



**Centrum voor de Evaluatie van Vaccinaties
Vaccin- & Infectieziekten Instituut
WHO Collaborating Centre for Prevention and
Control of Infectious Diseases**

Universiteit Antwerpen

1. Vaccineren tijdens de zwangerschap algemeen
2. Kinkhoest
3. Griep
4. De rol van de apotheker



1. Vaccineren tijdens de zwangerschap



Algemene regels

- **Risico op infectie:** epidemiologisch of individueel (preventieve maatregelen)
- **Risico verbonden aan vaccinatie** = theoretisch risico vs reëel risico
- Voordelen van vaccinatie wegen meestal op tegen de potentiële risico's op neveneffecten
Vooral als
 - er geen gegevens zijn om het theoretisch risico te documenteren (vb geïnactiveerde vaccins)
 - er reëel risico is op infectie
 - de infectie moeder of kind kan schaden

Algemene regels

- Elke vrouw zou voorbereid/beschermd moeten beginnen aan een zwangerschap: pre-conceptioneel consult (voeding-foliumzuur-*vaccinatie status*- serologische status- irreguliere antistoffen...)
- Moment van vaccinatie, indien nodig, en haalbaarheid! (zwangerschap- direct postpartum...)

Algemene regels

- Vaccins met **geïnactiveerd** materiaal zijn tot op heden onschadelijk voor foetus en zwangere vrouw
- **Geattenueerde (levende)** vaccins zijn gecontraïndiceerd bij zwangere vrouwen: 1 maand contraceptie, geruststelling bij blootstelling
- Immuun respons van een zwangere op een vaccin is even adequaat als bij een niet zwangere vrouw, maar op infectie niet

Vaccines in Pregnant Women and Research Initiatives

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and Center for Vaccine Awareness and Research, Texas Children's
Hospital, Houston, Texas

TABLE 1. Factors to Be Considered Before Implementing Maternal Immunization Program

Factor	Consideration
Safety	Inactivated vaccines are safe in pregnancy Live vaccines should be avoided 28 d before and during pregnancy
Immunogenicity	Does vaccine induce robust and durable immune response?
Timing of immunization	Maternal <i>and</i> infant disease burden high: immunize earlier Infant disease burden higher than maternal: immunize in early third trimester
Biological considerations	Placental transport minimal until 34 wk of gestation Amount of maternal antibody available for transport to infant Coexisting infection (eg, HIV and malaria ↓ placental transport) Antibody response*—placental transport of subclass IgG1 > IgG2 High maternal antibody levels likely to ↓ infant response to vaccines?
Implementation	Education for providers and public Acceptability to public Logistics and financing

*IgG1 response to protein antigens; IgG2 response to polysaccharide antigens; conjugation of a polysaccharide to a carrier protein (eg, conjugate vaccines) will induce IgG1 response.

HIV indicates human immunodeficiency virus; Ig, immunoglobulin.

**Healy,
Supplement COG 2012**

TABLE 2. Vaccines Recommended* or High Priority for Investigation† During Pregnancy

Vaccine	Safe	Immunogenic in Mothers	Placental Transport	Antibodies Persist?	Indication or Stage of Study
Tetanus-diphtheria toxoid*‡	Y	Y	> 100%	Y	Prevent maternal and neonatal tetanus
Influenza, inactivated*	Y	Y	94%-99%	≥ 2 mo	Prevent maternal and infant influenza
Meningococcal polysaccharide*§	Y	Y	30%-56%	3-4 mo	Phase 1 studies performed
Pneumococcal polysaccharide*§	Y	Variable by serotype	24%-89%	Y	Phase 1 studies performed
Acellular pertussis (Tdap) *	Y	Y	> 100%	ND	Prevent infant mortality from pertussis Phase 1 studies ongoing
Group B Streptococcus, conjugate† ¶	Y	Y	77%	≥ 2 mo	Phase 1 studies performed Phase 1 and 2 studies ongoing
<i>Haemophilus influenzae</i> type b, conjugate†	Y	Y	35%-61.5%	4-6 mo	Phase 1 studies performed
<i>Haemophilus influenzae</i> type b, polysaccharide†	Y	Y	44%	4-6 mo	Phase 1 studies performed
Meningococcal, conjugate†	ND	ND	ND	ND	ND
Pneumococcal conjugate†	ND	ND	ND	ND	ND
Respiratory syncytial virus†	Y	Moderately	> 100%	6 mo	Phase 1 studies performed

Reproduced from Healy and Baker.¹

‡ Not previously immunized or booster is required.

§ Underlying medical conditions.

|| Endemic or epidemic exposure.

¶ Results shown are for GBS type III conjugate vaccine, phase 1 and 2 trials ongoing for new candidate conjugate vaccines.

ND indicates not determined; Y, yes.



Overzicht

Polio	YES	Haemophilus	YES
Rubella	Contraindicated	Hepatitis A-B	YES
Measles	Contraindicated	Pneumococcus	YES
Mumps	Contraindicated	Yellow fever	Contraindicated
Tetanus	YES	Pertussis	YES
Influenza	YES	Varicella	Contraindicated



Rabies	YES	100% lethal!
Tick Borne Encephalitis	YES	Seasonality: high risk in Eastern Europe
Japanese encephalitis	YES	Prevention mosquitos!
Meningococcus	YES	Seasonality! Men-afrivac recommendation in meningitis belt (WER 2011 jan)
Cholera	Yes/No	50% immunogenicity, no obligation to immunize
TBC	Yes/No	Skintest/RX. Treatment treats foetus!
Small pox		No malformations
GBS GAS??		Phase II-III?
Anthrax		No data

Rubella

- Rubella infectie tijdens de ZS=risico voor de foetus
- Het vaccin is gecontraïndiceerd, maar vermoedelijk veilig
- Indicatie: postpartum vaccineren of voor de ZS



Rubella

- Geen congenitale defecten na toediening aan > 30.000 vrouwen (CDC)
- Infectie = 20 % malformaties
- Toevallige vaccinatie tijdens de ZS is geen reden voor abortus (Hamkar Vaccine 2006)
- Maar het vaccin is niet aanbevolen
- Indien vaccinatie van CBAW, moet 1 maand contraceptie worden gegeven (2-5% in België is niet immuun van de CBAW)

Summary of the data on the vaccination of unknowingly susceptible pregnant women§ during mass campaigns in the selected countries in the Region of the Americas

Country	Number of Vaccinated Women	Number of reported pregnant women who were vaccinated	Number of susceptible pregnant Women	Number of Live Births with follow up	Number of Infants with congenital infection*	Infants with CRS¶
Costa Rica (Badilla 2007)	800,000	3,810	163	93	0	0
Brazil	26,361,761	22,708	2,332	1,647	66 (4.0%)	0
El Salvador	1,400,000	909	59	59	1 (1.7%)	0
Ecuador	2,400,000	1,291	172	43	2 (0.9%)	0
Paraguay	1,862,178	945	148	119	0	0
Argentina	6,718,314	476	20	19	2 (11.7%)	0
Total	39,542,253	30,139	2894	1980	70 (3%)	0



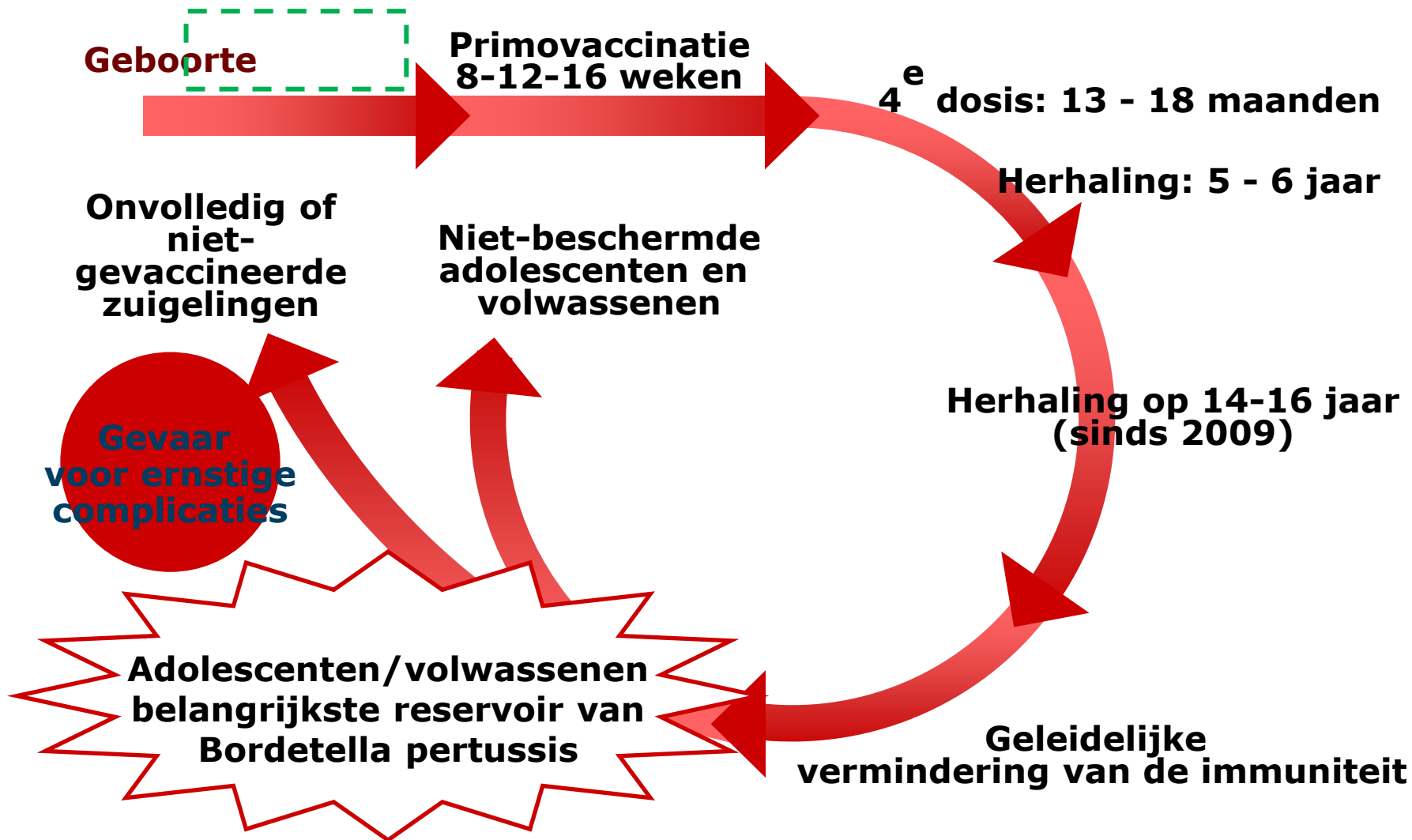
At the September 2010 session of the WHO Regional Committee for Europe, Member States unanimously adopted a resolution to renew their commitment and accelerate actions to eliminate measles and rubella in the European Region by 2015.



2. Kinkhoest

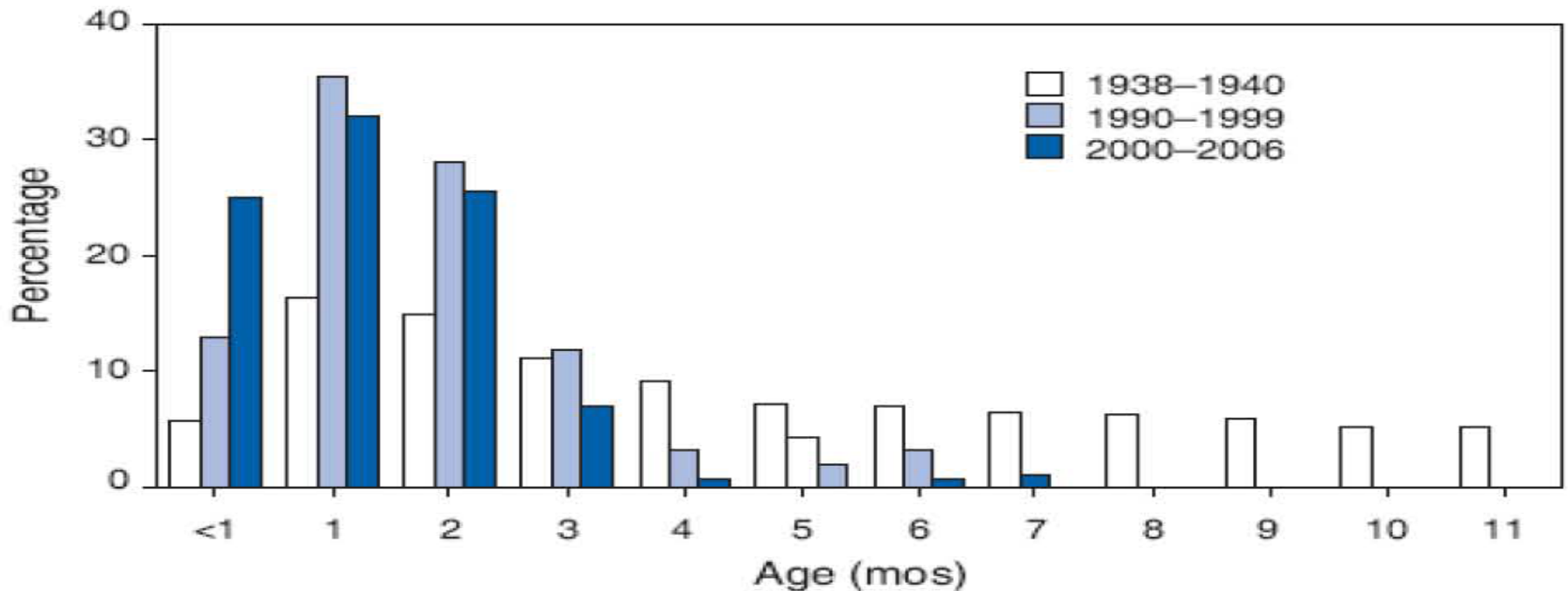


Epidemiologie



Complications

FIGURE 1. Proportion of reported infant pertussis deaths, by age — United States, 1938–1940,* 1990–1999,† and 2000–2006‡



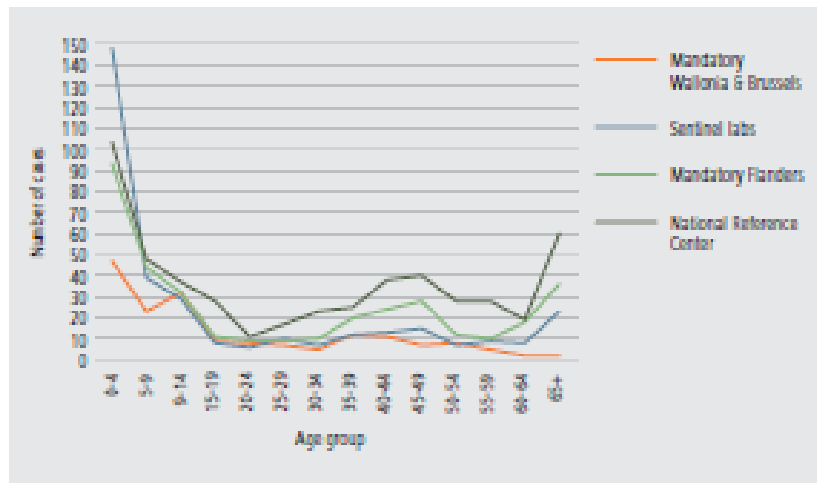
* **Source:** Sako W, Treuting WL, Witt DB, Nichamin SJ. Early immunization against pertussis with alum precipitated vaccine. *JAMA* 1945;127:379–84. N = 7,123 reported infant pertussis deaths.

† **Source:** Vitek CR, Pascual FB, Baughman AL, Murphy TV. Increase in deaths from pertussis among young infants in the United States in the 1990s. *Pediatr Infect Dis J* 2003; 22:628–34. N = 93 reported infant pertussis deaths.

‡ **Source:** CDC, unpublished data, 2007. N = 145 reported infant pertussis deaths.



Figuur 5 | Aantal gevallen van kinkhoest per leeftijdsgroep (in jaren), 2012, België (Nationale Referentiecentra, netwerk Peillaboratoria, verplichte melding)



N of cases 2012, per age category and source

Figuur 1 | Aantal gevallen van kinkhoest naargelang informatiebron, België, 2004-2012 (netwerk Peillaboratoria, verplichte melding, Nationale Referentiecentra)



N of cases 2004-2012, several sources

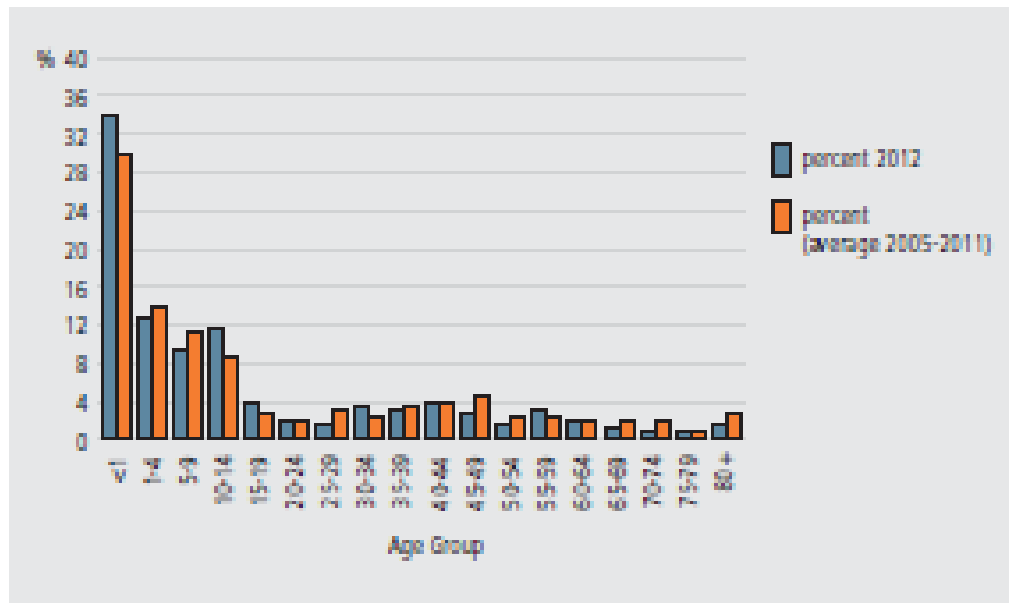
Incidence 2012: 10,8/100.000

Rapport WIV 2012, Krahe et al

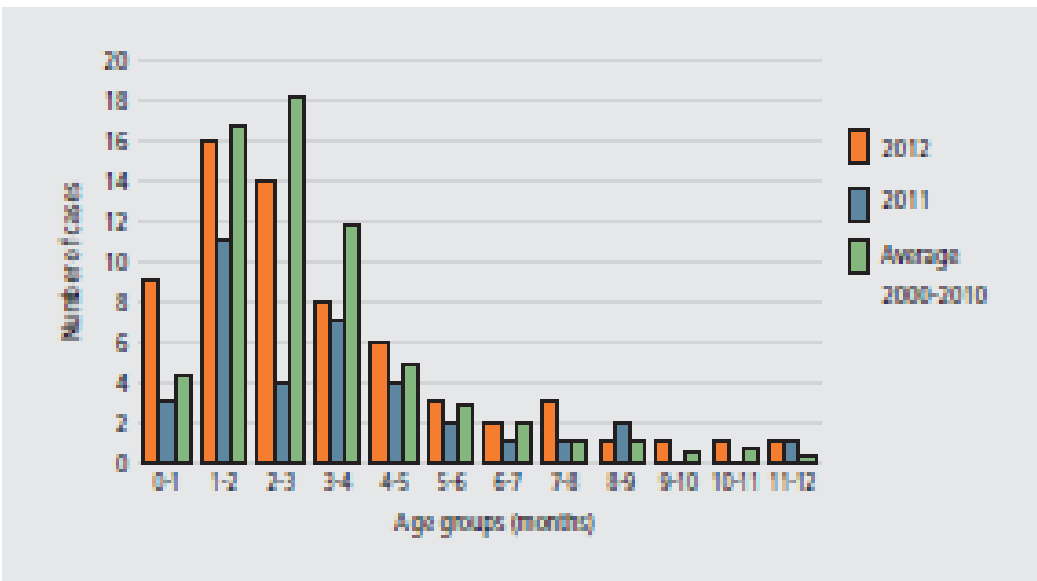


% of cases 2012, per age category

Figuur 4 | Leeftijdsverdeling van de gevallen van kinkhoest, in percentage, gemiddelde van 2005 -2011 en 2012, België (netwerk Peillaboratoria, WIV-ISP)



Figuur 6 | Aantal gevallen van kinkhoest bij kinderen < 12 maanden, België, 2000-2012 (Nationale Referentiecentra, UZ Brussel en WIV-ISP)



N of cases <1 year per month

Pertussis cases in Flanders (<50 years)

number of cases

600

500

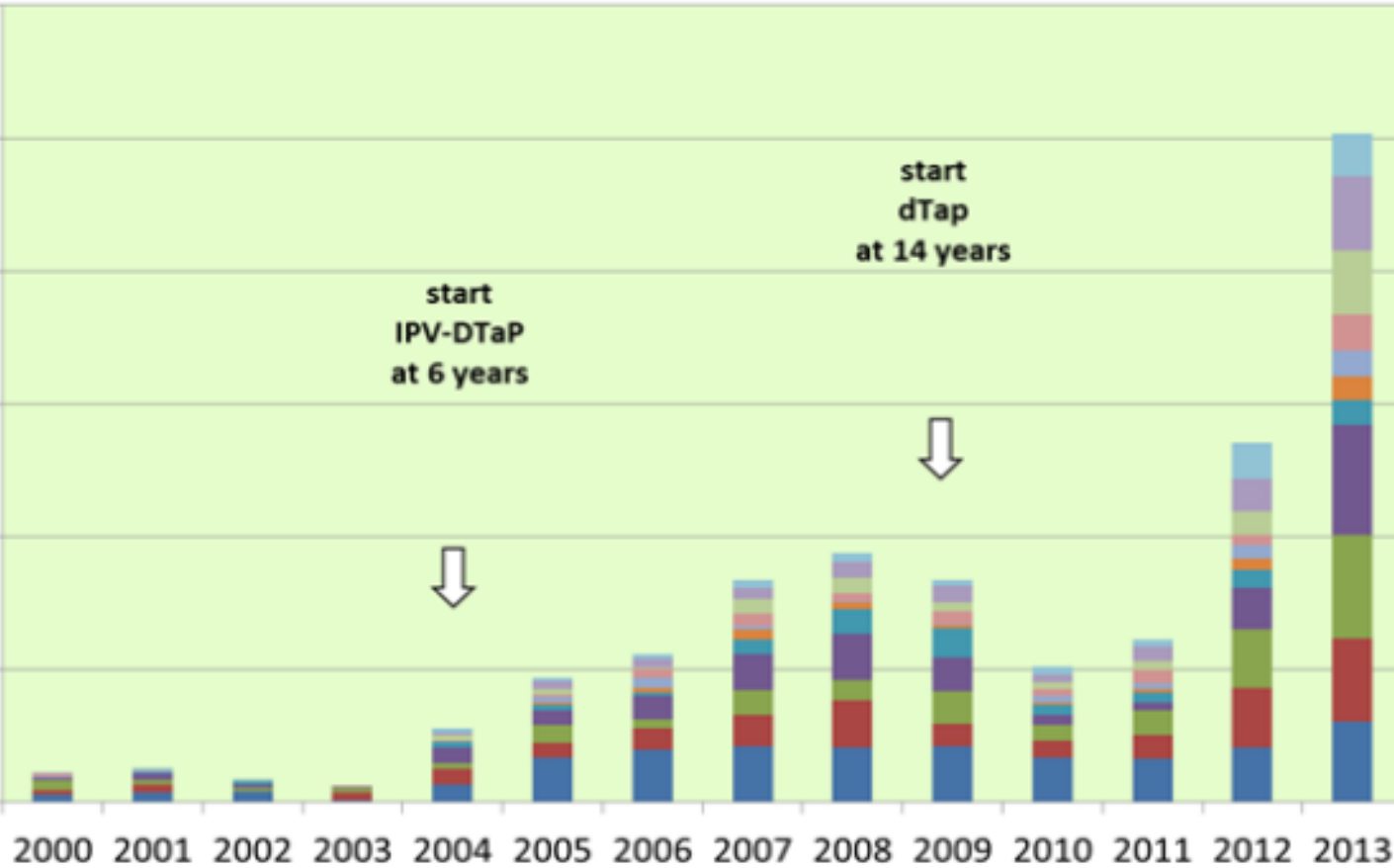
400

300

200

100

0



Top G, ESPID 2014

Pertussis cases in Flanders in 2013 (<50 years)

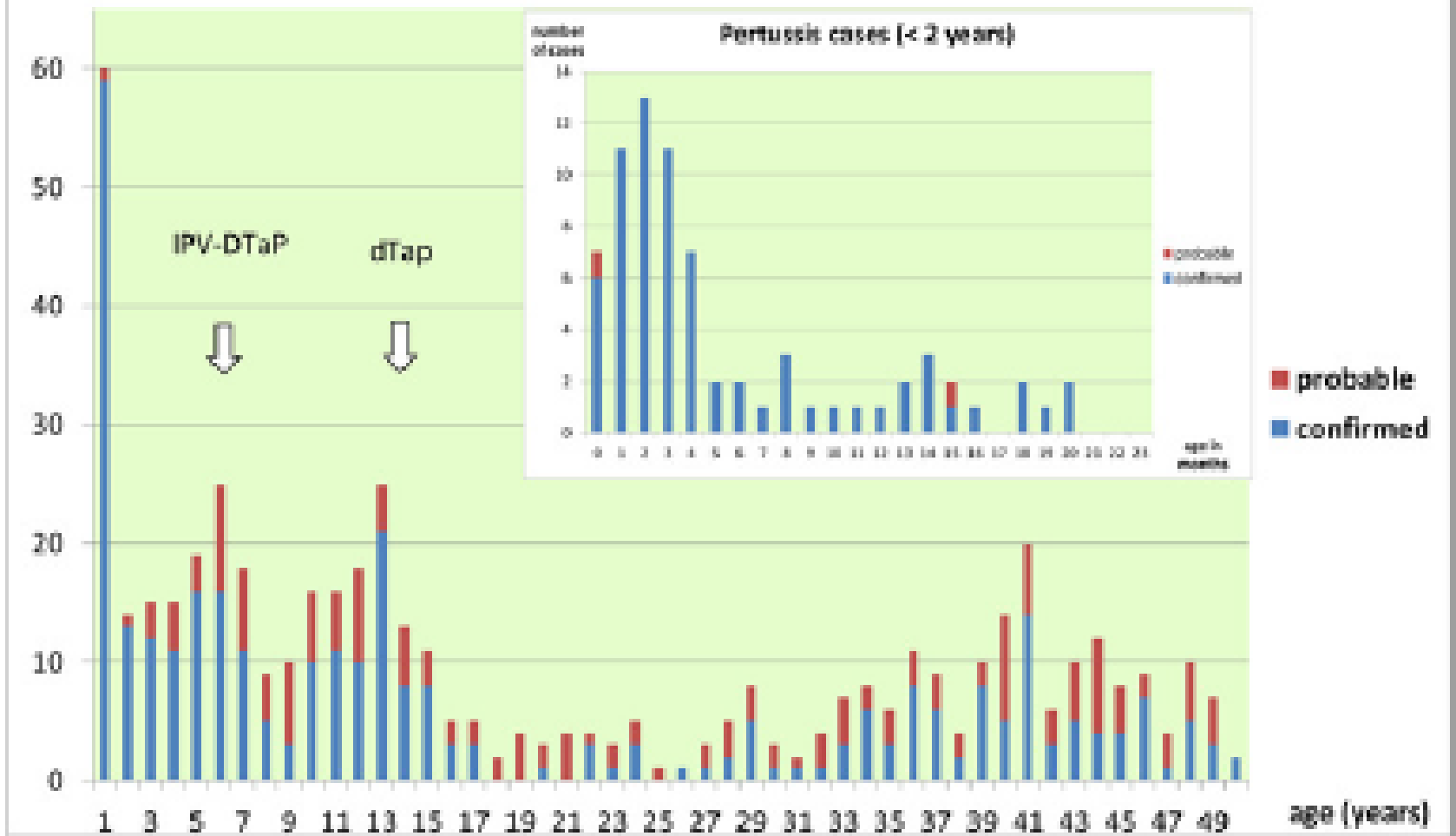


Figure 2: Age distribution of notified pertussis cases in 2013

Top, ESPID poster 2014

Tableau 1 : Cas de coqueluche déclarés en Wallonie en 2013 par catégorie d'âge

Age (ans)	Fréquence	Pourcentage	% cumulés
< 1	51	12,7%	12,7%
1 - 4	32	8,0%	20,7%
5 - 14	81	20,2%	40,8%
15 - 24	38	9,5%	50,3%
24 - 44	89	22,1%	72,4%
45 - 64	82	20,4%	92,8%
≥ 65	29	7,2%	100,0%
Total	402*	100,0%	100,0%

* 7 valeurs manquantes pour la date de naissance

Wallonie 2013: www.sante.cfwb.be

Table 1. *Number of sera with anti-PT IgG titres indicative of recent or acute pertussis infection*

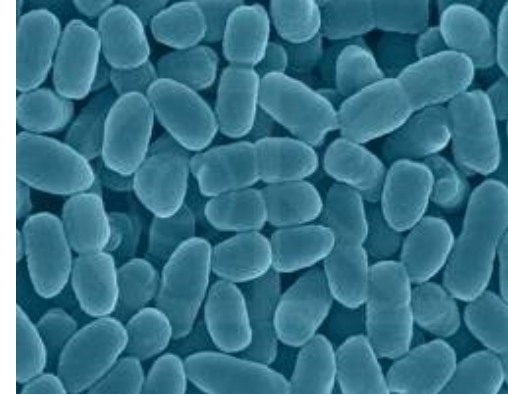
Region/province	> 50 IU/ml*	> 100 IU/ml†	% Positive
Flanders			
West Flanders	13	16	11·6
East Flanders	8	11	7·6
Wallonia			
Liège	12	6	7·2
Hainaut	13	14	10·8
Brussels Capital Region			
UZ Brussel	8	5	5·6
CHU Bruxelles	7	9	6·4

* Anti-PT IgG titre reflecting probable pertussis infection during the past 2 years.

† Anti-PT IgG titre reflecting probable acute pertussis infection.



Het vaccin



- wP vaccin versus aP vaccin

- Antigenisch actieve producten

- pertussis toxine
- filamenteus haemagglutinine
- adenylaat cyclase
- pertactine
- tracheaal cytotoxine
- fimbriae

gebruikt in vaccins
in verschillende combinaties

- Boostrix® en Boostrix IPV® op Belgische markt

- Geen correlate of protection

- Immuniteit

- na infectie: 4-20 jaar
- na vaccinatie: 4-12 jaar

Wendelboe PIDJ 2005; Hallander APMIS 2009



Vaccinatie beleid



Beleid in België



- **Zuigelingen** op 8 weken
- **Kinderen** op 4-6 jaar
- **Adolescenten** 14-16 jaar (2009)
- **Één dosis dTpa:**
 - Volwassenen die geen herhaling kregen op 14-16 jaar, ook die tetanus nodig hebben
 - Zwangere bij iedere zs (2013)
 - Volwassenen in contact met jonge kinderen (< 12 mnd)
 - Jonge & toekomstige ouders
 - Grootouders
 - Onthaalmoeders
 - Verzorgend personeel van pediatrie diensten/materniteiten/kinderdagverblijven





Strategieën om pasgeborenen te beschermen

- A. Vaccinatie bij de geboorte
- B. Cocoon vaccinatie
- C. Vaccinatie tijdens de zwangerschap





Zuigelingen vaccinatie

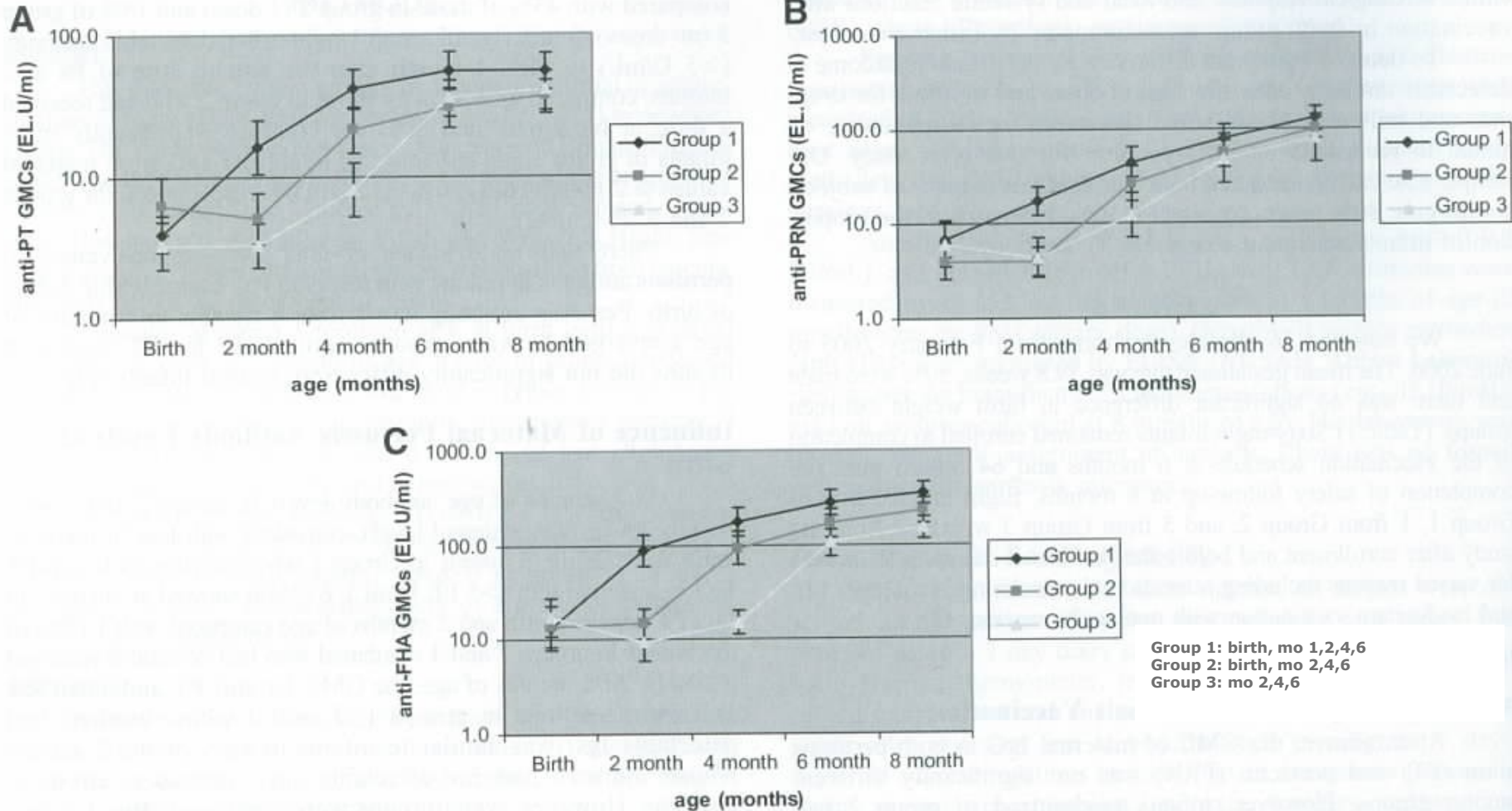


FIGURE 1. Anti-pertussis antibody geometric mean concentrations (GMCs) from birth until 2 months after completion of primary vaccination. A, Antibody response to pertussis toxin according to group and age; B, antibody response to pertactin according to group and age; C, antibody response to filamentous haemagglutinin according to group and age.

Table 1. Sources of infection in 106/166 (64%) households with infants < 6 months of age hospitalized for pertussis. For 12 households more than one primary case was identified.

Household member	Number
Mother (n=166)	40 (24%)
Father (n=157)	22 (13%)
Siblings 0-4 yr (n=93)	23 (14%)
Siblings 5-9 yr (n=86)	20 (12%)
Siblings 10-19 year (n=39)	11 (7%)
Other (n=27)	4 (3%)
Total	120 (73%)



Cocoon dekkingsgraad in Belgium



2012	Women	Men
Cocoon written proof	16,7%	21,2%

Informatie

Vaccinatie

• Ruim de helft (52,8%) van de respondenten kreeg informatie over de cocoonvaccinatiestrategie, hetzij door de gynaecoloog (56,8%), de vroedvrouw (31,8%), de kinderarts (12,1%) of de huisarts (11,7%).

• Net iets minder dan de helft van de vrouwen (46,8%) en hun partners (46,7%) werden gevaccineerd. De belangrijkste oorzaak voor niet-vaccinatie was het feit dat het vaccin niet werd aangeboden.

Vaccinatiegraad studie Theeten et al 2013

De mate waarin ouders werden geïnformeerd hing vooral af van het ziekenhuis waarin de bevalling plaatsgreep, en varieerde van amper 15% in het slechtst scorende ziekenhuis tot 84% in het best scorende.

De leeftijd, de nationaliteit en het hoogst behaalde diploma van de moeder waren geen voorspellende variabelen voor de vaccinatiegraad. Nogmaals wordt hier gewezen op de selectiebias binnen deze populatie.

Masterscriptie: Eveline Dhondt,
Promotoren : Isabel Leroux-Roels,
Geert Leroux-Roels
Centrum voor Vaccinologie UGe

De leeftijd, de nationaliteit en het hoogst behaalde diploma van de moeder waren geen significante voorspellende variabelen voor de informatiegraad in deze populatie van vooral hoogopgeleide vrouwen.

Het ziekenhuis waar de bevalling plaatsgreep had wél een grote invloed op de kans om gevaccineerd te zijn. De

vaccinatiegraad varieerde van 7,7% in het slechtst scorende ziekenhuis tot 91% in het best scorende.

Vax Info nr. 68 - Mei 2014

Vaccineren tijdens de zwangerschap

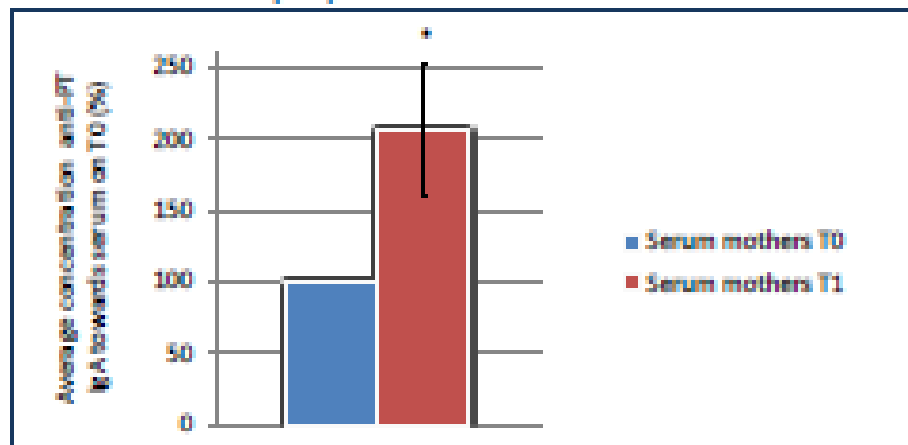


Borstvoeding

Poster@Bordetella2013,
September 2013, Dublin

ANTI-PT IgA UPON VACCINATION

*Concentration of anti-PT IgA in serum of the pregnant women on moment of vaccination (T0) and 4 weeks postvaccination (T1)



*Concentration of anti-PT SIgA in breast milk 8 weeks postpartum

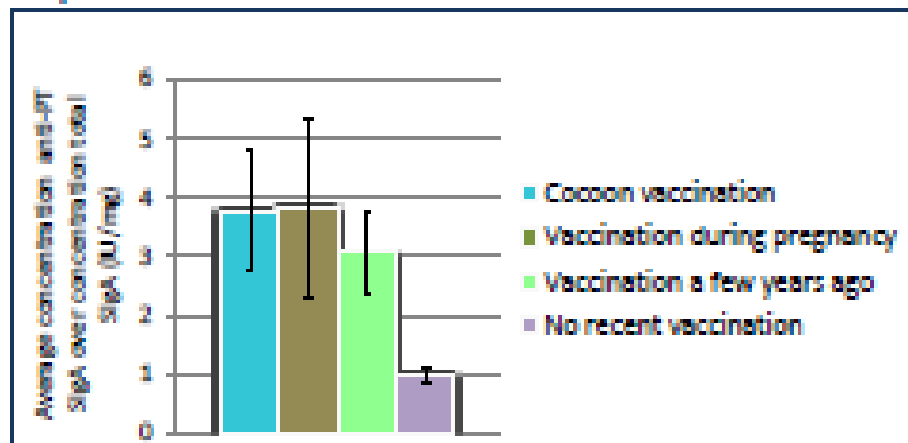


TABLE 1. Geometric Mean Titers (GMT) in Women and Children at Different Time Points for 3 Pertussis Antibodies (anti-PT, anti-FHA, anti-PRN) and *P* Values Indicating the Differences in GMT Between the Different Time Points (Paired Student *t* Test)

	anti-PT (95% CI) (Npos/N) (%) [*]	anti-FHA (95% CI) (Npos/N) (%) [*]	anti-PRN (95% CI) (Npos/N) (%) [*]
GMT women			
Prevaccination	3.6 (2.3–5.8) (7/24) (29%)	13.9 (8.3–23.5) (21/24) (87.5%)	14.4 (8.8–23.7) (18/24) (75%)
Postvaccination month 1	53.7 (23.2–89.5) (23/24) (96%)	913.5 (650–1283.8) (24/24) (100%)	586.9 (389–885.5) (24/24) (100%)
At next delivery	12.1 (7.3–19.9) (18/22) (81%)	133.2 (89–199.4) (22/22) (100%)	160.4 (94.6–271.8) (22/22) (100%)
<i>P</i> value pair 1 [†]	<0.0001	<0.0001	<0.0001
<i>P</i> value pair 2 [†]	<0.0001	<0.0001	<0.0001
<i>P</i> value pair 3 [‡]	<0.0001	<0.0001	<0.0001
GMT children			
Cord group A [‡]	6.1 (3.5–10.6) (12/22) (54%)	22.2 (12.9–38) (19/22) (86%)	20.3 (11.8–35) (19/22) (86%)
Cord group B [‡]	19.0 (11.7–30.7) (21/22) (95%)	247.0 (151–379) (22/22) (100%)	278.0 (154–502) (22/22) (100%)
<i>P</i> value both groups of cord samples	0.006	<0.0001	<0.0001
Infant group A, month 1 [‡]	3.1 (1.6–6.0) (5/14) (35%)	10.6 (5–22) (10/14) (71%)	9.8 (5–18) (8/14) (57%)
Infant group B, month 1 [‡]	10.3 (6.3–16.8) (18/22) (81%)	152.1 (104–220) (22/22) (100%)	167.4 (102–274) (22/22) (100%)
<i>P</i> value both groups of children	0.005	<0.0001	<0.0001

^{*}Npos = number of positive samples/N = total number of available samples and % positive samples.

[†]*P* value pair 1 = prevaccination and postvaccination month 1; *P* value pair 2 = postvaccination month 1 and at next delivery; *P* value pair 3 = prevaccination and at next delivery.

[‡]Group A: first born children, before the maternal booster dose; group B: second cohort of children, born after the maternal booster dose.

PT indicates pertussis toxin; FHA, filamentous hemagglutinin; PRN, pertactin; CI, confidence interval.

Op maand 1: halvering van titer

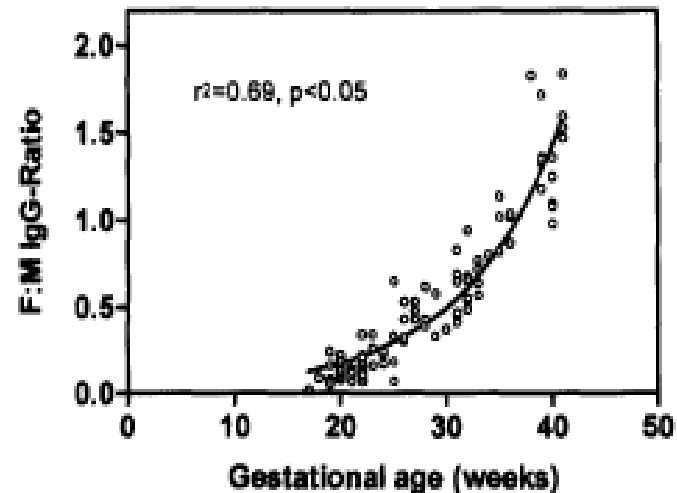


Vaccinatie tijdens de zwangerschap

Table 4
GMC and % 95 confidence intervals (CI) and placental transfer ratio (TR) of anti-pertussis antibodies in preterm subgroups and in the term group.

	Severely preterm (<32 weeks) (n: 42)	Late preterm (≥32 weeks) (n:58)	Term (≥37 weeks) (n: 100)
Anti-PT GMC (EU/ml)	9.76 ^a	16.32	19.46 ^a
95% CI	6.53–14.61	11.72– 22.73	15.73–24.10
Anti-FHA GMC (EU/ml)	13.54	15.33	19.18
95% CI	9.34–19.63	11.51– 20.41	15.58–23.62
Anti-PT placental TR	0.55 ^{b,c}	0.79 ^{b,d}	1.07 ^{c,d}
Anti-FHA placental TR	0.58 ^{e,f}	0.83 ^{e,g}	1.20 ^{f,g}

- ^a comparison of these 2 groups yielded a p value of 0.002.
- ^b comparison of the preterm subgroups yielded a p value of 0.006.
- ^c comparison of these groups yielded a p value of 0.0001.
- ^d comparison of these groups yielded a p value of 0.009.
- ^e comparison of the preterm subgroups yielded a p value of 0.01.
- ^f comparison of these groups yielded a p value of 0.0001.
- ^g comparison of these groups yielded a p value of 0.0001.



Historische data

Study	Year	No	Vaccine /Doses	Safety	Effectiveness
Lichty	1938	42	3 wP	Arm pain	Not reported
Cohen/ Mishulow	1941- 1946	~170	6 wP	Arm pain, lump, no adverse pregnancy outcomes	0/8 immunized and 3/6 unimmunized exposed infants developed pertussis
Kendrick	1945	57	3 wP	Not reported	Not reported
Adams	1947	16	3 wP	Not reported	Not reported
Cohen	1951	106	3 wP	Mild injection site; no adverse pregnancy outcomes	0/2 exposed infants of immunized women developed pertussis

TABLE 1**Newborn antibody levels stratified whether mothers Tdap**

Outcome Antibodies	Mother did not receive Tdap, mean (SEM) n = 52	Mother received Tdap, mean (SEM) n = 52	P value^a
Diphtheria	0.571 (0.157)	1.970 (0.291)	< .001
Tetanus	4.237 (1.381)	9.015 (0.981)	.004
PT	11.010 (1.796)	28.220 (2.768)	< .001
FHA	26.830 (4.022)	104.15 (21.664)	.002
PRN	24.700 (5.765)	333.01 (56.435)	< .001
FIM 2/3	82.83 (14.585)	1198.99 (189.937)	< .001

FHA, filamentous hemagglutinin; *FIM*, fimbriae; *PRN*, pertactin; *PT*, pertussis toxin; *Tdap*, tetanus, reduced diphtheria, and acellular pertussis antigens vaccine.

^a Significant at .05 level.

Gall. Effect of maternal immunization with Tdap. *Am J Obstet Gynecol* 2011.



Characteristic	Women		
	Pregnant		Nonpregnant Tdap (n = 32)
	Tdap Antepartum/Placebo Postpartum (n = 33)	Placebo Antepartum/Tdap Postpartum (n = 15)	

Table 4. Geometric Mean Concentration of Antibodies to Tdap Vaccine Antigens in Sera From Mothers and Infants, and Nonpregnant Women, by Study Group and Time of Sample Collection

Antigen ^a / Study Group	GMC (95% CI)							
	Prior to Immunization ^b	Pregnant and Nonpregnant Women			Infants			
		4 wk After Antepartum Tdap or Placebo ^b	At Delivery	2 Mo After Delivery	At Birth (Cord Blood)	2	Months 7 13	
Pertussis toxin, EU/mL								
Antepartum ^c	7.9 (4.9-12.6)	56.5 (40.0-79.9)	51.0 (37.1-70.1) ^f	53.1 (39.4-71.7) ^f	68.8 (52.1-90.8) ^f	20.6 (14.4-29.6)	64.9 (53.8-78.3)	80.1 (57.3-112.1)
Postpartum ^d	9.6 (5.2-17.6)	10.2 (5.6-18.7)	9.1 (4.6-17.8)	66.4 (42.2-104.8)	14.0 (7.3-26.9)	5.3 (3.0-9.4)	96.6 (56.7-164.6)	83.9 (50.0-140.8)
Nonpregnant	17.6 (12.5-24.7)	90.9 (69.1-119.7)						

Muñoz et al JAMA 2014

Anti-PT GMC in IU/mL (95%CI)	Group 1: Boostrix Belgium	Group 2: Control Belgium	Group3: Adacel Vietnam	Group 4: Control Vietnam	Difference group 1/3 (p value)
Prevacc	4.5 (3.1-6.4)	8.5 (5.6-13.1)	8.2 (6.4-10.6)	7.9 (6.0-10.4)	0.03
Postvacc	47.6 (38.7-58.7)	NA	33.1 (26.2-41.8)	NA	0.03
@ delivery	31.5 (25.8-38.5)	11.0 (8.0-15.2)	16.3 (12.7-20.9)	6.5 (4.5-9.4)	<0.01
Cord	100.5 (81.6-123.8)	24.9 (18.1-34.4)	21.9 (15.8-30.3)	6.2 (4.2-9.2)	<0.01
Mean ratio cord /maternal IgG	3.5	3.4	1.6	1.3	< 0.01

Leuridan et al ESPID 2014



De aanbevelingen



Reported Case Profiles, 2012 By Age, Weeks 1-52

Age	No. of Cases	%	Age Inc /100,000
< 1 yr	4994	10.3	126.7
1-6 yrs	8280	17.2	34.1
7-10 yrs	9532	19.8	58.5
11-19 yrs	14440	29.9	38.0
20+ yrs	10436	21.6	4.5
Unknown	595	(1.2)	N/A
Total	48277	100.0	15.2*

*Total age incidence per 100,000 calculated from 47,682 cases with age reported.

2012 Reported Pertussis Deaths By Age

Age	Deaths [†]
Infants, aged < 3 months:	15
Infants, aged 3-11 months:	1
Children, 1-4 years:	2
Adults, aged 55+ years:	2
Total	20

[†]Deaths reported through NNDDS to CDC.

^{††}11 of the 20 deaths were male.



DTaP Vaccination History of Pertussis Cases

Age	Unk	0 doses	1-2 doses	3+ doses	Total
	No. (%)	No. (%)	No. (%)	No. (%)	No.
6-11 mo	320(26)	131(11)	230(19)	539(44)	1220
1-4 yrs	1613(28)	540(9)	233(4)	3404(59)	5790
5-6 yrs	630(25)	180(7)	60(3)	1620(65)	2490
Total*	2563(27)	851(9)	523(5)	5563(59)	9500

*Percent calculated from total cases aged 6 months to 6 years, n=9,500.



ACIP (CDC), USA, Augustus 2011

- **Use of Tdap in pregnant women**
 - for pregnant women who previously have not received Tdap
 - **should administer Tdap during pregnancy, preferably during the third or late second trimester***. Alternatively, if not administered during pregnancy, Tdap should be administered immediately postpartum
- Reason: burden of disease
- UPDATE Oct 2012: **every** pregnancy



Figure 1. Provisional number of confirmed cases of pertussis, England and Wales, 2011 and 2012 by month

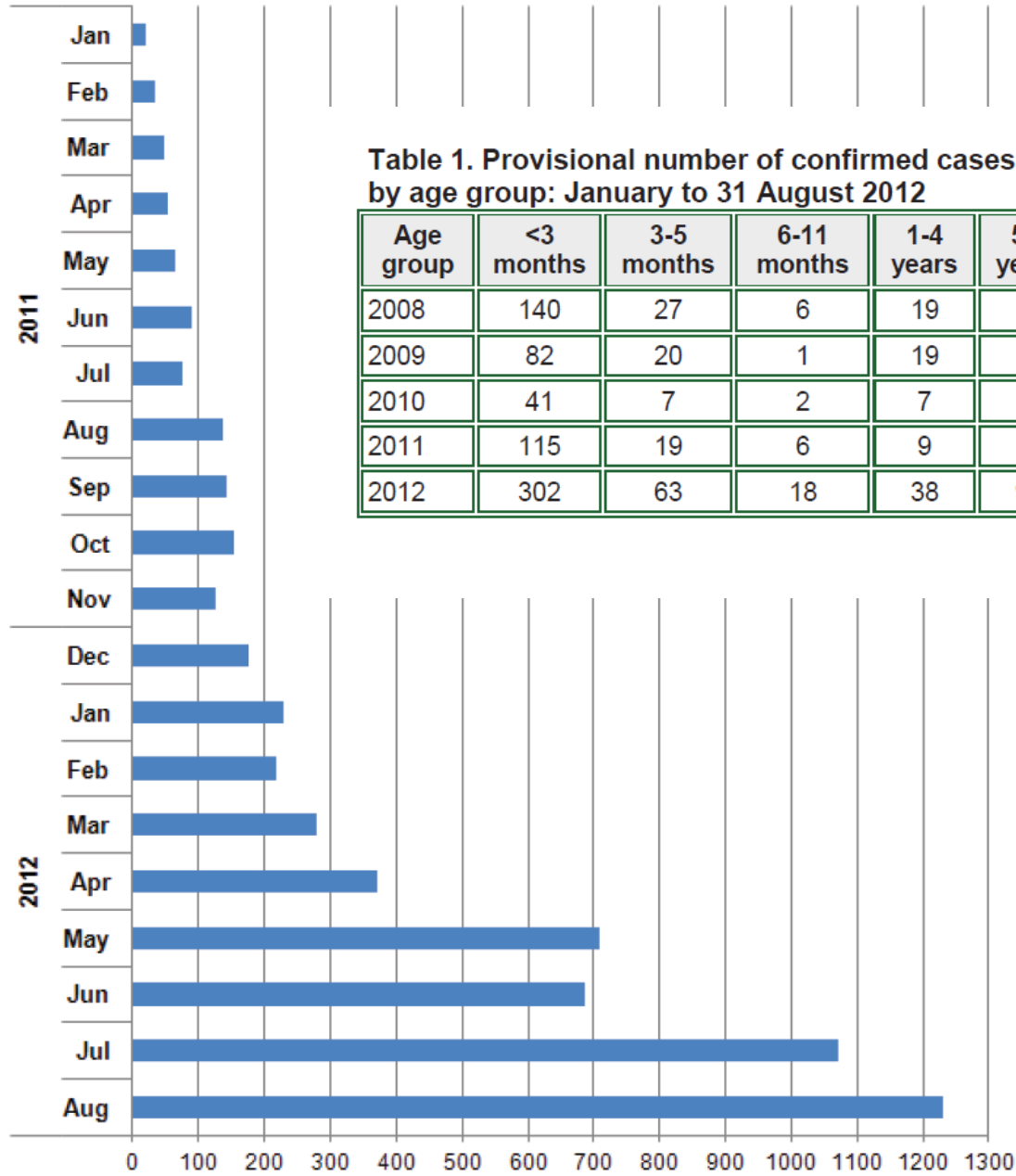
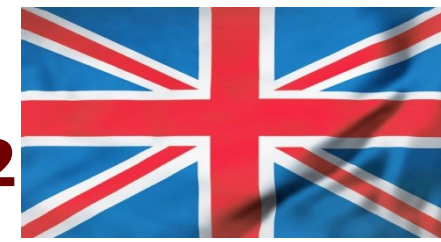


Table 1. Provisional number of confirmed cases of pertussis in England and Wales, 2008 to 2012 by age group: January to 31 August 2012

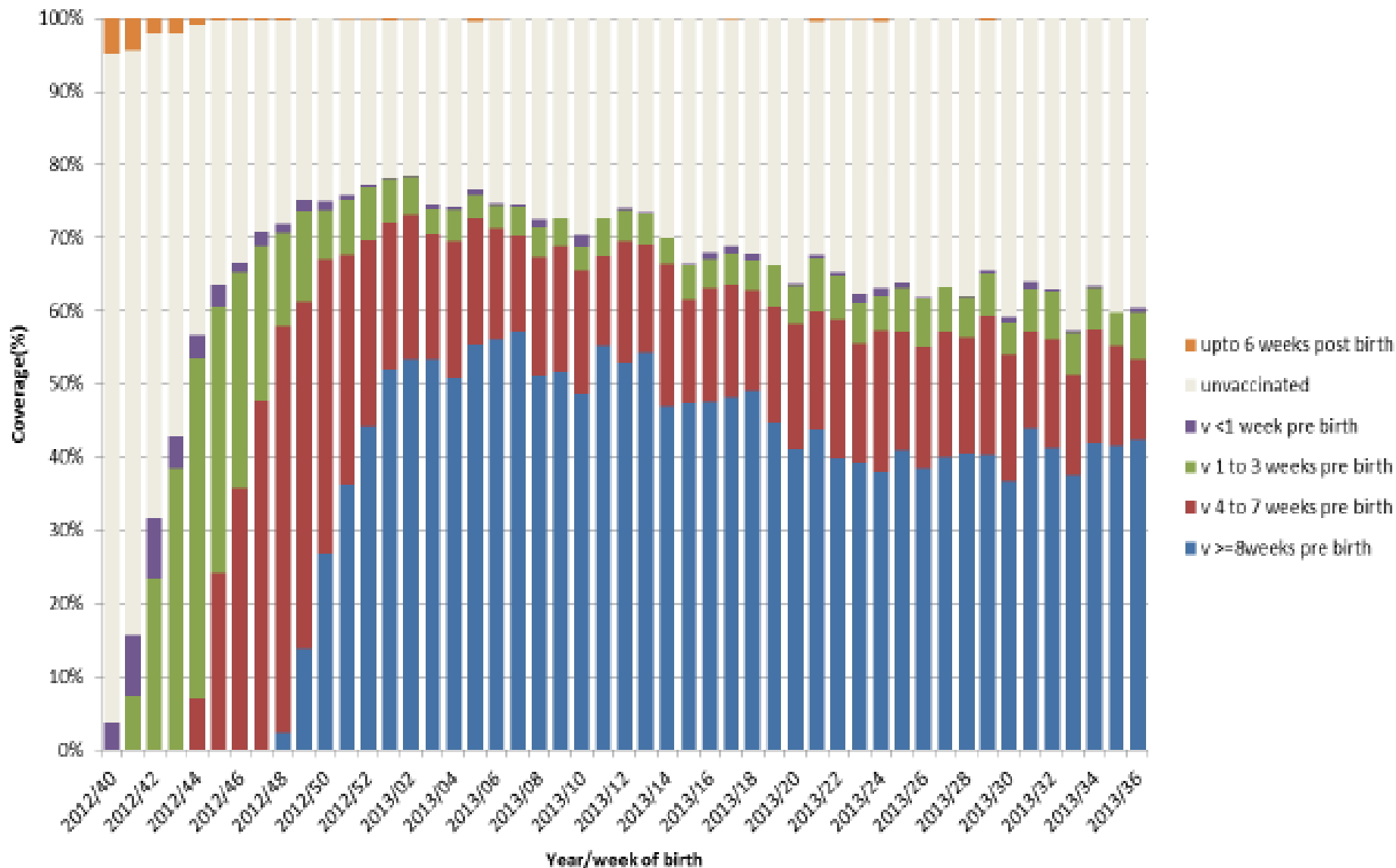
Age group	<3 months	3-5 months	6-11 months	1-4 years	5-9 years	10-14 years	15+ years	Not known	All ages
2008	140	27	6	19	14	104	317	-	627
2009	82	20	1	19	19	72	288	-	501
2010	41	7	2	7	9	31	156	-	253
2011	115	19	6	9	11	61	304	-	525
2012	302	63	18	38	95	496	3,778	1	4,791

14 infants died in 2012 (age 4-9 weeks)



- **Use of Tdap/IPV in pregnant women.**
 - Immunisation within weeks 28 to 32 of pregnancy may be optimal.
 - The committee considered that women with **repeat pregnancies** should be offered immunisation during **each** pregnancy as this would ensure maximal transplacental transfer of antibody.
- <http://www.dh.gov.uk/health/2012/09/whooping-cough-information/>
- **Reason:** most infant cases of pertussis continue to be below six weeks of age with a higher incidence in infants aged under three months than at any other point in over a decade; **nine confirmed deaths in infants under one year of age** have been reported up to week 39 in 2012, **all of whom were unvaccinated**

**% of mothers vaccinated by week of birth of infant (to 3/9/2013) and timing prior to delivery:
Data from the Clinical Practice Research Datalink which covers 12.5 million UK patients**



1. Preconceptionele vaccinatie is de meest ideale situatie.
2. Indien niet gebeurd, voorkeur voor vaccinatie tijdens de zwangerschap, **tussen 24 (suikertest) en 30 weken** is een goed moment.
 - a. Hierdoor is er voldoende productie van antistoffen bij de moeder met transfer naar de fetus, die de neonaat zullen beschermen tijdens de kritische eerste 2 maanden.
 - b. De vrees dat de neonaat onvoldoende antistoffen zou aanmaken door het maternale vaccin, is ongegrond.
 - c. De veiligheid van het vaccin tijdens de zwangerschap werd nu voldoende aangetoond.
3. Postnatale vaccinatie toont onvoldoende bescherming voor de kritieke periode neonataal.
4. **Vaccinatie gebeurt preferentieel door de huisarts. Indien het vaccin door de gynaecoloog wordt toegediend, dient registratie te gebeuren via <https://www.vaccinnet.be>**
5. Er wordt nog steeds aangeraden om de partner (terugbetaald) en grootouders te vaccineren omdat zij ook onvoldoende antistoffen zullen hebben.

Er wordt sinds enkele jaren een rappel voorzien voor tieners tussen 15-16 jaar via het CLB, waardoor dit een tijdelijke opdracht wordt.

HGR augustus 2013

- Voor iedere **zwangere vrouw** wordt kinkhoestvaccinatie tussen week 24 en week 32 van de zwangerschap aanbevolen, ongeacht of de vrouw voordien een herhalingsinenting kreeg.
- Indien de vaccinatie niet tijdens de zwangerschap wordt gegeven, wordt ze zo snel mogelijk postpartum toegediend als onderdeel van de cocoonstrategie.
- In geval de zwangere vrouw tijdens de zwangerschap werd ingeënt of men deze inenting onmiddellijk na de bevalling plant, blijft 'cocoonvaccinatie' voor **partner en andere adolescenten en volwassenen** die met de zuigeling in contact komen zeker aanbevolen. Deze 'cocoonvaccinatie' wordt best uitgevoerd een paar weken voor de bevalling.
- Er zijn momenteel geen gegevens beschikbaar over co-administratie van een kinkhoest vaccin en een griepvaccin bij zwangere vrouwen.

http://www.zorg-en-gezondheid.be/uploadedFiles/NLsite_v2/Ziekten/Vaccinaties/Informatie_voor_vaccinatoren/vaccinatie_fiche_volw_kinkhoest_20130830.pdf



Factoren die vaccinatie graad mee bepalen

- USA, retrospective cohort 1467 vrouwen: 82% gevaccineerd
- Kans om gevaccineerd te zijn is groter als:
 - griepvaccin gekregen
 - eerste zwangerschap
 - kaukasisch

Goldfarb et al AJOG May, 2014



Veiligheid

Study	Source data	N° during pregnancy	Gest age	Vaccine	AE	Interpretation
Zheteyeva 2012	VAERS 2005-2010	132	77% 1 ^e trim	Adacel en Boostrix	4% SAE, 15,5% spont sab	No unexpected pattern or unusual events
Wang 2011	Adacel Vaccine Pregnancy registry 6 years	539	All trim	Adacel	5% SAE	idem
Talbot 2010	Study Tdap HCW	16	All trim	Adacel	None	idem
Boostrix characteristics	GSK file	3	?	Boostrix	None	

US: ACIP : enhanced surveillance through VAERS/VSD.

Safety assessment by Medicines and Healthcare Regulatory Agency

Pregnant women with a record for a pertussis-containing vaccination from 01/10/2012 to 31/03/2013 were identified in the Clinical Practice Research Datalink. Stillbirth rates following vaccination were compared to published national background data. A matched cohort study, using historical unvaccinated controls, examining a range of pre-defined pregnancy-related adverse events was also conducted.

Follow up information on 17,560 vaccinated women. No adverse affects on fetal or obstetric outcomes identified

Table 3. Serious Adverse Events in Study Participants Receiving Tdap, by Study Group and Severity

	Antepartum		Postpartum		Nonpregnant Women (n = 32)
	Pregnant Women (n = 33)	Infants of Pregnant Women (n = 33)	Pregnant Women (n = 15)	Infants of Pregnant Women (n = 15)	
No. of participants with serious adverse events, No. (%) [95% CI]	7 (21.2) [8.9-38.9]	6 (18.2) [7.0-35.5]	2 (13.3) [1.7-40.5]	6 (40.0) [16.3-67.7]	1 (3.1) [<0.1-16.2]
No. of serious adverse events	7	7	2	10	1
No. with event by severity					
Mild	0	0	0	2	0
Moderate	3	2	1	5	0
Severe	3	5	1	0	1
Life-threatening	1	0	0	3	0
Event description by severity					
Mild				Atrial septum and ventricular septum defect Cardiomyopathy with biventricular hypertrophy ^b	
Moderate	Hypertension 48 d postvaccination Preterm contractions 33 d postvaccination Wound hematoma after cesarean delivery	Gastroenteritis requiring hospitalization Respiratory distress at birth	Vomiting requiring hospitalization 44 d after placebo injection	Bronchiolitis requiring hospitalization Respiratory distress/tachypnea ^c Anemia ^c Hypoglycemia ^b Poor feeding due to gastroesophageal reflux ^b	
Severe	Pregnancy-induced hypertension 30 d postvaccination Pancreatitis 3 mo after delivery Acute appendicitis 19 d after delivery	Choking with feeds requiring prolonged hospitalization Febrile seizures ^a Dehydration due to oral herpes simplex virus requiring hospitalization Bronchiolitis	Preterm labor requiring hospitalization 18 d after placebo injection		Pelvic fracture (motor vehicle crash)
Life-threatening	Fetal distress resulting in cesarean delivery 55 d postvaccination			Fetal distress resulting in cesarean delivery Fetal distress resulting in cesarean delivery ^d Bilateral pneumothoraces ^d	

Abbreviation: Tdap, tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.

^a One infant with febrile seizures had 2 distinct seizure events, both of severe severity.

^b The mild event of "cardiomyopathy with biventricular hypertrophy" and the 2 moderate events of "hypoglycemia" and "poor feeding" occurred in the same infant.

^c The 2 moderate events "respiratory distress/tachypnea" and "anemia" occurred in the same infant.

^d The 2 life-threatening events of "fetal distress" and "bilateral pneumothoraces" occurred in the same infant.



Munoz JAMA
2014

RESULTS

Women	Belgium	Vietnam
Tdap Vaccine	Boostrix [®]	Adacel [®]
Number vaccinated	54	51
Number of AE/N women	45/43 women	24/23 women
Mean duration of AE in days (min-max)	2,3 (1-10)	1,2 (1-2)
Number of SAE/N women	5/4 women	2/1 woman
Mean duration of SAE in days (min-max)	3,8 (1-9)	
Children	Belgium	Vietnam
Number	52 (2 twins)	27
Congenital disorders	0	0
Prematurity	1	1

- Of the 54 women in Belgium, 43 women showed at least 1 AE and 4 women showed at least 1 SAE. Of the 51 women in Vietnam, 23 showed at least 1 AE and 1 woman showed 2 SAE during pregnancy and at delivery.
- SAE in Belgium were 1 preeclampsia with 1 premature delivery, 1 deep venous thrombosis, 1 premature contractions episode and 1 preeclampsia at term. In Vietnam, 1 ovarian cyst with 1 premature delivery occurred.
- The reported AE in both countries were mild to moderate injection site pain and swelling. Fever was reported at day 1 after vaccination in 1 Belgian and 1 Vietnamese women.

DISCUSSION

- Reported AEFI do not differ from the expected side effects of the Tdap vaccine (both Adacel[®] and Boostrix[®]) in adults based on the SmPC (Summary of product characteristics) of both products.

In Belgium, 74% of the participants showed mild to moderate injection site pain and swelling. Compared to the data on the SmPC of Boostrix[®] this is an expected rate of reaction (23,7% - 80,6%)¹.

In Vietnam, 45% of the participants showed mild to moderate injection site pain and swelling. Compared to the data on the SmPC of Adacel[®] this is an expected rate of reaction (24,7%-65,7%)².

- Less AE and SAE are reported in Vietnamese women compared to Belgian women and the mean duration of the AE is shorter in Vietnamese women.
- There were 2 cases (3,7%) of preeclampsia in Belgian women, which is rather high compared to the background rate of preeclampsia in Belgium (2%). But due to the limited number of participants in the study, no conclusion can be drawn.
- The preliminary safety data in the offspring do not show an unexpected risk pattern, no congenital disorders were detected.

¹ http://us.gsk.com/products/assets/us_boostrix.pdf ;

² http://drug.fda.moph.go.th/zone_search/files/2C_5_52_NBC_Adacel.pdf

We acknowledge VliirUos (Flemish University Council: University Development Cooperation, Flanders, Belgium), FWO (Research Foundation Flanders, Belgium), and Nafosted (National Foundation for Science and Technology Development, Vietnam) for funding a joint research project in the field of maternal pertussis pertussis vaccination (grant number FWO.GA03212N)



Interferentie



Whole cell PT vaccine: + interference

- Sako W TW, Witt DB, et al. *Jama* **1945**;127:379-83.
- Provenzano RW WL, Sullivan CL. *NEJM* **1965**;273:959-65.
- **Englund JA**, et al. *Pediatrics* **1995** Sep;96(3 Pt 2):580-4.
- Saffar MJ, et al. *Indian pediatrics* **2007** Dec;44(12):916-8. **NO interference**

Acellular PT vaccine: no interference, studies ongoing in Canada, Mexico, Belgium, Vietnam

- Van Savage J, et al. *JID* **1990** Mar;161(3):487-92.
- **Englund JA**, et al. *Pediatrics* **1995** Sep;96(3 Pt 2):580-4.
- Van Rie A et al. *PIDJ* **2005** May;24(5 Suppl):S62-5.
- **Jones et al**, *Vaccine* **2014**
- **Hardy Fairbanks**, et al *PIDJ* **2013**
- **Muñoz et al** *JAMA* **2014**
- **Expected UK results January 2014 (ECDC Eurovaccine)**

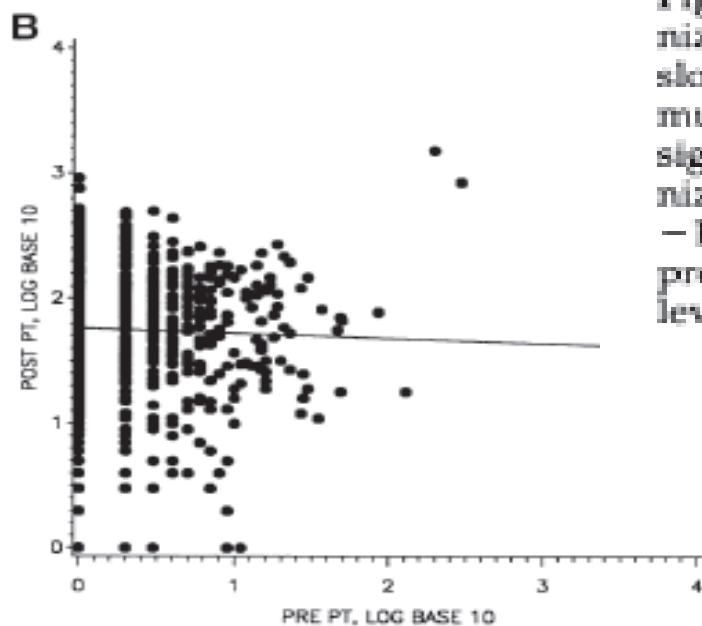
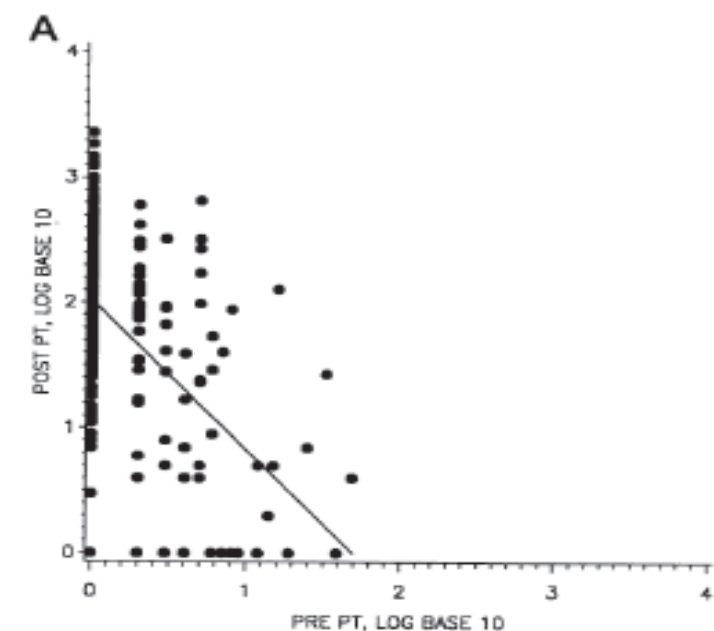


Figure. Relationship between preimmunization and postimmunization PT antibody levels after WCL (A) and DTaP (B). The slope of the linear regression for preimmunization versus postimmunization antibody is -0.04 for DTaP ($P = .26$), indicating no significant effect of preimmunization antibody on the postimmunization response. In contrast, the slope of the regression line is -1.19 for WCL ($P < .001$), indicating a significant negative effect of preimmunization antibody on the postimmunization antibody level. See Table 2 for the various regression coefficients (slopes).

Figure. Relationship between preimmunization and postimmunization PT antibody levels after WCL (A) and DTaP (B). The slope of the linear regression for preimmunization versus postimmunization antibody is -0.04 for DTaP ($P = .26$), indicating no significant effect of preimmunization antibody on the postimmunization response. In contrast, the slope of the regression line is



- RCT Muñoz et al JAMA 2014

Characteristic	Women		
	Pregnant		Nonpregnant Tdap (n = 32)
	Tdap Antepartum/Placebo Postpartum (n = 33)	Placebo Antepartum/Tdap Postpartum (n = 15)	

Table 4. Geometric Mean Concentration of Antibodies to Tdap Vaccine Antigens in Sera From Mothers and Infants, and Nonpregnant Women, by Study Group and Time of Sample Collection

Antigen ^a / Study Group	GMC (95% CI)							
	Prior to Immunization ^b	Pregnant and Nonpregnant Women				Infants		
		4 wk After Antepartum Tdap or Placebo ^b	At Delivery	2 Mo After Delivery	At Birth (Cord Blood)	2	Months	
						7	13	
Pertussis toxin, EU/mL								
Antepartum ^c	7.9 (4.9-12.6)	56.5 (40.0-79.9)	51.0 (37.1-70.1) ^f	53.1 (39.4-71.7) ^f	68.8 (52.1-90.8) ^f	20.6 (14.4-29.6) ^f	64.9 (53.8-78.3)	80.1 (57.3-112.1)
Postpartum ^d	9.6 (5.2-17.6)	10.2 (5.6-18.7)	9.1 (4.6-17.8)	66.4 (42.2-104.8)	14.0 (7.3-26.9)	5.3 (3.0-9.4)	96.6 (56.7-164.6)	83.9 (50.0-140.8)
Nonpregnant	17.6 (12.5-24.7)	90.9 (69.1-119.7)						



Effectiviteit van de strategie

Diermodel: bavianen

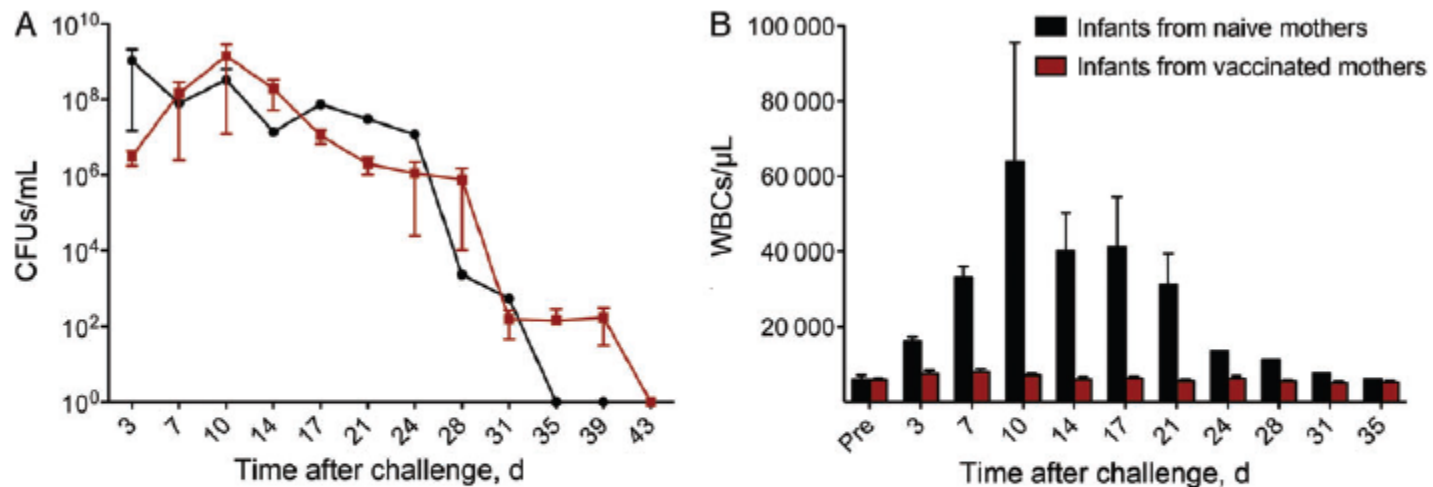
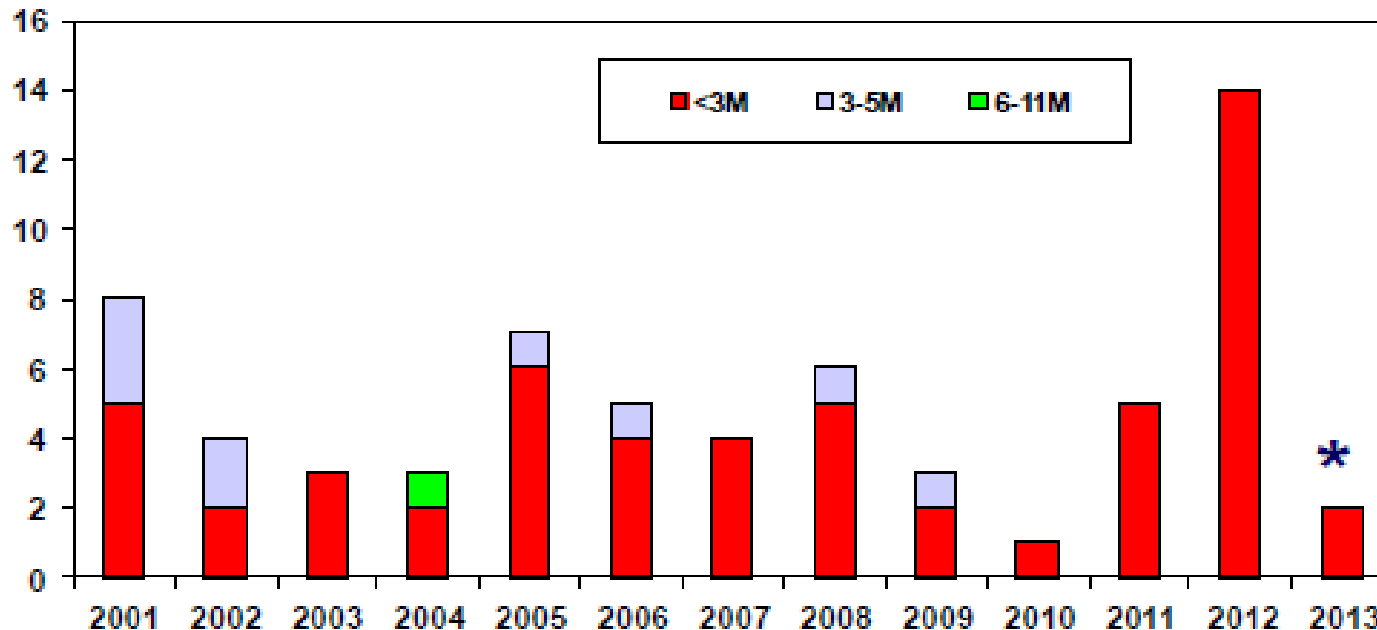


Figure 3. Maternal vaccination prevents leukocytosis but not colonization. Infant baboons were born to mothers that were vaccinated with the tetanus, diphtheria, acellular pertussis priming series and boosted during the third trimester (n = 7) or to unvaccinated mothers (n = 2). All animals were directly challenged with *Bordetella pertussis* at 5–6 weeks of age. *A*, Colonization was monitored by quantifying *B. pertussis* colony-forming units (CFUs) per milliliter in biweekly nasopharyngeal washes, with a limit of detection of 10 CFUs/mL. *B*, The mean circulating white blood cell (WBC) counts before and after challenge are shown for each group of animals (n = 2 per group). ***P* < .01 versus preinfection values from the same group.

Warfel et al JID March 2014

Reconciled deaths from pertussis in infants, England only



Sources: lab confirmed cases, certified deaths, Hospital episode statistics, GP registration details

* Both with unvaccinated mothers





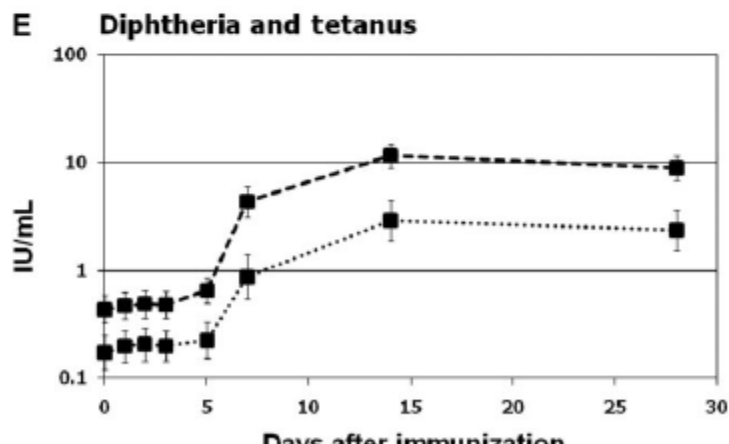
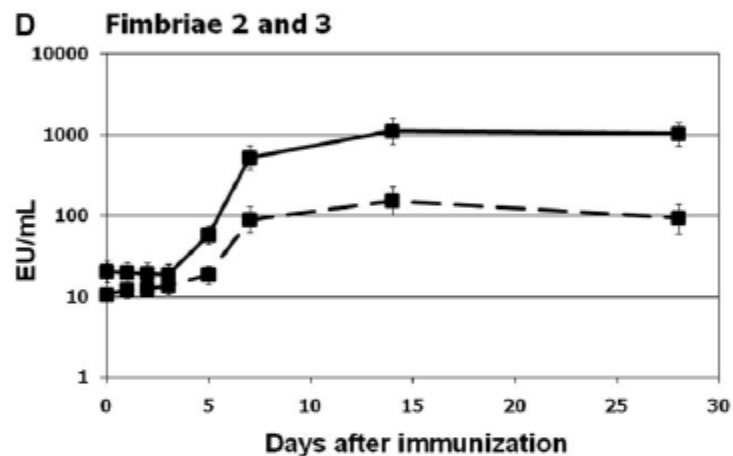
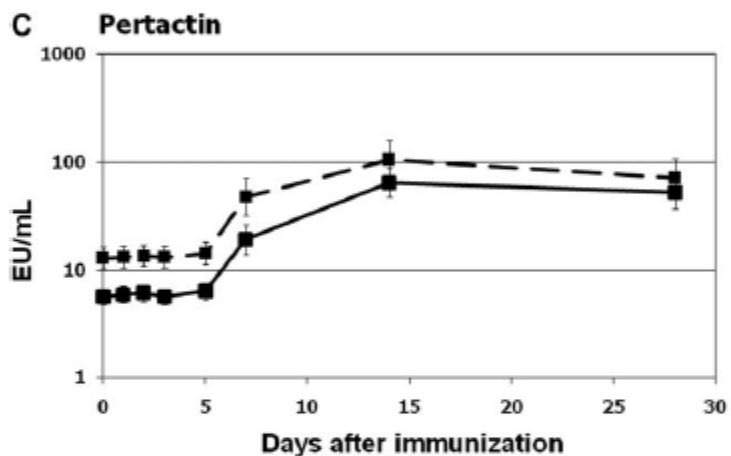
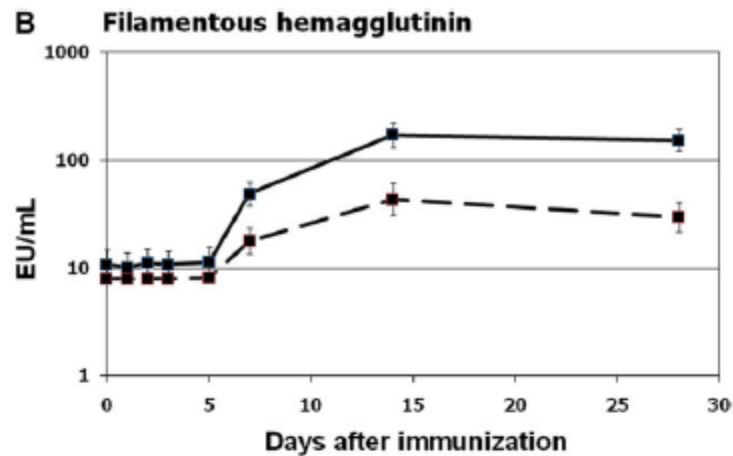
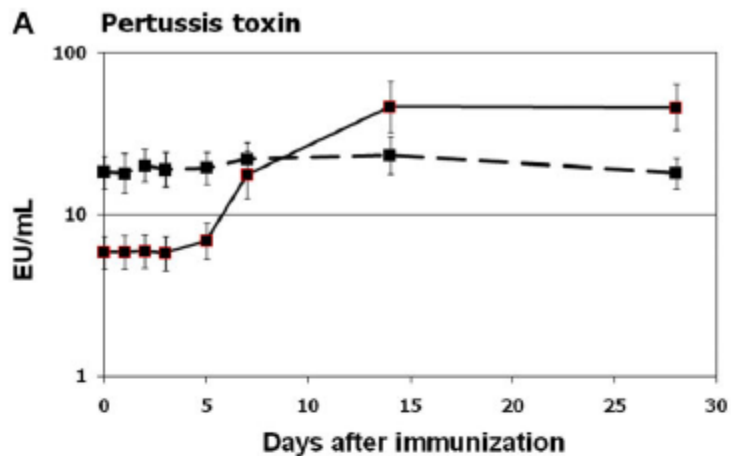
Timing of maternal immunisation	VE (95% CI)
At least 7 days before birth	91% (84% to 95 %)
At least 28 days before birth	91% (83% to 95%)
7 to 27 days before birth	91% (70% to 96%)
0-6 days before or 1-13 days after birth	38% (-95% to 80%)

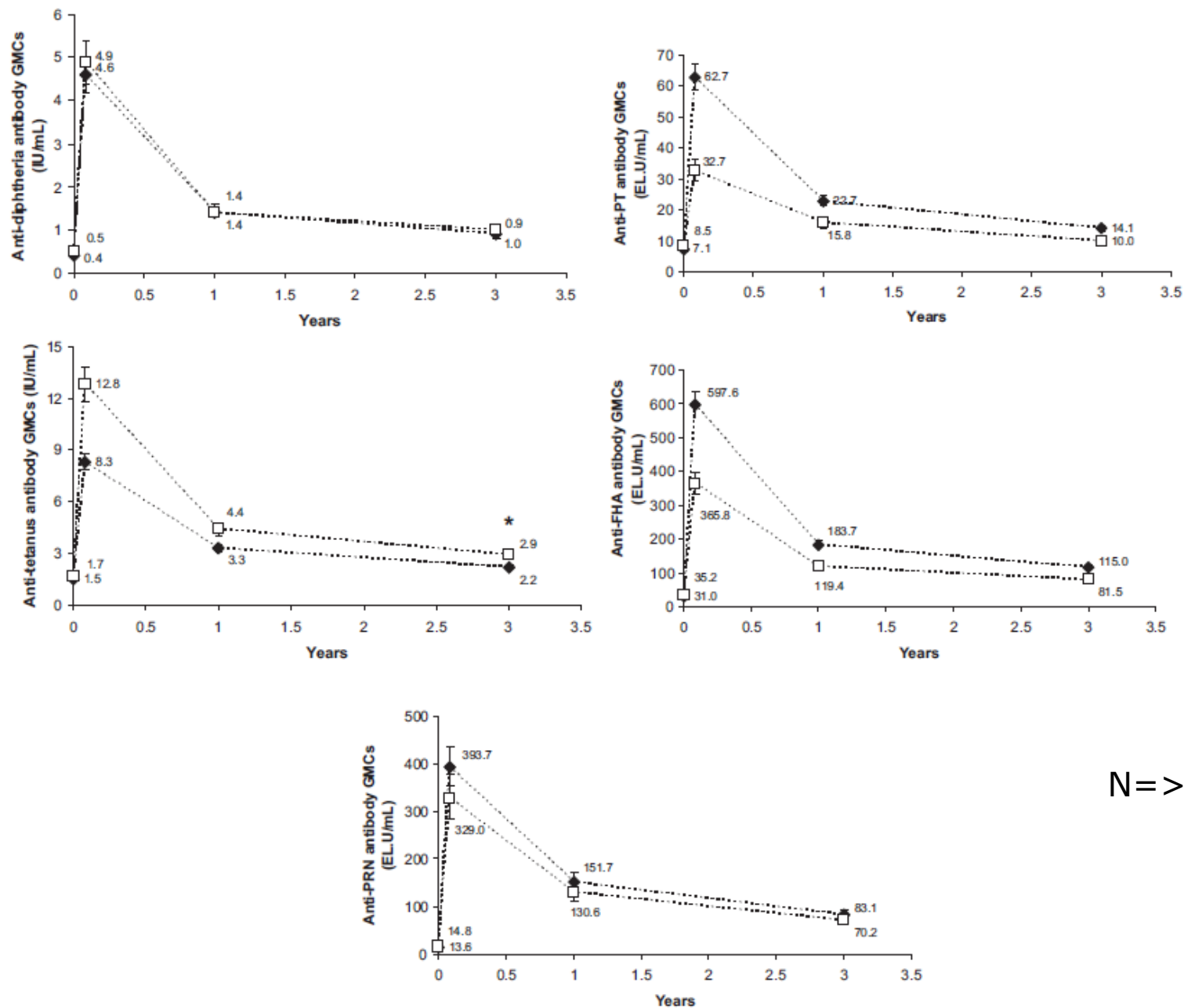


Timing



Halperin
2011 CID





N=>2000

Fig. 2. Antibody GMCs before and up to 3 years after vaccination with Tdap-B or Tdap-A (Year 3 ATP immunogenicity cohort). ◆, Tdap-B group; □, Tdap-A group. *Statistically significant difference between groups: the 95% CI for the between-group anti-tetanus GMC ratio (adjusted) excluded 1.



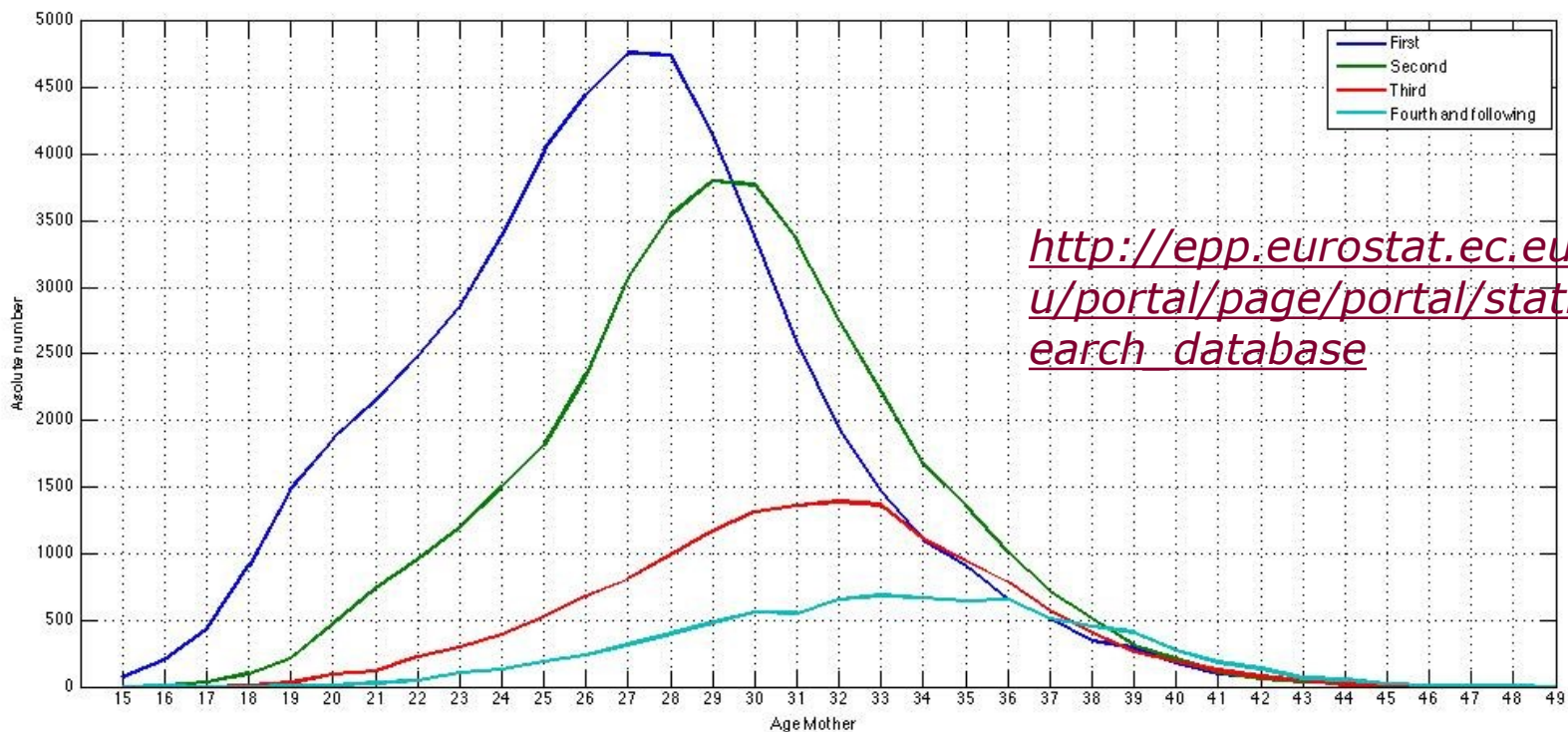
Herhaalde boosters

- Acip Juni 2013: herhaling bij iedere ZS → maternale antistoffen
- Veiligheid?
 - Herhaalde Tdap doses: (S)AE: vergelijkbaar met eerste herhalingsdosis en met Td

Halperin, PIDJ 2006
Beytout Vaccine 2009
Talbot Vaccine 2010
Theeten Vaccine 2007

- Data van herhaalde Td booster: geen verhoogd risico

Edsall JAMA 1967
Plotkin's vaccine 2013



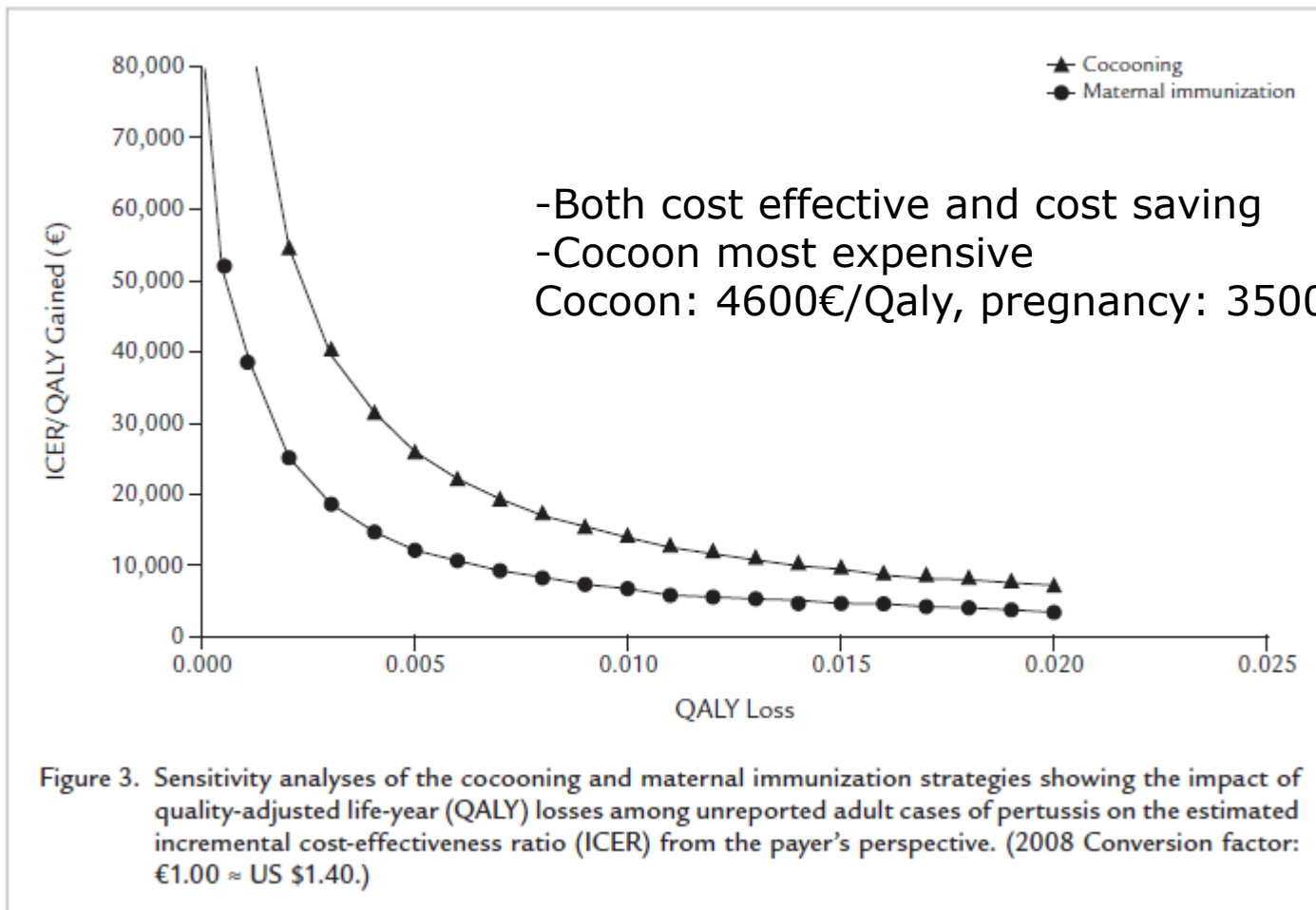
Aantal bevallingen in 2009 per leeftijd van moeder voor verschillende opeenvolgende kinderen.

- 1,85 kinderen per vrouw in België
- Gemiddeld 2 jaren tussen eerste en tweede kind en tussen tweede en derde kind.
- Hoe ouder de vrouwen zijn bij een eerste bevalling, hoe sneller een tweede kind volgt.
- 53.5% van de vrouwen krijgt meer dan 1 kind, 20.5% krijgt 3 kinderen en 7% krijgt 4 kinderen of meer.



Kosten

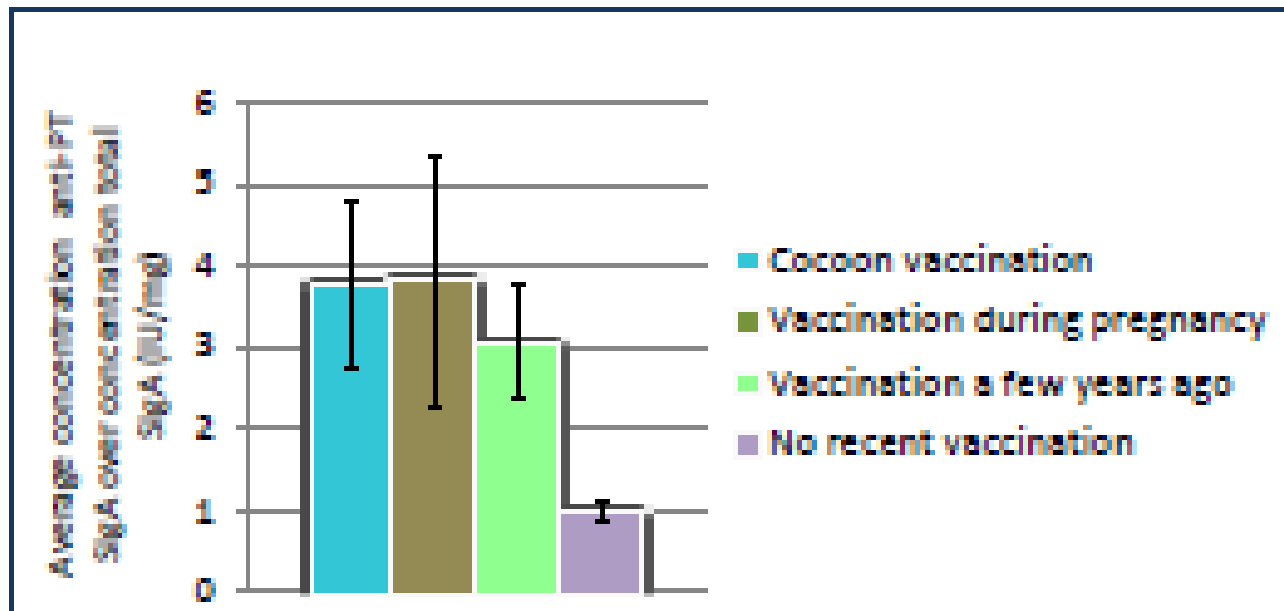




Westra TA Clinical Therapeutics 2010

Effect op borstvoeding

- Concentration of anti-PT SIgA in breast milk 8 weeks postpartum



Conclusie

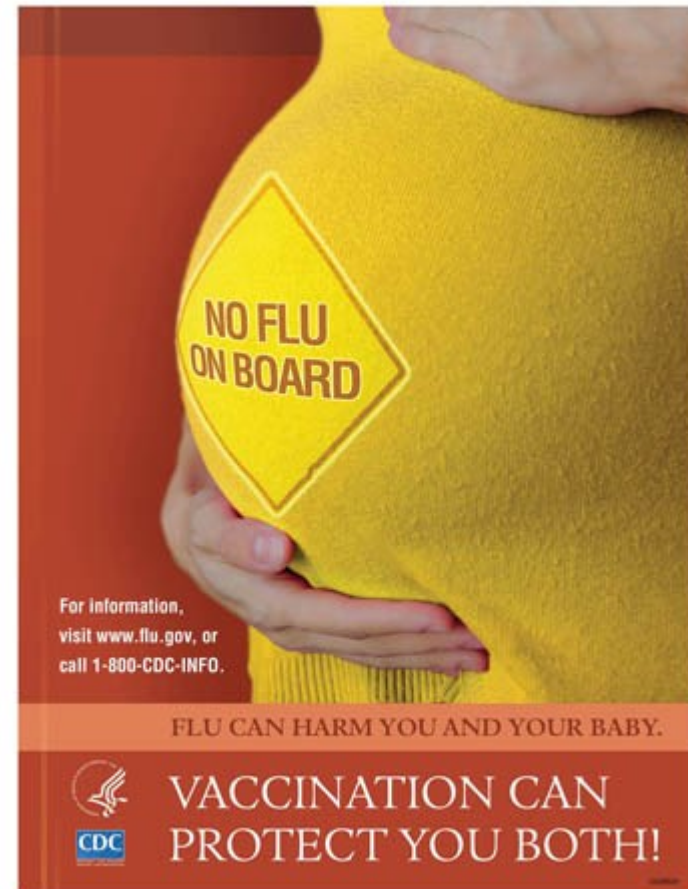
- Tdap tijdens de zwangerschap is veilig en effectief en kosten effectief
- Vaccinatie preferentieel tussen 24 en 32 weken zwangerschapsduur
- Gratis vanaf 1 juli via Vaccinnet voor Vlaanderen



3. GRIEP

influenza

- Influenza tijdens de ZS=
 - risico voor foetus
 - risico voor moeder
- Geen risico van vaccinatie
- Indicatie: iedere zwangere vrouw



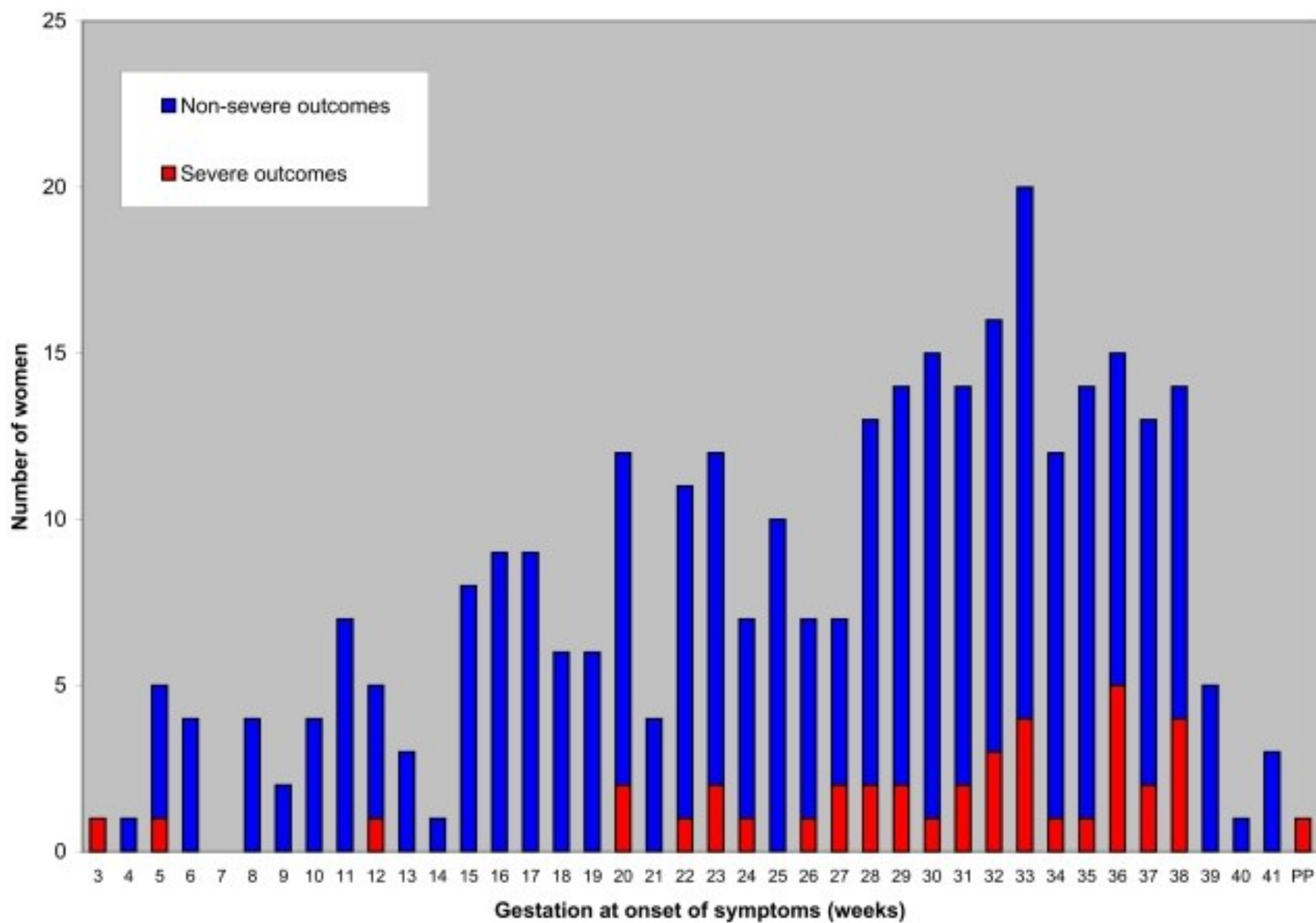
- Foetus
 - Verhoogd risico op abortus
 - Verhoogd risico op stillbirth
 - Verhoogd risico op prematuriteit
 - Vroege infectie: spina bifida, gespleten lip, verkorte ledematen
 - Later: neoplasie- shizophrenie
- Zwangere vrouwen: meer morbiditeit en mortaliteit door influenza (**H1N1**) ~media aandacht
- Postpartum risico stijging en ook bij neonaten
- Cave koorts in de zwangerschap! Paracetamol tot 6 gram/ dag



Influenza- vaccins



- Bijna allemaal geïnactiveerde vaccins
- Jaarlijks verschillende samenstelling
- Veilig tijdens de zwangerschap
- USA: alle zwangeren
- België: zwangeren in 2^o of 3^o trimester tijdens het griepseizoen (Oktober-Maart)
- Hoog risico zwangerschappen: ieder trimester



2009 H1N1 influenza in pregnant women.
Dubar G, et al. PLoS One. 2010 Oct 5;5(10)



EDITORIALS



Immunisation against influenza during pregnancy

The benefits outweigh the risks

Marian Knight *NIHR (National Institute for Health Research) research professor in public health*¹,
Boon Lim *consultant obstetrician*²

¹hospital, Tasmania, Australia



RESEARCH

Vaccination against pandemic A/H1N1 2009 influenza in pregnancy and risk of fetal death: cohort study in Denmark

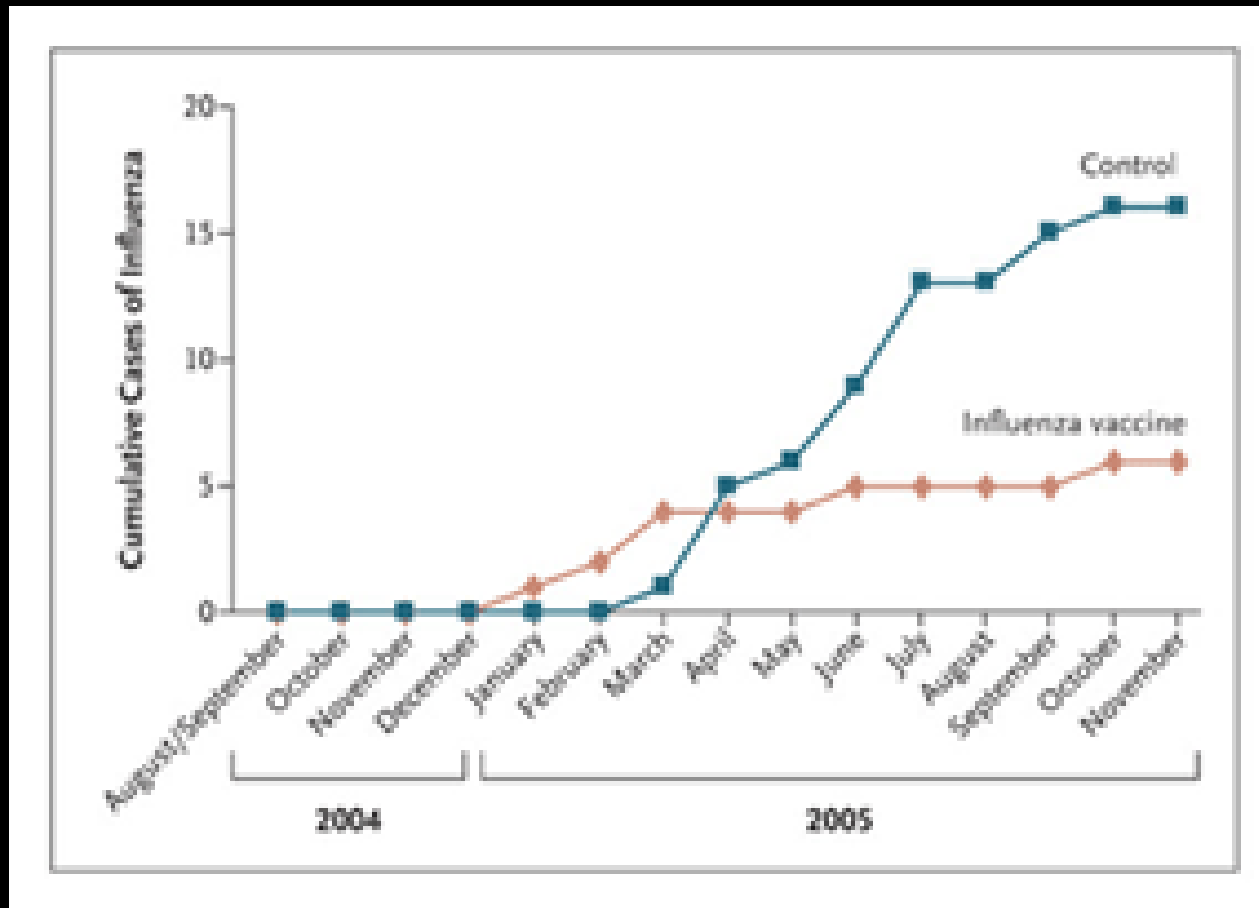
OPEN ACCESS

Björn Pasternak *registrar and postdoctoral fellow*^{1,2}, Henrik Svanström *statistician*¹, Ditte Mølgaard-Nielsen *researcher*¹, Tyra G Krause *consultant*³, Hanne-Dorthe Emborg *epidemiologist*³, Mads Melbye *professor*¹, Anders Hviid *senior investigator*¹

¹Department of Epidemiology Research, Statens Serum Institut, Artillerivej 5, 2300, Copenhagen, Denmark; ²Department of Clinical Sciences, Infectious Diseases Unit, Lund University, Malmö, Sweden; ³Department of Infectious Disease Epidemiology, Statens Serum Institut, Copenhagen, Denmark

- Denemarken
- 54.585 ZS
- Geen verhoogd risico na A/H1N1 2009 influenza vaccin, op:
 - foetale dood
 - spontane abortus
 - stillbirth

Cumulative Cases of Laboratory-Proven Influenza in Infants Whose Mothers Received Influenza Vaccine, as Compared with Control Subjects



Zaman K et al. *N Engl J Med* 2008;359:1555-1564.



THE NEW ENGLAND
JOURNAL OF MEDICINE



Review Steinhof et al Lancet 2014

- > 350.000 ZS gevaccineerd
- Significante reductie in prematuriteit en SGA

Meta-analyse Mertz et al: zwangeren hebben

- Verhoogd risico op hospitalisatie
 - Verhoogd risico op postpartum complicaties en dood door griep
 - Verhoogd risico op griep met complicaties bij neonaten
- gebrek aan goede studies die de effectiviteit meten van vaccinatie tegen seizoensgriep om de zwangeren te beschermen

WHO:

<http://www.who.int/mediacentre/factsheets/fs211/en/>



Effect op borstvoeding



Breast Milk Antibody and Neutralization Activity at One Year Postpartum after Antenatal Influenza Immunization. Mark Steinhoff, MD, FIDSA (ClinicalTrials.gov number, NCT00142389.)

Methods:

- The Mother's Gift study: prospective, blinded, randomized controlled trial
- 340 pregnant Bangladeshi mothers: trivalent inactivated influenza vaccine, or a control vaccine during the third trimester.
- breast milk at birth; 10 weeks, and 6 and 12 months.

Results: Influenza-specific IgA levels in breast milk were significantly higher in vaccinees than in controls;

GMCs: 3-6 fold higher throughout the 1 year observational period.

Virus neutralization titers in milk correlated with influenza-specific IgA levels.



TABLE

Vaccination coverage for first dose of pandemic influenza vaccine by target group, Italy, October 2009 to May 2010

Target groups	Number of first doses administered	Number of persons in target group	Vaccine coverage (%)
Healthcare personnel	165,562	1,069,264	15.5
Essential services personnel (e.g. police, firefighters, military corps)	72,181	1,228,155	5.9
Blood donors	6,329	742,349	0.8
Pregnant women in their second and third trimesters	23,016	189,915	12.1
Women who delivered in the previous 6 months or person who take cares of the baby	8,170	237,594	3.4
Individuals with at least one chronic underlying condition aged 6 months–65 years	549,167	4,309,466	12.7
Individuals with at least one chronic underlying condition aged >65 years	13,562	710,862	1.9
Children aged >6 months attending day-care centres	4,618	89,394	5.2
Children aged <18 years resident in long-term care facilities	1,120	10,155	11.0

20,657	7.7
7,671,581	0.3
4,642,188	0.1
20,921,580	4.2

Rizzo C, et al. Euro Surveill. 2010 Dec 9;15(49).

Mereckiene et al. Eurosurveillance, Volume 15, Issue 44, 04 November 2010. 81

TABLE 3

Vaccination coverage for seasonal influenza for clinical risk groups and/or HCW in 11 EU/EEA countries: national seasonal influenza vaccination surveys in Europe, January 2008 and July 2009^a

	Vaccination coverage for clinical risk groups (%)		Vaccination coverage for HCW (%)	
	Survey 2008	Survey 2009	Survey 2008	Survey 2009
the Netherlands	75.2	71.7	-	-
Norway ^b	50	50	-	-
Germany	48.5	49	27	23
Belgium	47	-	-	-
United Kingdom	42.1	45.3	14	13.4
France	35	52	48	-
Hungary	-	32.9	23.7	23.5
Ireland	27.6	-	20	-
Romania	-	-	-	89.4
Portugal	-	-	40	26
Spain	-	-	34.9	28.1

EEA: European Economic Area; EU: European Union; HCW: Healthcare workers

^a EU target for influenza season 2014-15 – 75%.

^b Vaccine coverage was calculated for the ≥65 age group and clinical risk groups together.

Influenza season provided for clinical groups for Survey 2008: Belgium 2003-4; Germany, Ireland – 2005-6; the remaining countries – 2006-7.

Influenza season provided for HCW for Survey 2008: France – 2004-5; Germany, Ireland – 2005-6; the remaining countries – 2006-7.

All countries reported vaccination coverage data for Survey 2009 for the 2007-08 influenza season.



4. De rol van de apotheker

- Portugal, Ierland, UK, USA: vaccinatie door apothekers
- Frankrijk
 - Comboroure et al pharma 2013
 - Studenten farmacie, N=293 (9,8% vd doelgroep)
 - 96% pro-vaccinatie, 69% is bereid te vaccineren in de praktijk, mits certificaat
- USA
 - Sinds 1990s: vaccinatie door apothekers
 - Hogere couverture
 - Ernst et al J American Pharm Assoc 1996
 - Influenza vaccination in a rural community

- Canada: afhankelijk van de staat
 - New Brunswick: de apotheker is vaccinator (certificaat)
 - Quebec: de apotheker mag niet vaccineren
- Portugal: influenza vaccinatie in de apotheek
- Ierland: sinds oktober 2011 mogen apothekers vaccineren
 - 1,400 opgeleide apothekers
 - 2013: 550 apotheken vaccineerden meer dan 9000 patienten.

Folia

- <http://www.bcfi.be/Folia/index.cfm?FoliaWelk=F40N11D&keyword=zwangerschap>
 - Beperkt effect van influenza vaccinatie tijdens de ZS? Hangt af van welk effect
- <http://www.bcfi.be/Folia/index.cfm?FoliaWelk=F40N02C&keyword=kinkhoest>
 - Nog verschillende strategieën open ter bescherming van de jonge zuigeling.

Besluit

- Vaccineren tijdens de zwangerschap is aanbevolen voor kinkhoest en griep
- Andere vaccins kunnen gegeven worden naargelang de noodzaak: reisgeneeskunde, blootstelling: levend afgezwakt versus inactieve vaccins
- De apotheker heeft in België een informerende en stimulerende rol aangaande vaccinaties in het algemeen en voor de zwangeren in het bijzonder.

Vragen?



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