfortable receiving HPV vaccines offered under a standing order policy. General and personal acceptance of standing orders for HPV vaccination was significantly higher among women who reported receiving HPV vaccine doses previously, but not by any demographic or experiential variables. Acceptability of standing orders for HPV vaccines was higher for series completion than initiation (88% vs. 70%, $p < 0.001$) and was more commonly supported for adult patients (79%) than for adolescents (43%). Acceptability of standing orders increased if the patient was first told that the provider 'strongly recommended the vaccine', even for a majority (52%) of those who generally were not comfortable receiving the vaccine using standing orders.
Conclusions
Because standing orders for HPV vaccine are generally acceptable to women attending Ob/Gyn clinics, to increase vaccination uptake among adults Ob/Gyn providers may want to consider adoption of standing orders for HPV vaccine, at least for series completion.

**Media and public reactions toward vaccination during the 'hepatitis B vaccine crisis' in China**

Original Research Article
Pages 1780-1785
Bin Chen, Jueman Mandy Zhang, Zhenggang Jiang, Jian Shao, Tao Jiang, Zhengting Wang, Kui Liu, Siliang Tang, Hua Gu, Jianmin Jiang
*Abstract*
Background
Public disputations affected vaccine confidence and vaccine rates particularly when adverse events occur. The vigorous development of Internet in China provides an opportunity to observe public reaction and sentiment toward vaccination when Kangtai Hepatitis B vaccine crisis happened and evolved to a widespread debate on the internet from December 12, 2013 to January 3, 2014.
Methods

This study conducted Internet surveillance by examining three daily indicators including the daily number of relevant online news article, Sina Weibo posts and Baidu search index during the crisis. We also analyzed the sentiments of relevant original microblog posts collected from Sina Weibo platform in the crisis.
Results
A total of 17 infant deaths were reported to associated with Hepatitis B vaccination. Three major waves of high media and public attention were detected. The daily indicators reached their peaks in the second wave after the relevant vaccine was suspended by the authority (from December 20 to December 29, 2013) with 23,200 daily online news reports, 34,018 Sina Weibo posts and 17,832 Baidu search indices. There were significant correlations between the daily amount of online news, Weibo posts, and Baidu searches ($p < .001$). The contents analysis suggested 1343 out of 1608 (83.5%) original Weibo posts expressed negative sentiment with almost 90% in the second wave.
Conclusion
This study found the Kangtai vaccine crisis raised great public attention and negative sentiment toward vaccinations on the internet in China. Policy change such as suspension of the suspected vaccine might trigger even greater reaction and more negative sentiment. The government should provide ways to address emerging public concerns after policy change to avoid misinformation and misunderstanding during such a vaccine crisis.

**Human papillomavirus vaccine uptake in boys and girls in a school-based vaccine delivery program in Prince Edward Island, Canada**

Original Research Article
Pages 1786-1790
Carol A. McClure, Mary-Ann MacSwain, Heather Morrison, Carolyn J. Sanford
*Abstract*
Background
In 2013, Prince Edward Island was the first province to introduce HPV vaccine universally to grade six boys in a school-based program. Because uptake rates in boys are unknown in this type of vaccination program, uptake of HPV vaccination in boys was measured and compared with uptake rates in girls and then analyzed with factors such as county, urban–rural location of the school, and school board to identify where the vaccine program could be improved.
Methods
HPV vaccination records from the provincial childhood immunization registry in PEI were merged with Department of Education data containing all grade six girls and boys in PEI. Vaccine uptakes between years and between sexes were compared using two sample tests of proportions. Logistic regression modeling which accounted for the hierarchical nature of the data was used to analyze associations between factors and uptake rates.
Results
Although uptake was high in boys and girls, a significantly greater proportion of girls (85%) received all three doses of the HPV vaccine compared to boys (79%; $p = 0.004$). The odds of grade six girls being fully vaccinated for HPV were 1.5 times greater than of grade six boys, and the odds of students in the English Language School Board receiving all three doses were more than twice as great as the odds of French Language School Board students.
Conclusions
HPV vaccination for boys in PEI has had a successful launch, almost reaching the Canadian Immunization Committee recommendations of >80% for the early years of a program. PEI has a highly organized Public Health Nursing program that is involved in all childhood and school-based vaccinations in PEI and in this context very high coverage rates were obtained. Areas to

target for improving uptake include the boys and the students in the French Language School Board.

**Parental vaccine hesitancy and acceptance of seasonal influenza vaccine in the pediatric emergency department**

Original Research Article
Pages 1802-1807
Bonnie Strelitz, Jesse Gritton, Eileen J. Klein, Miranda C. Bradford, Kristin Follmer, Danielle M. Zerr, Janet A. Englund, Douglas J. Opel

- *Abstract*

Background
Providing influenza vaccine to patients in the pediatric emergency department (PED) is one strategy to increase childhood influenza vaccine uptake. The Parent Attitudes about Childhood Vaccines (PACV) survey is a new tool to identify vaccine-hesitant parents that may facilitate influenza vaccine uptake in the PED.
Objective
To assess the feasibility of administering the PACV modified for influenza vaccination in the PED setting and to determine whether parental PACV scores are associated with patient receipt of influenza vaccine in the PED.
Methods
We conducted a cross-sectional study in the PED of a tertiary pediatric hospital in Seattle, WA during the 2013–2014 influenza season. English-speaking parents of children aged 6 months to 7 years who were afebrile, medically stable to be discharged home from the PED, and had not already received an influenza vaccine this season were administered a modified version of the PACV. PACV scores (0–100, higher score = higher hesitancy) were dichotomized (<50 and ≥50) consistent with previous validation studies. Feasibility was assessed by determining time to complete the PACV. Our primary outcome was influenza vaccine refusal in the PED. We used multivariable logistic regression to estimate unadjusted and adjusted odds ratios for association between vaccine refusal and dichotomized PACV scores.
Results
152 parent participants were included in the analysis. The median time for administering the PACV was 7 min. The median PACV score was 28, with 74% scoring <50. Parents who scored ≥50 on the PACV had increased odds of refusing the influenza vaccine compared to parents who scored <50 (adjusted OR [95% CI]: 6.58 [2.03–21.38]).
Conclusion
Administration of the PACV in the PED is feasible, and higher PACV scores in this setting are associated with increased influenza vaccine refusal.

**Vaccines — Open Access Journal**
(Accessed 28 March 2015)
http://www.mdpi.com/journal/vaccines
Article: **Tattoo Delivery of a Semliki Forest Virus-Based Vaccine Encoding Human Papillomavirus E6 and E7**
by Stephanie van de Wall, Mateusz Walczak, Nienke van Rooij, Baukje-Nynke Hoogeboom, Tjarko Meijerhof, Hans W. Nijman and Toos Daemen
Vaccines 2015, 3(2), 221-238; doi:10.3390/vaccines3020221 - published 24 March 2015

*Abstract*

The skin is an attractive organ for immunization because of the presence of antigen-presenting cells. Intradermal delivery via tattooing has demonstrated superior vaccine immunogenicity of DNA vaccines in comparison to conventional delivery methods. In this study, we explored the efficacy of tattoo injection of a tumor vaccine based on recombinant Semliki Forest virus replicon particles (rSFV) targeting human papillomavirus (HPV). Tattoo injection of rSFV particles resulted in antigen expression in both the skin and draining lymph nodes. In comparison with intramuscular injection, the overall antigen expression determined at the site of administration and draining lymph nodes was 10-fold lower upon tattoo injection. Delivery of SFV particles encoding the E6 and E7 antigens of human papillomavirus type 16 (SFVeE6,7) via tattooing resulted in HPV-specific cytotoxic T cells and in vivo therapeutic antitumor response. Strikingly, despite the observed lower overall transgene expression, SFVeE6,7 delivered via tattoo injection resulted in higher or equal levels of immune responses as compared to intramuscular injection. The intrinsic immunogenic potential of tattooing provides a benefit for immunotherapy based on an alphavirus.

**Value in Health**
March 2015 Volume 18, Issue 2, p137-354
http://www.valueinhealthjournal.com/current
[Reviewed earlier]

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## ***From Google Scholar & other sources: Selected Journal Articles, Newsletters, Dissertations, Theses, Commentary***

**International Journal of Infectious Diseases**
Volume 32, March 2015, Pages 5–12
Special Issue: Commemorating World Tuberculosis Day 2015
**Tuberculosis Vaccines–state of the art, and novel approaches to vaccine development**
Christopher da Costa, Barry Walker, Aurelio Bonavia
*Highlights*
:: The increasing global incidence of tuberculosis, including multi- and extensively-drug resistant disease, calls for renewed efforts to develop a safe and effective vaccine
:: Several new candidate vaccines are currently in preclinical stage development, with evaluation of novel approaches to vaccine delivery
:: Experimental medicine studies in human and non-human primate models of tuberculosis provide the potential for decreasing the time and cost of developing new vaccines, with increasing chances of late stage success
:: There is currently a wealth of promising candidate vaccines also in various phases of clinical development
*Summary*
The quest for a vaccine that could have a major impact in reducing the current global burden of TB disease in humans continues to be extremely challenging. Significant gaps in our knowledge and understanding of the pathogenesis and immunology of tuberculosis continue to undermine

efforts to break new ground, and traditional approaches to vaccine development have thus far met with limited success. Existing and novel candidate vaccines are being assessed in the context of their ability to impact the various stages that culminate in disease transmission and an increase in the global burden of disease. Innovative methods of vaccine administration and delivery have provided a fresh stimulus to the search for the elusive vaccine. Here we discuss the current status of preclinical vaccine development, providing insights into alternative approaches to vaccine delivery and promising candidate vaccines. The state of the art of clinical development also is reviewed.

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## ***Media/Policy Watch***

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

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

**Al Jazeera**
http://america.aljazeera.com/search.html?q=vaccine
*Accessed 28 March 2015*
[No new, unique, relevant content]

**The Atlantic**
http://www.theatlantic.com/magazine/
*Accessed 28 March 201*
[No new, unique, relevant content]

**BBC**
http://www.bbc.co.uk/
*Accessed 28 March 2015*
[No new, unique, relevant content]

**Brookings**
http://www.brookings.edu/
*Accessed 28 March 2015*
[No new, unique, relevant content]

**Council on Foreign Relations**
http://www.cfr.org/
*Accessed 28 March 2015*

*Testimony*
The Unfinished Health Agenda in Sub-Saharan Africa
by Thomas J. Bollyky March 19, 2015
In his testimony before the Senate Foreign Relations Subcommittee on Africa and Global Health Policy, Thomas J. Bollyky argues that continued U.S. and private sector leadership on the unfinished health agenda in Africa is as important now as it has been in the past and for the same reasons: a peaceful, inclusive economy presupposes healthier, more productive lives.

**The Economist**
http://www.economist.com/
*Accessed 28 March 2015*
[No new, unique, relevant content]

**Financial Times**
http://www.ft.com/home/uk
The true value of a life is not about the pharmaceutical costs
24 March 2015
The business model of the pharmaceutical industry has been based on drugs that alleviate the chronic diseases of the developed world, such as depression, hypertension and stomach acidity. By selling huge volumes of pills at moderate prices, companies could recover the expenditure involved in drug development and clinical trials and still make lavish profits. But only a few drugs fit that model. Many recent pharmacological discoveries are relevant to the acute illnesses of a few rather than the continuing ailments of the many. These are drugs such as Halavan, mainly used in patients with advanced metastatic breast cancer, and Sovaldi, a treatment for hepatitis C.

**Forbes**
http://www.forbes.com/
*Accessed 28 March 2015*
[No new, unique, relevant content]

**Foreign Affairs**
http://www.foreignaffairs.com/
*Accessed 28 March 2015*
[No new, unique, relevant content]

**Foreign Policy**
http://foreignpolicy.com/
*Accessed 28 March 2015*
[No new, unique, relevant content]

**The Guardian**
http://www.guardiannews.com/
*Accessed 28 March 2015*
[No new, unique, relevant content

**The Huffington Post**
http://www.huffingtonpost.com/

*Accessed 28 March 2015*
[No new, unique, relevant content]

**Mail & Guardian**
http://mg.co.za/
*Accessed 28 March 2015*
[No new, unique, relevant content]

**New Yorker**
http://www.newyorker.com/
*Accessed 28 March 2015*
[No new, unique, relevant content]

**New York Times**
http://www.nytimes.com/
*Accessed 28 March 2015*
[No new, unique, relevant content]

**Voice of America**
http://www.voanews.com/
WHO Denies It Delayed Declaration of Ebola Epidemic
Lisa Schlein
March 20, 2015 7:43 PM GENEVA—
The World Health Organization is vigorously denying accusations that it delayed declaring the Ebola epidemic in West Africa an international public health emergency for political reasons.
An article by the Associated Press said secretly obtained e-mails of internal documents indicated the WHO was afraid that declaring a global emergency could set off alarm bells, which could hurt countries' economies or interfere with the Muslim pilgrimage to Mecca.
WHO's spokeswoman on Ebola, Margaret Harris, told VOA that the assertion was categorically untrue…

**Wall Street Journal**
http://online.wsj.com/home-page?_wsjregion=na,us&_homepage=/home/us
*Accessed 28 March 2015*
The Key to Convincing Parents to Vaccinate Their Children
DREW HARRIS: The recent measles outbreak linked to Disneyland is drawing attention to the issue of families with unvaccinated children and the public policies that allow them to opt out of immunization mandates.
03/24/15
*The Experts*
Robert Kennedy Jr. speaks out against vaccine requirements
TRENTON, N.J. — Calling the federal agency that makes recommendations on vaccines a "sock puppet" for that industry, Robert Kennedy Jr. spoke out Monday against making it harder for parents to exempt their children from vaccinations.
03/23/15

**Washington Post**
http://www.washingtonpost.com/

*Accessed 28 March 2015*
[No new, unique, relevant content]

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*Support is also provided by a growing list of individuals who use this membership service to support their roles in public health, clinical practice, government, NGOs and other international institutions, academia and research organizations, and industry.*

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