VACCINAZIONI PER LE EPATITI VIRALI

UN RUOLO SCONTATO?

MARCO POZZI

SOD MALATTIE INFETTIVE E TROPICALI

AOU CAREGGI

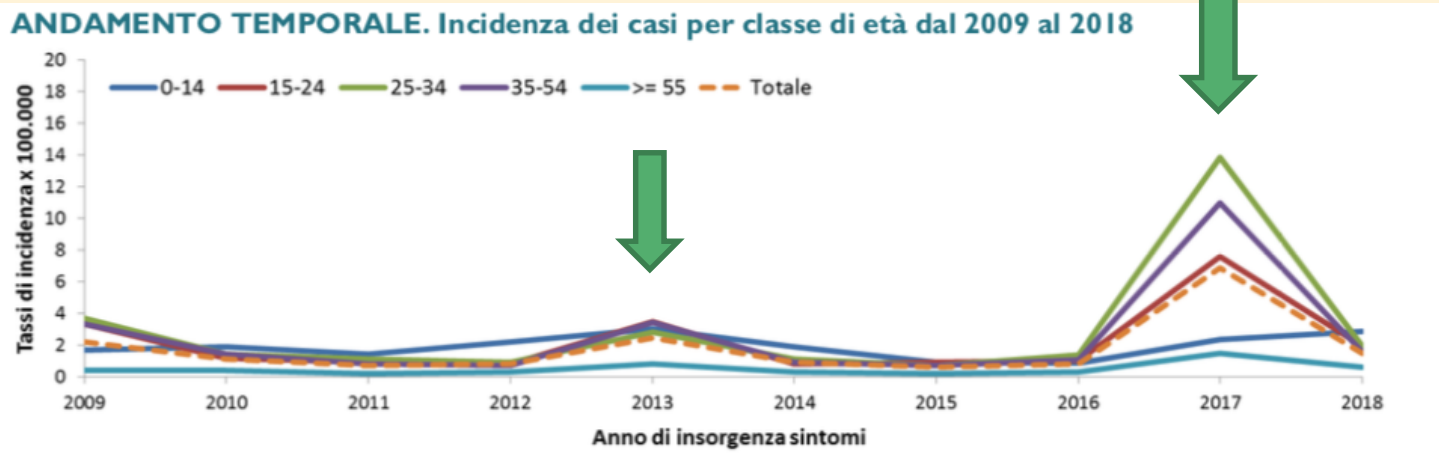
HEPATITIS A

KEY FACTS

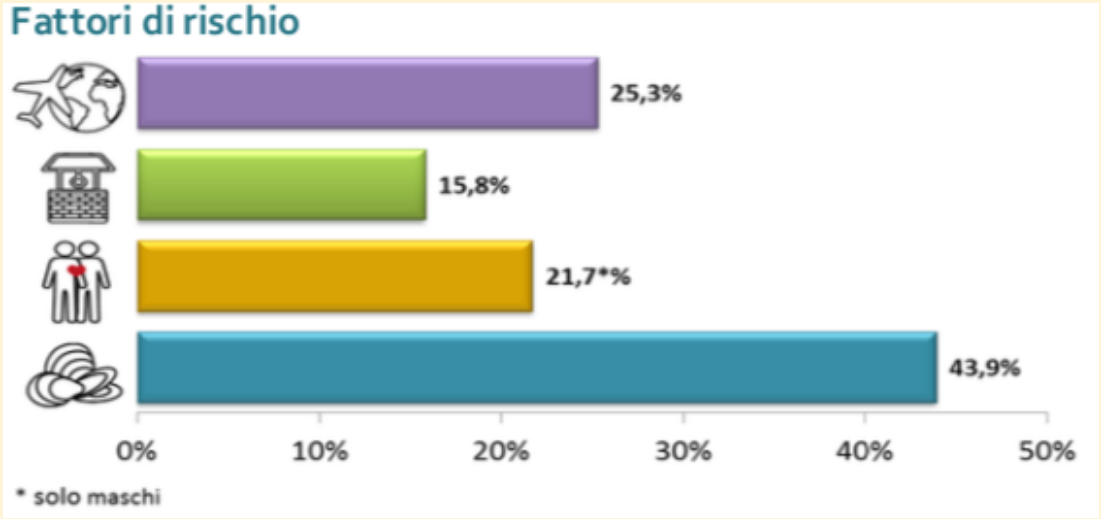
- Hepatitis A is a viral liver disease that can cause mild to severe illness.
- The hepatitis A virus (HAV) is transmitted through ingestion of contaminated food and water or through direct contact with an infectious person.
- Almost everyone recovers fully from hepatitis A with a lifelong immunity. However, a very small proportion of people infected with hepatitis A could die from fulminant hepatitis.
  WHO estimates that hepatitis A caused approximately 7 134 deaths in 2016 (accounting for 0.5% of the mortality due to viral hepatitis).
- The risk of hepatitis A infection is associated with a lack of safe water, and poor sanitation and hygiene (such as dirty hands).
- In countries where the risk of infection from food or water is low, there are outbreaks among men who have sex with men (MSM) and persons who inject drugs (PWIDs).
- A safe and effective vaccine is available to prevent hepatitis A.
- Safe water supply, food safety, improved sanitation, hand washing and the hepatitis A vaccine are the most effective ways to combat the disease. Persons at high risk, such as travelers to countries with high levels of infection, MSM and PWIDs can get vaccinated.

https://www.who.int/news-room/fact-sheets/detail/hepatitis-a

EPIDEMIOLOGY IN ITALY



Italy: low-endemic country
2017: 6.9x100000
2018: 1.5x100000



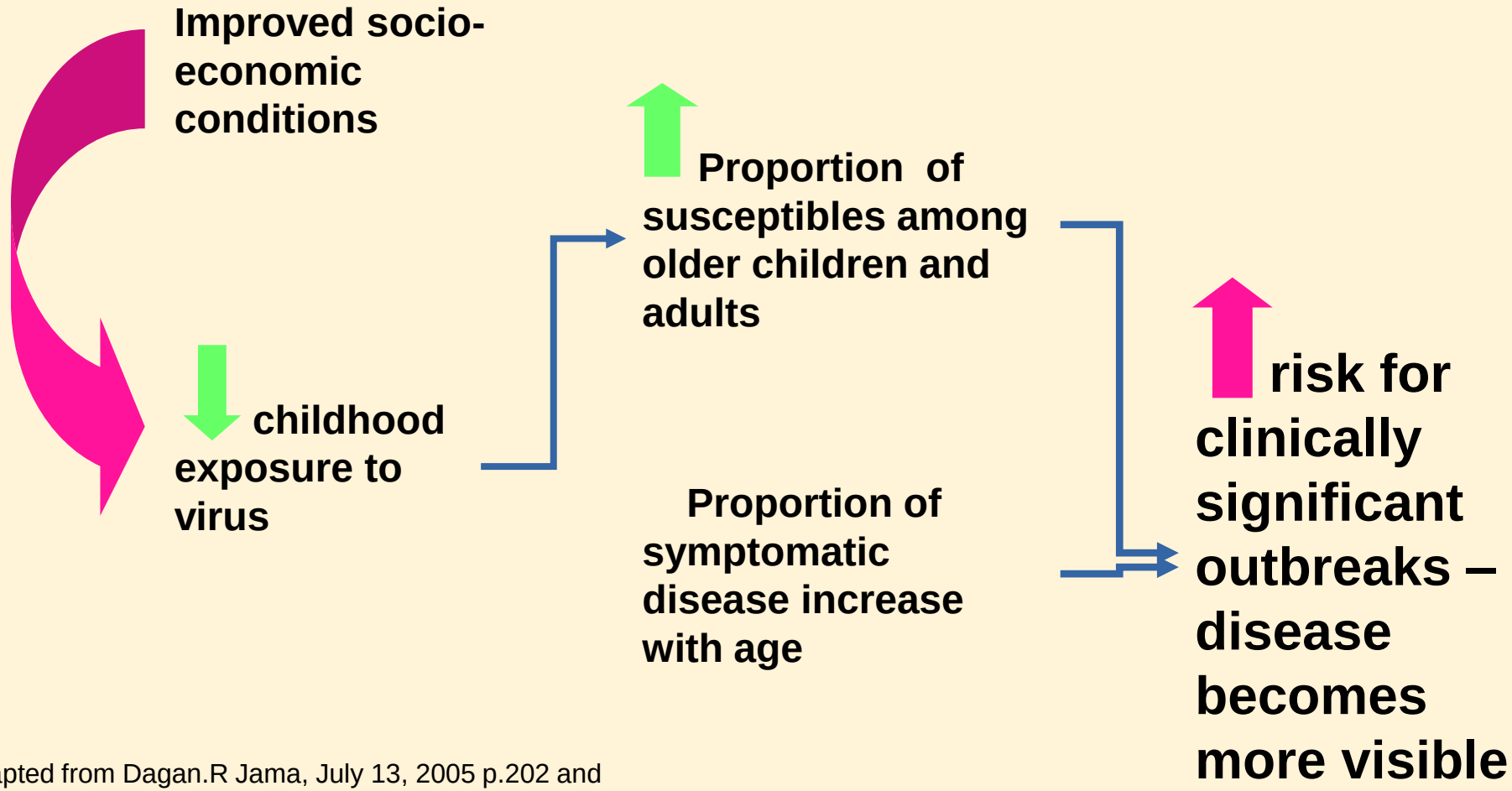
CHANGING EPIDEMIOLOGY IN EUROPE

→ PREVENTIVE MEASURES

- **Epidemiology driven by:**
  - Import through travellers
  - Import through returning children from high or intermediate countries
  - Outbreak stories: IDU, MSM, foodborne, …

- **Collective measures**
  - improve sanitation
  - control urban spread
  - prevent slum development
  - Universal HAV vaccination programs
- **Individual measures**
  - use good personal hygiene
  - handle food carefully
  - HAV vaccine

THE HEPATITIS A PARADOX



Adapted from Dagan.R Jama, July 13, 2005 p.202 and WHO/CDS/CSR/EDC/2000.7 p.20-217

HEPATITIS A VACCINES

- Schedule: 0-6 or 0-12 or 0-18m
- Inactivated or live attenuated
- Excellent immunogenicity
    - rapid seroconversion, flexible schedule
- Excellent safety record
- Can be offered starting at age 1y
- Efficiency in outbreak control and post-exposure prophylaxis
- Long-lasting protection: > 20 years f.u.
- No booster recommended

"To date, no data lend support to the need for booster doses of HAV vaccine in immunocompetent individuals who have received a full vaccination course"

Expert Consensus Statement on Hepatitis A Booster Policy

Epatite A

Vaccino				Indicazioni
Efficacia	Efficacia dopo	Durata	Limite di età	
94-100%	2° dose	[illegible]	/	Raccomandata ai viaggiatori in area endemica e ai gruppi a rischio.

Modalità di somministrazione: adulti e bambini sopra 10 anni di età: 1° dose alla data stabilita, 2° dose 6- 12 mesi dopo la prima

Principali precauzioni e controindicazioni	Effetti collaterali più comuni
Ipersensibilità a componenti del vaccino Dose ridotta nei bambini	Reazione locale Occasionalmente astenia, cefalea, febbre

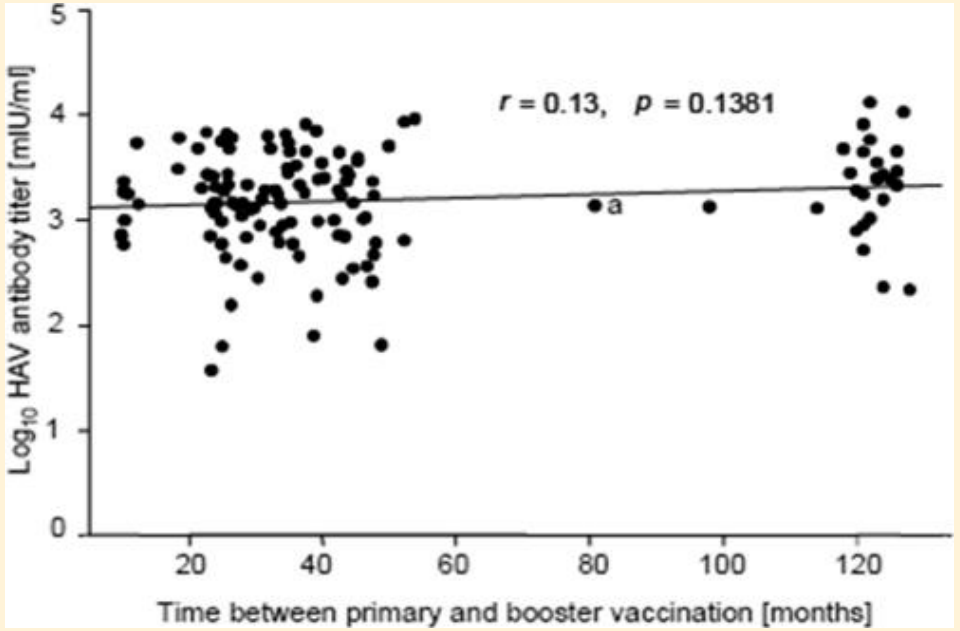
Epatite A + Epatite B

Vaccino				Indicazioni
Efficacia	Efficacia dopo	Durata	Limite	Indicata in speciali circostanze (esposizione professionale di medici, infermieri, ecc..), viaggiatori
> 94-100%	3° dose	> 10 anni	/	

Modalità di somministrazione: un ciclo vaccinale consiste in tre dosi: 1° dose alla data stabilita, 2° dose dopo un mese, 3° dose sei mesi dopo la prima; possibilità di ciclo rapido: 1° dose alla data stabilita, 2° dose dopo 7 giorni, 3° dose dopo 21 giorni e 4° dose a 12 mesi.

AFTER SINGLE DOSE: HOW LONG PROTECTED? WHAT IF ONE SINGLE DOSE IS FORGOTTEN?

- Increasing data, and good indications
  - Travel medicine: delayed second dose (up to 10.7 years)
    - Excellent anamnestic response to second dose
      - Not affected by the delay
      - Even after losing detectable antibodies
  - Single dose of live vaccine
    - Long-term persistence of antibodies and long-term effectiveness



ANTI-HAV AFTER BOOSTER DOSE OF INACTIVATED HEPA VACCINE, AS A FUNCTION OF TIME BETWEEN FIRST AND BOOSTER DOSE (> 12 DATA SOURCES)

Immune memory is probably induced by single dose vaccination.

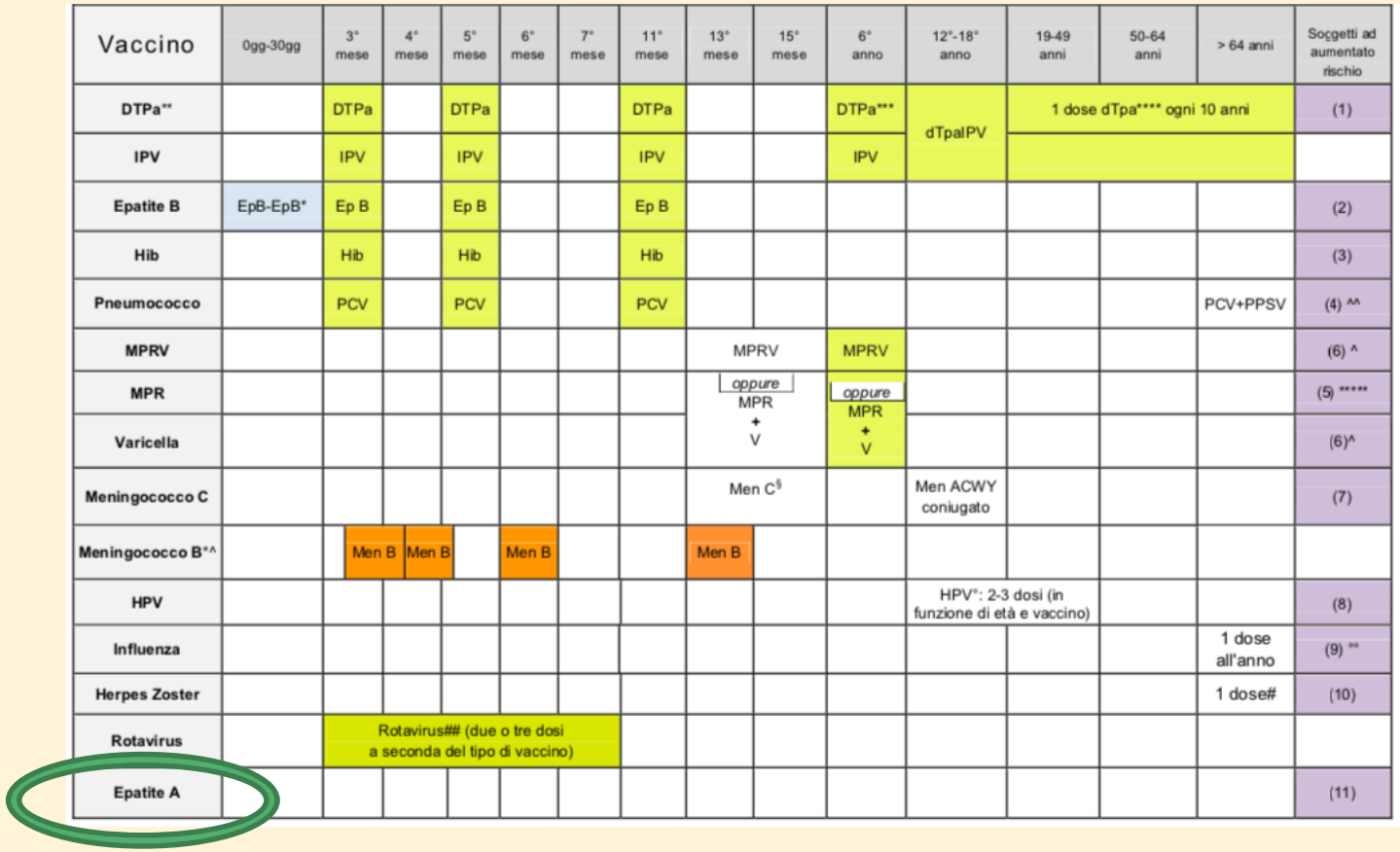
Beck 2003; Iwarson 2002; Iwarson 2004; Landry 2000; Orr 2006; Wang 2007; Williams 2003; Zhuang 2005, Hatz 2011, Herzog 2010, Sabanin 2010

Hatz et al. 2011

RACCOMANDAZIONI

Vaccino anti-epatite A

- Si consiglia l'effettuazione del vaccino per l'epatite A nelle seguenti categorie di soggetti con condizioni patologiche a rischio:
  - Soggetti affetti da epatopatia cronica (in conseguenza della maggiore suscettibilità di tali pazienti per l'insorgenza di forme fulminanti)
  - Pazienti con coagulopatie tali da richiedere terapia a lungo termine con derivati di natura ematica
  - Tossicodipendenti
  - Soggetti a rischio per soggiorni in aree particolarmente endemiche



Vaccino	0gg-30gg	3° mese	4° mese	5° mese	6° mese	7° mese	11° mese	13° mese	15° mese	6° anno	12°-18° anno	19-49 anni	50-64 anni	> 64 anni	Soggetti ad aumentato rischio
DTPa**		DTPa		DTPa			DTPa			DTPa***	dTpaIPV	1 dose dTpa**** ogni 10 anni			(1)
IPV		IPV		IPV			IPV			IPV					
Epatite B	EpB-EpB*	Ep B		Ep B			Ep B								(2)
Hib		Hib		Hib			Hib								(3)
Pneumococco		PCV		PCV			PCV							PCV+PPSV	(4) ^^
MPRV								MPRV		MPRV					(6) ^
MPR								*oppure* MPR + V		*oppure* MPR + V					(5) *****
Varicella															(6)^
Meningococco C								Men C§			Men ACWY coniugato				(7)
Meningococco B*^		Men B	Men B		Men B			Men B							
HPV											HPV°: 2-3 dosi (in funzione di età e vaccino)				(8)
Influenza														1 dose all'anno	(9) °°
Herpes Zoster														1 dose#	(10)
Rotavirus		Rotavirus## (due o tre dosi a seconda del tipo di vaccino)													
Epatite A															(11)

PNPV 2017-2019

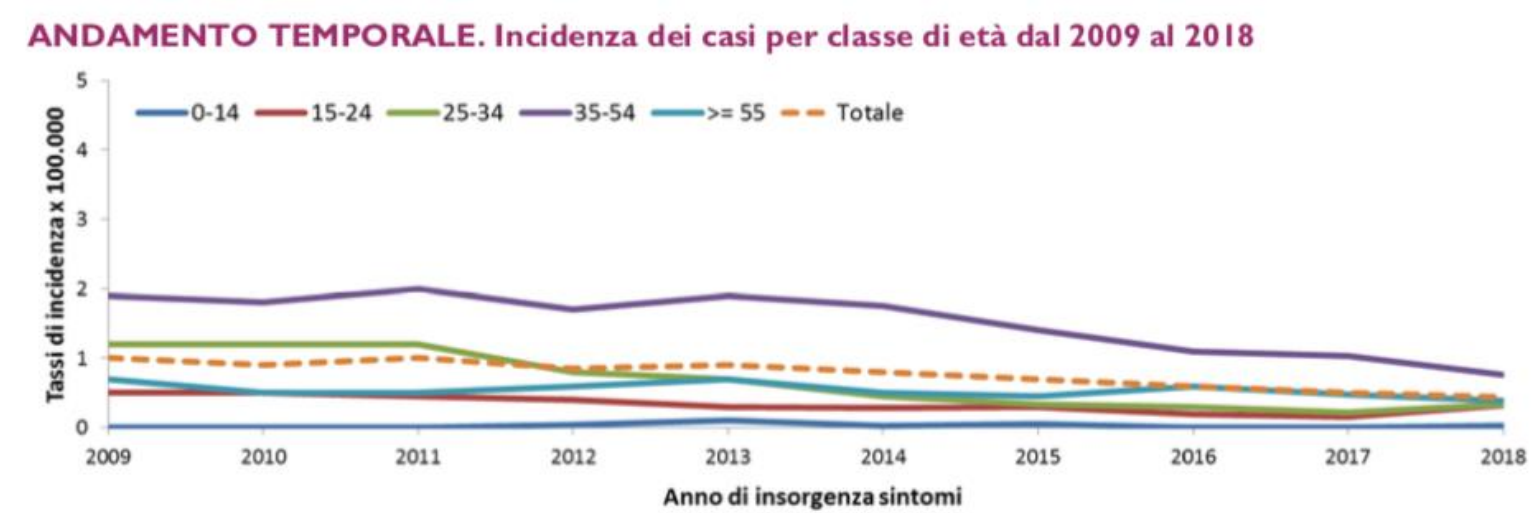
HEPATITIS B

KEY FACTS

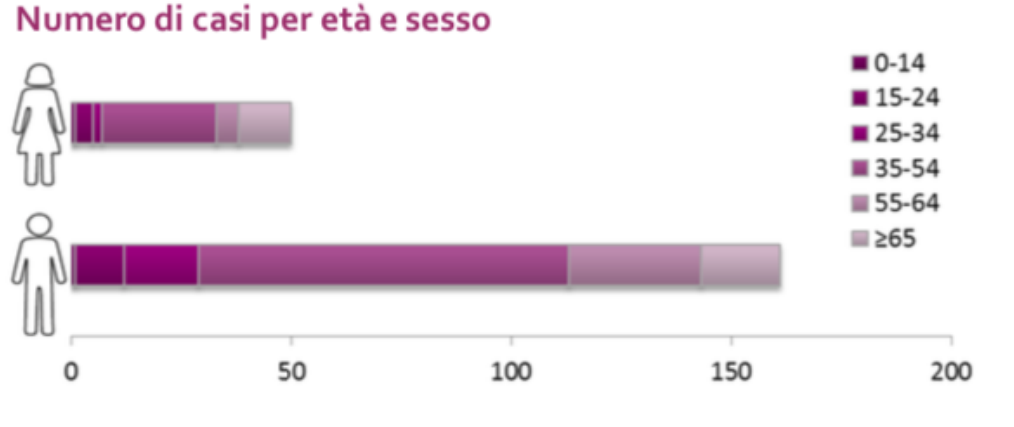
- Hepatitis B is a viral infection that attacks the liver and can cause both acute and chronic disease.
- The virus is most commonly transmitted from mother to child during birth and delivery, as well as through contact with blood or other body fluids.
- WHO estimates that in 2015, 257 million people were living with chronic hepatitis B infection (defined as hepatitis B surface antigen positive).
- In 2015, hepatitis B resulted in an estimated 887 000 deaths, mostly from cirrhosis and hepatocellular carcinoma (i.e. primary liver cancer).
- As of 2016, 27 million people (10.5% of all people estimated to be living with hepatitis B) were aware of their infection, while 4.5 million (16.7%) of the people diagnosed were on treatment.
- Hepatitis B can be prevented by vaccines that are safe, available and effective.

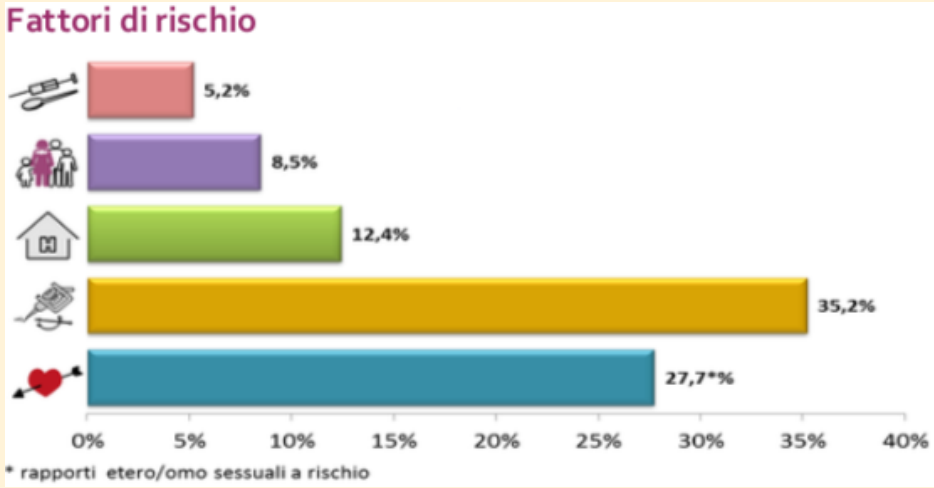
https://www.who.int/news-room/fact-sheets/detail/hepatitis-b

EPIDEMIOLOGY IN ITALY

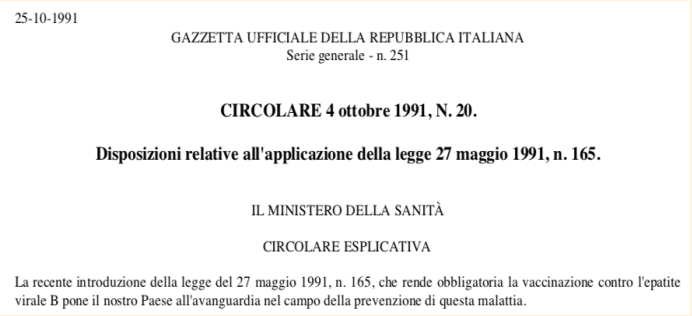


Italy: 0.4 x 100000





Vaccinazione anti-epatite B: la strategia italiana (Legge 27/05/1991 n.165)



25-10-1991

GAZZETTA UFFICIALE DELLA REPUBBLICA ITALIANA
Serie generale - n. 251

CIRCOLARE 4 ottobre 1991, N. 20.

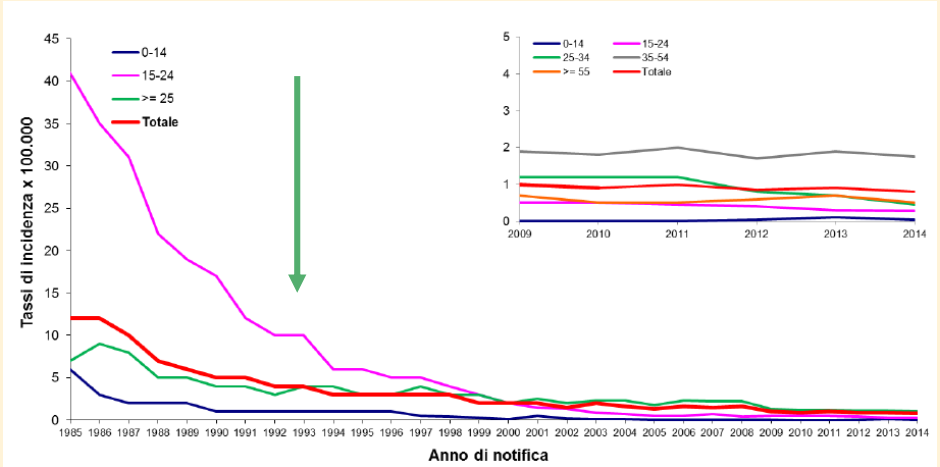
Disposizioni relative all'applicazione della legge 27 maggio 1991, n. 165.

IL MINISTERO DELLA SANITÀ

CIRCOLARE ESPLICATIVA

La recente introduzione della legge del 27 maggio 1991, n. 165, che rende obbligatoria la vaccinazione contro l'epatite virale B pone il nostro Paese all'avanguardia nel campo della prevenzione di questa malattia.

- Vaccinazione obbligatoria dei neonati al 3º mese - 5° mese -11°/12° mese (insieme alle altre vaccinazioni dell'infanzia)
- Vaccinazione obbligatoria degli adolescenti a 12 anni (3 dosi ai mesi 0, 1, 6)
- Screening per HBsAg nelle donne gravide
- Vaccinazione dei neonati da madre HBsAg+ alla nascita (4 dosi) (1)
- Vaccinazione gratuita nei gruppi a rischio (2)



Vaccinazione selettiva dei gruppi a maggior rischio

Vaccinazione universale dei nuovi nati

1983 **1988** **1991** **2003**

Identificazione dei gruppi a maggior rischio a cui offrire gratuitamente la vaccinazione

Interruzione della vaccinazione dei dodicenni

(1) Largamente praticata su base volontaria dal 1984-85

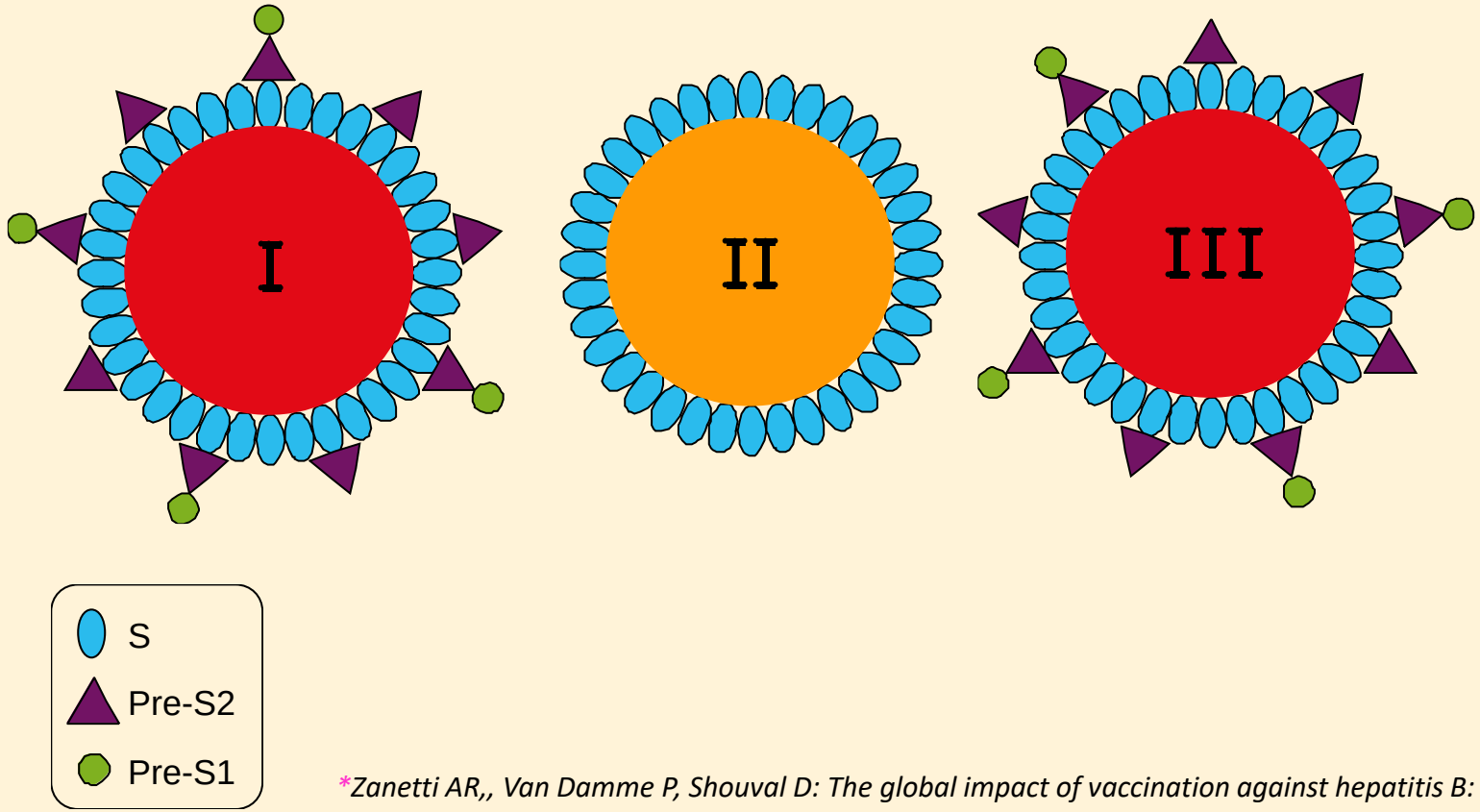
(2) Dal 1984 in alcune regioni, dal 1988 su tutto il territorio nazionale

Three generations of HBV vaccines

Plasma derived Vaccines 1980-1986

rDNA Yeast derived vaccines 1986-2017

rDNA Mammalian cell derived vaccines 2000-



*Zanetti AR,, Van Damme P, Shouval D: The global impact of vaccination against hepatitis B: A historical over view. Vaccine 2008;26:6266

TIPI DI VACCINO ANTI-EPATITE B

- **Plasma derivati (Vaccini di prima generazione)**
  - ottenuti da plasma di portatori cronici di HBV mediante trattamenti biochimici e biofisici
  - disponibili in quantità limitate
  - non omogeneità della fonte di materia prima

- **Ricombinanti (Vaccini di seconda generazione)**
  - lievito con inserimento della sequenza di DNA codificante la proteina 'small' dell'HBsAg (SHBs - non-glicosilata)
  - largamente disponibili a costi più bassi
  - consistenza tra lotti

Miliardi di dosi somministrate in tutto il mondo, con eccellenti risultati in termini di sicurezza ed immunogenicità

- **Ricombinanti derivati da cellule di mammifero (Vaccini di terza generazione)**
- (HBsAg, antigeni preS1, preS2)

– Hanno immunogenicità potenziata. Per adesso disponibili in pochi Paesi: Francia, Israele, alcuni Paesi del Sud-Est Asiatico

MOTIVI DI NON RISPOSTA AI VACCINI ANTI-EPATITE B

Nonostante l'ottima efficacia dei vaccini di "seconda generazione", esiste possibilità di fallimento vaccinale primario

I possibili motivi sono:

- inadeguata conservazione o somministrazione
- età avanzata
- obesità
- insufficienza renale
- epatopatia cronica
- immunosoppressione
- resistenza geneticamente determinata

PROTEZIONE : > 10 IU/L

- Misurata da 1 a 3 mesi dopo una adeguata schedula di immunizzazione.
- Neonati: 99%
- Bambini-adolescenti: 95-99%
- Adulti: < 95% (depending on age, BMI, smoking, genetic factors, …)

- **La non risposta alla immunizzazione può essere superata**
  - **aumentando la dose**
  - **effettuando dosi supplementari**
  - **mediante vaccinazione con proteine codificate dalla regione pre-S del genoma dell'HBV (vaccini di terza generazione)**

The Unmet Need: High-Risk Populations of Non-Responders & Low Responders to Conventional HBV Vaccination

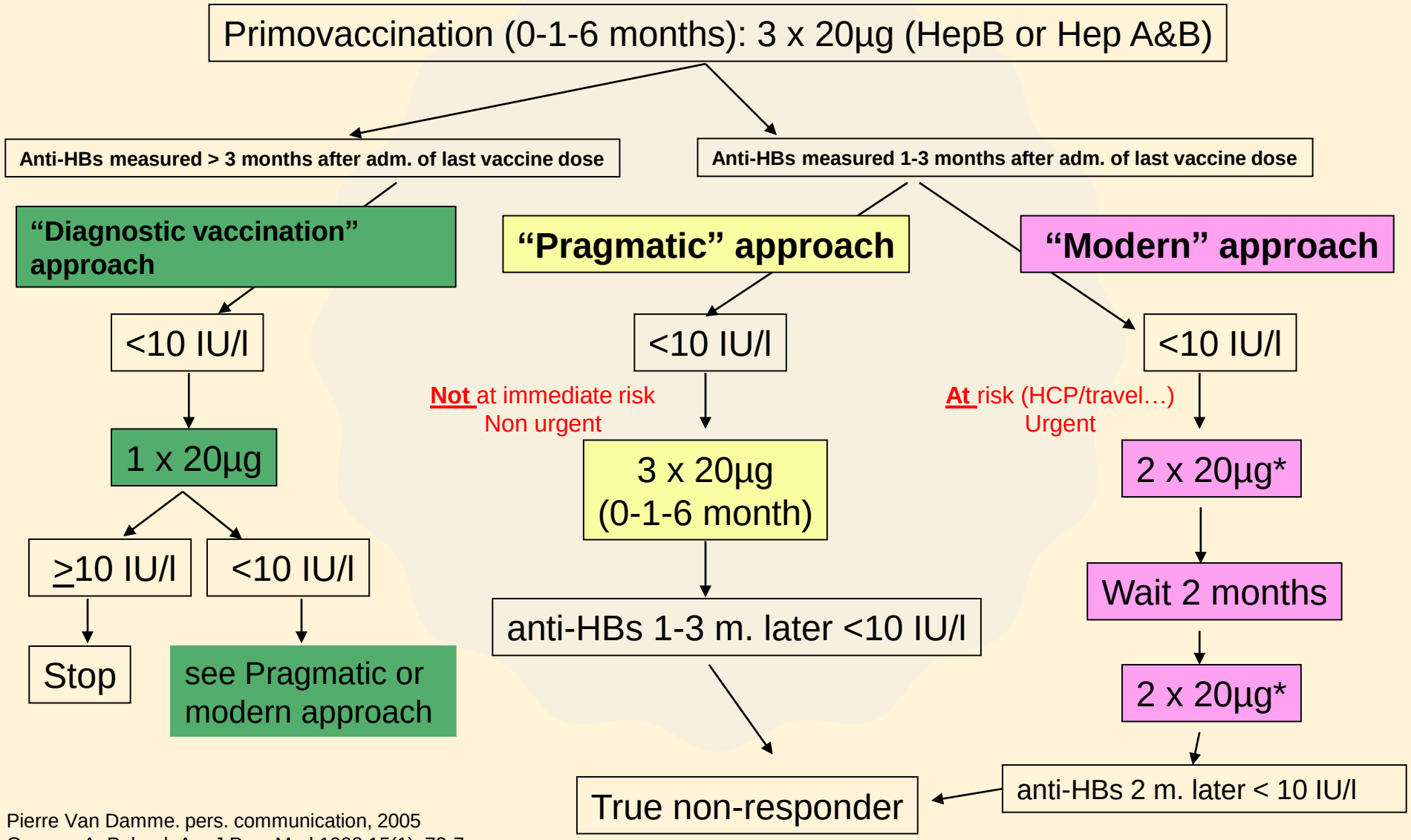
SEROPROTECTION RATES:

• Cancer patients (children)	~57%
• Patients with chronic liver disease	~50%
• Chronic renal failure & dialysis	34-81%
• Acute lymphocytic leukemia	~10%
• Bone marrow /stem cell transplant recipients	15-68%
• Pre-transplantation candidates	28-36%
• Post-transplantation patients	~10%
• HIV (children & adolescents)	~30%

- Miscellaneous (i.e. older healthcare workers engaged in exposure prone procedures; genetically determined non-responders, celiac disease, IBD)

https://www.vbivaccines.com/wp-content/uploads/2017/04/Sci-B-Vac-WVC-2017.pdf

HEPATITIS B: HYPO - NON RESPONDERS



Pierre Van Damme. pers. communication, 2005
Gregory A. Poland. Am J Prev Med 1998;15(1): 73-7
Kunal Das, R. K. Gupta, V. Kumar et al World J Gastroenterol 2003;9(5):1132-1134
Roland W. Ellis, Hepatitis B vaccines in Clinical Practice,1993

* Left & right deltoideus, concommitant

- New adjuvants* :
  - Fendrix GSK™ (MPL /A&QS21)
  - **Heplisav, Dynavax® (CpG ODNs TLR 9)**
  - MF 59 (oil in water)
  - AgB/RC 529 (MPL ,Corixa, Berna Biotech)
  - Cytokines (*GM-CSF, IL-2, IL-4, IL-12, IFN α, TLR 9 αg*)
  - Miscellaneous *(Cationic lipid, Virosomes ,HBcAg)*

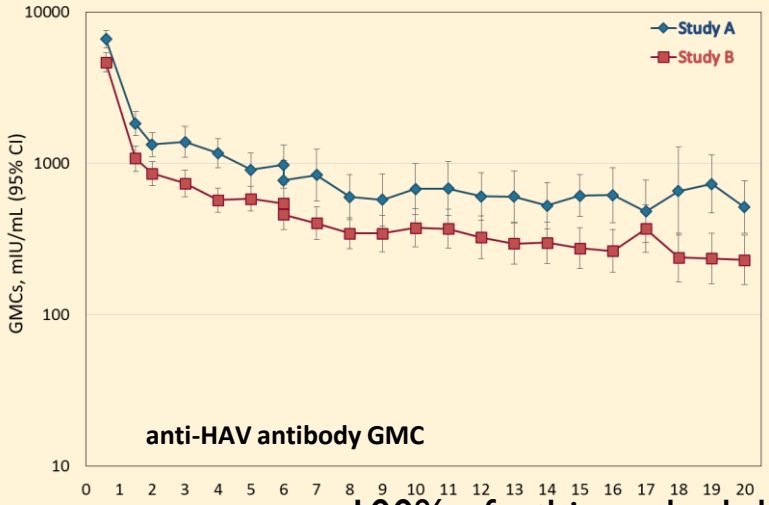
- Double or Triple antigen vaccines(Pre-S_1/Pre-S_2/S (with alum hydroxide)**:
  - **GenHevac B™ - France (Discontinued)**
  - **Hepagene™ - UK (Discontinued)**
  - **BioHep B/ HepImmune/ Sci B Vac® (licensed in Israel)**

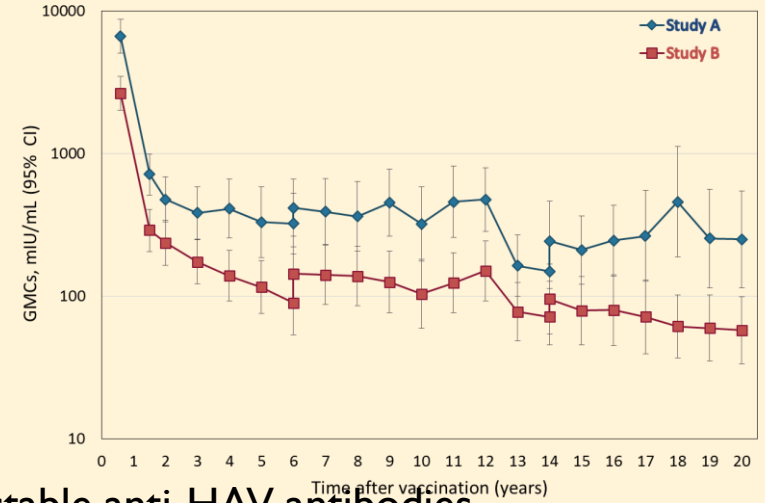
Table 2 Strategies to improve protection elicited by hepatitis B vaccination

Strategy	Product name (manufacturer)	References
Novel vaccine antigens		
PreS2-S	GenHevac-B (Pasteur)	[69]
PreS1–PreS2-S	SCI-B-Vac (SciGen)	[22, 57]
PreS1–PreS2-S	Hepagene (PowderJect)	[70]
Increased antigen dose		
40 µg	HBVAXPRO (Sanofi Pasteur MSD)	[71, 72]
Vaccination schedule		
Accelerated schedules		[73]
Alternative administration route		
Intradermal		[74, 75]
Adjuvants		
AS04	FENDrix (GSK Vaccines)	[33]
Immunostimulatory DNA sequences (ISS 1018)	HEPLISAV-B™ (Dynavax Technologies)	[49]

ANTI-HAV/HBV ANTIBODY PERSISTENCE AFTER 20 YEARS

- 20 years after *Twinrix*™ primary vaccination (0, 1, 6 months)





- 100% of subjects had detectable anti-HAV antibodies
- Over 96% of subjects had anti-HBs ≥10 IU/L

GMC, geometric mean concentration; HAV, hepatitis A virus; HBs ,hepatitis B surface. Twinrix is a trademark of GSK
Van Damme P, et al. NECTM 2016, oral presentation.

RACCOMANDAZIONI

Vaccino anti-epatite B

- I comportamenti ad incrementato rischio di infezione per cui si raccomanda la vaccinazione sono:
  - Conviventi e contatti di soggetti HBsAg positivi, indipendentemente dall'età
  - Vittime di punture accidentali con aghi potenzialmente infetti
  - Detenuti
  - Soggetti dediti alla prostituzione
  - Uomini che fanno sesso con uomini
  - Donatori di sangue appartenenti a gruppi sanguigni rari

Vaccino	0gg-30gg	3° mese	4° mese	5° mese	6° mese	7° mese	11° mese	13° mese	15° mese	6° anno	12°-18° anno	19-49 anni	50-64 anni	> 64 anni	Soggetti ad aumentato rischio
DTPa**		DTPa		DTPa			DTPa			DTPa***	dTpaIPV	1 dose dTpa**** ogni 10 anni			(1)
IPV		IPV		IPV			IPV			IPV					
Epatite B	EpB-EpB*	Ep B		Ep B			Ep B								(2)
Hib		Hib		Hib			Hib								(3)
Pneumococco		PCV		PCV			PCV							PCV+PPSV	(4) ^^
MPRV								MPRV		MPRV					(6) ^
MPR								*oppure* MPR + V		*oppure* MPR + V					(5) *****
Varicella															(6)^
Meningococco C								Men C§			Men ACWY coniugato				(7)
Meningococco B*^		Men B	Men B		Men B			Men B							
HPV											HPV°: 2-3 dosi (in funzione di età e vaccino)				(8)
Influenza														1 dose all'anno	(9) °°
Herpes Zoster														1 dose#	(10)
Rotavirus		Rotavirus## (due o tre dosi a seconda del tipo di vaccino)													
Epatite A															(11)

PNPV 2017-2019

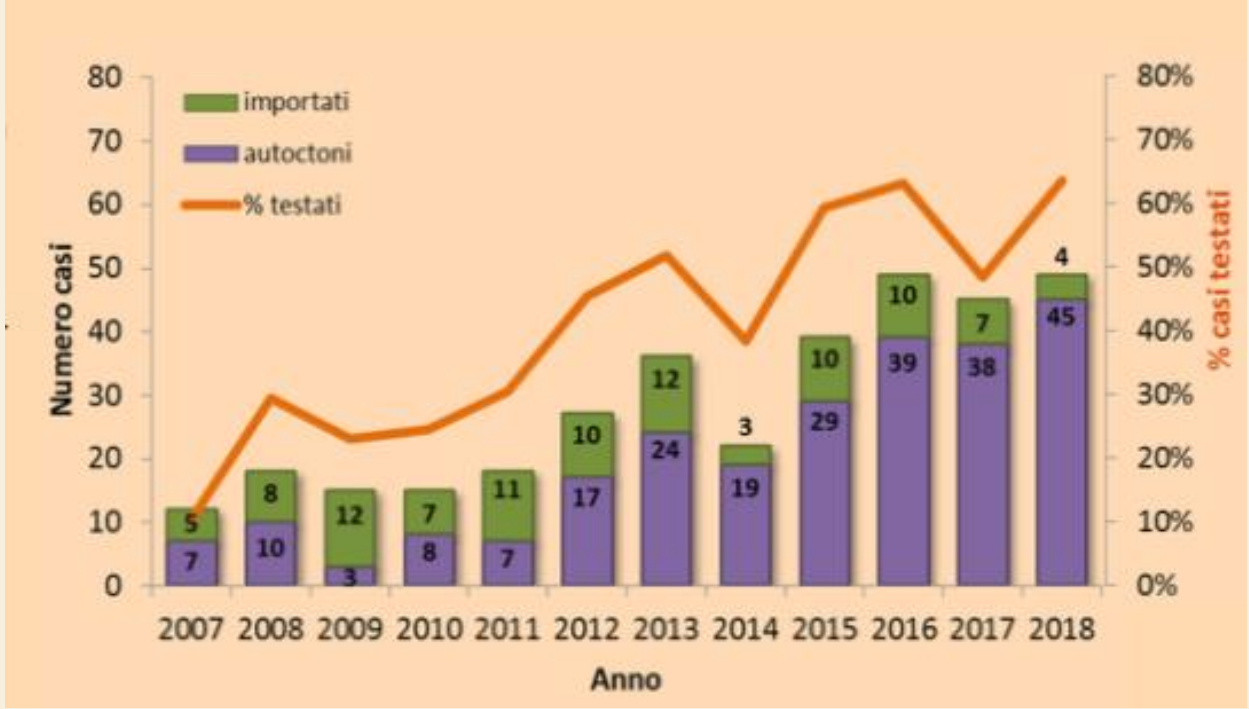
HEPATITIS E
KEY FACTS

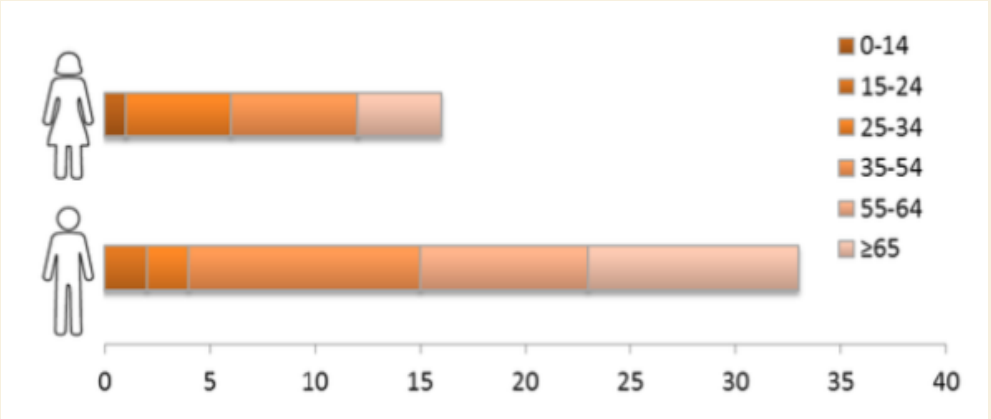
- Hepatitis E is a liver disease caused by infection with a virus known as hepatitis E virus (HEV).
- Every year, there are an estimated 20 million HEV infections worldwide, leading to an estimated 3.3 million symptomatic cases of hepatitis E (1).
- WHO estimates that hepatitis E caused approximately 44 000 deaths in 2015 (accounting for 3.3% of the mortality due to viral hepatitis).
- The virus is transmitted via the fecal-oral route, principally via contaminated water.
- Hepatitis E is found worldwide, but the disease is most common in East and South Asia.
- A vaccine to prevent hepatitis E virus infection has been developed and is licensed in China, but is not yet available elsewhere.

https://www.who.int/news-room/fact-sheets/detail/hepatitis-e

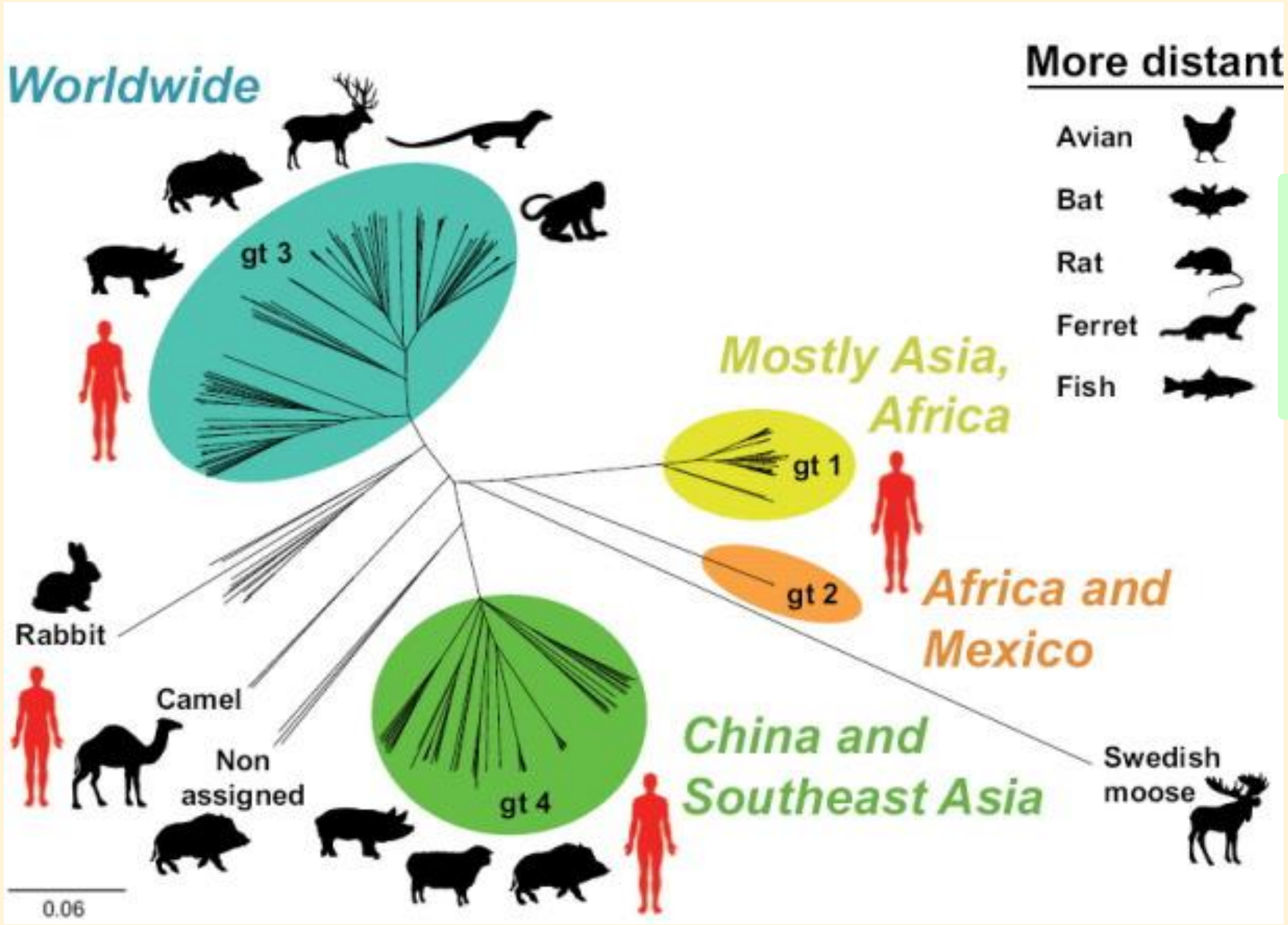
EPIDEMIOLOGY IN ITALY

- Continua nel 2018 il trend in aumento dei casi di epatite E notificati al SEIEVA. Questo aumento è a carico soprattutto di cittadini italiani, mentre solo pochi casi (4 nel 2018) sono legati a viaggi in zone endemiche per l'epatite E.





HEV: 7 GENOTYPES ,1 SEROTYPE



Developing countries
HEV G1-2

Developed countries
HEV G3-4

TRASMISSIONE

ZOONOSI→ Human HEV can infect pigs

Swine HEV can infect non-human primates

Individuals working with pig herds have higher risk of HEV infection

(Martinelli et al, 2011)

FOODBORNE DISEASE→ Histories of infection by eating Uncooked or undercooked:

-pig liver sold in grocery stores (Japan, USA)

-raw shellfish grown in a polluted areas (Japan, Spain)

-meat from wild deer and boar (Japan)

-pig liver sausage (France)

Contaminating virus is completely inactivated when commercial pig liver is boiled or stir-fried for 5'.
→ Inactivation at 71°C x 20' *IntJFoodMicrobiol 2008)*

- There is evidence of HEV transfusion transmission, but degree of its impact needs additional data
- Screening of donors is currently not considered cost-saving, but some countries do it (e.g. England, Ireland and France)

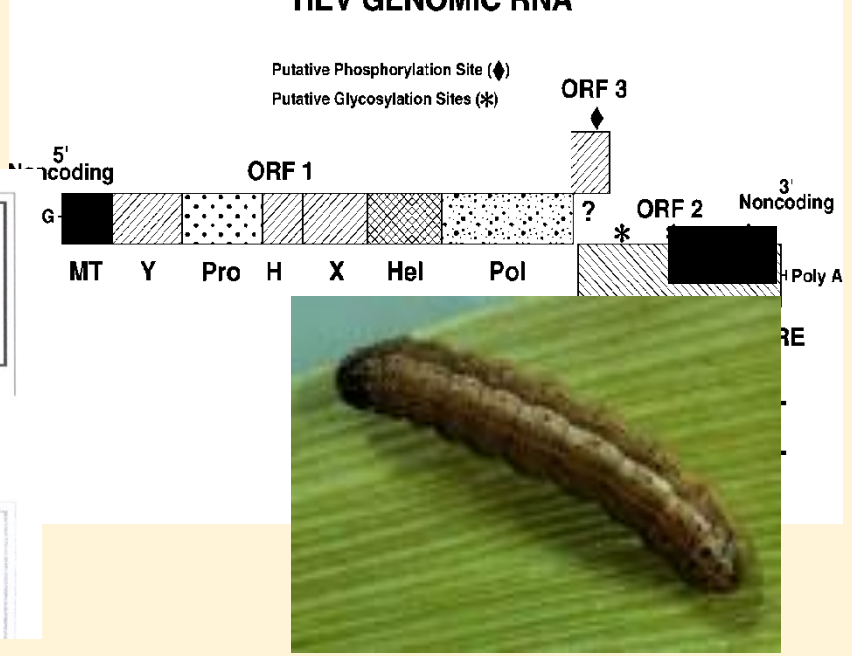
HEV vaccine - 1

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 1, 2007 VOL. 356 NO. 9

Safety and Efficacy of a Recombinant Hepatitis E Vaccine

Mrigendra Prasad Shrestha, M.B., B.S., Robert McNair Scott, M.D., Durga Man Joshi, M.D., Mammen P. Mammen, Jr., M.D., Gyan Bahadur Thapa, M.B., B.S., Narbada Thapa, Ph.D., Khin Saw Aye Myint, M.B., B.S., Marc Fourneau, B.S., Robert A. Kuschner, M.D., Sanjaya Kumar Shrestha, M.D., Marie Pierre David, M.S., Jitvimol Seriwatana, M.S., David W. Vaughn, M.D., Assad Safary, M.D., Timothy P. Endy, M.D., and Bruce L. Innis, M.D.



- Purified polypeptide (56KD; aa 112-607) produced in *Spodoptera frugiperda* cells infected with a recombinant Baculovirus containing HEV genomic sequence of the capsid antigen.
- Phase 2, double-blind, placebo controlled trial
- ~2000 nepalese healthy adults
- 3 doses of vaccine at 0, 1 and 6m
- Good safety and efficacy (95.5%)

HEV vaccine - 2

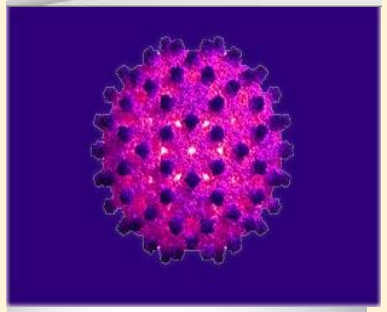
Efficacy and safety of a recombinant hepatitis E vaccine in healthy adults: a large-scale, randomised, double-blind placebo-controlled, phase 3 trial

Feng-Cai Zhu, Jun Zhang, Xue-Feng Zhang, Cheng Zhou, Zhong-Ze Wang, Shou-Jie Huang, Hua Wang, Chang-Lin Yang, Han-Min Jiang, Jia-Ping Cai, Yi-Jun Wang, Xing Ai, Yue-Mei Hu, Quan Tang, Xin Yao, Qiang Yan, Yang-Ling Xian, Ting Wu, Yi-Min Li, Ji Miao, Mun-Hon Ng, James Wai-Kuo Shih, Ning-Shao Xia

Lancet 2010; 376: 895-902

Jan.12.2012
China approved hepatitis E vaccine

- Truncated HEV capsid protein (30 KD; aa 368-607) expressed in *E. coli*.
- Randomized, double-blind, phase 3 trial
- 112,604 chinese healthy adults
- 3 doses of vaccine at 0, 1 and 6 m
- Vaccine efficacy 100%
- No serious adverse event



HEPATITIS C

KEY FACTS

-Hepatitis C is a liver disease caused by the hepatitis C virus (HCV): the virus can cause both acute and chronic hepatitis, ranging in severity from a mild illness lasting a few weeks to a serious, lifelong illness.

-Hepatitis C is a major cause of liver cancer.

-The hepatitis C virus is a bloodborne virus: the most common modes of infection are through exposure to small quantities of blood. This may happen through injection drug use, unsafe injection practices, unsafe health care, transfusion of unscreened blood and blood products, and sexual practices that lead to exposure to blood.

-Globally, an estimated 71 million people have chronic hepatitis C virus infection.

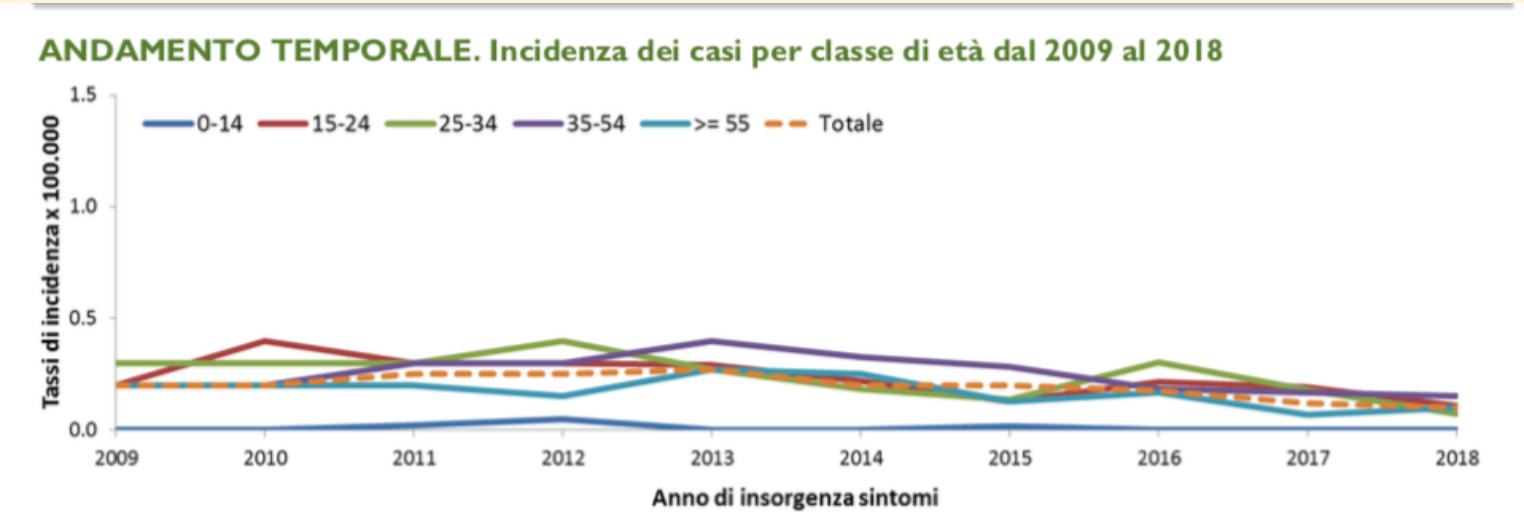
-A significant number of those who are chronically infected will develop cirrhosis or liver cancer.

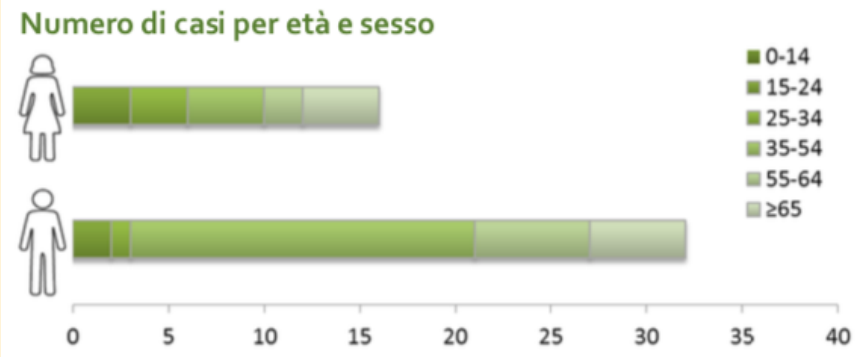
-WHO estimated that in 2016, approximately 399 000 people died from hepatitis C, mostly from cirrhosis and hepatocellular carcinoma (primary liver cancer).

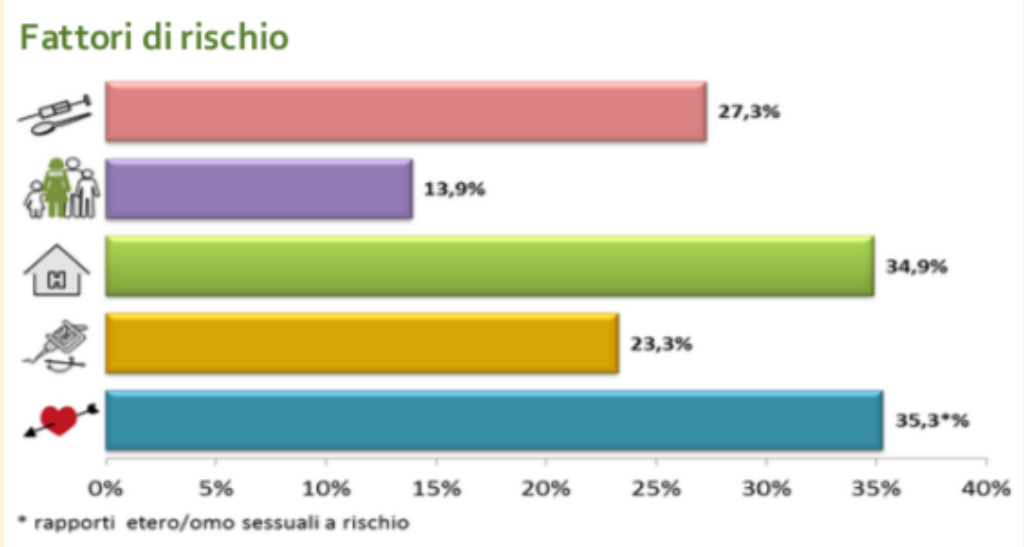
-Antiviral medicines can cure more than 95% of persons with hepatitis C infection, thereby reducing the risk of death from cirrhosis and liver cancer, but access to diagnosis and treatment is low.

-There is currently no effective vaccine against hepatitis C; however, research in this area is ongoing.

EPIDEMIOLOGY IN ITALY







BARRIERS TO HCV VACCINES DEVELOPMENT

- HCV genetic diversity (7 known genotypes and more than 80 subtypes)
- Limitations of HCV culture systems that pose challenges to production of a live-attenuated or inactivated whole HCV vaccine.
- Lack of in vitro systems and immunocompetent small animal models that facilitate determining whether vaccination induces protective immunity
- Incomplete understanding of protective immune responses
- Decades of research have revealed that HCV-specific $CD4^+$ helper T cells, $CD8^+$ cytotoxic T cells, and antibodies all play a role in protection against persistent HCV infection. Vaccine strategies to induce all 3 adaptive immune responses are in development.

Trial Evaluating Experimental Hepatitis C Vaccine Concludes

May 29, 2019

An experimental vaccine was not found to be effective at preventing chronic hepatitis C virus (HCV) infection in adults, according to results from a clinical trial sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health.

The trial began in March 2012 at sites in California and Maryland; a site in New Mexico was added in September 2015. The Phase 1/2 clinical trial was evaluating whether the experimental prime-boost vaccine known as AdCh3NSmut1/MVA-NSmut was safe and could prevent chronic HCV infection—defined as persistent presence of HCV in the blood for six months after initial detection of infection.

The trial enrolled 548 participants ages 18 to 45 years with a recent history of injecting drugs. The participants were randomly assigned to receive the experimental vaccine (a dose of AdCh3NSmut1 followed by a dose of MVA-NSmut 56 days later) or two placebo doses 56 days apart. Investigators report that 14 of the 275 participants in the experimental vaccine group and 14 of the 273 participants in the placebo group became chronically infected with HCV. The results indicate that the candidate vaccine failed to offer increased protection against chronic HCV infection compared to placebo. No vaccine-

COST-EFFECTIVE ANALYSIS

RESEARCH ARTICLE Open Access

The case for a universal hepatitis C vaccine to achieve hepatitis C elimination

Nick Scott[1,2*], David P. Wilson[1,2], Alexander J. Thompson[3,4], Eleanor Barnes[5,6], Manal El-Sayed[7], Adele Schwartz Benzaken[8], Heidi E. Drummer[1,9,10†] and Margaret E. Hellard[1,2,10,11†]

Abstract

Background: The introduction of highly effective direct-acting antiviral (DAA) therapy for hepatitis C has led to calls to eliminate it as a public health threat through treatment-as-prevention. Recent studies suggest it is possible to develop a vaccine to prevent hepatitis C. Using a mathematical model, we examined the potential impact of a hepatitis C vaccine on the feasibility and cost of achieving the global WHO elimination target of an 80% reduction in incidence by 2030 in the era of DAA treatment.

Methods: The model was calibrated to 167 countries and included two population groups (people who inject drugs (PWID) and the general community), features of the care cascade, and the coverage of health systems to deliver services. Projections were made for 2018–2030.

Results: The optimal incidence reduction strategy was to implement test and treat programmes among PWID, and in settings with high levels of community transmission undertake screening and treatment of the general population. With a vaccine available, the optimal strategy was to include vaccination within test and treat programmes, in addition to vaccinating adolescents in settings with high levels of community transmission. Of the 167 countries modelled, between 0 and 48 could achieve an 80% reduction in incidence without a vaccine. This increased to 15–113 countries if a 75% efficacious vaccine with a 10-year duration of protection were available. If a vaccination course cost US$200, vaccine use reduced the cost of elimination for 66 countries (40%) by an aggregate of US$7.4 (US$6.6–8.2) billion. For a US$50 per course vaccine, this increased to a US$9.8 (US$8.7–10.8) billion cost reduction across 78 countries (47%).

Conclusions: These findings strongly support the case for hepatitis C vaccine development as an urgent public health need, to ensure hepatitis C elimination is achievable and at substantially reduced costs for a majority of countries.

GRAZIE PER L’ATTENZIONE

UN RINGRAZIAMENTO A

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