GEBE AŞILAMASI

Dr. Funda Yetkin

İnönü Üniversitesi Tıp Fakültesi

Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Anabilim Dalı

Gebede İmmün Sistem

- Fetal tolerans
  - Yarı allograft fetüsün hayatta kalmasına olanak tanır
- Gebe kadını korur
- İmmün sistem baskılanmaz, düzenlenir
- Aşılara karşı gebe olmayan bireylerle benzer bağışıklık tepkisi

Chu HY. Birth Defects Res 2017; 109:379
R. Orefice. Best Pract Res Clin Obstet Gynaecol. 76 (2021) 3-12

Antikorların plasenta yolu ile geçişi;

- Annedeki konsantrasyon
- Antikor tipi
  - IgG1 taşınır
- Gebelik yaşı
- Fetal IgG konsantrasyonu
  - Gebeliğin ilk yarısında annedeki konsantrasyondan çok daha düşük
  - 28 -32. gebelik haftalarında annedeki seviyelerin yüzde 50'si
  - 36. haftada annedeki seviyelere eşit

Cyril Engmann.. ournal of Perinatology (2020) 40:844–857

frontiers in Immunology

REVIEW
published: 24 June 2020
doi: 10.3389/fimmu.2020.01282

Check for updates

Global Perspectives on Immunization During Pregnancy and Priorities for Future Research and Development: An International Consensus Statement

Bahaa Abu-Raya[1], Kirsten Maertens[2], Kathryn M. Edwards[3], Saad B. Omer[4],

- Düşük B hücresi seviyesi
- Üçüncü trimesterde B hücreli lenfopeni
- B hücre fonksiyonunda azalma
- Gebeliğin sonlarında toplam IgG düzeylerinde azalma
- Yüksek estradiol
  - Th2 hücre yanıtlarında artış
- Progesteron artışı
  - Th 1 hücre yanıtlarında inhibisyon
- Th 1 yanıtından Th2 yanıtına doğru aşamalı geçiş
- T hücresi fonksiyonunda azalma

Gebe Aşılaması

- İdeal olan
  - Gebe kalmadan önce yetişkin aşılama programına göre aşılanma
- Gebelik sırasında aşılama
  - Maruz kalma olasılığı yüksek
  - Anne ve/veya fetüs için riskli
  - Aşının zarar verme ihtimali düşük

Gebelikte aşılamayı etkileyen başlıca faktörler

MATERNAL ACCEPTANCE
- Perception of risk / severity of infection
- Access to vaccine provider
- Cost / health insurance

HEALTHCARE WORKER ACCEPTANCE
- Knowledge of recommendations
- Vaccine access and storage
- Reimbursement

MATERNAL IMMUNE RESPONSE TO VACCINATION

TRANSPLACENTAL TRANSFER OF VACCINE-SPECIFIC ANTIBODIES AND THEIR FUNCTION

INTERFERENCE WITH SUBSEQUENT INFANT IMMUNE RESPONSE TO VACCINATION

MATERNAL CLINICAL CONDITIONS
- Malaria, HIV infection, gestational hypertension, smoking

VACCINE SAFETY / ADVERSE EVENTS

TIMING OF IMMUNIZATION
- To achieve optimal immunity in mother and /or infant

GEOGRAPHICAL LOCATION
- Different circulating pathogen strains
- Different responses to vaccination
- Different local recommendations

SEASONALITY OF PATHOGENS TARGETED BY IMMUNIZATION
- Influenza, RSV

INDUCTION OF VACCINE-SPECIFIC ANTIBODIES IN BREAST MILK

Bahaa Abu-Raya. Front. Immunol. 2020; 11:1282.

FIGURE 1
Placental transfer of IgG antibodies from maternal to fetal circulation

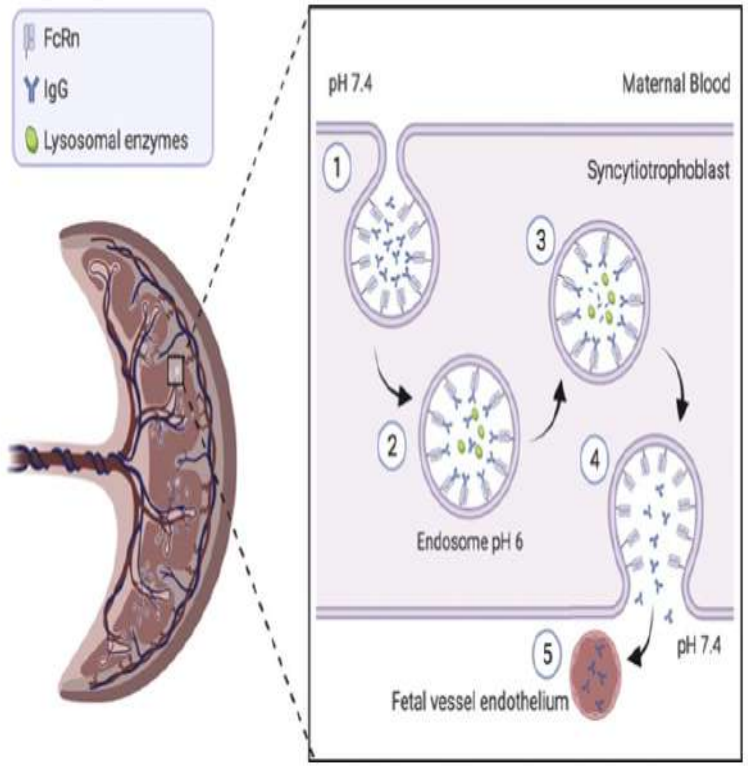
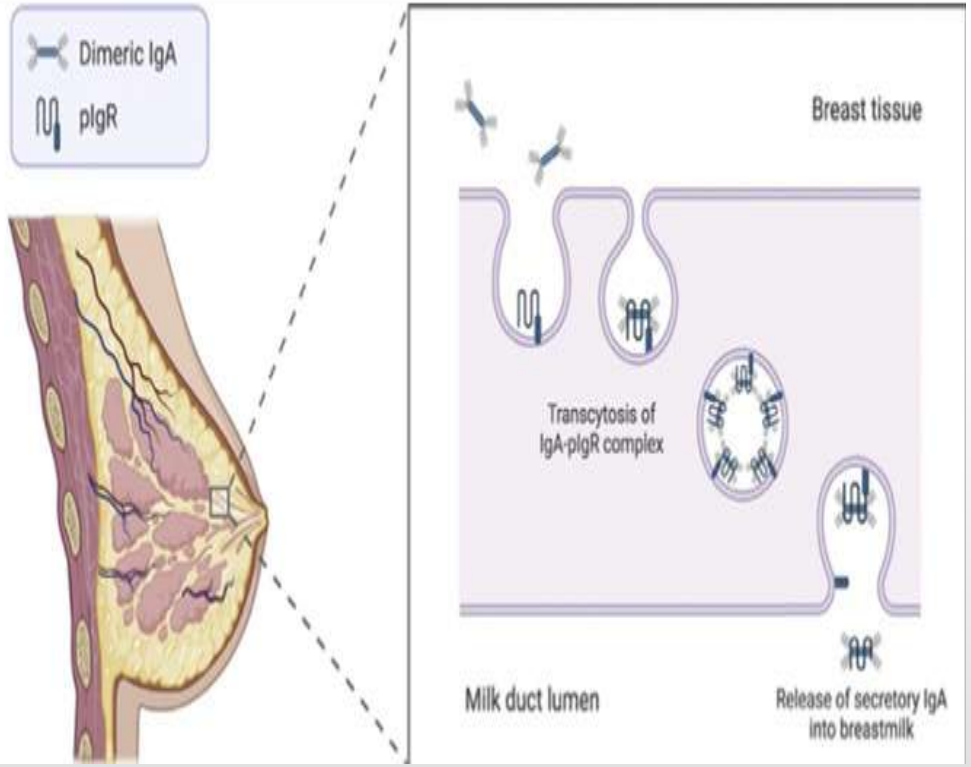


FIGURE 2
Transfer of secretory IgA antibodies from maternal breast tissue to breast milk



Etti M.Am J Obstet Gynecol 2022; 459-71

Gebelikte aşılamanın gerekçesi;

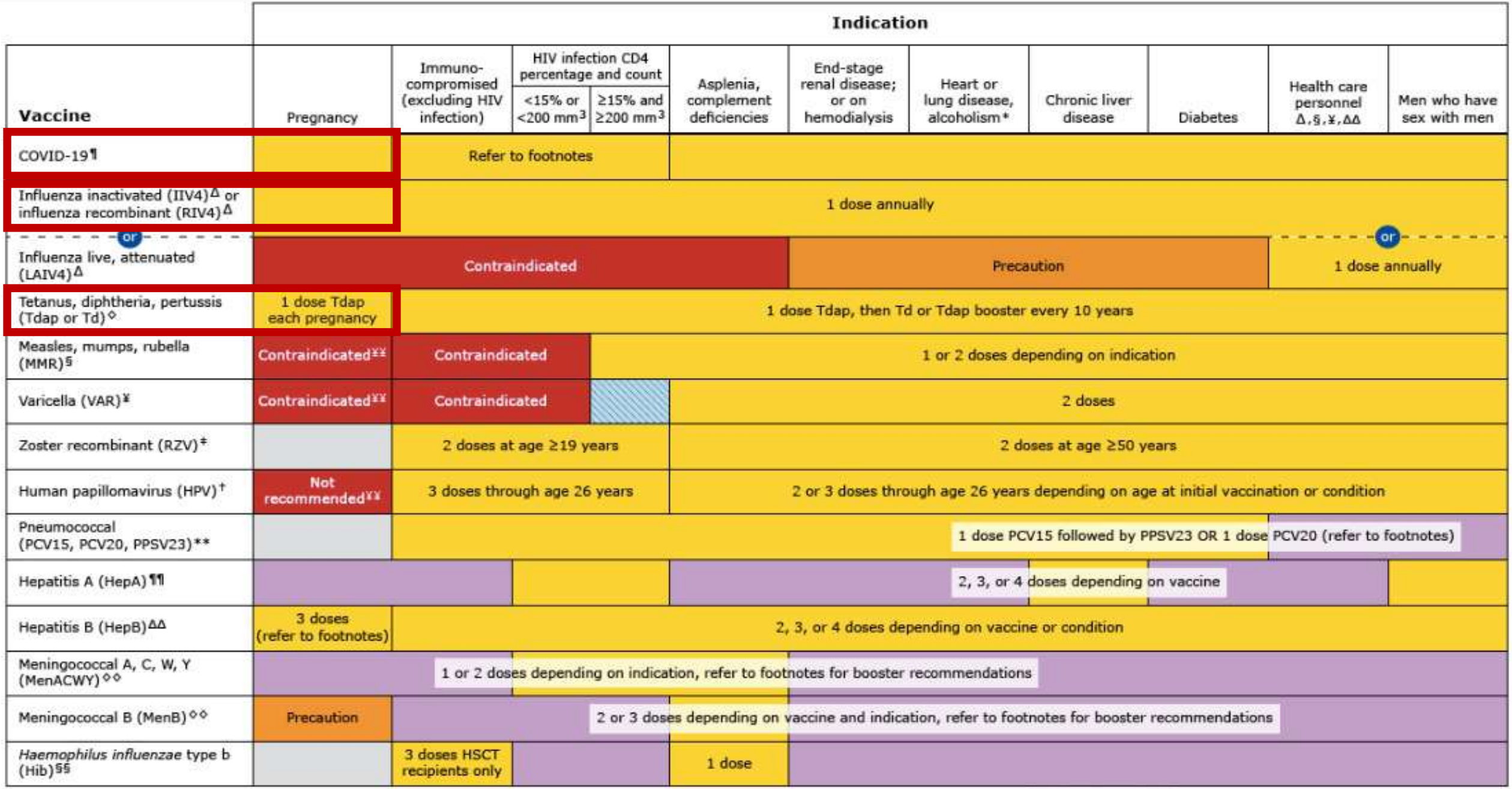
- Kadını gebelikte duyarlı olabileceği enfeksiyonlardan korumak
  - Fetusu
    - Konjenital enfeksiyondan korur
    - Annedeki enfeksiyonun diğer zararlı etkilerinden korur
- Bebeği yaşamın ilk aylarında enfeksiyondan korumak
  - Antikorlarının plasental ve anne sütü ile geçişi

Gebe kadınlar için rutin önerilen aşılar

Hastalık	Aşı türü	Öneri
▪ Tetanoz	▪ Toksoid	▪ Tüm gebe kadınlara ▪ Önceki aşılanma durumuna göre
▪ İnfluenza	▪ İnaktif	▪ Tüm gebe kadınlara ▪ Yüksek öncelikli
▪ Boğmaca	▪ Subunit adjuvanlı	▪ Tüm gebe kadınlara ▪ Aşılanamayacak kadar küçük bebeklerde hastalığının önlenmesi

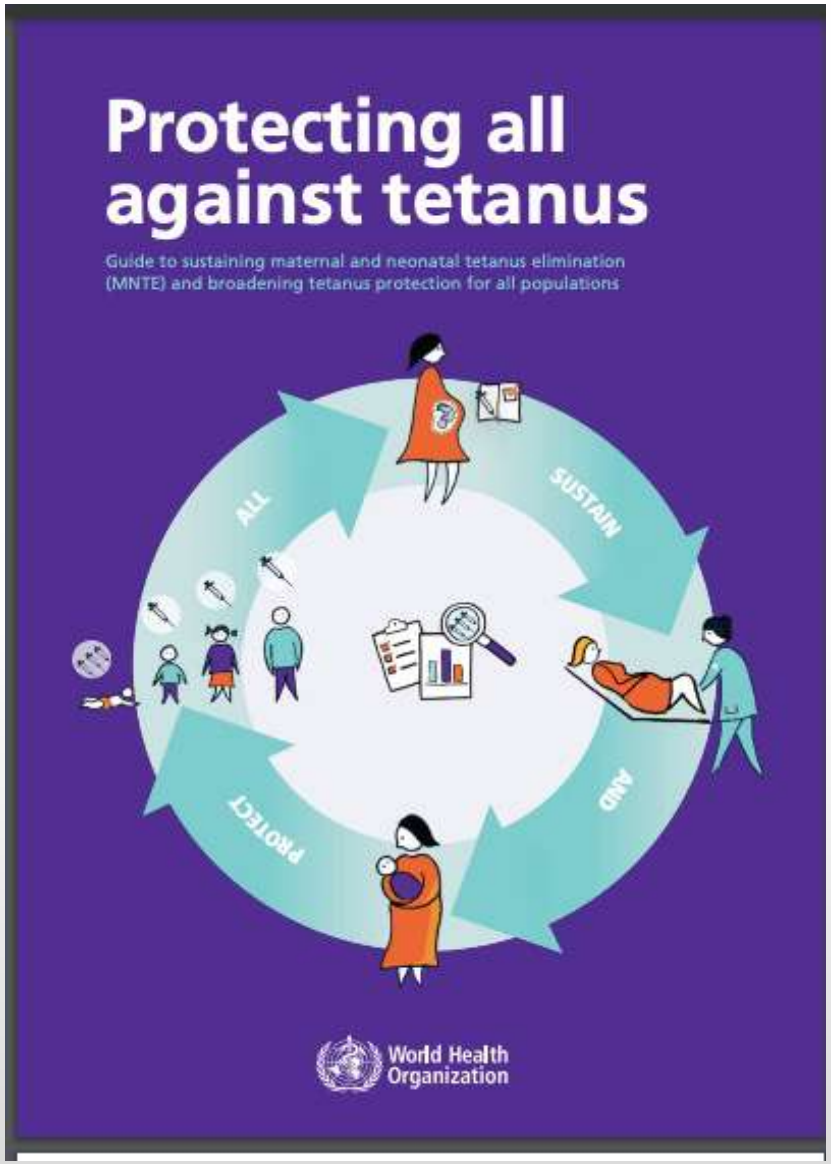
https://www.who.int/publications/i/item/WHO-HIS-2014.07

Recommended adult immunization schedule by medical condition and other indications - United States, 2023



Global elimination status of maternal and neonatal tetanus

“risk altındaki” 59 ülkeden 47'sinde ortadan kaldırıldı


Protecting all against tetanus
Guide to sustaining maternal and neonatal tetanus elimination (MNTE) and broadening tetanus protection for all populations
SUSTAIN
AND
PROTECT
ALL
World Health Organization


Countries achieving MNTE validation
Nepal
Togo
Vietnam
2005
2006
Egypt
Zambia
2007
Bangladesh
2008
Burundi
Comoros
Congo
Turkey
2009
Benin
Mozambique
Myanmar
2010
Ghana
Liberia
Senegal
Uganda
2011
Burkina Faso
Cameroon
China
G. Bissau
Tanzania
Timor Leste
2012
2nd elimination target

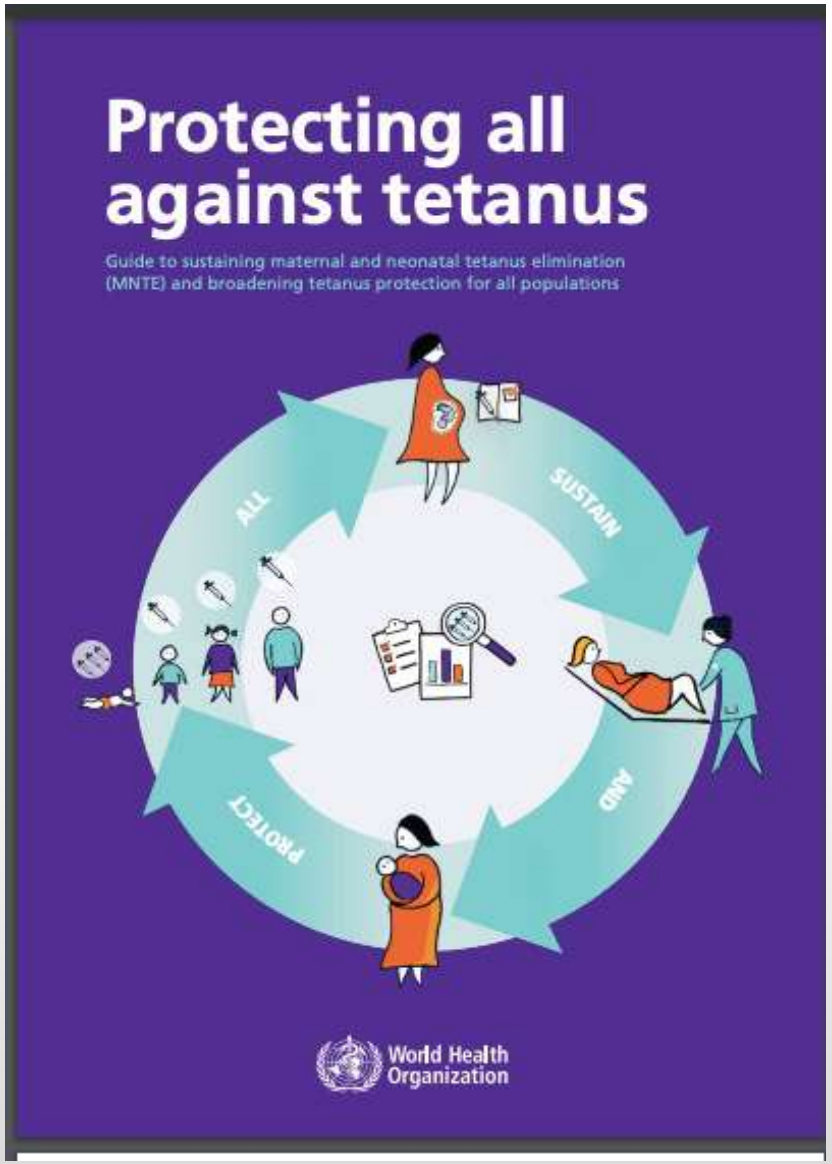


Table 5

TTCV vaccination schedule for WRA and pregnant women with unknown vaccination status or without previous exposure to TTCV[22]

Dose of TTCV	When to give	Expected duration of protection
TTCV 1	At first contact or as early in pregnancy as possible	None
TTCV 2	At least 4 weeks after TTCV1 (at the latest 2 weeks prior to birth)	1-3 years
TTCV 3	At least 6 months after TTCV2, or during subsequent pregnancy	At least 5 years
TTCV 4	At least 1 year after TTCV3, or during subsequent pregnancy	At least 10 years
TTCV 5	At least 1 year after TTCV4, or during subsequent pregnancy	For all childbearing age and much of adulthood

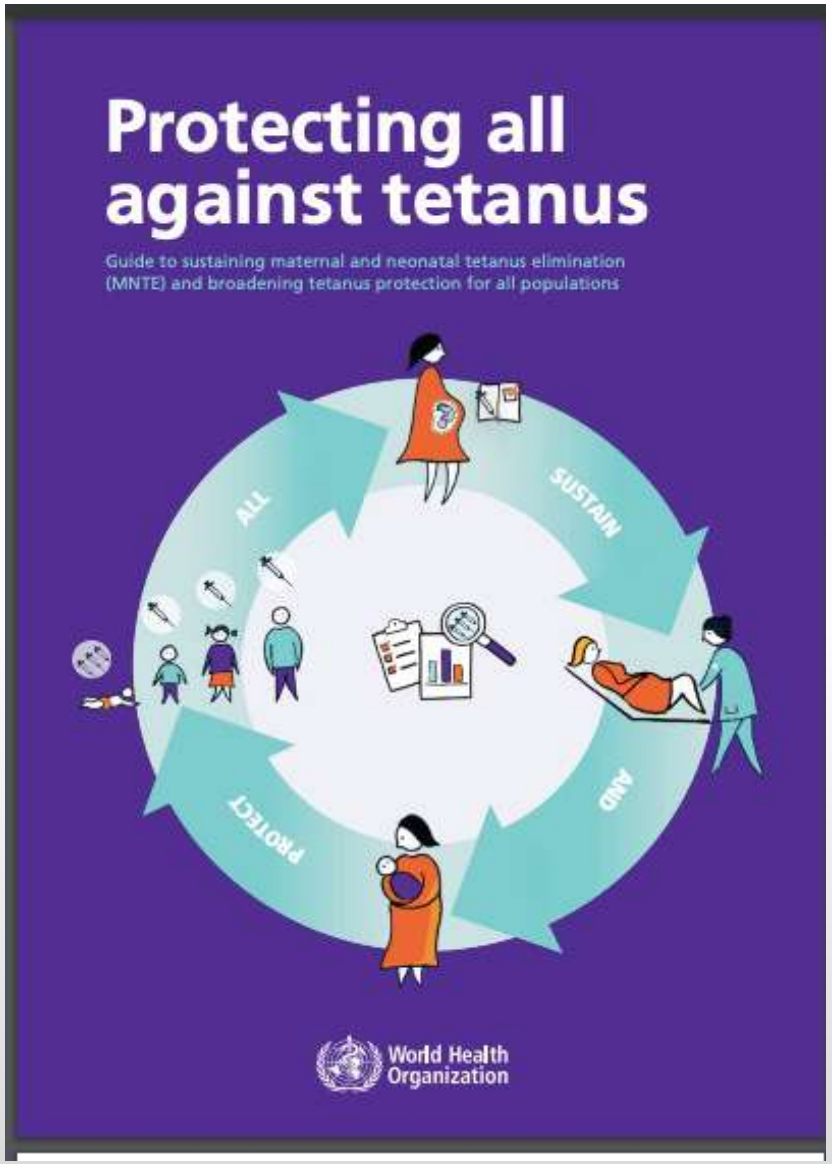


Table 6

TTCV vaccination schedule for partially vaccinated pregnant women[23]

Age of last vaccination	Previous vaccinations (from vaccination record)	Recommended TTCV doses	
		At present ANC contact/pregnancy	Later (with interval of at least one year)
Infancy	3 TTCV primary doses	2 doses of TTCV (minimum 4 week interval between doses)	1 dose of TTCV
Early childhood/ school age	3 TTCV primary doses + 1 booster (total of 4 TTCV doses)	1 dose of TTCV	1 dose of TTCV
School age	3 TTCV primary doses + 2 boosters (total of 5 TTCV doses)	1 dose of TTCV	None (fully protected)
Adolescence	3 TTCV primary doses + 3 boosters (total of 6 TTCV doses)	None (fully protected)	None (fully protected)

T.C.
SAĞLIK BAKANLIĞI
Temel Sağlık Hizmetleri Genel Müdürlüğü

Sayı : B100TSH0110005
Konu : Genişletilmiş Bağışıklama Programı Genelgesi

13.03.2009/7941

GENELGE
2009/17

Doğurganlık Çağı (15- 49 Yaş) /Gebe Kadınlardaki Tetanoz Aşı Takvimi

Doz sayısı	Uygulama zamanı	Koruma süresi
Td 1	Gebeliğin 4. ayında - İlk karşılaşmada	Yok
Td 2	Td 1'den en az 4 hafta sonra	1-3 yıl
Td 3	Td 2'den en az 6 ay sonra	5 yıl
Td 4	Td 3'den en az 1 yıl sonra ya da bir sonraki gebelikte	10 yıl
Td 5	Td 4'den en az 1 yıl sonra ya da bir sonraki gebelikte	Doğurganlık çağı boyunca

Boğmaca

- < 1 yaş bebeklerde morbidite ve mortalitenin önemli nedenlerinden
- < 6 ay bebeklerde en ciddi klinik
  - komplikasyonlar ve ölüm
- Bebeği korumak için gebe aşılaması
  - Aşılama zamanı önemli

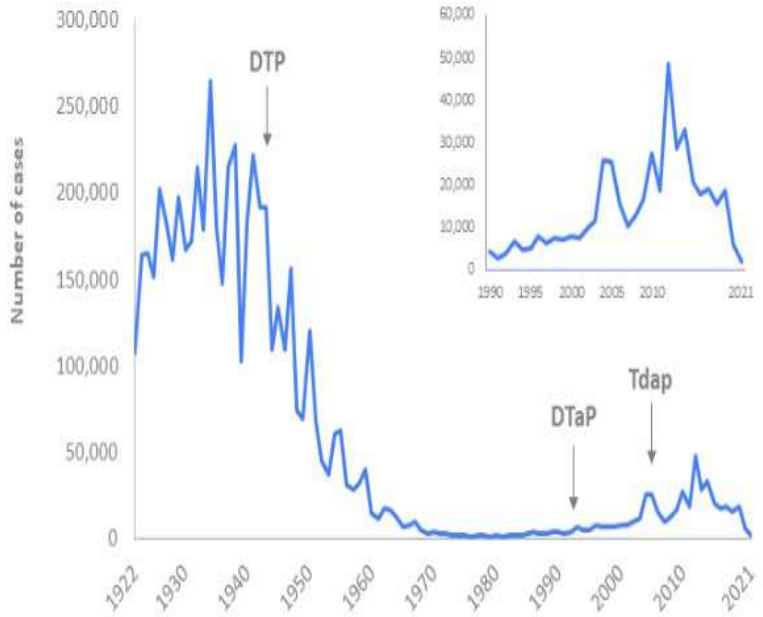
Table 2 Recommended Adult Immunization Schedule by Medical Condition or Other Indication, United States, 2023

Vaccine	Pregnancy	Immuno-compromised (excluding HIV infection)	HIV infection CD4 percentage and count		Asplenia, complement deficiencies	End-stage renal disease, or on hemodialysis	Heart or lung disease; alcoholism[a]	Chronic liver disease	Diabetes	Health care personnel[b]	Men who have sex with men
			<15% or <200 mm³	≥15% and ≥200 mm³							
COVID-19											
IIV4 or RIV4	1 dose annually										
or										or	
LAIV4						Precaution				1 dose annually	
Tdap or Td	1 dose Tdap, then Td or Tdap booster every 10 years										
MMR	1 or 2 doses depending on indication										
VAR	2 doses										
RZV	2 doses at age ≥50 years										
HPV	Recommended[c]	2 or 3 doses through age 26 years depending on age at initial vaccination or condition									
Pneumococcal (PCV15, PCV20, PPSV23)	1 dose PCV15 followed by PPSV23 OR 1 dose PCV20 (see notes)										
HepA	2, 3, or 4 doses depending on vaccine										
HepB	3 doses (see notes)	2, 3, or 4 doses depending on vaccine or condition									
MenACWY	1 or 2 doses depending on indication, see notes for booster recommendations										
MenB	Precaution	2 or 3 doses depending on vaccine and indication, see notes for booster recommendations									
Hib		3 doses HSCT[f] recipients only			1 dose						

- Her gebelikte
  - Tek doz Tdap
  - Tercihen 27-36. hafta

https://www.cdc.gov/vaccines/schedules/

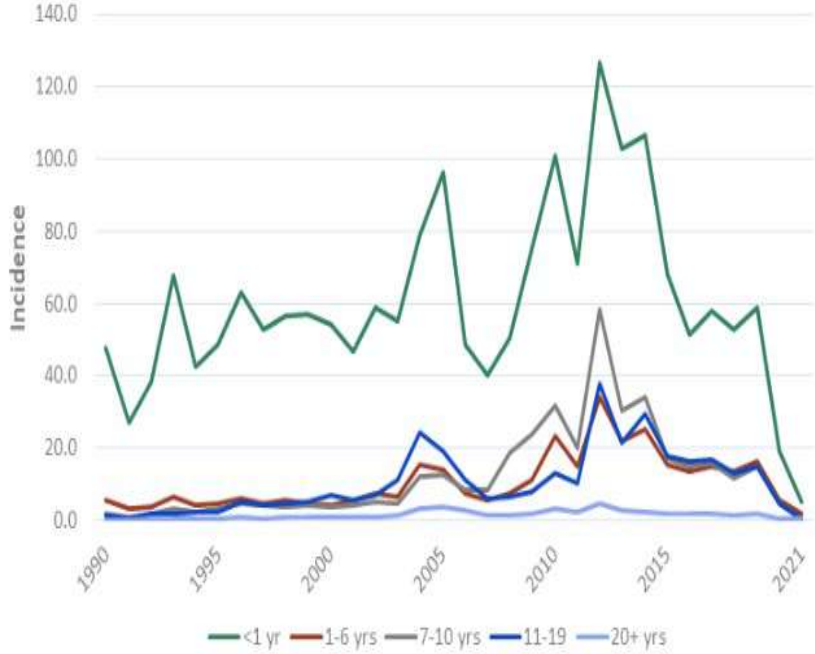
Reported NNDSS pertussis cases: 1922-2021



SOURCE: CDC, National Notifiable Diseases Surveillance System

1

Reported pertussis incidence by age group: 1990-2021



SOURCE: CDC, National Notifiable Diseases Surveillance System

2

https://www.cdc.gov/pertussis/images/incidence-graph

Clinical Infectious Diseases

MAJOR ARTICLE

Pertussis Infections Among Pregnant Women in the United States, 2012–2017

Tami H. Skoff,[1] Amanda E. Faulkner,[1,a] Jennifer L. Liang,[1] Meghan Barnes,[2] Kathy Kudish,[3] Ebony Thomas,[4] Cynthia Kenyon,[5] Marisa Hoffman,[6,b] Eva Pradhan,[7] Juventila Liko,[8] and Susan Hariri[1]

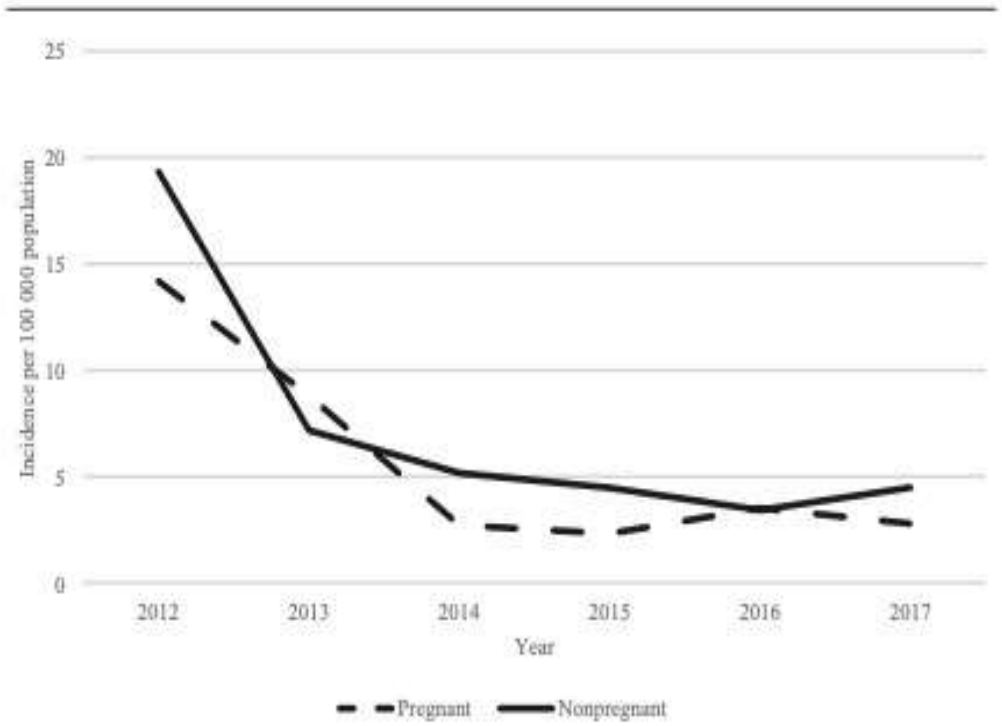


Figure 1. Pertussis incidences among women aged 18–44 years, by year and pregnancy status.

- 1 Ocak 2012-31 Aralık 2017
- 18-44 yaş arası kadın
- 1582 boğmaca vakası
- Gebe
  - 2,71/100 000 -14,2/100 000
- Gebe olmayan
  - 3,4/10 000- 19,3/100 000

CID. 2021;73(11):e3836–41

Clinical Infectious Diseases

MAJOR ARTICLE

Effectiveness of Prenatal Versus Postpartum Tetanus, Diphtheria, and Acellular Pertussis Vaccination in Preventing Infant Pertussis

Kathleen Winter,[1,2] Steve Nickell,[1] Michael Powell,[1] and Kathleen Harriman[1]

Background. Most severe a…fore initiation of the primary pertussis vaccine series. Women are recor…(Tdap) vaccine at the start of the third trimester of each pregnancy to …is recommendation was made by the Advisory Committee for Immu…ies in the United States have yet evaluated the effectiveness of this s…

Methods. We evaluated a c… in the California Immunization Registry to determine whether infa…ion had a lower risk of pertussis at <8 weeks of age than infants born …artum.

Results. Tdap vaccination received at 27–36 weeks gestation was found to be 85% (95% confidence interval, 33%–98%) more effective than postpartum Tdap vaccination at preventing pertussis in infants <8 weeks of age . Vaccination at 27–36 weeks gestation was more effective at preventing pertussis in infant than vaccination during the second trimester.

Conclusions. Tdap vaccination at 27–36 weeks gestation was 85% more effective than postpartum vaccination at preventing pertussis in infants <8 weeks of age. Efforts should be made by prenatal care providers to provide Tdap vaccine to pregnant women during routine prenatal visits at the earliest opportunity between 27 and 36 weeks gestation.

- 27-36. gebelik haftalarında uygulanan Tdap, boğmacayı önlemede daha etkili
  - Doğum sonrası Tdap aşılamasından
  - İkinci trimesterdeki Tdap aşılamasından

CID. 2017;64(1):3–8

Vaccine 39 (2021) 2555–2560

Contents lists available at ScienceDirect

Vaccine

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

Clinical repercussions in pertussis infants post-Tdpa vaccination of pregnant woman: An immunization success?

Katiuscia Araujo de Miranda Lopes [a,*], Paulo Neves Baptista [b], Renata de Medeiros Nascimento [c],

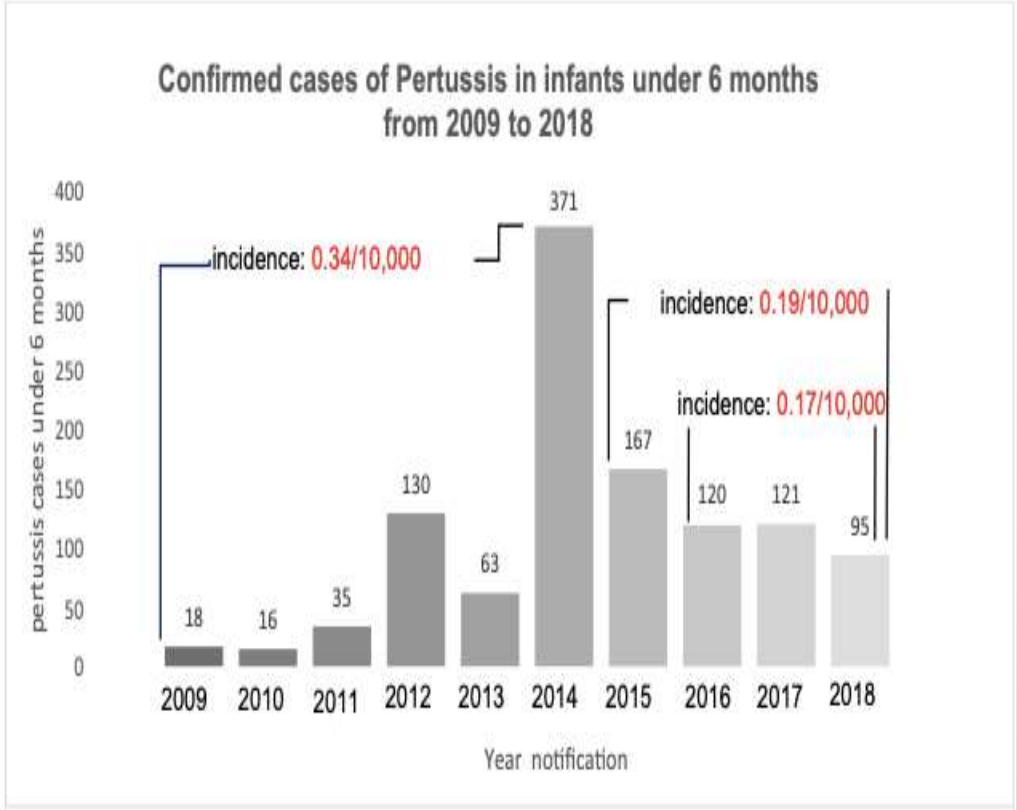


Chart 1. Epidemiological curve of pertussis cases in infants under 6 months from 2009 to 2018.

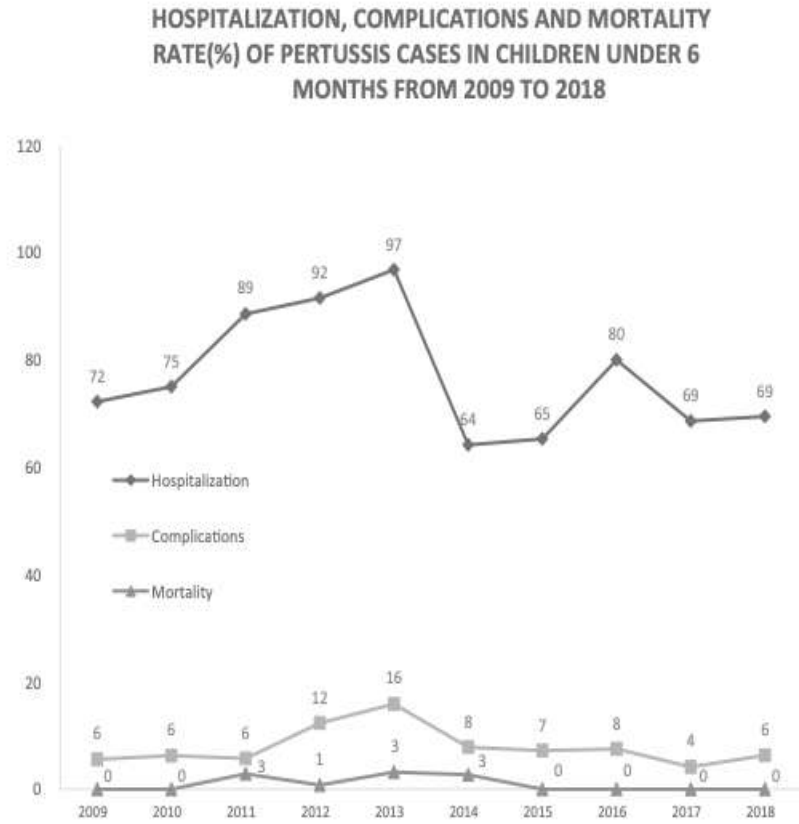


Chart 2. Hospitalization, complications, and mortality rates of pertussis cases from 2009 to 2018 in infants under 6 months.

FIGURE 1 | Countries with recommendations for immunization against pertussis in pregnancy by official authorities (for South America, pertussis immunization during pregnancy is recommended by The Pan American Health Organization). This figure was inspired by G. Amirthalingham and K. Maertens and created by K. Maertens.

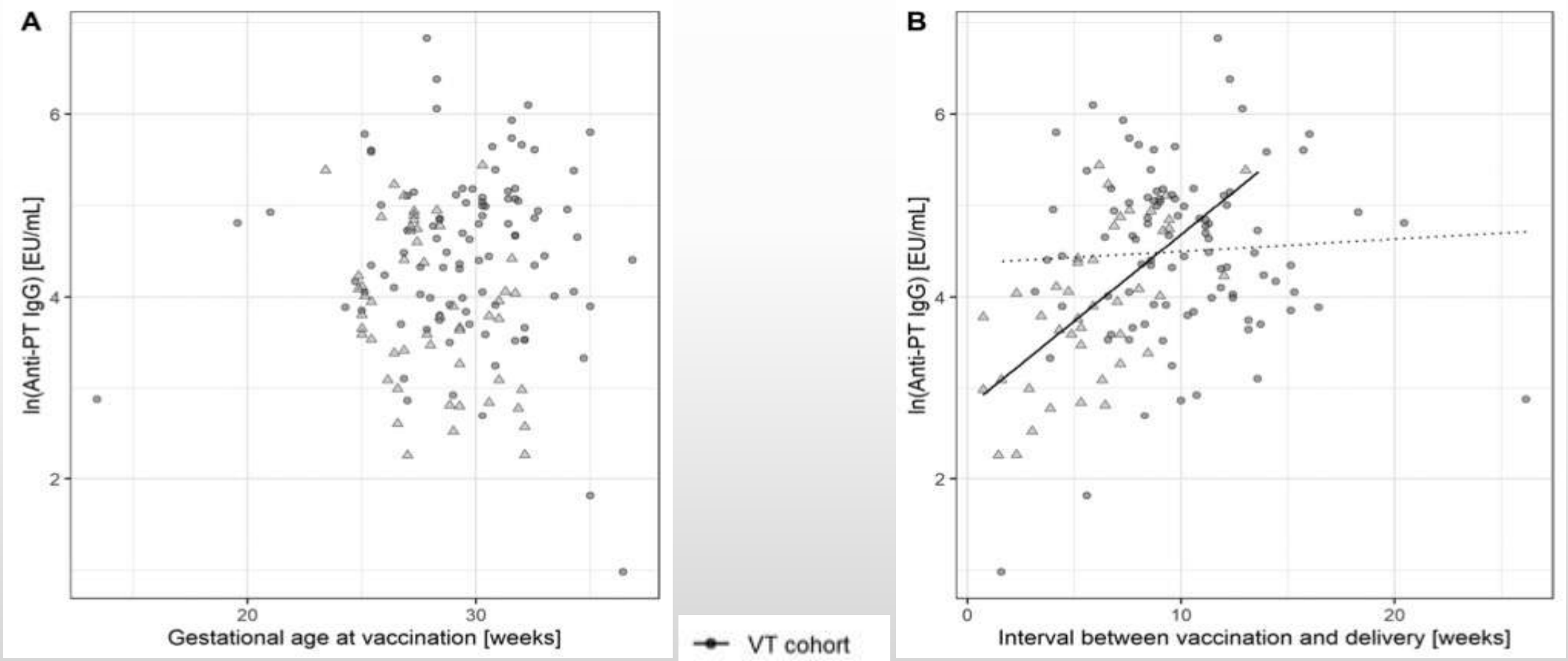
.

Bahaa Abu-Raya, Front. Immunol. 2020; 11:1282.

Clinical Infectious Diseases
MAJOR ARTICLE

Pertussis Immunization During Pregnancy: Assessment of the Role of Maternal Antibodies on Immune Responses in Term and Preterm-Born Infants

Kirsten Maertens,[1] Marjolein R. P. Orije,[1] Sereina A. Herzog,[2,3] Ludo M. Mahieu,[4] Niel Hens,[2,5] Pierre Van Damme,[1] and Elke Leuridan[1]



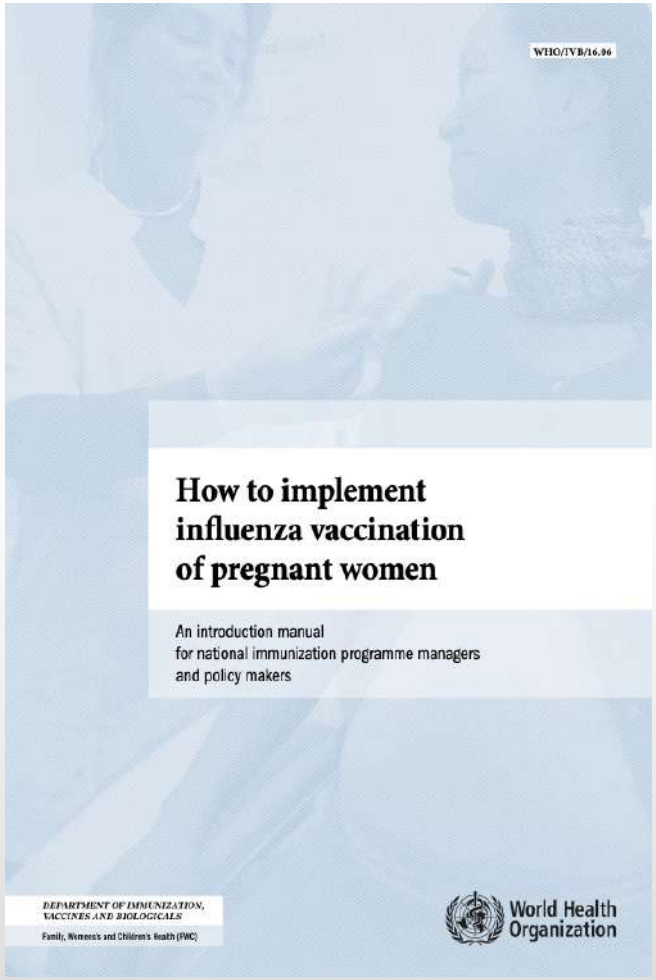
CID. 2022;74(2):189-98

Table 2 Recommended Adult Immunization Schedule by Medical Condition or Other Indication, United States, 2023

Vaccine	Pregnancy	Immuno-compromised (excluding HIV infection)	HIV infection CD4 percentage and count		Asplenia, complement deficiencies	End-stage renal disease, or on hemodialysis	Heart or lung disease; alcoholism[a]	Chronic liver disease	Diabetes	Health care personnel[b]	Men who have sex with men
			<15% or <200 mm³	≥15% and ≥200 mm³							
COVID-19		See Notes									
IIV4 or RIV4					1 dose annually						
LAIV4						Precaution				or 1 dose annually	
Tdap or Td	pregnancy				, then Td or Tdap booster every 10 years						
MMR	Contraindicated*	Contraindicated			1 or 2 doses depending on indication						
VAR	Contraindicated*	Contraindicated			2 doses						
RZV		2 doses at age ≥19 years			2 doses at age ≥50 years						
HPV	Not Recommended*	3 doses through age 26 years			2 or 3 doses through age 26 years depending on age at initial vaccination or condition						
Pneumococcal (PCV15, PCV20, PPSV23)		1 dose PCV15 followed by PPSV23 OR 1 dose PCV20 (see notes)									
HepA					2, 3, or 4 doses depending on vaccine						
HepB	3 doses (see notes)	2, 3, or 4 doses depending on vaccine or condition									
MenACWY		1 or 2 doses depending on indication, see notes for booster recommendations									
MenB	Precaution	2 or 3 doses depending on vaccine and indication, see notes for booster recommendations									
Hib		3 doses HSCT[c] recipients only			1 dose						

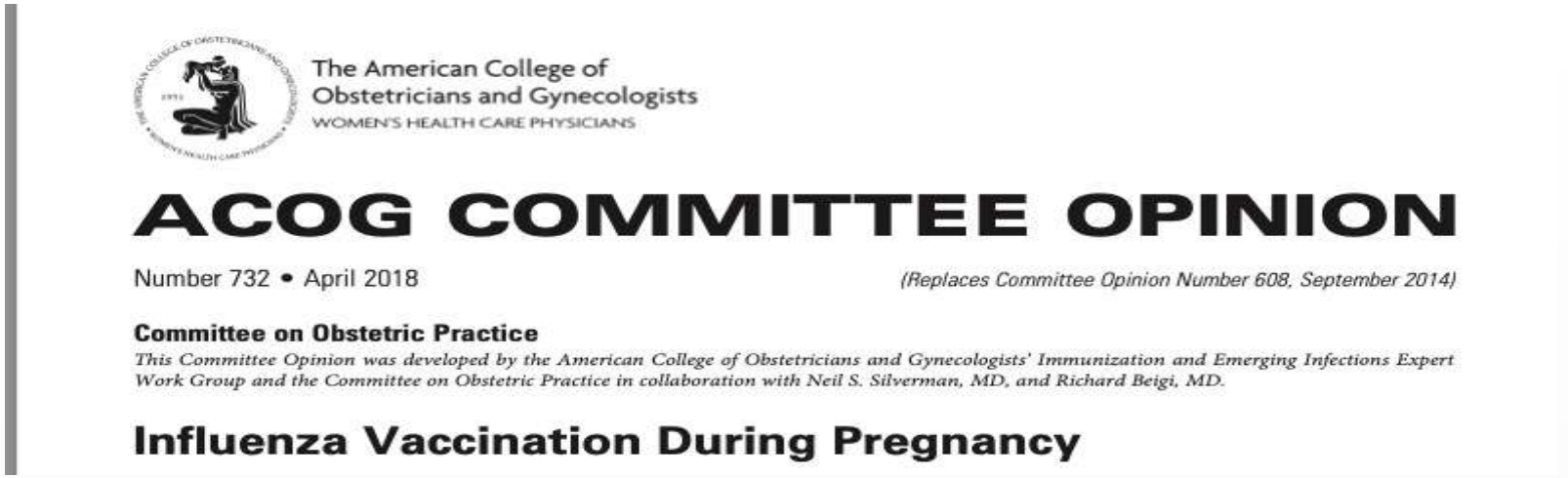
- İnfluenza mevsimi boyunca
- Hamilelik evrelerine bakılmaksızın

https://www.cdc.gov/vaccines/schedules/



WHO's influenza recommendations aim to protect vulnerable high-risk groups from severe disease [1]. WHO published a position paper on influenza vaccine in 2012, identifying pregnant women as the highest priority group for countries considering the initiation or expansion of programmes for seasonal influenza vaccination. Influenza vaccination of pregnant women will protect both the mother and her young infant against influenza [2]. Currently there is no licensed

- DSÖ 2012 yılında hamile kadınları en yüksek öncelikli grup olarak tanımladı.
- Gebelikte grip aşısı;
  - Hem anneyi, hem de bebeğini gribe karşı korur



The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

ACOG COMMITTEE OPINION

Number 732 • April 2018

(Replaces Committee Opinion Number 608, September 2014)

Committee on Obstetric Practice

This Committee Opinion was developed by the American College of Obstetricians and Gynecologists' Immunization and Emerging Infections Expert Work Group and the Committee on Obstetric Practice in collaboration with Neil S. Silverman, MD, and Richard Beigi, MD.

Influenza Vaccination During Pregnancy

- Gebenin grip aşısı,
- Kadınlar ve yeni doğan bebekler için doğum öncesi bakımın önemli bir bileşeni
- Sağlık hizmeti sağlayıcıları, hamile kadınlara aşının güvenliği ve yararları konusunda danışmanlık yapmalı

İnfluenza

- Gebe ve doğum sonrası kadında
  - Griple ilişkili morbidite ve mortalite yüksek

- Grip aşısı,
  - Annenin grip hastalığı ve hastaneye kaldırılma riskini azaltır
  - Gebelik sonuçlarını iyileştirir
  - Bebeğin doğumdan sonraki birkaç ay korunmasını sağlar

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effectiveness of Maternal Influenza Immunization in Mothers and Infants

K. Zaman, M.B., B.S., Ph.D., Eliza Roy, M.B., B.S., D.C.H.,

Clinical Infectious Diseases

MAJOR ARTICLE

Influenza Vaccine Effectiveness in Preventing Influenza-associated Hospitalizations During Pregnancy: A Multi-country Retrospective Test Negative Design Study, 2010–2016

Clinical Infectious Diseases® 2018;68(9):1444–53

Mark G. Thompson,[1] Jeffrey C. Kwong,[2,3,4,5,6] Annette K. Regan,[7,8] Mark A. Katz,[9,10,11] Steven J. Drews,[12,13] Eduardo Azziz-Baumgartner,[1]

Lancet Infect Dis. 2017 September ; 17(9): 981–989. doi:10.1016/S1473-3099(17)30252-9.

Year-round influenza immunisation during pregnancy in Nepal: a phase 4, randomised, placebo-controlled trial

Mark C Steinhoff, Joanne Katz, Janet A Englund, Subarna K Khatry, Laxman Shrestha,

- Anne ve bebekte influenza benzeri hastalıkta azalma

Human Reproduction, Vol.29, No.4 pp. 809–823, 2014
Advanced Access publication on December 22, 2013 doi:10.1093/humrep/det455

human reproduction **META-ANALYSIS** ***Reproductive epidemiology***

Influenza and congenital anomalies: a systematic review and meta-analysis

J.M. Luteijn*, M.J. Brown, and H. Dolk

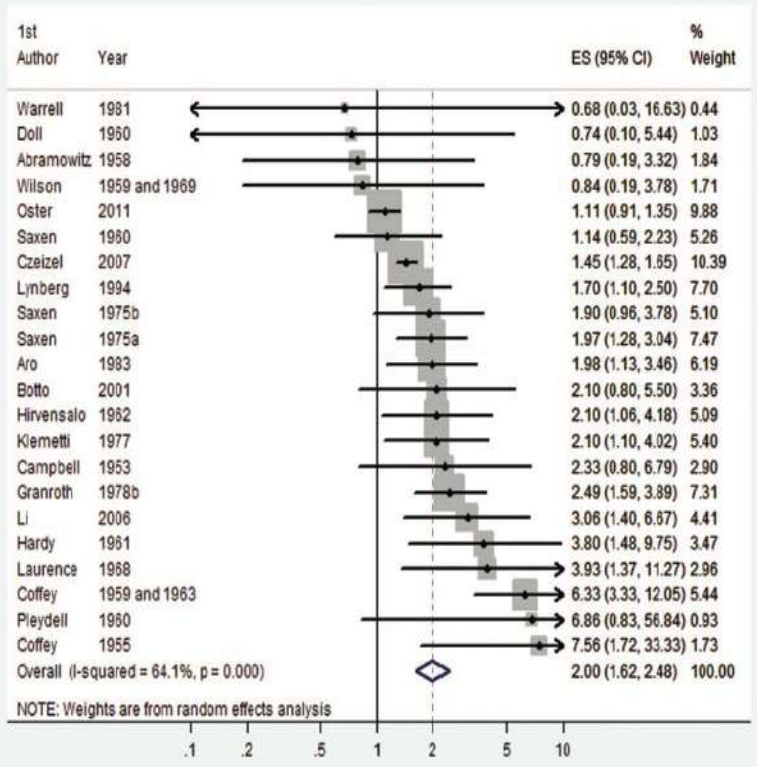


Figure 2 Forest plot of non-chromosomal CA following first trimester influenza exposure. ES, effect size.

MAIN RESULTS AND THE ROLE OF CHANCE: First trimester maternal influenza exposure was associated with an increased risk of any congenital anomaly [adjusted odds ratio (AOR) 2.00, 95% CI: 1.62–2.48], neural tube defects [odds ratio (OR) 3.33, 2.05–5.40], hydrocephaly (5.74, 1.10–30.00), congenital heart defects (1.56, 1.13–2.14), aortic valve atresia/stenosis (AOR 2.59, 1.21–5.54), ventricular septal defect (AOR 1.59, 1.24–2.14), cleft lip (3.12, 2.20–4.42), digestive system (1.72, 1.09–2.68) and limb reduction defects (2.03, 1.27–3.27). An increased risk for cleft lip (but not for cleft palate) was also reported by ecological studies not included in the meta-analysis. Study outcomes reported for 27 subgroups of congenital anomaly could not be included in the meta-analysis. Visual inspection of funnel plots did not suggest evidence for publication bias.

Birth Defects Res. 2019 January 15; 111(2): 88–95. doi:10.1002/bdr2.1445.

Outcomes of infants born to women with influenza A(H1N1)pdm09

Kim Newsome[1], **C. J. Alverson**[1], **Jennifer Williams**[1], **Anne F. McIntyre**[1], **Anne D. Fine**[2],

Results: 490 pregnant women with influenza, 1,451 women without reported influenza with pregnancies in the same year, and 1,446 pregnant women without reported influenza with prior year pregnancie… …ensive care unit (ICU; *n* = … …ight infants, and i… …djusted relative risk, … …me year comparisons, … …alized women not a… …t outcomes.

Conclusion … …ore likely to have advers… …for influenza vaccination during pregnancy.

- Yoğun bakım ünitesine kabul edilen 2009 H1N1 influenzalı kadınlarda
  - Erken doğum (<37 hafta)
  - Düşük doğum ağırlıklı bebek
  - Apgar skorları <=6 olan bebekler

  daha yüksek oranda

Vaccine 38 (2020) 1601–1613

Contents lists available at ScienceDirect

Vaccine

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

Review

The effectiveness of influenza vaccination in pregnancy in relation to child health outcomes: Systematic review and meta-analysis

J.R. Jarvis [a,b,*], R.B. Dorey [a,e], F.D.M. Warricker [c], N.A. Alwan [b,d,1], C.E. Jones [a,e,1]

- Anne aşılaması
- Bebeklerde laboratuvar olarak doğrulanmış gripte %34'lük (%15-50) genel bir azalma ile ilişkili

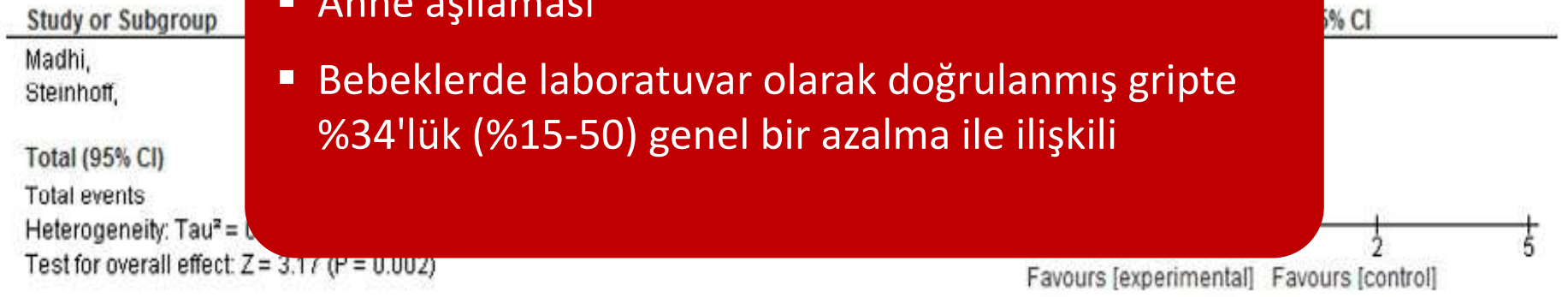


Fig. 2. Forest plot of pooled results for maternal influenza vaccination and LCI in infants.

FORMAL SYSTEMATIC REVIEW (COMMISSIONED OR NON-COMMISSIONED)

WILEY

Optimal timing of influenza vaccine during pregnancy: A systematic review and meta-analysis

Will Cuningham[1,2,3] | Nicholas Geard[2,3,4] | James E. Fielding[2,3] | Sabine Braat[3,5]

- Farklı trimesterlerde aşılananlarda serokonversiyon oranlarında önemli ölçüde farklılık yok
- Kord kanında gribe karşı nötralize edici antikorların geometrik ortalama titreleri
  - Üçüncü trimesterde aşılananlarda ilk trimesterde aşılananlara göre 1,44 kat daha yüksek

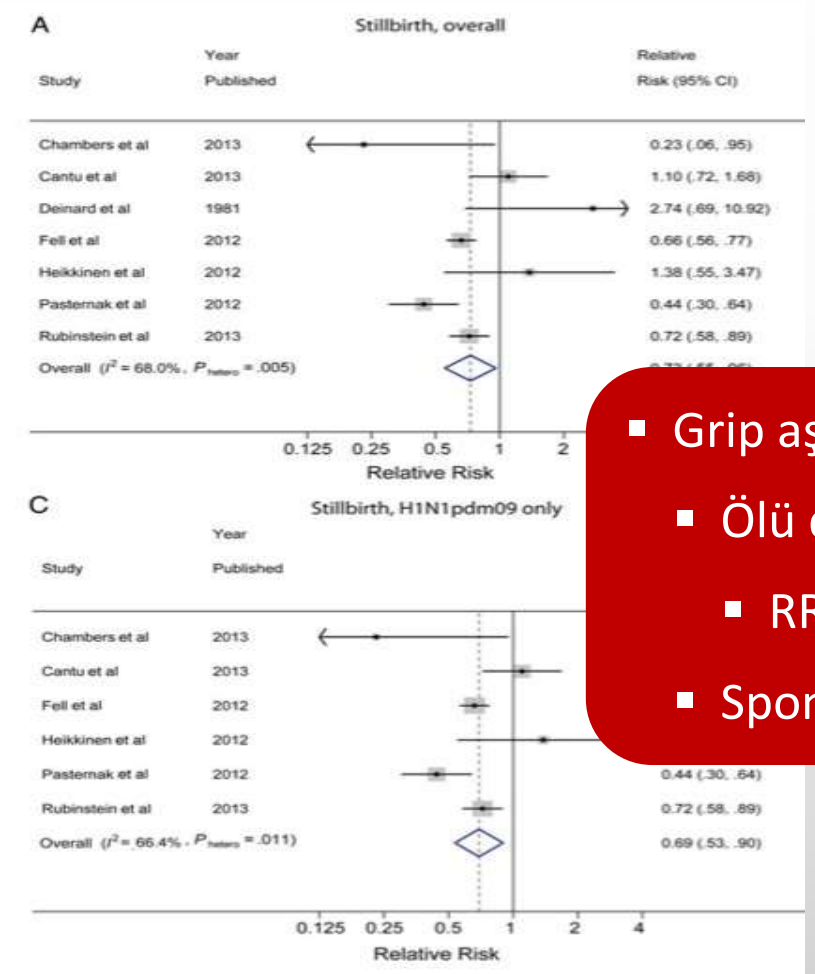
Influenza Other Respi Viruses. 2019;13:438–452

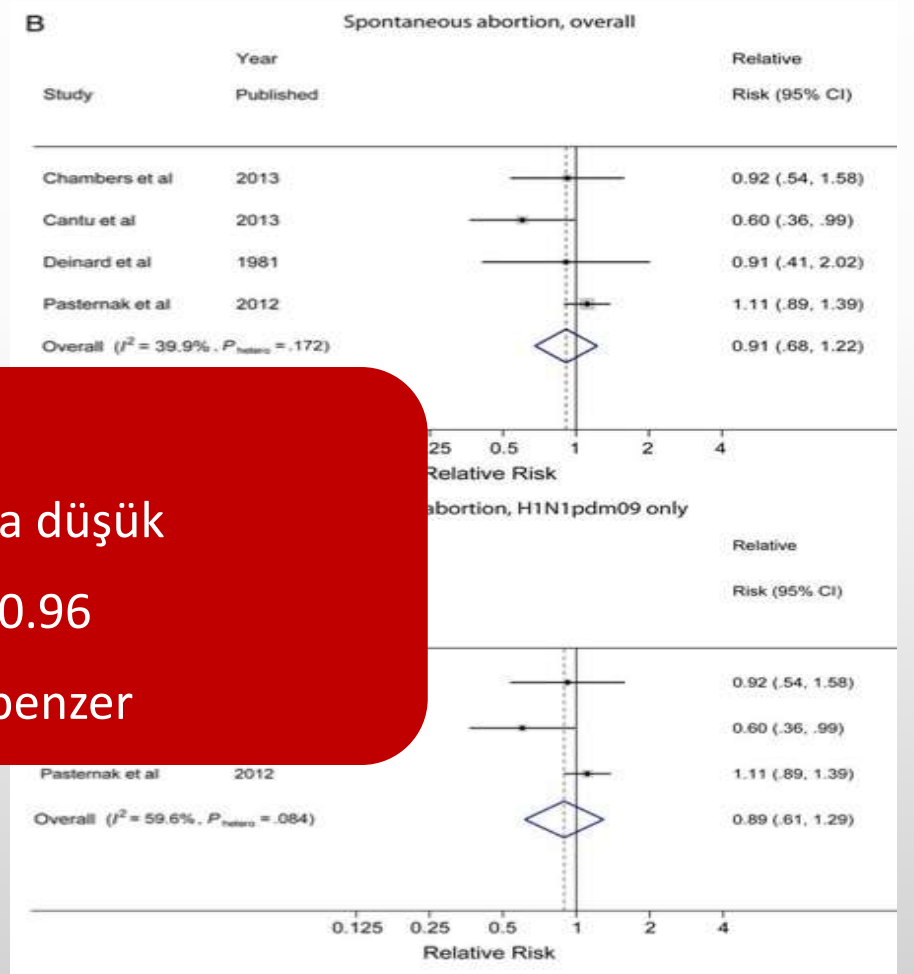
REVIEW ARTICLE

Maternal Influenza Immunization and Birth Outcomes of Stillbirth and Spontaneous Abortion: A Systematic Review and Meta-analysis

Kristin N. Bratton,[1,2] Melissa T. Wardle,[1,2] Walter A. Orenstein,[1,2,3,4] and Saad B. Omer[1,2,5]

Clinical Infectious Diseases® 2015;60(5):e11–9





- Grip aşısı alanlarda
  - Ölü doğum olasılığı daha düşük
    - RR 0.73, %95 CI 0.55-0.96
  - Spontan abortus oranı benzer

Table 2 Recommended Adult Immunization Schedule by Medical Condition or Other Indication, United States, 2023

Vaccine	Pregnancy	Immuno-compromised (excluding HIV infection)	HIV infection CD4 percentage and count		Asplenia, complement deficiencies	End-stage renal disease, or on hemodialysis	Heart or lung disease; alcoholism[a]	Chronic liver disease	Diabetes	Health care personnel[b]	Men who have sex with men
			<15% or <200 mm³	≥15% and ≥200 mm³							
COVID-19											
IIV4 or RIV4					1 dose annually						
or										or	
LAIV4						Precaution				1 dose annually	
Tdap or Td					dose Tdap, then Td or Tdap booster every 10 years						
MMR	Contraindicated*	Contraindicated			1 or 2 doses depending on indication						
VAR	Contraindicated*	Contraindicated			2 doses						
RZV		2 doses at age ≥19 years			2 doses at age ≥50 years						
HPV	Not Recommended*	3 doses through age 26 years			2 or 3 doses through age 26 years depending on age at initial vaccination or condition						
Pneumococcal (PCV15, PCV20, PPSV23)		1 dose PCV15 followed by PPSV23 OR 1 dose PCV20 (see notes)									
HepA					2, 3, or 4 doses depending on vaccine						
HepB	3 doses (see notes)	2, 3, or 4 doses depending on vaccine or condition									
MenACWY		1 or 2 doses depending on indication, see notes for booster recommendations									
MenB	Precaution	2 or 3 doses depending on vaccine and indication, see notes for booster recommendations									
Hib		3 doses HSCT[c] recipients only			1 dose						

- Gebeler
- Emzirenler
  - COVID-19 aşısı önerilmekte

https://www.cdc.gov/vaccines/schedules/

TABLE 2

Summary of COVID-19 vaccines and evidence of safety and recommendations for use in pregnancy

Vaccine platform	Commercial developer (candidate name)	Mechanism of action	Assessment of safety in pregnancy	Recommendations for use during pregnancy
mRNA	Pfizer/BioNTech (BNT162b2)	Nucleoside-modified mRNA expressed in lipid nanoparticles that encodes the spike protein for the SARS-COV-2 virus	Pfizer/BioNTech commenced a global Phase 3 study recruiting pregnant women in early 2021	Initial safety data supports the safe use of mRNA vaccines in pregnant women
	Moderna (mRNA-1237)	Nucleoside-modified mRNA encoding the pre-fusion stabilized spike (S) protein and the S1–S2 cleavage site encapsulated within a lipid nanoparticle	Real-world data from >90,000 women have not identified any safety signals[22]	
Nonreplicating viral vector	Oxford-AstraZeneca (AZD1222)	Modified chimpanzee adenovirus (replication deficient) containing the gene encoding the spike (S) protein	Pregnancies that occurred in clinical trials were recorded and followed up until 3 months after birth. Compared with women who received the control vaccine, there was no increased risk of miscarriage and no instances of stillbirth.[23]	No previous studies among pregnant women. However, adenovirus-vectored Zika vaccine studies in pregnant mice did not identify any safety signals

Etti M.Am J Obstet Gynecol 2022; 459-71

TABLE 2

Summary of COVID-19 vaccines and evidence of safety and recommendations for use in pregnancy

Vaccine platform	Commercial developer (candidate name)	Mechanism of action	Assessment of safety in pregnancy	Recommendations for use during pregnancy
	Janssen (Ad26.COV2.S)	Recombinant, replication-incompetent human adenovirus type 26 that encodes the full length of the stabilized conformation of the spike (S) protein		
	Sputnik V (Gam-COVID-Vac)	Combined recombinant adenovirus-based vaccine (rAd5 and rAd26), both containing the gene encoding the full-length spike (S) protein		
Protein subunit	Novavax (NVX-Cov2373)	Full length recombinant spike (S) protein nanoparticle administered with a saponin-based adjuvant (Matrix-M)	No direct safety data available	Recombinant vaccines are generally considered safe for use during pregnancy Safety of saponin-based adjuvant in pregnancy unknown
Inactivated whole virus	Sinovac (CoronaVac)	Inactivated whole virus particle containing aluminum hydroxide adjuvant	No direct safety data available	Inactivated vaccines generally considered safe for use during pregnancy.
	Sinopharm (BBIBP-CorV)	Inactivated whole virus particle containing aluminum hydroxide adjuvant		Aluminum hydroxide (used in human papillomavirus vaccine) and CpG 1018 (used in hepatitis B virus vaccine adjuvants) both considered safe for use during pregnancy
	Valneva (VLA2001)	Inactivated whole virus particle containing aluminum hydroxide and CpG 1018 adjuvants		Safety of the Alhydroxiquim-II adjuvant unknown in pregnancy
	Bharat Biotech (BBV152)	Inactivated whole virus particle containing Alhydroxyquim-II adjuvant		

Etti M.Am J Obstet Gynecol 2022; 459-71

Pregnancy outcomes and vaccine effectiveness during the period of omicron as the variant of concern, INTERCOVID-2022: a multinational, observational study

Jose Villar, Constanza P Soto Conti, Robert B Gunier, Shabina Ariff, Rachel Craik, Paolo I Cavoretto, Stephen Rauch, Serena Gandino, Ricardo Nieto,

Lancet 2023; 401: 447–57

	All women: effectiveness against laboratory-confirmed COVID-19		All women: effectiveness against moderate COVID-19 symptoms*		All women: effectiveness against severe COVID-19 symptoms, referral for higher care, ICU admission, or death†		Women diagnosed with COVID-19: effectiveness against severe symptoms, referral for higher care, ICU admission, or death†	
	N	VE (95% CI)	N	VE (95% CI)	N	VE (95% CI)	N	VE (95% CI)
All vaccines combined								
Unvaccinated	632	0 (ref)	213	0 (ref)	85	0 (ref)	65	0 (ref)
Partially vaccinated	145	5% (0–18)	41	26% (0–46)	13	35% (0–64)	9	33% (0–67)
Completely vaccinated	535	9% (0–18)	171	20% (1–34)‡	36	48% (22–65)‡	10	74% (48–87)‡
Booster vaccination	233	30% (19–39)‡	71	48% (32–61)‡	7	76% (47–89)‡	2	91% (65–98)‡
mRNA vaccine								
Partially vaccinated	84	0 (0–17)	18	32% (0–57)	6	35% (0–72)	5	29% (0–71)
Completely vaccinated	352	11% (0–21)‡	75	41% (22–55)‡	18	56% (27–74)‡	6	79% (49–91)‡
Booster vaccination	152	32% (20–42)‡	35	54% (34–68)‡	4	81% (47–93)‡	1	94% (56–99)‡
Non-replicating viral vector vaccine								
Partially vaccinated	39	0 (0–13)	11	0 (0–40)	2	61% (0–90)	1	27% (0–89)
Completely vaccinated	94	2% (0–20)	52	0 (0–4)	6	60% (2–83)‡	2	56% (0–91)
Booster vaccination	56	20% (0–38)	25	25% (0–52)	3	49% (0–84)	1	76% (0–96)
Inactivated virus vaccine								
Partially vaccinated	9	28% (0–61)	5	4% (0–62)	2	0 (0–70)	0	NA
Completely vaccinated	86	0 (0–20)	43	0 (0–8)	12	8% (0–52)	2	66% (0–93)
Booster vaccination	24	27% (0–51)	10	31% (0–66)	0	NA	0	NA

Models adjusted for maternal age, overweight or obesity, presence or absence of any pre-existing medical condition, and country. ICU=intensive care unit. VE=vaccine effectiveness. NA=not applicable due to no cases. *Moderate COVID-19 symptoms are defined as fever, chest pain, or shortness of breath, and not showing any severe symptoms.†Severe COVID-19 symptoms are defined as having been admitted to hospital during pregnancy for either respiratory disease, respiratory tract infection, or requiring antibiotic or antiviral treatment. ‡p<0·05.

Table 2: **VE (%) against laboratory-confirmed COVID-19 diagnosis, moderate and severe maternal COVID-19 symptoms, and maternal referral to higher level of care, ICU admission, or death, according to vaccine type and regimen**

Interpretation COVID-19 in pregnancy, during the first 6 months of omicron as the variant of concern, was associated with increased risk of severe maternal morbidity and mortality, especially among symptomatic and unvaccinated women. Women with complete or boosted vaccine doses had reduced risk for severe symptoms, complications, and death. Vaccination coverage among pregnant women remains a priority.

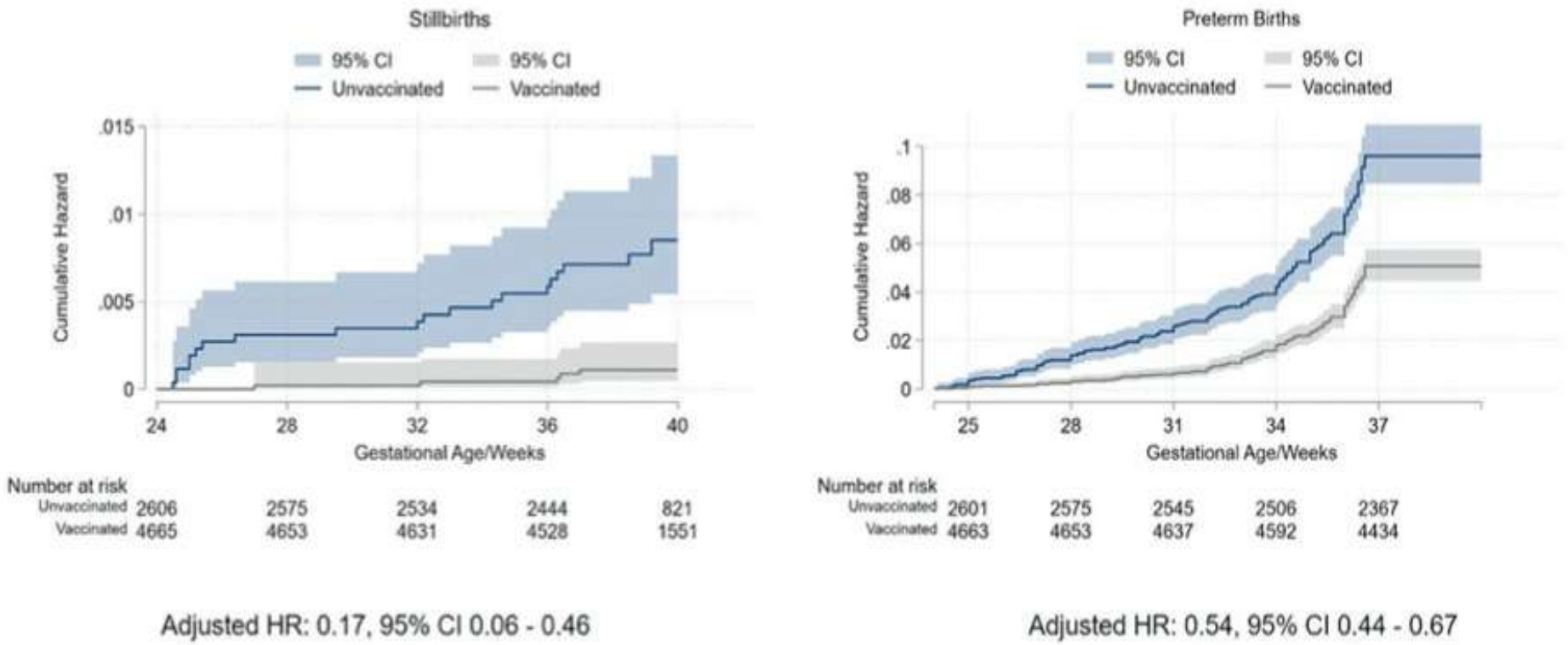
- Tam veya güçlendirilmiş aşı ile
  - Ciddi semptomlar, komplikasyonlar ve ölüm riski azalmış
- Gebe kadınların aşılanması öncelik olmaya devam ediyor

OBSTETRICS

Reductions in stillbirths and preterm birth in COVID-19—vaccinated women: a multicenter cohort study of vaccination uptake and perinatal outcomes

Lisa Hui, MBBS, PhD; Melvin B. Marzan, BSc, MSc; Daniel L. Rolnik, PhD; Stephanie Potenza, MD; N

FIGURE 6
Hazard ratio plots for stillbirth and preterm birth for women vaccinated before 24 weeks' gestation



Am J Obstet Gynecol 2023;228:585.e1-17.

OBSTETRICS

Reductions in stillbirths and preterm birth in COVID-19—vaccinated women: a multicenter cohort study of vaccination uptake and perinatal outcomes

Lisa Hui, MBBS, PhD; Melvin B. Marzan, BSc, MSc; Daniel L. Rolnik, PhD; Stephanie Potenza, MD; N

CONCLUSION: COVID-19 vaccination during pregnancy was associated with a reduction in stillbirth and preterm birth, and not associated with any adverse impact on fetal growth or development. Vaccine coverage was substantially influenced by known social determinants of health.

- Gebede COVID-19 aşısı
  - Ölü doğum ve erken doğum oranlarında azalma
  - Fetal büyüme veya gelişme üzerinde olumsuz etki ile ilişkili değil

ARTICLE

https://doi.org/10.1038/s41467-022-30052-w OPEN

Systematic review and meta-analysis of the effectiveness and perinatal outcomes of COVID-19 vaccination in pregnancy

SYSTEMATIC REVIEW OPEN

Systematic review and meta-analysis of neonatal outcomes of COVID-19 vaccination in pregnancy

Dingning Zhang[1,2,3,4], Tingting Huang[1,2,3,4], Zhihui Chen[1,2,3], Lulu Zhang[1,2,3], Qi Gao[1,2,3], Ge Liu[1,2,3], Jun Zheng[1,2,3]✉ and Fangrui Ding[1,2,3]✉

Pediatric Research (2023) 94:34–42; https://doi.org/10.1038/s41390-022-02421-0

SYSTEMATIC REVIEW

Effectiveness and safety of COVID-19 vaccine in pregnant women: A systematic review with meta-analysis

BJOG. 2023;130:348–357.

Mara Tormen[1,2] | Cristina Taliento[2] | Stefano Salvioli[3,4] | Irene Piccolotti[2] |

Endemik ülkelerde veya salgınlarda önerilen aşılar-I

Hastalık	Aşı türü	Öneri
▪ Kolera	▪ İnaktif	▪ Gebe ve emziren kadınlar oral kolera aşısı kampanyalarına dahil edilmeli ▪ Potansiyel fayda yüksek, risk düşük
▪ Ebola	▪ Replike olmayan/ yetersiz replike	▪ Üç yeni aday aşı var ▪ Gebe ve emziren kadınlar klinik araştırma protokollerine dahil edilmeli
▪ Hepatit E	▪ Rekombinant, adjuvanlı	▪ Gebe kadınlar yüksek risk grubunda ▪ Kullanılması dikkate alınmalı

https://www.who.int/publications/i/item/WHO-HIS-2014.07

Endemik ülkelerde veya salgınlarda önerilen aşılar-II

Hastalık	Aşı türü	Öneri
▪ Menenjit A	▪ Konjuge	▪ Menenjit kuşağında yaşayan gebe ve emziren kadınlar ▪ MenA konjuge aşısını almaktadır
▪ Kuduz	▪ İnaktif	▪ Gebe ve emziren kadınlarda ▪ Kuduz aşıları ve kuduz immünoglobulini güvenli ve etkili
▪ Kene kaynaklı ensefalit	▪ İnaktif	▪ Görülme sıklığı yüksek (yılda >5 vaka/100.000 nüfus) bölgelerde ▪ Gebe ve emziren kadınlarda kullanılmalı
▪ Sarıhumma	▪ Canlı zayıflatılmış	▪ Endemik bölgelerde veya salgınlarda ▪ Aşılamanın yararları, aşı ilişkili virüsün fetüse bulaşma riskinden daha fazla

https://www.who.int/publications/i/item/WHO-HIS-2014.07

Gebelikte özel kullanım için klinik çalışmaları süren aşılar

Hastalık	Aşı türü	Öneri
▪ Grup B streptokok (GBS)	▪ Konjuge	▪ Yenidoğanda erken ve geç başlangıçlı GBS enfeksiyonunu önlemek için ▪ Erken doğum ve ölü doğumlar üzerindeki potansiyel etki
▪ Respiratuvar Sinsityal Virüs (RSV)	▪ Subunit ± adjuvanlı	▪ Küçük bebeklerde şiddetli RSV hastalığını önlemek için

https://www.who.int/publications/i/item/WHO-HIS-2014.07

ORIGINAL ARTICLE

Prefusion F Protein–Based Respiratory Syncytial Virus Immunization in Pregnancy

Eric A.F. Simões, M.D., Kimberly J. Center, M.D., Alan T.N. Tita, M.D., Ph.D.,

Table 2. Efficacy of Maternal Vaccination against RSV-Associated Lower Respiratory Tract Illness in the U.S. Cohort of 508 Infants.

Efficacy End Point	RSVpreF Vaccine (N=405)	Placebo (N=103)	Estimated Vaccine Efficacy (95% CI)
	number of infants with event		*percent*
Any medically attended RSV-associated lower respiratory tract illness*	3	5	84.7 (21.6 to 97.6)
Medically attended severe RSV-associated lower respiratory tract illness†	1	3‡	91.5 (–5.6 to 99.8)

CONCLUSIONS

RSVpreF vaccine elicited neutralizing antibody responses with efficient transplacental transfer and without evident safety concerns. (Funded by Pfizer; ClinicalTrials.gov number, NCT04032093.)


Group B Streptococcus
Vaccine Development
Technology
ROADMAP
Priority activities for development,
testing, licensure and global availability
of Group B streptococcus vaccines
2017
World Health
Organization
GROUP B
STREPTOCOCCUS
VACCINE
TECHNOLOGY
ROADMAP

TABLE 4

Vaccines contraindicated during pregnancy

Vaccine (platform)	Reason for contraindication	Safety considerations
BCG (live attenuated virus)	Contains live culture preparation of the BCG strain of *Mycobacterium bovis*	No harmful effects have been observed in pregnant women. However, safety in pregnancy has not been formally evaluated.[162]
Human papilloma virus (recombinant virus-like particle)	No safety data available to support use in pregnancy. Not recommended by the CDC for administration during pregnancy.	No evidence of increased risk of adverse pregnancy or fetal outcomes following administration during pregnancy.[163,164] If inadvertent administration during pregnancy, delay remaining doses until after pregnancy.
Measles, mumps, and rubella (live attenuated virus)	Contains live attenuated mumps, measles, and rubella viruses	No evidence of increased risk of adverse pregnancy or fetal outcomes (including congenital rubella syndrome) following administration during pregnancy.[98] Pregnancy testing is not recommended before vaccine administration of vaccine. However, recipients are advised not to become pregnant for at least 28 days after vaccine dose.[20,47]
Varicella (live attenuated virus)	Contains live attenuated varicella-zoster virus.	Data from Merck/CDC Pregnancy Registry have not identified any increased risk of congenital varicella syndrome.[20,165]
Zoster (recombinant glycoprotein)	No safety data available to support use in pregnancy. Not recommended by CDC for administration during pregnancy.	Data from Merck/CDC Pregnancy Registry has not identified any increased risk of congenital varicella syndrome.[20]

Etti M.Am J Obstet Gynecol 2022; 459-71

Brief Report

Major Birth Defects after Vaccination Reported to the Vaccine Adverse Event Reporting System (VAERS), 1990 to 2014

Pedro L. Moro*[1], Janet Cragan[2], Paige Lewis[1], and Lakshmi Sukumaran[1]

Background: Major birth defects are important infant outcomes that have not been well studied in the postmarketing surveillance of vaccines given to pregnant women. We assessed the presence of major birth defects following vaccination in the Vaccine Adverse Event Reporting System (VAERS), a national spontaneous reporting system used to monitor the safety of vaccines in the United States. **Methods:** We searched VAERS for reports of major birth defects during January 1, 1990, through December 31, 2014. We excluded birth defects from vaccines that had been studied in pregnancy registries or other epidemiological studies (e.g., human papilloma virus, varicella, measles/mumps/rubella, and anthrax vaccines). Birth defects were categorized into trimester of vaccination and classified based on the organs and/or systems affected. If several birth defects affecting different systems were described, we classified those as multiple body systems. Empirical Bayesian data mining was used to assess for disproportionate reporting. **Results:** We identified 50 reports of major birth defects; in 28 reports, the vaccine was given during the first trimester; 25 were reports with single vaccines administered. Birth defects accounted for 0.03% of all reports received by VAERS during the study period and 3.2% of pregnancy reports; reported defects affected predominately the musculoskeletal ($N = 10$) or nervous ($N = 10$) systems. No unusual clusters or specific birth defects were identified. **Conclusion:** This review of the VAERS database found that major birth defects were infrequently reported, with no particular condition reported disproportionally. Birth defects after routine maternal vaccination will continue to be monitored in VAERS for signals to prompt future studies.

Birth Defects Research 109:1057–1062, 2017.

Key words: birth defects; epidemiology; surveillance; vaccine; vaccine safety

Vaccine 39 (2021) 85–120

Contents lists available at ScienceDirect

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

Review

Pregnant women & vaccines against emerging epidemic threats: Ethics guidance for preparedness, research, and response ☆

Carleigh B. Krubiner [a,1,*], Ruth R. Faden [a,b], Ruth A. Karron [b], Margaret O. Little [c], Anne D. Lyerly [d]