RISULTATI A LUNGO TERMINE DELLA VACCINAZIONE HBV

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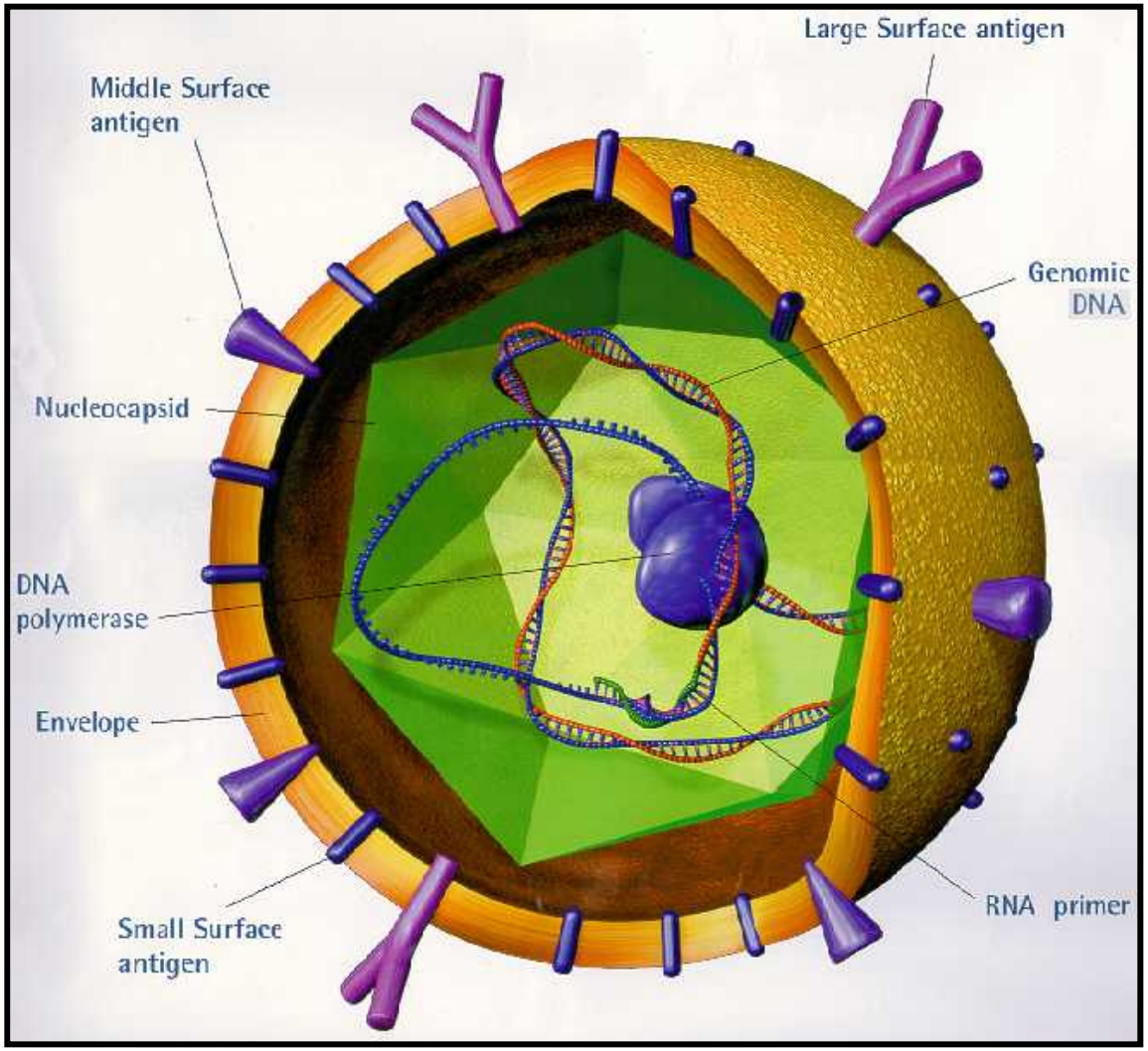
Hepatitis B virus



del: 16/05/2013

Sanità news

Organo di Informazione di Socitel

ALLARME DELL'OMS PER IL NUOVO CORONAVIRUS

Si aggravano le condizioni del secondo francese contagiato dal virus della ''nuova Sars'', peggiorate durante la notte nell'ospedale di Lille, dove è ricoverato. Il paziente è sottoposto a respirazione artificiale. Grave, ma stabile è invece il primo paziente, un uomo di 65 anni nel quale l'infezione si era manifest...

CON IL CAMBIO DELL'ADIUVANTE IL VACCINO PER LA PERTOSSE DIVENTA PIU' EFFICACE

L'ESPOSIZIONE AL CADMIO POTREBBE AUMENTARE L'INCIDENZA DI MALATTIE EPATICHE

AL VIA UN VACCINO SPERIMENTALE PER LA MALATTIA DI LYME

UN NUOVO FARMACO PER IL TUMORE AL POLMONE

UN BATTERIO PER CONTRASTARE L'OBESITA'

L'INQUINAMENTO INCIDE SULLA RESISTENZA ALL'INSULINA

IN ARRIVO NUOVE PROCEDURE PER GLI ATTESTATI DI MALATTIA

Entra in vigore dal 4 giugno 2013 la nuova procedura per la consultazione online degli attestati di malattia dei dipendenti, da parte di aziende e lavoratori. Con il Messaggio n.7485, l'INPS annuncia infatti un nuovo formato per l'invio telematico dei certificati al SAC, il sistema di accoglienza

IDENTIFICATE CELLULE IMMUNITARIE CHE CONTRASTANO L'HERPES GENITALE

Identificate cellule immunitarie che

MENO RISCHI DI PRESSIONE ALTA PER

News dall'Istituto Superiore di Sanità

Hepatitis B profilaxis

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Hepatitis B profilaxis

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Hepatitis B profilaxis

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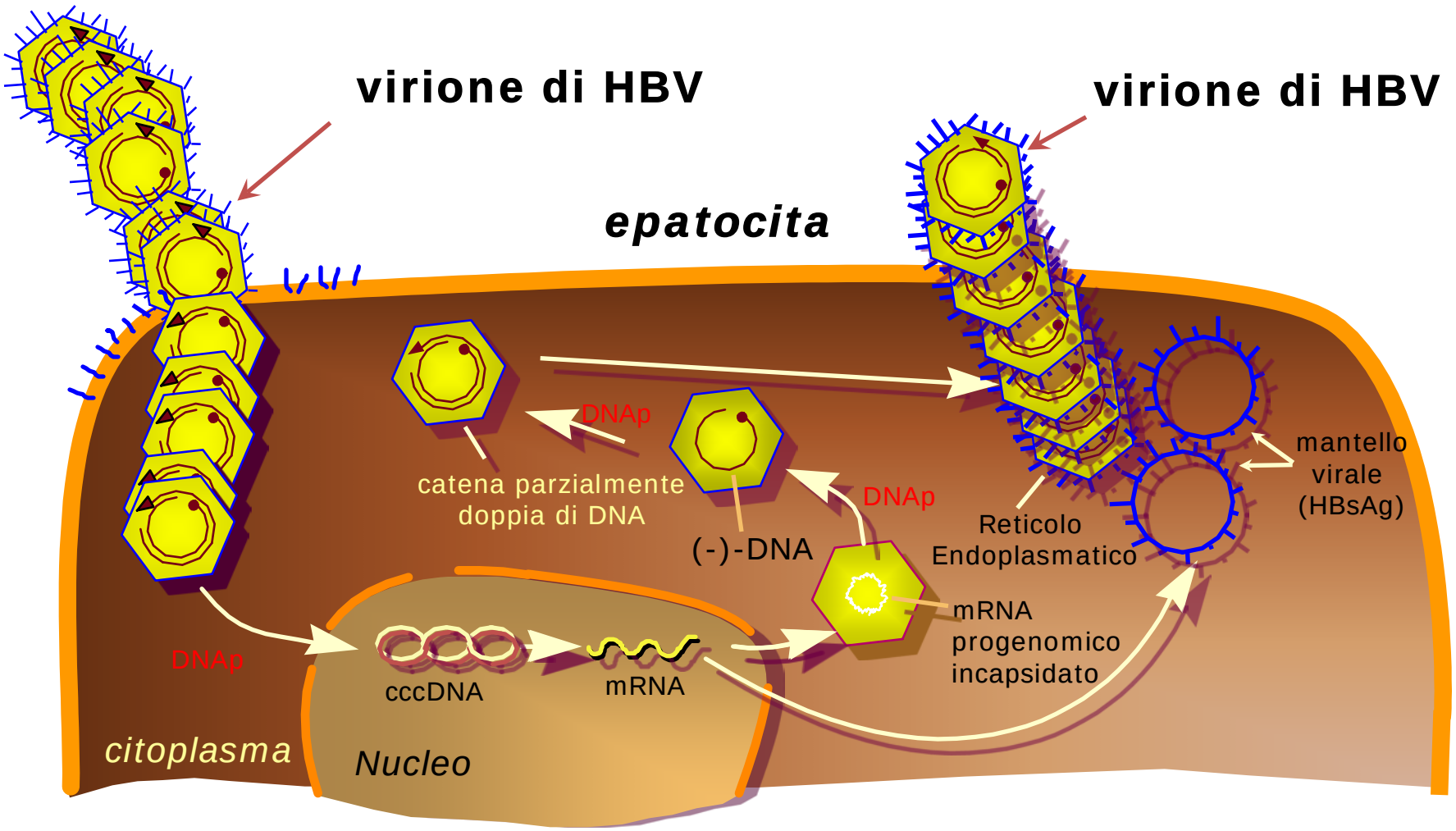
Hepatitis B profilaxis

REGIONE AUTONOMA DELLA SARDEGNA. PROVVEDITORATI AGLI STUDI DI SASSARI E NUORO, UNIVERSITA' DI CAGLIARI (Istituti di Igiene e Medicina Preventiva e di Biologia dell'Età Evolutiva) E DI SASSARI (Istituto di Igiene e Medicina Preventiva) Progetto Epatite B - Sardegna . L'educazione alla salute nella Scuola sarda. Stampacolor, Muros, 1987.

Ciclo replicativo del virus dell'epatite B



cccDNA: covalently closed circular DNA

Prevalenza di portatori cronici di HBV

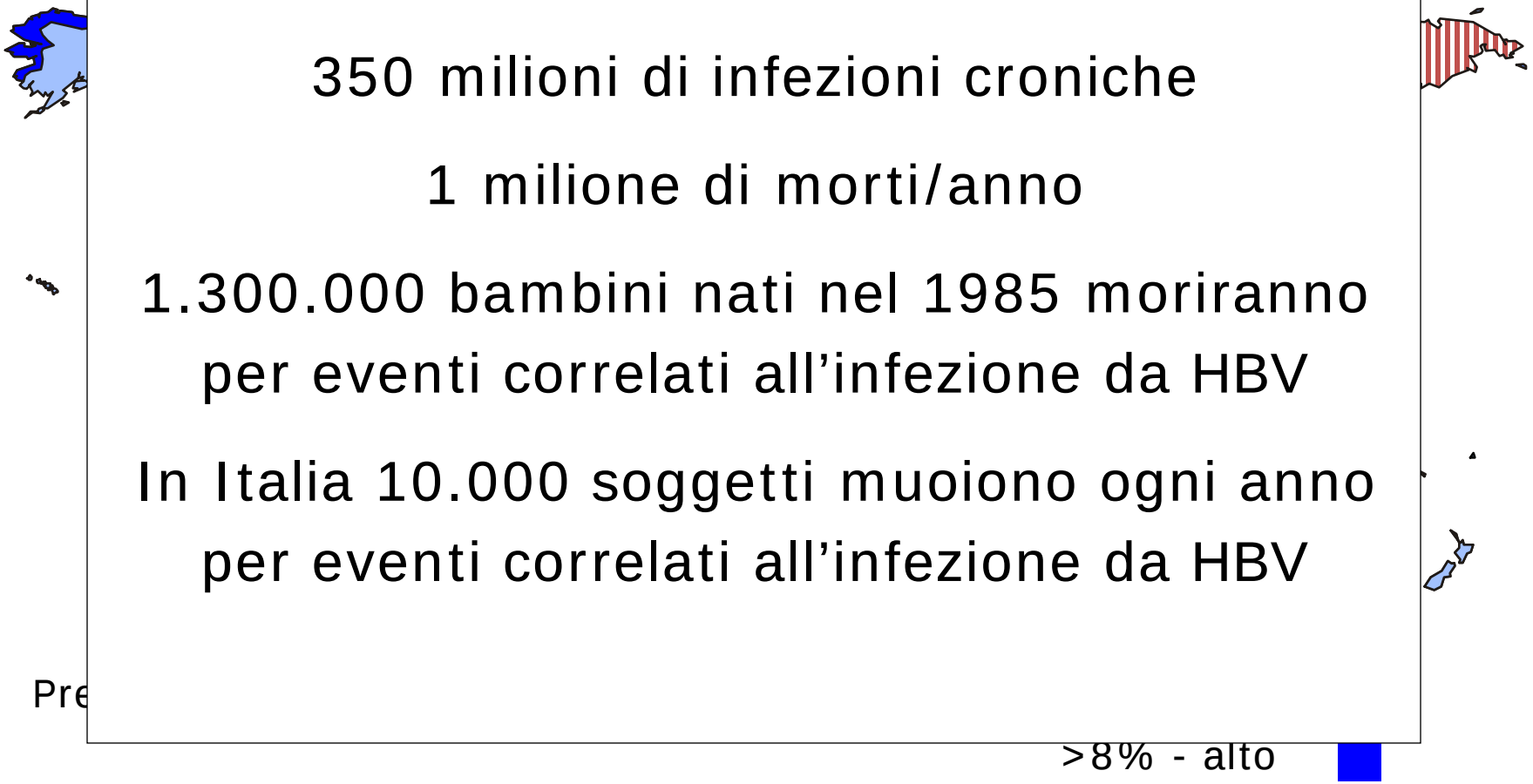
2 miliardi pazienti infetti

350 milioni di infezioni croniche

1 milione di morti/anno

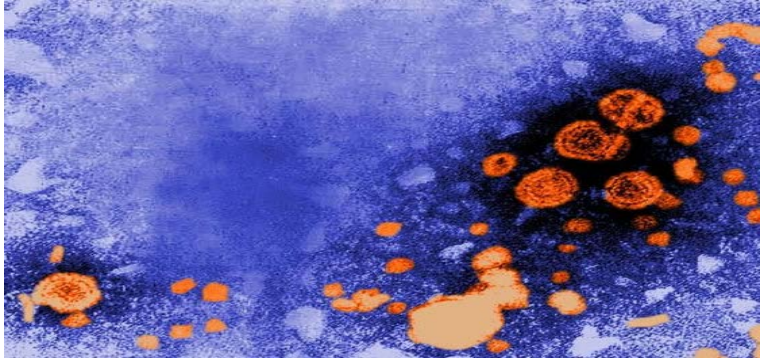
1.300.000 bambini nati nel 1985 moriranno per eventi correlati all'infezione da HBV

In Italia 10.000 soggetti muoiono ogni anno per eventi correlati all'infezione da HBV

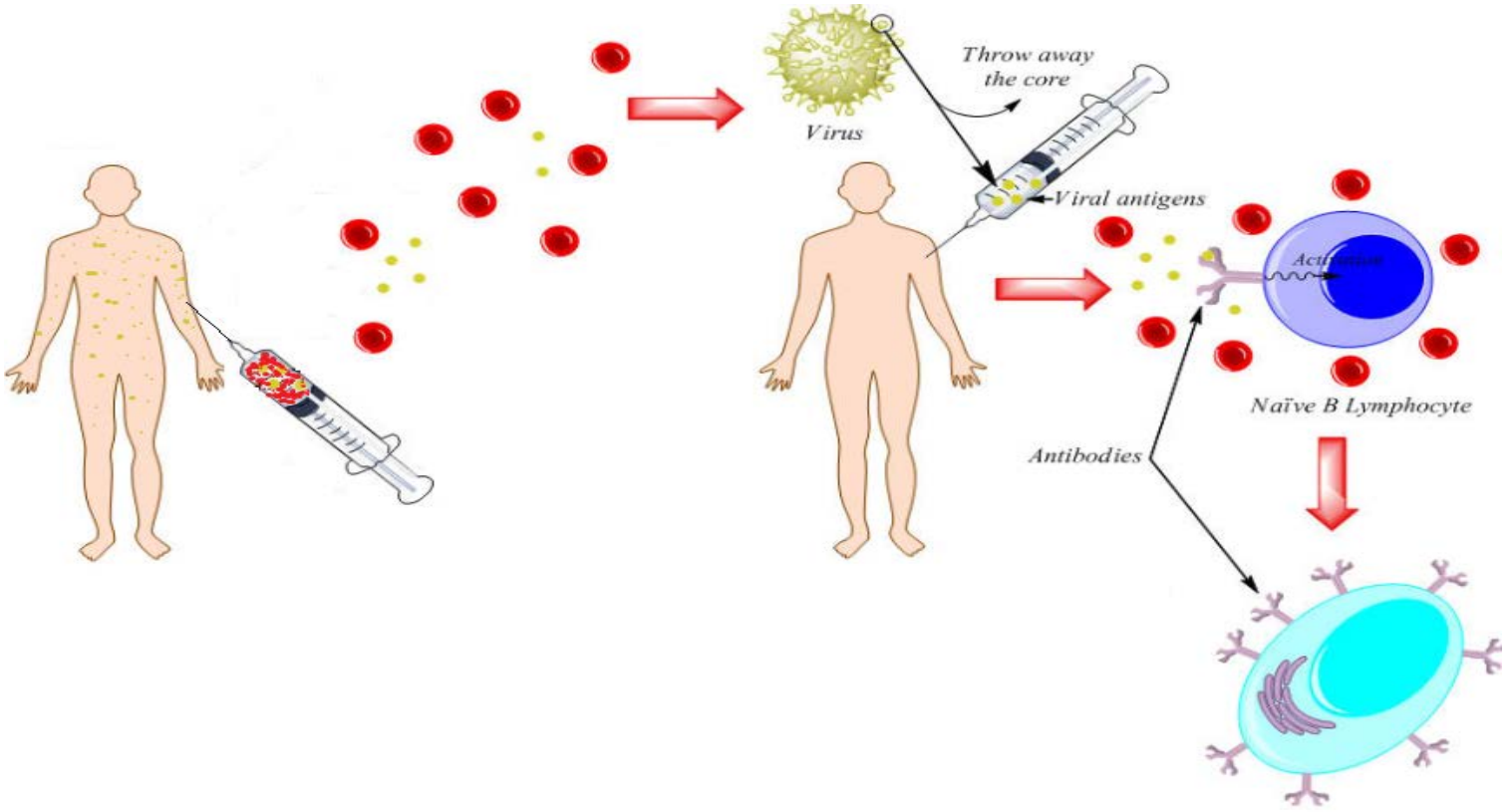


U.S. Center for Disease Control

Blumberg 1965 Ag Au



Vaccino plasmaderivato anti-epatite B (Prima generazione 1981)



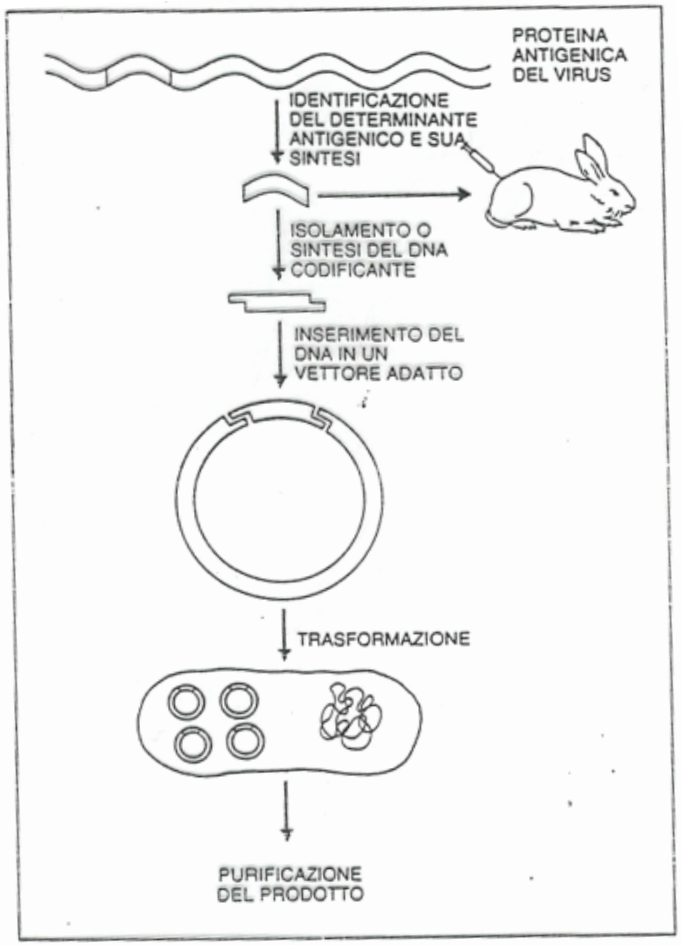
Tipi di vaccino anti-epatite B

- **Plasma derivati (Vaccini di prima generazione-1981)**
  - ottenuti da plasma di portatori cronici di HBV mediante trattamenti biochimici e biofisici
  - disponibili in quantità limitate
  - non omogeneità della fonte di materia prima

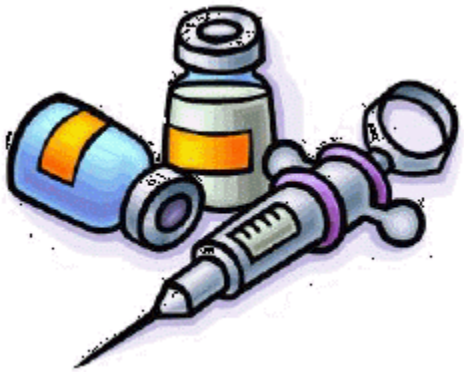
- **Ricombinanti (Vaccini di seconda generazione 1986)**
  - lievito con inserimento della sequenza di DNA codificante la proteina ‘small’ dell’HBsAg (SHBs - non-glicosilata)
  - largamente disponibili a costi più bassi
  - consistenza tra lotti
  - di recente si stanno producendo vaccini ricombinanti contenenti anche proteine “grandi” e “intermedie”

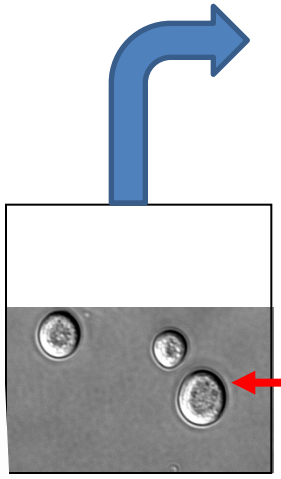
Miliardi di dosi somministrate in tutto il mondo, con eccellenti risultati in termini di sicurezza ed immunogenicità

Primo vaccino ricombinante



Solo una piccola parte di una proteina virale ne costituisce il determinante antigenico. Una volta identificato, esso può venire sintetizzato chimicamente e quindi iniettato in animali da laboratorio in modo da verificare la sua capacità di protezione contro le particelle virali. È quindi possibile risalire al DNA che codifica il frammento peptidico e inserirlo in un adatto vettore. La molecola ibrida può, a sua volta, essere introdotta in cellule batteriche che saranno in grado di sintetizzare quantità rilevanti di prodotto proteico. Questo potrà essere purificato e commercializzato come vaccino contro le particelle virali a cui la proteina appartiene.

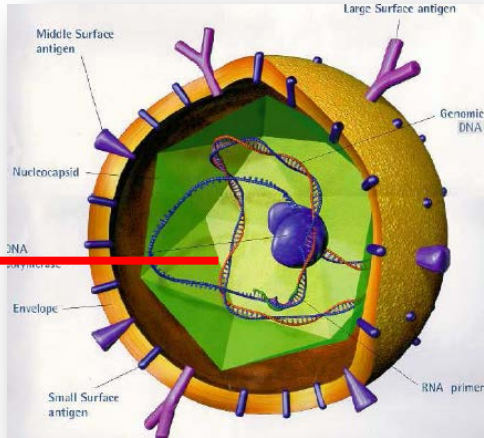




Saccaromyces cerevisiae

Gene S
Codificante per
Proteina “small”

Plasmide



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SETTEMBRE 1985 - **Evidenza della efficacia della vaccinazione anti-epatite B somministrando il vaccino negli stessi tempi delle vaccinazioni obbligatorie in Italia (difterite, tetano, polio) (*Piazza M. et al.* Lancet 1985*; i: 949-951; Piazza M. et al.* Lancet 1985; ii: 1120-1121)**

GENNAIO 1987 - **Applicazione del protocollo di vaccinazione dei nuovi nati nella città di Afragola (NA), ove l'endemia di epatite B era elevata (percentuale dei portatori di HBsAg >13%) con eccellenti risultati (*Piazza M. et al.* Lancet 1988)**

GENNAIO 1988 - L'Organizzazione Mondiale della Sanità (WHO) raccomanda che nei Paesi con prevalenza dei portatori di HBV maggiore del 2% (in Italia era del 5%) la vaccinazione contro l'epatite B dovrebbe essere integrata nei programmi di vaccinazione dell'infanzia.

MAGGIO 1991 - Promulgazione della vaccinazione obbligatoria dei nuovi nati contro l'epatite B in Italia

DECRETI, DELIBERE E ORDINANZE MINISTERIALI

MINISTERO DELLA SANITÀ

DECRETO 3 ottobre 1991.

Protocollo per l'esecuzione delle vaccinazioni contro l'epatite virale B.

PROTOCOLLO DI ESECUZIONE DELLE VACCINAZIONI

La vaccinazione contro l'epatite B può essere eseguita secondo la schedula prevista per ciascun vaccino registrato.

Per gli scopi che si prefigge la legge 27 maggio 1991, n. 165, sembra tuttavia opportuno seguire protocolli di vaccinazione il più possibile uniformi, che vengono di seguito riportati:

1) *Nuovi nati che devono effettuare le vaccinazioni dell'obbligo:*

Con ogni tipo di vaccino si esegue lo schema Piazza che prevede di regola la immunizzazione al 3°, 5° e 11° mese di vita contemporaneamente alle altre vaccinazioni obbligatorie (polio-difterite-tetano). Dose pediatrica.

2) *Nati da madre HBsAg positiva:*

Con ogni tipo di vaccino si segue il seguente schema:

1ª dose alla nascita (contemporaneamente alla somministrazione di immunoglobuline in altra sede);

2ª dose dopo un mese;

3ª dose subito dopo il compimento del secondo mese di vita, in concomitanza con le vaccinazioni antipolio-difterite-tetano;

4ª dose all'undicesimo mese in concomitanza con le suddette vaccinazioni.

Dose pediatrica.

3) *Bambini sotto i 10 anni, appartenenti ai gruppi a rischio, e già sottoposti alle altre vaccinazioni obbligatorie (polio-difterite-tetano):*

Si segue lo schema: mese 0, 1, 6.

Dose pediatrica.

4) *Soggetti di età superiore ai 10 anni (adolescenti della coorte dell'obbligo, adolescenti e adulti delle categorie a rischio):*

Si esegue lo schema: 0, 1, 6.

Dose per adulti.

5) *Soggetti dializzati o immunocompromessi:*

Lo schema base è: mese 0, 1, 6 impiegando una dose doppia rispetto a quella usata per l'adulto normorispondente, tenendo presente che il contenuto in alluminio non deve comunque superare 1,25 mg/dose.

Al fine di ottenere una risposta sierologica adeguata ulteriori dosi di rinforzo potranno essere decise, caso per caso in base ai risultati del monitoraggio sierologico dell'anti-HBs.

6) *Soggetti vittime di punture accidentali con aghi o strumenti appuntiti, potenzialmente infetti o che hanno avuto altre esposizioni, per le quali è importante conseguire difese immunitarie nel più breve tempo possibile:*

Lo schema più collaudato, con tutti i tipi di vaccino, è quello mese: 0, 1, 2 completato da un rinforzo fra il sesto e dodicesimo mese.

Dose per adulti.

L'opportunità di somministrare contemporaneamente immunoglobuline specifiche va valutato caso per caso.

Sopra i dieci anni, tutti i tipi di vaccino devono essere inoculati nel deltoide; nel neonato, nei muscoli della coscia (regione esterna quadricipite).

Tutte le preparazioni dei vaccini debbono essere conservate tra +2 °C e +8 °C; non devono essere assolutamente congelate.

I periodici aggiornamenti previsti all'art. 2 del presente decreto indicheranno i tempi e le modalità di somministrazione ed eventuali dosi di richiamo.

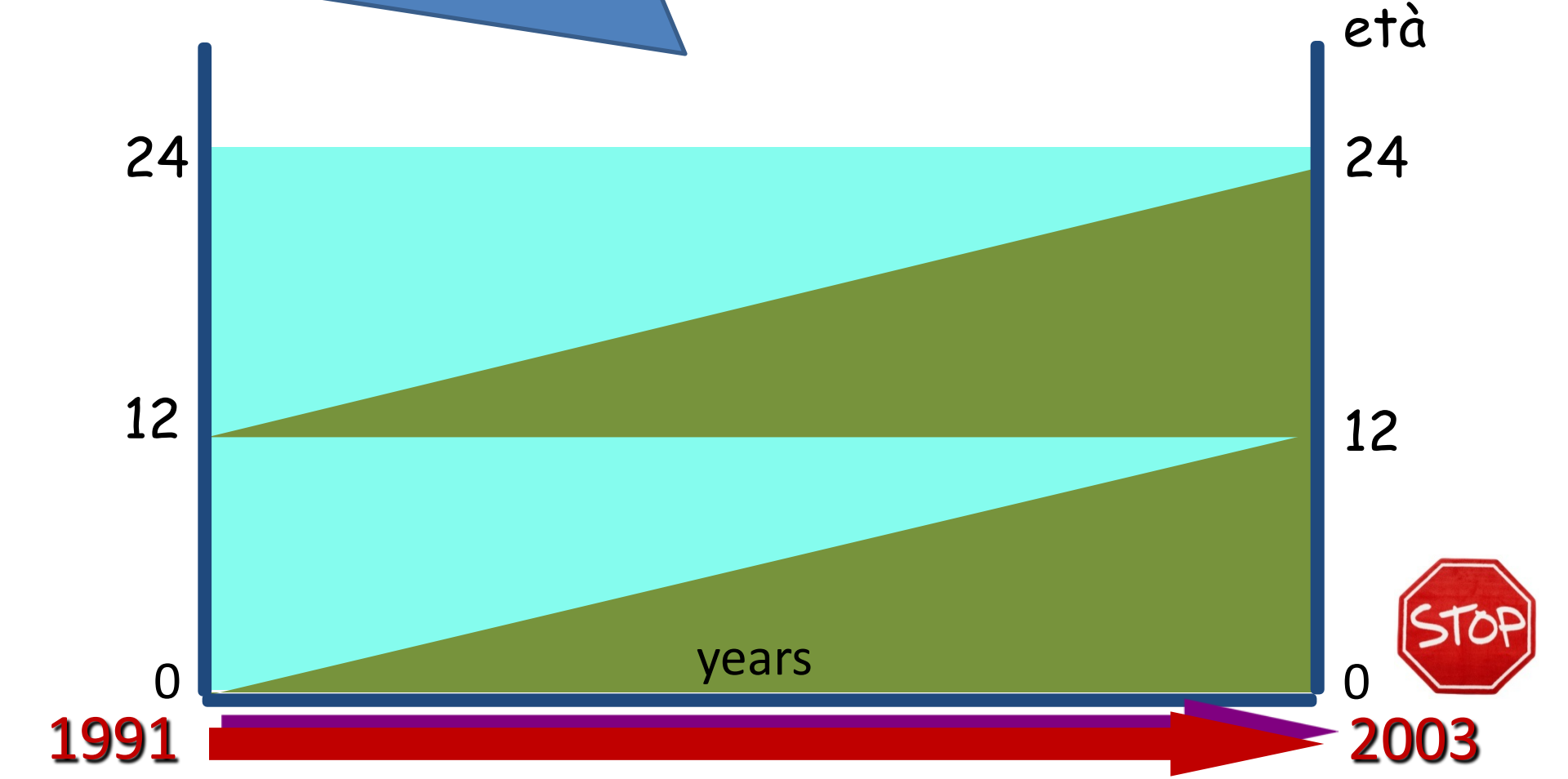
91A4646

DECRETO 4 ottobre 1991.

Offerta gratuita della vaccinazione contro l'epatite virale B alle categorie a rischio.

Strategia italiana di Vaccinazione Universale contro HBV

La vaccinazione universale contro l'infezione da è stata raccomandata per tutti I neonati in Italia nel 1991. Durante il periodo 1991-2003, la vaccinazione è stata raccomandata anche per gli adolescenti (12 anno di vita).



Alla fine del 2003, la prima coorte di neonati vaccinati nel 1991 ha raggiunto (12 anni) l'età target per gli adolescenti. Così la vaccinazione per gli adolescenti è stata interrotta.

Copertura vaccinale anti HBV in Italia (3 dosi al 24 mese di età): coorte 1991

The Italian Vaccine Coverage Survey Working Group. Childhood vaccination coverage in Italy: results of a seven-region survey, Bull WHO 1994;72:885–95

Table 3: **Percentage coverage of first and third doses of diphtheria–tetanus, poliovirus, and hepatitis B vaccines, by region, for children aged 12–23 months**[a]

		Campania			Lombardy				
Vaccine[b]	Abruzzi	Naples	Other	Liguria	Milan	Other	Marches	Molise	Tuscany
DT1	99.5 (98.6–100)[c]	98.6 (97.0–100)	99.1 (97.8–100)	99.5 (96.6–100)	100	100	100	100	100
DT3	95.2 (91.1–99.3)	77.1 (71.0–83.2)	87.2 (82.5–91.9)	96.7 (94.1–99.2)	91.0 (85.4–96.6)	94.8 (88.8–100)	98.6 (97.0–100)	95.2 (92.2–98.3)	95.2 (91.6–98.9)
OPV1	99.5 (98.6–100)	98.6 (97.0–100)	98.1 (96.3–99.9)	99.5 (98.6–100)	100	100	100	99.5 (98.6–100)	100
OPV3	97.6 (95.7–99.6)	77.6 (71.5–83.7)	88.2 (83.7–92.6)	96.7 (94.1–99.2)	91.0 (85.4–96.6)	97.6 (95.3–100)	98.6 (97.0–100)	94.3 (90.9–97.7)	95.2 (91.6–98.9)
HBV1	89.2 (80.9–97.4)	84.4 (76.4–92.4)	79.3 (67.5–91.1)	94.0 (88.7–99.3)	96.6 (91.8–100)	99.2 (97.7–100)	95.7 (89.8–100)	82.3 (71.6–93.9)	98.3 (90.7–100)
HBV3	62.5 (51.3–74.8)	62.3 (53.9–70.7)	63.1 (50.4–75.7)	85.9 (78.7–93.2)	79.3 (68.8–89.8)	92.2 (87.9–96.0)	87.1 (78.7–95.6)	68.3 (56.3–80.2)	81.0 (68.3–93.8)

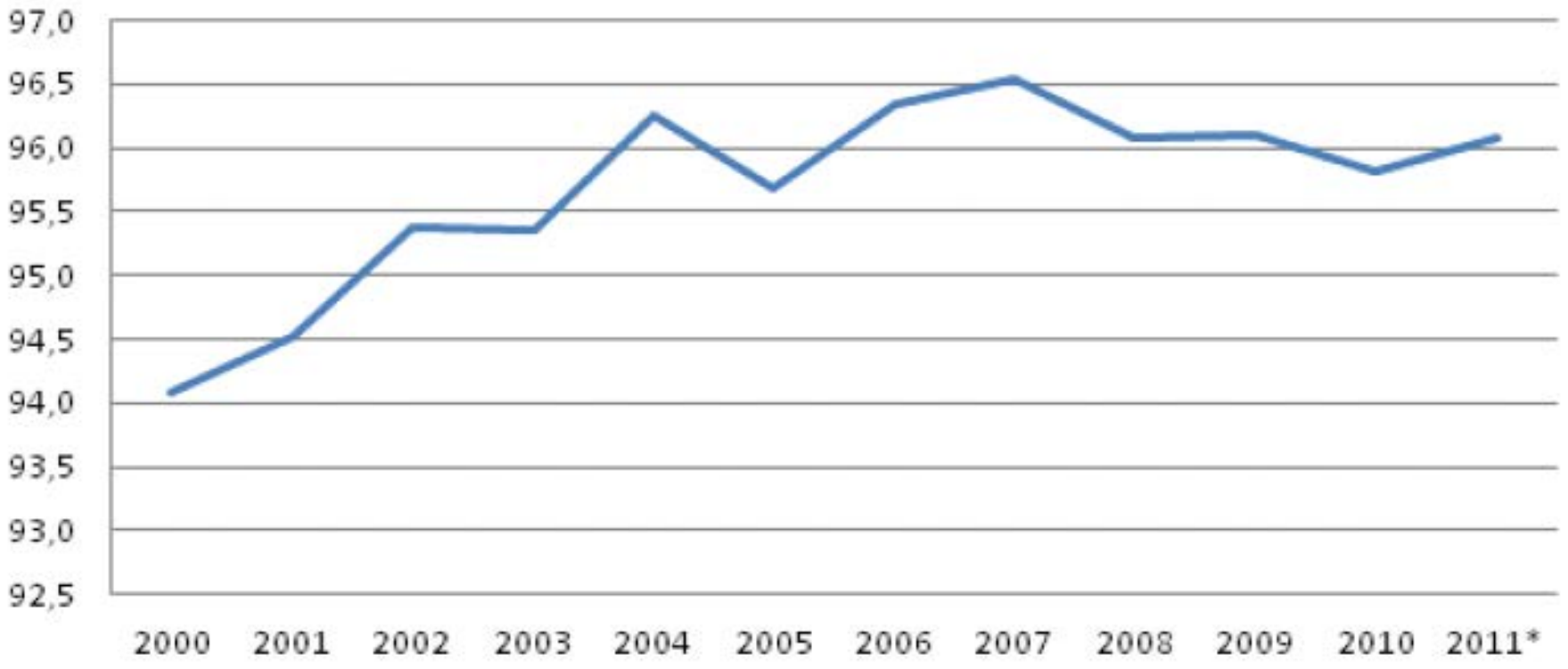
Copertura vaccinale anti HBV in Italia (3 dosi al 24 mese di età): coorte 1996

Coverage with three doses of hepatitis B vaccine (95%confidence intervals) at 24 months of age in 20 Italian Regions, 1998 (source: 5)

	Mean (95% CI)
Abruzzo	94.8% (91.4–98.2)
Basilicata	99.1% (97.8–100)
Bolzano	85.6% (80.6–90.7)
Calabria	94.8% (91.7–97.9)
Campania	97.6% (81.3–93.9)
Emilia R.	97.6% (95.7–99.6)
Friuli V.G	97.6% (95.7–99.6)
Liguria	97.6% (95.3–100)
Lombardia	97.6% (95.7–99.6)
Marche	94.8% (90.4–99.1)
Molise	89.1% (82.0–96.3)
Piemonte	98.6% (95.8–100)
Puglia	93.0% (89.1–96.9)
Sardegna	95.2% (92.4–98.0)
Sicilia	91.1% (86.1–96.1)
Toscana	95.2% (92.4–98.0)
Trento	98.1% (96.3–99.9)
Umbria	98.6% (97.0–100)
Val d'Aosta	100
Veneto	97.6% (95.7–99.6)

Salmaso S, Rota MC, Ciofi degli Atti ML, Tozzi AE, Kreidl P. and the ICONA Study Group: infant immunisation coverage in Italy: estimates by simultaneous EPI cluster surveys of regions. Bull WHO 1999;77:843–51

Copertura vaccinale anti HBV in Italia (3 dosi al 24 mese di età): coorti 2000-2011

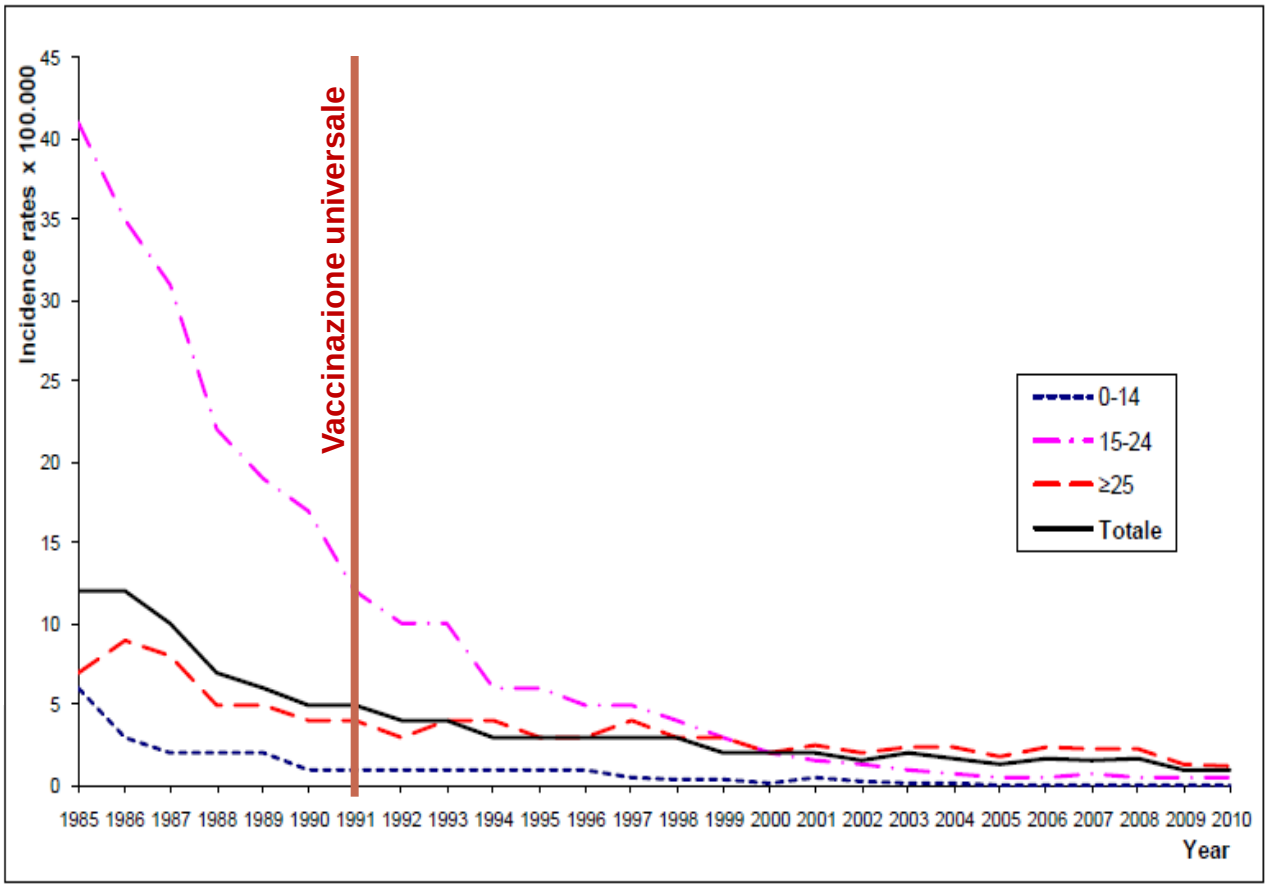


Ministero della Salute

http://www.salute.gov.it/imgs/C_17_pagineAree_811_listaFile_itemName_11_file.pdf
Accessed May 3, 2013

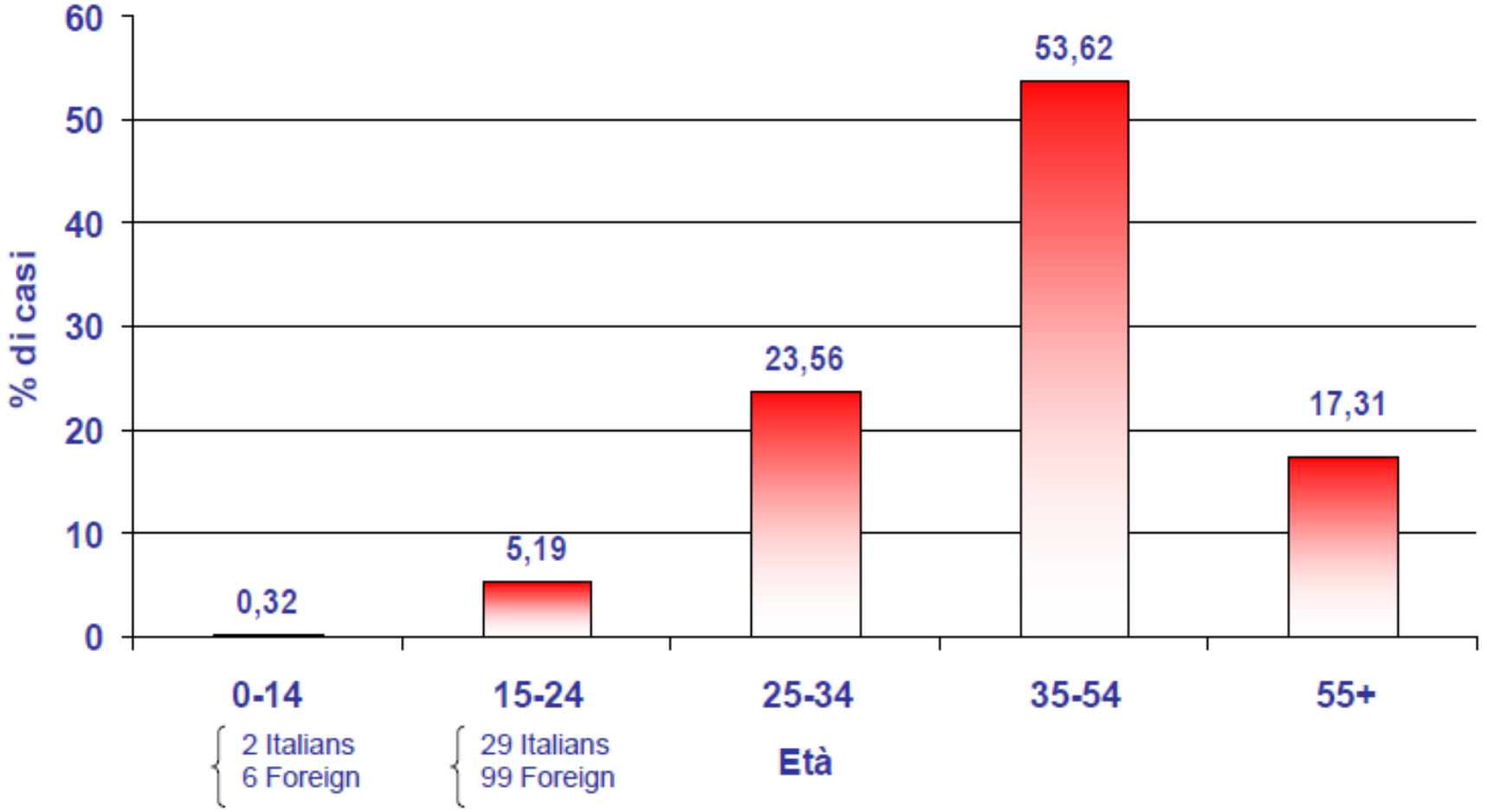
Incidenza di epatite acuta B (X 100.000 abitanti) Per età ed anno di notifica (1985-2010) SEIEVA

Year	Age			
	0-14	15-24	≥25	Tot
1985	6	41	7	12
1986	3	35	9	12
1987	2	31	8	10
1988	2	22	5	7
1989	2	19	5	6
1990	1	17	4	5
1991	1	12	4	5
1992	1	10	3	4
1993	1	10	4	4
1994	1	6	4	3
1995	1	6	3	3
1996	1	5	3	3
1997	0,5	5	4	3
1998	0,4	4	3	3
1999	0,3	3	3	2
2000	0,1	2	2	2
2001	0,5	1,5	2,5	2
2002	0,2	1,3	2	1,5
2003	0,1	0,9	2,3	2
2004	0,1	0,7	2,3	1,6
2005	0,02	0,5	1,8	1,3
2006	0,02	0,5	2,3	1,6
2007	0,05	0,7	2,2	1,5
2008	0,05	0,45	2,2	1,6
2009	0,01	0,5	1,3	1
2010	0,0	0,5	1,2	0,9

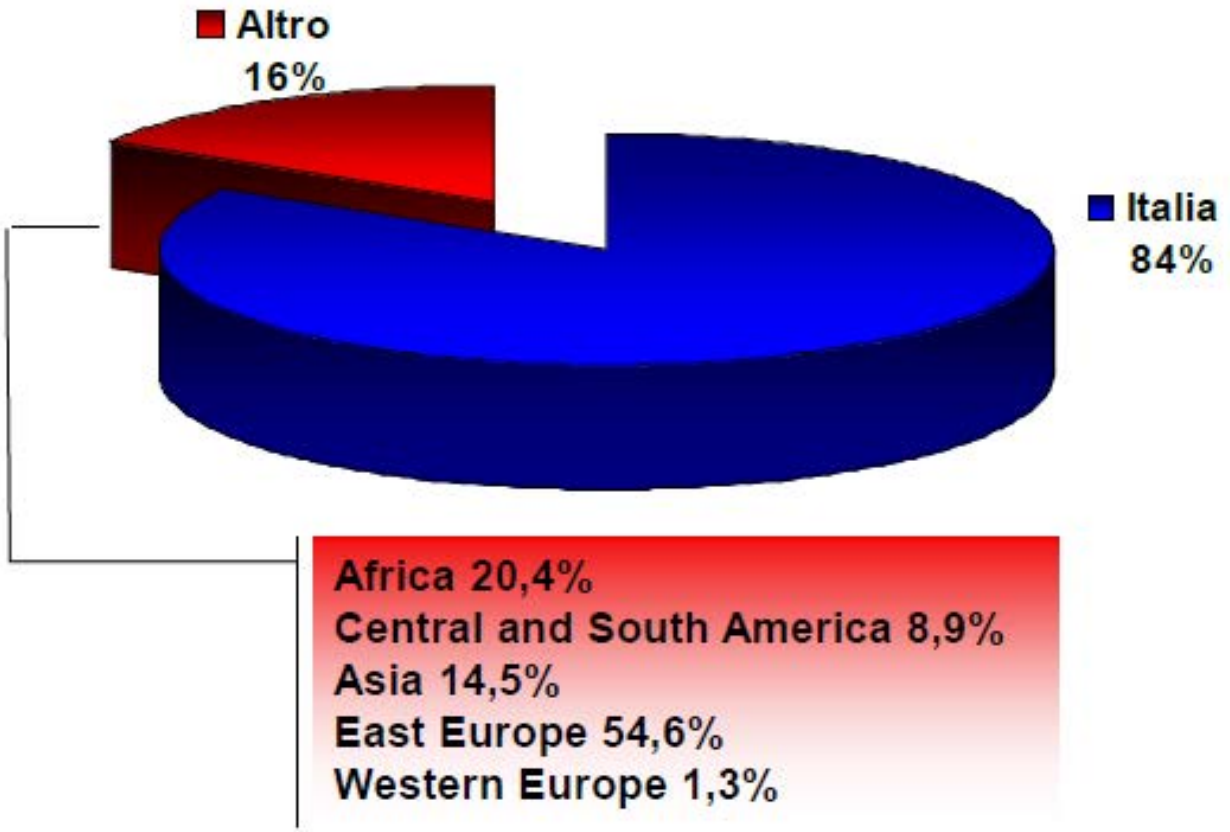


In Italia, tra il 1985 ed il 2010, si è osservato un declino dell'incidenza di epatite B. Il decremento ha interessato maggiormente il gruppo15-24 anni (quello maggiormente esposto al rischio fino al 1998).

Distribution of notified Hepatitis B cases by age
SEIEVA 2006-2010



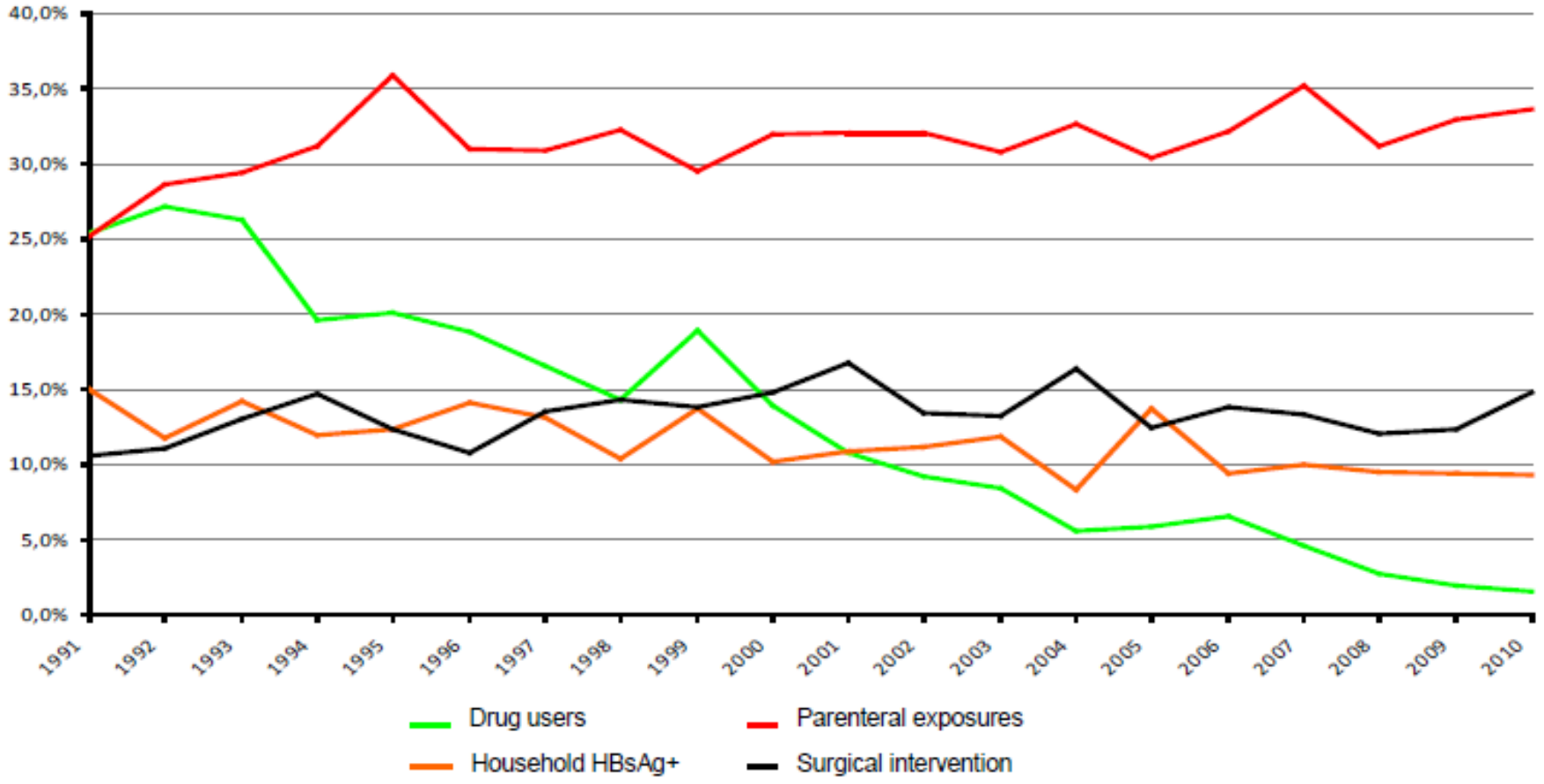
Cases of notified acute hepatitis B by nazionality SEIEVA 2006-2010



Risk factors for acute hepatitis B
SEIEVA 2006 - 2010

Risk factors	O.R.	(C.I.)	P.A.R.
I.V. drug users	2,2	(1,3 - 3,9)	2,1%
Surgical Intervention	1,7	(1,3 - 2,4)	5,5%
Other nosocomial exposures	1,8	(1,2 - 2,8)	4,2%
Other parenteral exposures	2,4	(1,9 - 2,9)	20,1%
Dental Therapy	1,5	(1,2 - 1,8)	9,4%
Household of HBsAg+	6,4	(3,8 - 10,5)	10,1%
Never/occasional condom use	3,2	(2,5 - 4,1)	13,8%

Frequency of reported risk factors by year
SEIEVA 1991-2010



Viral Hepatitis Prevention Board, Milan, Italy, November 17-18, 2011:
Hepatitis B vaccination: a completed schedule enough to control HBV lifelong?
Italy: Impact of universal vaccination programmes on the epidemiology of hepatitia B in Italy (SEIEVA results)
Alfonso Mele (Instituto Superiore di Sanita, Roma, Italy

Alfonso Mele
Istituto Superiore di Sanità

Trasmissione dell'HBV in Italia, SEIEVA 2009

Tipo di fattore di rischio	Fattore di rischio	Age							
		0-14		15-24		25 e +		Tot	
		n°	(%)	n°	(%)	n°	(%)	n°	(%)
Oro-fecale	Consumo di frutti di mare	0	(0)	6	(30)	149	(41)	155	(40)
	Contatto con itterico nelle sei settimane	0	(0)	0	(0)	8	(2)	8	(2)
	Notte fuori città	0	(0)	6	(32)	114	(31)	120	(31)
Parenterale o sessuale	Trasfusione sangue	0	(0)	0	(0)	8	(2)	8	(2)
	Interventi chirurgici	0	(0)	1	(5)	50	(13)	51	(12)
	Ospedalizzazione	0	(0)	1	(5)	32	(8)	33	(8)
	Other parenteral exposures	0	(0)	8	(38)	127	(33)	135	(33)
	Terapia odontoiatrica	1	(100)	3	(14)	124	(33)	128	(32)
	Uso di droghe E.V.	0	(0)	3	(14)	6	(2)	9	(2)
	Convivente Tossicodipendente	0	(0)	0	(0)	6	(2)	6	(2)
	Contatto con itterico nei sei mesi	0	(0)	2	(11)	22	(6)	24	(6)
	Sexual partners	0	(0)	6	(33)	128	(38)	134	(38)
	Convivente di soggetto HBsAg+	0	(0)	3	(21)	28	(9)	31	(10)
	Convivente di soggetto HCV+	0	(0)	0	(0)	9	(3)	9	(3)
	Tot* **	1		23		399		424	

* I casi possono avere più di un fattore di rischio
** Piercing, tatuaggi, agopuntura, manicure/pedicure, rasatura dal barbiere
*** Per alcuni casi l'informazione relativa ad alcuni fattori di rischio non è disponibile

Esposizione parenterale (piercing, tatuaggi, agopuntura, pedicure, etc.), cure odontoiatriche e promiscuità sessuale sono I fattori di rischio prevalenti. I soggetti a maggior rischio sono gli over 25 anni.

RISULTATI DELLA VACCINAZIONE CONTRO L'EPATITE B IN ITALIA (II)

La percentuale dei portatori di HBsAg si è ridotta:

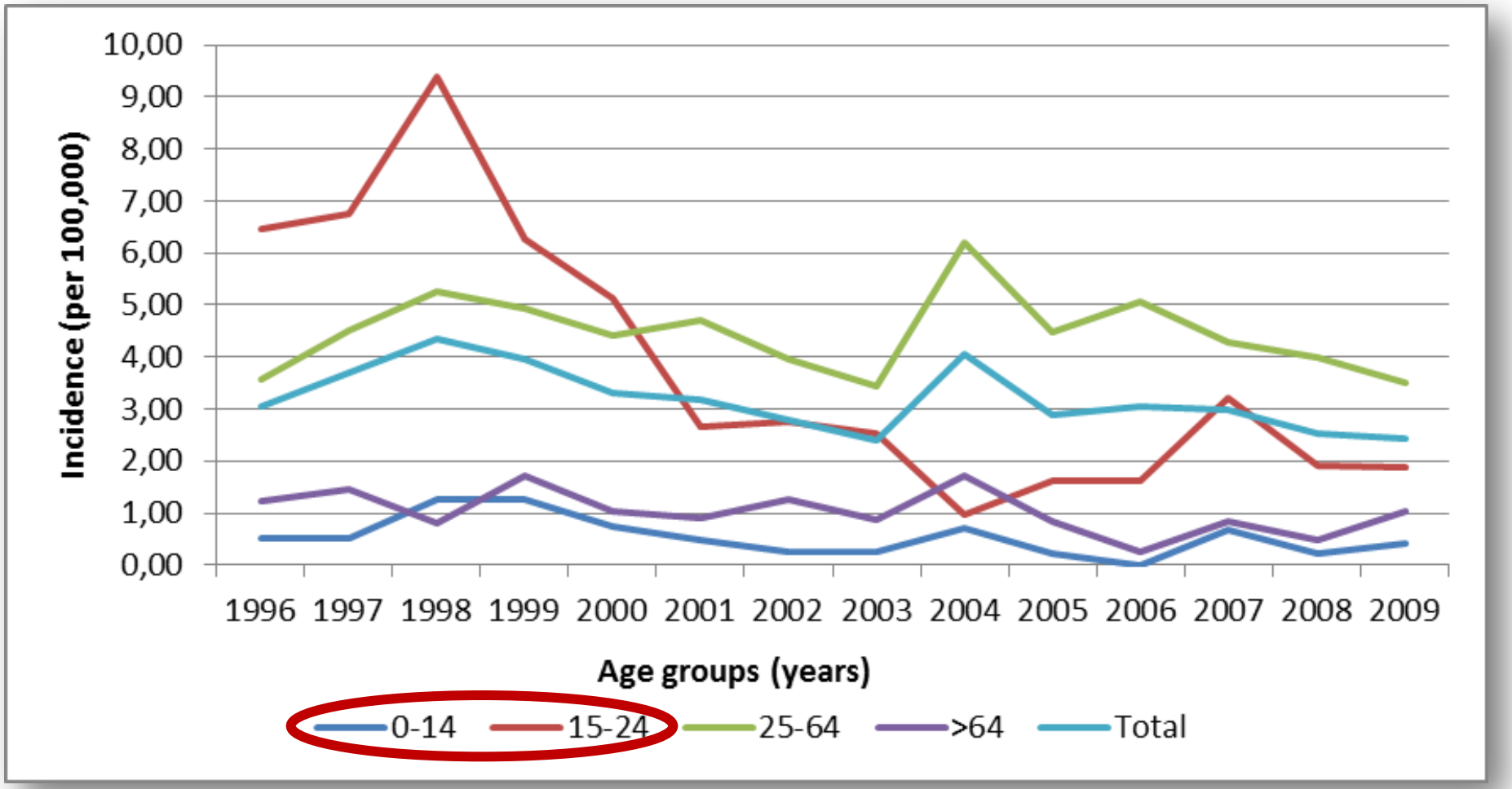
1980 - 5% → **1997 - 0,9%**

(Squarcione S., 1997; Da Villa G, 1998)

Ad Afragola, l' incidenza dell'epatite acuta B è crollata da 63 casi /100.000 abitanti prima della vaccinazione a 1 caso /100,000 (negli utlimi 5 anni).

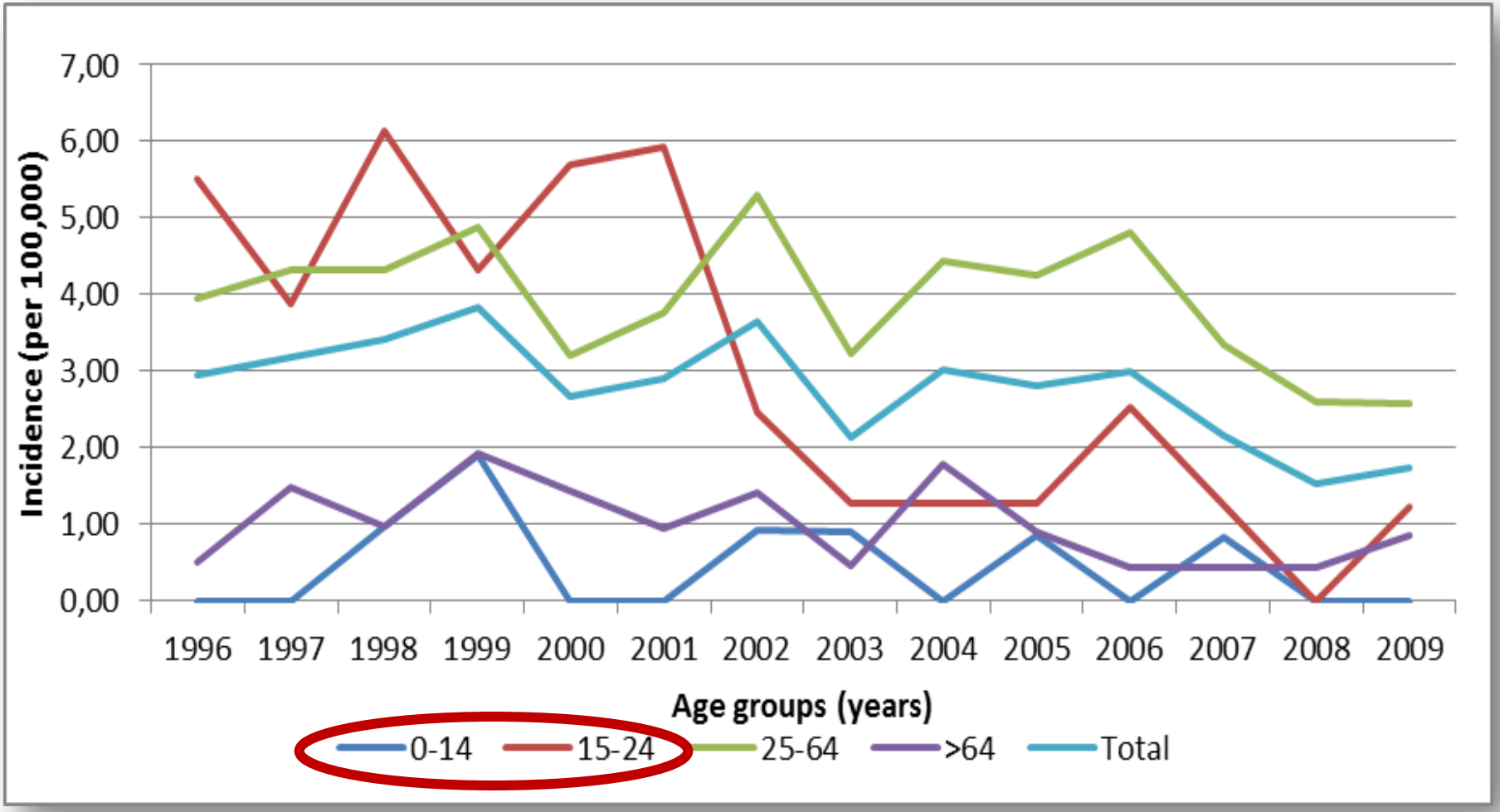
Anche la percentuale dei portatori di HBsAg si è ridotta da 13,4% del 1978 ad 1,85% nel 1999 e con essa le sequele croniche dell'infezione (Da Villa G., 2000).

Un esempio regionale
Incidenza di epatite B in Toscana



Ministry of Health

Incidenza di epatite B in provincia di Firenze



Ministry of Health

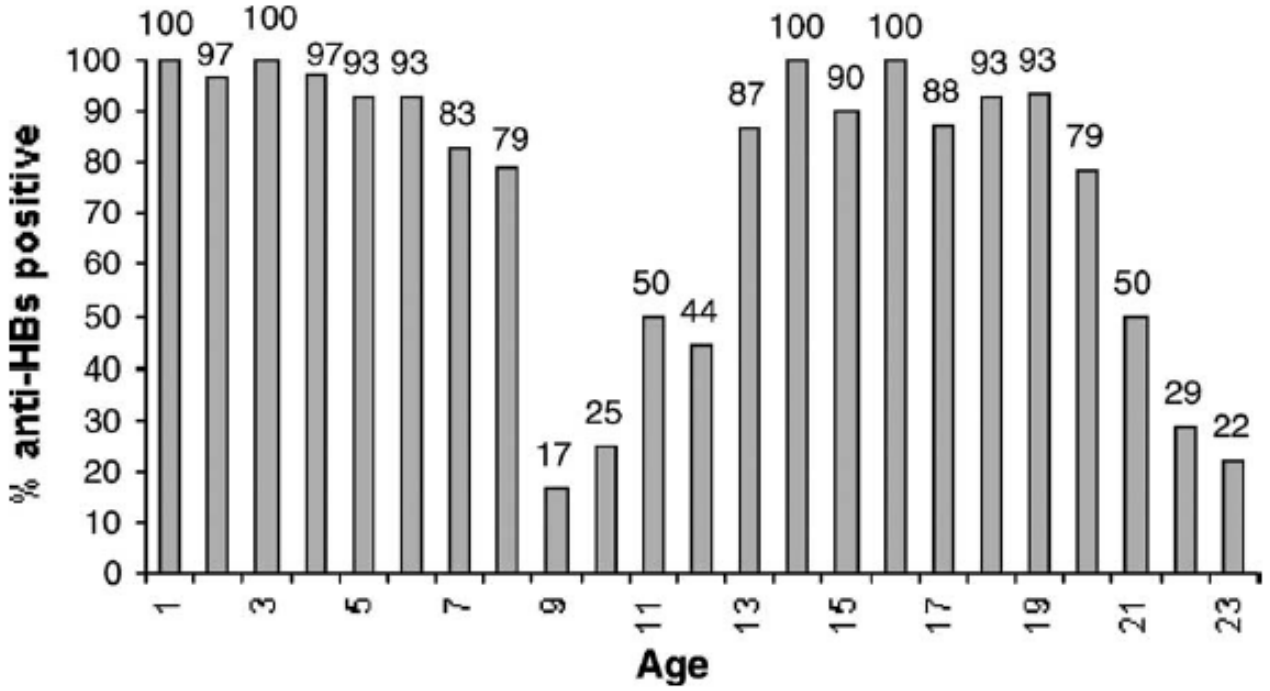
ELSEVIER

Vaccine 21 (2003) 685–691

www.elsevier.com/locate/vaccine

Impact of universal vaccination programmes on the epidemiology of hepatitis B: 10 years of experience in Italy

Paolo Bonanni [a,*], Giovanna Pesavento [a], Angela Bechini [a], Emilia Tiscione [a], Francesco Mannelli [b], Cristiana Benucci [b], Antonella Lo Nostro [a]



Prevalence of anti-HBs reactivity (≥10 mIU/ml) in anonymous sera collected from subjects aged 1–23 years living in Florence (year 2000).

Un'analisi su sieri anonimizzati rivela l'eccellente livello di immunità verso HBV acquisita dalle coorti di età incluse nel programma di vaccinazione universale, che spiega il declino osservato nelle curve di incidenza.

20 anni dopo l'implementazione della vaccinazione universale in Toscana

RESEARCH PAPER

Human Vaccines & Immunotherapeutics 9:3, 1–6; March 2013; © 2013 Landes Bioscience

Sero-epidemiology of hepatitis B markers in the population of Tuscany, Central Italy, 20 years after the implementation of universal vaccination

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Introduction

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In recent years, the European Centre for Disease Prevention and Control reported a decrease of new cases of hepatitis B in Western and Eastern Europe.[2] Particularly, the reduction of hepatitis B incidence can be explained by the adoption of effective vaccination programs against HBV infection, to a greater emphasis on the use of condoms to prevent sexually transmitted infections, to implementation of health promotion campaigns and to the compliance to universal precautions and use of disposable health devices. As a matter of facts, in 1995, 6.7 cases of hepatitis B per 100,000 inhabitants were reported in Europe; in 2007, that number dropped to 1.5 cases per 100,000 inhabitants.[2]

Vaccination strategies for control of HBV infection were initially focused on the immunization of high-risk groups (like men who have sex with men, health care workers, intravenous drug users, people with multiple sex partners, people living in households with chronic carriers etc.) and newborns to HBsAg carrier mothers who were screened during pregnancy. In 1992, the WHO recommended that all countries should introduce HBV universal vaccination in their national immunization programs, in addition to immunization of people at increased behavioral or professional risk of exposure to HBV.[3,4]

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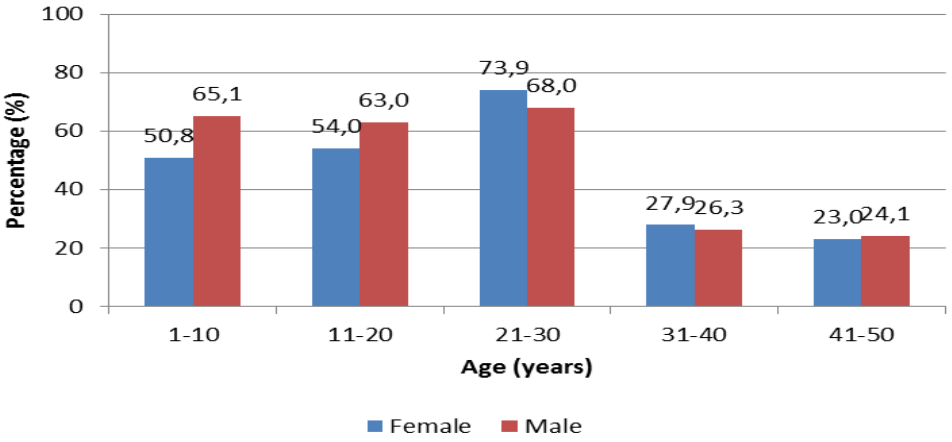
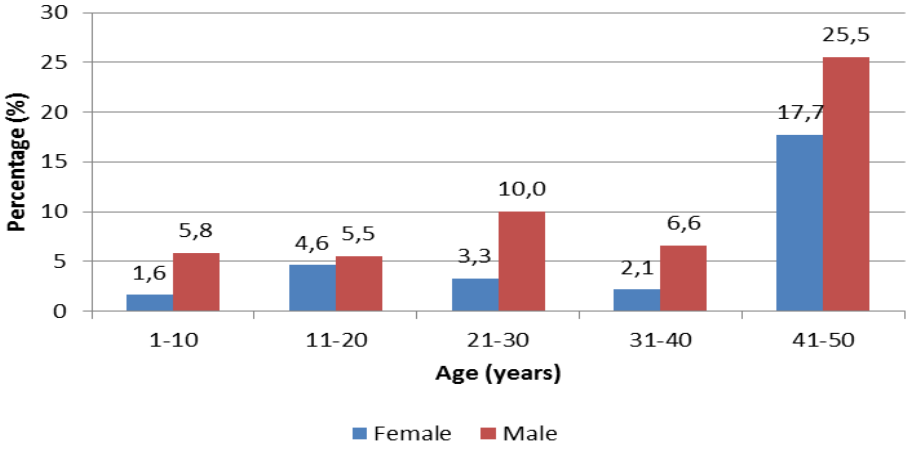
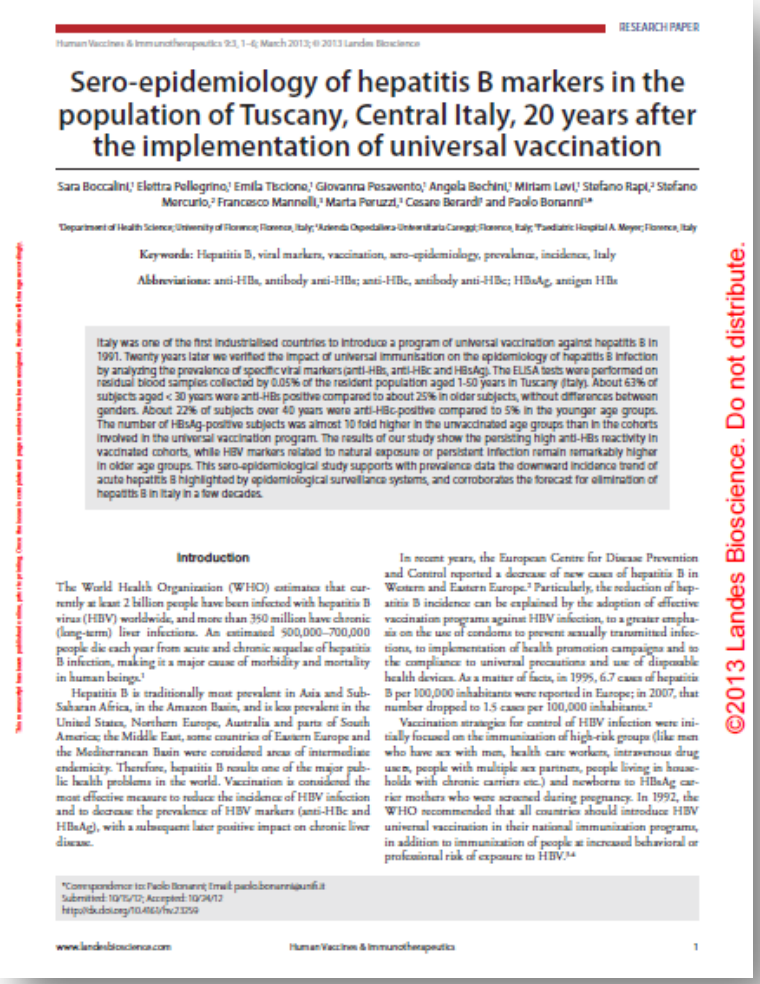
Submitted: 10/15/12; Accepted: 10/24/12
http://dx.doi.org/10.4161/hv.23259

Prevalenza di anti-HBs



Prevalenza di anti-HBc





RESEARCH PAPER

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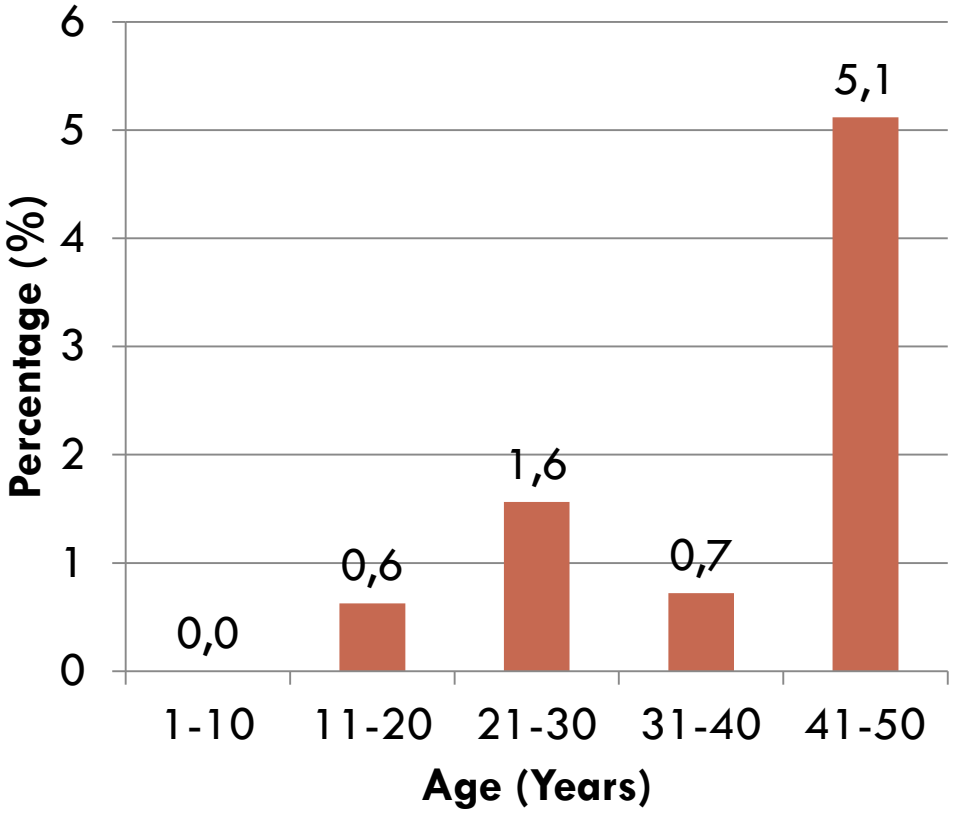
Submitted: 10/15/12; Accepted: 10/24/12
http://dx.doi.org/10.4161/hv.23759

20 anni dopo l'implementazione della vaccinazione universale in Toscana

Prevalenza di HBs Ag



Il numero di soggetti HBsAg-positivi è risultato circa 10 volte più alto nei non vaccinati rispetto alle coorti target della vaccinazione

Impatto economico della vaccinazione HBV in Italia

ELSEVIER

Vaccine 17 (1999) 1734–1738

Immunization programme against hepatitis B virus infection in Italy: cost-effectiveness

G. Da Villa*, A. Sepe

Italian Institute for Prevention of Liver Diseases, WHO Collaborating Center, Via Generale Orsini, 42, 80132 Naples, Italy

Saving of assistance and social expenditure associated with AVH in Italy from 1991 to 1996

	1985–1990	1991–1996	Saving
No. cases	35,614	17,608	18,006
Assistance cost	400,658,000	198,090,000	202,568,000
Social cost	82,558,000	40,818,000	41,740,000

Thousand USD.

6 years later the implementation (1996)

In the light of these preliminary results, the saving of costs due to the fall in AVH cases amounts to 2/3 of expenditure on vaccination. Moreover, observing the incidence trend of new infections in the last few years, we can estimate a progressive further increase in savings. But the main economic goal of vaccination will be reached starting from 2006, after 15 years of immunization, when we will begin to save money in the treatment of cirrhosis and HCC too.

Da Villa, 1999

Impatto economico della vaccinazione HBV a 20 anni dall'implementazione

- **1991**: introduzione della vaccinazione universale

Oggi: **20 anni più tardi**

  - **Quali sono stati i costi sostenuti e quelli evitati a 20 anni dall'introduzione?**
  - **E' stata giustificata dal punto di vista clinico ed economico?**

→ **analisi economica "a posteriori" con ulteriori benefici clinici/economici fino al 2059**

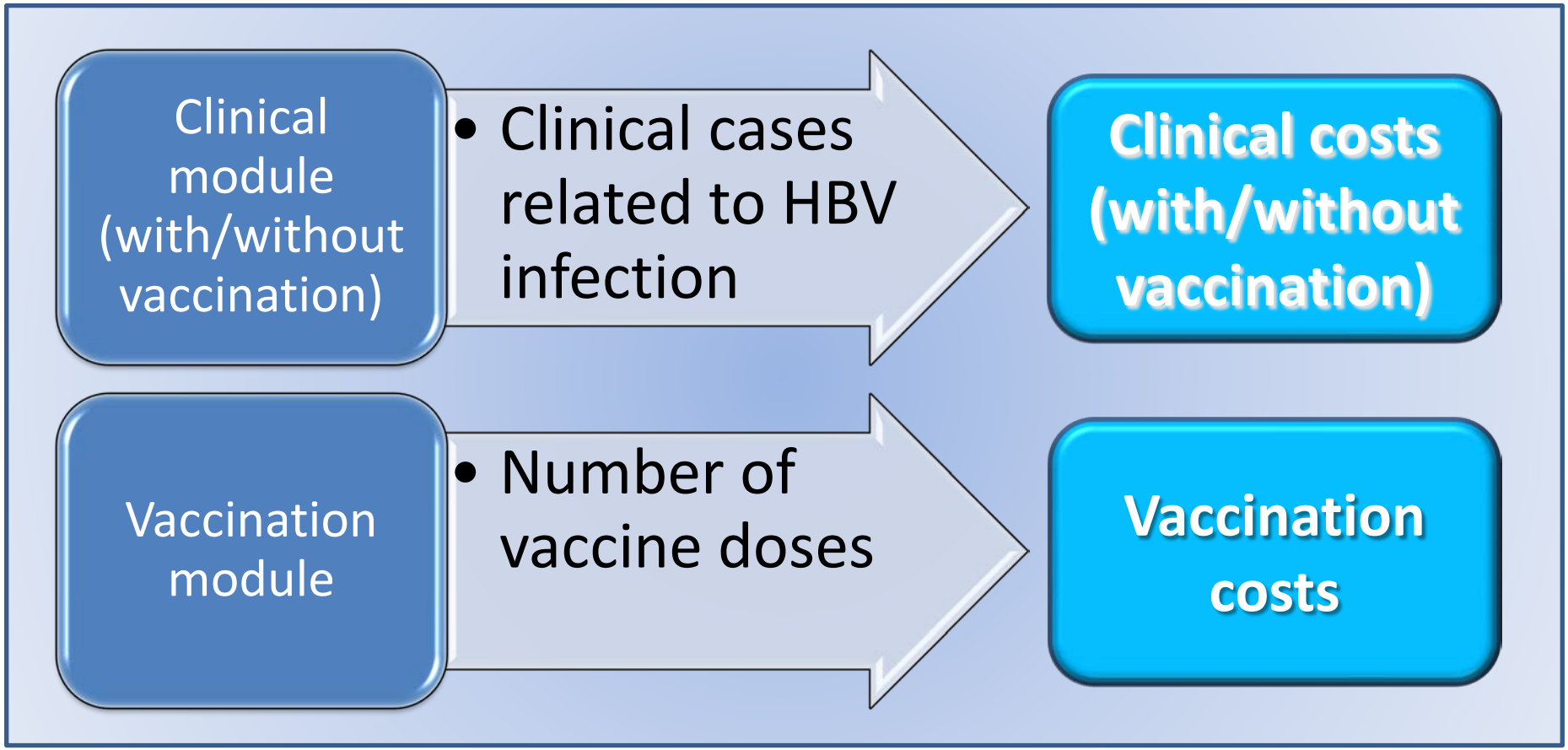
Analyzed scenarios

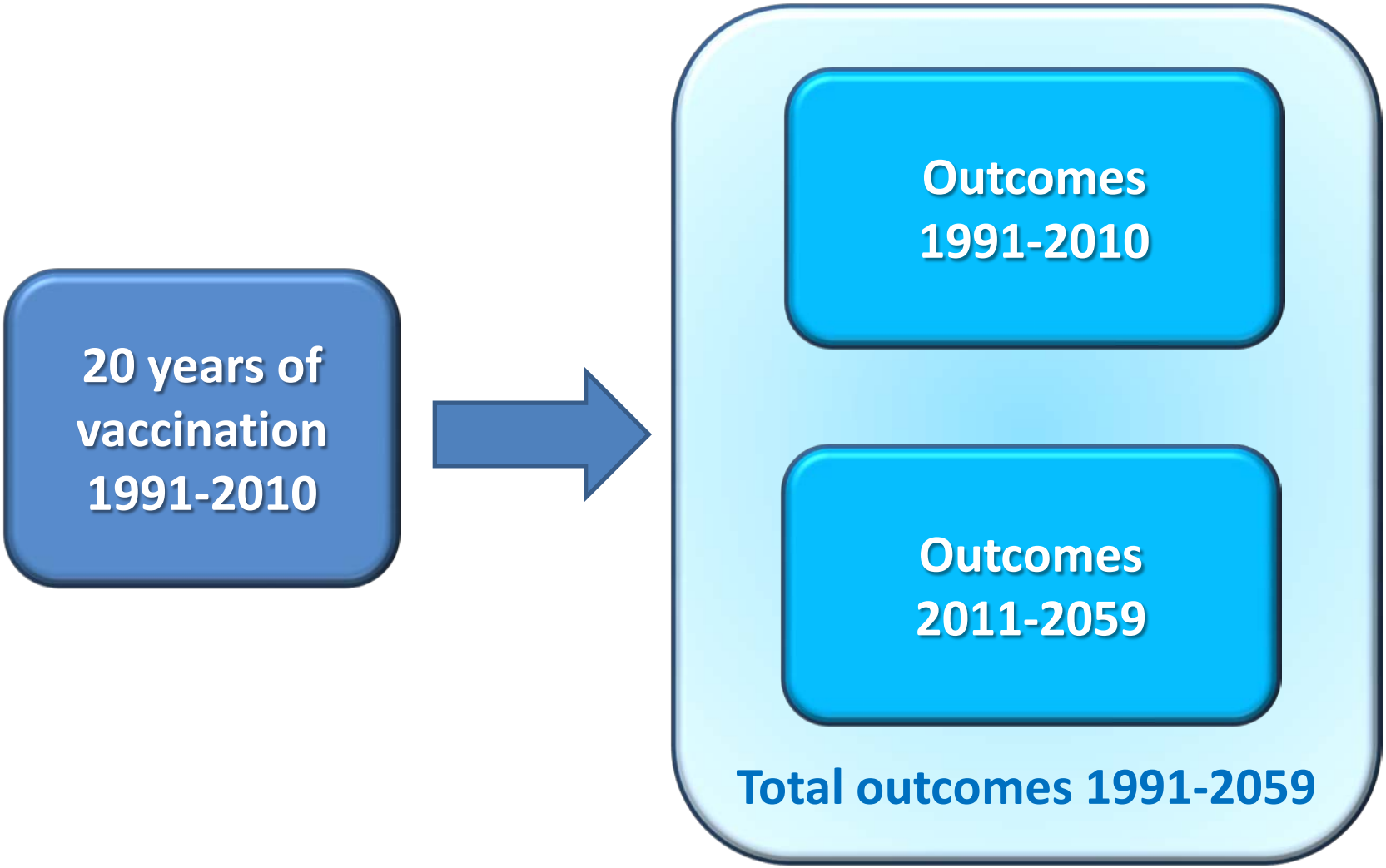
- **Vaccination program in Italy (1991-2010)**

versus

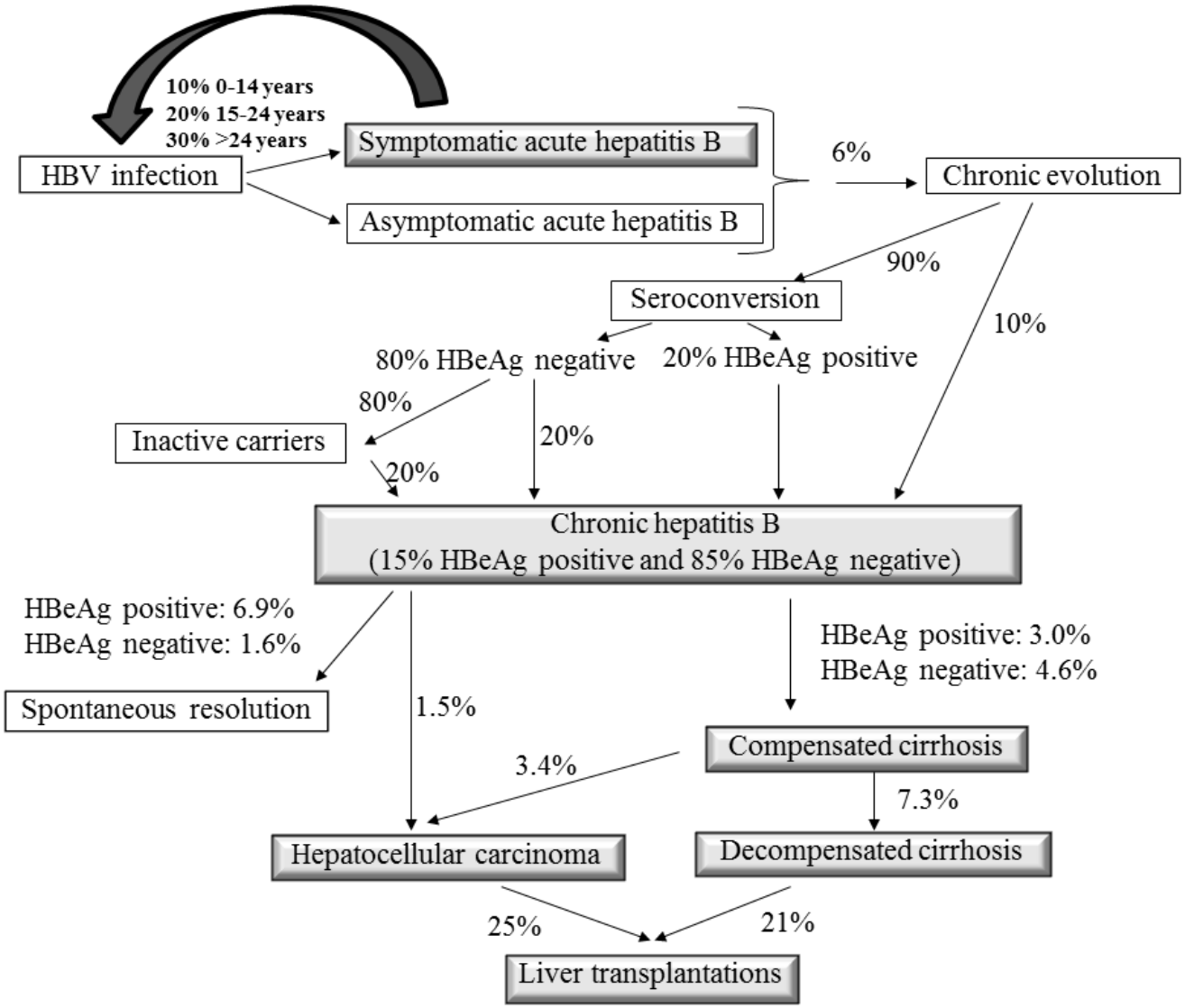
- **No vaccination program (1991-2010):** in the scenarios of slowly decreasing hepatitis B incidence due to some impact of other preventive interventions

Mathematical model




20 years of vaccination 1991-2010
Outcomes 1991-2010
Outcomes 2011-2059
Total outcomes 1991-2059

Natural history of hepatitis B



Impatto economico della vaccinazione HBV in Italia a 20 anni

RESEARCH PAPER

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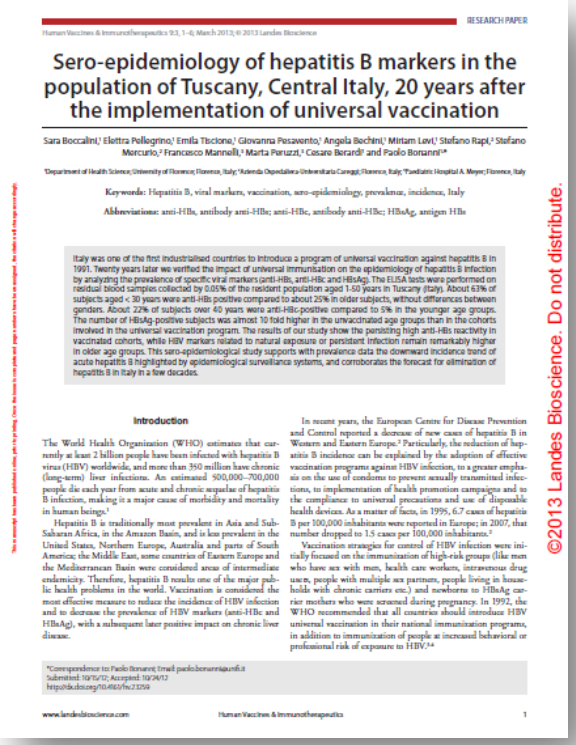
Submitted: 10/15/12; Accepted: 10/24/12
http://dx.doi.org/10.4161/hv.23259

Table 1. Total number of clinical cases related to HBV infection in Italy

Clinical Cases	No-vaccination	Vaccination	Avoided cases	% reduction
HBV infection	168,930	42,038	126,892	75
AHB	43,140	28,520	14,621	34
CHB	5,465	1,360	4,105	75
CC	129	59	70	54
DC	9	4	5	54
HCC	86	22	64	74
LT	24	7	17	72



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Submitted: 10/15/12; Accepted: 10/24/12
http://dx.doi.org/10.4161/hv.23259

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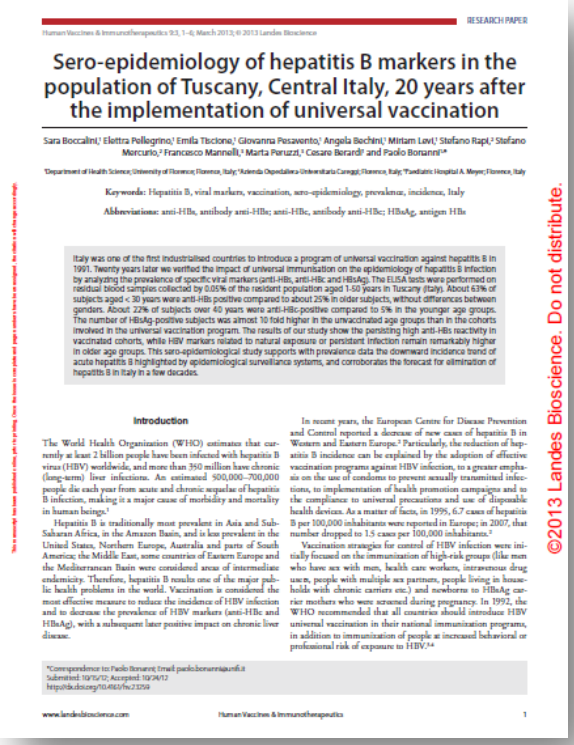
Table 2. Clinical costs during the period 1991–2010, 2011–2059 and 1991–2059 according to NHS and Societal perspective in the no-vaccination and vaccination scenario

PAST COSTS (1991–2010)				
NHS perspective				
	No-vaccination	**Vaccination**	**Avoided costs**	**% reduction**
AHB	572,051,723	362,160,953	209,890,771	37
CHB	649,157,949	210,059,569	439,098,380	68
CC	18,485,689	8,914,521	9,571,168	52
DC	1,193,807	575,700	618,107	52
HCC	8,330,359	2,830,361	5,499,999	66
LT	3,135,545	1,117,773	2,017,771	64
Total	***1,252,355,072***	***585,658,877***	***666,696,195***	***53***
Societal perspective				
	No-vaccination	**Vaccination**	**Avoided costs**	**% reduction**
AHB	689,926,159	436,786,229	253,139,930	37
CHB	763,780,696	247,150,087	516,630,609	68
CC	21,749,733	10,488,571	11,261,162	52
DC	1,404,599	677,353	727,247	52
HCC	9,801,263	3,330,121	6,471,141	66
LT	3,681,249	1,311,056	2,370,193	64
Total	***1,490,343,698***	***699,743,417***	***790,600,281***	***53***



RESEARCH PAPER

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FUTURE COSTS (2011–2059)

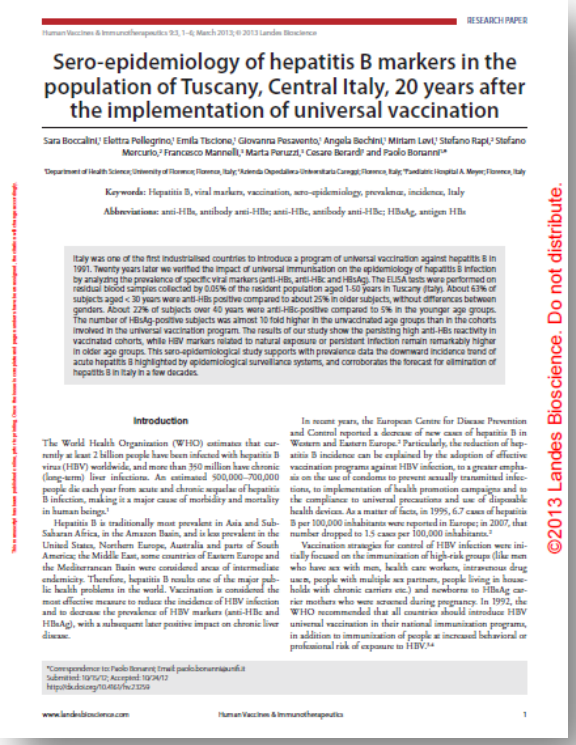
NHS perspective

	No-vaccination	Vaccination	Avoided costs	% reduction
AHB	0	0	0	0
CHB	1,407,135,406	312,317,653	1,094,817,753	78
CC	19,147,161	8,519,755	10,627,406	56
DC	795,200	342,980	452,219	57
HCC	61,994,027	16,534,566	45,459,461	73
LT	5,855,495	1,471,071	4,384,425	75
Total	***1,494,927,289***	***339,186,025***	***1,155,741,264***	***77***

Societal perspective

	No-vaccination	Vaccination	Avoided costs	% reduction
AHB	0	0	0	0
CHB	1,655,595,315	367,464,028	1,288,131,288	78
CC	22,528,002	10,024,100	12,503,902	56
DC	935,609	403,541	532,069	57
HCC	73,523,198	19,623,408	53,899,790	73
LT	6,546,747	1,625,042	4,921,705	75
Total	***1,759,128,872***	***399,140,118***	***1,359,988,754***	***77***

Note: costs assessed during 2011–59 are limited to those that acquired HBV during the 1991–2010 period.



RESEARCH PAPER

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TOTAL COSTS (1991–2059)				
NHS perspective				
	No-vaccination	**Vaccination**	**Avoided costs**	**% reduction**
AHB	572,051,723	362,160,953	209,890,771	37
CHB	2,056,293,355	522,377,222	1,533,916,133	75
CC	37,632,849	17,434,276	20,198,573	54
DC	1,989,007	918,681	1,070,326	54
HCC	70,324,386	19,364,927	50,959,459	72
LT	8,991,040	2,588,844	6,402,196	71
Total	***2,747,282,361***	***924,844,902***	***1,822,437,459***	***66***
Societal perspective				
	No-vaccination	**Vaccination**	**Avoided costs**	**% reduction**
AHB	689,926,159	436,786,229	253,139,930	37
CHB	2,419,376,011	614,614,115	1,804,761,896	75
CC	44,277,735	20,512,671	23,765,064	54
DC	2,340,208	1,080,893	1,259,315	54
HCC	83,324,461	22,953,529	60,370,932	72
LT	10,227,996	2,936,098	7,291,898	71
Total	***3,249,472,570***	***1,098,883,535***	***2,150,589,035***	***66***

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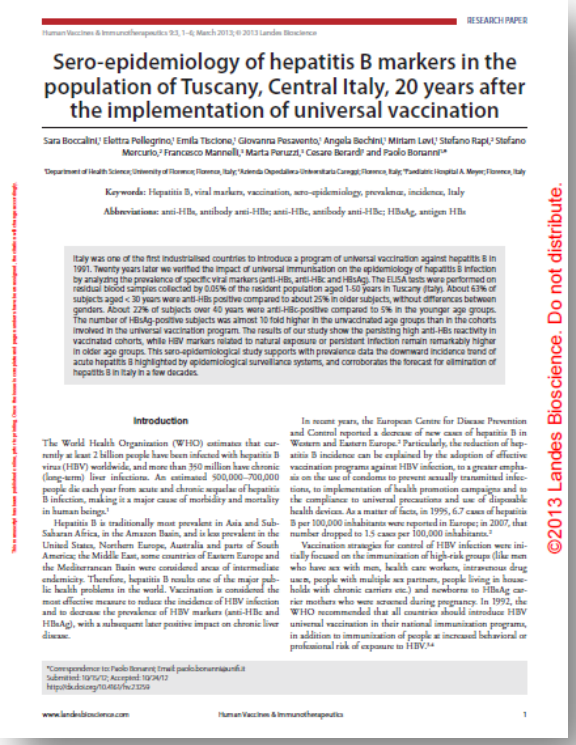

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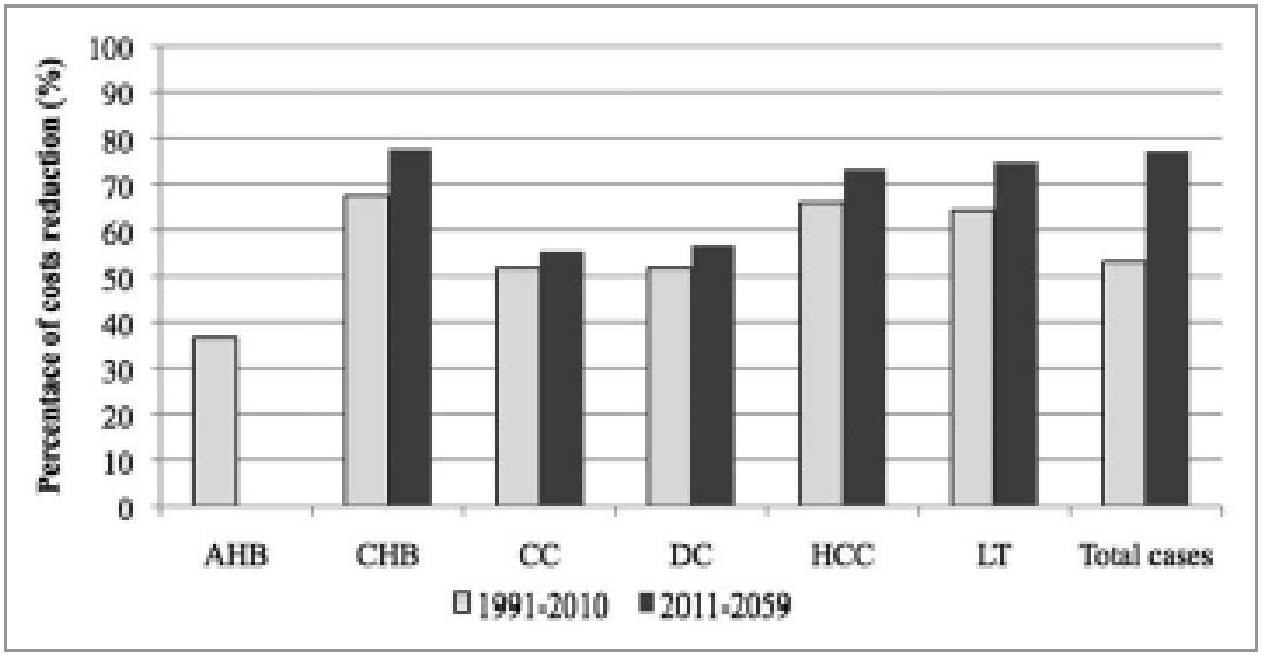

Figure 1. Percentage of clinical costs reduction due to implementation of the vaccination program in past and future years.

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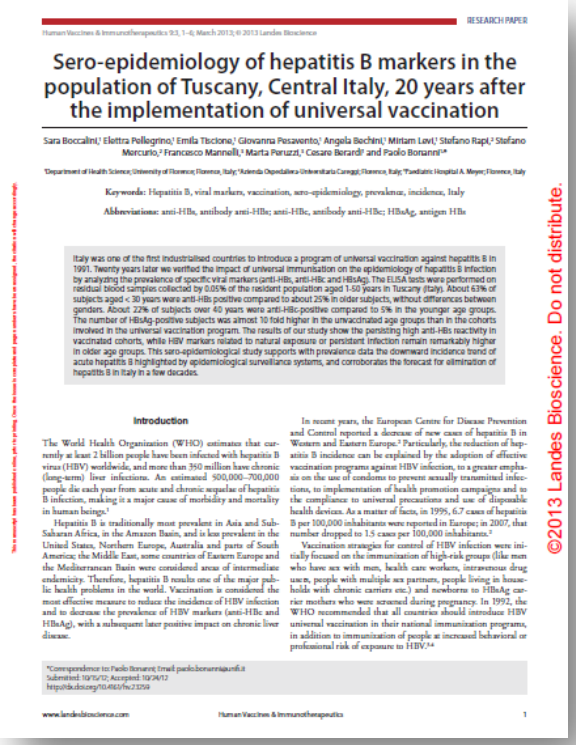

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Table 3. Savings during the first 20 y of the vaccination program (1991–2010) and overall saving (1991–2059)

Savings during the first 20 y of the vaccination program (1991–2010)		
	NHS perspective	**Societal perspective**
Clinical savings	666,696,195	790,600,281
Vaccination cost	655,675,042	872,002,316
Net costs	*-11,021,153*	*81,402,035*
ROI/BCR	**1.02**	**0.91**
Overall savings (1991–2059)		
	NHS perspective	**Societal perspective**
Clinical savings	1,822,437,459	2,150,589,035
Vaccination cost	655,675,042	872,002,316
Net costs	*-1,166,762,417*	*-1,278,586,719*
ROI/BCR	**2.78**	**2.47**

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Introduction

The World Health Organization (WHO) estimates that currently at least 2 billion people have been infected with hepatitis B virus (HBV) worldwide, and more than 350 million have chronic (long-term) liver infections. An estimated 500,000–700,000 people die each year from acute and chronic sequelae of hepatitis B infection, making it a major cause of morbidity and mortality in human beings.[1]

Hepatitis B is traditionally most prevalent in Asia and Sub-Saharan Africa, in the Amazon Basin, and is less prevalent in the United States, Northern Europe, Australia and parts of South America; the Middle East, some countries of Eastern Europe and the Mediterranean Basin were considered areas of intermediate endemicity. Therefore, hepatitis B results one of the major public health problems in the world. Vaccination is considered the most effective measure to reduce the incidence of HBV infection and to decrease the prevalence of HBV markers (anti-HBc and HBsAg), with a subsequent later positive impact on chronic liver disease.

In recent years, the European Centre for Disease Prevention and Control reported a decrease of new cases of hepatitis B in Western and Eastern Europe.[2] Particularly, the reduction of hepatitis B incidence can be explained by the adoption of effective vaccination programs against HBV infection, to a greater emphasis on the use of condoms to prevent sexually transmitted infections, to implementation of health promotion campaigns and to the compliance to universal precautions and use of disposable health devices. As a matter of facts, in 1995, 6.7 cases of hepatitis B per 100,000 inhabitants were reported in Europe; in 2007, that number dropped to 1.5 cases per 100,000 inhabitants.[2]

Vaccination strategies for control of HBV infection were initially focused on the immunization of high-risk groups (like men who have sex with men, health care workers, intravenous drug users, people with multiple sex partners, people living in households with chronic carriers etc.) and newborns to HBsAg carrier mothers who were screened during pregnancy. In 1992, the WHO recommended that all countries should introduce HBV universal vaccination in their national immunization programs, in addition to immunization of people at increased behavioral or professional risk of exposure to HBV.[3,4]

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Submitted: 10/15/12; Accepted: 10/24/12

http://dx.doi.org/10.4161/hv.23259

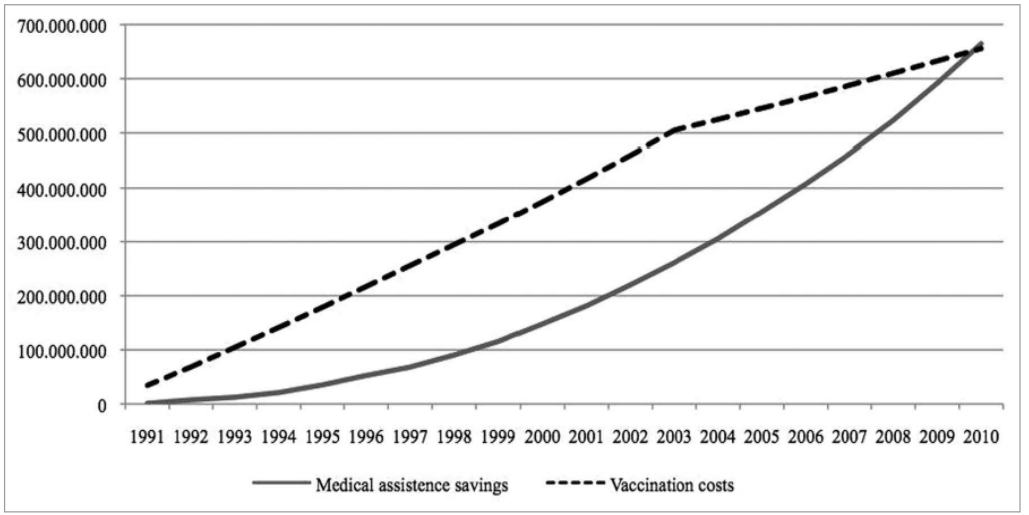


Figure 2. Cumulative clinical savings and vaccination costs in the NHS perspective during the period 1991–2010.

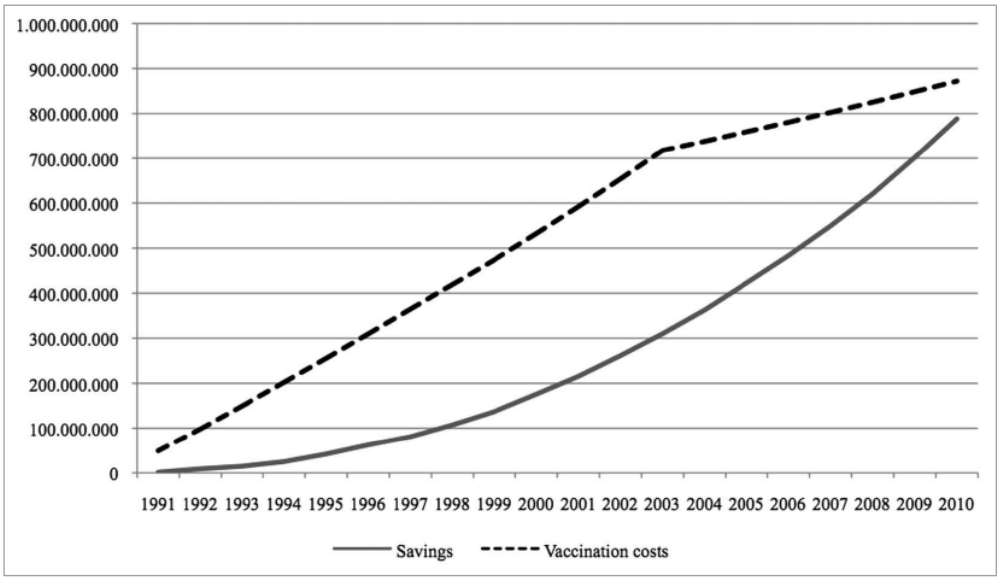
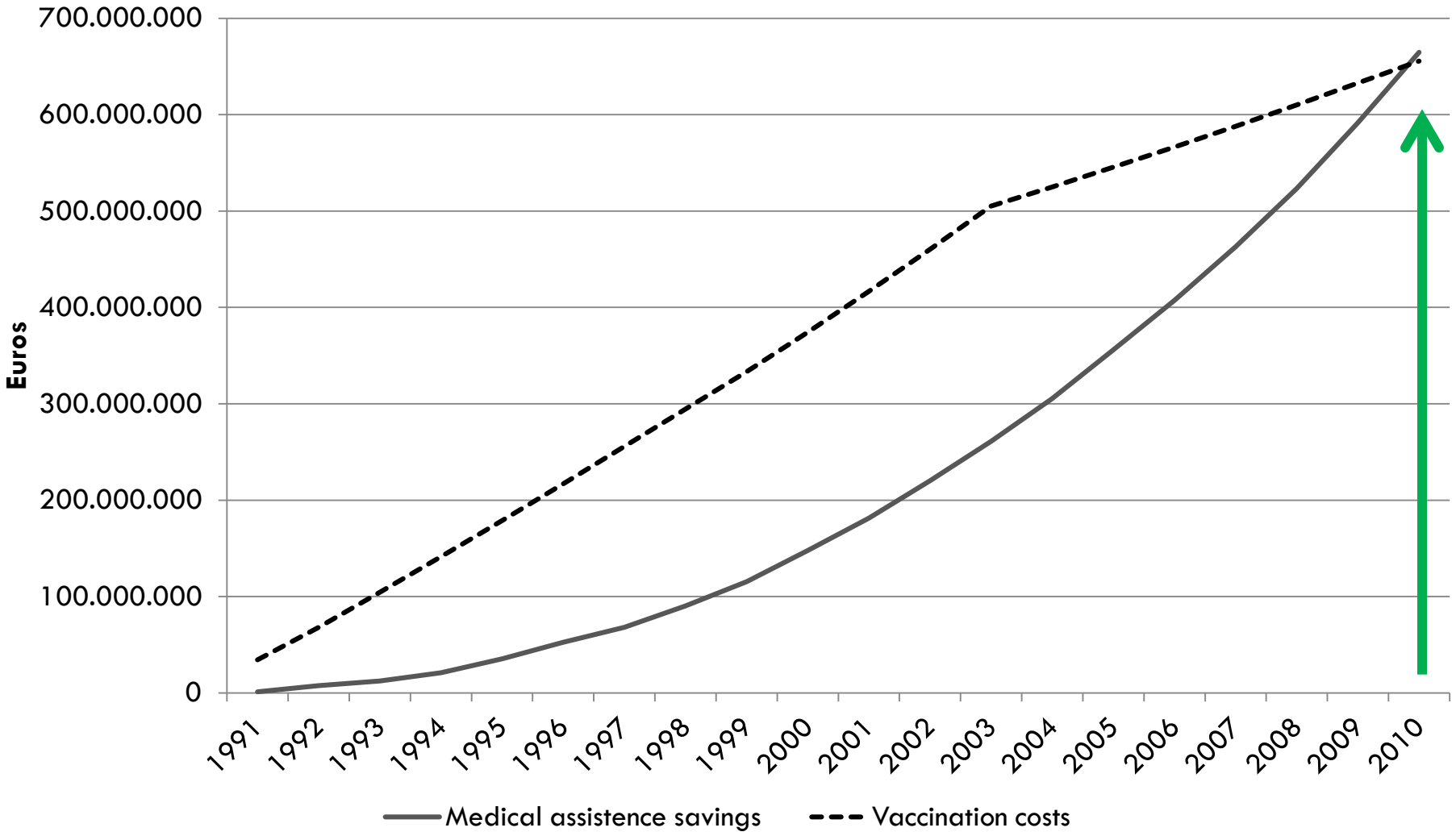


Figure 3. Cumulative clinical savings and vaccination costs in the Societal perspective during the period 1991–2010.

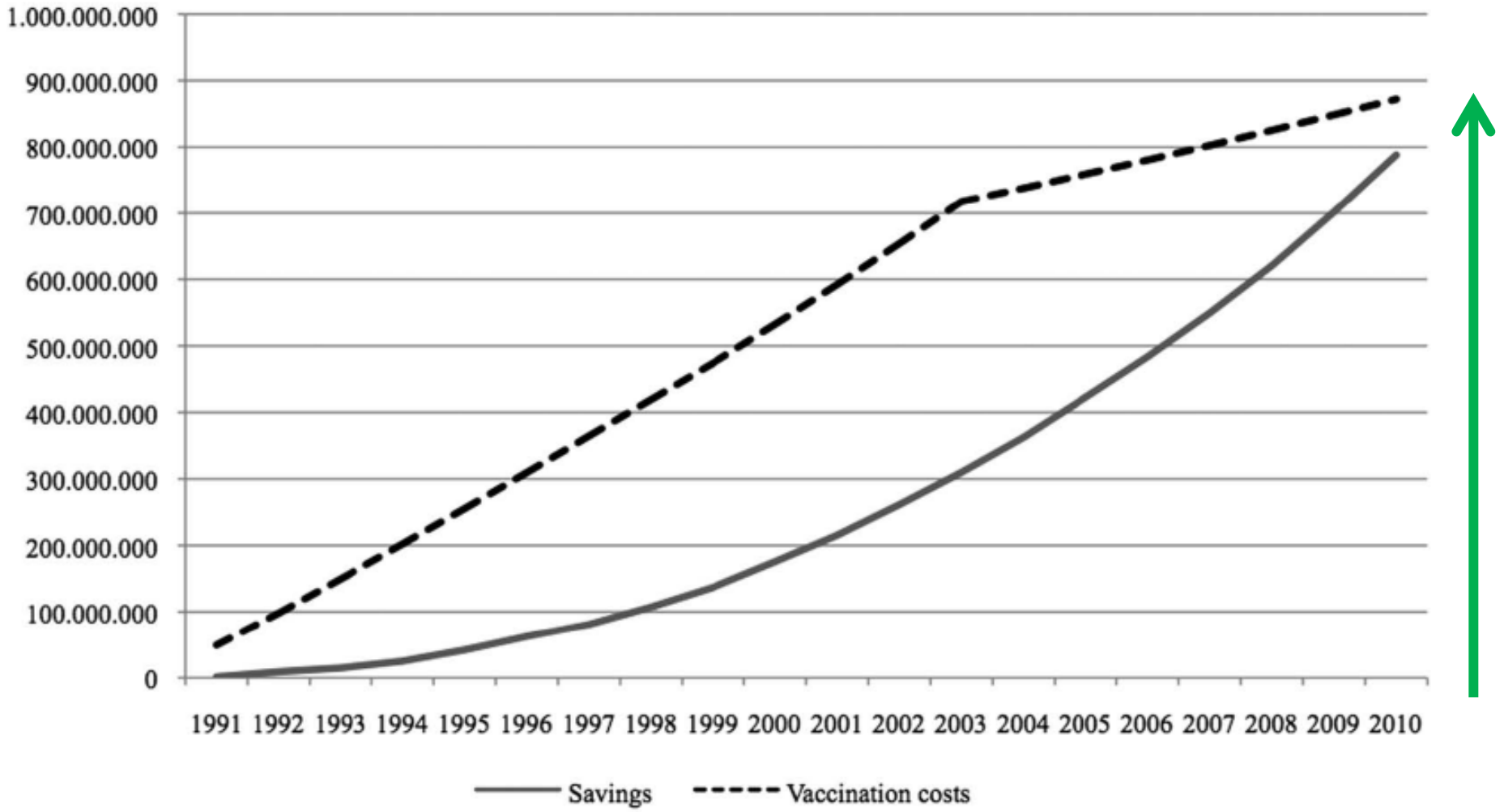
Savings (1991-2059)

	Payer perspective	Societal perspective
Clinical savings	1.822.437.459	2.150.589.035
Vaccination cost	655.675.042	872.002.316
Savings	*1.166.762.417*	*1.278.586.719*
Savings per avoided infection	9.195	10.076
Savings per vaccinated subject	68,26	74,80
Savings per administered vaccine dose	22,68	24,85
ROI/BCR	**2,78**	**2,47**

Cumulative costs and savings (Payer perspective 1991-2010)



Cumulative costs and savings
Societal perspective (1991-2010)



Sensitivity analysis

NHS perspective	N. HBV infection avoided	Net savings (1991-2010)	Net savings (1991-2059)	Savings per avoided infection (1991-2010)	Savings per avoided infection (1991-2059)	ROI (1991-2010)	ROI (1991-2059)
Baseline results	126.892	11.021.153	1.166.762.417	87	9.195	1,02	2,78
Adolescent vaccination coverage (95%)	126.892	-5.268.429	1.150.472.835	-42	9.067	0,99	2,71
>% symptomatic subjects (+10%)	88.351	-128.629.092	676.047.683	-1.456	7.652	0,80	2,03
Median age of chronic evolution (36 years)	126.892	11.021.153	1.080.801.052	87	8.517	1,02	2,65
Societal perspective	**N. HBV infection avoided**	**Net savings (1991-2010)**	**Net savings (1991-2059)**	**Savings per avoided infection (1991-2010)**	**Savings per avoided infection (1991-2059)**	**BCR (1991-2010)**	**BCR (1991-2059)**
Baseline results	126.892	-81.402.035	1.278.586.719	-642	10.076	0,91	2,47
Adolescent vaccination coverage (95%)	126.892	-109.211.314	1.250.777.440	-861	9.857	0,88	2,39
>% symptomatic subjects (+10%)	88.351	-245.709.317	701.172.609	-2.781	7.936	0,72	1,80
Median age of chronic evolution (36 years)	126.892	-81.402.035	1.177.470.063	-642	9.279	0,91	2,35

Limitations of the study (I)

- We did not take into account the turning from monovalent hepatitis B vaccine to combined vaccines, which might have changed the cost of the hepatitis B component (although probably not in a substantial way)

- The cost for treatment calculated based on the figures of 1990 and updated according to the annual inflation rate does not take into account the progressive availability of new (expensive) drugs for chronic hepatitis B

Limitations of the study (II)

- No effect of co-infections from HCV, HDV, HIV, or from alcohol and illegal drug consumption were taken into account in the model
- Life expectation for chronic hepatitis patients (not for cirrhosis and liver cancer) was considered equal to healthy people
- Overall, our model is probably highly conservative regarding the economic impact of vaccination (i.e. we probably underestimated economic benefits of the vaccination programme)

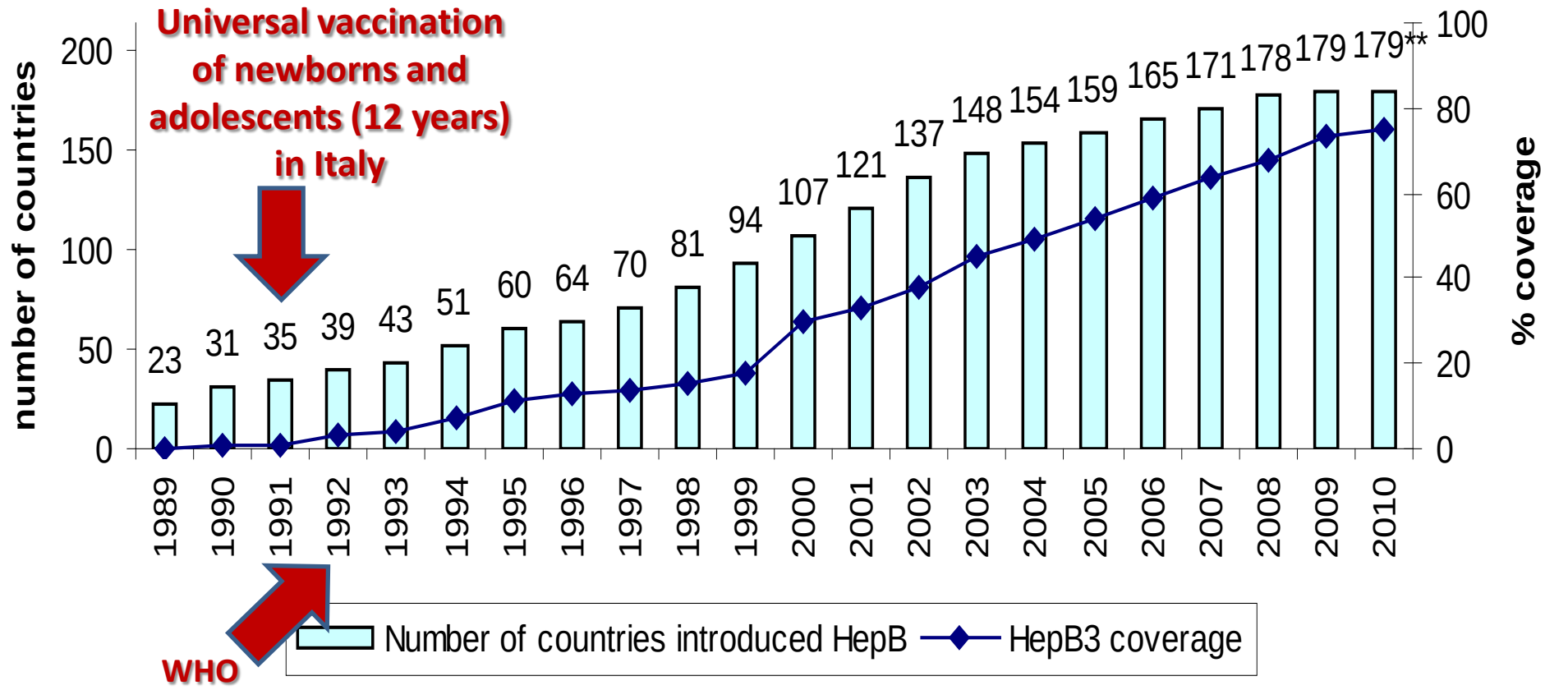
Conclusions

- **The introduction of universal hepatitis B vaccination in Italy was clinically and economically favorable during the first 20 years of adoption.**

- **Further clinically and economic benefits for this first period of vaccination will be increasingly evident in the future (chronic hepatitis, cirrhosis, hepatocellular carcinoma cases avoided and no longer requiring treatment).**

- **In the payer perspective, we certainly already reached the break-even point, and we are now progressively saving more and more money.**

Country introduction HepB* and global infant HepB3 coverage, 1989-2010



Source: WHO/UNICEF coverage estimates 2010 revision. July 2011; and IVB Database, 193 WHO Member States. Date of slide: 2 August 2011

* Year of introduction can be the year of partial introduction

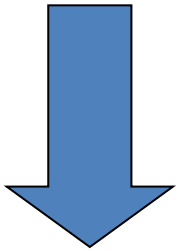
** Includes India and the Sudan with partial introduction excluding 3 countries where HepB administered for adolescence

RISULTATI DELLA VACCINAZIONE DI MASSA NELLE AREE IPERENDEMICHE

La vaccinazione di massa contro l'epatite B ha ridotto drasticamente la prevalenza della epatite cronica B in età pediatrica in: Gambia (dal 10% allo 0.6%), Taiwan, Cina, Indonesia, Senegal, Thailandia, Alaska e Malaysia (MMWR 2003; Ng et al., 2005)

A Taiwan, la vaccinazione di massa contro l'epatite B ha ridotto drasticamente ($p<0.001$) l'incidenza di cancro del fegato in età pediatrica (Huang K e Lin S, 2001).

COSA E' SUCCESSO NEI PAESI CHE AVEVANO ADOTTATO LA STRATEGIA DI VACCINARE SOLO I GRUPPI A RISCHIO?



FALLIMENTO

Miriam Alter in un editoriale pubblicato su Annals of Internal Medicine scrive: "le esperienze hanno dimostrato che la vaccinazione solo degli adulti e dei bambini a rischio non è stata efficace nel ridurre l'incidenza della malattia" (*Alter MJ*, 2003)

CLINICAL THERAPEUTICS®/VOL. 23, NO. 3, 2001

Hepatitis B Vaccines: Assessment of the Seroprotective Efficacy of Two Recombinant DNA Vaccines

Toby Coates, FRACP,[1] Rosamund Wilson, PhD,[2]
Guy Patrick, MRCP(UK), FRACP, PhD,[3]
Francis André, MBBS, MI Biol, FRC Path,[4]
and Virginia Watson, MR PharmS[5]

ABSTRACT

Background: In universal vaccination programs, when there is no postvaccination serologic assessment of response, there must be confidence that the vaccines used provide a high degree of seroprotection.

Objective: This parallel analysis of 2 recombinant hepatitis B vaccines (Engerix B® and Recombivax®/HB-Vax II®) was conducted to review the seroprotective efficacy of each vaccine in defined populations.

Methods: Clinical studies of the 2 vaccines published as manuscripts or conference abstracts in the public domain between January 1986 and April 1999 were identified retrospectively by unrestricted screening of journals through BIOSIS®, MEDLINE®, and EMBASE® and the Internet. Unpublished or internal company data were excluded to maintain impartiality. The studies were reviewed and analyzed. The studies were not assessed for quality other than a judgment of their eligibility for inclusion in the analysis. The primary outcome measure was the proportion of subjects in defined populations who showed an early seroprotective response to currently licensed vaccination schedules. Summary statistical analyses of seroprotective response rates and 95% CIs were calculated for each vaccine for each population. Seroprotective response was defined by an anti-hepatitis B surface antigen titer ≥10 IU/L measured between 1 and 3 months after the final vaccination. Because the study was designed specifically to review published immunogenicity data, safety data were not assessed. The study was not designed to demonstrate superiority of one vaccine over the other.

Sono stati rivisti 181 studi clinici con circa 33,000 soggetti vaccinati con 2 diversi vaccini lievito derivati

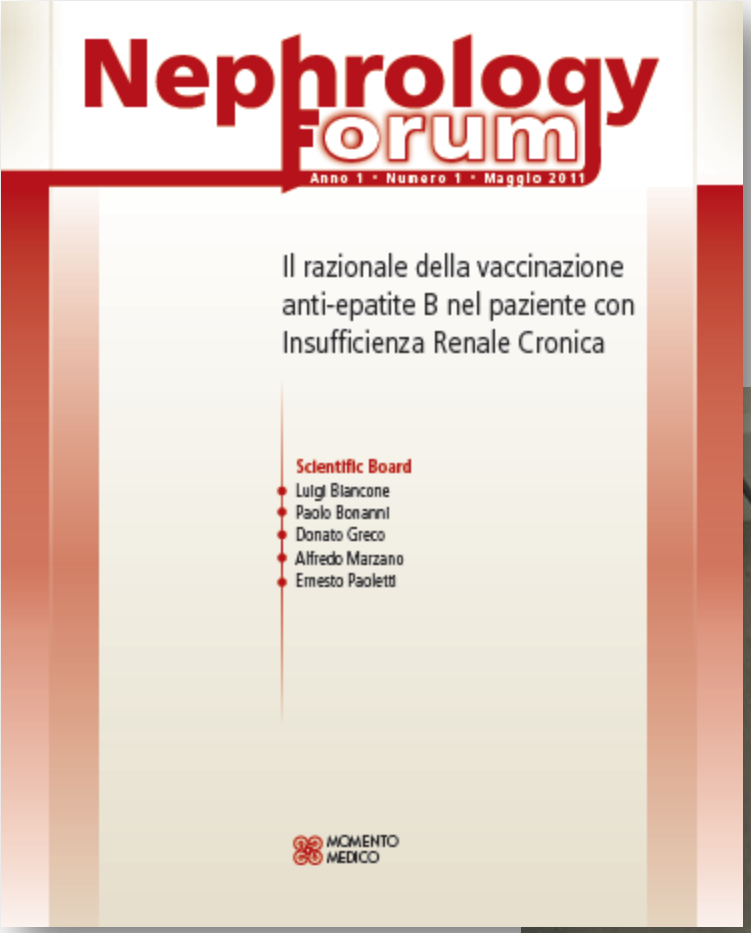
La sieroprotezione (>10 mIU/ml) è stata raggiunta nel 95.8% e 94.3% rispettivamente utilizzando la schedula a 3 dosi a 0, 1 e 6 mesi

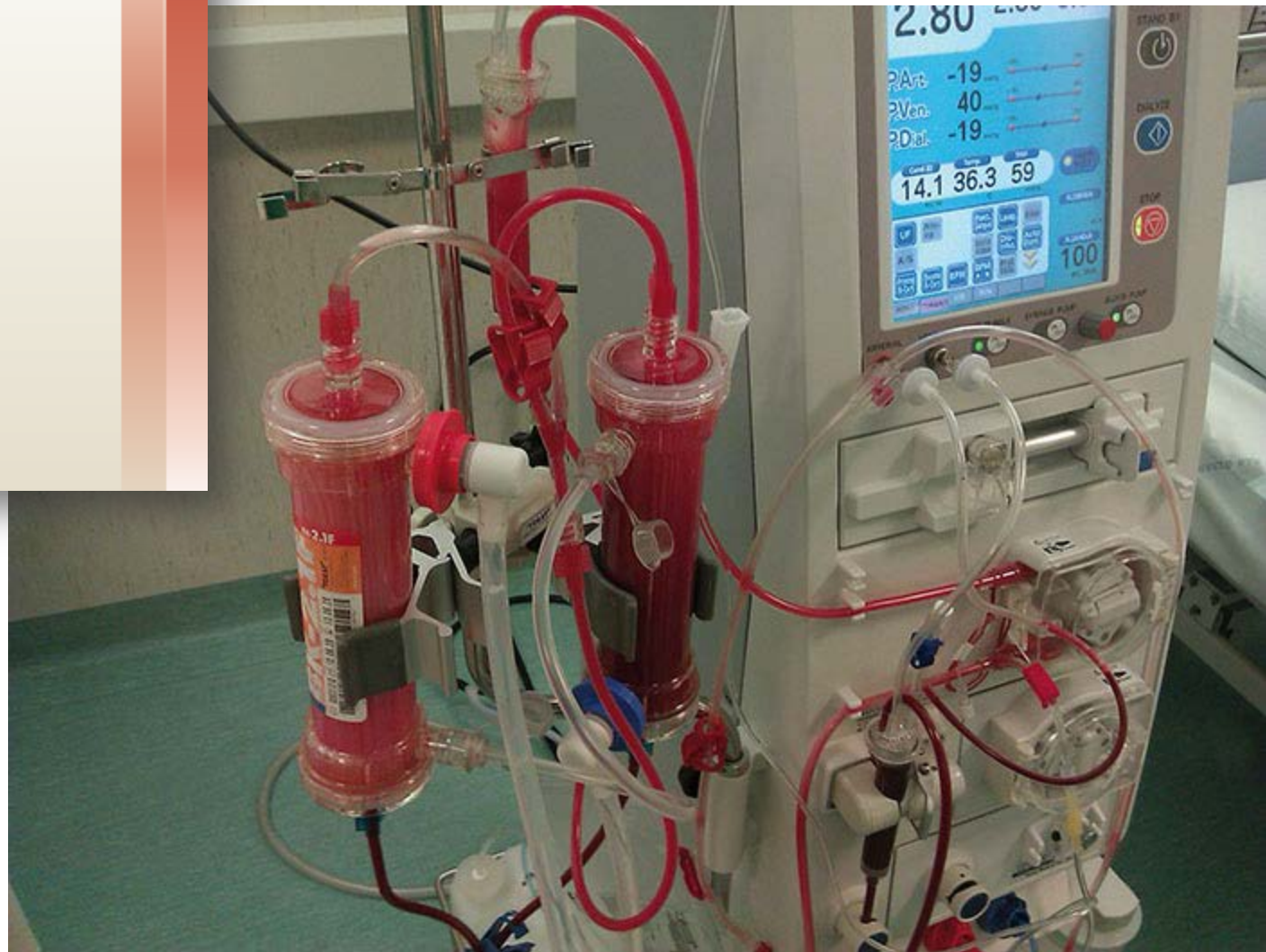
Il livello di non risposta nei bambini e negli adulti è risultato basso

ASPETTI PECULIARI

- **EMODIALIZZATI**
- **NON RESPONDERS**
- **OPERATORI SANITARI**
- **MIGRANTI**

EMODIALIZZATI





Inquadriamo il problema:
La vaccinazione anti-HBV nel paziente con IRC

- Il numero di soggetti in dialisi in Italia è circa **40.000-50.000**[1,2]
- Ogni anno circa **6.200** nuovi soggetti entrano in dialisi[1]
- La SIN stima che almeno il **20%** dei soggetti dializzati in Italia, quindi altamente a rischio per l'epatite B, NON sia stato vaccinato[2]
- Un recente studio, condotto in tutti i centri nefrologici regionali del Lazio, conferma che il 18% dei pazienti non risulta vaccinato contro l'HBV, ma in particolare che il 50% dei soggetti infettati era stato vaccinato, indice di una mancata risposta al vaccino[3]
- In Italia i pazienti con IRC sono stimati in >2 milioni; inoltre, si stima che oltre 200 mila individui abbiano IRC ancora lieve ma siano futuri candidati alla dialisi[4]

1. http://www.salute.gov.it/resources/static/focus/200/ATTI_per_web.pdf
2. Società Italiana di Nefrologia
3. Petrosillo INMI Spallanzani, 14 Dic 2010. disponibile al sito:https://www.asplazio.it/asp_online/tut_soggetti_deb/files/files_dialisi/convegno_14_12_2010/4_Rischio_Infettivologico.pdf
4. Greco D. Neprhology 2011

Raccomandazioni e Guidelines per la profilassi dell'Epatite B nel paziente con IRC in Italia

- **Sottoporre a screening per HBV** tutti i soggetti sottoposti a dialisi e/o a trapianto renale[1,2]
- **Attivare la vaccinazione dei soggetti HBsAg-negativi**, ricorrendo a protocolli vaccinali rinforzati oppure a vaccini potenziati con adiuvanti, registrati specificamente per i pazienti nefropatici[1,2]
- **Prevedere il monitoraggio** dei soggetti HBsAg-positivi inattivi sottoposti a dialisi[1,2]

A livello Internazionale:

- L'***European Renal Association*** raccomanda la vaccinazione anti-HBV nei pazienti con IRC progressiva preferibilmente prima di iniziare l'emodialisi[3]
- I **Centers for Disease Control and Prevention** raccomandano di vaccinare tutti i soggetti affetti da IRC in pre-dialisi a dialisi[4]

1. Carosi G et al. Dig Liver Dis 2011 Apr; 43 (4): 259-65
2. Fabrizi F et al. J Artif Organs 2008; 31: 386-94
3. ERA. Nephrol Dial Trans 2002 (S7); 17: 78-81
4. MMWR 2001; 50: 1-43

Offerta della vaccinazione anti-Epatite B ai soggetti con IRC, in Italia

- Il nuovo Piano Nazionale Vaccini 2012-14 conferma l'offerta attiva e gratuita della vaccinazione HBV ai nefropatici cronici

- Esistono diverse modalità di offerta della vaccinazione HBV tra le Regioni oltre a quella praticata dalle ASL:
  - prescrizione del vaccino da parte del medico curante ed il ritiro del vaccino dalla ASL o dalla farmacia da parte del paziente
  - vaccinazione diretta del nefropatico da parte del centro nefrologico che ha in cura il paziente
  - vaccinazione presso il centro dialisi da parte degli operatori del centro vaccinale, per i pazienti che hanno difficoltà a recarsi al centro vaccinale

- **Manca una vera offerta attiva della vaccinazione da parte dei servizi vaccinali**: questi servizi non si muovono alla ricerca dei soggetti da vaccinare, ma vaccinano i richiedenti
- **Non in tutti i nefropatici viene effettuata la verifica anticorpale** della risposta al vaccino dopo la prima dose e quindi, non tutti i pauci o non-responder completano il ciclo vaccinale.

1. Piano Nazionale Vaccini 2012-14
2. Greco D. Nephrology 2011

Quali sono gli svantaggi dei vaccini anti-Epatite B “tradizionali”, nei dializzati?

- Una immunogenicità scarsa
- Necessità di una dose doppia di vaccino convenzionale
- Perdita dell’immunità dopo 12-15 mesi dalla vaccinazione[1]
- Necessità di una dose booster qualora gli anticorpi contro l‘antigene di superficie (anti-HBsAg o HBsAb) risultino inferiori a 10 IU/L[2]

1. Ramezani A et al, 2008; http://onlinelibrary.wiley.com/doi/10.1111/j.1744-9987.2008.00560.x/abstract
2. Tsouchchnikas I et al, 2007; http://www.traveldoctoronline.net/loss-of-hepatitis-b-immunity-in-hemodialysis-patients-acquired-either-naturally-or-after-vaccination-MTc5Njk0OTA=.htm

Quali strategie adoperare per superare gli svantaggi dei vaccini anti-Epatite B “tradizionali”, nei dializzati?

- Aumentare il numero delle dosi
- Aumentare la dose di vaccino (doppia)
- Usare vie di somministrazione diverse (intradermica)
- Usare antigeni pre-S1 e pre-S2
- Usare un adiuvante più potente

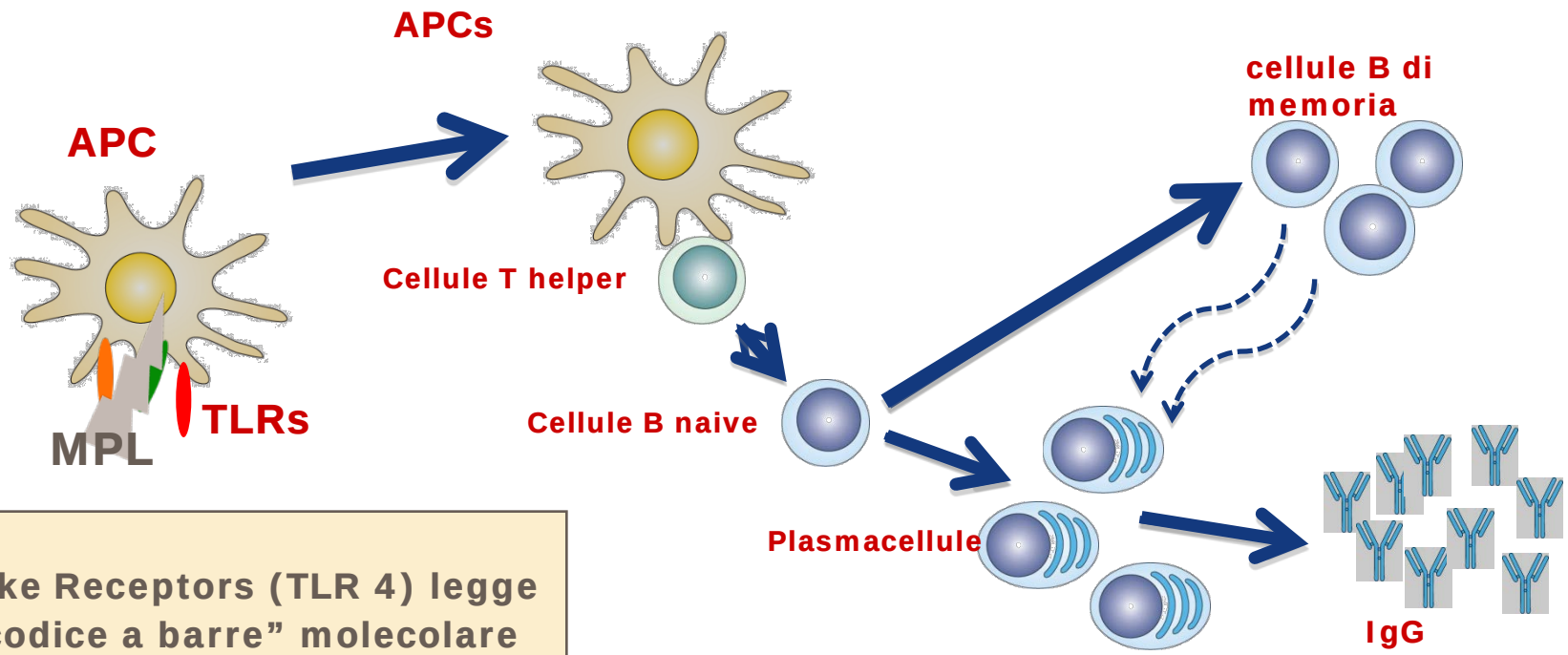
Perchè impiegare un vaccino adiuvato nei soggetti con IRC?

- Le frequenti ospedalizzazioni aumentano il rischio di contrarre l'Epatite B anche in fase di pre-dialisi[1]
- Il rischio di cronicizzazione è particolarmente alto nei soggetti dializzati, rispetto alla popolazione generale (60% *vs* 5–10%)[2]
- Si tratta di pazienti immunodepressi[3]
- Hanno in genere una risposta immune al vaccino bassa, proprio a causa del loro stato di immunodepressione[3]
- Altri co-fattori possono indurre una ridotta risposta immune:
  - obesità, età, malnutrizione, fumo di sigaretta, infezione pre-esistente da HCV o HIV

1. Girndt M, Kohler H. Semin Nephrol 2002; 22: 340–50
2. Zacks SL, Fried MW. Infect Dis Clin North Am 2001; 15: 877–99
3. MMWR 2001; 50: 1–43

L'adiuvante AS04

➢ **Il MPL amplifica la risposta immunitaria mirata verso l'antigene con il quale è co-somministrato**



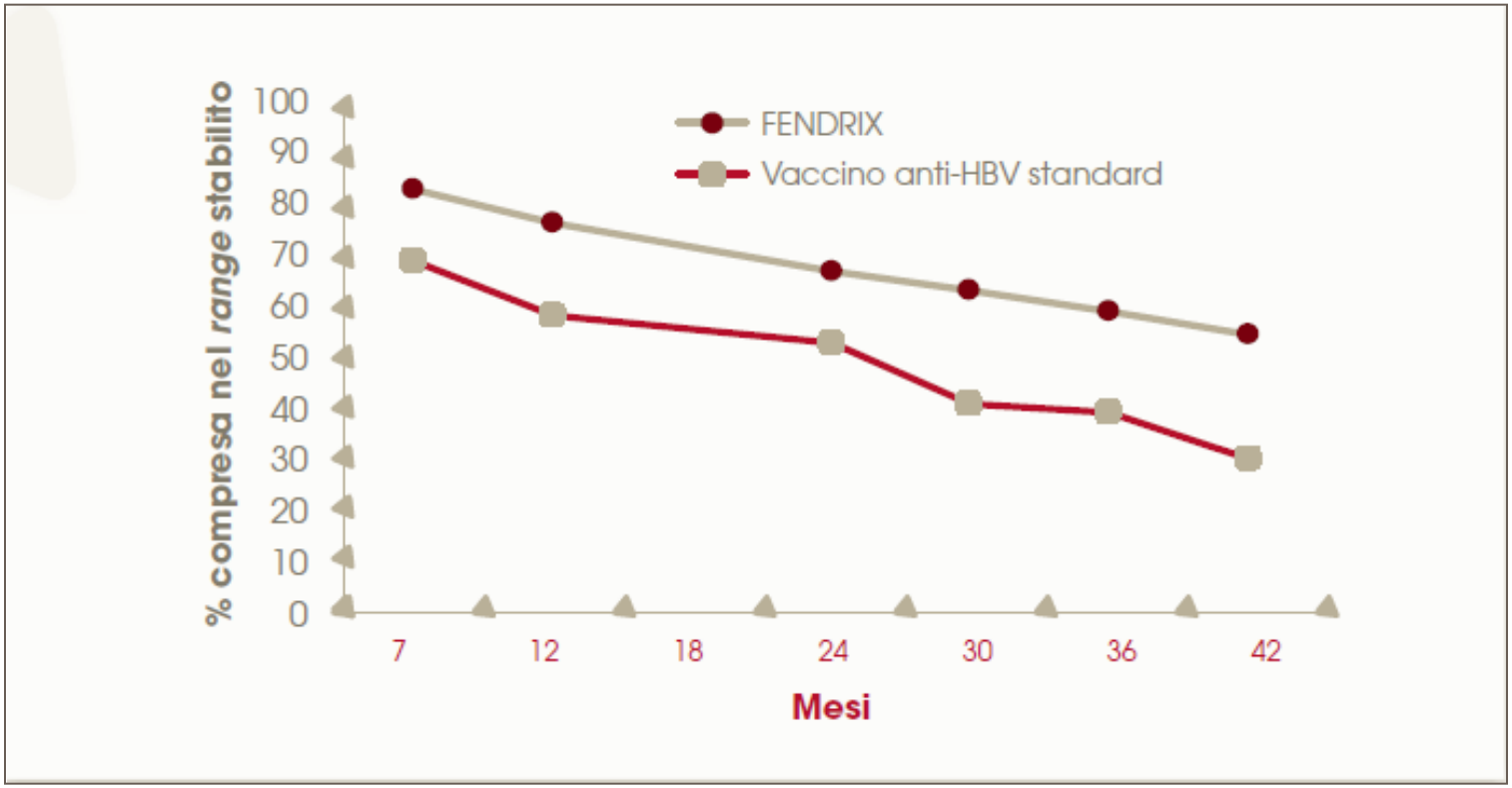
Toll-Like Receptors (TLR 4) legge il "codice a barre" molecolare

T. Seya, T. Akazawa, T. Tsujita, M. Matsumoto, Evid Based Complement Alternat Med 3, 31 (2006)
B. Pulendran, R. Ahmed, Cell 124, 849 (2006)
C. Janeway, Immunobiology, the immune system in health and disease. (Garland Science, 2004)

I vantaggi del sistema adiuvante

in pazienti in pre-emodialisi ed emodialisi

Percentuale di pazienti con anti-HBs ≥100mUI/mL durante il periodo di *follow-up*



- **54,1% dei pazienti sottoposti a vaccinazione primaria con Fendrix ha presentato anti-HBs ≥100 mUI/mL 42 mesi dopo la vaccinazione iniziale rispetto al 29% dei pazienti nel gruppo trattato con Engerix B**

Kong NCT et al. Kidney Intern 2008; 73: 856-863

Determinanti del rischio di infezione in lavoratori esposti ad agenti biologici

p = prevalenza dell'agente infettante nel "materiale" oggetto della lavorazione

E = frequenza di esposizione efficace al rischio (probabilità di avere un incidente)

t = efficacia di trasmissione dell'agente a seguito di una singola esposizione a rischio

S = proporzione degli operatori suscettibili all'infezione

Rischio = p x E x t x S

…ridurre la prevalenza dell'agente infettante, ridurre il numero di esposizioni e di suscettibili (con la vaccinazione)

DECRETO LEGISLATIVO 9 aprile 2008 , n. 81

Attuazione dell'articolo 1 della legge 3 agosto 2007, n. 123, in materia di tutela della salute e della sicurezza nei luoghi di lavoro.

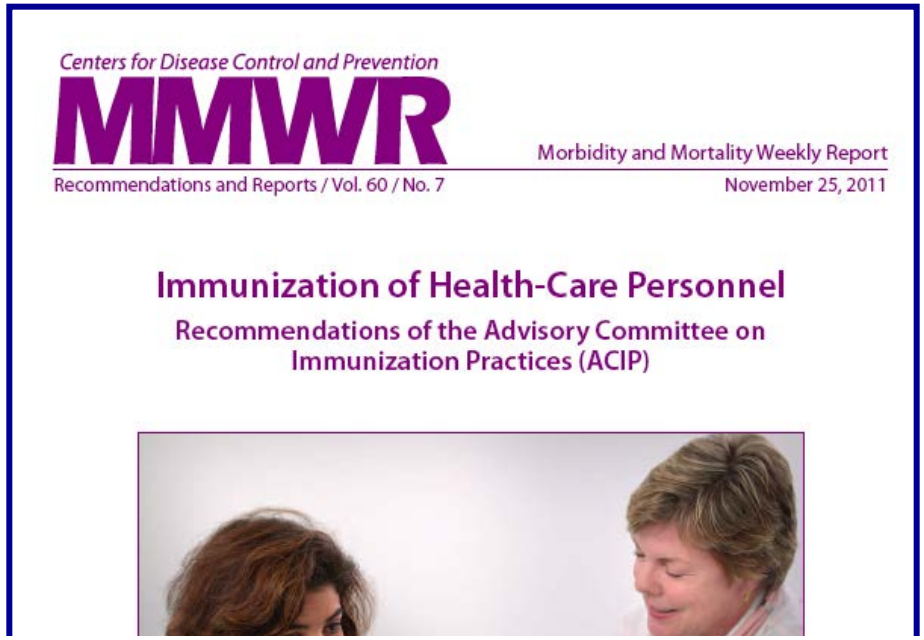
Art. 279.

Prevenzione e controllo

1. I lavoratori addetti alle attivita' per le quali la valutazione dei rischi ha evidenziato un rischio per la salute sono sottoposti alla sorveglianza sanitaria.

2. Il datore di lavoro, su conforme parere del medico competente, adotta misure protettive particolari per quei lavoratori per i quali, anche per motivi sanitari individuali, si richiedono misure speciali di protezione, fra le quali:

a) la messa a disposizione di vaccini efficaci per quei lavoratori che non sono gia' immuni all'agente biologico presente nella lavorazione, da somministrare a cura del medico competente;



Healthcare Personnel Vaccination Recommendations[1]

Vaccine	Recommendations in brief
Hepatitis B	Give 3-dose series (dose #1 now, #2 in 1 month, #3 approximately 5 months after #2). Give IM. Obtain anti-HBs serologic testing 1–2 months after dose #3.
Influenza	Give 1 dose of influenza vaccine annually. Give inactivated injectable influenza vaccine intramuscularly or live attenuated influenza vaccine (LAIV) intranasally.
MMR	For healthcare personnel (HCP) born in 1957 or later without serologic evidence of immunity or prior vaccination, give 2 doses of MMR, 4 weeks apart. For HCP born prior to 1957, see below. Give SC.
Varicella (chickenpox)	For HCP who have no serologic proof of immunity, prior vaccination, or history of varicella disease, give 2 doses of varicella vaccine, 4 weeks apart. Give SC.
Tetanus, diphtheria, pertussis	Give a one-time dose of Tdap as soon as feasible to all HCP who have not received Tdap previously. Give Td boosters every 10 years thereafter. Give IM.
Meningococcal	Give 1 dose to microbiologists who are routinely exposed to isolates of *N. meningitidis*. Give IM or SC.

Ministero della Salute

Le vaccinazioni per gli operatori sanitari

Gli operatori sanitari, a causa del loro contatto con i pazienti e con materiale potenzialmente infetto, sono a rischio di esposizione a malattie infettive prevenibili con vaccinazione.
L'obiettivo di un adeguato intervento di immunizzazione nel personale sanitario è fondamentale per la prevenzione ed il controllo delle infezioni.
Programmi di vaccinazione ben impostati possono, infatti, ridurre in modo sostanziale il numero degli operatori suscettibili ed i conseguenti rischi sia di acquisire pericolose infezioni occupazionali, sia di trasmettere patogeni prevenibili con la vaccinazione ai pazienti o ad altri operatori.

2012 - 2014

EPATITE B

Gestione dei non-responders

(ACIP; MMWR 2011, vol. 60, RR-7)

- **Fino a 3 dosi addizionali** per raggiungere titoli di anti-HBs > 10 mUI/ml ed indurre la memoria immunologica (25-50% con una dose; 44-100% con tre dosi) (Clemens 1997; Goldwater 1997)
- Il tasso cumulativo di risposta a un nuovo ciclo di 3 dosi è risultato pari al 69% (Averhoff 1998)
- Nei non rispondenti non sono raccomandati più di due cicli completi

Sorveglianza SIOP-SIROH 2010 (Piemonte)

- Incidenti percutanei 3/100 operatori e 2.9/1000 ricoveri
- Pazienti fonte-nota: 84.6% delle esposizioni percutanee (2.4% HBsAg positivi)
- Copertura vaccinale :

	2002	2010
Operatori sanitari	86.7%	86.3%
Squadra esterna pulizie	41.7%	27.3%
Ausiliari	69.8%	80.0%

PROCEDURE "EXPOSURE PRONE"

Sono definite "exposure prone" quelle procedure (EPP) che possono esporre il paziente al sangue dell'operatore.

Procedure in cui le mani di un operatore, anche se indossa i guanti, possono venire a contatto con strumenti taglienti o la punta di un ago oppure con tessuti taglienti, quali le spicole ossee o dentarie, allinterno di una cavità corporea di un paziente, una ferita o uno spazio anatomico confinato, dove le mani o le dita possono non essere completamente visibili in ogni momento

ISS-Consensus Conference 1999; CDC 1991; CDC 2012

TABLE 1. Cases of surgeon-to-patient transmission of hepatitis B virus (HBV) in which the surgeon's HBV DNA was quantified

Location of reported case (yr)	Profession	HBV DNA (GE/ml)*	HBV e-antigen	Quantification technique	Time sample taken after transmission
United States (1992)†	Thoracic surgery resident	1.0×10^9	Positive	Semi-quantitative PCR dot-blot hybridization, with comparison serum containing 108 chimpanzee-infectious particles	4 mos
United Kingdom (1990–1997)§	Cardiothoracic surgeon	10^9	Positive	Semi-quantification by end-point dilution	6 mos
	General surgeon	10^8	Positive		>8 wks
	General surgeon	10^9	Positive		Unknown
	General surgeon	10^7	Positive		Unknown
	Cardiothoracic surgeon	10^5	Positive		Unknown
United Kingdom (1988, 1993–1995)¶	General surgeon	1.0×10^7	Negative	Liquid hybridization and enzyme-linked oligonucleotide assay	12 wks
	Gynecologist	4.4×10^6	Negative		Unknown
	Gynecologist	5.5×10^6	Negative		Unknown
	General surgeon	2.5×10^5	Negative		12 wks
United Kingdom (1999)**	Surgeon	1.03×10^6	Negative	Lightcycler PCR	Unknown
Netherlands (1998–1999)††	Surgeon	5.0×10^9	Positive	Limited dilution PCR	1 yr
United Kingdom (1988–1997)§§	Surgeon	1.12×10^8	Negative	Chiron Quantiplex Branched DNA assay and Roche Amplicor HBV DNA monitor assay	At least 3 mos after transmission in all surgeons
	Surgeon	2.55×10^5			
	Surgeon	6.72×10^5			
	Surgeon	6.35×10^4			
	Surgeon	4.20×10^8¶¶			
	Surgeon	9.47×10^8			
United States (2008)***	Orthopedic surgeon	1.79×10^7	Positive	Versant 3.0 third generation branched DNA assay	14 wks

Casistica 1992-2008: HBV DNA virus load> 10^5 GE/ml

TABLE 2. Recommendations for the management of health-care providers (HCP) with hepatitis B virus (HBV) infection*

HBV-infected HCP	SHEA (2010)	ACS (2004)	Europe (2003)†	Canada (2000)	United Kingdom (2000)	United States (1991)
Management of HBV-infected HCP performing EPP						
Hepatitis B e-antigen	Not required to be negative	Not required to be negative	Required to be negative	Required to be negative	Required to be negative	Required to be negative
HBV DNA	$<10^4$ GE/ml	—	Variable by country $<10^2$–$<10^4$ GE/ml	$<10^5$ GE/ml initially and $<10^3$ GE/ml on therapy	$<10^3$ GE/ml	(test not available)
Frequency of monitoring	6 mos	—	3 mos if doing EPP; 12 mos for other HCP	—	12 mos	—
Expert panel	Yes	Yes	Yes	Yes	—	Yes

No restrizioni nella professione (tranne Exposure Prone)
Se EPP: controllo periodico di HBV DNA load
HBeAg negativo e HBV DNA load < 10^3-10^4 GE /ml

HBV E FLUSSI MIGRATORI

Secondo i dati dell' ISTAT (2004), in Italia il numero degli immigrati legali supera 1.900.000 persone (pari a circa il 3% della popolazione italiana)

Il numero degli immigrati illegali ????

Patologie infettive prevenibili con la vaccinazione ed immigrati

J Med Virol. 2009

Evolving Clinical Landscape of Chronic Hepatitis B: A Multicenter Italian Study

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- Crossectionalmulticentersurvey on 1,386 HBsAg chronic carriers
- 21 referral centers
- 6-month period

Results

- HBeAg-positive subjects were more likely to be younger, immigrants, co-infected with HIV and with higher HBV DNA and ALT levels compared to HBeAgnegativecases

Discussion

- About 35,000 new HBsAg carriers are expected, that is, 170,000–200,000 HBsAg carriers based on a 5–6% prevalence in incomingpopulations

J. Med. Virol. 81:1999–2006, 2009.
http://onlinelibrary.wiley.com/doi/10.1002/jmv.21643/pdf

VARIANTI DI HBV E VACCINAZIONE

Si è temuto che il virus B potesse mutare e quindi selezionare un ceppo che non era neutralizzato dal vaccino. Infatti, infezioni da tale ceppo (detto mutante del gene "s") sono state segnalate in nati da madri infette, nonostante che tali nati fossero stati vaccinati con il classico vaccino contro l'epatite B.

Tali segnalazioni hanno fatto temere che, applicando la vaccinazione di massa, questa potesse aumentare la comparsa dei mutanti.

Con il procedere degli studi e delle ricerche è stato dimostrato che tale pericolo non esiste.

(Hsu, 2004; Basuni 2004)

VARIANTI DI HBV E VACCINAZIONE

In conclusione possiamo affermare che oggi non esiste alcun mutante di HBV che possa rendere inefficace la vaccinazione universale

CONCLUSIONI

Oggi 160 Nazioni adottano lo stesso schema di vaccinazione impiegato per la prima volta dall'Italia

Diversi miliardi di dosi sono state somministrate con eccezionali indici di sicurezza ed efficacia

In Italia l'incidenza dell'epatite acuta B è diminuita da 5,4 casi/ 100.000 abitanti nel 1990 a 1,4 casi/ 100.000 abitanti nel 2004 e vi è stata anche una significativa riduzione dei portatori cronici

E' il primo vaccino capace di prevenire il cancro

I mutanti di HBV non rendono inefficace il programma di vaccinazione di massa

VACCINI ESAVALENTI DELL'INFANZIA

Oggi sono ampiamente utilizzati i vaccini pediatrici esavalenti, attivi contro difterite, poliomielite, tetano, epatite B, pertosse e malattie invasive da Hemophilus influenzae di tipo b.

La risposta anticorpale (intesa come percentuale di sieroconversione e titolo medio di anti-HBs) è buona nei bambini vaccinati con vaccini esavalenti , compresi i nati prematuri

(Ropero AM, J Clin Virol 2005; Omenaca F, Pediatrics 2005)

Si auspica in un futuro non lontano la scomparsa dell’epatite B acuta, cronica, della cirrosi epatica e del cancro del fegato