Update vaccinatiebeleid anno 2019

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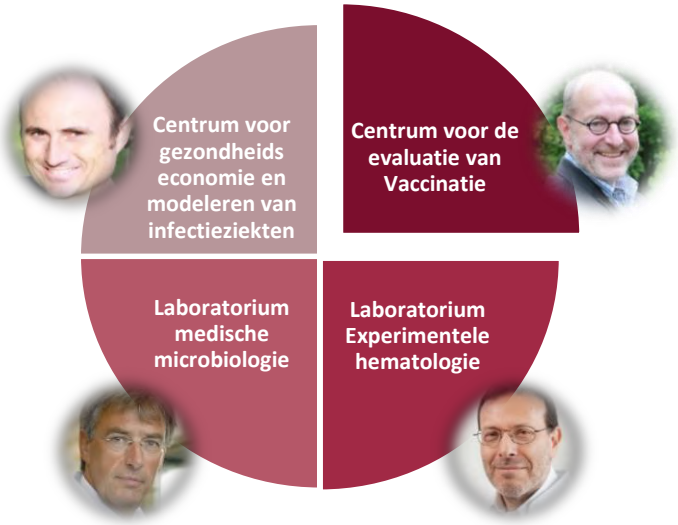
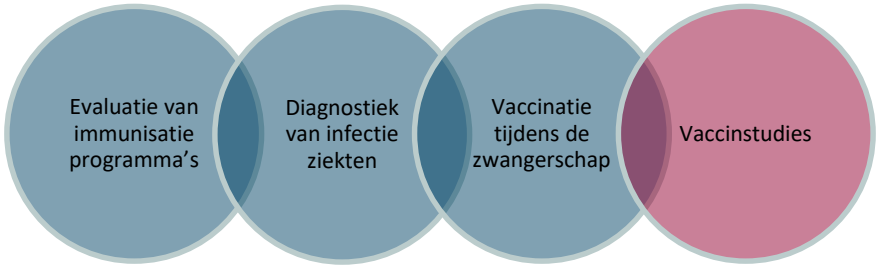
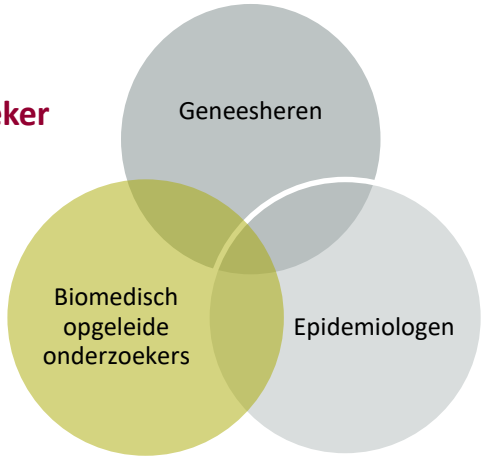
UAntwerpen

VAXINFECTIO





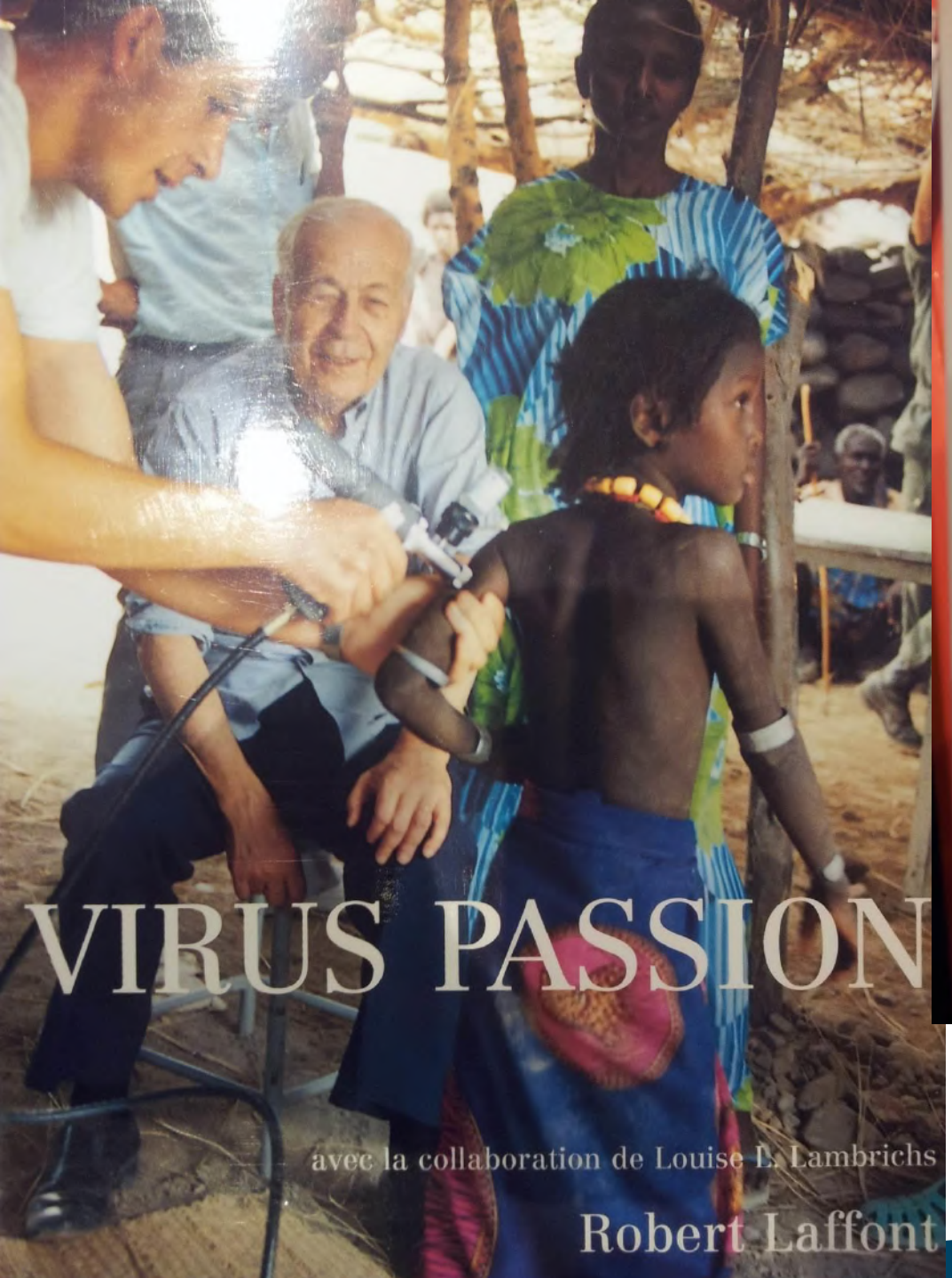
Onderzoekers



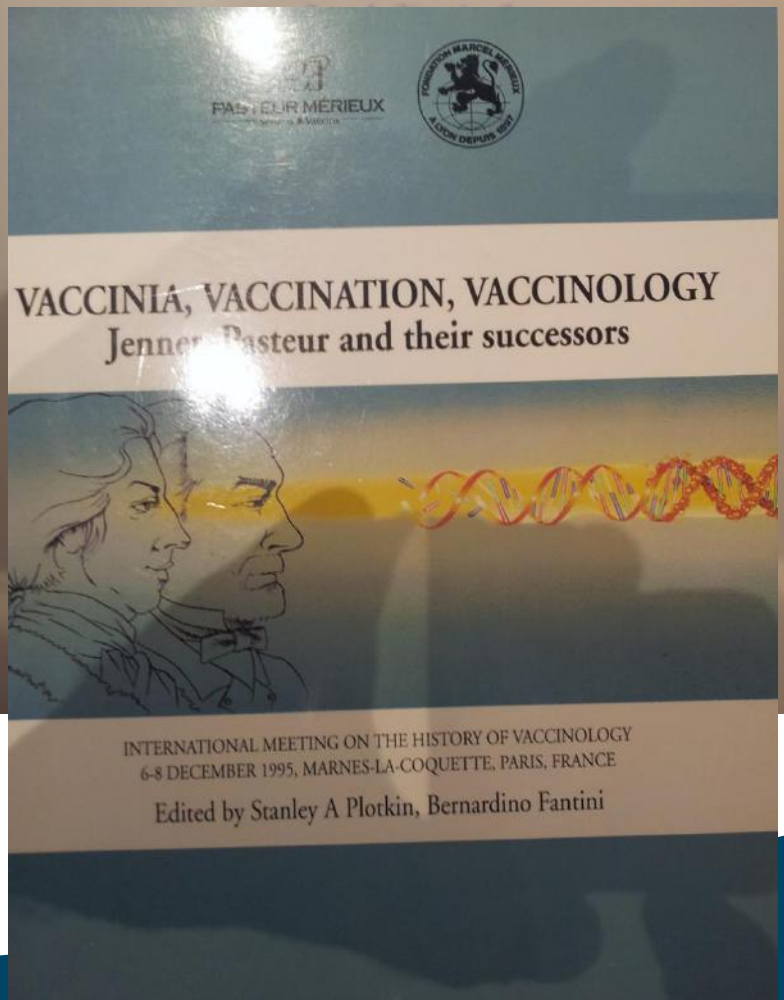
Inhoud en doelstellingen

- Historiek
- Samenstelling van vaccins - polio
- Soorten vaccins/ antigenen
- Concept ‘groepsimmuniteit’
- Nieuwe vaccins
- Vaccin-toediening
- Vaccinatieschema België en Vlaanderen

Enkele mijlpalen in de vaccinologie!



L'AVENTURE DE LA VACCINATION



“variolation”

- Eerste melding van een soort vaccinatie was rond de 7° eeuw:
  - Boedisten dronken slangengif met de bedoeling immuniteit te verkrijgen tegen gif (oraal vaccin!)
- Eerste melding van ‘variolisatie’ vinden we in de 16° eeuw (Brahmin-kaste bij de Hindus, Indië):
  - Men nam gedroogde pus van pokken-pustels en bracht dit in in de huid van de ‘gevaccineerde’, om deze zodoende te immuniseren tegen de pokken.
  - Dit bleek te werken maar 2 à 3% overleed na interventie (tegen 10% na de ziekte)

“variolation”

In 1742 verschijnt in “The golden mirror of medicine” een Chinese tekst met de beschrijving van vier verschillende vormen van inoculatie tegen pokken die **sinds 1695** plaatsvinden in China:

- verkruimelde korstjes van pokken-pustels werden in katoen gewikkeld en in de neus gestopt,
- verkruimelde korstjes werden in de neus geblazen,
- de onderkleding van een kind dat ziek was, werd een aantal dagen onder een gezond kind gelegd,
- een stuk katoen wordt ingesmeerd met de vesikel-inhoud van een pokken-pustel en in de neus gestopt.

= nasale vaccinatie “avant la lettre”!

“variolation”: overwaaien naar het Westen!

- Lady Montagu was zelf het slachtoffer geweest van pokken (1715): “she was left without eyelashes and a deeply pitted skin”. Haar broer was eraan overleden.
- “les filles qui n’étaient plus mariables par leur laideur repoussante!”
- = zeer gedreven voorstander van pokkenvariolatie! (cfr patiëntenlobby)
- Echtgenote van de Britse ambassadeur in Constantinopel, waar ze in contact kwam met de variolatietechniek (zoontje gevaccineerd in Turkije)

“variolation”: overwaaien naar het Westen!

- 1721: Eenmaal in Engeland, dochter gevaccineerd (publiekelijk!)
- 1721: kinderen van de koning van Engeland worden gevarioliseerd!
  - Na eerst de techniek toe te passen op 6 ter dood veroordeelden (3 mannen en 3 vrouwen), en 5 weeskinderen!
- 1721-1723: 474 mensen geïnoculeerd (9 overlijdens)
- “démonstration de courage” (Voltaire)
- Dure techniek: 3000€
- Aanleren aan derden: 12.000€

1746: “London smallpox and inoculation hospital”

1752-1768: 100-1000 inoculaties per jaar!

1754: positief advies van de College of Physicians (zolang isolatie was voorzien)

1750: Frankrijk – **eerste anti-vaccin bewegingen**! Ook in de UK. Naast intellectuele beweging ten voordele van de variolisatie!

1767:

- Robert Sutton: ipv nasaal – huidprikje!
- 400 inocualties per dag!

The Cow-Pock — or — *the Wonderful Effects of the New Inoculation!* — Vide. the Publications of y Anti-Vaccine Soc

variolation

UK, 1774: a cattle breeder, Benjamin Jesty:

- Himself immune to smallpox after contracting cowpox from his herd
- To avoid a smallpox outbreak he deliberately inoculated his wife and two children with cowpox. And he succeeded!
- He knew that milkmaids seemed protected from smallpox after they had contracted cowpox!

variolation

UK, 1774: a cattle breeder, Benjamin Jesty:

- Without being a scientist he observed that cowpox and variola/smallpox are related (orthopox) viruses
- “And that immunity to a moderately harmless disease could confer protection against another far more dangerous disease!” = first real vaccination!
- Also the smallpox vaccine virus ‘vaccinia’ is a related orthopox virus

Jenner, medische praktijk in Berkeley (1749-1823)

3 belangrijke observaties:

- er waren mensen bij wie de inoculatie met pokkenvirus niet ‘pakte’. Ze ontwikkelden geen papels of andere milde tekens.
- nochtans hadden veel van deze mensen wel cowpox opgelopen (vaccinia’) door koeien te melken die aan cowpox leden.
- Cowpox is overdraagbaar op de mens en is goedaardig!

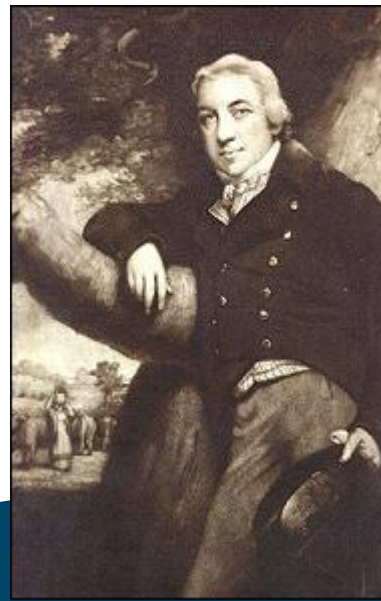
“The cow pox protects the human constitution from the infection of the smallpox” (1798) – boek want publicatie geweigerd!

Jenner, medische praktijk in Berkeley (1749-1823)

- Hij wou mensen ‘vaccineren’ met de inhoud van koepokkenpustels om vervolgens te zien of zij nog vatbaar waren voor pokken.
- Toeval wil dat er rond die periode er een epidemie was van vaccinia in een boerderij vlakbij zijn praktijk.

De verantwoordelijke koe is Blossom (Gloster ras), een van de slachtoffers, Sarah Nelmes.

De geïnoculeerde is een jongetje van 8 jaar, James Phipps. Hij heeft de eerste dagen na de vaccinatie via arm-to-arm transfer wat last, axillair aan de kant van de inoculatie, maar voorts geen probleem.

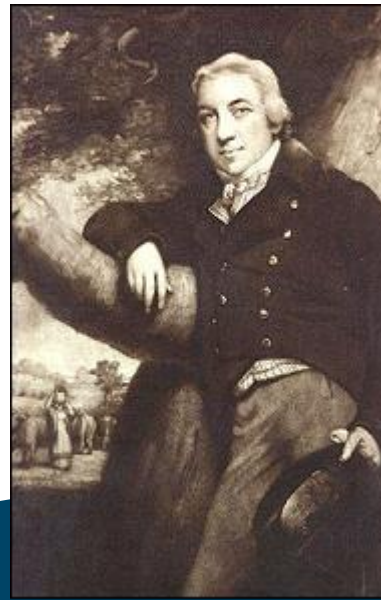


Jenner, medische praktijk in Berkeley (1749-1823)

- Wat later zal Jenner James inoculeren met het pokkenvirus. (= human challenge study)
- James doet een matige reactie, zonder enig probleem. Dit herhaalt Jenner nog een paar maanden later, met hetzelfde resultaat.

Phipps had immuniteit verkregen tegen pokken.

Het woord vaccinatie (vacca = koe) heeft eerst het woord inoculatie vervangen enkel voor deze interventie, later op voorstel van Pasteur voor alle vaccins.



World's Greatest 1000 Creation Scientists 2000

LOUIS PASTEUR

Medicine • Chemistry • Physics
Bacteriology • Immunology

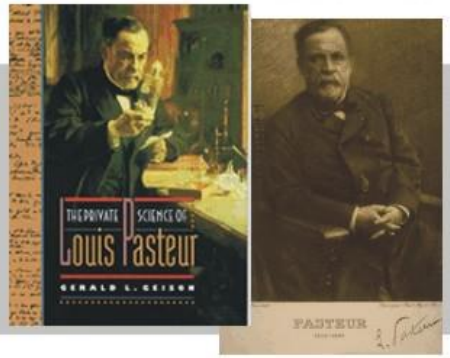
1822 - 1895

"Greatest biologist of all time"

- **Contributed more to the saving of human lives than any other man**
- **Germ theory of disease**
- **Law of Biogenesis**
  Disproved "spontaneous generation"
- **"Pasteurization" of food**
- **Developed vaccines for:**
  Rabies - Diphtheria - Anthrax *and more*
- **Opposed Darwinism**

"Here was a life, within the limits of humanity, well-nigh perfect. He worked incessantly. He went through poverty, bereavement, ill health and opposition. He lived to see his doctrines current over all the world. Yet here was a man whose spiritual life was no less admirable than his scientific life."

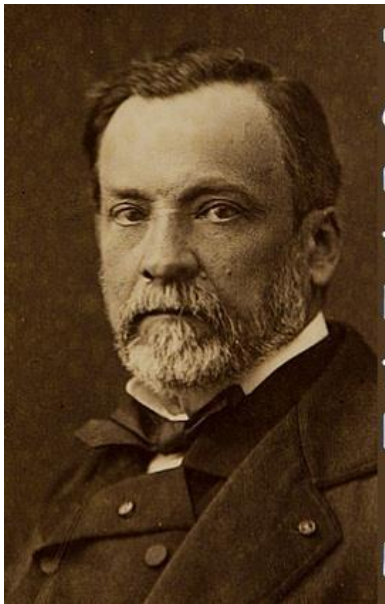
– Stephen Paget, English surgeon



"Could I but know all, I would have the faith of a Breton peasant woman."

"The more I study nature, the more I stand amazed at the work of the Creator."

– Louis Pasteur

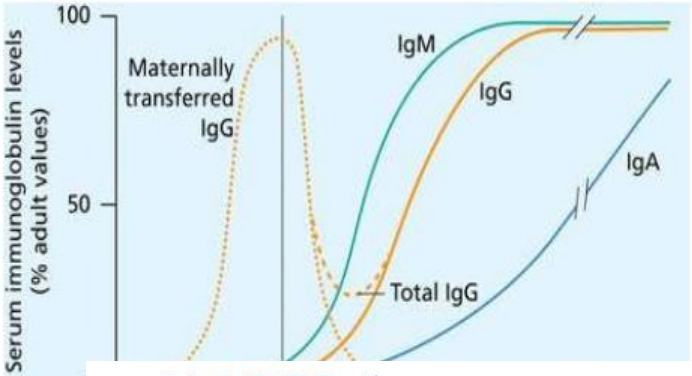


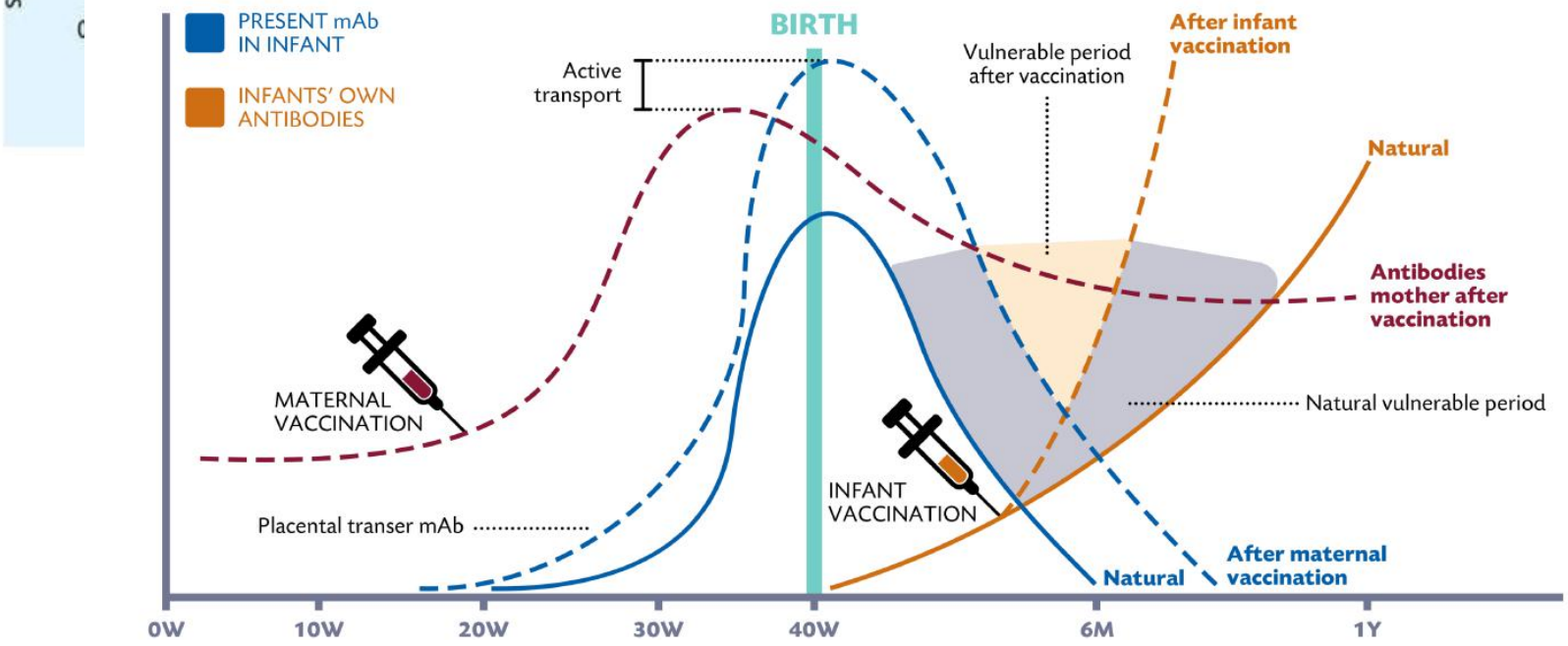
"When I approach a child, he inspires in me two sentiments; tenderness for what he is, and respect for what he may become."

Louis Pasteur

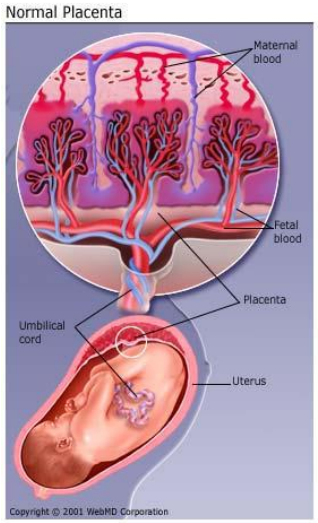
Pasteur (1822-1895)

- Worked on the attenuation of the chicken cholera bacterium
- Introduced the **concepts of attenuation** – modification through passages/heating/… - renewed virulence – the need to replace person to person vaccination with something safer, less likely to transmit other diseases.
- developed a anthrax vaccine for cattle!
- Developed a rabies vaccine for humans!


Serum immunoglobulin levels (% adult values)
100
50
Maternally transferred IgG
IgM
IgG
IgA
Total IgG


PRESENT mAb IN INFANT
INFANTS' OWN ANTIBODIES
BIRTH
Active transport
Vulnerable period after vaccination
After infant vaccination
Natural
Antibodies mother after vaccination
MATERNAL VACCINATION
Natural vulnerable period
INFANT VACCINATION
Placental transer mAb
Natural
After maternal vaccination
0W
10W
20W
30W
40W
6M
1Y

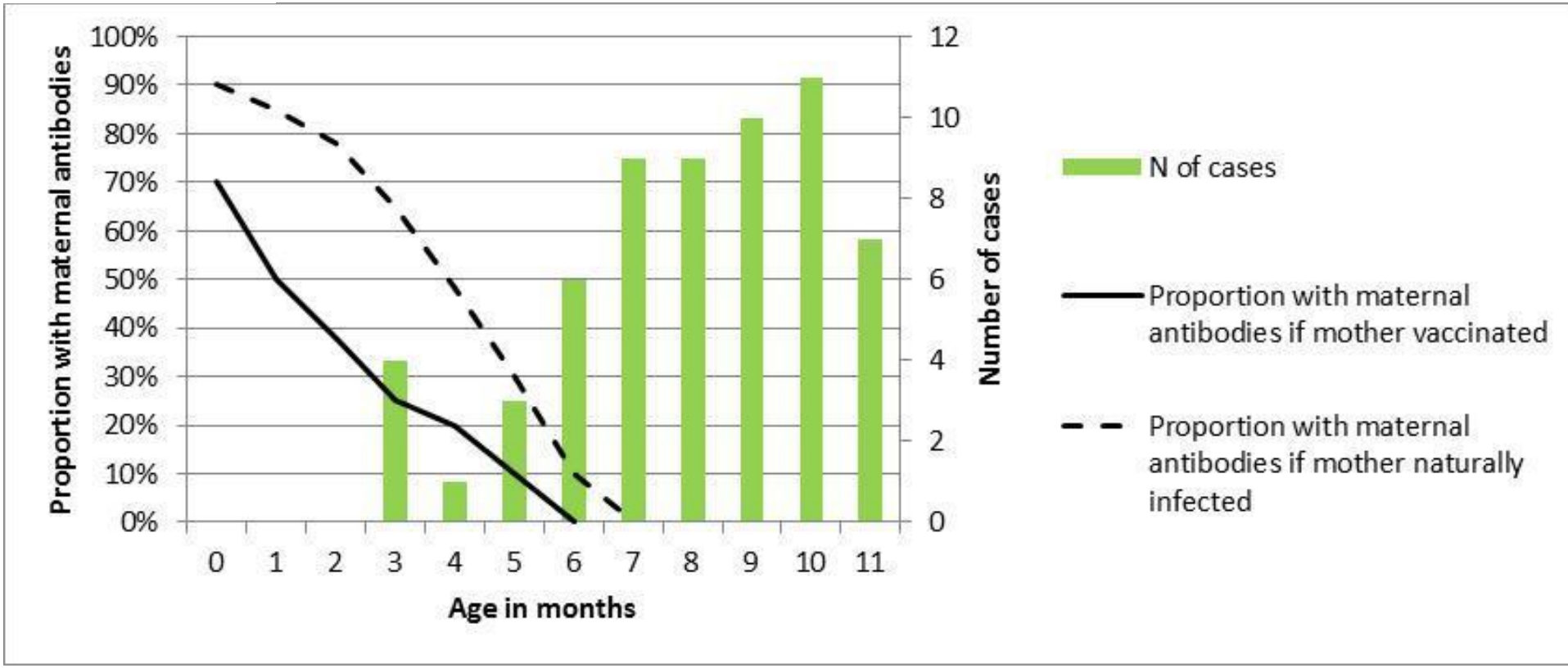
Placental transport



- start at 16 weeks
- 35 weeks: foetal IgG >maternal concentrations
- IgG 1 ratio 1.8:1
- premature babies receive fewer antibodies

(Leineweber B et al. PIDJ 2004; Linder N et al. Vaccine 2004)

Proportie zuigelingen (≤ 12 m) met maternale mazelen antistoffen en aantal gevallen van mazelen in 2011 uitbraak (≤ 12 m of age)



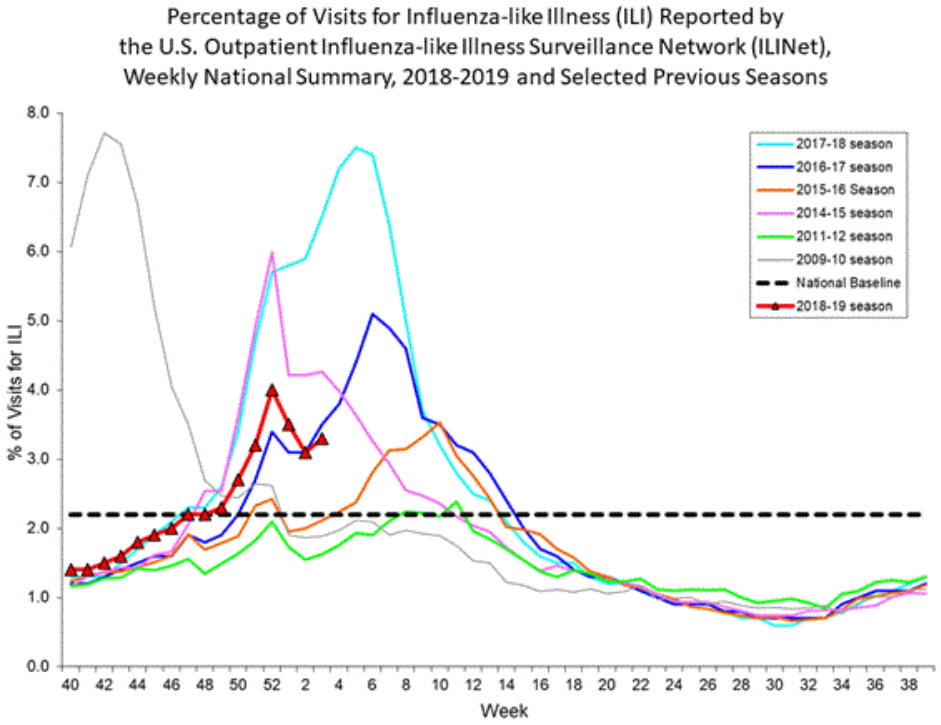
Solid line: proportion with measles antibodies in children from vaccinated mothers
Dotted line: proportion with measles antibodies in children from naturally immune mothers (Leuridan, Vaccine 2012)
Columns: number of measles cases (N=60) by age in months during the 2011 measles outbreak in Belgium

Vaccinatie tijdens de zwangerschap: het heden

±2009: aanbeveling om een influenza (griep) vaccin te geven tijdens de zwangerschap

Risico voor de zwangere vrouw
- Ernstigere griep symptomen
- Hoge koorts
- Ademhalingsproblemen
- Sterfte

Risico voor het ongeboren kind
- Miskraam
- Doodgeboorte
- Prematuriteit
- Geboorten afwijkingen



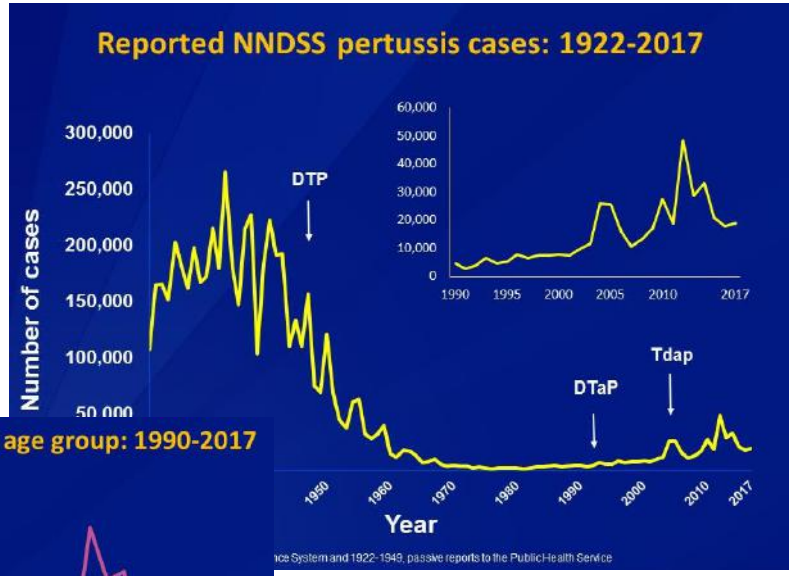
Pertussis

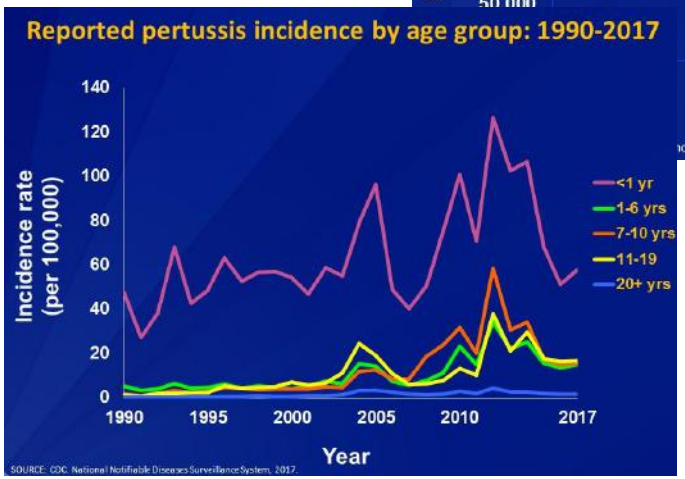
Vaccinatie tijdens de zwangerschap: het heden

±2011: aanbeveling om een kinkhoest vaccin te geven tijdens de zwangerschap

Risico voor de zwangere vrouw
- Ernstige hoestbuien
- Ademhalingsproblemen

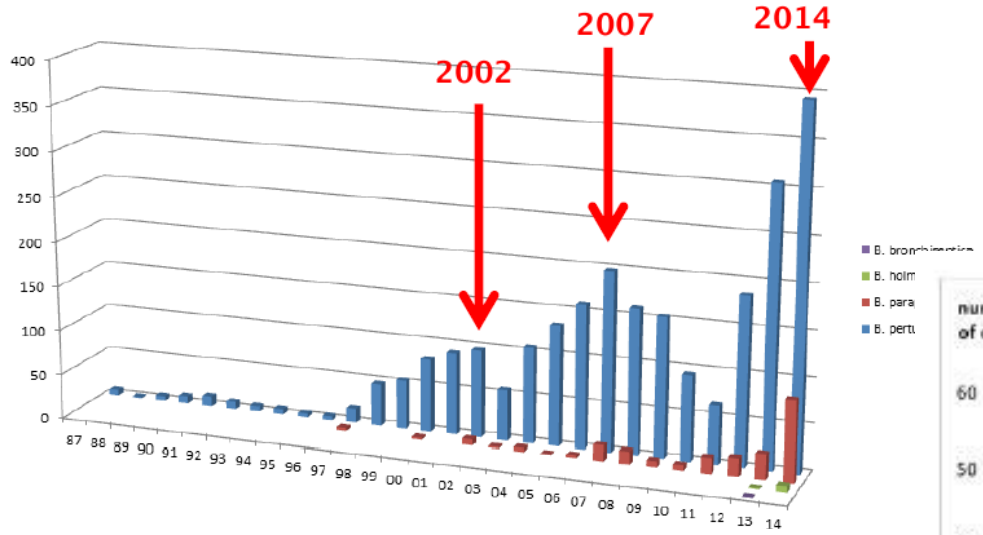
Risico voor het pasgeboren kind
- Ademhalingsproblemen, zuurstofgebrek door ernstige hoestbuien
- Hersenletsels
- Overlijden

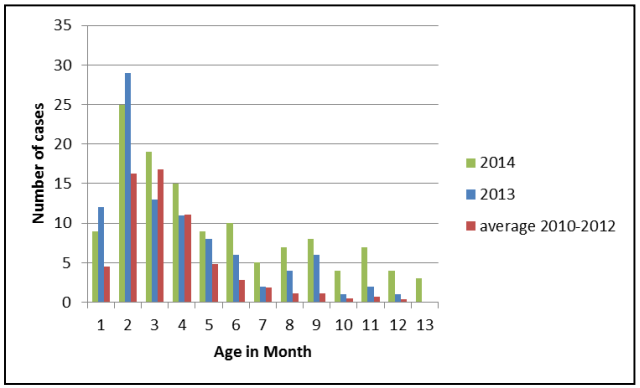




Epidemiology of pertussis

Cyclus installation? An outbreak/5 to 7 years?





Nationaal referentie laboratorium
Met dank aan Prof Dr Denis Pierard en Dr Kris Huygen

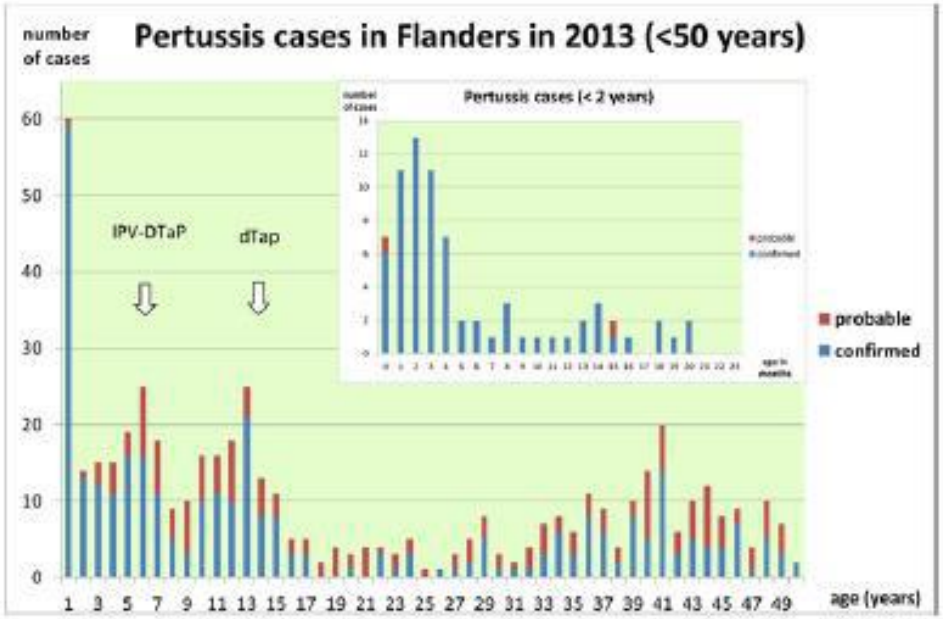
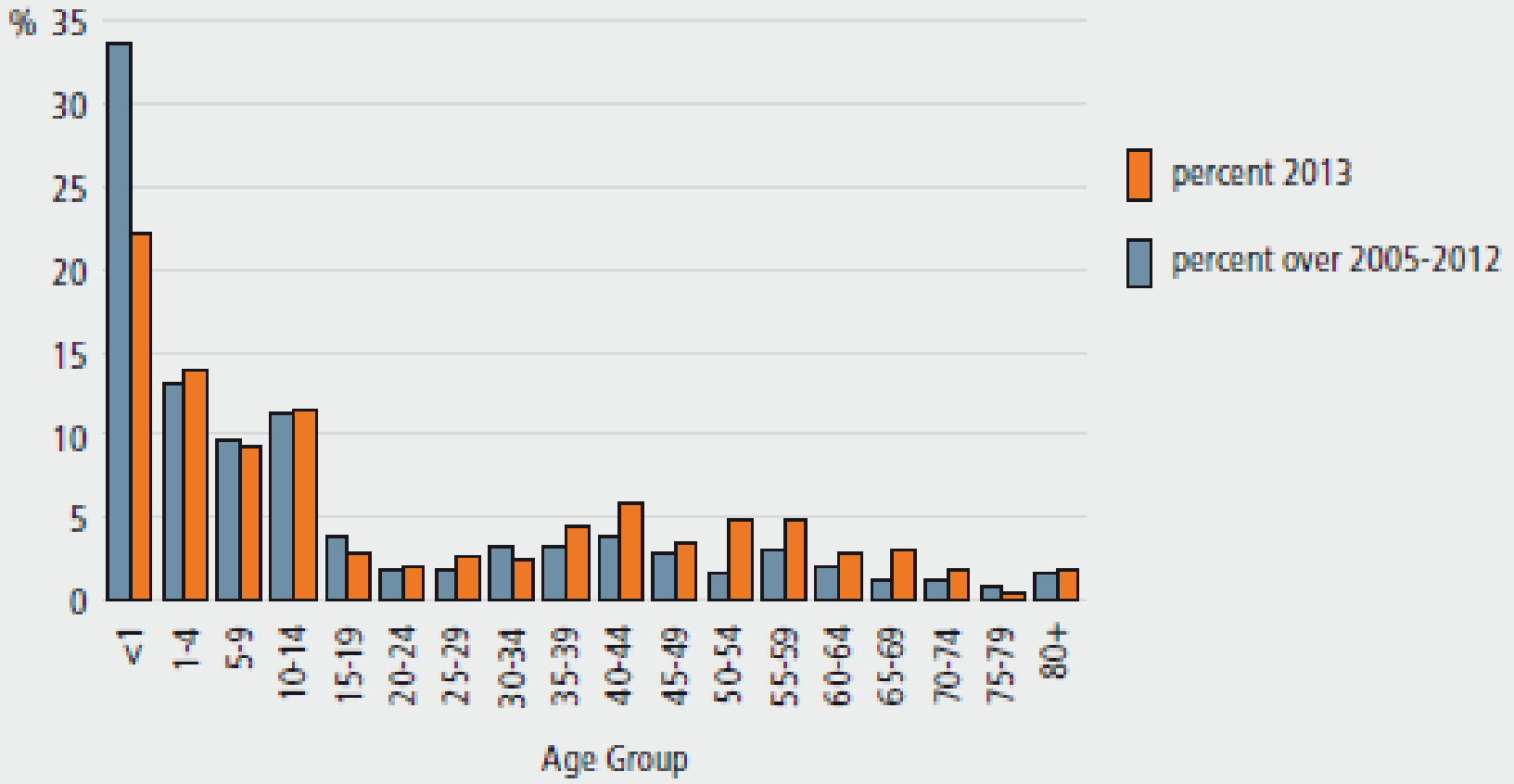


Figure 2: Age distribution of notified pertussis cases in 2013

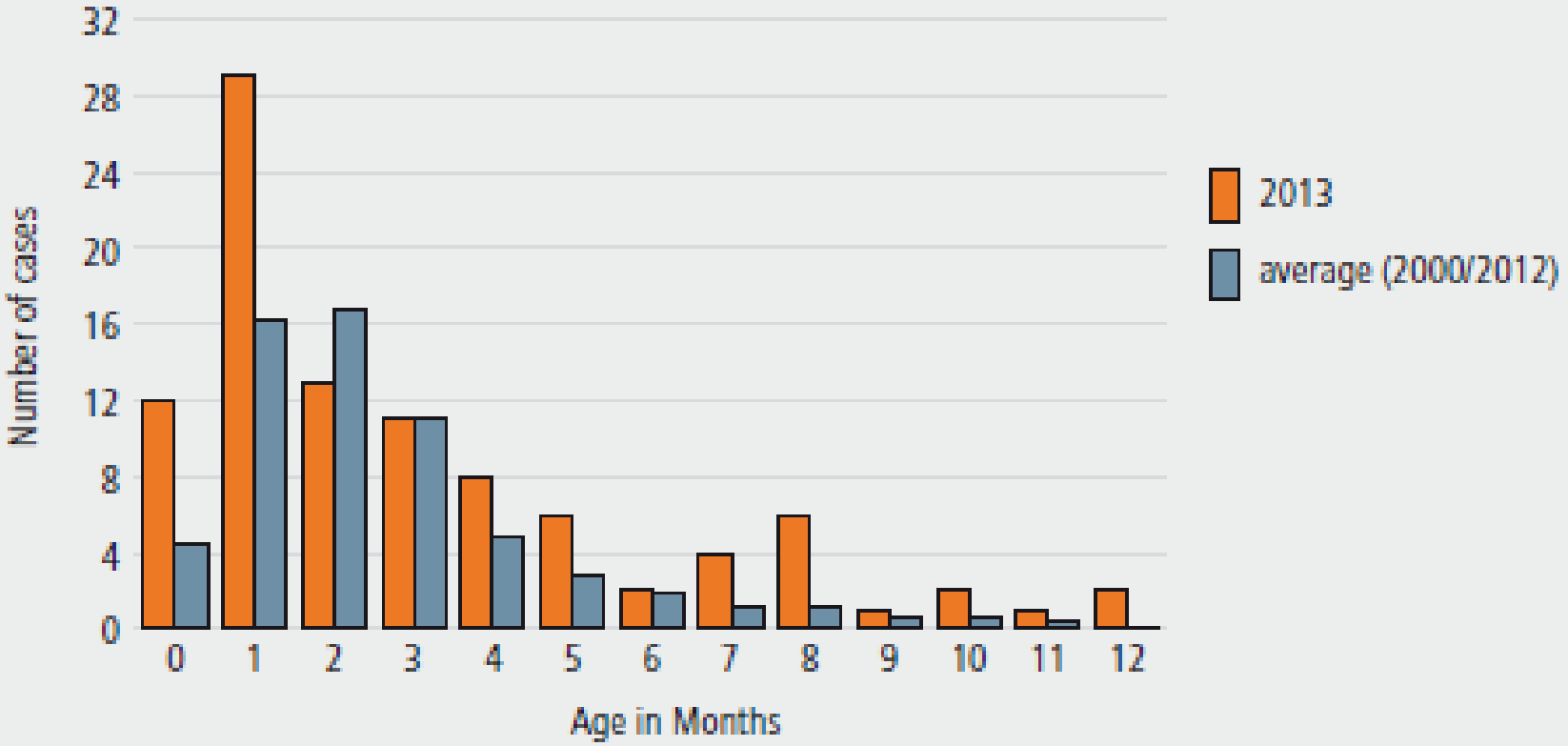
Sabbe M. Grammens T, Braeye T, Bleyenheuft C, Quoilin S et al. Infectieziekten bij kinderen, die voorkomen kunnen worden door vaccinatie. Jaarrapport 2014, in press. Wetenschappelijk Instituut Volksgezondheid, Brussel. 2015. D/2015/2505/05.

Figuur 5 | Relatieve leeftijdsverdeling van de gevallen van kinkhoest, in percentage, België, 2005-2012 en 2013, België (Netwerk Peillaboratoria WIV-ISP)



"infectieziekten bij kinderen, die voorlomen kunnen worden door vaccinatie" – WIV-ISP – jaarrapport 2013

Figuur 4 | Aantal gevallen van kinkhoest bij kinderen jonger dan 1 jaar, per levensmaand, 2010-2012 en 2013, België (Nationale referentiecentra UZ Brussel en WIV-ISP)



"infectieziekten bij kinderen, die voorlomen kunnen worden door vaccinatie" – WIV-ISP – jaarrapport 2013

Effectiveness on hospitalisation, caused by pertussis disease among young infants

Timing of maternal immunisation	VE (95% CI)
At least 7 days before birth	91% (84% to 95 %)
At least 28 days before birth	91% (83% to 95%)
7 to 27 days before birth	91% (70% to 96%)
0-6 days before or 1-13 days after birth	38% (-95% to 80%)

Amirthalingam et al Lancet 2015

Zwangerschapsvaccinatie aanbevelingen in België

Influenza vaccin

Zwangere vrouwen worden aanbevolen om zich te laten vaccineren tijdens het griepseizoen ongeacht de fase van de zwangerschap.

Kinkhoest vaccin

Zwangere vrouwen worden aanbevolen zich te laten vaccineren bij elke zwangerschap voorkeur tussen 24-32 weken, ongeacht of de vrouw voordien een herhalingsinenting kreeg.

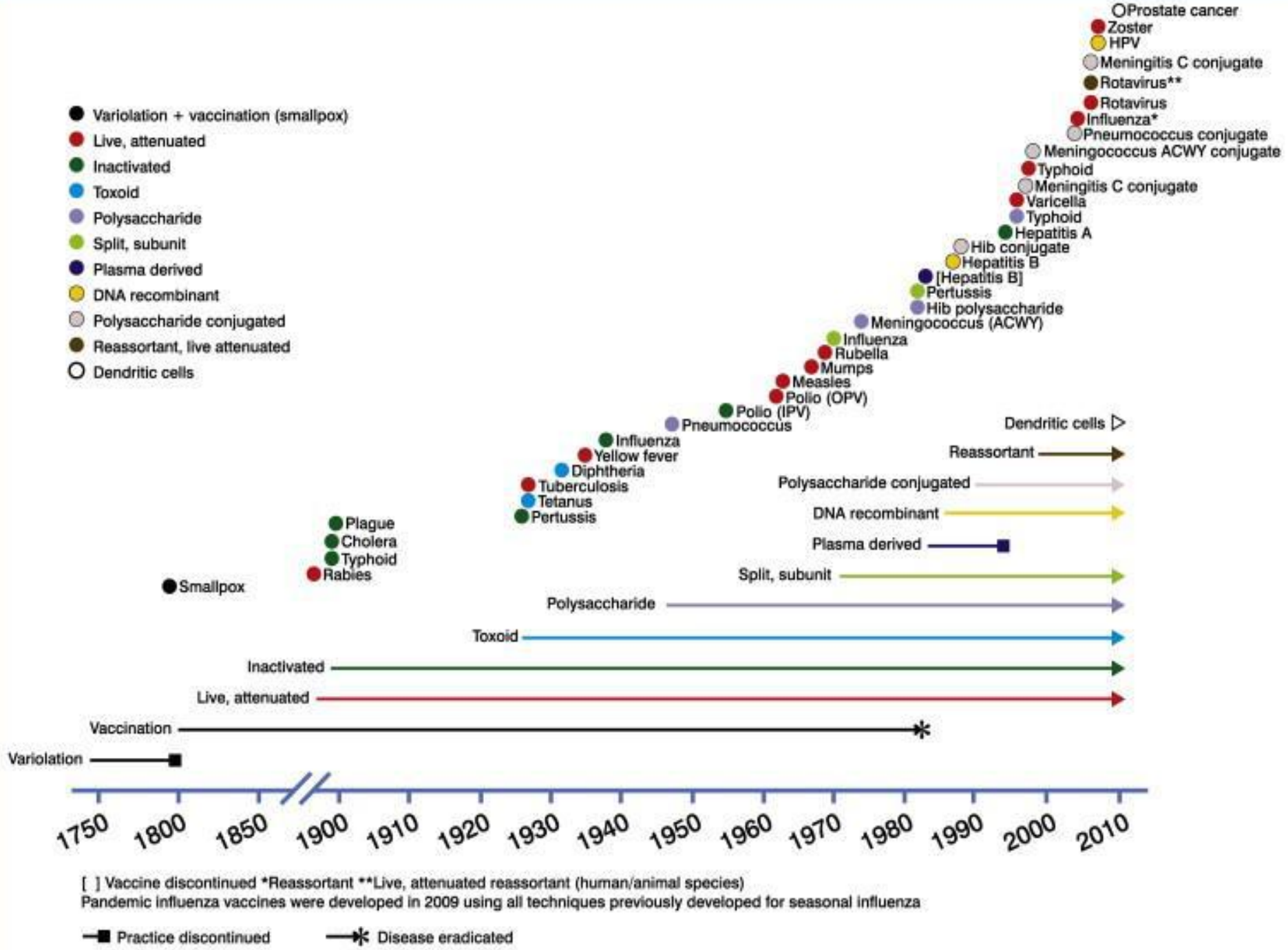
- Indien de vaccinatie niet tijdens de zwangerschap wordt gegeven, wordt ze zo snel mogelijk postpartum toegediend.

Vaccinatiegraad zwangere vrouwen

Vaccinatiegraad kinkhoest- en griepvaccinatie tijdens de zwangerschap, Vlaanderen 2016

Vergelijk moeders bevallen in 2016 vs 2014

Vlaanderen	jonge moeders	Moeders jonge kinderen*
Bevallen in	2016	2014
Kinkhoest	69.3	57.6
Griep	47.2	15.9



[ ] Vaccine discontinued *Reassortant **Live, attenuated reassortant (human/animal species)
Pandemic influenza vaccines were developed in 2009 using all techniques previously developed for seasonal influenza

Practice discontinued Disease eradicated

Wat is een vaccin?

= een product dat actieve immuniteit produceert, waardoor het individu beschermd is tegen ziekte of infectie

Hoe werkt een inenting ?

Doel van vaccinatie

Opwekken immunologisch antwoord

- antigen-specifiek

De gevaccineerde beschermen

- tegen infectie met een ziektekiem
  - transmissie van de ziektekiem is uitgeschakeld
- tegen ziekte door de ziekte kiem
  - transmissie is nog mogelijk
- tegen aspecten/symptomen van de ziekte
  - De ziektekiem kan nog steeds ziekte veroorzaken

Voorbeelden?

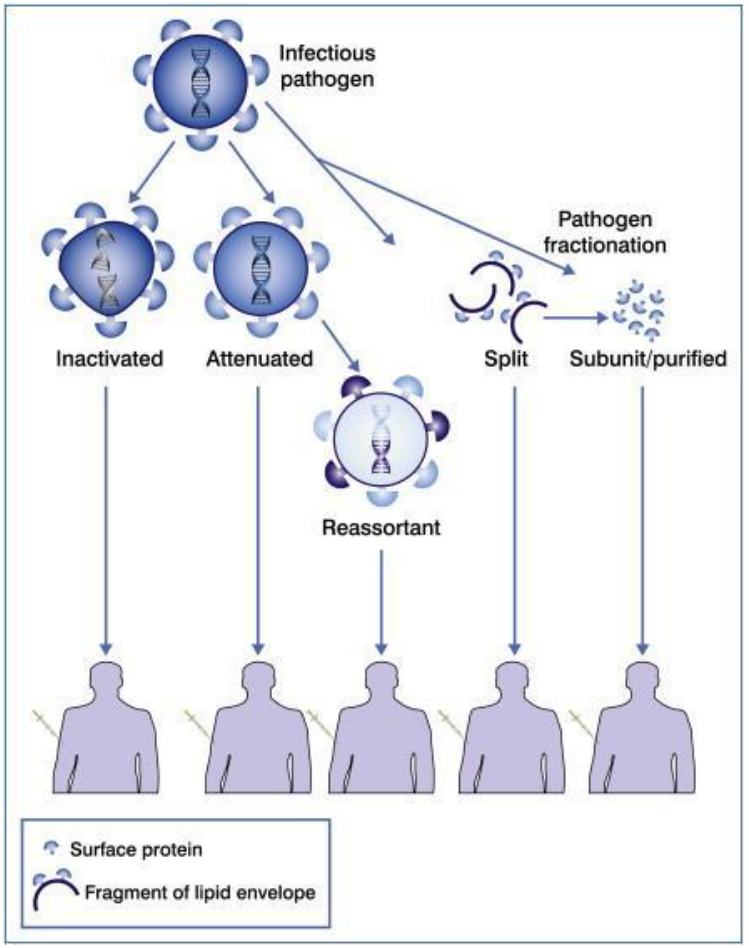
⇒ Pokken, orale polio, mazelen, difterie…

⇒ Pertussis(kinkhoest), geïnactiveerd polio vaccin, influenza

⇒ Influenza

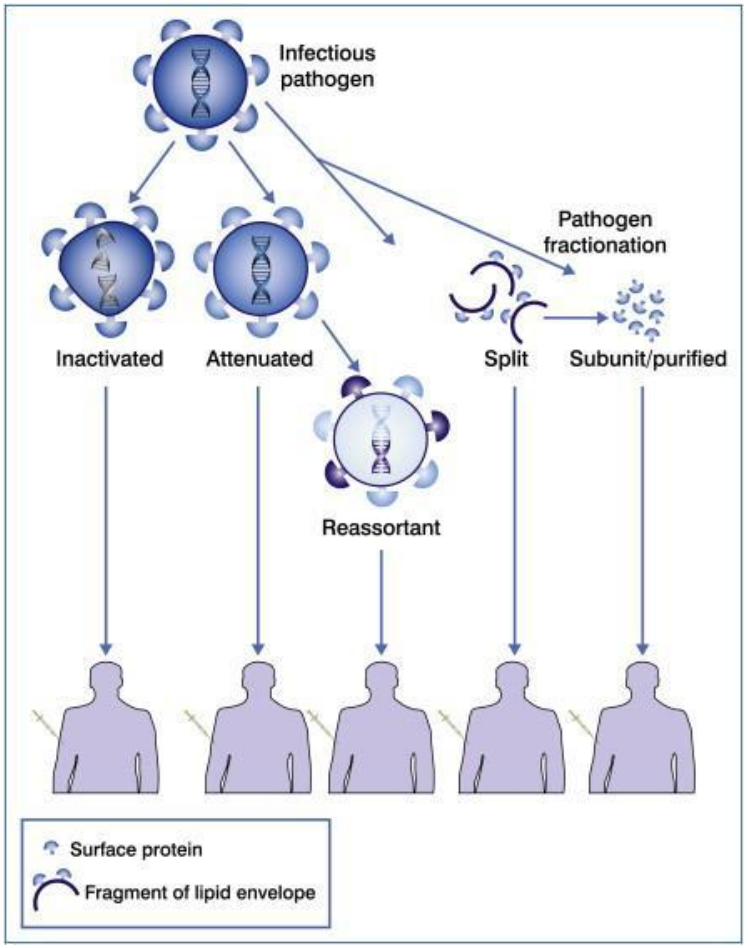
Soorten vaccins

- Geïnactiveerde vaccins
  = de pathogeen (= ziekmakende bacterie of virus) werd gedood/geinactiveerd met behulp van formaline of hitte …
- Levend geattenueerde vaccins
  = door middel van het pathogeen verschillende keren op te kweken *in vitro* of *in vivo* sluipen er mutaties in de ziektekiem, waardoor het zijn virulentie verliest.
- Split vaccins
  = Enkele delen van het pathogeen werden verwijderd
- Subunit vaccins
  = enkel de antigenen die verantwoordelijk zijn voor het opwekken van antilichamen warden behouden in het vaccin



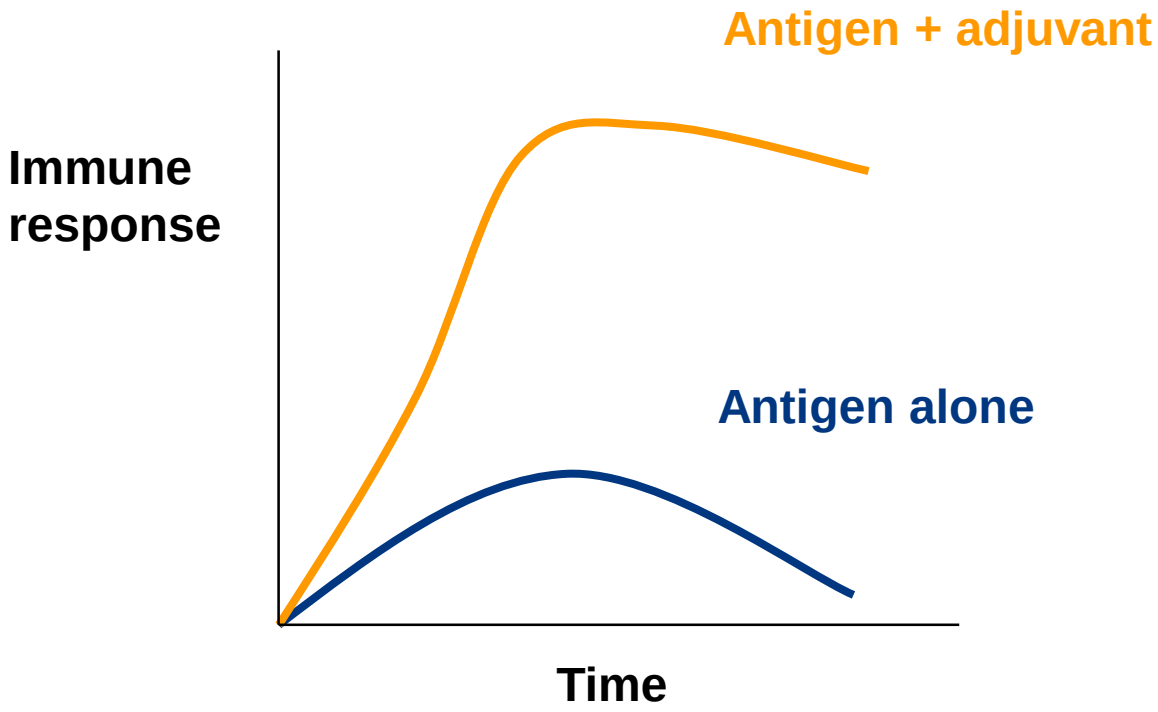
Soorten vaccins

- Geïnactiveerde vaccins
  - + Zeer reactief (herkenning van de volledige ziektekiem)
  - - Meer kans op neveneffecten
  - - Adjuvantia nodig
- Levend geattenueerde vaccins
  - + Zeer reactief (herkenning van de volledige ziektekiem)
  - - De ziekte kiem kan zich nog verder delen
  - - Meer kans op neveneffecten
- Split vaccins
  - + Minder kans op neveneffecten
  - - Adjuvantia nodig
- Subunit vaccins
  - + Minder kans op neveneffecten
  - - Adjuvantia nodig



Why do we need adjuvants ?

Pulendran B, Ahmed A. Cell 2006; 124:849-863



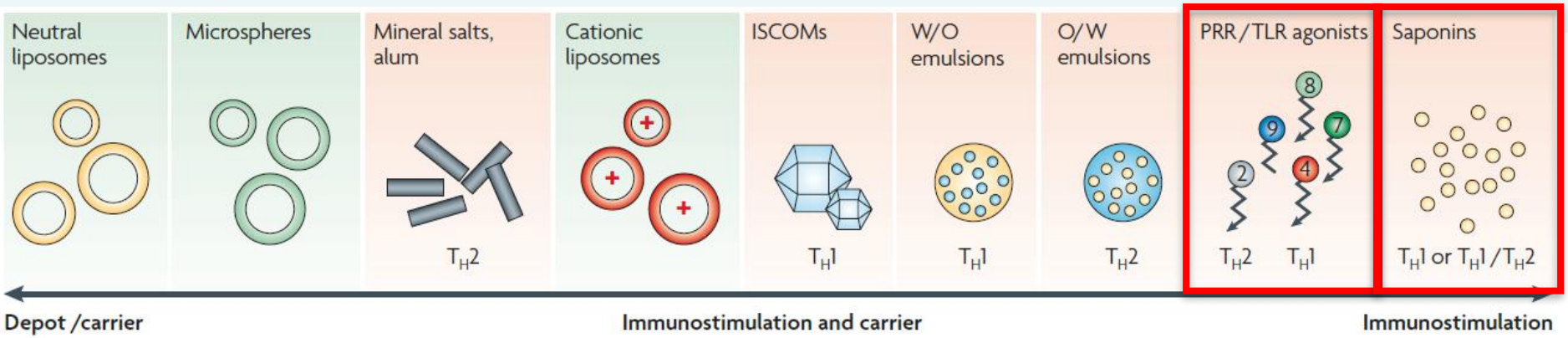
Adjuvants enhance the protection provided by vaccines by promoting rapid, long-lasting and broad immunity

Corradin G, Del Giudice G. Curr Med Chem. 2005;4:185-191

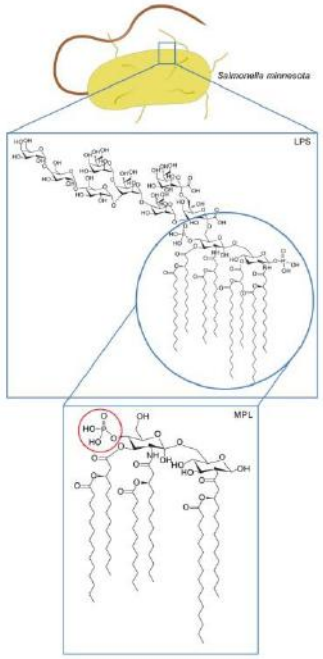
Adjuvantia

- Aluminum salts
  - Most widely used
  - Best documented
  - Used since more than 80 years
- Emulsions: MF59 (oil in water) - FLUAD
- Saponins: QS21
- Endotoxin-based adjuvans:
  - Monophosphoryl Lipid A = lipopolysaccharide from a gram- bacteria
  - AS04 = MPL + Al – FENDRIX
  - AS01; AS02; AS03; ….

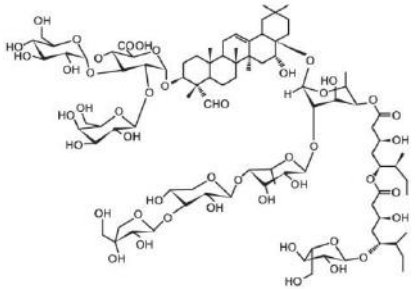
Immunostimulatory adjuvants



MPL
TLR 4 agonist

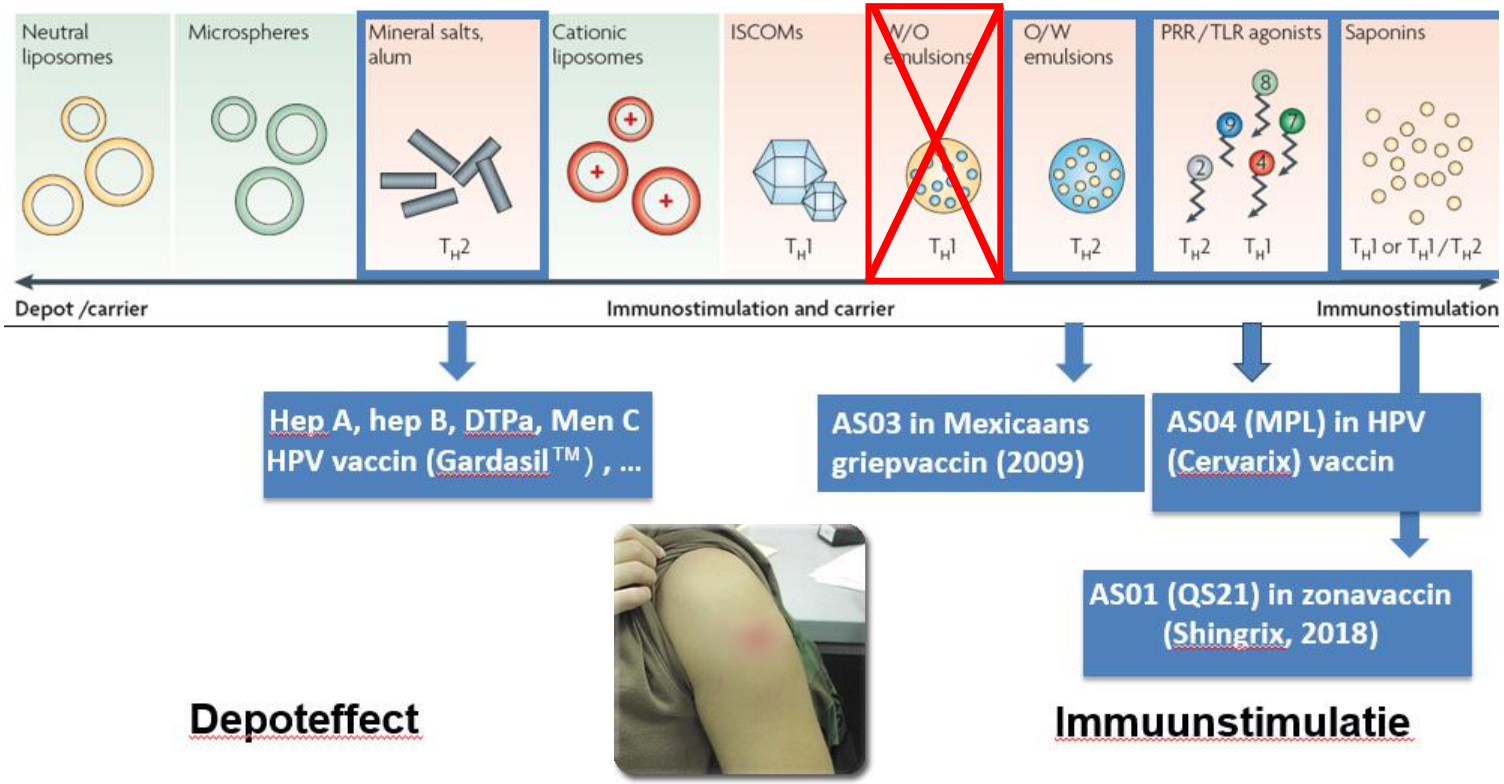


Saponin QS21
from plants



Quillaja Saponaria Molina

Types adjuvantia



Guy. Nat Rev Microbiol 2007; 5: 505-517

Overview of Adjuvant Systems (AS)

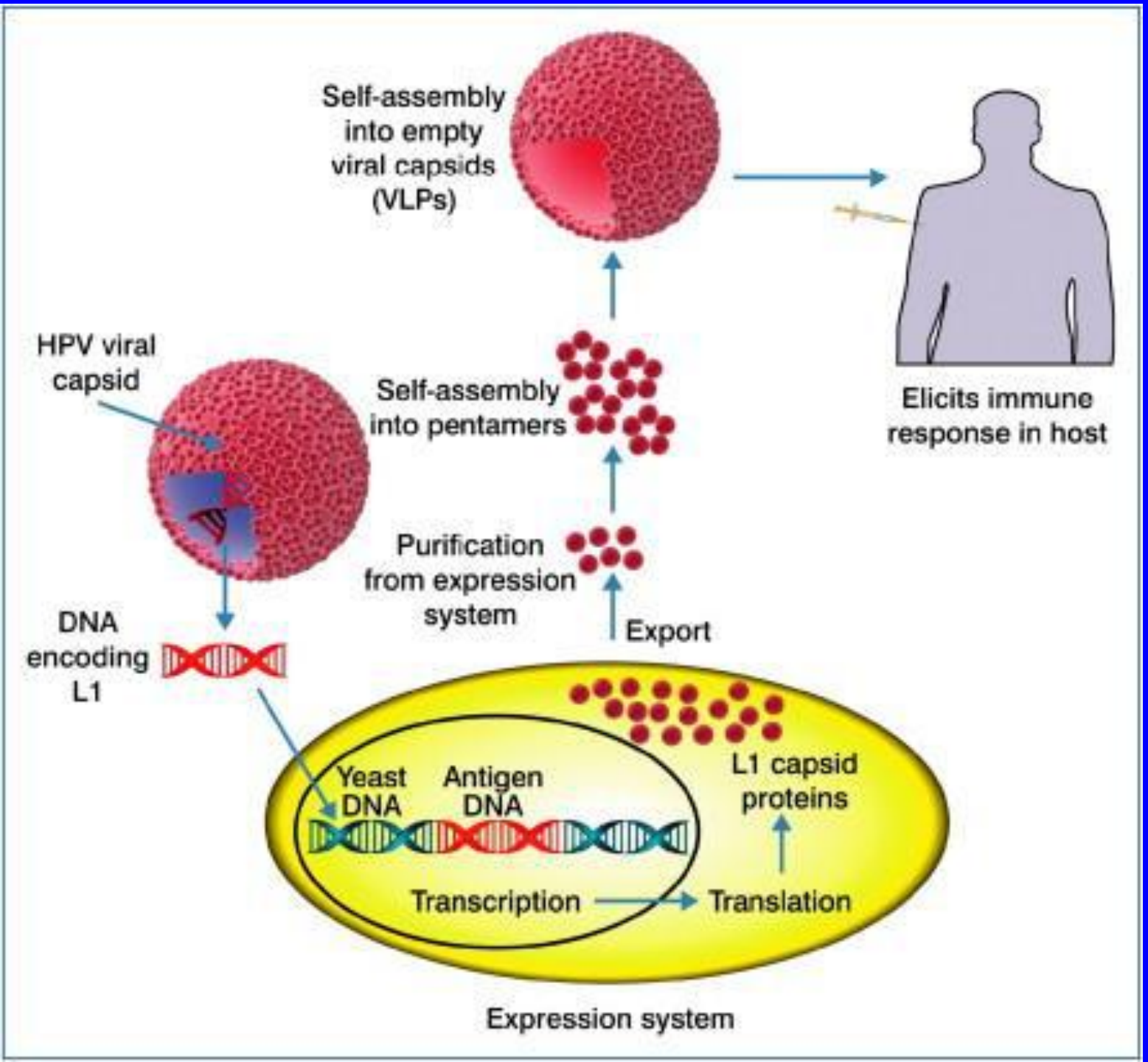
Name	Alum	Lipo somes	O/W emulsion (squalene, α-tocopherol)	TLR 4 agonist (MPL)	Saponin (QS21)	Immune response	Example
AS01		X		X	X	CMI, incl CTL	HIV, TB, VZV
AS02			X	X	X	CMI, incl CTL	Malaria
AS03			X			Humoral Th1	Pandemic influenza (Pandemrix)
AS04	X			X		Humoral, incl B cell memory	HBV (Fendrix) HPV (Cervarix) HSV

Garçon et al. Expert Rev Vaccines 2012; 11: 349-66; Garçon et al. Expert Rev Vaccines 2011; 10: 471-86; Garçon et al. Expert Opin Biol Ther 2011. 11: 667-77

Short peptide antigens

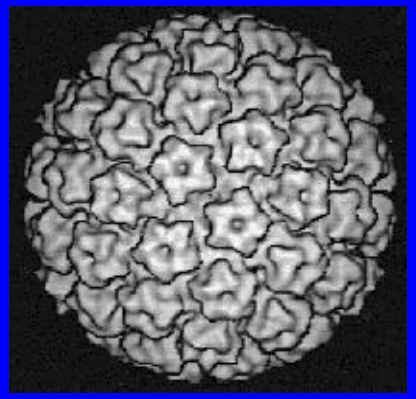
- Produced by recombinant DNA technology
- For viruses like HBV and HPV
- Gene encoding for HBsAg is sequenced and introduced in yeast – cloning of gene for HBsAg in yeast
- HBsAg produced by these cells, split, purified

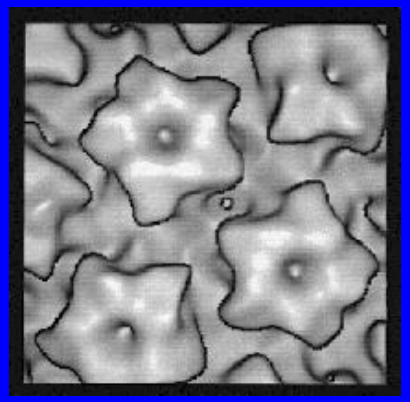
- Aggregate in particulate antigens – VLP
- More immunogenic than soluble proteins
- Need of adjuvans

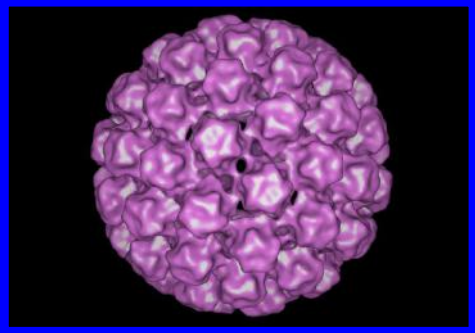

Self-assembly into empty viral capsids (VLPs)
Elicits immune response in host
HPV viral capsid
Self-assembly into pentamers
Purification from expression system
Export
DNA encoding L1
L1 capsid proteins
Yeast DNA
Antigen DNA
Transcription
Translation
Expression system

Human Papilloma Virus (HPV)

- Non-enveloped capsid made-up of 72 pentagonal capsomers







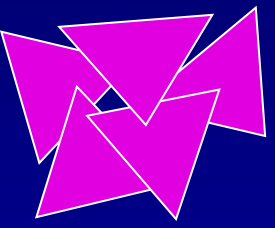
Syrjänen and Syrjänen. Papillomavirus infections in human pathology. Wiley & Sons 2000, Chichester:11-46.

Assembly of Virus-like Particles

Structural model of papilloma VLP

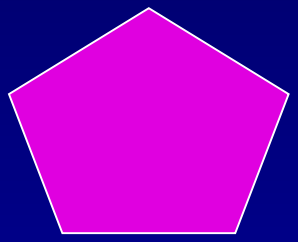
Virus-Like Particle
(~20,000 kD)

L1 proteins
(55 to 57 kD)



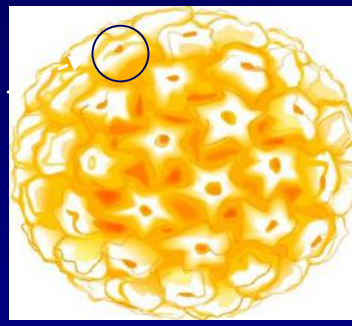
5 x L1

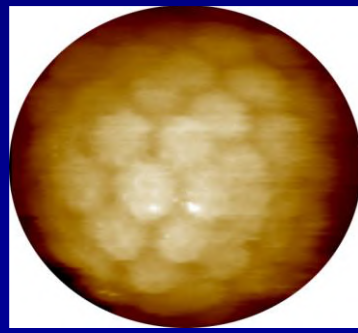
L1 capsomere
(~280 kD)



72
capsomeres

(Atomic force microscopy image of a single VLP)





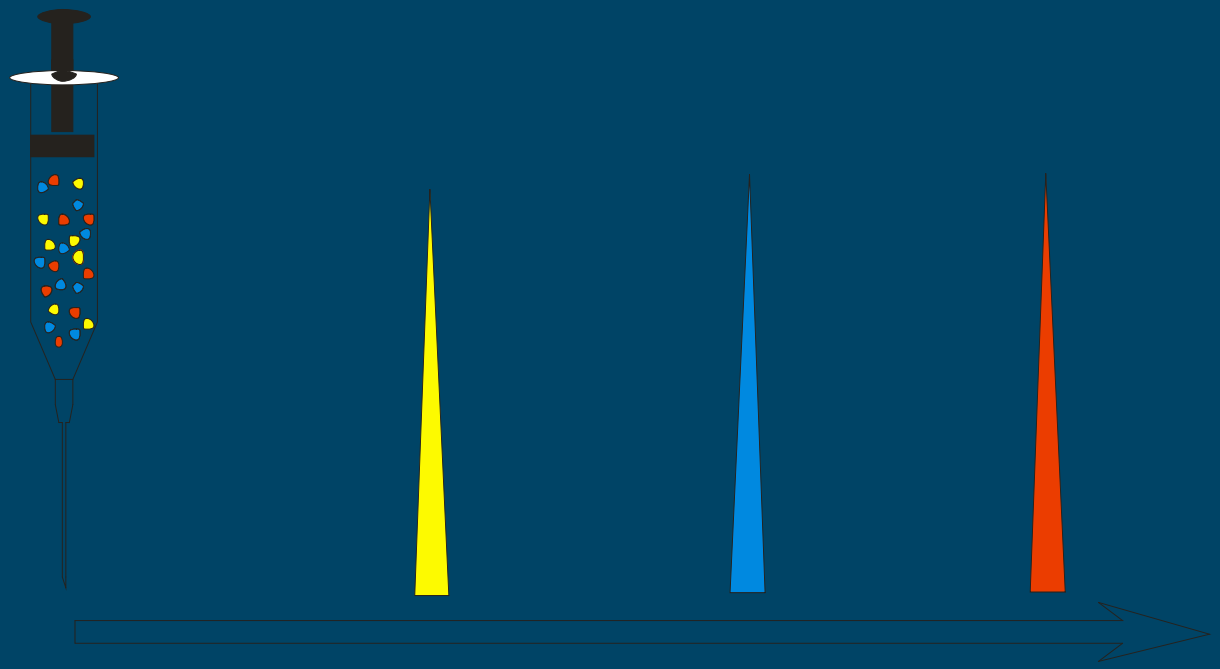
Atomic force miscroscopic picture: Merck Research Laboratories).
1. Kirnbauer et al. Proc Natl Acad Sci USA 1992;89:12180–4. 2.Kirnbauer et al. J Virol 1993;67:6929–36. 3. Galloway. In Current Research on Papillomaviruses. (Ed). C. Lacey. Leeds Medical Information, Leeds University Press, Leeds, 1996:113–9. 4. Brown et al. Virology 1996;222:43–50. 5 Carter et al. Clin Dermatol 1997;15:249–59.

Future vaccines

- Evolution in the way of administration:
  - Mucosal, eatable, ID, inhalation, jetguns, topical applications, …
- Use of new adjuvants
- DNA vaccines
  - Cloning of a gene that codes for a protein able to induce immune response
  - Injection of DNA, incorporation in human cells, expression of the gene, production of the protein, induction of the immune system
  - Human cell is used as a production unit
- Pulsed release of Ag
- Combination vaccines
- Therapeutic vaccines
  - Cancer, allergy, MS, …

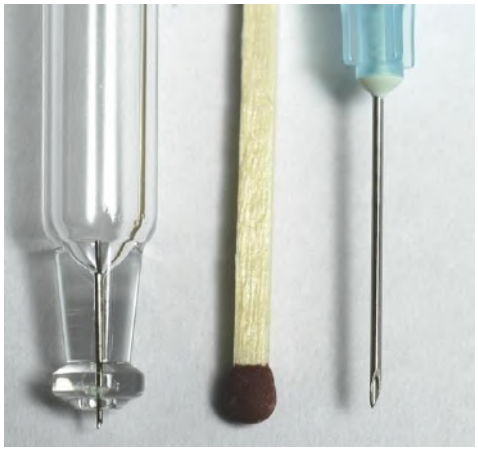
Self-Exploding Microcapsules

single shot vaccination to avoid booster



Soluvia, Becton-Dickinson

ID microneedle
30 G,
1.5 mm length



IM needle
25 G,
16 mm length

Since 2010:

- Soluvia exclusively licensed to Sanofi Pasteur
- Intanza® / Fluzone ® (= Flu vaccine)

VAX-ID – assembled device

3D render

Vaccine 37 (2019) 581–586

Contents lists available at ScienceDirect

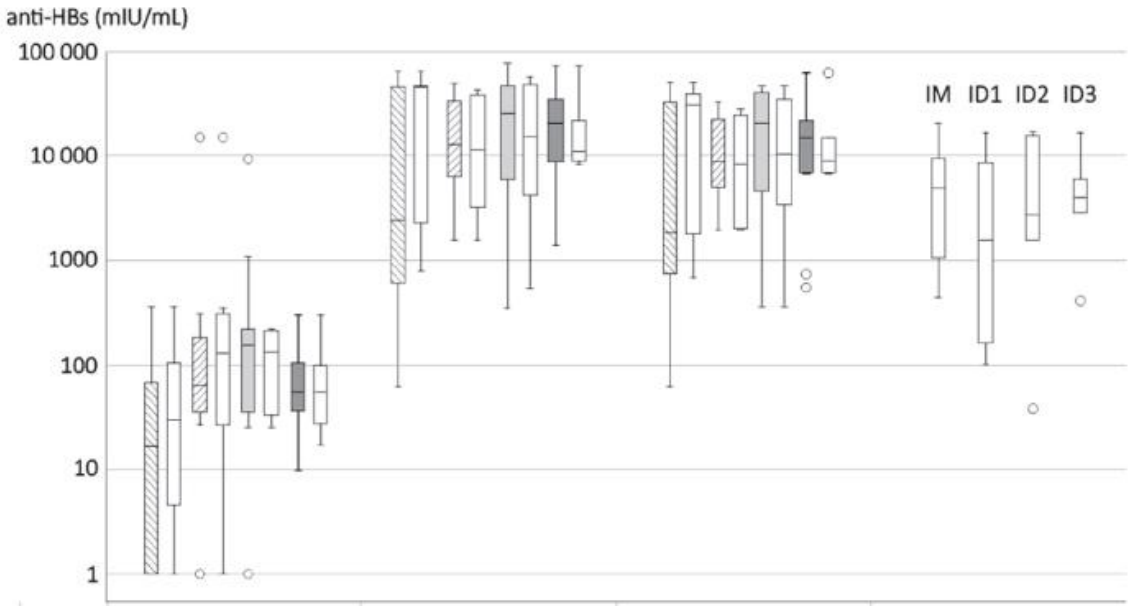
Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Immunogenicity and safety of intradermal delivery of hepatitis B booster vaccine using the novel drug delivery device VAX-ID™

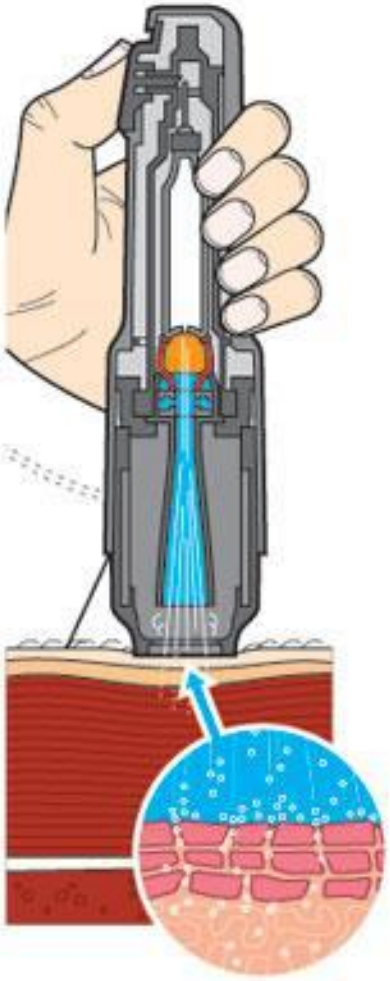
T.J.S. Van Mulder [a,b,*], K. Withanage [b], K.C.L. Beyers [a,c], V.V.J. Vankerckhoven [a,b], H. Theeten [b], P. Van Damme [b]

[a] Novosanis, Bijkhoevelaan 32c, BE-2110 Wijnegem, Belgium
[b] Centre for the Evaluation of Vaccination, Vaccine & Infectious Disease Institute, University of Antwerp, Campus Drie Eiken, Universiteitsplein 1, BE-2610 Wilrijk, Belgium
[c] Voxdale, Bijkhoevelaan 32c, BE-2110 Wijnegem, Belgium



Study group	N	Day 0 GMC (95% CI)	Day 14 GMC (95% CI)	Day 30 GMC (95% CI)	Day 210 GMC (95% CI)

Nasale vaccins: bv. Attenuated flu vaccine, UK 2013



Oral administration

Rotavirus vaccination (2 products: Rotarix and RotaTeq)

Role of vaccination in disease control

- Reduce the number of susceptibles
- Protect against infectious diseases
- Protect against carriership
- Reduce morbidity and mortality
- Control transmission
- Potential to eliminate
- Pontential to eradicate
  - Host?
  - Transmission?
  - Tools?

Impact of Vaccines in the 20th & 21st Centuries

Comparison of 20th Century Annual Morbidity & Current Morbidity

Disease	20th Century Annual Morbidity*	2017 Reported Cases†	% Decrease
Smallpox	29,005	0	100%
Diphtheria	21,053	0	100%
Pertussis	200,752	15,808	92%
Tetanus	580	31	95%
Polio (paralytic)	16,316	0	100%
Measles	530,217	122	>99%
Mumps	162,344	5,629	97%
Rubella	47,745	9	>99%
CRS	152	2	99%
Haemophilus influenzae	20,000 (est.)	22§	>99%

* *JAMA*. 2007;298(18):2155-2163

† CDC. *National Notifiable Diseases Surveillance System, Week 52, 2017 Weekly Tables of Infectious Disease Data*. Atlanta, GA. CDC Division of Health Informatics and Surveillance, 2018. Available at: www.cdc.gov/nndss/infectious-tables.html. Accessed on January 4, 2018.

§ *Haemophilus influenzae* type b (Hib) <5 years of age. An additional 11 cases of Hib are estimated to have occurred among the 237 notifications of Hi (<5 years of age) with unknown serotype.

Belangrijk aspect van vaccinatie!

Groepsimmuniteit

= wanneer een voldoende groot deel van de populatie immuniteit heeft tegen de ziektekiem, zullen zij ervoor zorgen dat deze ziektekiem de onbeschermde individuen van de populatie niet zal bereiken.

Rijksinstituut voor Volksgezondheid en Milieu
Ministerie van Volksgezondheid, Welzijn en Sport

Wat is groepsimmuniteit?

Voorwaarden:

- Mens op mens overdraagbare pathogenen
- At random verspreiding van onbeschermde individuen

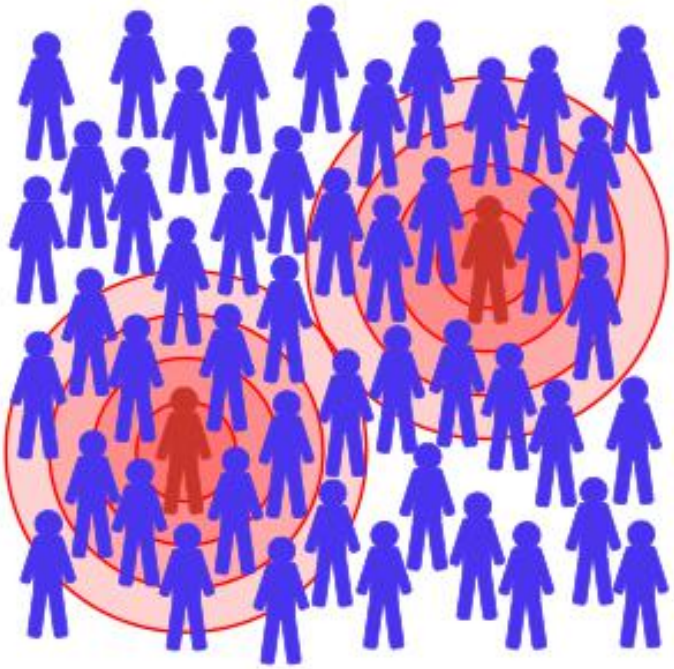
Biedt bescherming aan:

- Ongevaccineerde mensen
- Immuun gecompromitteerde patiënten (kankerpatiënten, immuundeficiëntie stoornissen …)
- Pasgeborenen

= not immunized, but still healthy

= immunized and healthy

= not immunized, sick, and contagious



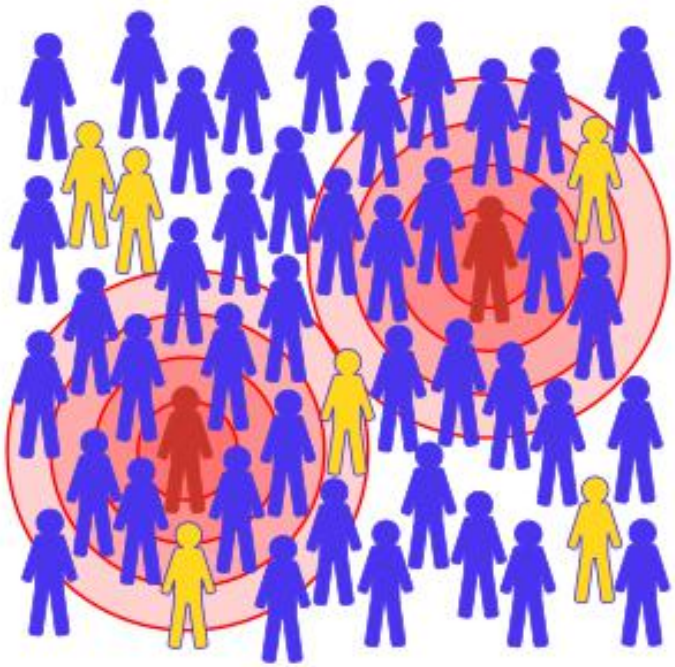
No one is immunized.

Contagious disease spreads through the population.

= not immunized, but still healthy

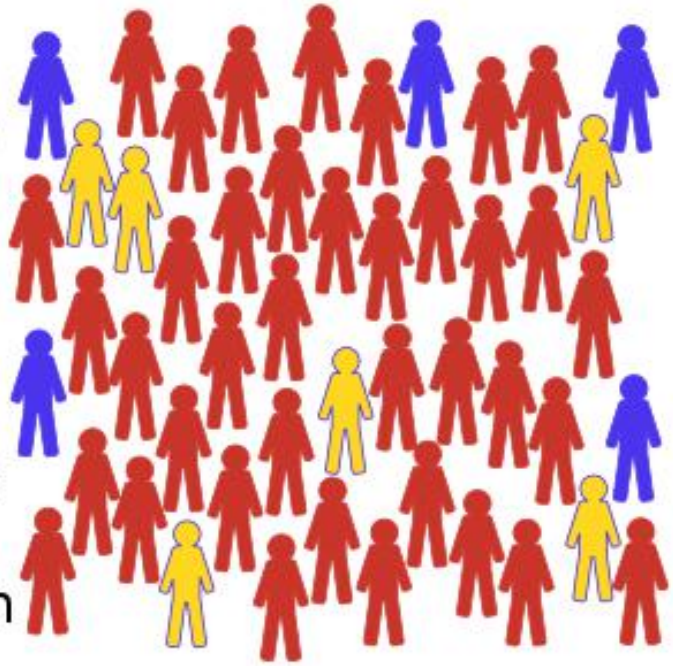
= immunized and healthy

= not immunized, sick, and contagious



Some of the population gets immunized.

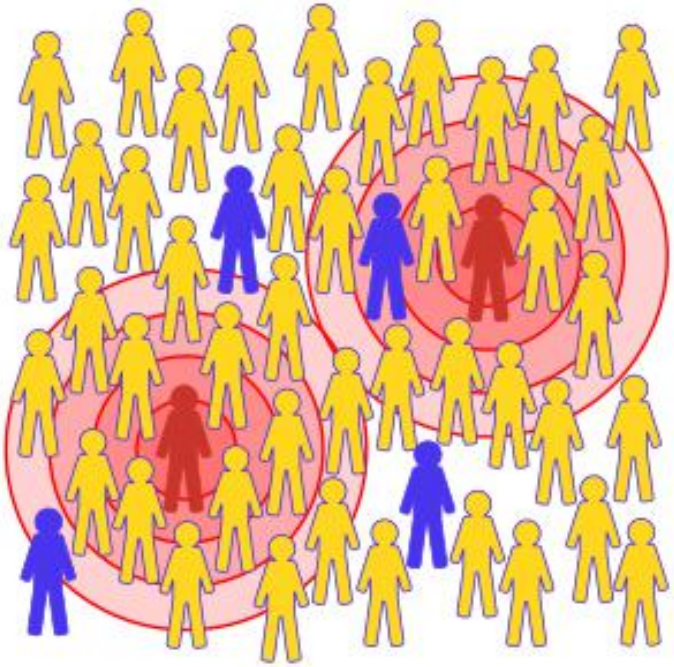
Contagious disease spreads through some of the population



= not immunized, but still healthy

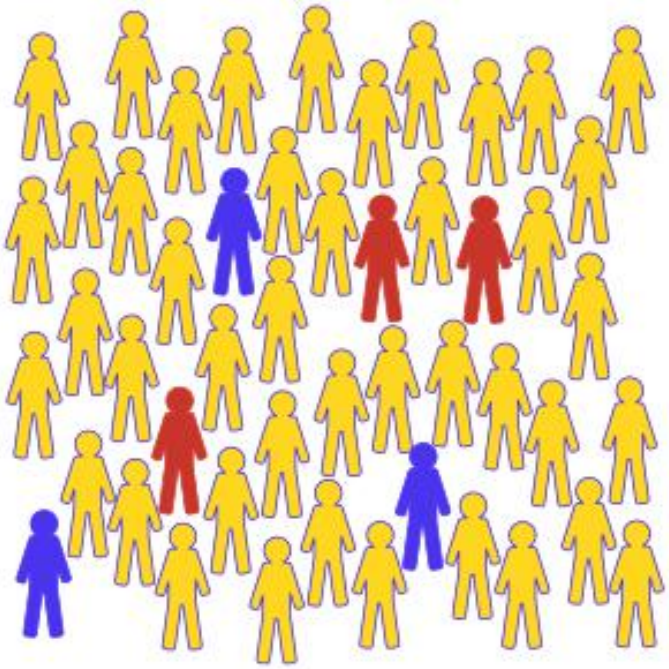
= immunized and healthy

= not immunized, sick, and contagious



Most of the population gets immunized.

Spread of contagious disease is contained.



- **Estimated Herd Immunity thresholds for vaccine preventable diseases**

Disease	Transmission	R_0	Herd immunity threshold
Diphtheria	Saliva	6-7	85%
Measles	Airborne	12-18	83 - 94%
Mumps	Airborne /droplet	4-7	75 - 86%
Pertussis	Airborne droplet	12-17	92 - 94%
Polio	Fecal-oral	5-7	80 - 86%
Rubella	Airborne droplet	5-7	80 - 85%
Smallpox	Social contact	6-7	83 - 85%

- R_0 is the basic reproduction number, or the average number of secondary infectious cases that are produced by a single index case in completely susceptible population

The Expanded Program on Immunization (EPI)

Gestart in 1974 door WHO

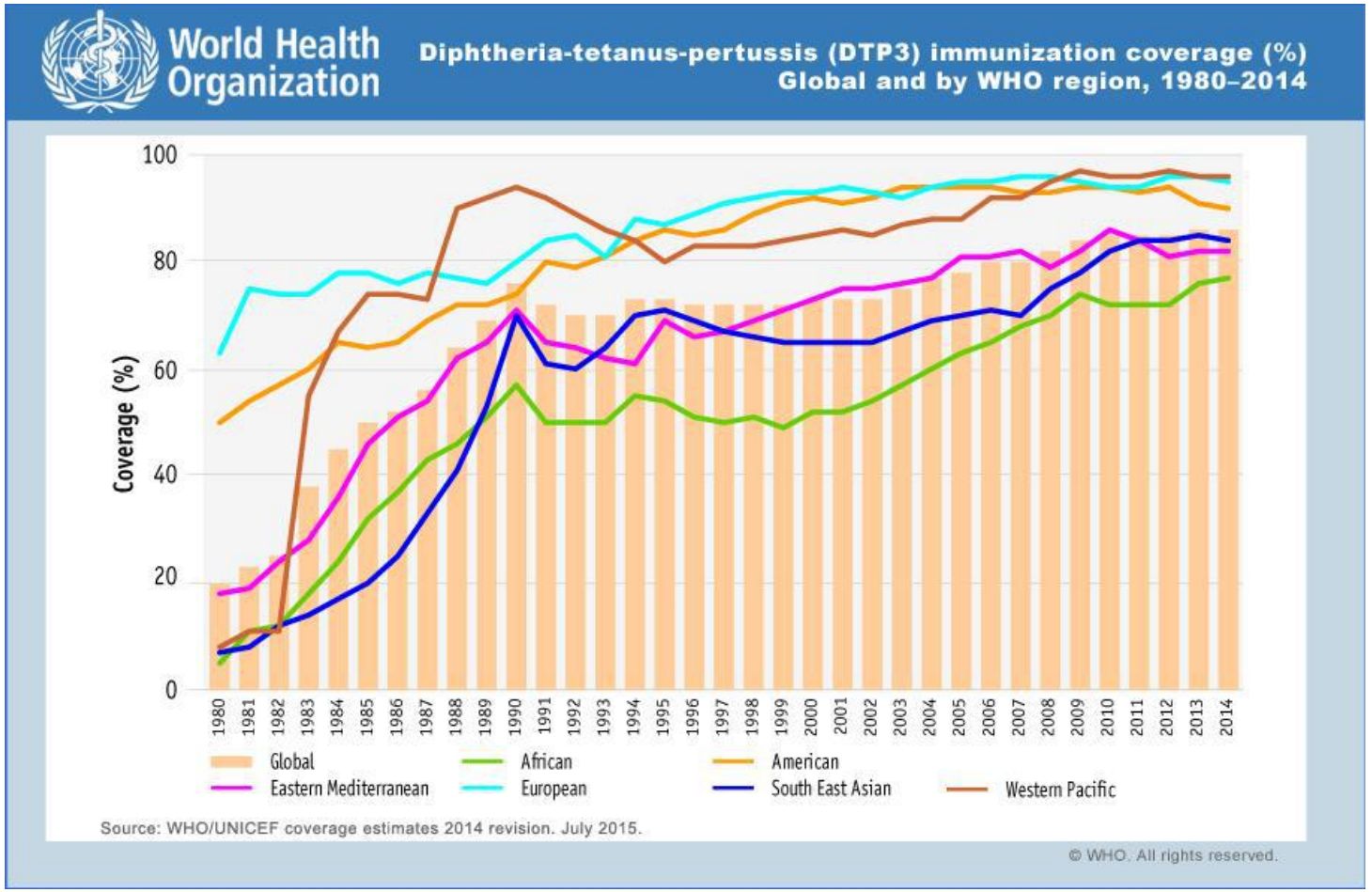
- Een wereldwijde doelstelling voor universele immuni
  tegen difterie, tetanus, pertussis(kinkhoest), polio, ma
- Toen <5% van de kinderen onder 1 jaar gevaccineerd tegen deze infectieziekten

In 1990: 80% van 130 miljoen kinderen werden gevaccineerd voor hun eerste verjaardag.

= meer dan 3 miljoen kindersterfte gevallen/jaar voorkomen.

The Expanded Program on Immunization (EPI)

- In 2014:
  - ±**85**% van de kinderen wereldwijd kreeg 1 dosis van het mazelen vaccin voor 1 jaar.
  - ± **86**% (115 miljoen) kinderen wereldwijd kregen 3 dosissen difterie-tetanus-pertussis(kinkhoest) vaccin
  - **129/194** deelnemende landen bereikte ± **90**% couverture voor het difterie-tetanus-pertussis(kinkhoest) vaccin


World Health Organization
Diphtheria-tetanus-pertussis (DTP3) immunization coverage (%)
Global and by WHO region, 1980–2014
Coverage (%)
100
80
60
40
20
0
1980 1981 1982 1983 1984 1985 1986 1987 1988 1989 1990 1991 1992 1993 1994 1995 1996 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014
Global
African
American
Eastern Mediterranean
European
South East Asian
Western Pacific
Source: WHO/UNICEF coverage estimates 2014 revision. July 2015.
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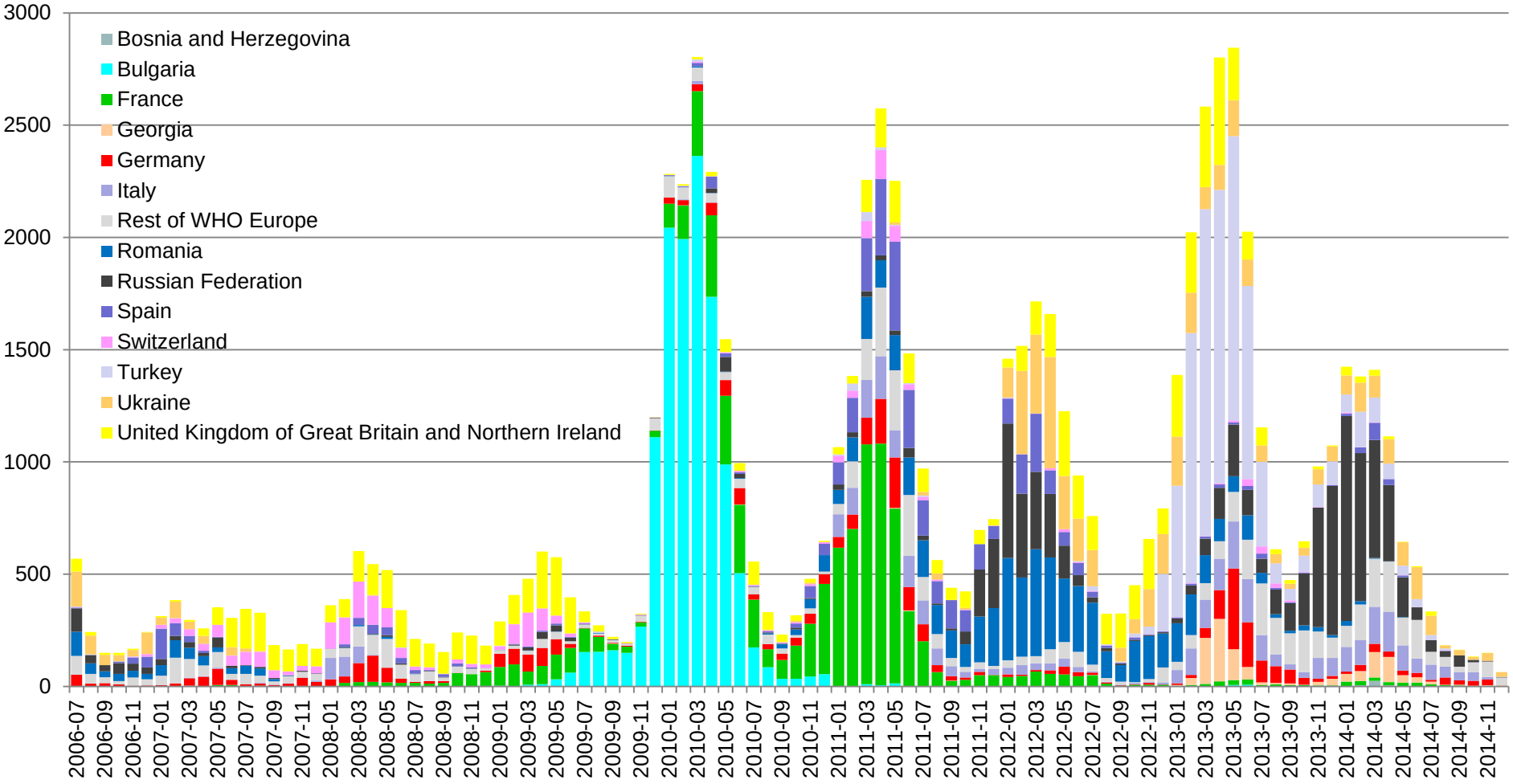
Voorbeelden van vaccineerbare aandoeningen

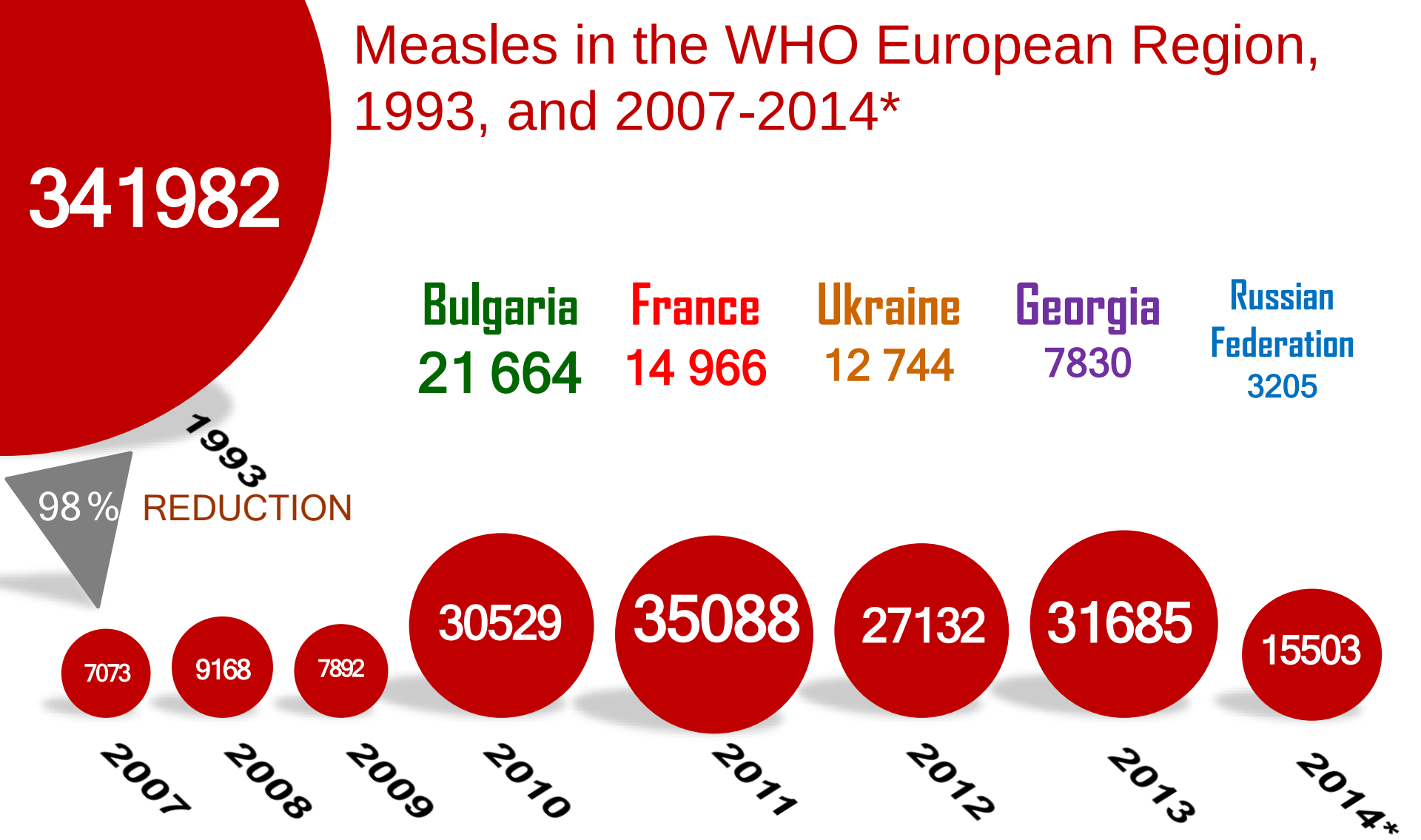
Mazelen

Measles cases by month and year, WHO European Region, 2006-2014



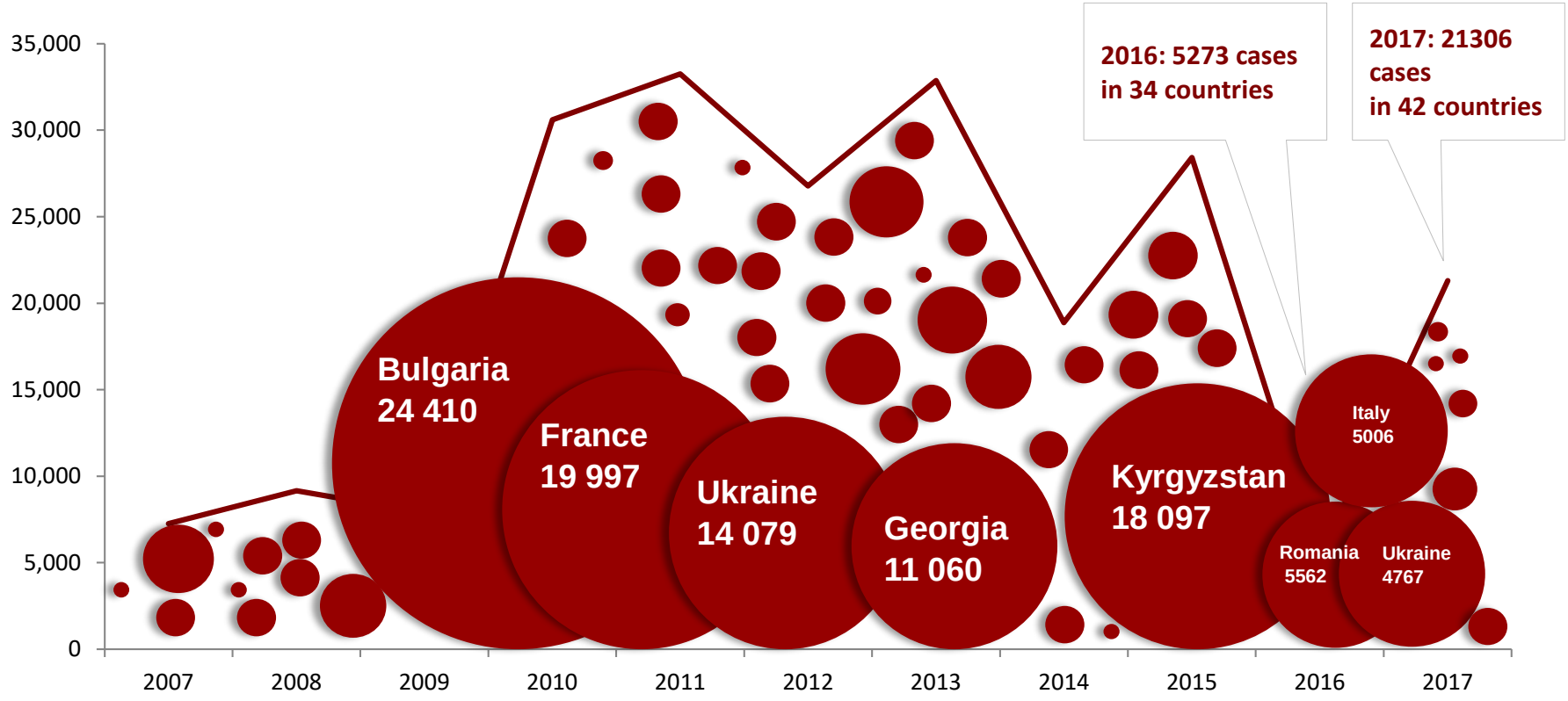
Source: MR reporting to WHO European region Update Date : 28-Jan-2015. Data for 2014 is provisional.

Measles in the WHO European Region, 1993, and 2007-2014*



*Provisional data for 2014 Jan-Nov

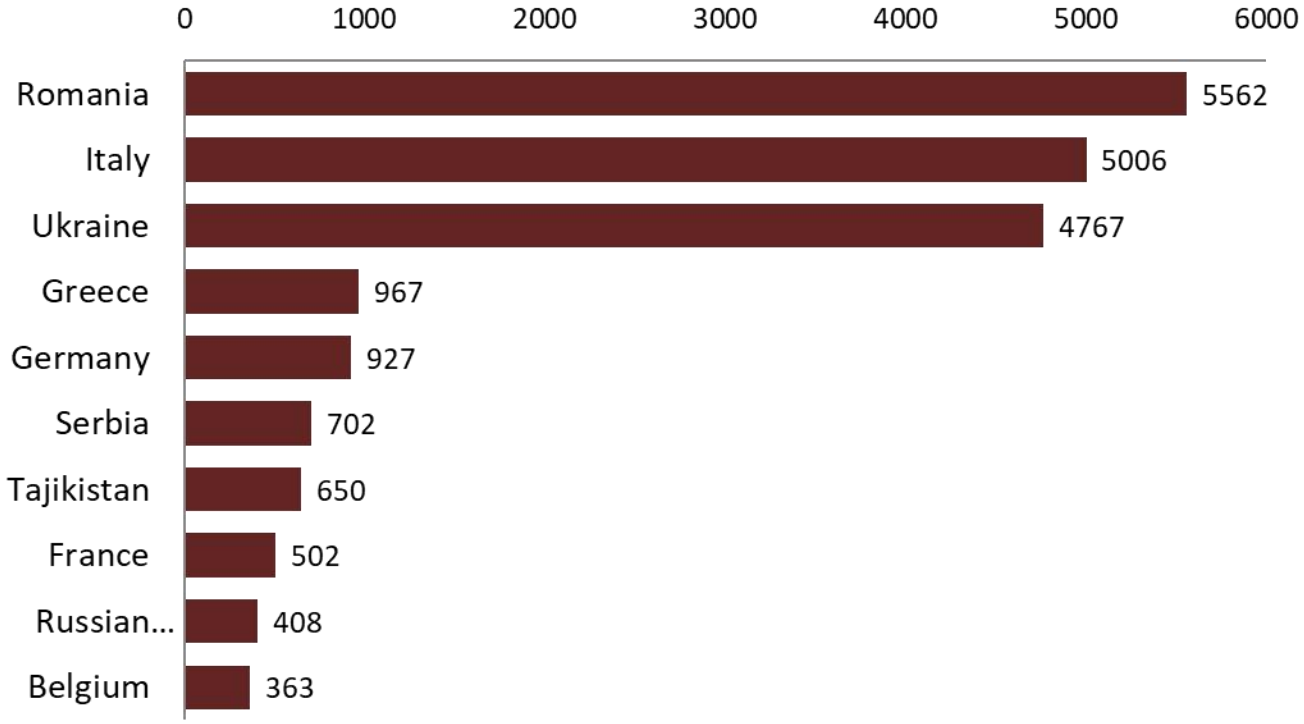
Number of measles in the WHO European Region, 2007-2017*



Data source: CISID, extracted 2 February 2018

* Data for 2017 is preliminary

Top 10 countries with measles cases, WHO European Region, 2017*

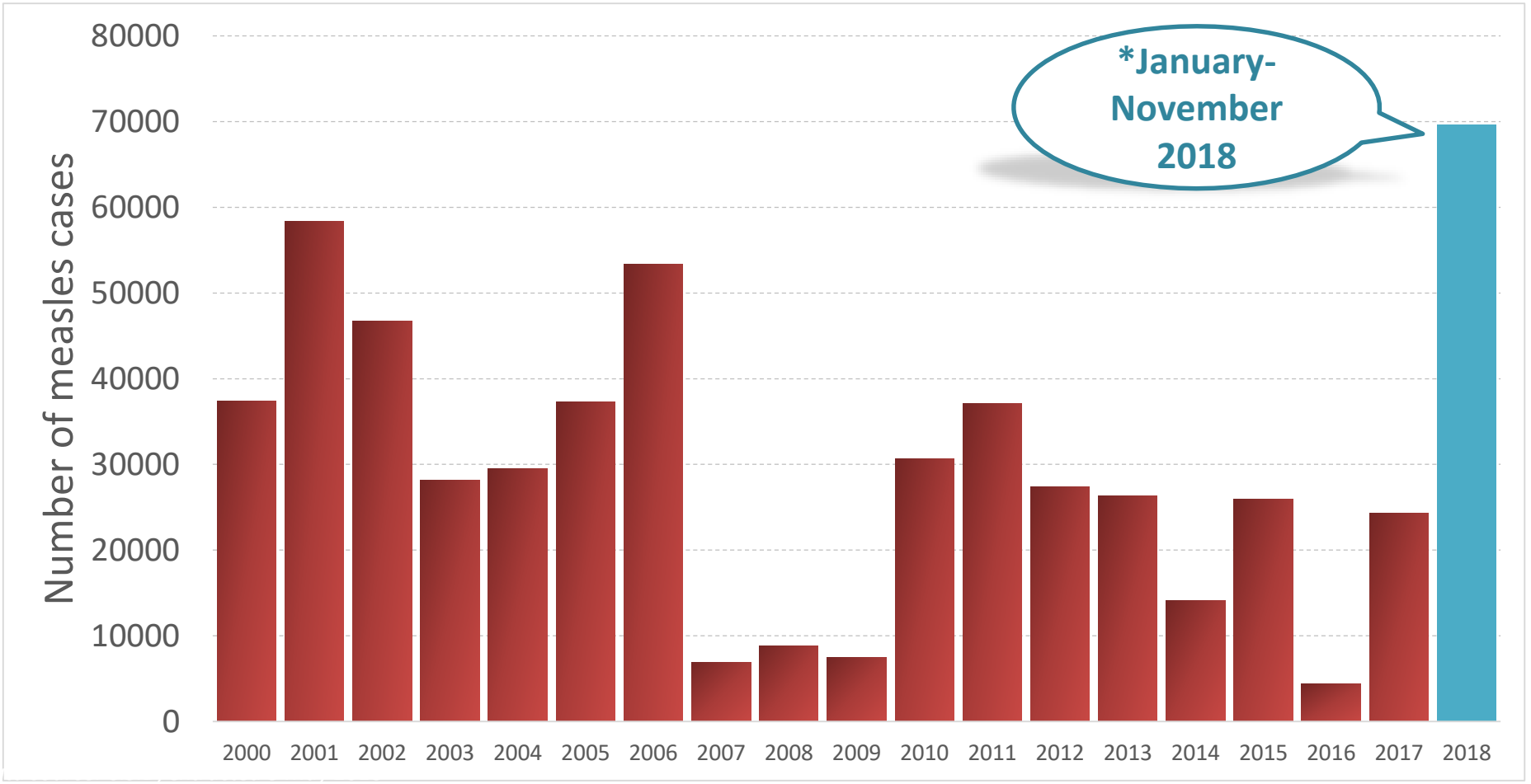


72% of cases in the Region in **3** countries *(n=15,335)*

Data source: CISID, extracted 2 February 2018

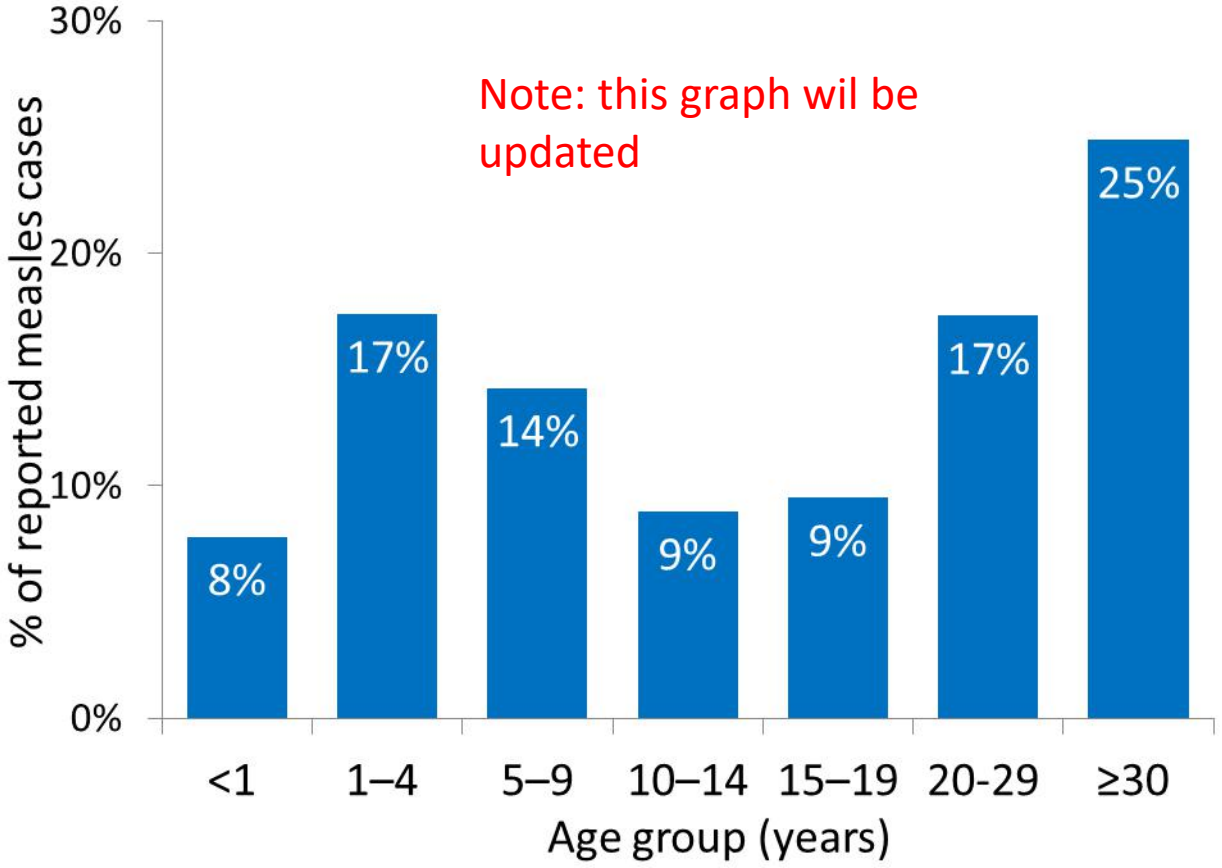
* Data for 2017 is preliminary

Number of measles in the WHO European Region, 2000-2018*

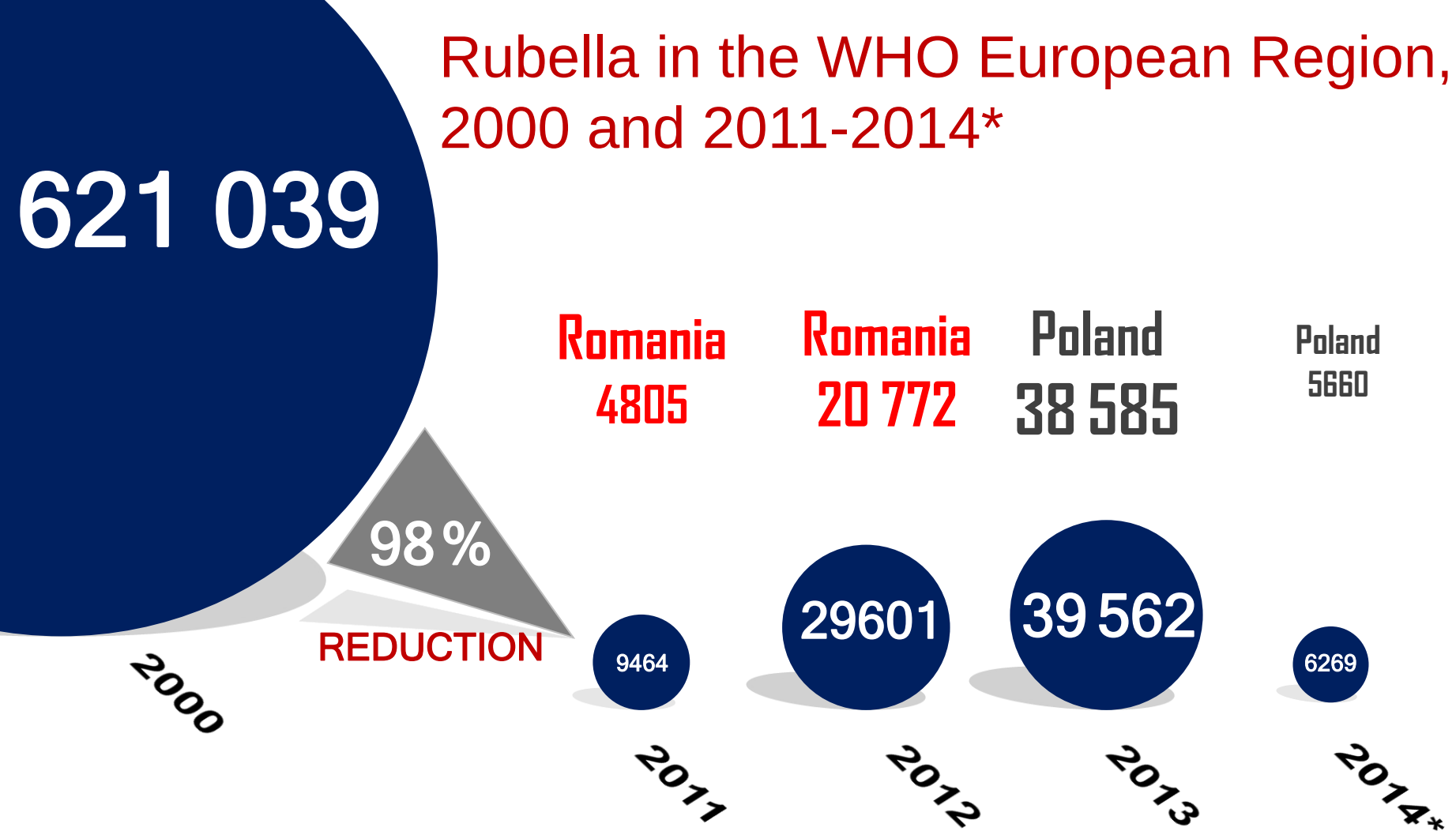


Source: http://www.who.int/immunization/monitoring_surveillance/data/en/

Age distribution and vaccination status of measles, WHO European Region, 2017 *(n=22,351)*



Rubella in the WHO European Region, 2000 and 2011-2014*



*Provisional data for 2014 Jan-Nov

Rubella in the WHO European Region, 2000 & 2010-2017*

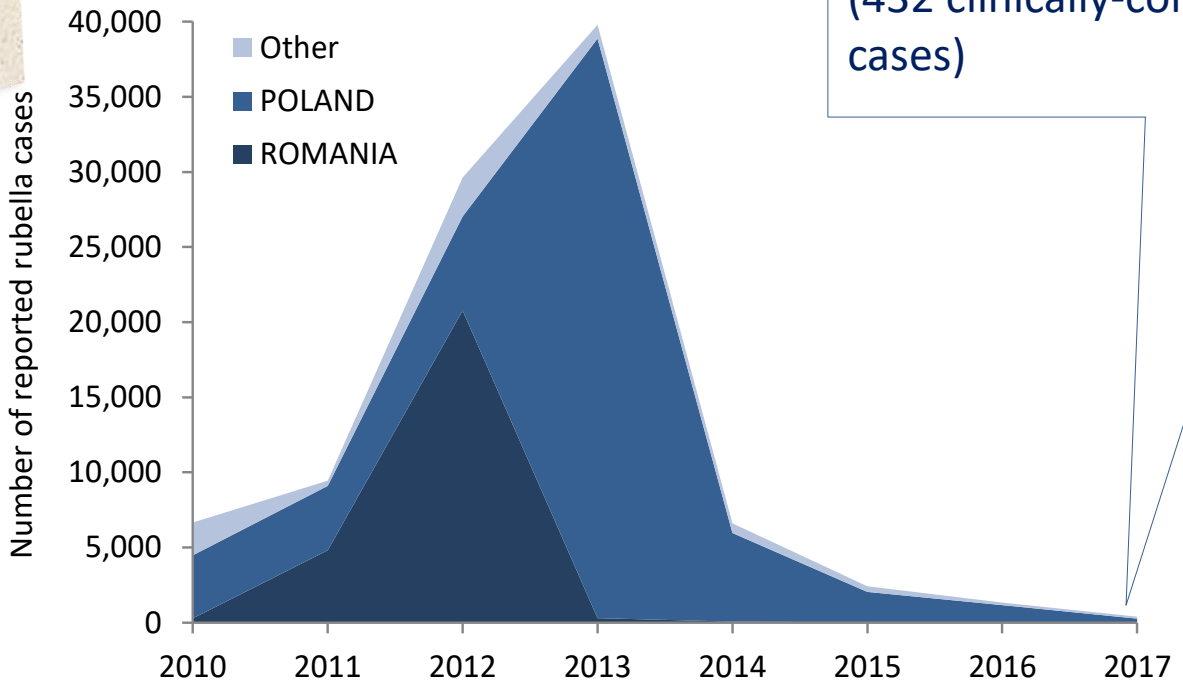
621 039 cases in 2000

99.8%

REDUCTION 2000-2016

649 reported cases in 2017

67% reported by Poland (432 clinically-compatible cases)



Data source: CISID, extracted 2 February 2018

* Data for 2017 is preliminary

Vaccinatieschema in België/Vlaanderen

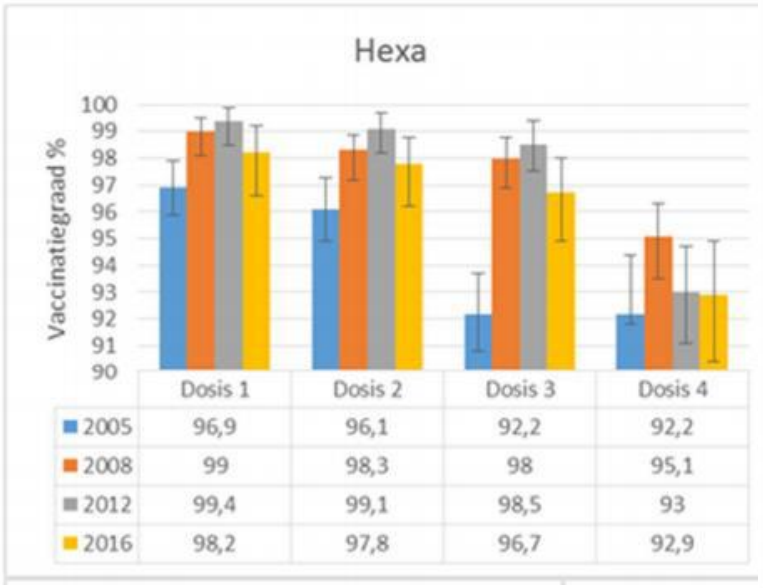
Centre for the Evaluation of Vaccination
Vaccine & Infectious Disease Institute
University of Antwerp

Vaccinatie tegen	8 wkn	12 wkn	16 wkn	12 mnd	13/15 mnd[8]	5-7 jr[1]	10-13 jr	14-16 jr[3]
Poliomyelitis								
Difterie (kroep)								
Tetanus (klem)								
Pertussis (kinkhoest)								
Haemophilus Influenzae B (hersenvliesontsteking)								
Hepatitis B (geelzucht)								
Pneumokokken		 (7)						
Rotavirus[4]		 (5)	 (5)					
Mazelen							(2) 	
Bof (dikoor)								
Rodehond (rubella)								
Meningokokken type C (hersenvliesontsteking)								
Humaan Papillomavirus[6] (baarmoederhalskanker)								

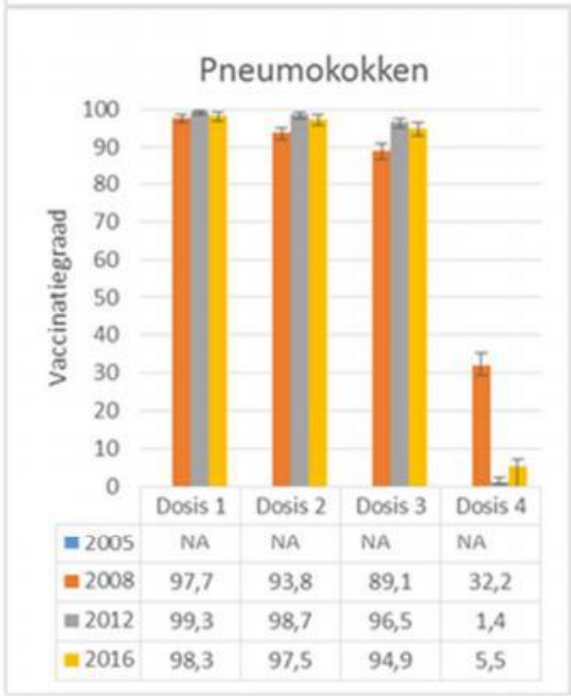
Vaccinatie tegen	8 wkn	12 wkn	16 wkn	12 mnd	15 mnd	5-7 jr[1]	10-13 jr	14-16 jr[4]
Poliomyelitis	x	x	x		x	x		
Difterie (kroep)	x	x	x		x	x		x[5]
Tetanus (klem)	x	x	x		x	x		x
Pertussis (kinkhoest)	x	x	x		x	x		x[5]
Haemophilus Influenzae B	x	x	x		x			
Hepatitis B (geelzucht)	x	x	x		x		xx[3]	
Pneumokokken 7-serotypes	x		x	x				
Rotavirus[6]	x	x	x[7]					
Mazelen				x			x[2]	
Bof (dikoor)				x			x[2]	
Rodehond (rubella)				x			x[2]	
Meningokokken type C					x			
Humaan Papillomavirus[8]							xxx	

Vaccinatiegraad in Vlaanderen

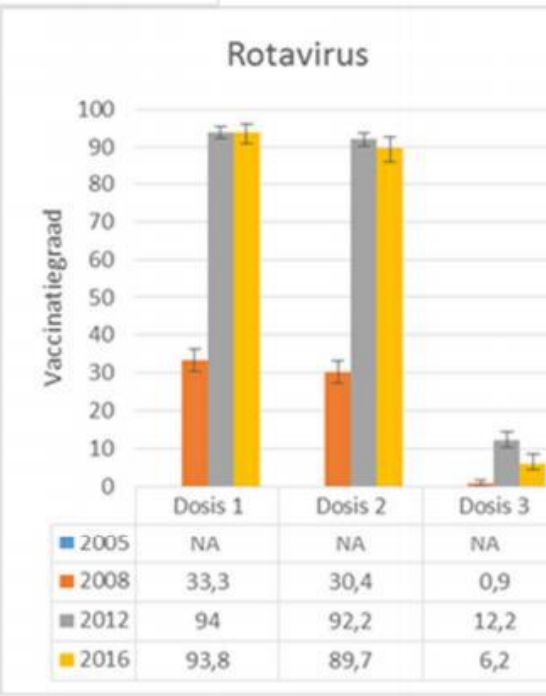
Bij jonge kinderen in de opeenvolgende metingen tussen 2005 tot 2016



	Dosis 1	Dosis 2	Dosis 3	Dosis 4
2005	96,9	96,1	92,2	92,2
2008	99	98,3	98	95,1
2012	99,4	99,1	98,5	93
2016	98,2	97,8	96,7	92,9

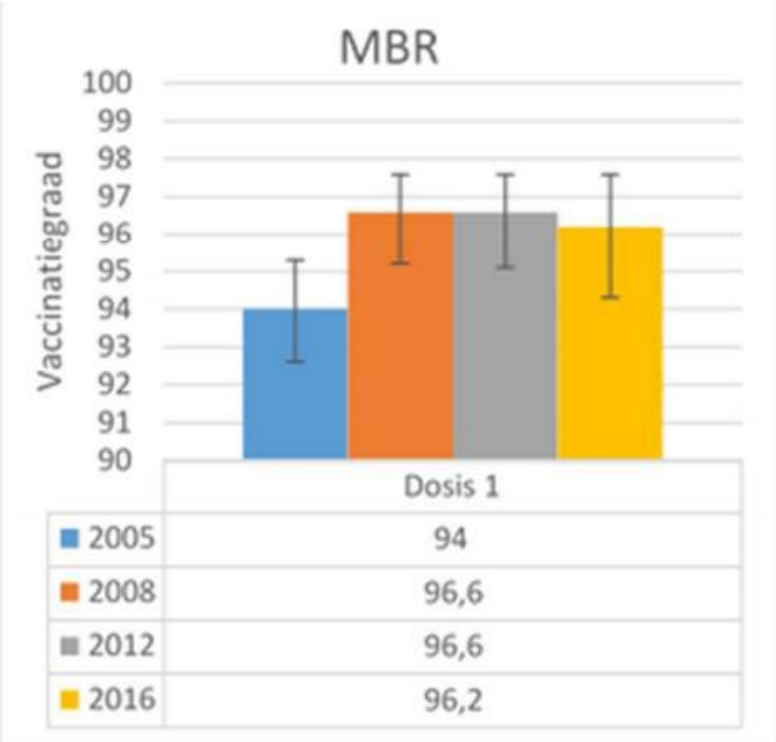


	Dosis 1	Dosis 2	Dosis 3	Dosis 4
2005	NA	NA	NA	NA
2008	97,7	93,8	89,1	32,2
2012	99,3	98,7	96,5	1,4
2016	98,3	97,5	94,9	5,5

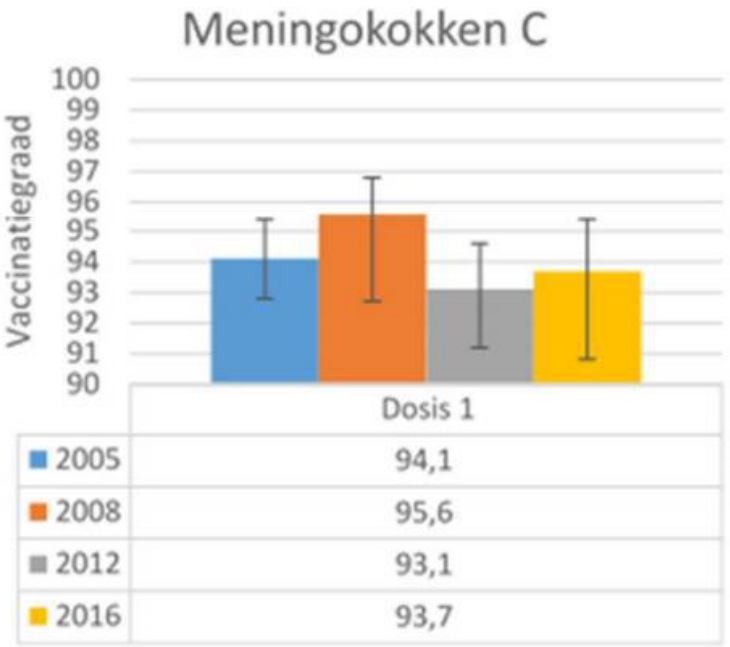


	Dosis 1	Dosis 2	Dosis 3
2005	NA	NA	NA
2008	33,3	30,4	0,9
2012	94	92,2	12,2
2016	93,8	89,7	6,2

Vaccinatiegraad in Vlaanderen



	Dosis 1
2005	94
2008	96,6
2012	96,6
2016	96,2



	Dosis 1
2005	94,1
2008	95,6
2012	93,1
2016	93,7

Vaccine confidence

University of Antwerp

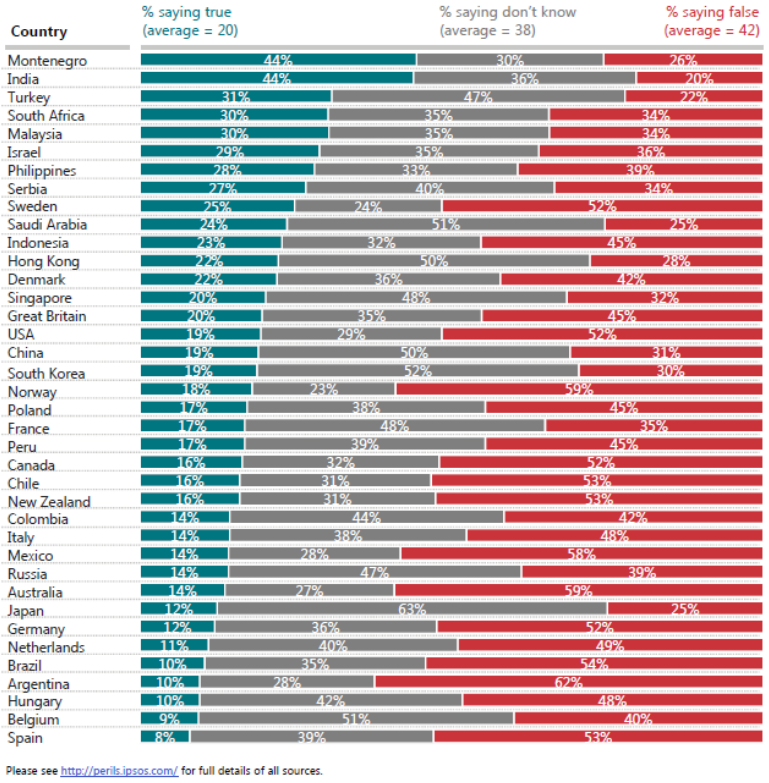
Problemen in het vaccinatie landschap

Do you think the following statement is true or false?

Some vaccines cause autism in healthy children

Nearly six in ten people across the countries as a whole say they are unsure or believe that there is a link between vaccines and autism in healthy children, despite the claim being widely discredited.

Some countries, particularly Montenegro and India, have very high levels of belief in the claim.



Please see http://perils.ipsos.com/ for full details of all sources.

Vaccin ~ autisme

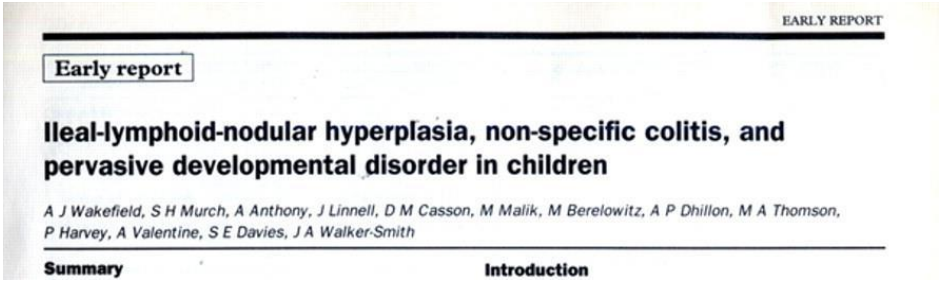
1998

Publicatie van artikel in The Lancet (!)

12 kinderen: ontwikkelingsstoornissen en darmklachten na BMR-vaccin

Persconferentie in Londens ziekenhuis

Beperkt opgepikt door media



EARLY REPORT

Early report

Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children

A J Wakefield, S H Murch, A Anthony, J Linnell, D M Casson, M Malik, M Berelowitz, A P Dhillon, M A Thomson, P Harvey, A Valentine, S E Davies, J A Walker-Smith

Summary **Introduction**

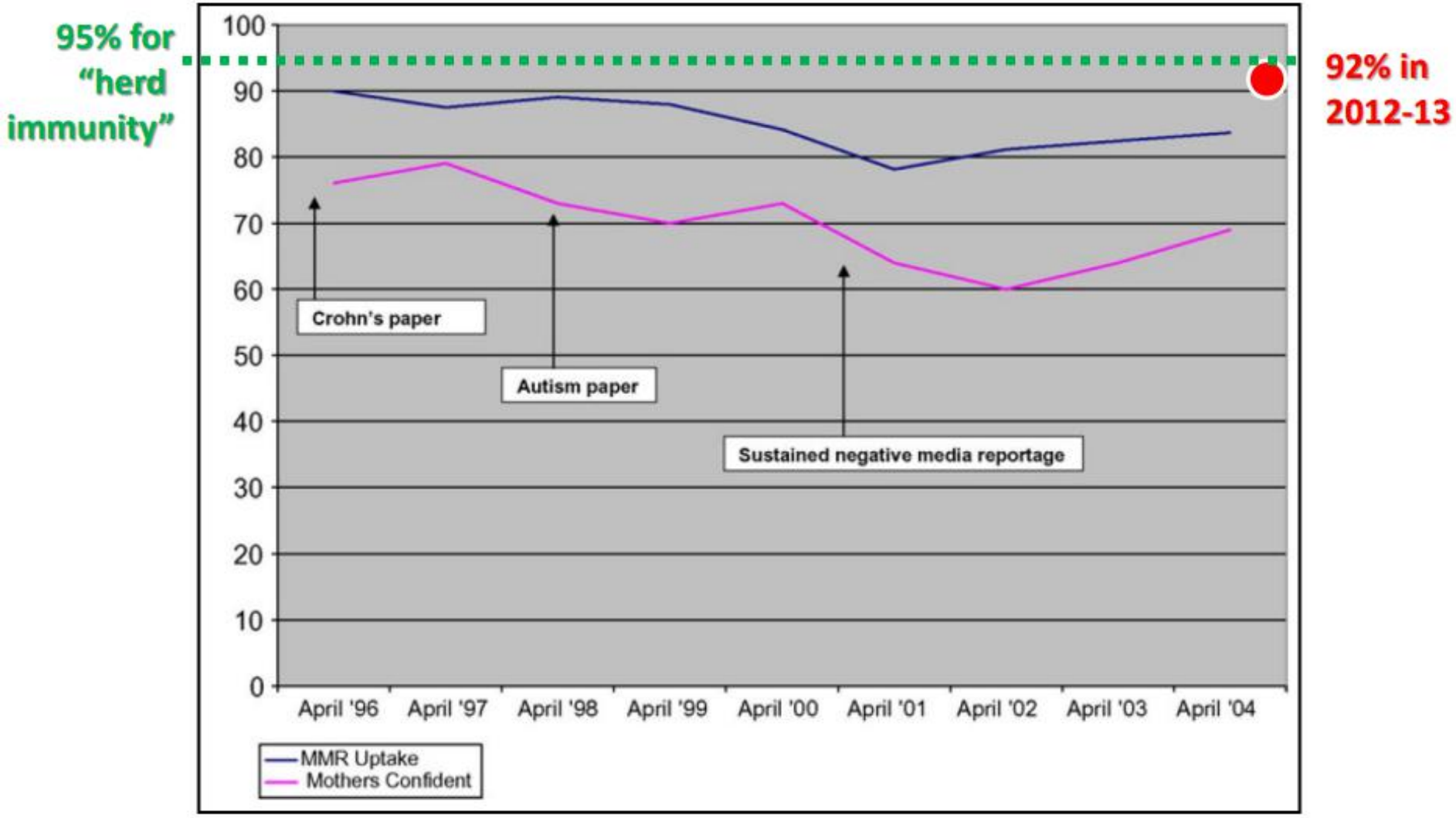
2001-2002

Wakefield publiceert kleinere artikels, suggererend dat vaccinatie onveilig is

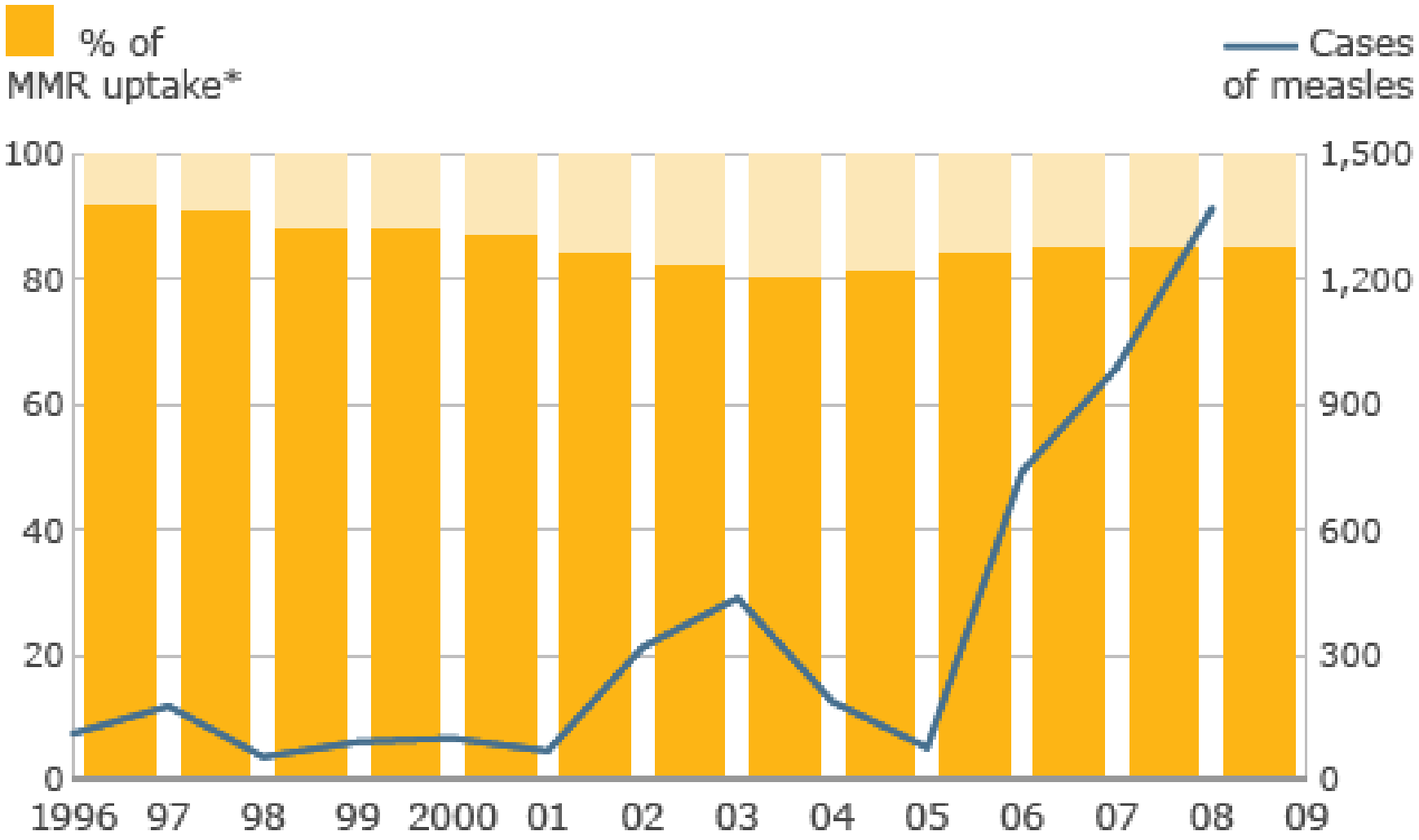
Enorme (onzorgvuldige) media-aandacht!

Leo Blair

U.K. MMR Vaccination Rates
(Smith et al., 2007)



MMR and measles



*figures relate to financial years 1996/97, 1997/98 etc

Source: HPA

THE LANCET

The Lancet, Volume 351, Issue 9103, Pages 637 - 641, 28 February 1998
doi:10.1016/S0140-6736(97)11096-0

FAKE NEWS

This article was retracted

RETRACTED: Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children

Dr AJ Wakefield FRCS [a], SH Murch MB [b], A Anthony MB [a], J Linnell PhD [a], DM Casson MRCP [b], M Malik MRCP [b], M Berelowitz FRCPsych [c], AP Dhillon MRCPath [a], MA Thomson FRCP [b], P Harvey FRCP [d], A Valentine FRCR [e], SE Davies MRCPath [a], JA Walker-Smith FRCP [a]

Summary

Background

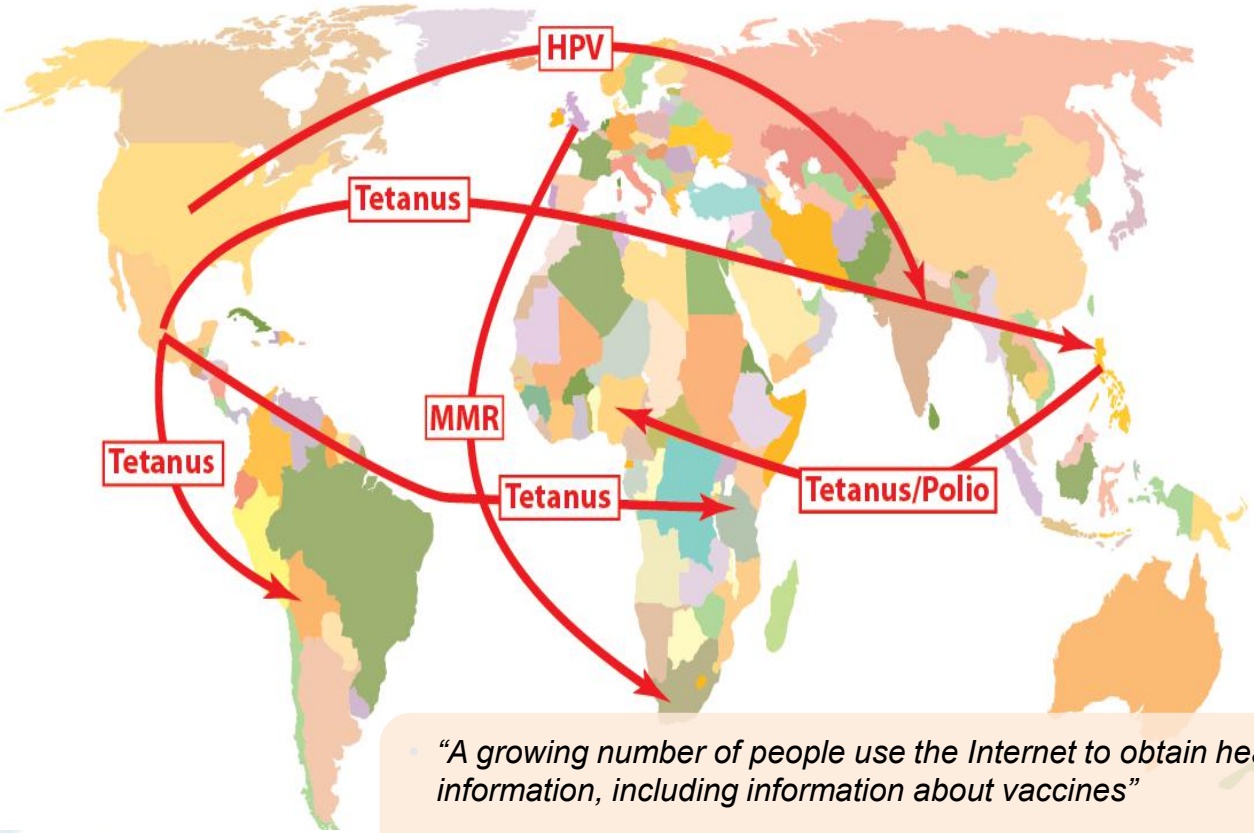
We investigated a consecutive series of children with chronic enterocolitis and regressive developmental disorder.

Methods

12 children (mean age 6 years [range 3–10], 11 boys) were referred to a paediatric gastroenterology unit with a history of normal development followed by loss of acquired skills, including language, together with diarrhoea and abdominal pain. Children underwent gastroenterological, neurological, and developmental assessment and review of developmental records. Ileocolonoscopy and biopsy sampling, magnetic-resonance imaging (MRI), electroencephalography (EEG), and lumbar puncture were done under sedation. Barium follow-through radiography was done where possible. Biochemical, haematological, and immunological profiles were examined.

RETRACTED

Perceptions of vaccine risk travel globally



- *"A growing number of people use the Internet to obtain health information, including information about vaccines"*
- Betsch C. *Vaccine* 2012; 30: 3723–6

Changed Global Environment

- Broader environment of **distrust**
- The public is increasingly **challenging "quality" and "safety"** of commodities
- Stronger **"right to know" environment** - growing civil society demands on access to information
- **Everyone is an expert** through social media
- Hard to **validate** circulating information

Analysis of anti-vaccination sentiment: n=197
trust – alternatives – safety - conspiracy

(Hoffman B et al; Vaccine 2019 (in press)

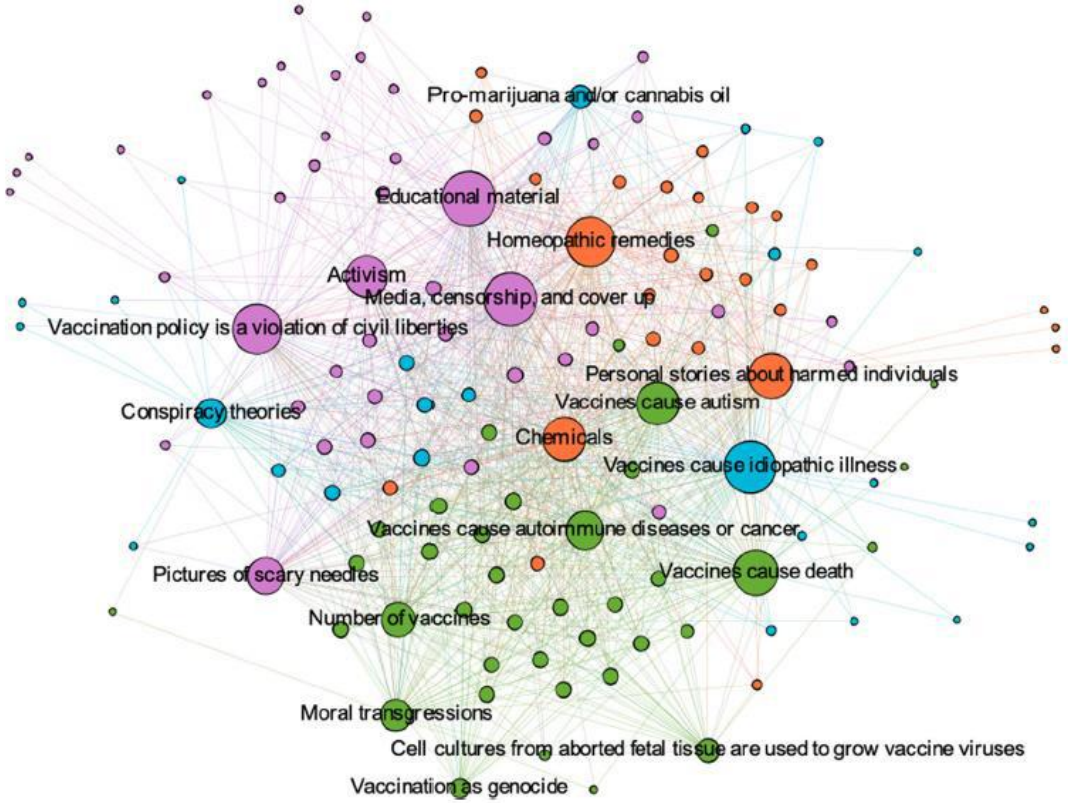
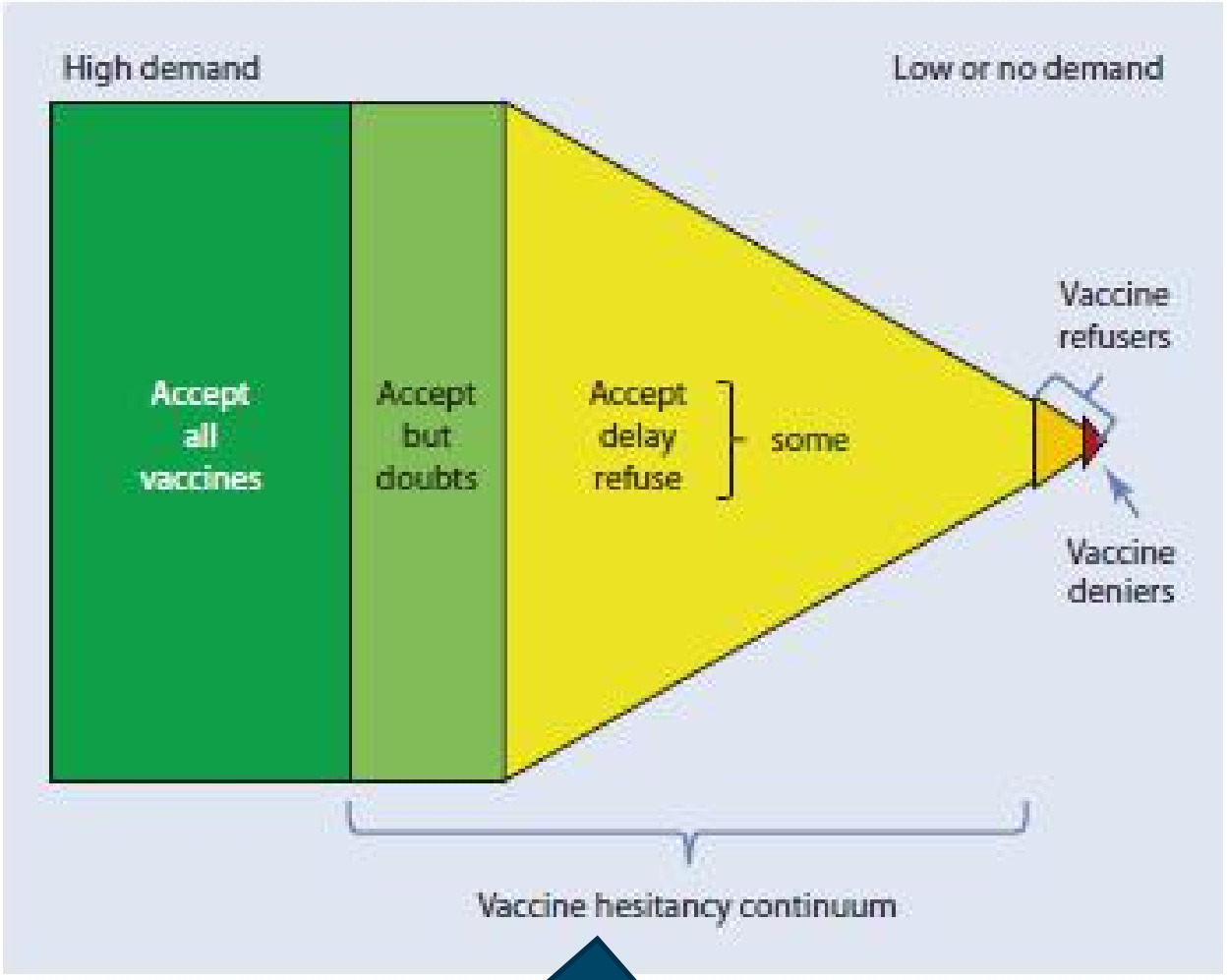
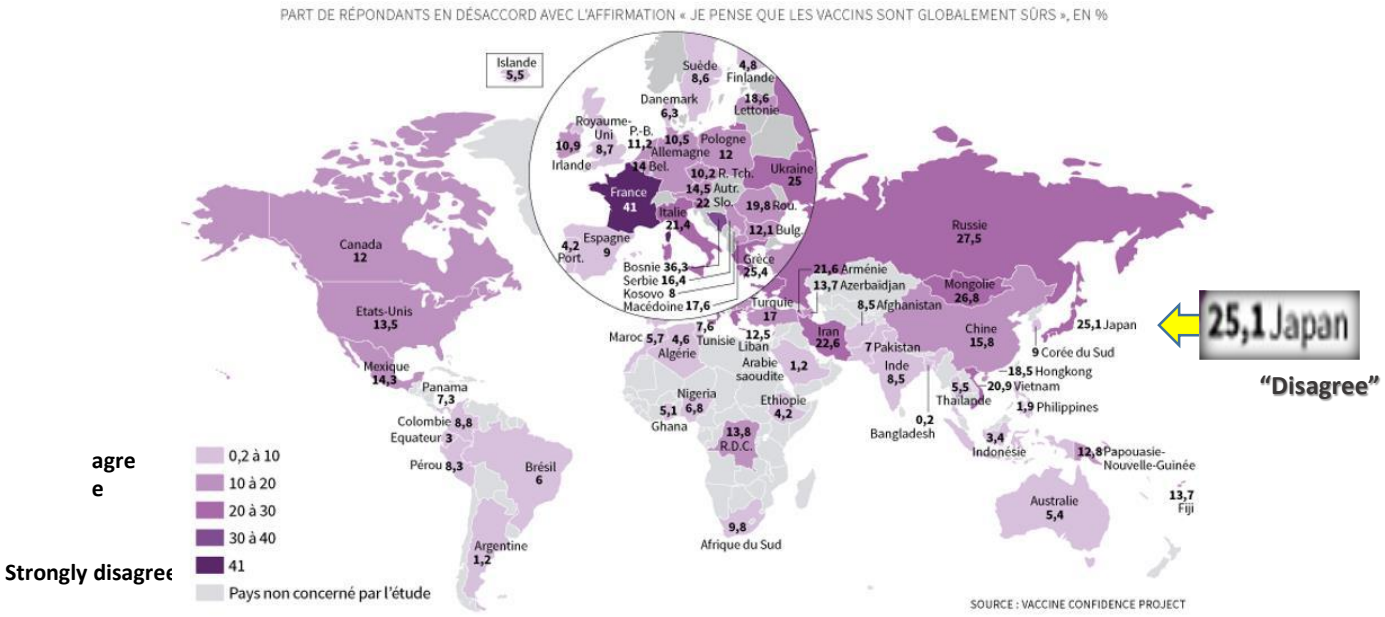


Fig. 4.1 History of vaccine acceptance in Europe. Noni Mac Donald, ► www.sabin.org/sites/sabin.org/files/1-vaccine_hesitancy_final_draft_7_jan26_2017.pdf



Disagree wih “Vaccines are safe?” - 2015

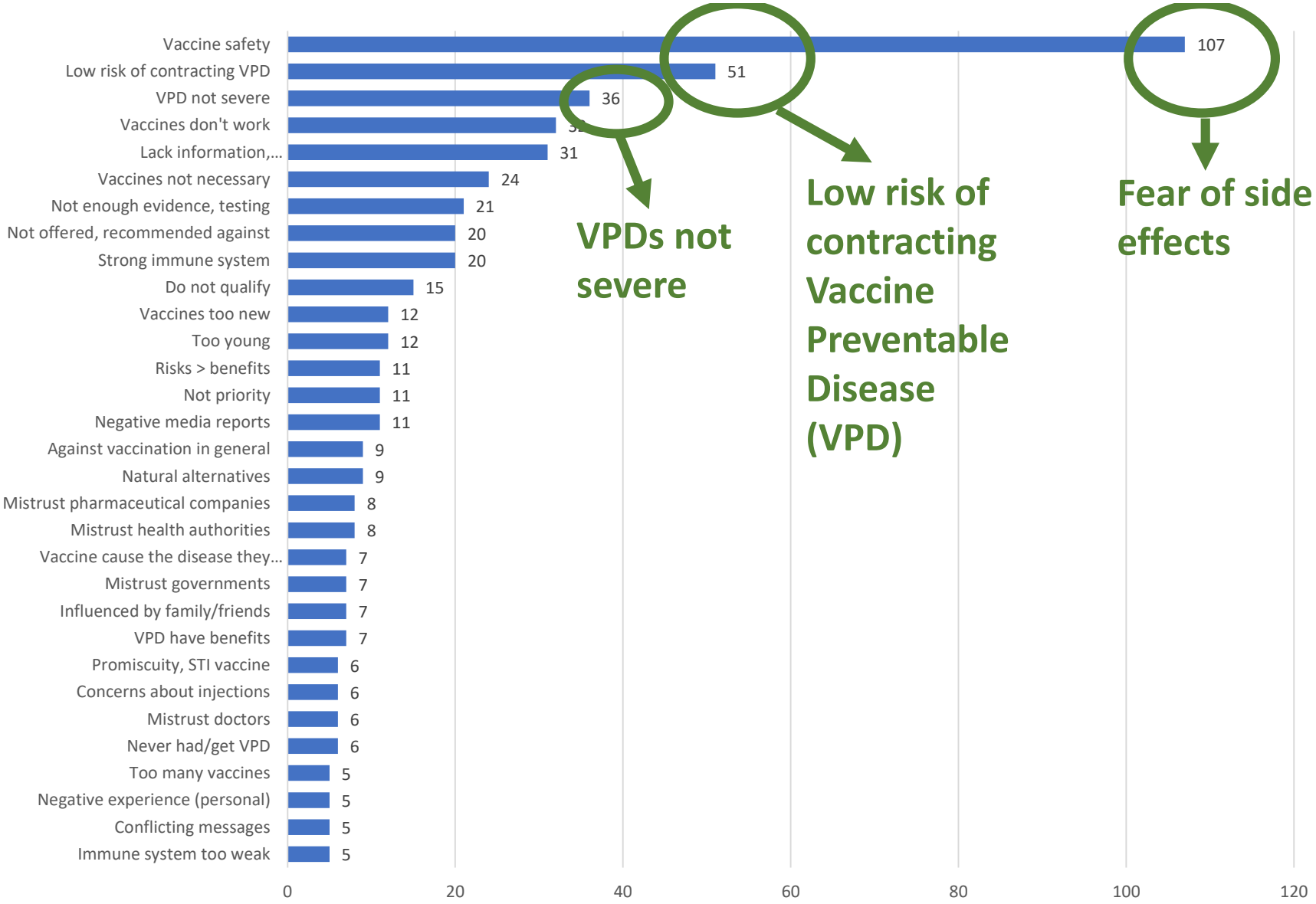


Larson et al. *State of Vaccine Confidence 2016 .* EBioMedicine 12 (2016) 295–301

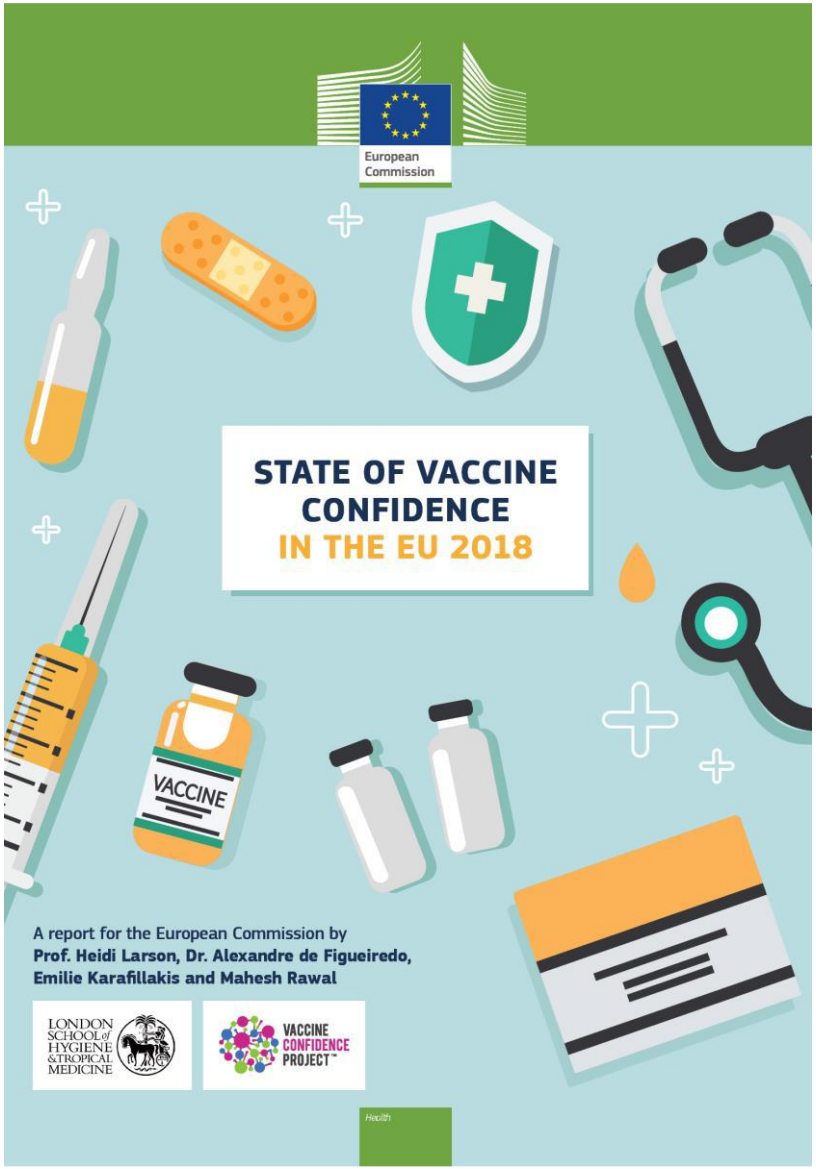
MAP: http://www.lemonde.fr/sante/article/2016/09/09/plus-de-quatre-francais-sur-dix-estiment-que-les-vaccins-ne-sont-pas-surs_4994856_1651302.html

What drives low confidence?

Frequency of concerns: number of qualitative studies where concerns were mentioned + number of quantitative studies where more than 20% of participants mentioned those concerns



Karafillakis & Larson. The benefit of the doubt or doubts over benefits? Vaccine 2017; 35 (37): 4840-4850


European Commission
STATE OF VACCINE CONFIDENCE
IN THE EU 2018
VACCINE
A report for the European Commission by
Prof. Heidi Larson, Dr. Alexandre de Figueiredo,
Emilie Karafillakis and Mahesh Rawal
LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE
VACCINE CONFIDENCE PROJECT™
Health

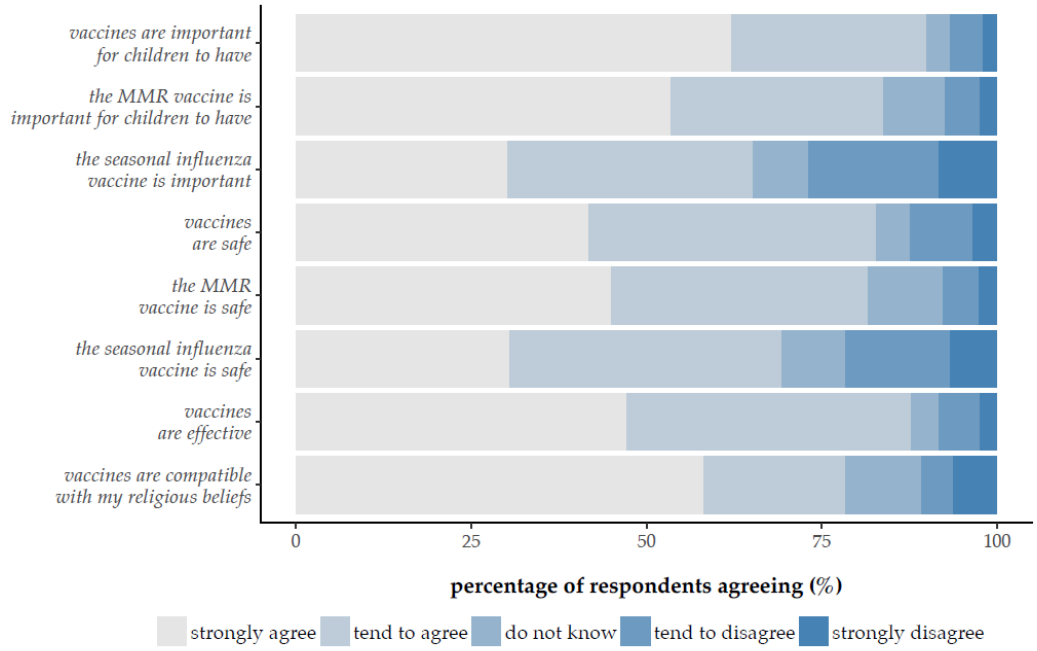
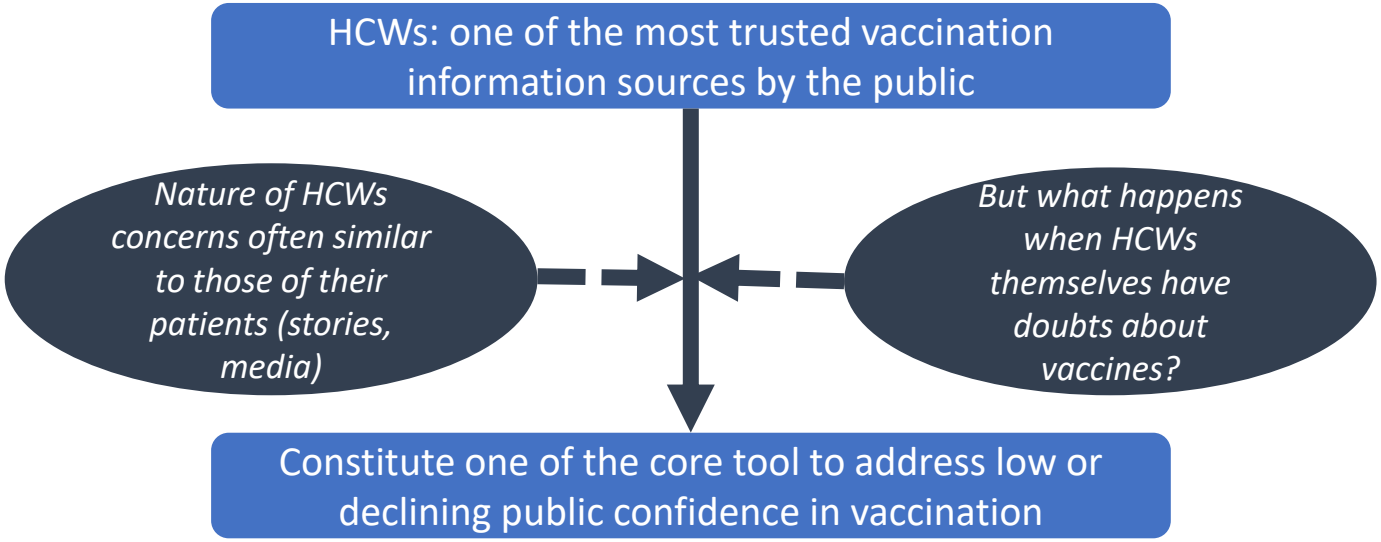


Figure 3: **The majority of the EU public agree that vaccines are important, safe, and effective**. Most of the EU public either strongly or tend to agree that vaccines – including the MMR and seasonal influenza vaccines – are important, safe, and effective. However, the seasonal influenza vaccine is viewed as both less important and less safe than the MMR vaccine and vaccines generally.

Why a paradox?

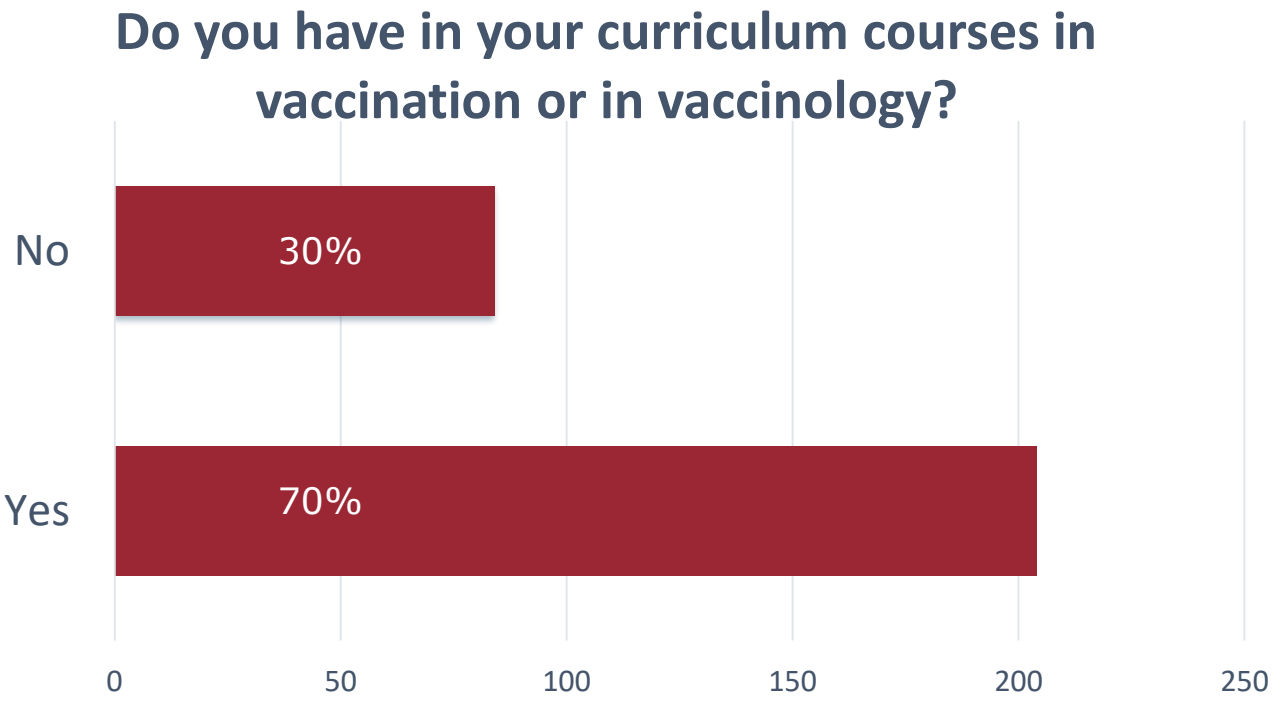


We find a correlation between GP confidence and confidence among general public in the survey: countries whose GPs hold higher confidence in vaccines tend to have a larger proportion of the public expressing positive vaccination beliefs. We provide rankings of member states by overall level of confidence in the safety of vaccines and provide raw data summaries for each member state.

Health care provider's confidence: vaccination or not!

	Health care provider		
parents		confident	Non-confident
	confident		
	Non-confident		

Online EU survey via Medical Students' Associations - 2018



IFMSA
International Federation of Medical Students' Associations

EMSA
European Medical Students' Association

Do you consider yourself confident to reply to people questioning or against vaccines?

	Bachelor students (n = 107)	Master students (n = 133)	Total (n = 240)
Yes	66/107 = 62%	103/133 = 77%	169/240 = 70%
No	22/107 = 21%	17/133 = 13%	39/240 = 16%
I don't know	19/107 = 18%	13/133 = 10%	32/240 = 13%

Toen & Nu

- Informatie
- Educatie
- Luisteren naar hun bezorgdheden

Take home message

- Don’t overestimate the **knowledge of** (future) HCP* about vaccines in general
- We need to measure systematically **vaccine confidence in HCP**
- **Be prepared** when introducing a new vaccine in a country/region
- The **work isn’t finished** once a vaccine is succesfully introduced

* GPs, pediatricians, school doctors, pharmacists, nurses, midwives, medical and para-medical students

Meer weten over vaccinatie weigering?

Erendoctoraat: Heidi Larson

@universiteit antwerpen

4 April 9.30-11.30