Safety and perception - who are the great enemies of HPV vaccination programmes?

Paolo Bonanni

Department of Health Sciences
University of Florence, Italy
‘Primum non nocere’
Thomas Sydenham

‘First, do no harm’

Easier said than done!
‘Things we don’t know we don’t know’
Donald Rumsfeld

Distinctive characters of vaccines when compared to drugs

- Biological products

- Administration to healthy subjects (usually children or adolescents) - the reason why even minimal adverse events are perceived as non tolerable

- Preventive aim, not therapeutic

- Act at the individual, but also at the population level
  - modify the immune status
  - reduce the circulation of the infectious agent
  - modify the epidemiology of the disease

Healthy life styles (?)

“Something’s just not right—our air is clean, our water is pure, we all get plenty of exercise, everything we eat is organic and free-range, and yet nobody lives past thirty.”
There are concerns about the safety of vaccines because they are given to large populations of healthy people.
ACETAMINOPHEN
Freq adverse events (1-9%)
- Rinitis
- Severe dyspnea
- Paroxystic bronchial spasm
- Gastrointestinal haemorrhage
- Dyspepsia
- Abdominal pain
- Ulcus
- Etc

FDA labelling – last access 2010
The universal application of vaccines makes their safety of utmost importance.

The ‘herd immunity’ (and, for HPV, the future public health impact and simplification of screening programs) can only be achieved if public confidence in the safety of the vaccine is secure.

‘First, do not harm’
Safety is assessed at every step of vaccine development and indefinitely after licensure.

Preclinical: 5–15 years

Clinical: 5–15 years

Post-licensure: For entire life-cycle

Safety assessment and monitoring

Adverse Events Following Immunization (AEFI) Classification

- **Vaccine reaction:**
  - Event caused or precipitated by the vaccine when given correctly
  - Caused by inherent properties of the vaccine

- **Programme error:**
  - Event caused by an error in vaccine preparation, handling, or administration

- **Coincidental event:**
  - Event that happens after immunization but not caused by the vaccine (chance association)

- **Injection reaction:**
  - Event from anxiety about, or pain from the injection itself rather than the vaccine

- **Unknown:**
  - Cause cannot be determined

# Frequency and severity of AEFI

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Severity</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common</td>
<td>Mild</td>
<td>Aim of reactogenicity studies</td>
</tr>
<tr>
<td>Rare</td>
<td>Mild</td>
<td>No/little interest</td>
</tr>
<tr>
<td>Common</td>
<td>Serious</td>
<td>Should never be observed</td>
</tr>
<tr>
<td>Rare</td>
<td>Serious</td>
<td>Aim of reactogenicity studies</td>
</tr>
</tbody>
</table>

AEFI, adverse event following immunisation

Passive Vaccine Surveillance

- **Voluntary reporting of AEs** by healthcare providers, vaccinees, and others (parents, relatives, friends etc.)¹,a
  - Direct reporting to manufacturer²
  - National surveillance systems (eg, Australian TGA database, US VAERS)¹,³,⁴
  - Multinational databases (eg, VigiBase of WHO’s PIDM)⁴,⁵

- **Designed to identify new or rare AEs and changes in rates of previously reported AEs**¹,⁴,a

- **Limitations** include variability of reporting, reporter bias, potential underreporting⁶

- **AE causality** cannot be determined because of limited nature of data reported¹,⁶

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INDEX TERMS
- AEs
- PIDM
- TGA
- VAERS


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AEs reported to VAERS have no established cause-and-effect relationship with vaccine administration.
Active Vaccine Surveillance

- **Systematic procedure** for actively seeking and identifying clinically significant events that occur within a defined period and/or population\(^1,2\)
  - Manufacturer **postmarketing trials**\(^2\)
  - **Large linked databases** (eg, US Vaccine Safety Datalink and PRISM systems, UK General Practice Research Database)\(^1,3,4\)

- Can assess whether a specific AE is significantly associated with vaccination\(^1,2,a\)

\(^a\)AEs reported to VAERS have no established cause-and-effect relationship with vaccine administration. AE=adverse event; PRISM=Post-Licensure Rapid Immunization Safety Monitoring.

Continued evaluation of adverse events reported by the authorities

**EU and national authorities**

- **Detection**
  - Reports of adverse events
- **Validation**
  - Cause of the event? Not caused by the vaccines
  - Cause by the vaccine?
- **Interpretation**
  - Change in benefit:risk ratio?
- **Action**
  - No change in use
  - e.g. additional warnings, restricted use

**GPs, Nurses, Pharmacists**

**Manufacturer**

**Public**

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GP, general practitioner

Concerns about immune-mediated disorders

• Theoretical risk of adverse immunological responses that may lead to immune-mediated disorders, linked to
  – Homology of the antigen to a human protein, or
  – Non-specific immune enhancement properties of the adjuvant used
Safety monitoring of adjuvanted vaccines

- Identify AEs of ‘special interest’
- Focus on autoimmune/autoinflammatory diseases
  - Neuro-inflammatory disorders (e.g. optic neuritis, transverse myelitis)
  - Musculoskeletal and connective tissue diseases (e.g. RA, SLE, Wegener’s disease)
  - GI disorders (e.g. Crohn’s disease, ulcerative colitis)
- Establish enhanced case reporting throughout entire study period for potential autoimmune-related AEs
- Surveillance: active vs. passive; data-linkage
- Consider longer safety follow-up period
  - 6–12 months or longer

AE, adverse event; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; GI, gastrointestinal

Adapted from Marion F Gruber, PhD, Acting Director, OVRR/CBER/, Vaccine Forum, Washington 2012. Available at: http://www.fda.gov/downloads/EmergencyPreparedness/MedicalCountermeasures/UCM292045.pdf (accessed April 2014);
Vaccine safety is continuously monitored

- Continuous vaccine safety monitoring is in place to rapidly identify and evaluate potentially occurring rare and/or serious adverse events temporally linked to vaccination (e.g. sudden deaths, immune-mediated disorders such as Guillain-Barré syndrome, narcolepsy)

- When needed, studies are triggered to assess safety signals and distinguish possible causes from likely coincidence

# Safety of human papillomavirus vaccines: a review

Michela Stillo, Paloma Carrillo Santuste & Pier Luigi Lopalco

10.1517/14740338.2015.1013532 © 2015 Informa UK, Ltd. ISSN 1474-0338, e-ISSN 1744-764X

## Table 3. Human papilloma virus vaccines safety reviews.

<table>
<thead>
<tr>
<th>Author</th>
<th>Title</th>
<th>Year of publication</th>
<th>Type of study</th>
<th>Place</th>
<th>Population</th>
<th>Vaccine type</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weber et al.</td>
<td>Childhood vaccination-associated adverse events by sex: A literature review</td>
<td>2014</td>
<td>Review</td>
<td>12 studies</td>
<td>HPV/16/18 and HPV/11/16/18</td>
<td>AE: The most frequent local adverse event was injection-site pain; the incidence of adverse events did not increase with increasing number of doses Injection-site adverse event (especially pain) and mild self-limited systemic symptoms (such as myalgia and headache) occur commonly after vaccination and should be anticipated. None of these symptoms is more common in bHPVv Pain, the most common injection-site AE, occurred more frequently with vaccine (61% vaccine; 75% placebo-alum; 45% placebo-saline). No differences were seen in the incidence of the most common non-serious AEs-headache and pyrexia</td>
<td>SAE: No specific safety concern identified except for the Gee et al. [94] observation of an elevated risk of 1.98 for venous thromboembolism</td>
</tr>
<tr>
<td>Macartney et al.</td>
<td>Safety of human papillomavirus vaccines: a review</td>
<td>2016</td>
<td>Review</td>
<td>/</td>
<td>HPV/16/18 and HPV/11/16/18</td>
<td>Consistent with the findings of the review no evidence supported an association of HPV vaccine with other outcomes, such as onset chronic diseases</td>
<td></td>
</tr>
<tr>
<td>Lee et al.</td>
<td>Clinical trial and post-licensure safety profile of a prophylactic Human Papillomavirus (HPV) 16 and 18 virus-like particle vaccine</td>
<td>2010</td>
<td>Review of five clinical trials</td>
<td>21,480 girls and boys</td>
<td>HPV/16/11/16/18</td>
<td>SAE occurred in 0.05% in vaccine group ad in 0.02% in placebo group. Of 18 deaths (0.1% vaccine; 0.1% placebo), all were considered unrelated to study treatment. New medical conditions which were potentially consistent with autoimmune phenomena were reported in 2.4% of both vaccine and placebo recipients. Almost all the case-reports of SAE had weak or moderate strength of evidence for causality</td>
<td></td>
</tr>
<tr>
<td>Agostinetti et al.</td>
<td>Safety of human papillomavirus (HPV) vaccines: A review of the international experience so far</td>
<td>2009</td>
<td>Review based on national and international agencies</td>
<td>US, Canada, Australia, Europe, Germany, France, UK</td>
<td>HPV/11/16/18 and HPV/16/18</td>
<td>Pre-licensure data: Injection site symptoms were the most reported symptoms in any one of the studies, they were reported more frequently in the vaccine group than in the control group. General symptoms were slightly higher in the vaccine group</td>
<td></td>
</tr>
</tbody>
</table>

AE: Adverse event; bHPVv: Bivalent HPV vaccine; SAE: Serious adverse event.
Main evidences on HPV vaccines safety (1)

- Both vaccines are safe and well tolerated.
- Site injection symptoms are the most frequent AEs reported, pain being the most frequently referred. Symptoms usually disappear shortly after vaccination and the incidence decreases with the second and third dose of vaccine.
- General symptoms such as headache, syncope and fever are reported from 10 to 30% of cases, although no significant difference has been observed between vaccination and control groups.
- The incidence of SAEs is variable but in most cases causal association is not proven. Additionally, the occurrence of these events is similar in both vaccine and control groups.
Main evidences on HPV vaccines safety (2)

- For specific categories of SAE (ADs, venous thromboembolism, neurological syndromes) the absence of correlation with the vaccination has already been demonstrated.

- No deaths from the introduction of the two vaccines have been attributed to HPV vaccination, but some cases have been poorly investigated leaving room for speculation, which could damage vaccination programs.

- Some studies on the safety of the vaccine in groups other than the primary target population (men, women older than 25 years, HIV+ girls) have already been published and have given satisfactory results comparable with those in the primary target population.
The incidence of chronic pain resembling complex regional pain syndrome reported in Japan (24 cases reported to date) is being investigated, but so far the expert advisory committee has not been able to ascertain a causal relationship with vaccination.

March 12, 2014

Global Advisory Committee on Vaccine Safety
Statement on the continued safety of HPV vaccination

As with all new vaccines, the Global Advisory Committee on Vaccine Safety has been reviewing the safety of HPV vaccines since they were first licensed in 2006. The World Health Organization (WHO) recommends the introduction of HPV vaccination into national immunization programmes where prevention of cervical cancer is a public health priority and the introduction is programmatically feasible [1]. While early detection of pre- and cancerous cells through screening programs has helped decrease incidence rates of cervical cancer in women aged 25-45 in the UK, for example [2], that decrease has plateaued in the past decade. While safety concerns about HPV vaccines have been raised, these have systematically been investigated: to date, the GACVS has not found any safety issue that would alter any of the current recommendations for the use of the vaccine.
We have forgotten the seriousness of some diseases
Vaccine Hesitancy Determinant Categories

**Trust** in vaccines, in delivery system, in the policy-makers who decide which vaccines are needed and when.

**Complacency**

Perceived risks VPD low; vaccination not deemed a necessary preventive action. Other life/health responsibilities higher priority at time.

**Convenience**

Physical access-availability, affordability, willingness to pay; geographical access, ability to understand (language, health literacy); appeal of immunization services.

**Confidence**

SAGE Working Group Vaccine Hesitancy 2014
Risk communication and vaccines: which are the issues?

- ‘Vaccines are victims of their own success’
- The power of temporal association (‘post hoc, ergo propter hoc’ - after that, therefore due to that)
- Individual freedom of choice vs. public health interest
- Voluntary risk (controllable) is more accepted than involuntary risk
- Some parents prefer the ‘Omission bias’ to active decision for immunisation
- Allegations will not disappear. They need to be treated as a chronic phenomenon with periodical flares
Why so much alarm for vaccines?

- Despite our daily encounters with microbial antigens, vaccines still seem unnatural and frightening to some people.
- Perception of risk is amplified in today’s setting.
- The public’s (and the media’s) understanding of immunisation is superficial.

Courtesy of NCIRS
For HPV does it have to do with cultural / religious barriers?
HPV vaccine will lead young girls to promiscuity!

Right, and bird flu vaccine will lead them to lay eggs.
HPV Vaccine Doesn’t Alter Sexual Behavior, Study Finds

By ANAHAD O’CONNOR

Sexual Activity–Related Outcomes After Human Papillomavirus Vaccination of 11- to 12-Year-Olds

WHAT’S KNOWN ON THIS SUBJECT: Concerns persist about sexual disinhibition after human papillomavirus (HPV) vaccination of preteenage girls. Self-reported surveys have indicated few anticipated behavior changes after HPV vaccination. Little is known about sexual activity-related clinical outcomes after HPV vaccination.

WHAT THIS STUDY ADDS: Utilizing managed care organization electronic data, we evaluated the incidence of adverse outcomes of sexual activity little difference in those who did not receive vaccination.

PEDIATRICS Volume 130, Number 5, November 2012
Does HPV vaccination increase promiscuity?

- HPV vaccination in the recommended ages was not associated with increased rates of sexual activity-related outcomes

Incidence rate ratios comparing HPV vaccine-exposed* to –unexposed girls

<table>
<thead>
<tr>
<th>Sexual activity-related outcomes</th>
<th>Adjusted incidence rate ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testing/Diagnosis/Counseling</td>
<td></td>
</tr>
<tr>
<td>Diagnosis only</td>
<td></td>
</tr>
<tr>
<td>Chlamydia testing</td>
<td></td>
</tr>
<tr>
<td>Chlamydia diagnosis</td>
<td></td>
</tr>
<tr>
<td>Pregnancy testing</td>
<td></td>
</tr>
<tr>
<td>Pregnancy diagnosis</td>
<td></td>
</tr>
<tr>
<td>VD-NOS diagnosis</td>
<td></td>
</tr>
<tr>
<td>Counseling on contraceptives</td>
<td></td>
</tr>
</tbody>
</table>

* Girls vaccinated (≥ 1 dose of HPV vaccine) at age 11-12 years; 3-year follow-up for outcomes
Testing/Diagnosis/Counseling = Testing/Diagnosis/Counseling for any medical outcomes relating to sexual activity VD-NOS = venereal disease, not otherwise specified

How should we handle public concerns about vaccine safety?

There is no substitute for science in the refutation of myth

Science activities very rarely deal with zero/no risk

Honesty and clarity
Head and heart need addressing

Refer to experience

The fact that we do not know everything about vaccines does not imply that we know nothing…

What did diseases do before we had vaccines?
Challenges in vaccine development

- Temporal association of adverse events after vaccination
  - a temporal association is not sufficient to establish cause and effect
  - true cause and effect relationship assessments are needed to avoid elevating a hypothesis of risk above the very real risk of vaccine-preventable diseases
  - ‘background’ occurrence of an event (disease) must always to be taken into consideration
Pertussis vaccination: potential mistaken association with Sudden Infant Death Syndrome in France

Associations with other conditions are inevitable, but not necessarily causally linked with vaccination.

When a large population is vaccinated, naturally occurring diseases are likely to coincide with vaccination.

Estimated risk of selected diseases in young girls/women (9–18 years) assuming vaccination with a saline placebo according to the indicated US scheme for HPV 6/11/16/18 vaccine based on US rates for ER visits and hospitalisations without vaccination.

HPV vaccination and events that may be mistaken for adverse events

50-60 adolescents (9-18 years) per each 100,000 are admitted with diabetes each year.

LAST MINUTE NEWS – THE SENSATIONAL
- She won lotto big prize after HPV vaccination
- “It was just after the 2nd shot”, she said
Surveillance is essential to generate signals and hypotheses but not to prove them!

Incidence of events in vaccinated subjects = \( \frac{a}{a + b} \)

Incidence of events in non-vaccinated subjects = \( \frac{c}{c + d} \)
Investigating adverse events

• Hypothesis testing
  – Well-designed controlled epidemiological studies
  – Require a clear hypothesis
  – Determine whether there is evidence of an association and if so, the size of the effect

• Methods
  – Case-control studies
  – Cohort studies
  – Case-only methods
Signal detection from passive surveillance

Quantitative Signal Detection

Implementation of calculations to support quantitative signal detection

Proportional Reporting Ratio (PRR)

95% PRR Confidence Interval

$X^2$ (Chi Square Test)

Incidence of an AE after receiving a given drug

Incidence of same AE in the whole surveillance database

AE, adverse event

Features of a Postmodern Society

- Distrust of science
- Greater attention to risk
- Better access to real-time information
- Readiness to recur to the judiciary

J.A. Muir Gray Lancet 1999; 354:1550-1553
Risk Perception

• Science is secondary to value judgments that people make concerning risks.

• None of the leading factors of how people make decisions are technical or scientific.

• Source credibility is key.

• As a result, communication about risk must be developed through a process that essentially works backwards from the value judgments people make about risk information.

Source: Bruce Gellin, Vanderbilt University School of Medicine
Why is vaccine criticism increasing?

- Usefulness of vaccines is challenged.
- ‘Authority’ is scrutinised (post-modern phenomenon)
  - scientific authority and integrity of scientists and experts
- Increasing interest in alternative medicine
- Increase in diagnosis of autism due to increased disease awareness and changes to diagnostic criteria
Why is vaccine criticism increasing?

- The World Wide Web contains freely available information that encourages vaccine refusal or emphasises the dangers of vaccines.
- The media may sensationalise vaccine safety issues, or may fail to provide perspective.

HPV vaccine: Rapid response to public concern

“In other words, efficient and timely communication is crucial in order to stop possible rumours about adverse events due to vaccination. This is a very important message I would like to convey to countries that are planning to introduce HPV vaccination.”

ECDC Director’s Presentation. Overview of HPV vaccination from an EU and ECDC perspective. HPV Summit at Excellence in Paediatrics, December 5, 2013

Schoolgirl dies after cervical cancer vaccination
- HPV vaccine batch quarantined as ‘precautionary measure’
- Vaccination part of national immunisation programme

The Guardian, Tuesday 29 September 2009

Girl who died after cervical cancer injection had tumour in her chest
- Death of girl due to underlying medical condition, inquest hears

The Guardian, Thursday 1 October 2009

Reasons for vaccination rejection

- Perception that disease is not harmful
- Low perception of risk of acquiring the disease
- Belief in natural medicine
- Lack of knowledge about immunisation
- Perception that vaccine is harmful (autism, macrophagic myofasciitis)
- Lack of knowledge on how vaccines are formulated (use of substances derived from animal or human fetal cells)

Adapted from Ernst et al. Identifying clusters of high vaccination exemption rates among schools and their determinants. Available at: http://www.azdhs.gov/phs/oids/training/documents/2012/ErnstKacey.pdf (accessed April 2014)
Anti-vaccine movements are nothing new

- Vaccine opposition is
  - a long standing issue
  - started mid-1800s with strong backlash to the smallpox mandatory vaccination in England

*Courtesy of James Gillray, Library of Congress, Prints and Photographs division*
Innovation in communication methods have since emerged: the internet and social media

- Vaccine opponents now have the ability to use cyber interaction to share views
- A Google search leads to vaccine critical sites in about 1 of 5 hits on immunisation
- The internet may have more influence than reported, particularly when personal narratives are used

Influence of digital social media in Eastern Europe on vaccine confidence

Allocation of arguments in English-speaking anti-vaccination discussions

Distribution of anti-vaccine discussions by channel: English networks

What can be done?

- Effective use of personal narratives in support of immunisation
- Leverage interactivity on the web and use it in support of immunisation (e.g. regular tweets on new research)
- Trust is crucial
  - Take more time to understand how sources of pro-immunisation information can be increased
  - Healthcare workers remain the most trusted and used source of information
  - Build trust

Adapted from Butler. Contrasting the anti-vaccine movements. Presented at ESCMID 2013, Prague

www.chainofprotection.org
I vaccini anti HPV, somministrati prima dell'esposizione al virus, prevenendo le lesioni genitali precancerose (del collo dell'utero, della vulva e della vagina), di fatto riducono notevolmente la possibilità di sviluppo di neoplasia maligna. Inoltre, il vaccino quadrivalente, previene anche le lesioni condilomatose in entrambi sessi.
The importance of effective communication campaigns: UK example – national press

The new HPV vaccine, which protects against cervical cancer, will save hundreds of women's lives every year.

This vaccine, along with the cervical screening programme, will help protect women for life.

The annual vaccination programme for girls aged 12 to 13 (school year 6) starts this autumn.

Over the next 3 years, it will also be offered to other girls aged 13 to 18.

Arm your daughter against cervical cancer. Your daughter's school or local NHS will provide more information before the vaccination is due.

For more information about the HPV vaccine visit www.nhs.uk/HPV or call the helpline on 0845 602 3303.

Armed for life.

Courtesy Prof. David Salisbury
The importance of effective communication campaigns: UK example – online advertorials
The importance of effective communication campaigns: UK example – ‘Habbo Hotel’
Ease of access helps reduce inequities

Cervical screening participation by socio-economic status, Victoria

HPV coverage by socio-economic status, Victoria

Quintile 1: lowest
Quintile 5: highest

Local initiatives to help improve coverage: An Italian example

Coverage rate 4 years after introduction of HPV vaccination programme is lower than expected: 64%

Understand reasons behind low HPV vaccination uptake

Educate about HPV vaccination to allow informed decision
Local initiatives to help improve coverage: An Italian example

- Provide ‘non-responder’ database
- Call Center: Contact family of ‘non-responder’
- Family: Give reason for not vaccinating & book vaccination or counselling session
- LHU: Local Health Unit

LHU: Local Health Unit
Local initiatives to help improve coverage: An Italian example

• Outcome

<table>
<thead>
<tr>
<th></th>
<th>Requested</th>
<th>Coverage Increase¹</th>
<th>Period</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Calabria</strong></td>
<td>Vaccination</td>
<td>24.5%</td>
<td>1997</td>
</tr>
<tr>
<td></td>
<td>Counselling</td>
<td>16%</td>
<td>1998</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>6 months</td>
</tr>
<tr>
<td><strong>Genoa</strong></td>
<td>Vaccination</td>
<td>23.1%</td>
<td>1997</td>
</tr>
<tr>
<td></td>
<td>Counselling</td>
<td>18%</td>
<td>2000</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3 months</td>
</tr>
</tbody>
</table>

• Motivators for not taking the vaccine

- Aversion to vaccine: 20%
- HCP did not support vaccination: 19%
- Girls too young: 7%
- Long term coverage: 7%
- Others: 13%
- Vaccine too new: 30%
- Vaccine not safe: 4%
What can be done?

Ensure healthcare workers are well educated on vaccine benefits vs. risks

Promote transparency and accountability in vaccine decision making

Tell stories – *recall and anchor*
- Provide resources
- Explain evidence
- Be credible
- Be opportunistic
- Be convincing
- Be caring

- Build trust
- Address concerns and conspiracies
- Be transparent and clear

Adapted from Butler. Contrasting the anti-vaccine movements. Presented at ESCMID 2013, Prague
Main determinant in HPV vaccination

HCP active recommendation

Table 4
Predictors of HPV vaccination for all respondents ($N = 530$).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>$p$-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Student status (yes versus no)</td>
<td>2.79</td>
<td>1.53–5.09</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Personal importance of vaccine (very important versus other)</td>
<td>7.69</td>
<td>4.22–14.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Physician discussion and recommendation (yes versus no)</td>
<td><strong>93.50</strong></td>
<td>39.10–223.60</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Rosenthal et al. Vaccine 2010
‘Decision scale’ for the implementation of vaccination programmes

Risk (theoretical) of rare adverse events

Evidence of vaccination benefits

This also does not enhance confidence in vaccines and vaccination.

Vaccine “A” from company “A”

Vaccine “B” from company “B”
“Test everything; hold fast what is good”

Saint Paul

First Letter to Thessalonians, 5, 21