



DEPARTAMENTO DE
MICroBiologia
UNIVERSIDADE DE SÃO PAULO



Vacinas contra agentes virais

Enrique Boccardo

Depto. de Microbiologia

ICB/USP.

eboccardo@usp.br

UM POUCO DE HISTÓRIA...



- A varíola era endêmica na China
- 1000 AC
- Aplicação da “variolation”

UM POUCO DE HISTÓRIA...



- O 14 de Maio de 1796 Edward Jenner utilizou material infectado com “cowpox” (da mão de Sarah Nemes) para vacinar James Phipps (8 anos)
- O 1º de Julio de 1796, Jenner inoculou James com material obtido apartir de um caso de varíola.
- James não foi infectado

A vacinação contra a varíola foi adotada quase universalmente no século XIX

VACINAS

Definição de **Imunização**:

- procedimento através se induz a resistência imune do corpo contra uma doença específica. Pode ser **passiva** ou **ativa**.
- Na imunização **passiva** o organismos não é “desafiado”. Acontece pela administração de soro ou imunoglobulinas de um indivíduo imune (ex., tétanos, sarampo, ebola, Lassa, SARS-CoV-2, mordidas de cobra, raiva, etc.).
- A imunização passiva natural acontece pela transferência de anticorpos maternos antes de após o nascimento.

VACINAS

A imunização **ativa** acontece pela ativação do sistema imune. Assim, o organismo adquire resistência contra doenças específicas ativação da **resposta imune adquirida** (humoral e celular).

A imunização **ativa** pode acontecer de maneira natural ou artificial (vacinas).

Definição de **vacina** (uma das possíveis):

- preparação antigénica, que inoculada (administrada) num indivíduo induz uma resposta imunitária protetora específica para um ou mais agentes infecciosos.

Resposta imune: **Adquirida**

Resposta humoral

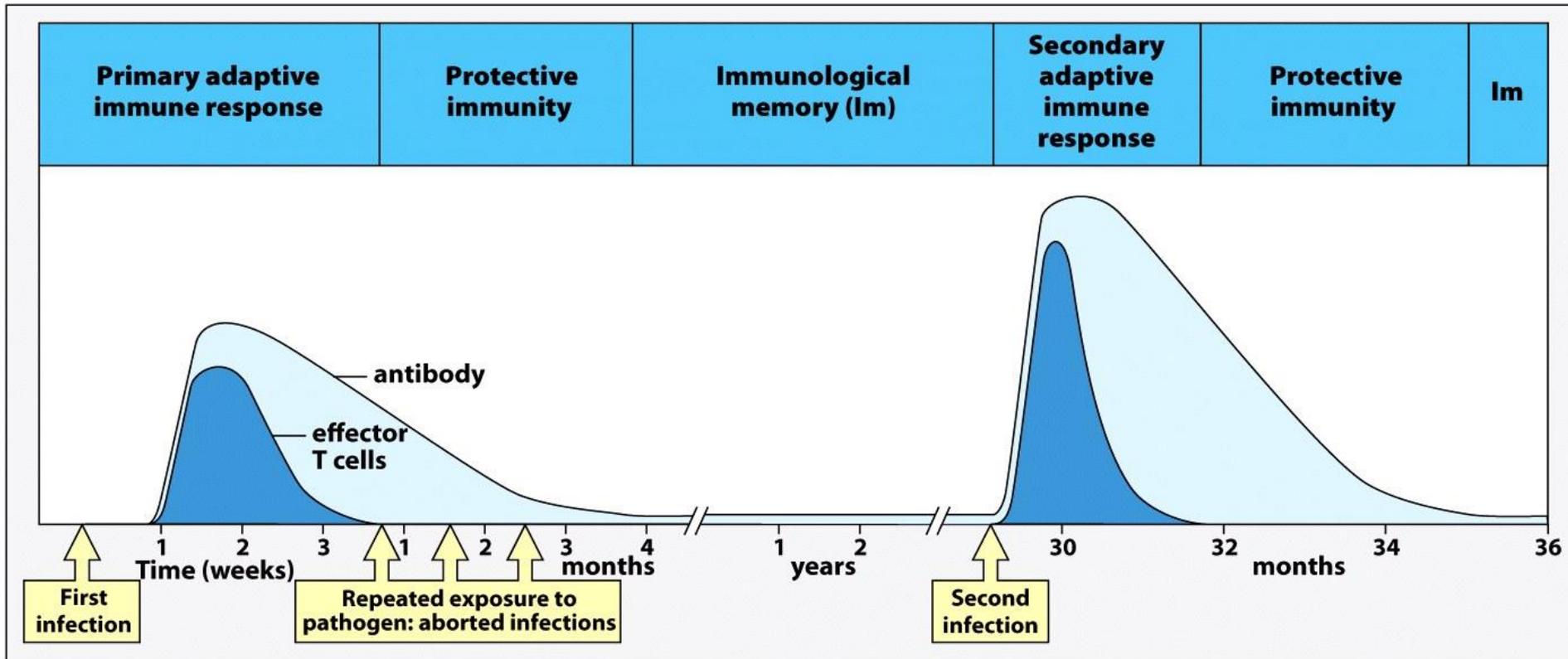
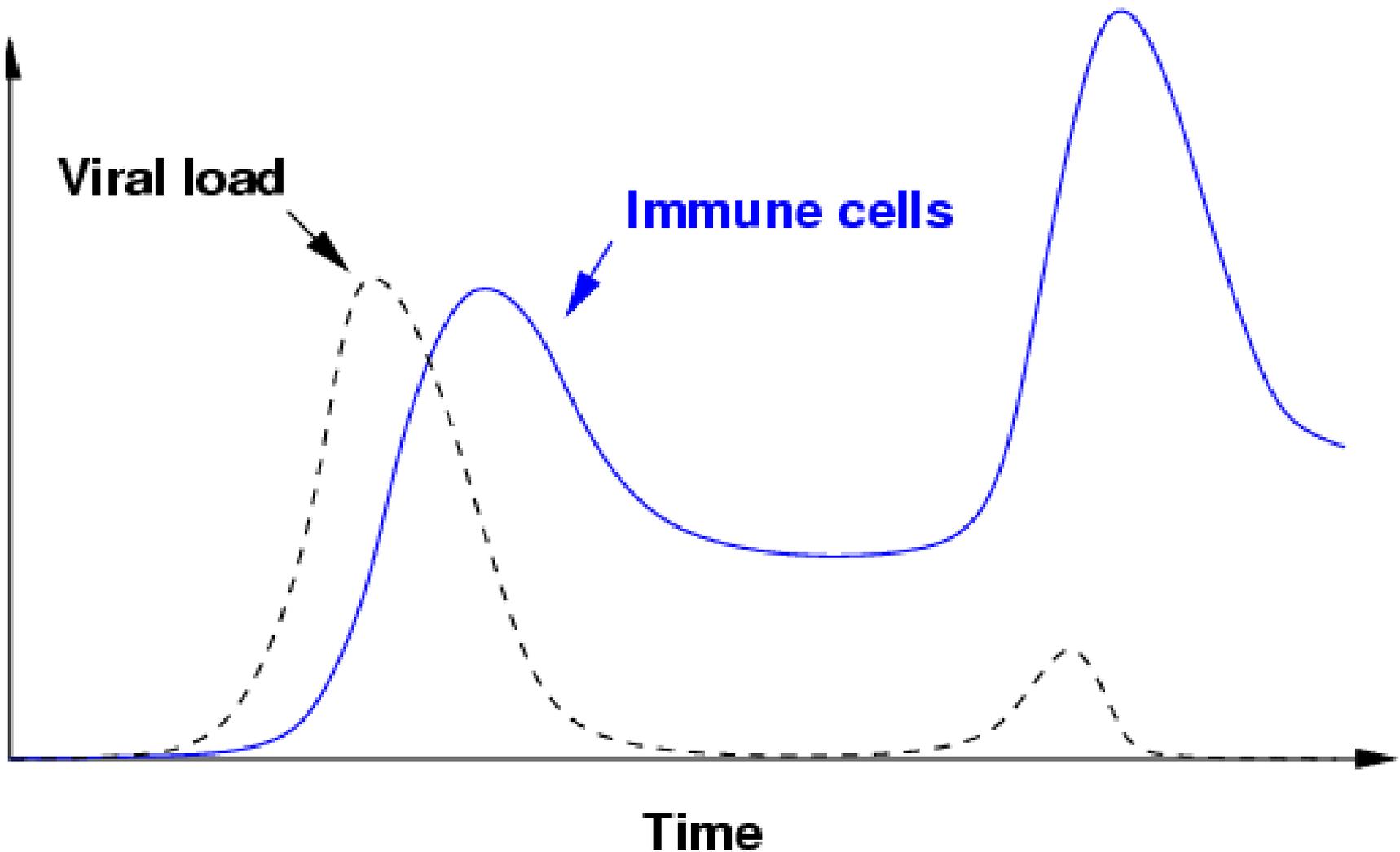


Figure 10.18 The Immune System, 3ed. (© Garland Science 2009)

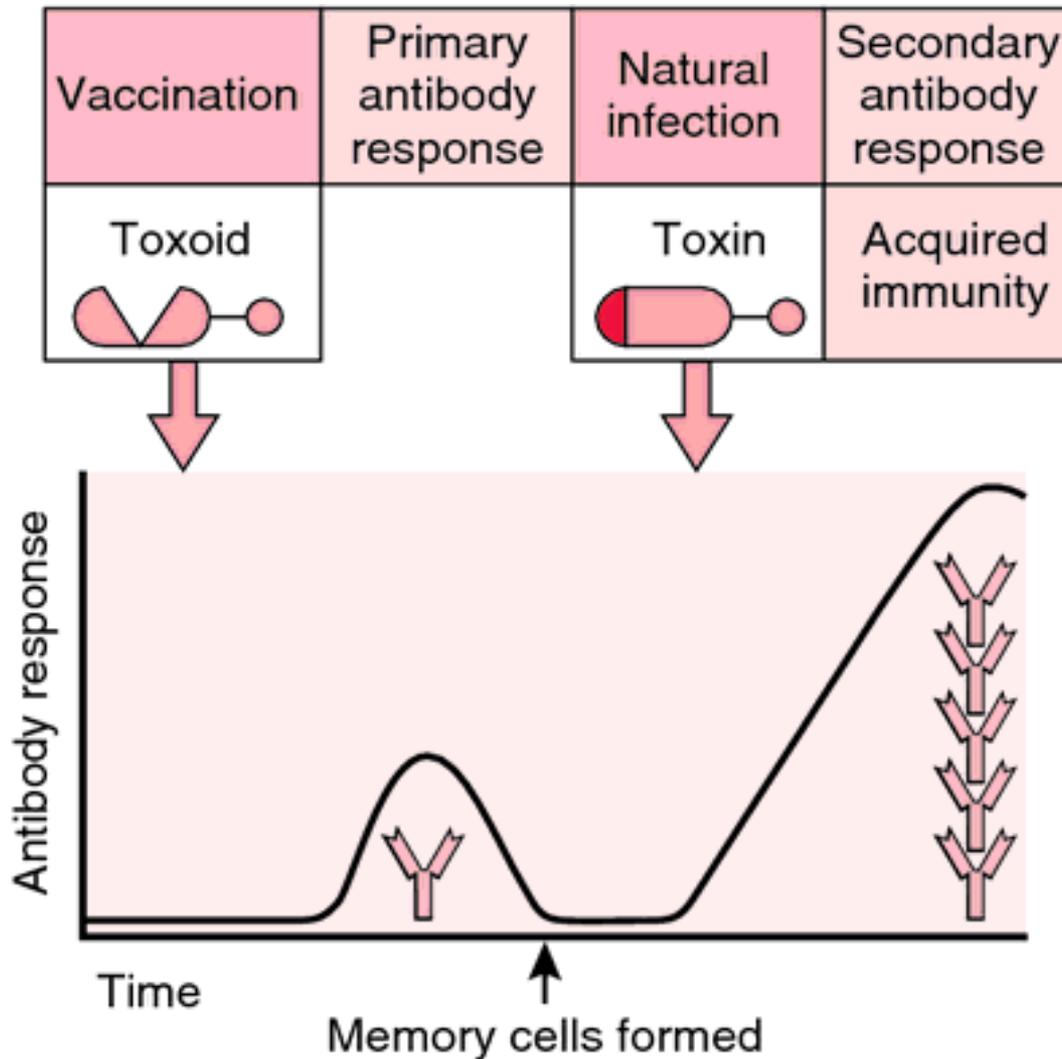
Resposta imune: **Adquirida**

Resposta humoral



Resposta imune: **Adquirida**

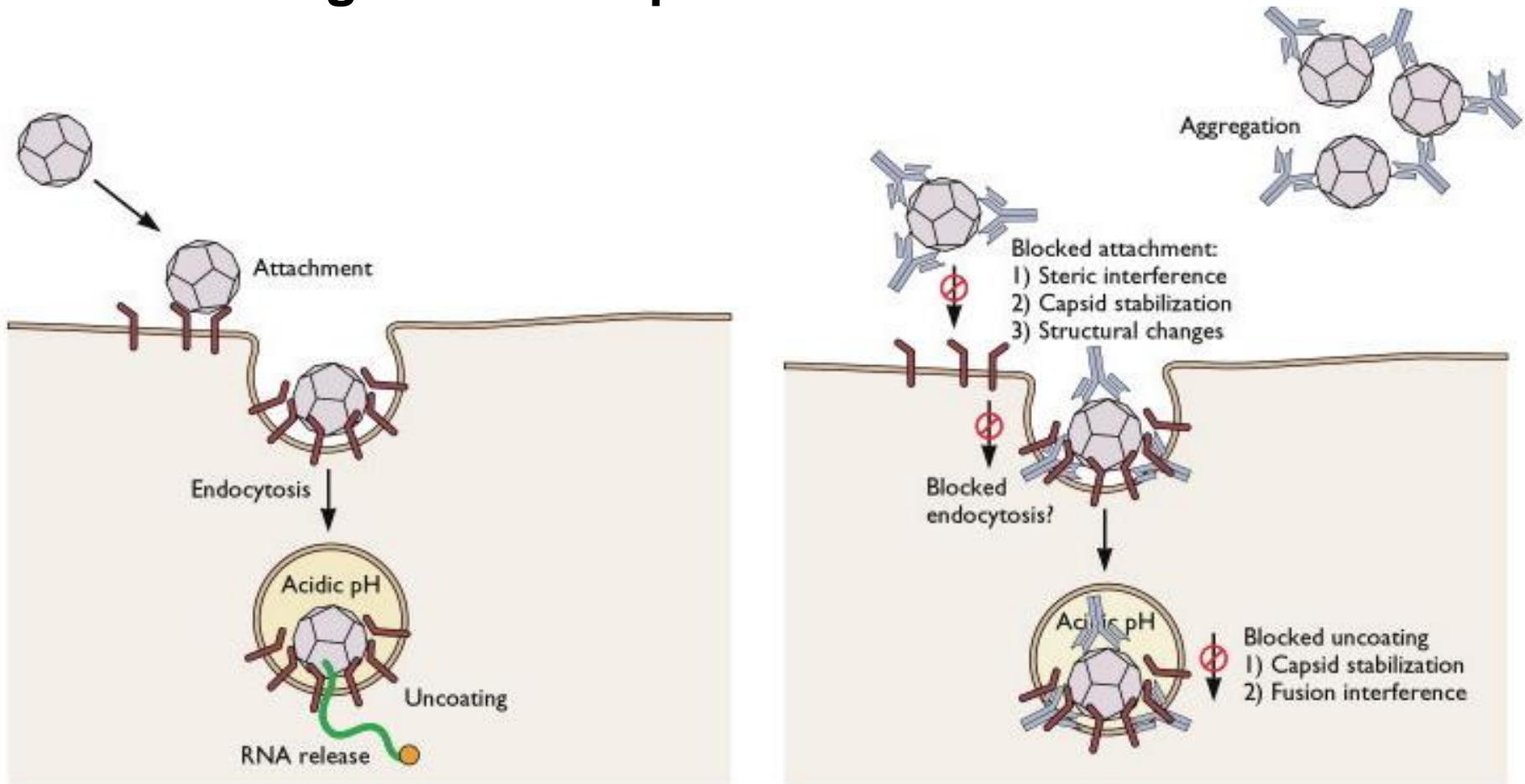
Resposta humoral



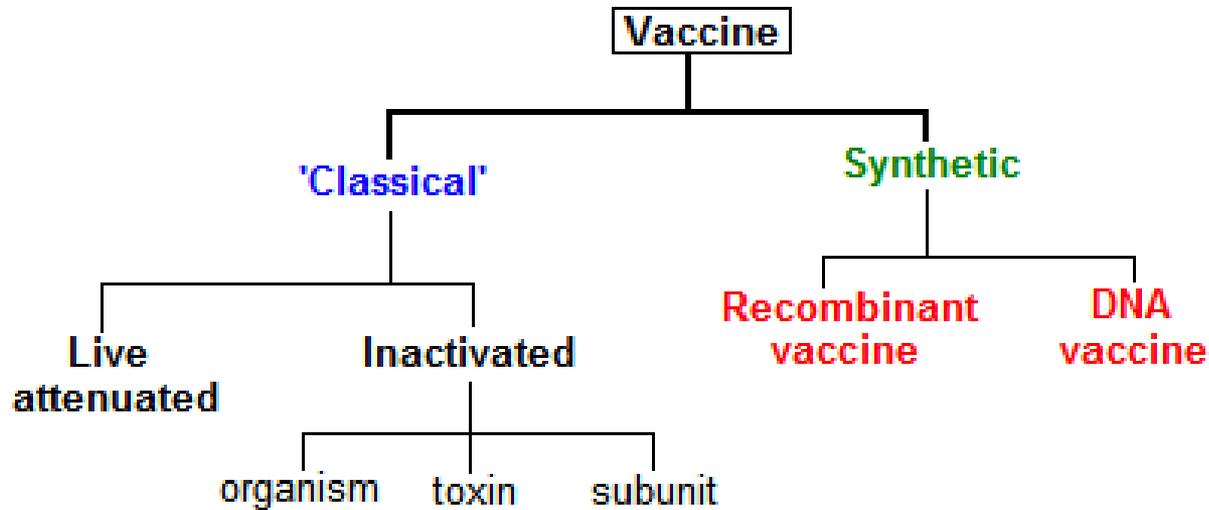
Resposta imune: **Adquirida**

Resposta humoral

Alguns anticorpos são neutralizantes

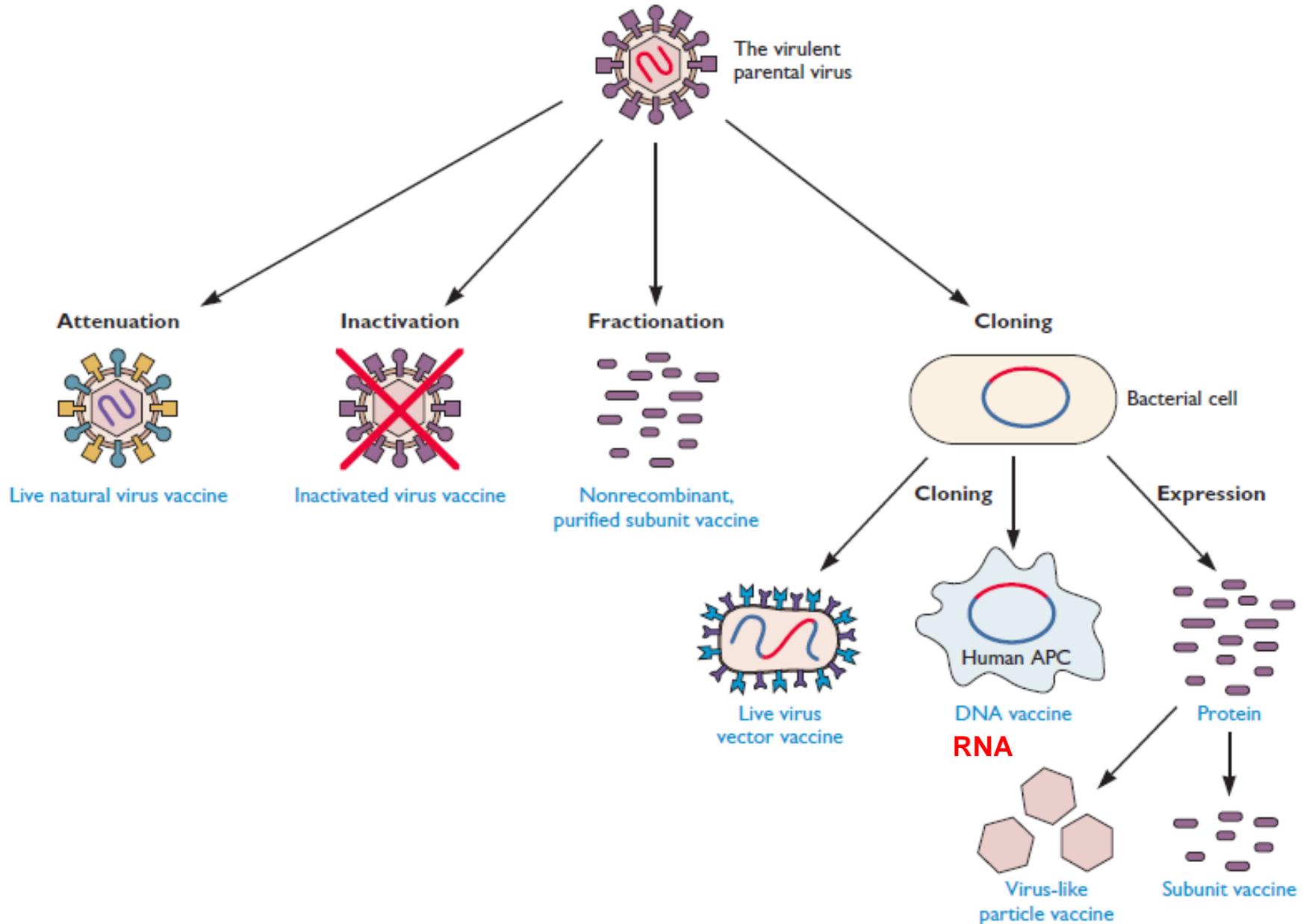


TIPOS DE VACINAS



- Vacinas vivas atenuadas
- Vacinas inativadas
- Vacinas baseadas em subunidades
- Vacinas de toxóides
- Vacinas conjugadas
- Vacinas de DNA
- Vacinas de vetores recombinantes

TIPOS DE VACINAS

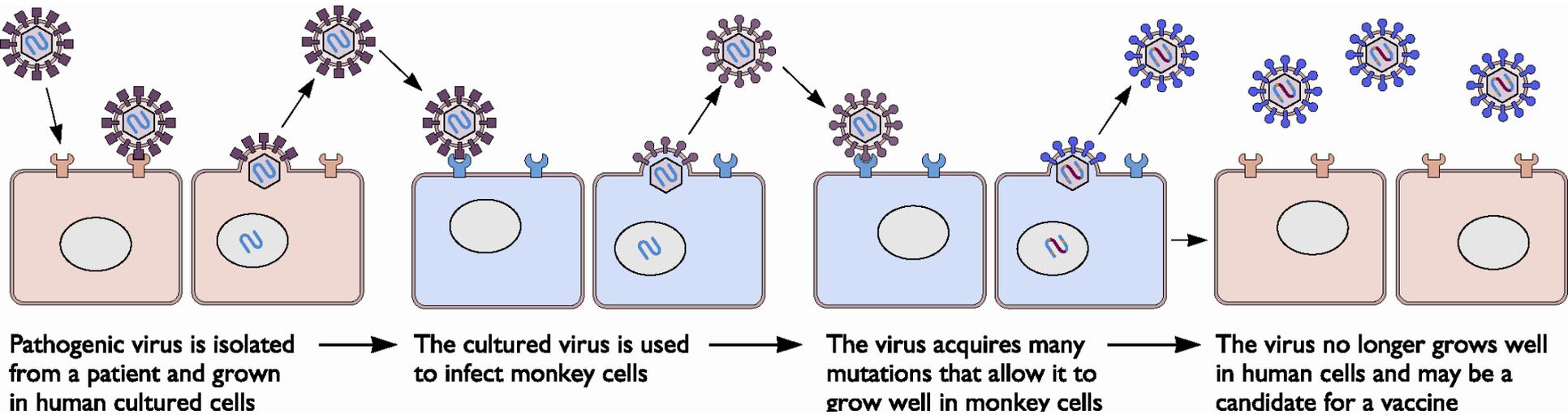


TIPOS DE VACINAS

- Vacinas vivas atenuadas
 - VZV, OPV, YFV
 - “heterólogas” ex., Variola
- Vacinas inativadas
- Vacinas baseadas em subunidades
- Vacinas de toxóides
- Vacinas conjugadas
- Vacinas de DNA
- Vacinas de RNA
- Vacinas de vetores recombinantes

TIPOS DE VACINAS

Vacinas vivas atenuadas



TIPOS DE VACINAS

Live attenuated (LAV)

- Tuberculosis (BCG)
- Oral polio vaccine (OPV)
- Measles
- Rotavirus
- Yellow fever

Inactivated (killed antigen)

- Whole-cell pertussis (wP)
- Inactivated polio virus (IPV)

Influenza
Covid-19 (Coronavac)

Subunit (purified antigen)

- Acellular pertussis (aP),
- *Haemophilus influenzae* type B (Hib),
- Pneumococcal (PCV-7, PCV-10, PCV-13)
- Hepatitis B (HepB)

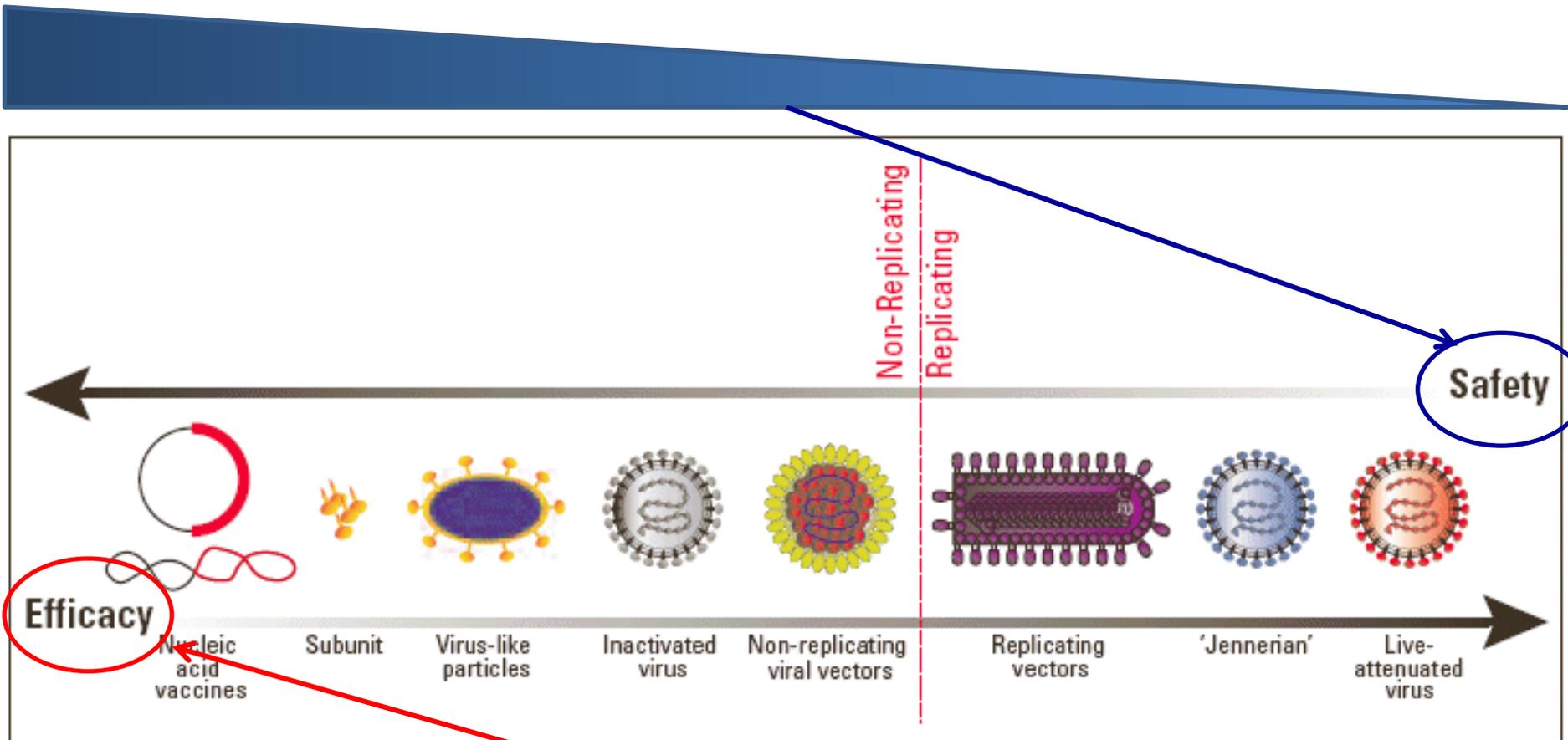
HPV

Toxoid (inactivated toxins)

- Tetanus toxoid (TT),
- Diphtheria toxoid

TIPOS DE VACINAS

Vantagens e desvantagens



TIPOS DE VACINAS

Vantagens e desvantagens

Vacinas vivas atenuadas

IMMUNE RESPONSE



- ◆ Live microorganisms provide continual antigenic stimulation, giving sufficient time for memory cell production.
- ◆ Attenuated pathogens are capable of replicating within host cells.

Excellent immune response

SAFETY AND STABILITY



- ◆ Attenuated pathogens can revert to original form and cause disease.
- ◆ Potential harm to individuals with compromised immune systems (eg. HIV).
- ◆ Sustained infection (BCG - local lymphadenitis).
- ◆ Contamination of tissue culture.
- ◆ Immunization errors (Reconstitution, cold chain).
- ◆ Usually not given in pregnancy

Less safe compared to inactivated vaccines

TIPOS DE VACINAS

Vantagens e desvantagens

Vacinas inativadas

IMMUNE RESPONSE



- ◆ May not always induce an immune response at first dose.
- ◆ Response may not be long-lived, requiring several doses of vaccine.

Less strong immune response compared to live vaccines

SAFETY AND STABILITY



- ◆ Have no live components, **no risk** of inducing the disease.
- ◆ Safer and more stable than LAVs.

Excellent stability profile

VACINAS licenciadas nos Estados Unidos

Table 8.3 Viral vaccines licensed in the United States

Disease or virus	Type of vaccine	Indications for use	Schedule
Adenovirus	Live attenuated, oral	Military recruits	One dose
Hepatitis A	Inactivated whole virus	Travellers, other high-risk groups	0, 1, and 6 mo
Hepatitis B	Yeast-produced recombinant surface protein	Universal in children, exposure to blood, sexual promiscuity	0, 1, 6, and 12 mo
Influenza	Inactivated viral subunits	Elderly and other high-risk groups	One dose seasonally
Influenza	Live attenuated	Children 2–8 yr old, not previously vaccinated with influenza vaccine	Two doses at least 1 mo apart
		Children 2–8 yr old, previously vaccinated with influenza vaccine	One dose
		Children, adolescents, and adults 9–49 yr old	One dose
Japanese encephalitis	Inactivated whole virus	Travelers to or inhabitants of high-risk areas in Asia	0, 7, and 30 days
Measles	Live attenuated	Universal vaccination of infants	12 mo of age; 2nd dose, 6 to 12 yr of age
Mumps	Live attenuated	Universal vaccination of infants	Same as measles, given as MMR
Papilloma (human)	Yeast- or SF9-produced virus-like particles	Females 9–26 yr old	Three doses
Rotavirus	Live reassortant	Healthy infants	2, 3, and 6 mo or 2 and 4 mo of age depending on vaccine
Rubella	Live attenuated	Universal vaccination of infants	Same as measles, given as MMR
Polio (inactivated)	Inactivated whole viruses of types 1, 2, and 3	Changing: commonly used for immunosuppressed where live vaccine cannot be used	2, 4, and 12–18 mo of age, then 4 to 6 yr of age
Polio (live)	Live, attenuated, oral mixture of types 1, 2, and 3	Universal vaccination; no longer used in United States	2, 4, and 6–18 mo of age
Rabies	Inactivated whole virus	Exposure to rabies, actual or prospective	0, 3, 7, 14, and 28 days postexposure
Smallpox	Live vaccinia virus	Certain laboratory workers	One dose
Varicella	Live attenuated	Universal vaccination of infants	12 to 18 mo of age
Varicella-zoster	Live attenuated	Adults 60 yr old and older	One dose
Yellow fever	Live attenuated	Travel to areas where infection is common	One dose every 10 yr

Vaccines Licensed for Use in the United States

Product Name	Trade Name
Adenovirus Type 4 and Type 7 Vaccine, Live, Oral (/vaccines-blood-biologics/vaccines/adenovirus-type-4-and-type-7-vaccine-live-oral)	No Trade Name
Anthrax Vaccine Adsorbed (/vaccines-blood-biologics/vaccines/biothrax)	Biothrax
BCG Live (/vaccines-blood-biologics/vaccines/bcg-vaccine)	BCG Vaccine
BCG Live (/vaccines-blood-biologics/vaccines/tice-bcg)	TICE BCG
Cholera Vaccine Live Oral (/vaccines-blood-biologics/vaccines/vaxchora)	Vaxchora
COVID-19 Vaccine, mRNA (/vaccines-blood-biologics/comirnaty)	Comirnaty
COVID-19 Vaccine, mRNA (/vaccines-blood-biologics/spikevax)	SPIKEVAX

<u>Dengue Tetravalent Vaccine, Live (/vaccines-blood-biologics/dengvaxia)</u>	DENGVAXIA
<u>Diphtheria & Tetanus Toxoids Adsorbed (/vaccines-blood-biologics/vaccines/diphtheria-and-tetanus-toxoids-adsorbed)</u>	No Trade Name
<u>Diphtheria & Tetanus Toxoids & Acellular Pertussis Vaccine Adsorbed (/vaccines-blood-biologics/vaccines/infanrix)</u>	Infanrix
<u>Diphtheria & Tetanus Toxoids & Acellular Pertussis Vaccine Adsorbed (/vaccines-blood-biologics/vaccines/daptacel)</u>	DAPTACEL
<u>Diphtheria & Tetanus Toxoids & Acellular Pertussis Vaccine Adsorbed, Hepatitis B (recombinant) and Inactivated Poliovirus Vaccine Combined (/vaccines-blood-biologics/vaccines/pediarix)</u>	Pediarix
<u>Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed and Inactivated Poliovirus Vaccine (/vaccines-blood-biologics/vaccines/kinrix)</u>	KINRIX
<u>Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed and Inactivated Poliovirus Vaccine (/vaccines-blood-biologics/vaccines/quadracel)</u>	Quadracel
<u>Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed, Inactivated Poliovirus, Haemophilus b Conjugate [Meningococcal Protein Conjugate] and Hepatitis B [Recombinant] Vaccine (/vaccines-blood-biologics/vaxelis)</u>	VAXELIS

[Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed, Inactivated Poliovirus and Haemophilus b Conjugate \(Tetanus Toxoid Conjugate\) Vaccine \(/vaccines-blood-biologics/vaccines/pentacel\)](#) Pentacel

[Ebola Zaire Vaccine, Live \(/vaccines-blood-biologics/ervebo\)](#) ERVEBO

[Haemophilus b Conjugate Vaccine \(Meningococcal Protein Conjugate\) \(/vaccines-blood-biologics/vaccines/haemophilus-b-conjugate-vaccine-meningococcal-protein-conjugate\)](#) PedvaxHIB

[Haemophilus b Conjugate Vaccine \(Tetanus Toxoid Conjugate\) \(/vaccines-blood-biologics/vaccines/acthib\)](#) ActHIB

[Haemophilus b Conjugate Vaccine \(Tetanus Toxoid Conjugate\) \(/vaccines-blood-biologics/vaccines/hiberix\)](#) Hiberix

[Hepatitis A Vaccine, Inactivated \(/vaccines-blood-biologics/vaccines/havrix\)](#) Havrix

[Hepatitis A Vaccine, Inactivated \(/vaccines-blood-biologics/vaccines/vaqta\)](#) VAQTA

[Hepatitis A Inactivated and Hepatitis B \(Recombinant\) Vaccine \(/vaccines-blood-biologics/vaccines/twinrix\)](#) Twinrix

Hepatitis B Vaccine (Recombinant) (</vaccines-blood-biologics/vaccines/recombivax-hb>) Recombivax HB

Hepatitis B Vaccine (Recombinant) (</vaccines-blood-biologics/prehevbrio>) PREHEVBRIO

Hepatitis B Vaccine (Recombinant) (</vaccines-blood-biologics/vaccines/engerix-b>) Engerix-B

Hepatitis B Vaccine (Recombinant), Adjuvanted (</vaccines-blood-biologics/vaccines/heplisav-b>) HEPLISAV-B

Human Papillomavirus Quadrivalent (Types 6, 11, 16, 18) Vaccine, Recombinant (</vaccines-blood-biologics/vaccines/gardasil>) Gardasil

Human Papillomavirus 9-valent Vaccine, Recombinant (</vaccines-blood-biologics/vaccines/gardasil-9>) Gardasil 9

Human Papillomavirus Bivalent (Types 16, 18) Vaccine, Recombinant (</vaccines-blood-biologics/vaccines/cervarix>) Cervarix

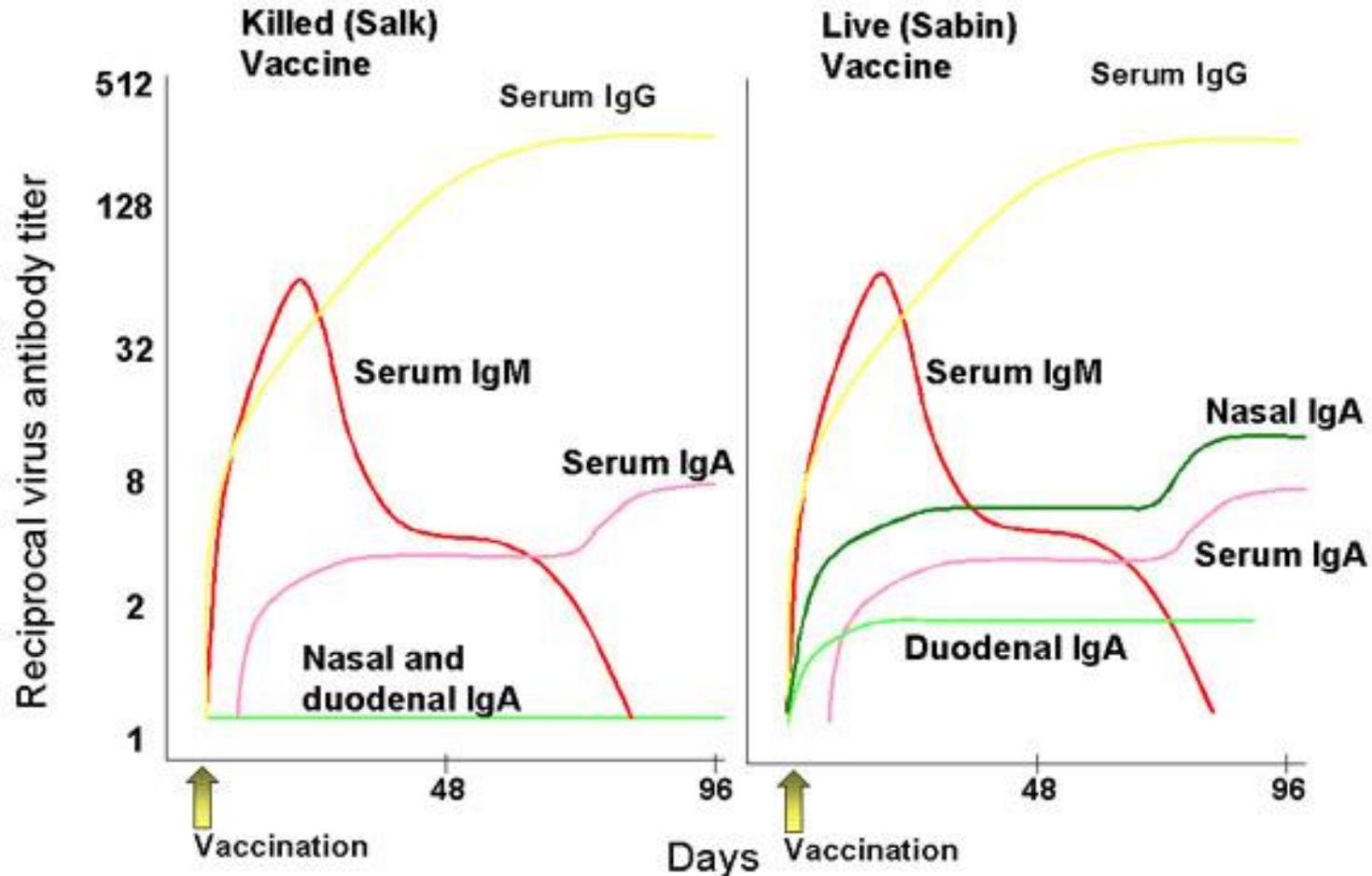
Influenza A (H1N1) 2009 Monovalent Vaccine (</vaccines-blood-biologics/vaccines/influenza-h1n1-2009-monovalent-vaccine-csl-limited>) No Trade Name

Influenza A (H1N1) 2009 Monovalent Vaccine (</vaccines-blood-biologics/vaccines/influenza-h1n1-2009-monovalent-vaccine-medimmune-llc>) No Trade Name

Influenza A (H1N1) 2009 Monovalent Vaccine (/vaccines-blood-biologics/vaccines/influenza-h1n1-2009-monovalent-vaccine-id-biomedical-corporation-quebec)	No Trade Name
Influenza A (H1N1) 2009 Monovalent Vaccine (/vaccines-blood-biologics/vaccines/influenza-h1n1-2009-monovalent-vaccine-novartis-vaccines-and-diagnostics-limited)	No Trade Name
Influenza A (H1N1) 2009 Monovalent Vaccine (/vaccines-blood-biologics/vaccines/influenza-h1n1-2009-monovalent-vaccine-novartis-vaccines-and-diagnostics-limited)	No Trade Name
Influenza Virus Vaccine, H5N1 (/vaccines-blood-biologics/vaccines/influenza-virus-vaccine-h5n1-national-stockpile) (for National Stockpile)	No Trade Name
Influenza A (H5N1) Virus Monovalent Vaccine, Adjuvanted (/vaccines-blood-biologics/vaccines/influenza-h5n1-virus-monovalent-vaccine-adjuvanted)	No Trade Name
Influenza A (H5N1) Monovalent Vaccine, Adjuvanted (/vaccines-blood-biologics/audenz)	AUDENZ
Influenza Vaccine, Adjuvanted (/vaccines-blood-biologics/flud-quadrivalent)	Flud Quadrivalent
Influenza Vaccine, Adjuvanted (/vaccines-blood-biologics/vaccines/flud)	Flud
Influenza Vaccine (/vaccines-blood-biologics/vaccines/afluria-quadrivalent-afluria-quadrivalent-southern-hemisphere)	Afluria Quadrivalent, Afluria Quadrivalent Southern Hemisphere

TIPOS DE VACINAS

Vantagens e desvantagens



TIPOS DE VACINAS

Vantagens e desvantagens

Vacinas de subunidades

IMMUNE RESPONSE



- ◆ Must determine which combination of antigenic properties will produce an effective immune response with the correct pathway.
- ◆ A response may be elicited, but with no guarantee that memory will form for future responses.

Less strong immune response compared to LAVs

SAFETY AND STABILITY



- ◆ Have no live components, **no risk** of inducing the disease.
- ◆ Safer and more stable than LAVs.

Excellent stability profile

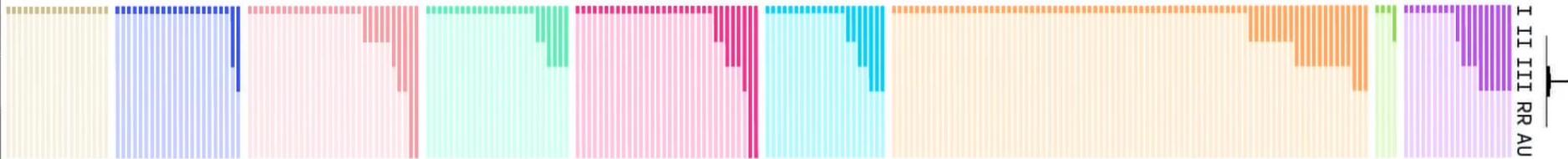
VACINAS vs. MEDICAMENTOS

	Vacina	Medicamento
Ação	Preventiva	Terapêutica
Benefício	Individual e coletivo O efeito não é perceptível (não contrai a doença)	Individual O efeito é visível (normalmente ocorre melhoria)
Indivíduos	Saudáveis	Doentes

CARACTERÍSTICAS DE UMA VACINA EFICAZ

Segura	Não deve causar doença
Poucos efeitos colaterais	
Deve induzir uma resposta imune protetora	Proteger aos vacinados Gerar memória
Aspectos práticos	Custo!!! Biologicamente estável!!! De fácil administração.

SARS-CoV-2 virus vaccines



251 vaccines in development, 61 in clinical testing, 11 in use

Leading Vaccines

■	BioNTech/Pfizer	Authorized
■	Moderna	Authorized
■	Oxford/AstraZeneca	Authorized
■	Janssen Pharma	Authorized
■	Sinovac/Instituto Butantan	Phase III
■	Wuhan Inst./Sinopharm	Phase III
■	Beijing Inst./Sinopharm	Phase III
■	Gamaleya Research Inst.	Phase III
■	CanSino Biologics	Phase III
■	Novavax	Phase III

VACCINE CATEGORIES

- Inactivated Virus
- Live Attenuated Virus
- Protein Subunit
- DNA-Based
- RNA-Based
- Replicating Viral Vector
- Non-Replicating Viral Vector
- Virus-Like Particle
- Other Vaccines

PHASES

- I Phase One
- II Phase Two
- III Phase Three
- RR Regulatory Review
- AU Authorized

Data as of 3/24/21

Exemplo do Papilomavírus Humano (HPV)

Impacto do HPV nas populações

HPV

- ~100% Carcinomas da cérvix uterina.
 - 80-90% Carcinomas de ânus.
 - 50-70% Carcinomas de vagina.
 - 20-30% Carcinomas de vulva.
 - 20-30% Carcinomas de pênis.
 - 10-40% Carcinomas de Cabeça e Pescoço.
 - 100% Verrugas genitais.
 - 100% Papilomatose respiratória recorrente.
- ~640.000 casos/ano.
 - 4,5% de todos os cânceres (8,6% M vs. 0,9% H).
 - 29,5% dos cânceres de origem infecciosa.

HPV e patologias em mulheres e homens

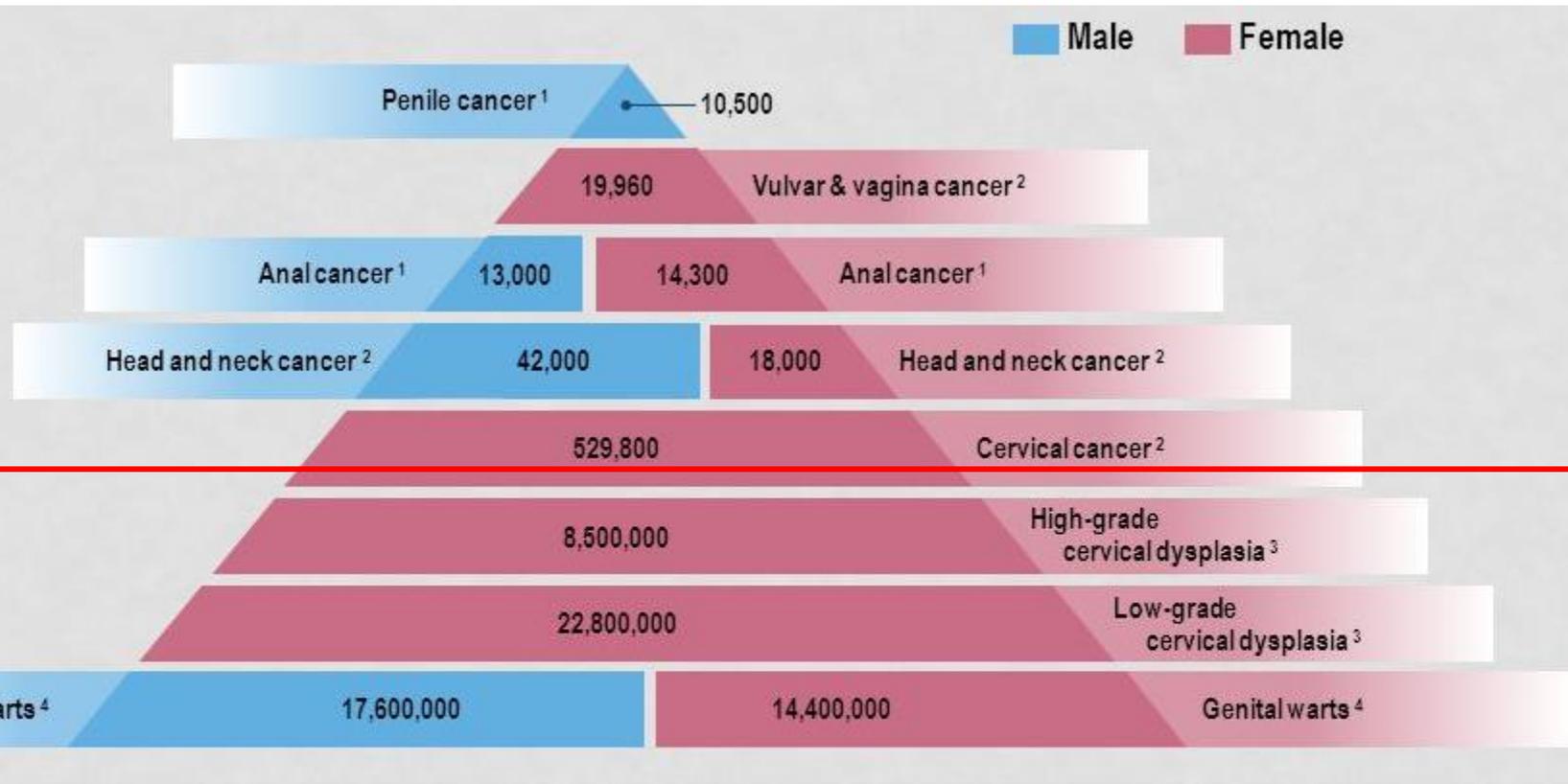
- Estimativa global (2008) de novos casos atribuíveis ao HPV por sítio anatômico.

Anatomic site	Number of new cases in 2008	Number of new cases attributed to HPV	Attributable fraction
Uterine cervix	530.000	530.000	100 %
Vulva	27.000	12.000	43 %
Anal canal	27.000	24.000	88 %
Penile	22.000	11.000	50 %
Vagina	13.000	9.000	70 %
Oropharynx*	85.000	22.000	15-70 %
TOTAL	700.000	610.000	86 %

*includes the tonsil and base of tongue

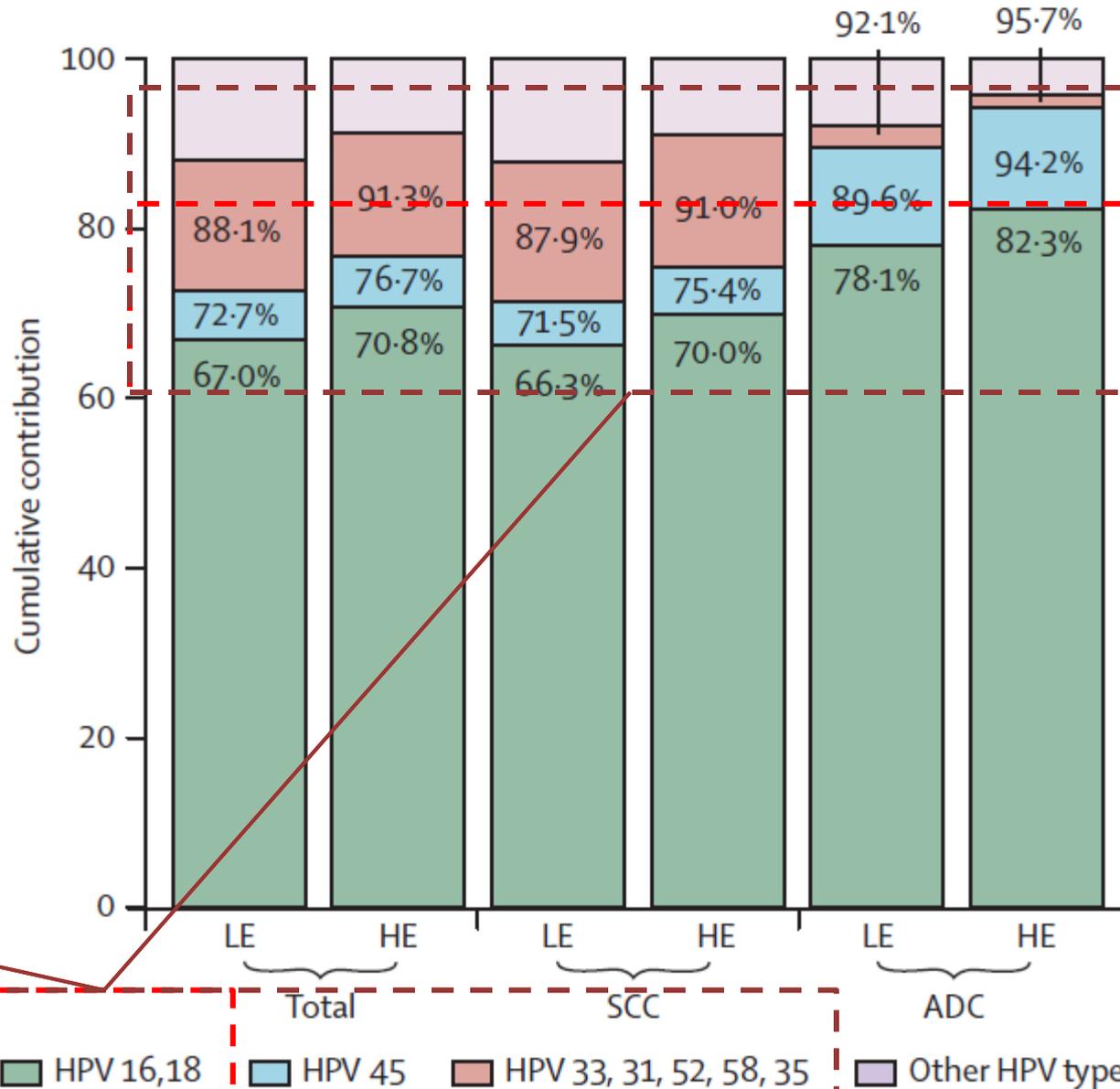
HPV e patologias em mulheres e homens

Estimativa global de novos casos por ano

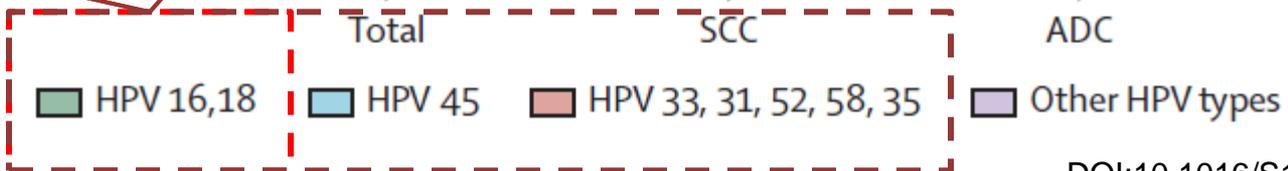


1. Parkin DM et al. Vaccine. 2006;24(Suppl 3):S3/11–S3/25. 2. WHO/ICO Information Centre on HPV and Cervical Cancer (HPV Information Centre). Human Papillomavirus and Related Cancers in World. Summary Report 2010. 3. World Health Organization. Geneva, Switzerland: World Health Organization; 1999:1–22. 4. World Health Organization (WHO). Executive summary: the state of world health. 1995. http://www.who.int/whr/1995/media_centre/executive_summary1/en/index3.html#. Accessed June 7, 2012.

Tipos de HPV em cânceres do colo do útero



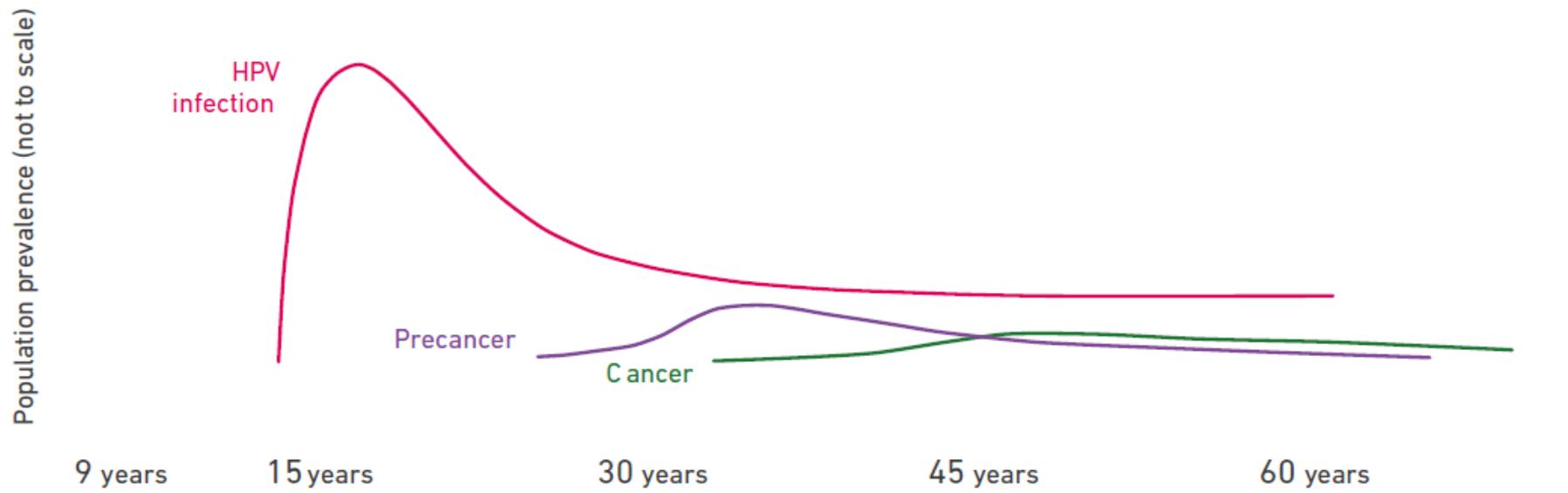
~90% dos CCU



Impacto do HPV nas populações

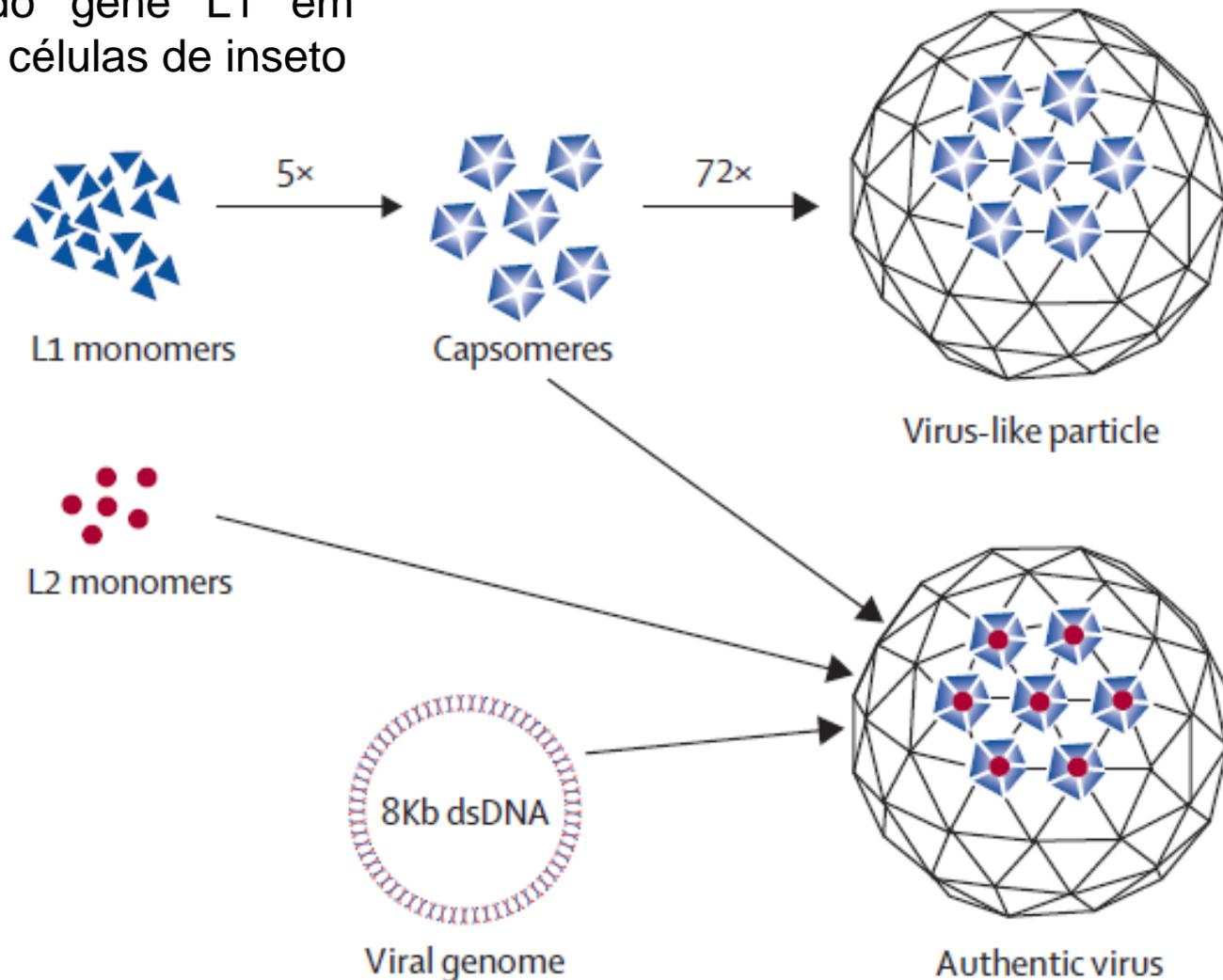
- HPVs 16 e 18 são mais oncogênicos e persistem mais do que outros tipos de HPV de alto risco.
- A maioria (>85%) dos casos de câncer de colo uterino acontece em regiões menos desenvolvidas.
- HPVs de alto risco causam uma proporção significativa de cânceres, tanto em mulheres quanto em homens.

Como enfrentar o câncer de colo uterino?

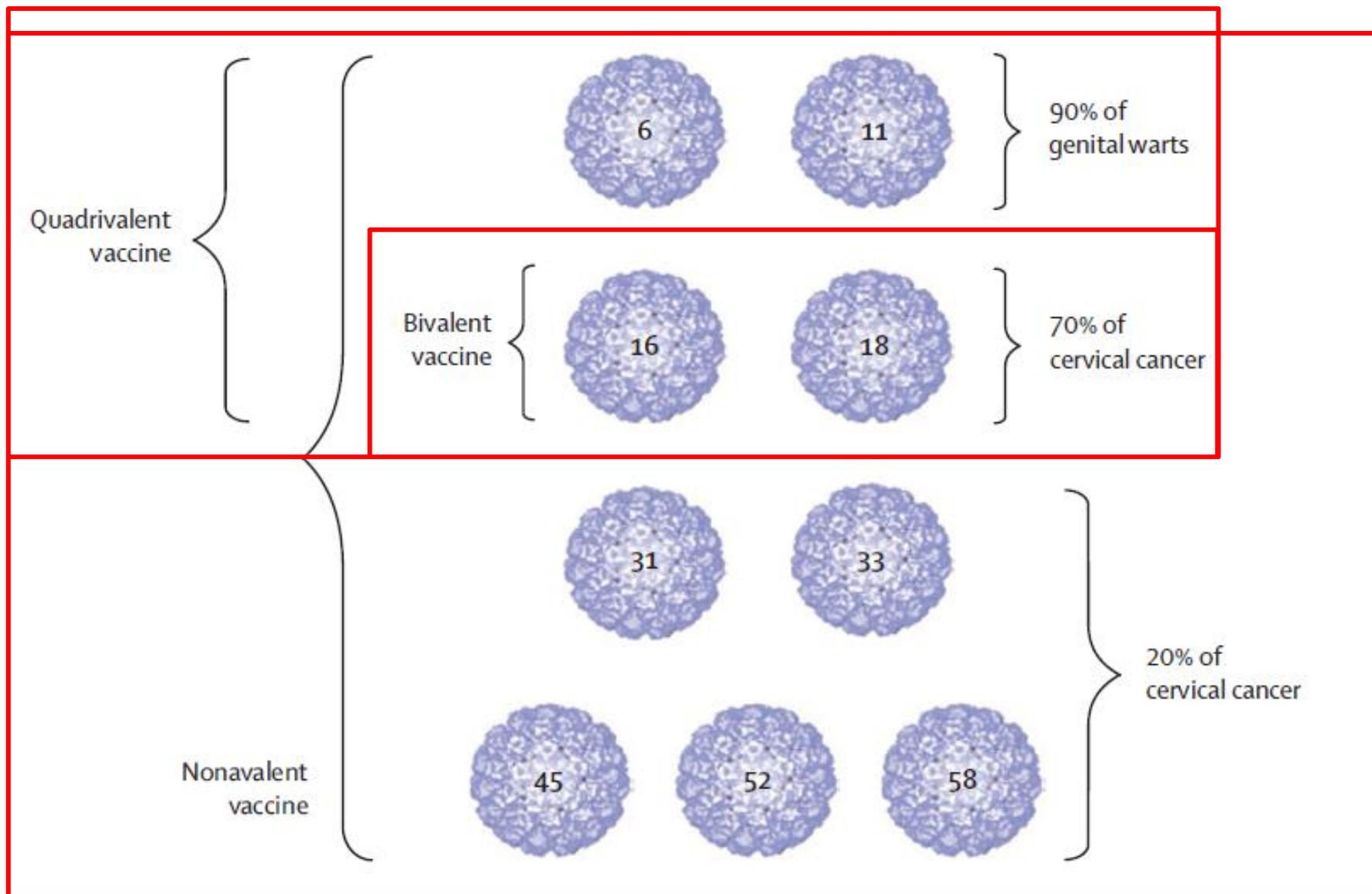


Estratégia para desenvolvimento de vacinas profiláticas: VLPs

- Expressão do gene L1 em leveduras ou células de inseto



Vacinas profiláticas: potencial de proteção



Vacinas profiláticas Licenciadas: Características e potencial de proteção

	2vHPV vaccine	4vHPV vaccine	9vHPV vaccine
Company	GlaxoSmithKline	Merck	Merck
Brand name	Cervarix	Gardasil, Silgard	Gardasil 9
L1 virus-like particle types	HPV- 16/18	HPV-6/11/ 16/18	HPV-6/11/ 16/18/31/33/45/52/58
Cross-protection	HPV-31/33/45	HPV-31	Unknown
Adjuvant	ASO4 (0.5 mg aluminium hydroxide and 50 µg 3-O-desacyl-4"-monophosphoryl lipid A [MPL])	0.225 mg aluminium hydroxyphosphate sulfate	0.5 mg aluminium hydroxyphosphate sulphate

A vacinação interrompe a transmissão do HPV

- Australia (2007): Programa Nacional de Vacinação (4vHPV) de meninas e mulheres (12-26 anos)

Presentations with warts in men and women <21

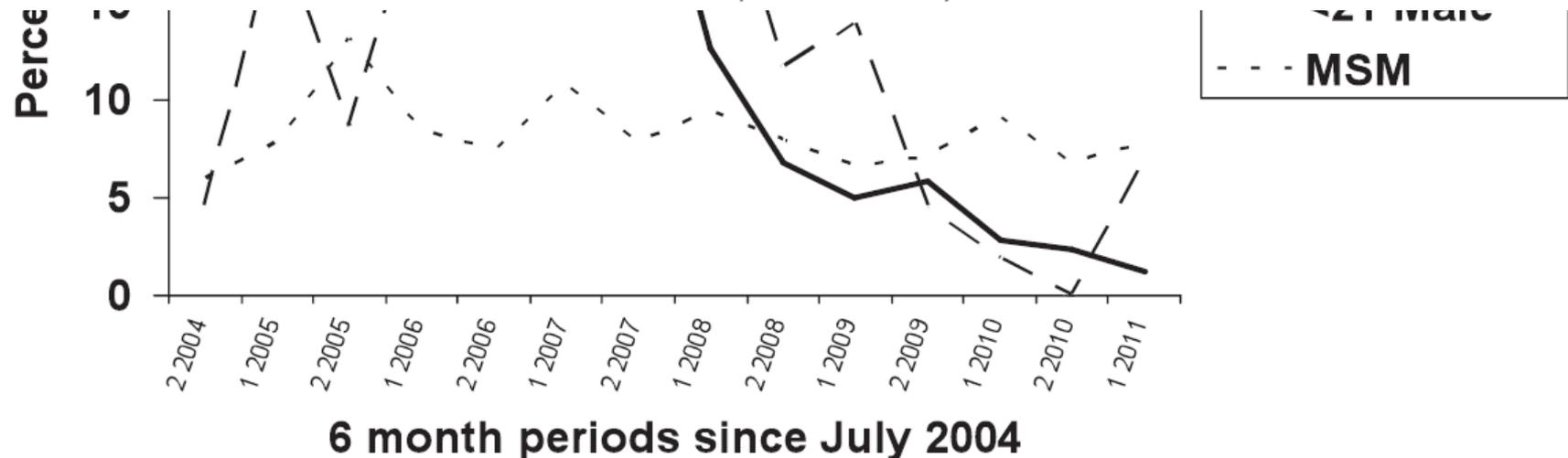
Epidemiology



ORIGINAL ARTICLE

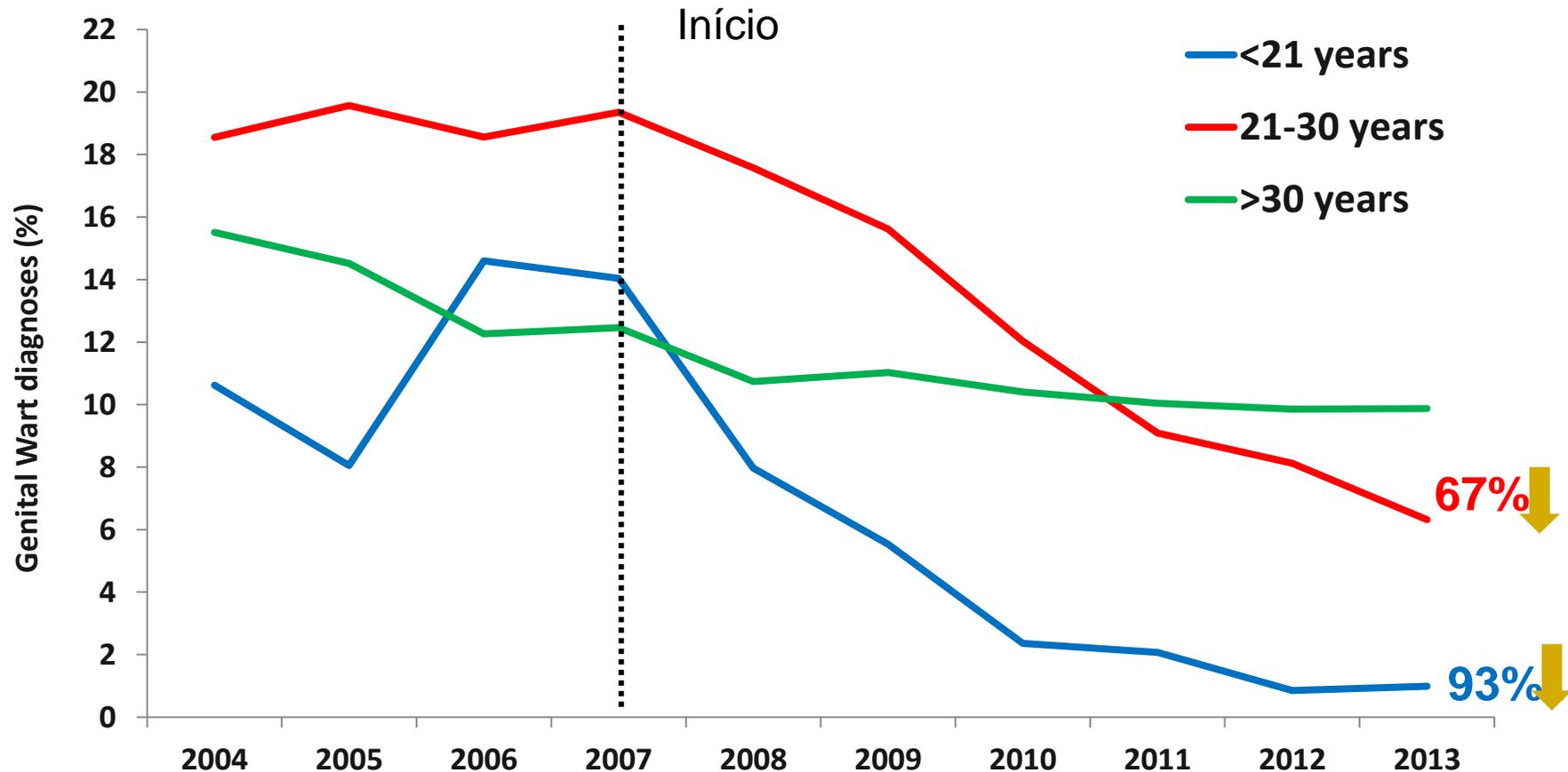
The near disappearance of genital warts in young women 4 years after commencing a national human papillomavirus (HPV) vaccination programme

Tim R H Read,¹ Jane S Hocking,² Marcus Y Chen,¹ Basil Donovan,³
Catriona S Bradshaw,⁴ Christopher K Fairley¹



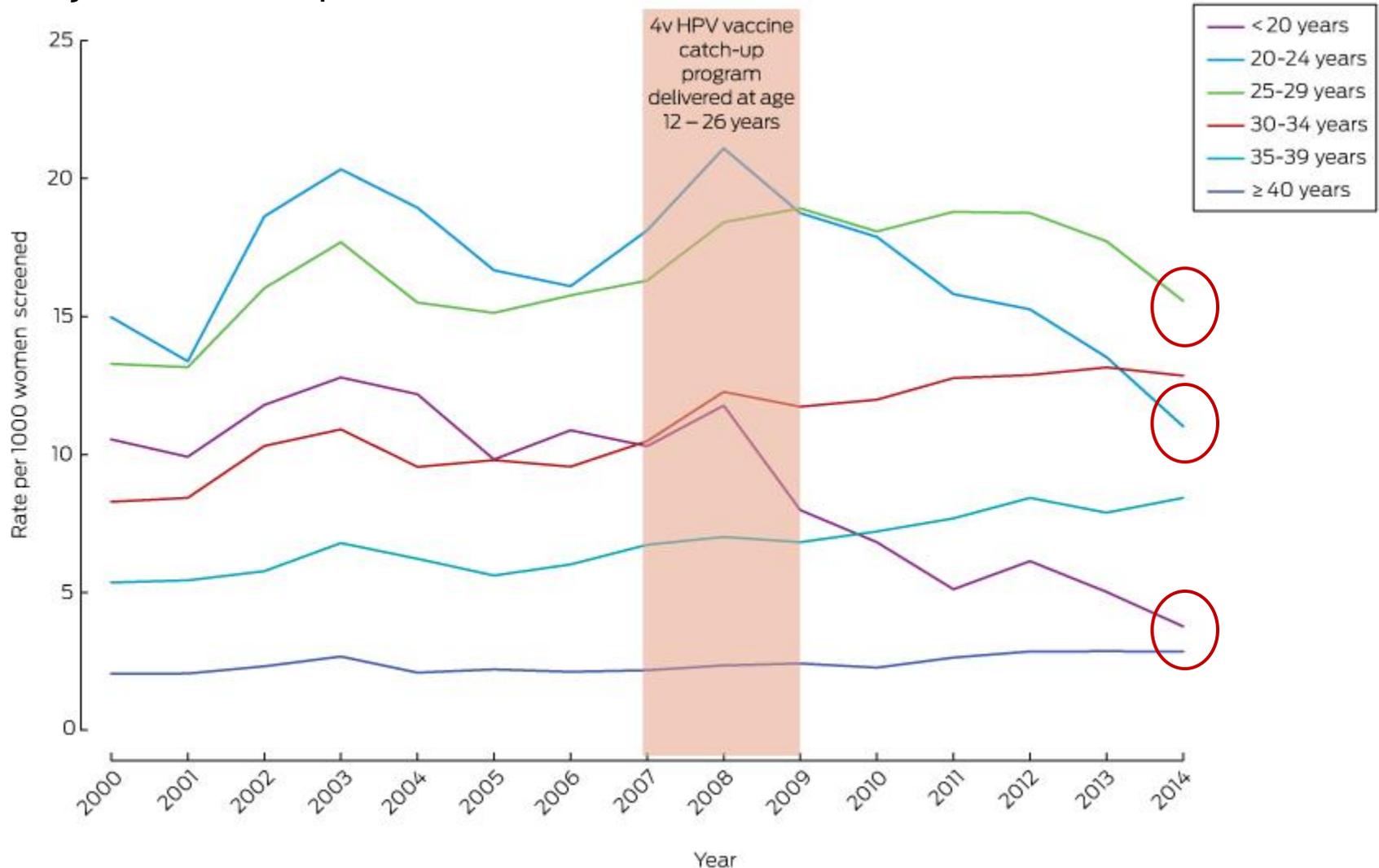
A vacinação interrompe a transmissão do HPV

- Austrália (2007): Programa Nacional de Vacinação (4vHPV) de meninas e mulheres (12-26 anos).
- Redução de verrugas genitais em homens heterossexuais australianos.



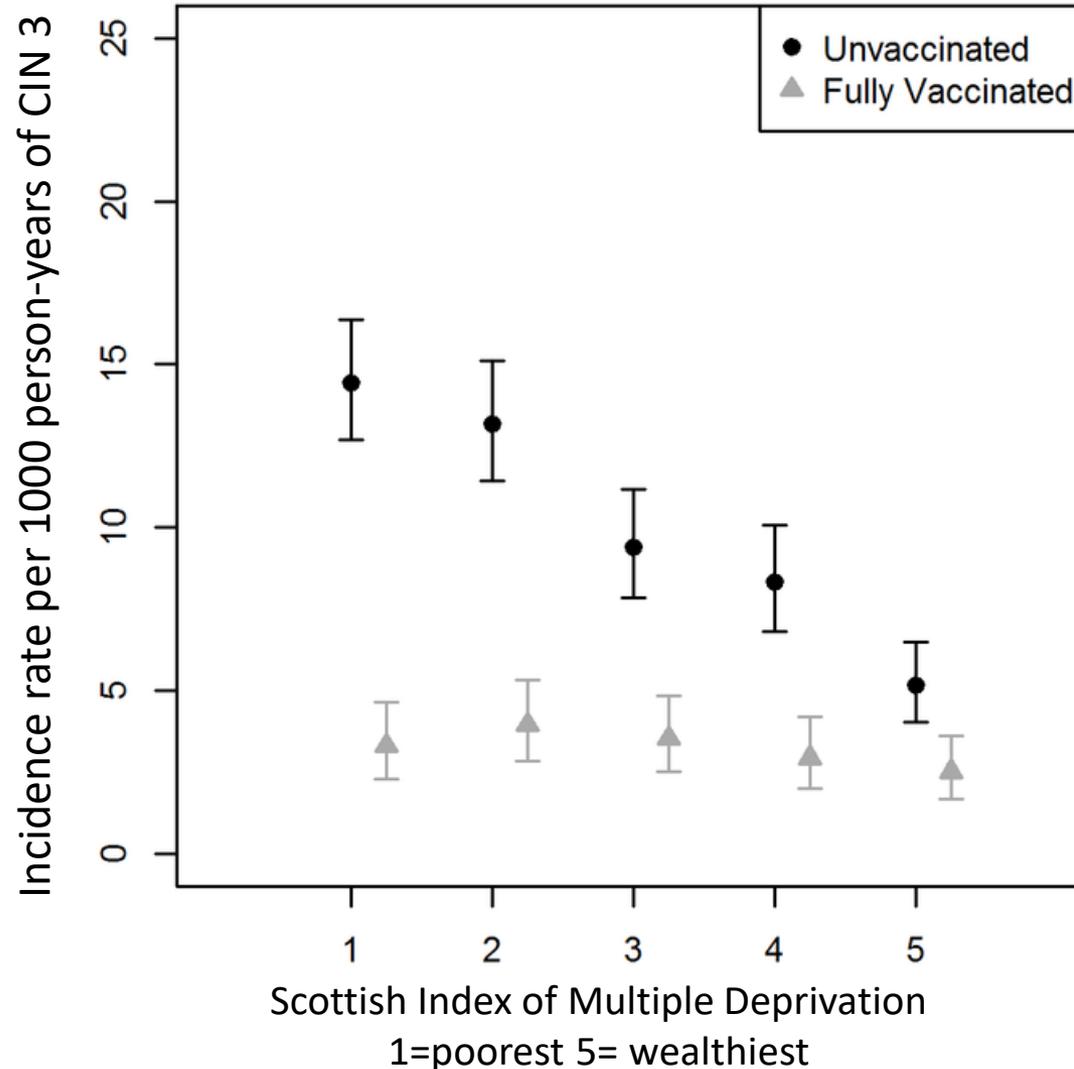
A vacinação interrompe a transmissão do HPV

- Australia (2007): Programa Nacional de Vacinação (4vHPV) de meninas e mulheres (12-26 anos).
- Redução de lesões precursoras do câncer cervical.



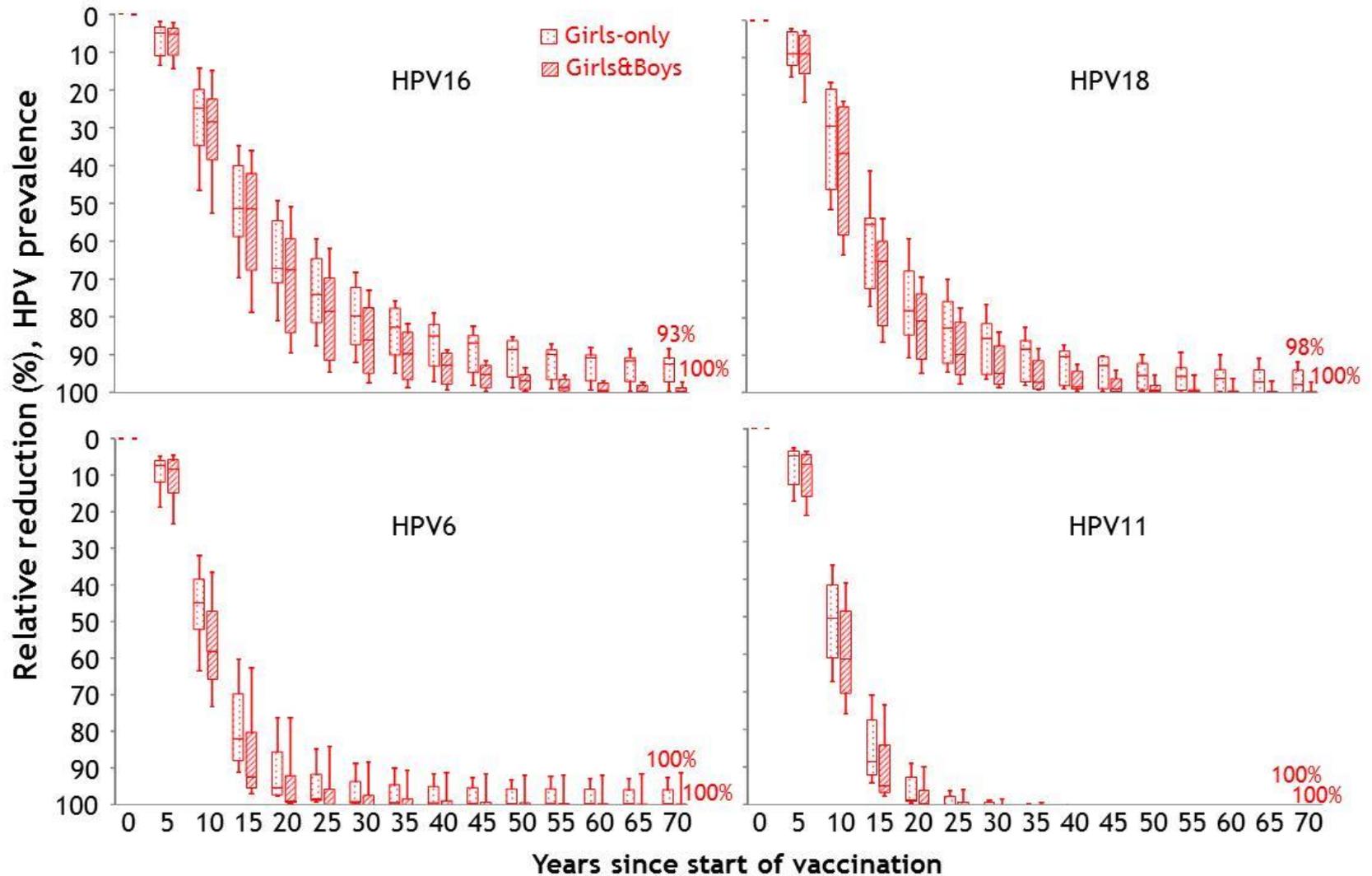
A vacinação interrompe a transmissão do HPV

- Escócia: Vacinação (2vHPV) reduz a incidência de lesões precursoras do câncer cervical. Diminuição da desigualdade.



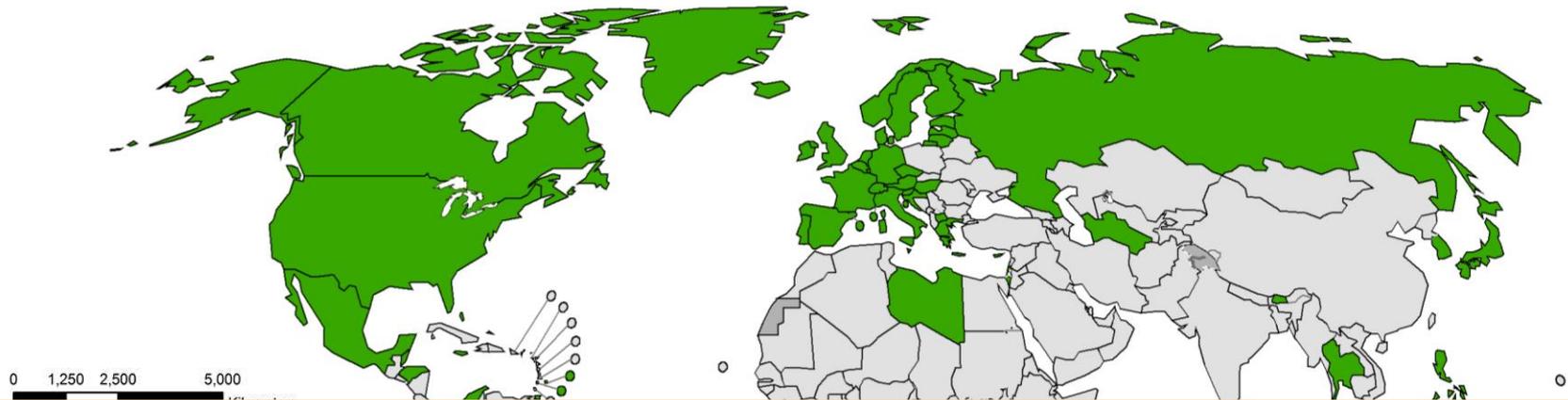
A vacinação interrompe a transmissão do HPV

- É possível a eliminação de HPV16, HPV18, HPV6 e HPV11 se 80% de meninas e meninos forem vacinados.

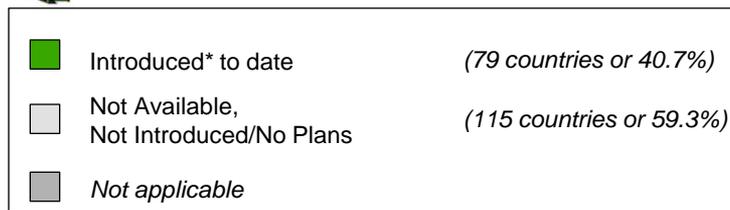


Vacinas profiláticas contra HPV: realidade Mundial

79 Países adotaram vacinas contra HPV em seus programas nacionais de imunização (Janeiro de 2018)



- Apenas 5% da população mundial recebeu a vacina. Isto aconteceu principalmente em países desenvolvidos.



* Includes partial introduction



Vacinas profiláticas contra HPV: situação no Brasil.

Vacinação contra o HPV no Brasil

População elegível para receber gratuitamente a vacinação contra HPV^{1,2}

População	Faixa etária	Número de doses	Intervalo entre doses
Meninos	11-14 anos (2019)*	2 doses	0 e 6 meses
Meninas	9-14 anos	2 doses	0 e 6 meses
Vivendo com HIV/AIDS	Homens e Mulheres 9-26 anos	3 doses	0, 2, 6 meses
Transplantados de órgãos sólidos	Homens e Mulheres 9-26 anos	3 doses	0, 2, 6 meses
Transplantados de medula óssea	Homens e Mulheres 9-26 anos	3 doses	0, 2, 6 meses
Paciente oncológicos	Homens e Mulheres 9-26 anos	3 doses	0, 2, 6 meses

* Até 2020, a faixa etária masculina será ampliada gradativamente para meninos a partir de nove anos de idade

1. Ministério da Saúde amplia vacinação em todas as faixas etárias . Available at

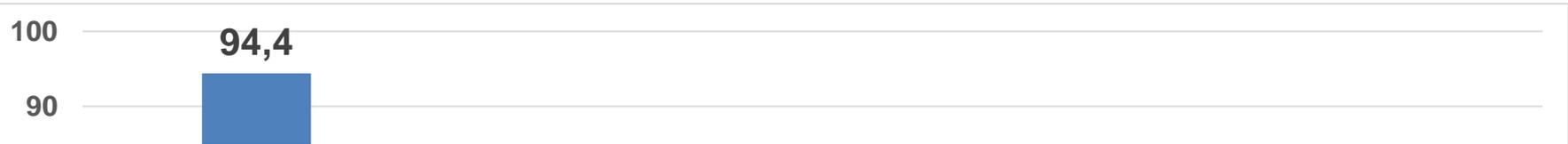
<http://portalarquivos.saude.gov.br/images/pdf/2017/marco/03/Novo-calendario-vacinal-de-2017.pdf> [Accessed 14 March 2017].

2. MS. Available at <http://www.brasil.gov.br/saude/2017/01/tire-duvidas-sobre-a-vacinacao-contr-o-hpv-para-meninos> [Accessed 14 March 2017].

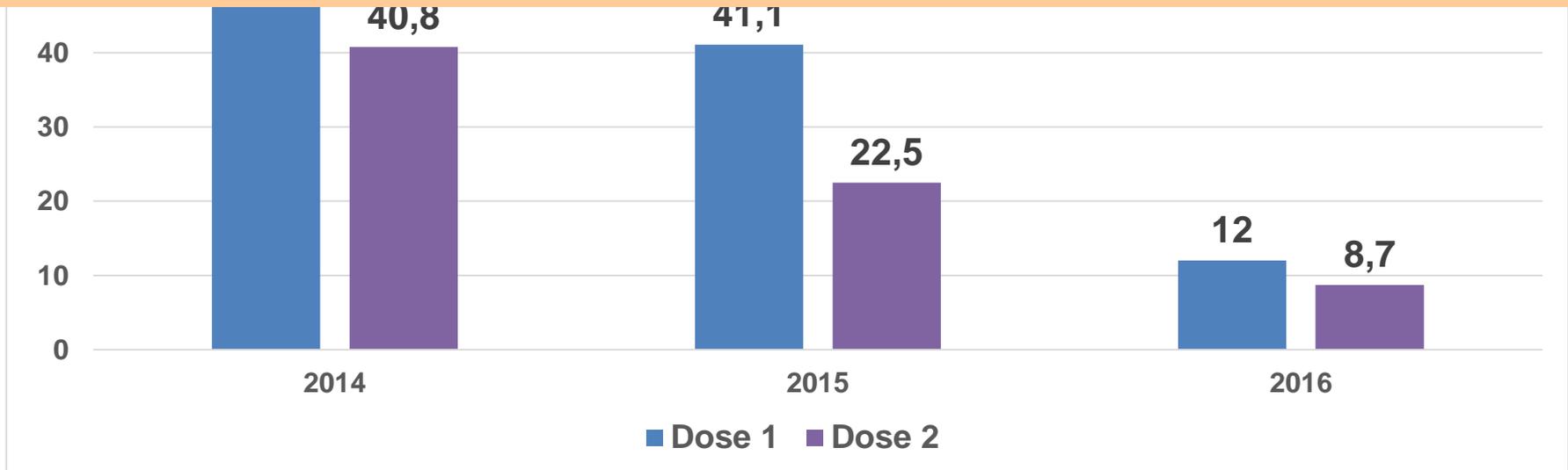


Cobertura da vacina de HPV no Brasil

(SI-PNI, Ministério da Saúde 2014-2016)



- Em agosto de 2018, apenas 43% das meninas e 17% dos meninos tinham recebido as duas doses da vacina



Resumindo, as vacinas profiláticas contra HPV:

- São eficazes para prevenir a infecção.
- São eficazes para prevenir lesões precursoras.
- São seguras.
- Mas...chegam a quem mais precisa delas?
- Duração da proteção?
- Não substituem programas de rastreamento.

Recommended Childhood and Adolescent Immunization Schedule UNITED STATES • 2006

Vaccine ▼	Age ►	Birth	1 month	2 months	4 months	6 months	12 months	15 months	18 months	24 months	4-6 years	11-12 years	13-14 years	15 years	16-18 years
Hepatitis B ¹	HepB		HepB	HepB	HepB ¹	HepB	HepB	HepB	HepB	HepB	HepB	HepB Series	HepB Series	HepB Series	HepB Series
Diphtheria, Tetanus, Pertussis ²				DTaP	DTaP	DTaP		DTaP			DTaP	Tdap	Tdap	Tdap	Tdap
<i>Haemophilus influenzae</i> type b ³				Hib	Hib	Hib ³	Hib								
Inactivated Poliovirus				IPV	IPV	IPV	IPV	IPV	IPV	IPV	IPV				
Measles, Mumps, Rubella ⁴							MMR				MMR	MMR	MMR	MMR	MMR
Varicella ⁵							Varicella					Varicella	Varicella	Varicella	Varicella
Meningococcal ⁶												MCV4	MCV4	MCV4	MCV4
Pneumococcal ⁷				PCV	PCV	PCV	PCV				PCV	PPV	PPV	PPV	PPV
Influenza ⁸							Influenza (Yearly)					Influenza (Yearly)	Influenza (Yearly)	Influenza (Yearly)	Influenza (Yearly)
Hepatitis A ¹												HepA Series	HepA Series	HepA Series	HepA Series

Quadrivalent HPV Vaccine

This schedule indicates the recommended ages for routine administration of currently licensed childhood vaccines, as of December 1, 2005, for children through age 18 years. Any dose not administered at the recommended age should be administered at any subsequent visit when indicated and feasible. ■ Indicates age groups that warrant special effort to administer those vaccines not previously administered. Additional vaccines may be licensed and recommended during the year. Licensed combination vaccines may be used whenever

any components of the combination are indicated and other components of the vaccine are not contraindicated and if approved by the Food and Drug Administration for that dose of the series. Providers should consult the respective ACIP statement for detailed recommendations. Clinically significant adverse events that follow immunization should be reported to the Vaccine Adverse Event Reporting System (VAERS). Guidance about how to obtain and complete a VAERS form is available at www.vaers.hhs.gov or by telephone, 800-822-7967.

■ Range of recommended ages ■ Catch-up immunization ■ 11-12 year old assessment

Profilaxia contra vírus causadores de Tumor

Vacinas profiláticas disponíveis para HBV e HPV

- Seguras
- Bem toleradas
- Eficazes
 - >45 anos de seguimento (HBV)
 - ~15 anos de seguimento (HPV)
- **Caras** (HPV)

OBRIQADO!!!