

**10° Corso A.O.G.O.I.
9° Turin IAN DONALD Course**

**TEST DI SCREENING
E DI DIAGNOSI PRENATALE
FRA PASSATO E FUTURO**

***PRENATAL SCREENING
AND DIAGNOSTIC TESTS BETWEEN
THE PAST AND THE FUTURE***

**Torino, 15-16 marzo 2024
Hotel NH S. Stefano**



Prevenzione per la salute di mamma e bambino: Vaccini

Elsa Viora

14 maggio 1796 Edward Jenner



Edward Jenner che vaccina suo figlio tra le braccia di Mrs Jenn Welcome

Two centuries of vaccination: historical and conceptual approach and future perspectives

2024

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TYPE Review

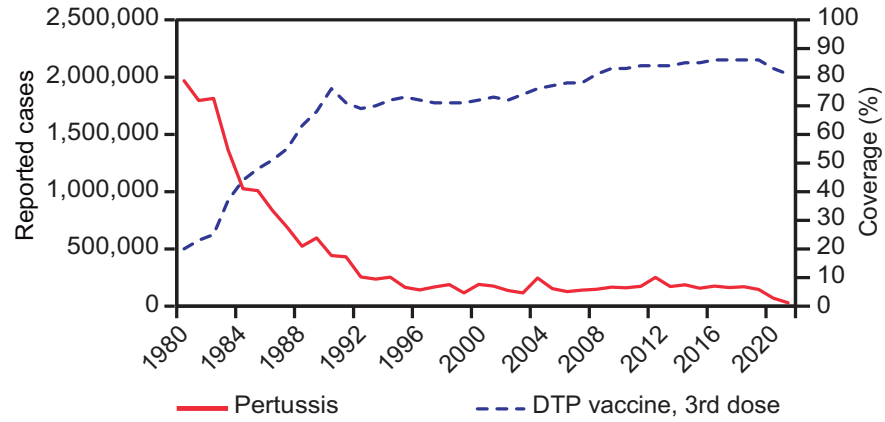
PUBLISHED 09 January 2024

DOI 10.3389/fpubh.2023.1326154

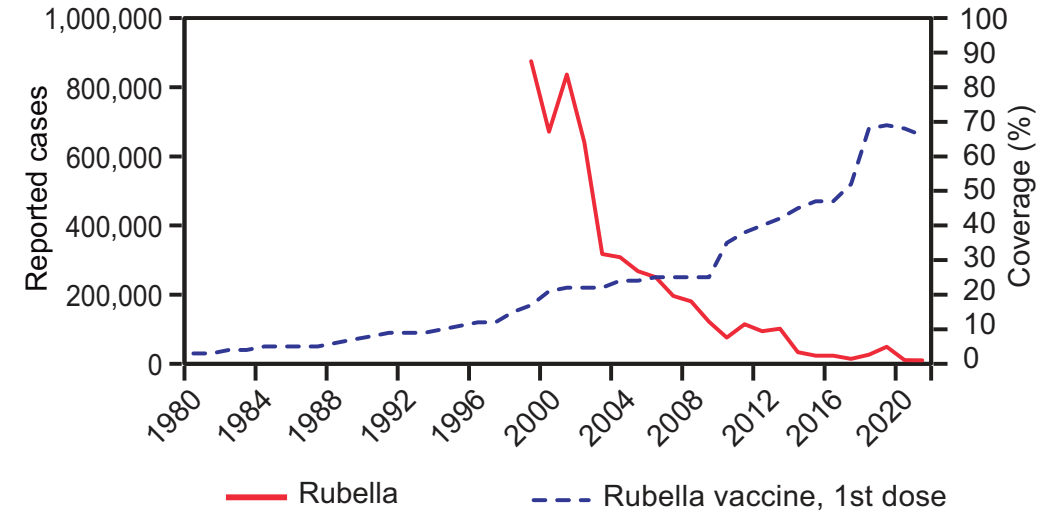
Pathogen	Disease	Year	Developer(s)	Vaccine type
Variola virus	Smallpox	1796	Edward Jenner	Vaccine based on bovine smallpox virus
Rabies virus	Rabies	1885	Louis Pasteur and Émile Roux	Attenuated vaccine
<i>Salmonella enterica</i> Serovar Typhi	Typhoid fever	1896	Richard Pfeiffer and Almroth Wright	Inactivated vaccine
<i>Vibrio cholerae</i>	Cholera	1896	Wilhelm Kolle	Inactivated vaccine
<i>Yersinia pestis</i>	Bubonic plague	1897	Waldemar Haffkine	Inactivated vaccine
<i>Mycobacterium tuberculosis</i>	Tuberculosis	1921	Albert Calmette and Camille Guérin	Attenuated vaccine based on <i>Mycobacterium bovis</i>
<i>Corynebacterium diphtheria</i>	Diphtheria	1923	Gaston Ramon	Toxoid vaccine that protects against the toxin
<i>Clostridium tetani</i>	Tetanus	1925	Gaston Ramon	Toxoid vaccine that protects against the toxin
<i>Bordetella pertussis</i>	Pertussis	1930s	Pearl Kendrick and Grace Eldering	Whole-cell inactivated vaccine
Yellow fever virus	Yellow Fever	1937	Max Theiler	Attenuated vaccine (17D strain)
Polio virus	Poliomyelitis	1955	Jonas Salk	Inactivated vaccine that protects against all 3 serotypes
Polio virus	Poliomyelitis	1960	Albert Sabin	Oral attenuated vaccine that protects against all 3 serotypes
Measles virus	Measles	1954–1960	John F. Enders and Samuel L. Katz	Attenuated vaccine; part of the MMR vaccine
Mumps virus	Mumps	1967	Maurice Hilleman	Attenuated vaccine; part of the MMR vaccine
Rubella virus	Rubella	1969	Stanley Plotkin	Attenuated vaccine (RA 27/3 strain); part of the MMR vaccine

Varicella-Zoster virus	Varicella	1974	Michiaki Takahashi	Attenuated vaccine (Oka strain)
<i>Neisseria meningitidis</i> serogroups A, C, W, and Y	Meningitis	1981		Polysaccharide vaccine
Hepatitis B virus	Hepatitis B	1982	Baruch Blumberg and Irving Millman	Subunit vaccine based on viral surface protein
<i>Streptococcus pneumoniae</i>	Pneumonia	1983	Robert Austrian et al.	Polysaccharide vaccine against 23 serotypes
<i>Haemophilus influenzae</i> type b	Pneumonia, meningitis, and other illnesses	1985	David H. Smith, Porter Anderson, et al.	Polysaccharide vaccine
<i>Haemophilus influenzae</i> type b	Pneumonia, meningitis, and other illnesses	1987		Conjugate polysaccharide vaccine
<i>Vibrio cholerae</i>	Cholera	1991	Jan Holmgren et al.	Vaccine containing killed whole cell of <i>V. cholerae</i> O1 and cholera toxin B subunit
<i>Bordetella pertussis</i>	Pertussis	1992	Rino Rappuoli et al.	Acellular vaccine
Hepatitis A virus	Hepatitis A	1990s	Various developers	Inactivated vaccines
<i>Neisseria meningitidis</i> serogroup C	Meningitis	1999		Conjugate polysaccharide vaccine
<i>Streptococcus pneumoniae</i>	Pneumonia	2000		Conjugate polysaccharide vaccine against seven serotypes
<i>Neisseria meningitidis</i> serogroups A, C, W, and Y	Meningitis	2005		Conjugate polysaccharide vaccine
Rotavirus	Gastroenteritis	2006	Various developers	Attenuated vaccine against rotavirus and reassortant vaccine
Human Papillomavirus (HPV)	Human papillomavirus-associated cancers	2006	Ian Frazer and Jian Zhou	Subunit vaccine based on viral proteins; protects against cervical cancer and other HPV-associated cancers
<i>Neisseria meningitidis</i> serogroup B	Meningitis	2013		Subunit vaccine plus outer membrane vesicles.
SARS-CoV-2	COVID-19	2020–2021	Various developers	Various technologies: inactivated vaccines, mRNA vaccines, and non-replicating viral vector vaccines.
Respiratory syncytial virus (RSV)	Cold-like symptoms, pneumonia.	2023		Subunit vaccine based on the prefusion F protein.

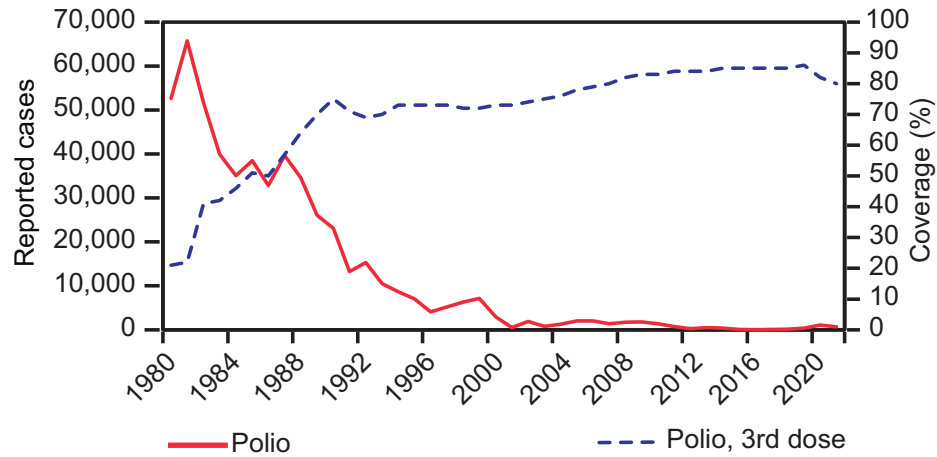
C Pertussis



F Rubella



D Polio



History has demonstrated that vaccines are one of the most powerful tools in humanity's arsenal against infectious diseases. Their continued success depends not only on scientific innovation but also on maintaining public trust and acceptance. As we move forward, it is imperative to learn from past experiences, both triumphs and setbacks, to ensure safe and effective vaccines are accessible for all.

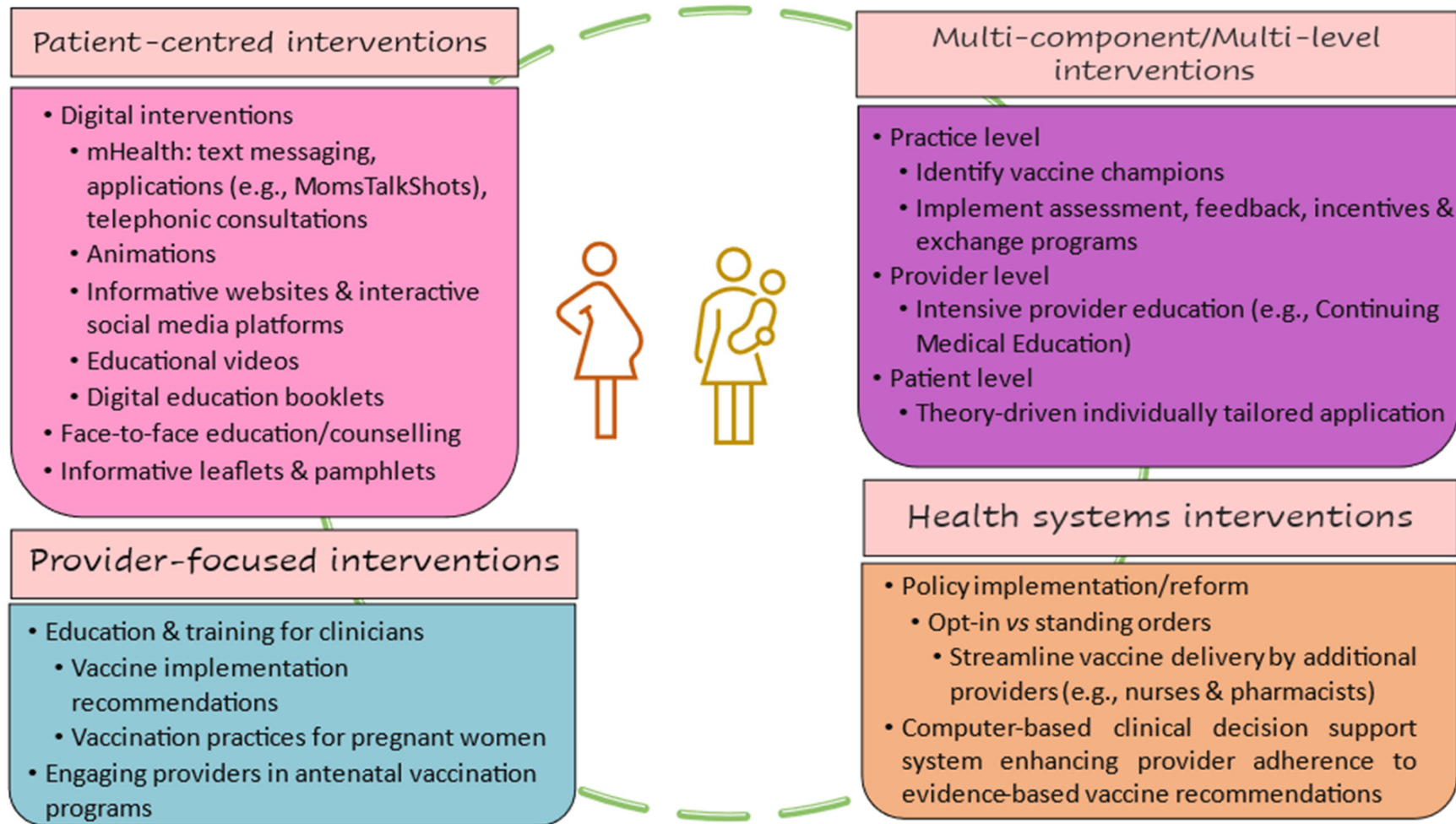


Figure 3. Different types of interventions included in this scoping review.

Vaccine *hesitancy*: problema di salute mondiale

Il vantaggio del vaccino (*evitare una malattia, ridurre il rischio di complicanze gravi*)

è anche il suo limite (*proposto ad una popolazione di sani*)

Vaccine *hesitancy*: problema di salute mondiale

OMS

- nel 2012 ha istituito un gruppo di lavoro specifico sul tema, denominato Strategic Advisory Group of Experts (**Sage**) on Immunization, guidato da un Segretariato congiunto Oms/Unicef
- ad agosto 2015 ha pubblicato tutto il materiale su un numero monografico della rivista *Vaccine* dedicato interamente all'esitazione vaccinale (*WHO Recommendations Regarding Vaccine Hesitancy*)

2023

Review

Interventions to Improve Knowledge, Attitudes, and Uptake of Recommended Vaccines during Pregnancy and Postpartum: A Scoping Review

Imen Ayouni ^{1,2,*}, Edina Amponsah-Dacosta ² , Susanne Noll ², Benjamin M. Kagina ² and Rudzani Muloiwa ^{1,2} 

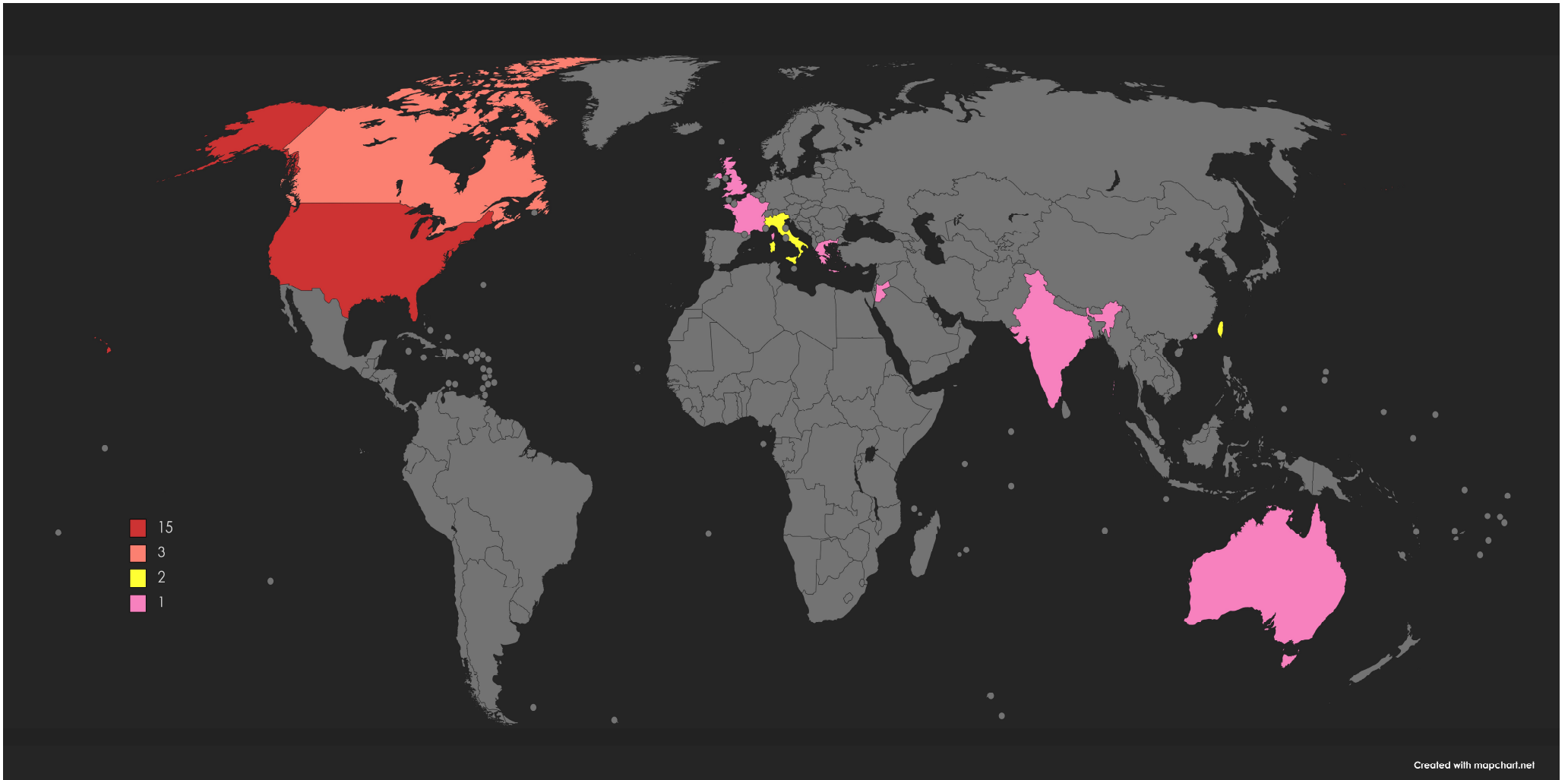
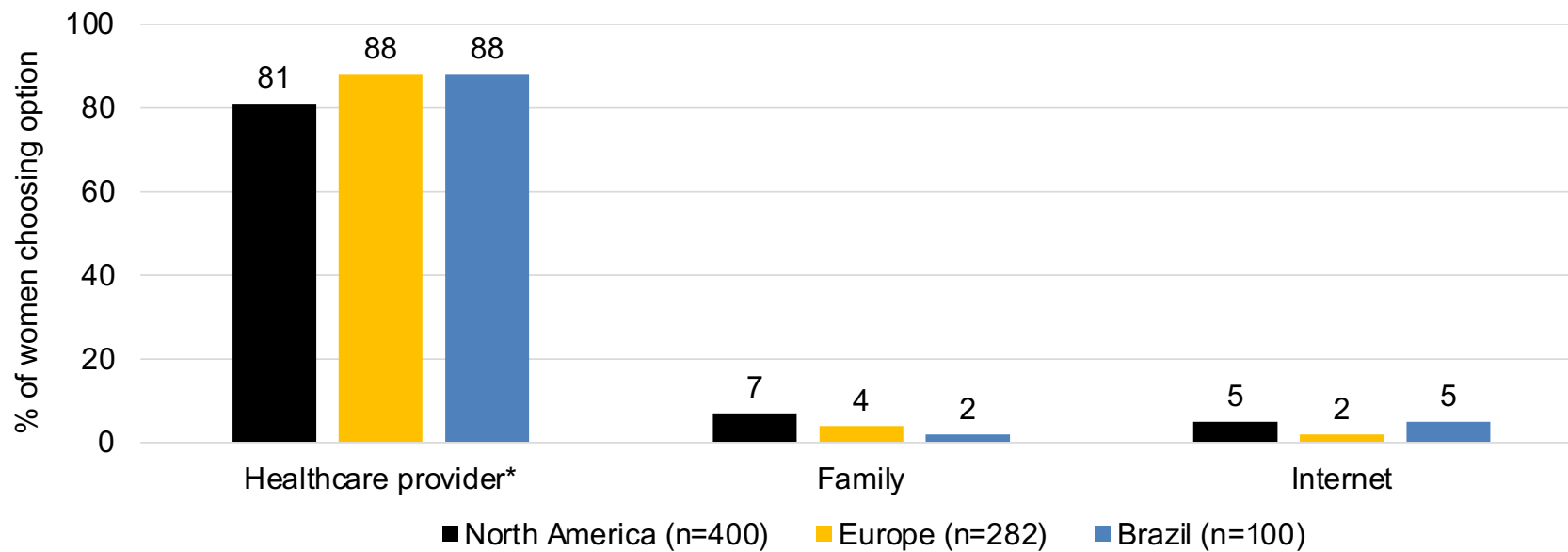


Figure 2. Number of intervention studies by country.

Online survey

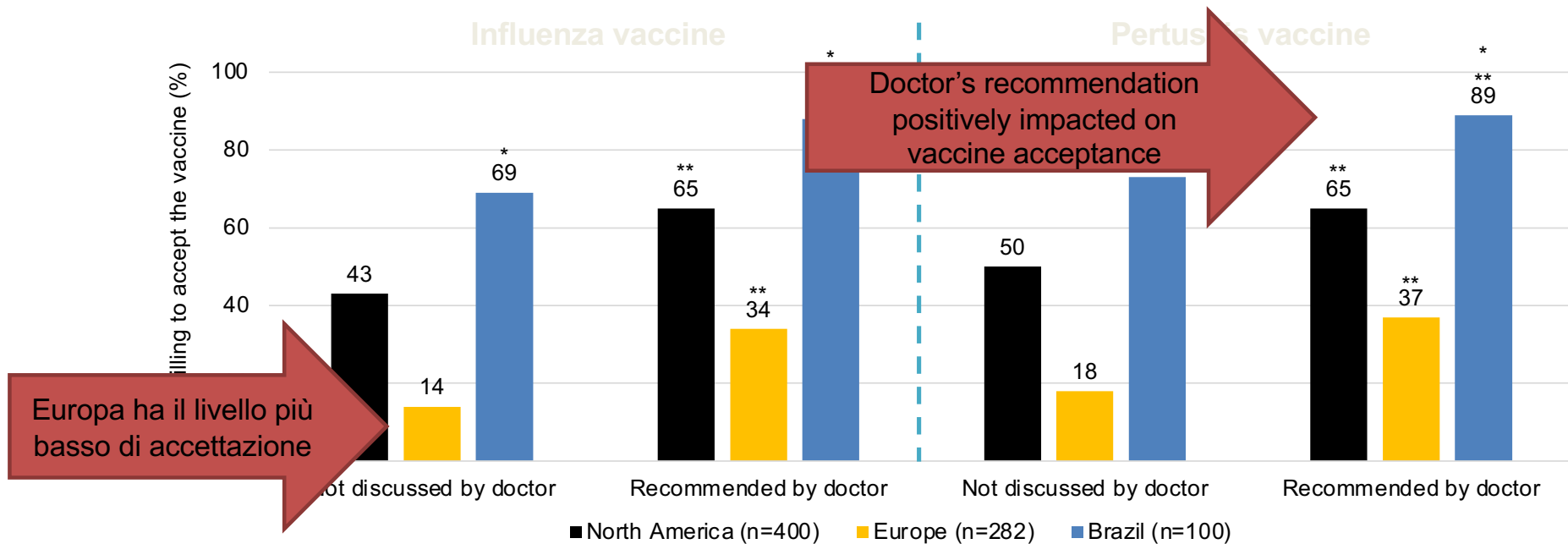
782 donne in gravidanza in Nord America, Europa e Brasile
Chi è la fonte di informazione più credibile sui vaccini in gravidanza?



*Physician or midwife/nurse practitioner.

Patwardhan M, Gonik B. J Womens Health Safety Res 2019;3:90–8.

Accettazione dei vaccini fra le donne in gravidanza varia fra le aree geografiche ma è universalmente migliorata se raccomandata dal medico



*p<0.05 for comparisons between North America, Europe and Brazil; **p<0.05 for comparisons between "Recommended by doctor" and "Not discussed by doctor" for each vaccine. Patwardhan M, Gonik B. J Womens Health Safety Res 2019;3:90-8.

Vaccines During Pregnancy

Influenza (the flu) and pertussis (whooping cough) are serious illnesses, but the flu shot and the whooping cough shot (also called Tdap*) can keep you healthy and help protect your newborn. All women should get these shots during pregnancy.



THE FLU VACCINE IS

- Safe for pregnant women and their babies when given during any trimester of pregnancy
- Effective at preventing serious flu illness in pregnant women

HOW DOES IT PROTECT MY BABY?

- The flu vaccine creates antibodies that are passed to a fetus, which gives protection against the flu until a baby can get the flu shot at age 6 months.

THE WHOOPING COUGH (Tdap*) VACCINE IS

- Safe for pregnant women and their babies
- Recommended between 27 weeks and 36 weeks of each pregnancy

HOW DOES IT PROTECT MY BABY?

- The Tdap vaccine creates antibodies that are passed to a fetus, which gives protection against whooping cough until a baby can get his or her first whooping cough shot at age 2 months.

PROTECT YOURSELF AND YOUR BABY. GET YOUR FLU AND WHOOPING COUGH (Tdap) SHOTS DURING EACH PREGNANCY.

Visit www.acog.org/immunization for more information on vaccines during pregnancy and other adult vaccines.

*Tdap is a combination vaccine that contains tetanus, diphtheria, pertussis, and acellular whooping cough antigens.

The flu shot is a separate vaccine.

For more information on the flu shot, visit www.cdc.gov/flu. For more information on Tdap, visit www.cdc.gov/vaccines/imz/adm/tdap.

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VACCINES— GET THE FACTS

FACT

Pregnant women who get the flu can become much sicker than nonpregnant women who get the flu. Pregnant women with flu complications have more medical visits and more hospitalizations. The flu shot offers you the best protection.

FACT

Babies younger than 1 month have the highest risk of severe disease and of dying from whooping cough. A baby cannot be vaccinated until he or she is 2 months old, so the baby's best protection is you getting the Tdap shot during pregnancy.

FACT

Getting shots during pregnancy will not make you sick or harm your fetus. Current research shows that vaccines do not cause pregnancy problems, birth defects, or autism in children. Vaccines have been used for many years in millions of pregnant women.



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

ACOG COMMITTEE OPINION SUMMARY

Number 718 • September 2017

(Replaces Committee Opinion Number 566, June 2013)

For a comprehensive overview of these recommendations, the full-text version of this Committee Opinion is available at <http://dx.doi.org/10.1097/AOG.0000000000002301>.



Scan this QR code with your smartphone to view the full-text version of this Committee Opinion.

Committee on Obstetric Practice Immunization and Emerging Infections Expert Work Group

This Committee Opinion was developed by the Immunization and Emerging Infections Expert Work Group and the Committee on Obstetric Practice, with the assistance of Richard Beigi, MD.

Update on Immunization and Pregnancy: Tetanus, Diphtheria, and Pertussis Vaccination



FOR PROFESSIONALS www.immunize.org / FOR THE PUBLIC www.vaccineinformation.org



www.immunize.org/catg.d/p4040.pdf
Item #P4040 (11/3/2023)





UK Health
Security
Agency



Pregnant?



Immunisation helps
to protect you and
your baby from
infectious diseases

Immunise against:
Flu (Influenza)
Whooping cough
(Pertussis)
German measles
(Rubella)

This leaflet describes
the vaccinations
that help protect
you and your baby
during and after
pregnancy.

Pregnant? – Vaccinations before, during and after your pregnancy

COVID-19 Vaccines While Pregnant or Breastfeeding

Updated July 14, 2022 [Español](#) | [Other Languages](#) [Print](#)

What You Need to Know

- COVID-19 vaccination is recommended for all people 6 months and older. This includes people who are pregnant, breastfeeding, trying to get pregnant now, or might become pregnant in the future. CDC also recommends COVID-19 vaccines for infants 6 months and older whose mother was vaccinated or had a COVID infection before or while pregnant.
 - [If you are pregnant or were recently pregnant](#), you are more likely to get very sick from COVID-19 compared to people who are not pregnant. Additionally, if you have COVID-19 during pregnancy, you are at increased risk of complications that can affect your pregnancy and developing baby.
 - Getting a COVID-19 vaccine can help protect you from getting very sick from COVID-19.
 - People who are pregnant should [stay up to date](#) with their COVID-19 vaccines, including getting a COVID-19 booster shot when it's time to get one.
- [Evidence](#) continues to build showing that:
 - COVID-19 vaccination during pregnancy is safe and effective.
 - There is currently no evidence that any vaccines, including COVID-19 vaccines, cause fertility problems in women or men.

On This Page

Vaccinare per proteggere

Position Paper



Nuove sfide nella prevenzione per mamma e neonato.
Investire nelle vaccinazioni raccomandate in gravidanza.
L'influenza.



Associazione dei Ginecologi Italiani:
spedali, del territorio e liberi professori



Position Paper
Nuove sfide nella prevenzione per mamma e neonato.
Investire nelle vaccinazioni raccomandate in gravidanza.
La pertosse.



The American College of
Obstetricians and Gynecologists
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Update on Immunization and Pregnancy: Tetanus, Diphtheria, and Pertussis Vaccination

VACCINAZIONI IN GRAVIDANZA

proteggila per proteggerli

Documento congiunto redatto dal gruppo di lavoro
SIGO, SIMP, AOGOI, AGUI, SITI, SIN, FNOPO, Rete Interaziendale Milano
Materna Infantile (RIMMI), Vivere Onlus, Cittadinanzattiva



Perche'?

Il vaccino ha il ruolo di

- evitare la malattia (o le complicanze gravi)
- indurre una risposta immunitaria (Ab, cellulo-mediata)

Quali differenze per le donne?

Bisogna pensare alle conseguenze di eventuale recettività ad agente patogeno che possa creare problemi durante la gravidanza



Quali?

- Rosolia/Morbillo/Parotite (MPR)
- Varicella
- Difterite-tetano-pertosse (dTpa)
- Influenza
- Covid-19

- HPV
-

Quando?

- In età infantile
- In età fertile
- Durante la gravidanza
- In puerperio

Perché si offre vaccino in gravidanza?



Per proteggere la madre:

infezioni che sono potenzialmente gravi per madre e feto (influenza, tetano)

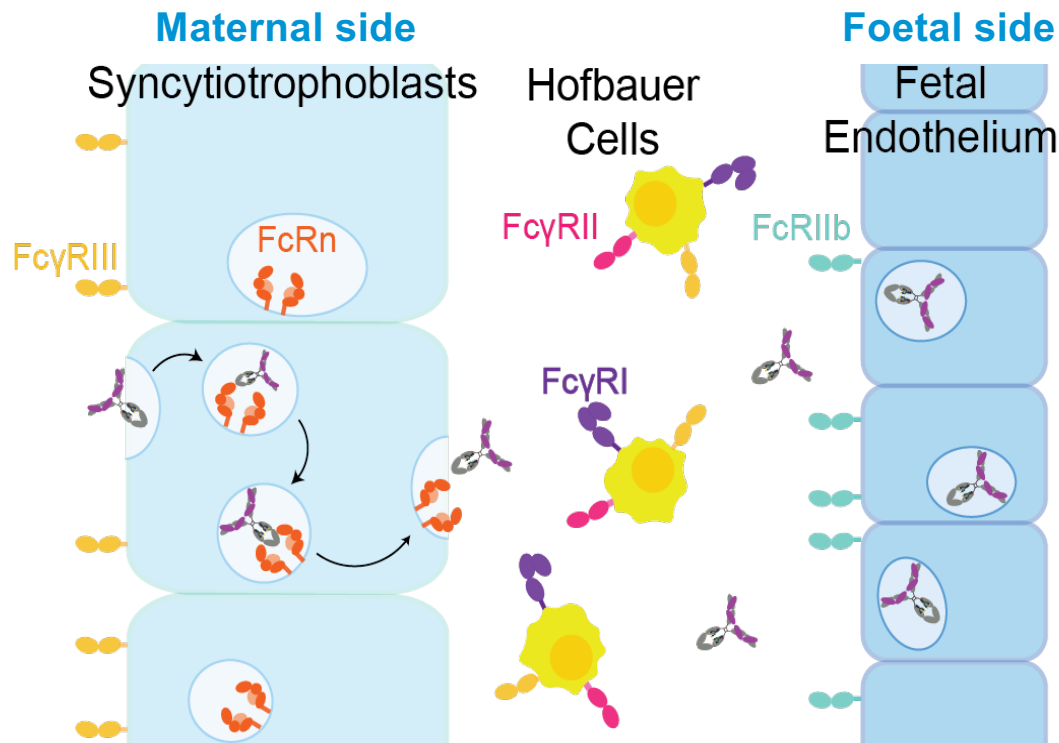
Per proteggere il feto/neonato attraverso la madre:

Feto - immunità passiva mediante gli Ab vaccino-specifici che passano attraverso la placenta

Neonato - attraverso il latte materno per proteggere il bambino nei primi mesi di vita prima delle vaccinazioni che danno immunità attiva (influenza, pertosse, tetano)



Passaggio Ab materni attraverso la placenta



Selective transfer of IgG*:¹⁻⁴

- Subclass IgG1 > 4 > 3 > 2
- Vaccines with protein antigens > vaccines with polysaccharide antigens because they induce IgG2
- Affected by maternal clinical condition (HIV, malaria, hypergammaglobulinaemia)
- May be impacted by glycosylation status, molecular structure and effector function of IgG?

Transfer of antibodies and immune complexes provides:¹

- Immunity against toxins and pathogens
- Tolerance to commensals
- Tolerance to allergens
- A starting point for immune system development

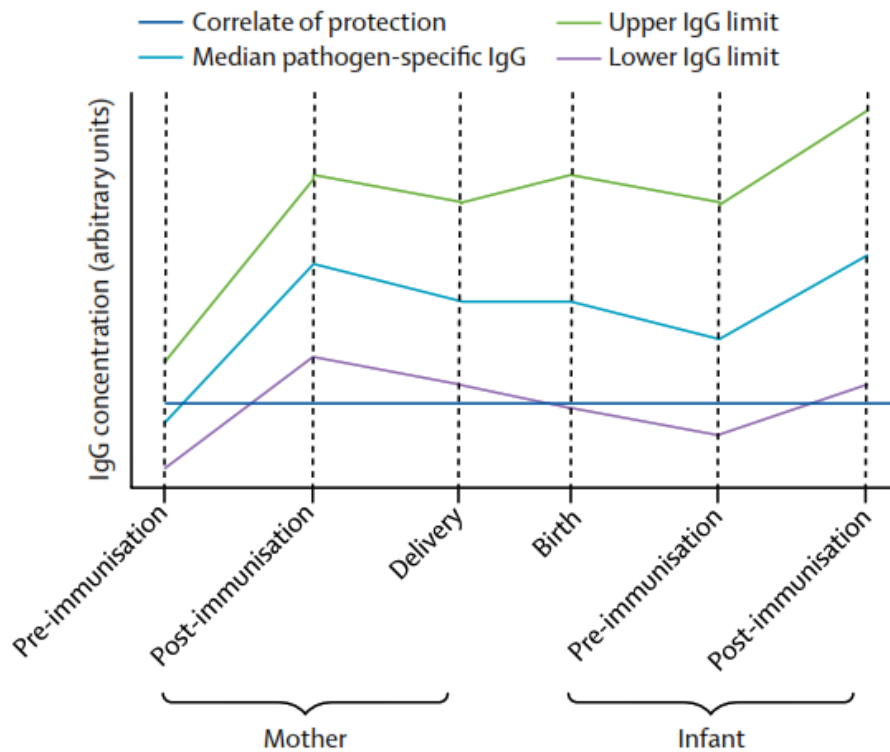
*IgG is the only antibody type that is transferred directly across the placenta.⁴ FcRn, neonatal Fc receptor; IgG, immunoglobulin G.

1. Jennewein MF, et al. Semin Immunopathol 2017;39:605–13; 2. Abu-Raja B, et al. Front Immunol 2020;11:1282;

3. Maertens K, et al. Eur J Pediatr 2020;179:235–42; 4. Marchant A, et al. Lancet Infect Dis 2017;17:e197–e208.

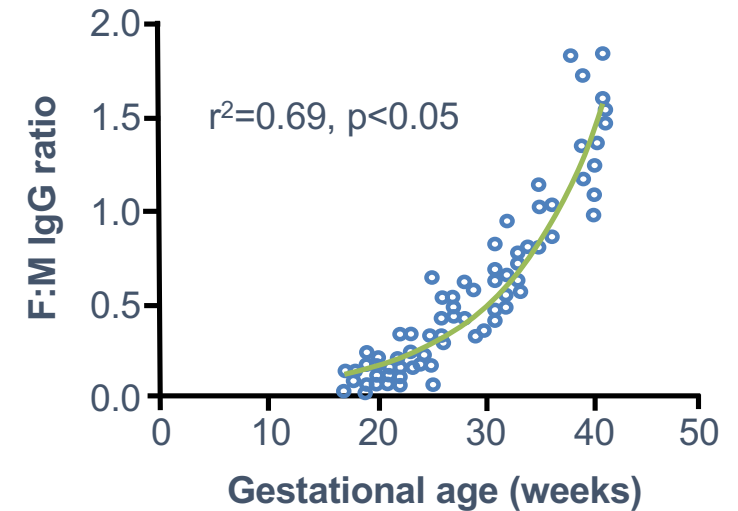
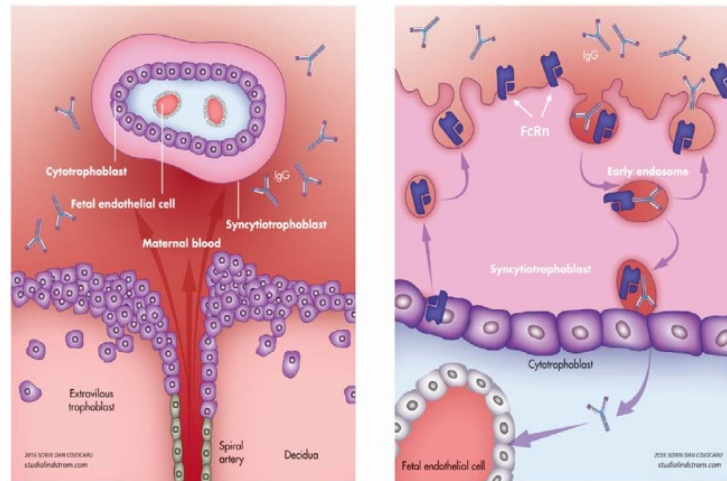
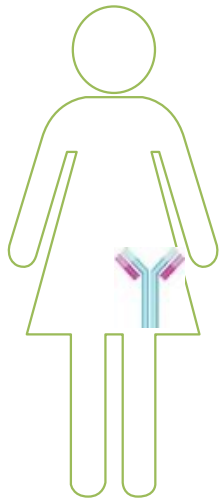
Vaccinazione delle donne in gravidanza aumenta il livello di Ab nel feto

Effect of vaccination in pregnancy on antibody levels in the mother and infant



- An ideal vaccine should raise the **maternal antibody concentration** to above the level needed to provide immunity throughout the pregnancy
- Ideally, maternal vaccination should also increase and **maintain the antibody concentration in newborns** to a level needed to provide immunity until the primary series of infant immunisations

Livello di Ab materni nei feti dipende da livello Ab nel sangue materno, placenta ed età gestazionale



Maternal titre and other antibody-specific factors^{1,2}

Placental health (transplacental transfer of IgG via FcRn receptors)¹⁻³

Gestational age (IgG transfer ↑ as pregnancy progresses*)^{1,4}

Maternal antibody titre depends on vaccination status and time since last vaccination/disease²

*Transfer of maternal antibodies starts from around week 17 of pregnancy and increases with gestation.⁵ FcRn, neonatal Fc receptor; F:M, foetal:maternal; IgG, immunoglobulin G..

1. Marchant A, et al. Lancet Infect Dis 2017;17:e197–e208; 2. Maertens K, et al. Eur J Pediatr 2020;179:235–42.; 3. Ciobanu AM, et al. Diagnostics (Basel). 2020;10:583;

4. Malek A, et al. Am J Reprod Immunol 1996;36:284–55; 5. Buchy P, et al. Int J Infect Dis 2020;92:1–12.

Vaccini raccomandati in gravidanza

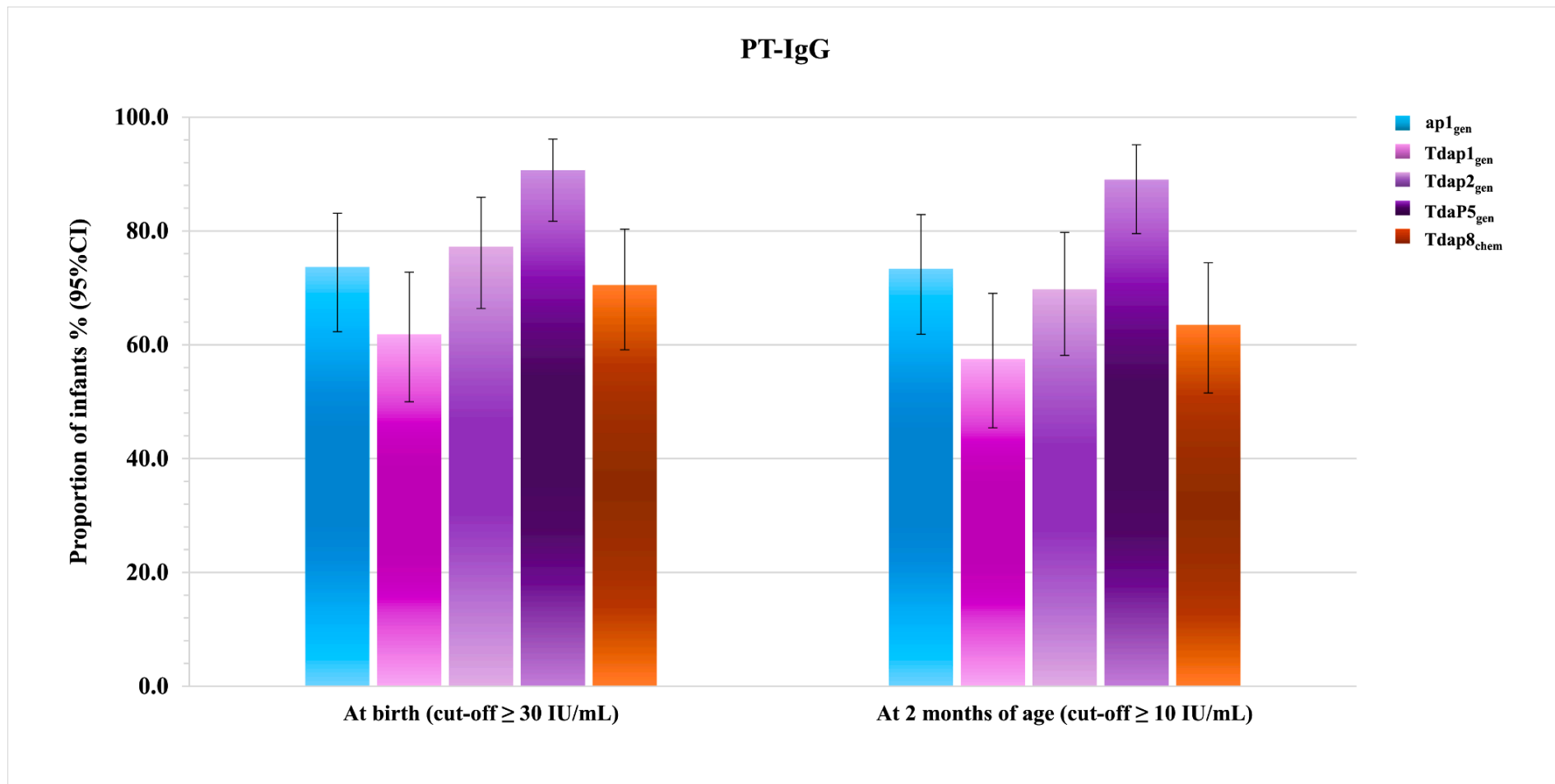
- ✓ Influenza
- ✓ Pertosse

devono essere ripetuti ad **ogni** gravidanza

2024

Effective and safe transfer of maternal antibodies persisting two months postpartum following maternal immunization with different doses of recombinant pertussis-containing vaccines

Kulkanya Chokephaibulkit ^{a,b,1}, Thanyawee Puthanakit ^{c,1}, Surasith Chaithongwongwatthana ^d, Niranjan Bhat ^f, Yuxiao Tang ^f, Suvaporn Anugulruengkitt ^c, Chenchit Chayachinda ^e, Sanitra Anuwutnavin ^e, Keswadee Lapphra ^b, Supattra Rungmaitree ^b, Monta Tawan ^c, Indah Andi-Lolo ^f, Renee Holt ^f, Librada Fortuna ^{g,*}, Chawanee Kerdsomboon ^g, Vilasinee Yuwaree ^g, Souad Mansouri ^g, Pham Hong Thai ^g, Bruce L. Innis ^f



¹ If the cord blood was not obtained at the time of delivery, an infant blood draw would be collected within 72 hours of birth

Fig. 2. Proportion of infants with cut-off levels of anti-PT antibody at birth¹ and at 2 months of age.

PT_{gen} containing vaccines (aP5_{gen}, Tdap5_{gen} and Tdap2_{gen}) are licensed for booster use in adolescents and adults including pregnant women and the elderly. The availability of affordable low-dose ap1_{gen} and Tdap1_{gen} vaccines could make maternal pertussis vaccination more accessible in low-middle income countries.

12-11-2019



0033045-12/11/2019-DGPRE-MDS-P

Ministero della Salute

**OGGETTO: Vaccinazioni raccomandate per le donne in età fertile e in gravidanza
Aggiornamento novembre 2019**

Con la presente nota si integrano e aggiornano le indicazioni già fornite con la Circolare del 21/11/2018, prot. 34074.

Scopo del presente documento è ribadire l'importanza delle vaccinazioni come strumento di promozione della salute della donna in età fertile, in previsione e durante la gravidanza, proteggendo se stessa e il nascituro da alcune specifiche patologie infettive.

È stato osservato che le madri trasferiscono anticorpi al prodotto del concepimento, offrendogli così un certo grado di protezione contro malattie quali morbillo, difterite e poliomielite. Gli anticorpi materni sono in grado di proteggere i neonati dalle infezioni, e modificare la severità delle relative malattie infettive nei bambini, per un periodo di tempo variabile, a seconda del livello di trasmissione placentare e del tasso di decadimento degli anticorpi acquisiti passivamente. La trasmissione transplacentare di anticorpi è un processo selettivo, attivo e intracellulare, che inizia intorno alla 17^a settimana di gestazione e progressivamente aumenta, fino alla 40^a settimana, quando le IgG fetali raggiungono livelli più elevati rispetto a quelle materne. Tuttavia, i livelli di IgG fetali sono influenzati da diversi fattori, tra cui concentrazione delle immunoglobuline nel sangue materno, anomalie della placenta, tipo di vaccino eventualmente ricevuto, età gestazionale al parto e tempo intercorso tra vaccinazione e parto.

Vaccinazioni in età fertile		Note
Raccomandate	MPR e varicella	Se non vaccinata e anamnesticamente negativa anche solo a una delle malattie elencate. Ritardare la gravidanza di 4 settimane dopo la vaccinazione
	dTpa	Richiamo ogni 10 anni
	HPV	Nel corso del 12° anno di vita. Raccomandato anche recupero in caso di non vaccinazione in quella età, possibilmente prima dell'inizio dell'attività sessuale
Vaccinazioni in gravidanza		
Raccomandate	dTpa	Dalla 27 ^a alla 36 ^a settimana di gestazione, idealmente intorno alla 28 ^a settimana, e ad ogni gravidanza, indipendentemente dall'anamnesi positiva per malattia o pregressa vaccinazione
	influenza inattivato	In qualsiasi epoca della gravidanza
Controindicate	Vaccini vivi attenuati (MPR, Varicella, zoster), BCG ⁴ , encefalite giapponese ⁵	Vaccini MPR, Varicella, zoster se somministrati non costituiscono indicazioni all'interruzione volontaria di gravidanza
Non raccomandate per dati non disponibili	HPV, Tifo orale (se necessario, preferire la formulazione a subunità iniettabile), pneumococco	Se somministrate non costituiscono indicazioni all'interruzione volontaria di gravidanza
Possibili se beneficio maggiore del rischio	Epatite A, epatite B, IPV ⁶ , meningococco, TBE ⁷ , rabbia, colera, febbre gialla ⁸	Se somministrate non costituiscono indicazioni all'interruzione volontaria di gravidanza

Vaccinazioni nel puerperio*		
Raccomandate	MPR e varicella	Se la donna non è stata vaccinata e se anamnesticamente negativa anche solo a una delle malattie elencate
	dTpa	Se la donna non è stata vaccinata durante la gravidanza. In tale evenienza è altresì opportuna la vaccinazione dei contatti stretti

* L'allattamento non è una controindicazione alla vaccinazione

PNPV 2023-2025

Intesa, ai sensi dell'articolo 8, comma 6, della legge 5 giugno 2003, n. 131, tra il Governo, le regioni e le Province autonome di Trento e di Bolzano, sul documento recante «Piano nazionale di prevenzione vaccinale (PNPV) 2023-2025» e sul documento recante «Calendario nazionale vaccinale». (Rep. atti n. 193/CSR del 2 agosto 2023). (23A04685)

(G.U. Serie Generale , n. 194 del 21 agosto 2023)

Obiettivi del Piano

- mantenere lo stato Polio free
- raggiungere e mantenere l'eliminazione di morbillo e rosolia
- rafforzare la prevenzione del cancro della cervice uterina e delle altre malattie HPV correlate
- raggiungere e mantenere le coperture vaccinali target rafforzando Governance, Reti e percorsi di prevenzione vaccinale
- promuovere interventi vaccinali nei gruppi di popolazione ad alto rischio per patologia, favorendo un approccio centrato sulle esigenze del cittadino/paziente
- ridurre le diseguaglianze e prevedere azioni per i gruppi di popolazione difficilmente raggiungibili e/o con bassa copertura vaccinale
- completare l'informatizzazione delle anagrafi vaccinali regionali e mettere a regime l'anagrafe vaccinale nazionale
- migliorare la sorveglianza delle malattie prevenibili da vaccino
- rafforzare la comunicazione in campo vaccinale
- promuovere nei professionisti sanitari la cultura delle vaccinazioni e la formazione in vaccinologia.

2023-2025

Take-home messages (1)

I vaccini rappresentano un importante strumento di prevenzione

- dei difetti congeniti
- di malattie materno-fetoneonatali

N.B. L'offerta attiva (informazione adeguata, indicazione scritta in cartella) aumenta sensibilmente la copertura vaccinale

Take-home messages (2)

- ✓ Alle bambine sono **raccomandati** i vaccini previsti del calendario vaccinale, se ciò non è stato fatto vanno offerti i vaccini
 - alla prima visita ginecologica
 - in puerperio
 - ✓ Alle donne in gravidanza sono **raccomandati** i vaccini per pertosse (dTpa) ed influenza secondo le modalità previste
- N.B. Il vaccino anti-influenza può essere eseguito in contemporanea al vaccino anti-Covid

Grazie a tutte/i.....

*To avoid criticism say nothing, do nothing, be nothing
(Elbert Hubbard, 1856-1915)*

Arrivederci al 14-15 marzo 2025!

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