

# Name: Prof. Dr. med. Heiner Wedemeyer



**Country:** Germany

**Affiliation:** Hannover Medical School

**Function:** Professor and Chairman of the Department of Gastroenterology, Hepatology, Infectious Diseases and Endocrinology

**Main expertise (1-2 lines):** Liver diseases with a main focus on viral hepatitis, liver transplantation and hepatocellular carcinoma. Currently, he serves as the Managing Director of the German Hepatitis C Registry.

# Vaccination against hepatitis B as prevention for hepatocellular carcinoma

Heiner Wedemeyer

Hannover Medical School

**Dept. of Gastroenterology, Hepatology, Infectious Diseases & Endocrinology**  
*including GI Oncology, Liver Transplantation, Nutrition Medicine, Intensive Care*



# Transparency/Conflicts of Interest

## Roles/Function in scientific organisations/foundations

President German Gastroenterology Association

Co-Editor Journal of Hepatology

CEO spin-off of the German Liver Foundation (“Leberstiftungs-GmbH”)

UEG National Member Forum

## Industry Honoraria for consulting or speaking (last 5 years):

Abbott, AbbVie, Biomarin, Biotest, BMS, Falk Foundation, Gilead, JJ/Janssen-Cilag, GSK, Lilly, Novo Nordisk, Merck/MSD, Pfizer, Roche, Takeda, Vir

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## DZIF-HepNet Study House

Petra Dörge, Julia Kahlhöfer, Svenja Hardtke

## Koç University Medical School in Istanbul

Cihan Yurdaydin

## Deutsche Leberstiftung/Leberstiftungs GmbH

Bianka Wiebner, Yvonne Serfert, Dietrich Hüppe, Heinz Hartmann, Peter Hofmann

## DFG SFBs 738, 900, TR209

### Several BMBF-funded consortia

### Exc Cluster RESIST

## DZIF TTU Hepatitis

Stephan Urban, Maura Dandri, Lena Allweiss

## HDV-1000

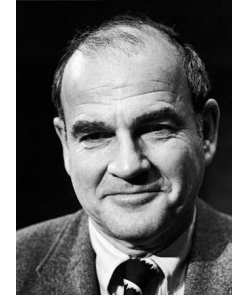
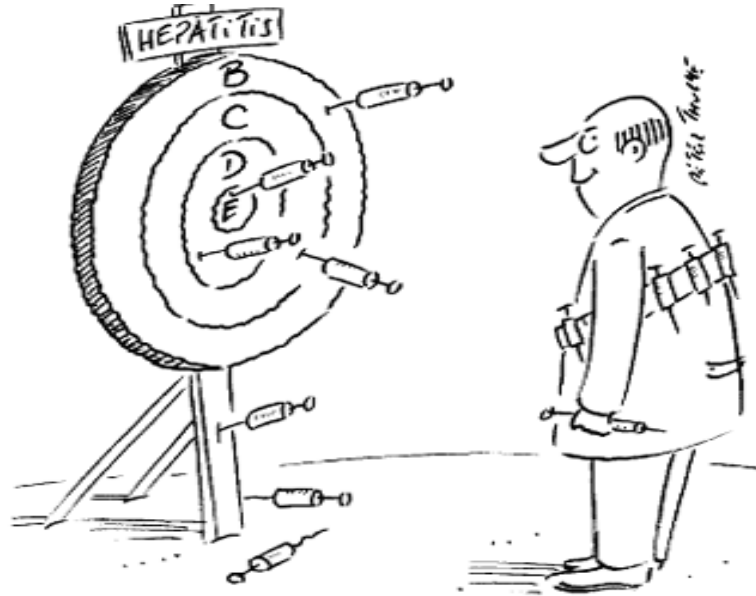
P. Lampertico, F. Zoulim, K Aggarwal, S. Aleman, F. Caruntu, K. Deterding, A. Wranke

## THE D-SOLVE Consortium

P. Lampertico, M. Cornberg, J. Debarry, H. Kefalakes, L. Sandmann, Y. Li, S. Aleman, J. Lupberger, N. Björkstrom, T. Baumert, F. Caruntu







**Viral Hepatitis:**  
**Research and development of vaccines and antiviral  
treatments are unique success stories**

# Major Achievements in Viral Hepatitis

- Vaccines against HAV, HBV, (HEV)
- Control of HBV replication is possible
- Cure of HCV infection is possible
- Reduction of hepatic decompensation
- prevent clinical complications: extrahepatic symptoms
- Reduction of viral-associated liver cancer
- Liver transplantation for viral hepatitis: only HDV is left...

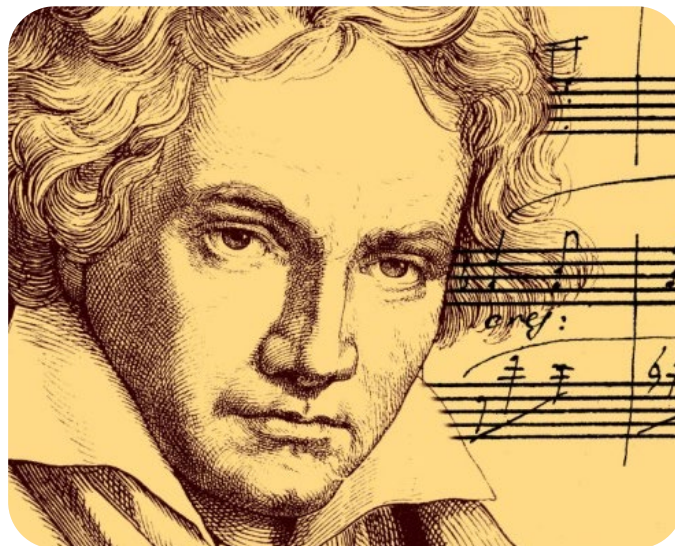
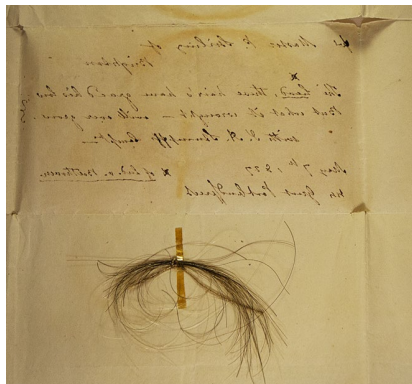


# Major Achievements in Viral Hepatitis

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- Control of HBV replication is possible
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- Reduction of hepatic decompensation
- prevent clinical complications: extrahepatic symptoms
- **Reduction of viral-associated liver cancer**
- Liver transplantation for viral hepatitis: only HDV is left...

March 26: Beethoven died in Vienna in 1827

B = **B**eethoven\*



\*Begg et al. *Curr Biol.* 2023 Mar 13;S0960-9822(23)00181-1. doi: 10.1016/j.cub.2023.02.041.

## Article

## Genomic analyses of hair from Ludwig van Beethoven

Tristan James Alexander Begg,<sup>1,6,24,\*</sup> Axel Schmidt,<sup>2</sup> Arthur Kocher,<sup>9,22,24</sup> Maarten H.D. Lamuseau,<sup>3,14,15,16</sup> Göran Runfeldt,<sup>4</sup> Paul Andrew Maier,<sup>4</sup> John D. Wilson,<sup>5,28</sup> Rodrigo Barquera,<sup>9</sup> Carlo Maj,<sup>2,27</sup> András Szolek,<sup>18,19</sup> Michael Sager,<sup>4</sup> Stephen Clayton,<sup>5,24</sup> Alexander Peltzer,<sup>26</sup> Ruoyun Hui,<sup>8,20</sup> Julia Ronge,<sup>12</sup> Ella Reiter,<sup>6</sup> Căcilia Freund,<sup>24</sup> Marta Burri,<sup>24</sup> Franziska Aron,<sup>24</sup> Anthi Tiliakou,<sup>9,24</sup> Joanna Osborn,<sup>1</sup> Doron M. Behar,<sup>21</sup>

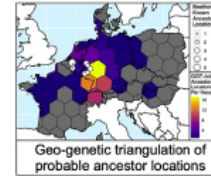
(Author list continued on next page)

## Authentication testing



## Analyses of 24-fold genome of Ludwig van Beethoven

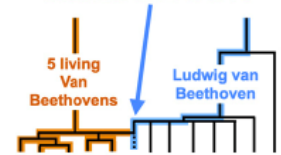
## Genetic ancestry



> 99% European ancestry  
Resembles Western/Central Europeans

## Genetic genealogy

Extra-pair paternity event  
between 1572 & 1770



## Heritable disease risk

Liver disease risk in  
*PNPLA3* and  
*HFE* genes

Interaction between genetic  
risk and alcohol  
consumption



## Ancient pathogens

Infection with  
hepatitis B virus

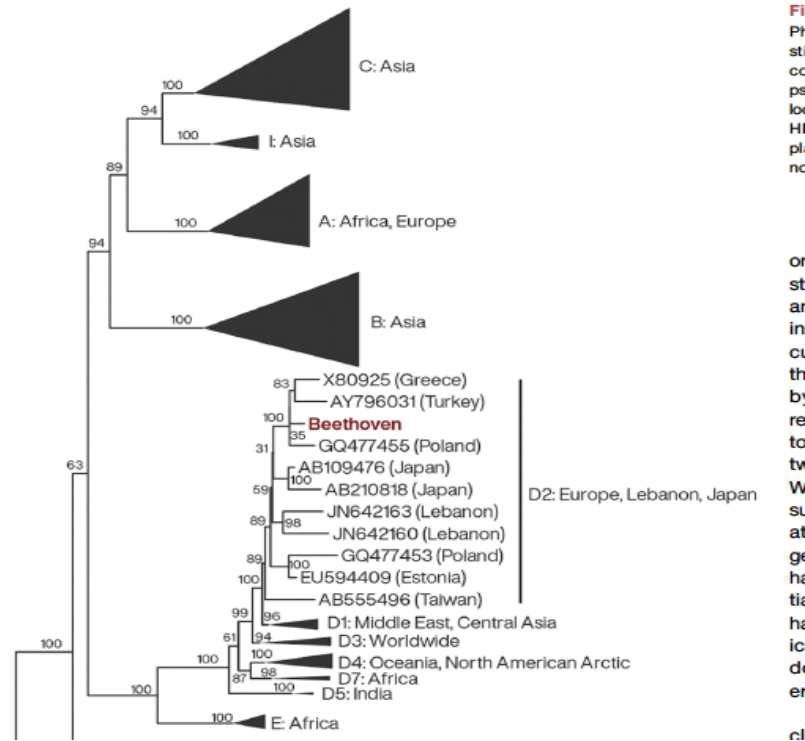


Targeted capture of hepatitis B virus DNA

HBV DNA fragments

# Beethoven was infected with HBV Genotype D

*Begg TJA et al., Curr Biol. 2023 Mar 13;S0960-9822(23)00181-1*



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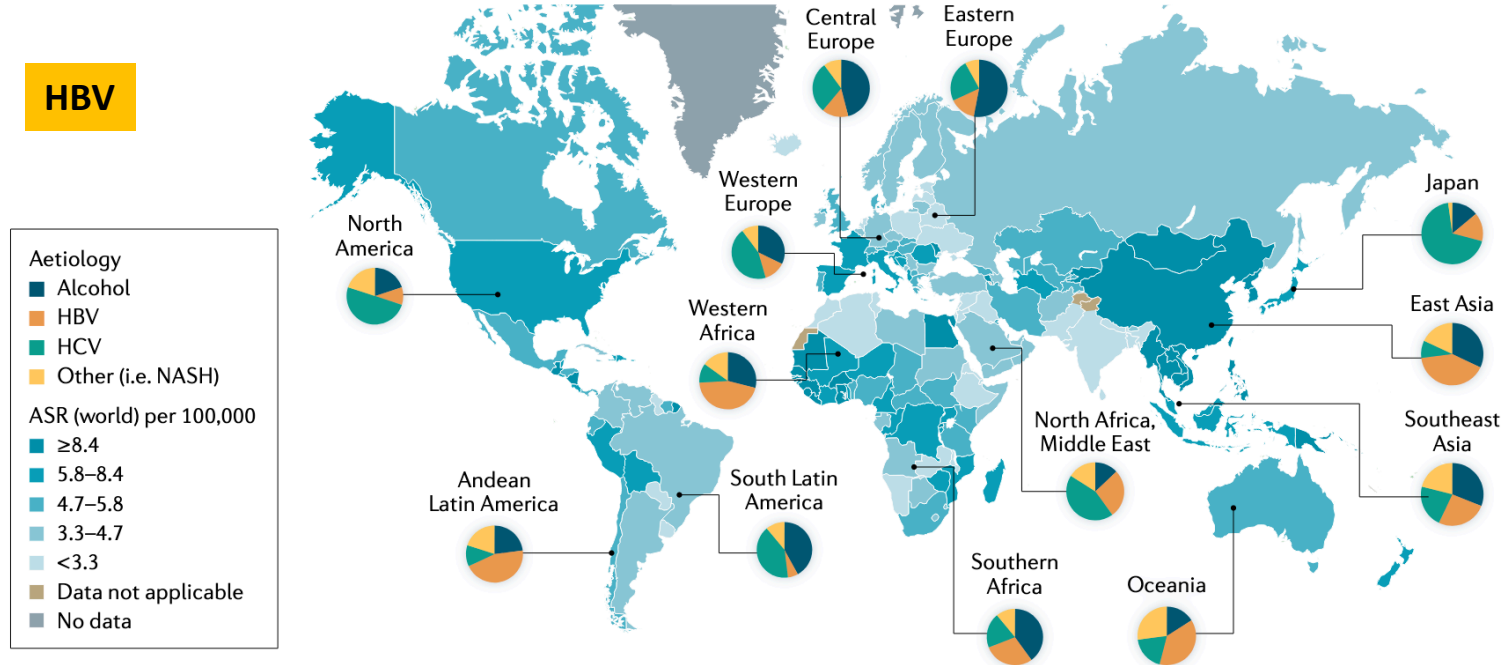
## Viral Hepatitis 2025

**At least 40 Million new infections with a hepatitis virus every year!**

**More than 300 Million are chronically infected with a hepatitis virus!**

**More than 1 Million deaths due to viral hepatitis every year!**

# HBV infection is still a major cause of HCCs world-wide



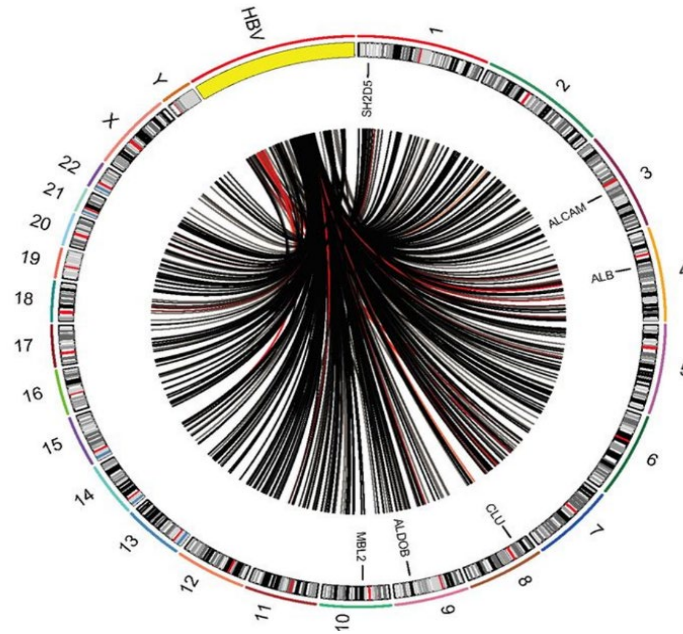
Llovet et al. *Nat Rev Dis Primers*. 2021 Jan 21;7(1):6.



# Hepatitis B and Cancer

**It's more than hepatitis, fibrosis and cirrhosis**

# HBV integration and the risk to develop HCC



Yu X et al., *Gut*. 2024;73(5):797-809.

# **Viral Hepatitis: Where to go from here?**

Acute/Chronic  
Hepatitis

Complications  
of cirrhosis

Cancer

Extrahepatic  
manifestations

Immunology

Natural  
History

Co-Morbidities

Virology

Viral  
Hepatitis

Antiviral  
therapy

Diagnostics

Patho-  
physiology

Transplantation  
Immun-Modulation

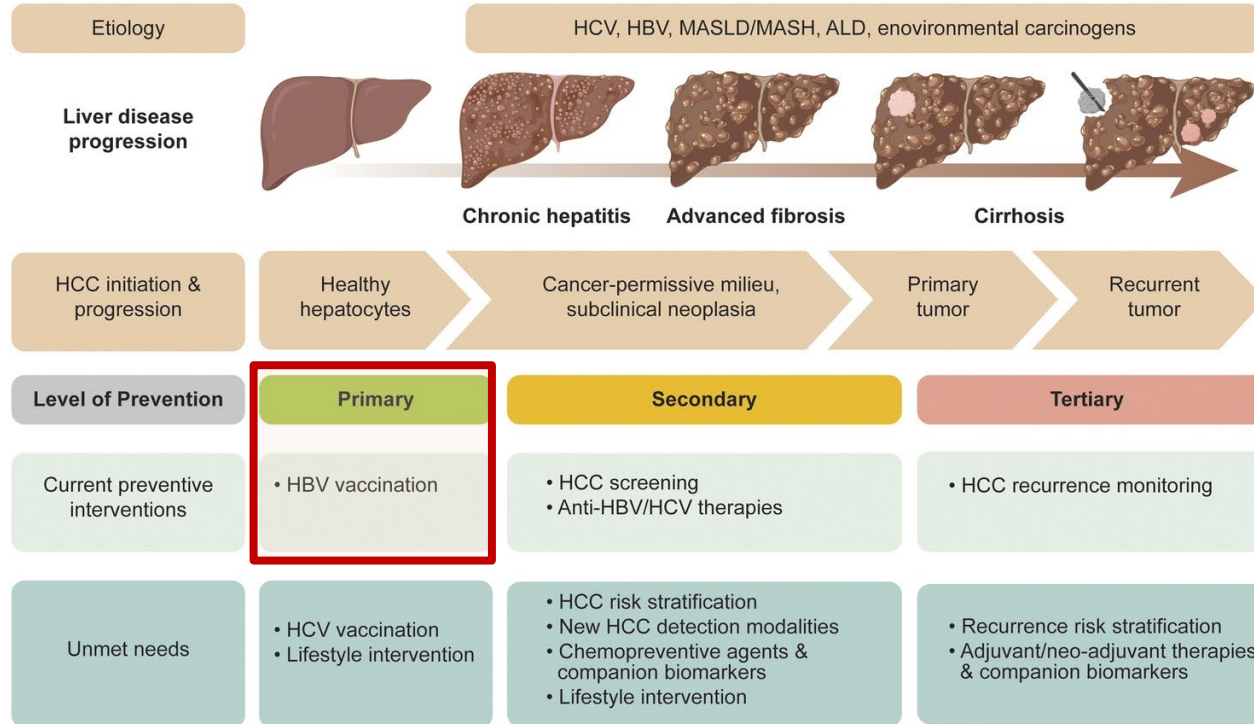
„Public Health“

Epidemiology

Prevention

Elimination

# HBV vaccination is the only primary prevention against HCC with proven efficacy!



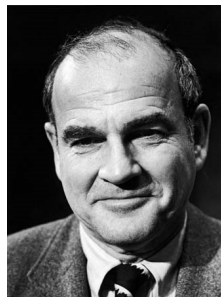
Hepatitis A

Hepatitis B

Hepatitis C

Hepatitis D

Hepatitis E



Krugman S, Giles JP, Hammond J.  
Viral hepatitis, type B (MS-2 strain).  
Studies on active immunization.  
JAMA. 1971 Jul 5;217(1):41-5.

Maupas P, Goudeau A, Coursaget P, Drucker J,  
Bagros P.  
Immunisation against hepatitis B in man.  
Lancet. 1976 Jun 26;1(7974):1367-70.

Szmunes W, .., Kellner A. Hepatitis B vaccine:  
demonstration of efficacy in a controlled  
clinical trial in a high-risk population in the  
United States.  
N Engl J Med. 1980 Oct 9;303(15):833-41. doi:



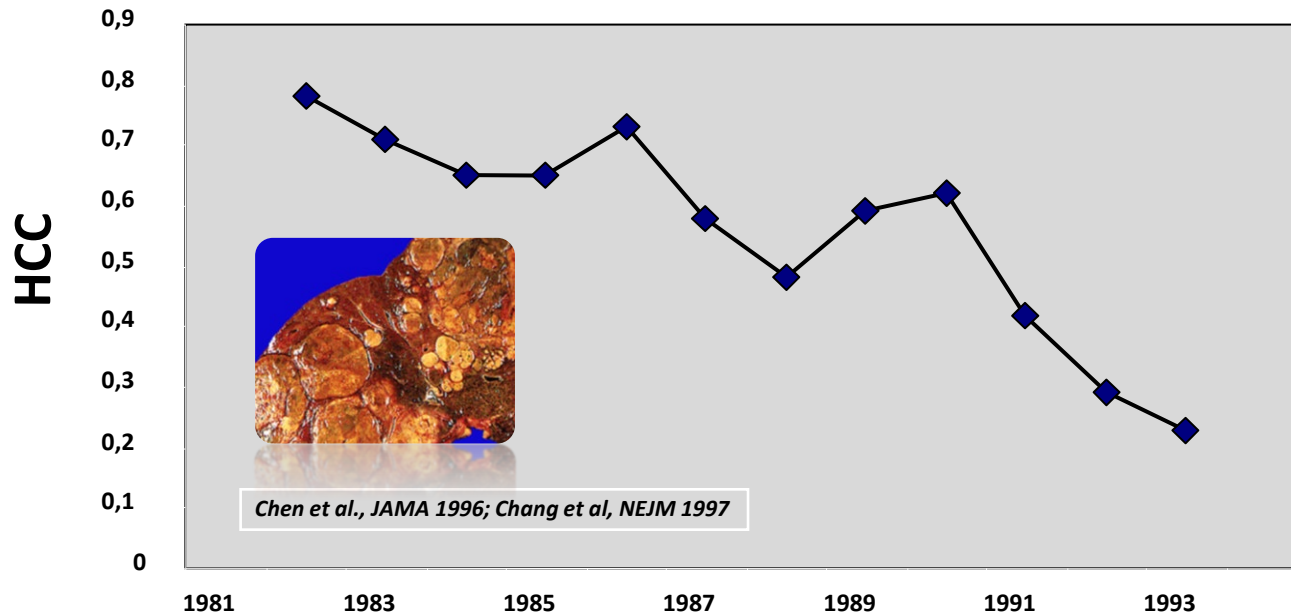
# Hepatitis B Vaccine

## The first vaccine reducing the risk of cancer!

Journal of Hepatology 51 (2009) 615–616

EASL International Recognition Awardee 2009

**Prof. Ding-Shinn Chen**



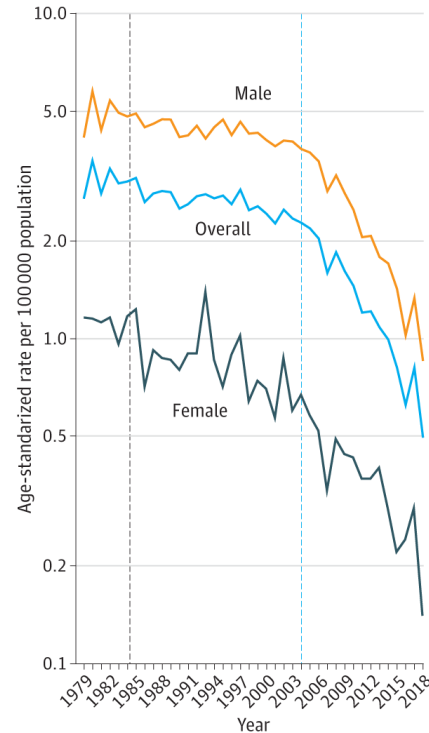
# Hepatitis B Vaccine

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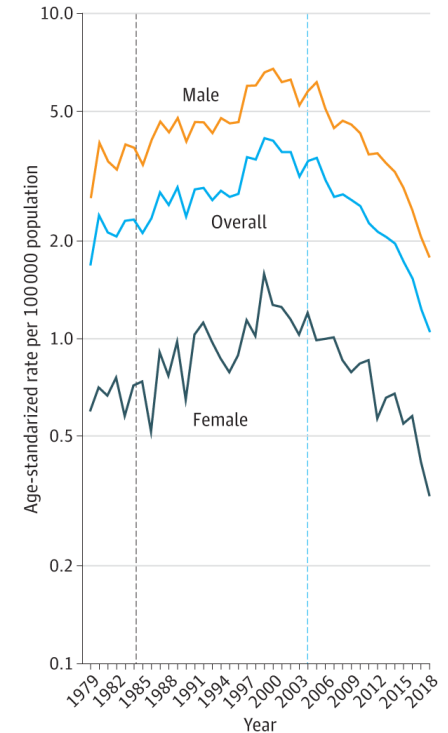
Taiwan:

HCC mortality and incidence  
male vs. female

**B** Hepatocellular carcinoma mortality



**C** Hepatocellular carcinoma incidence



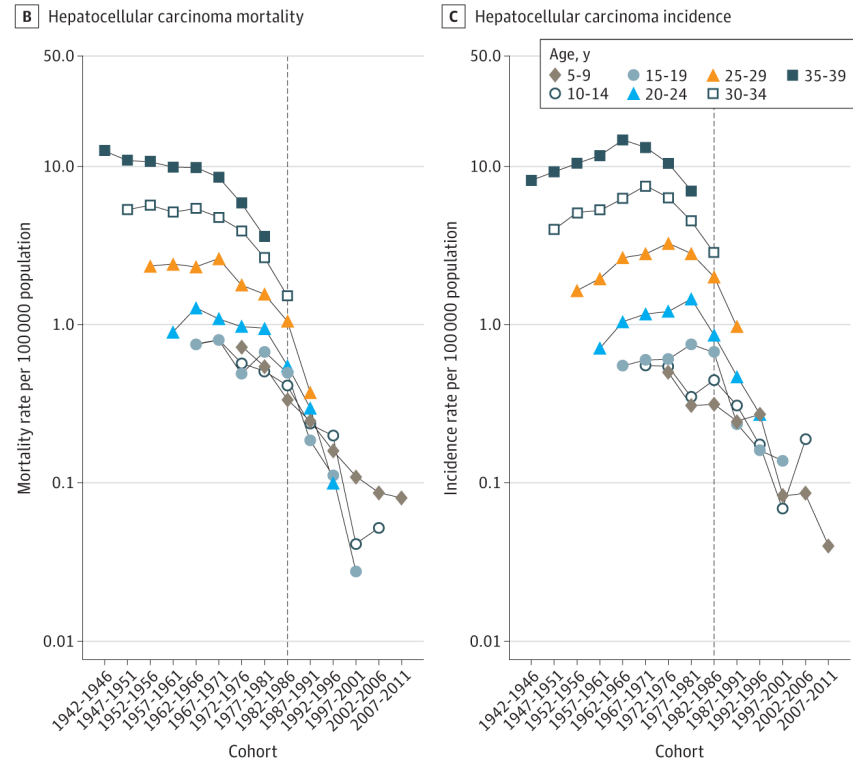
# Hepatitis B Vaccine

## The first vaccine reducing the risk of cancer!

Taiwan:

HCC mortality and incidence

Age groups

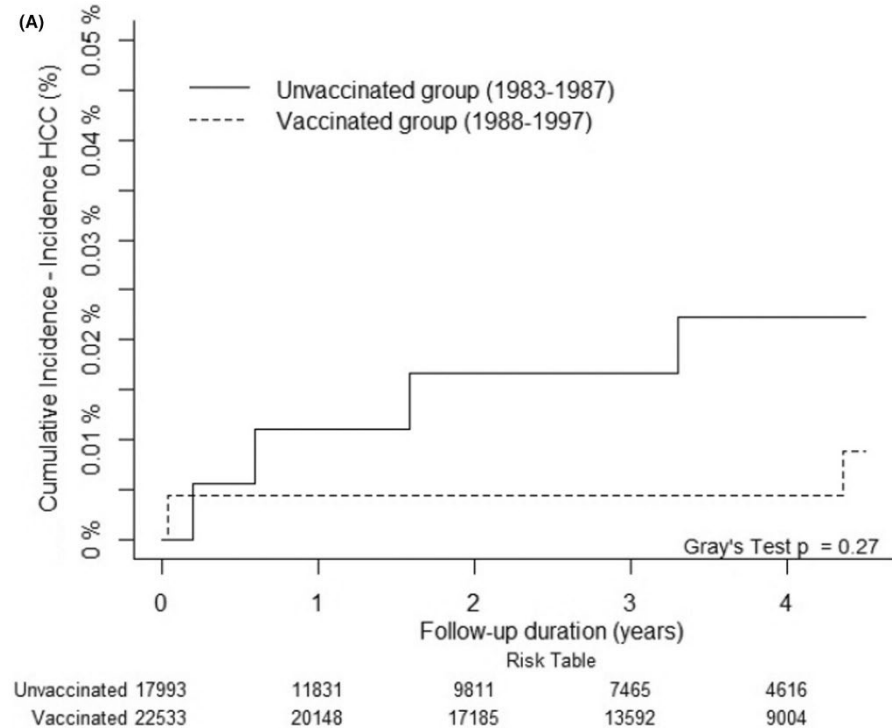


# Hepatitis B Vaccine

## The first vaccine reducing the risk of cancer!

Hong Kong:

unvaccinated vs.  
vaccinated individuals



## Hepatitis B Vaccine

The first vaccine reducing the risk of cancer!

### Japan:

Tajiri H, Tanaka H, Brooks S, Takano T.

**Reduction of hepatocellular carcinoma** in childhood after introduction of **selective vaccination against hepatitis B virus** for infants born to HBV carrier mothers.

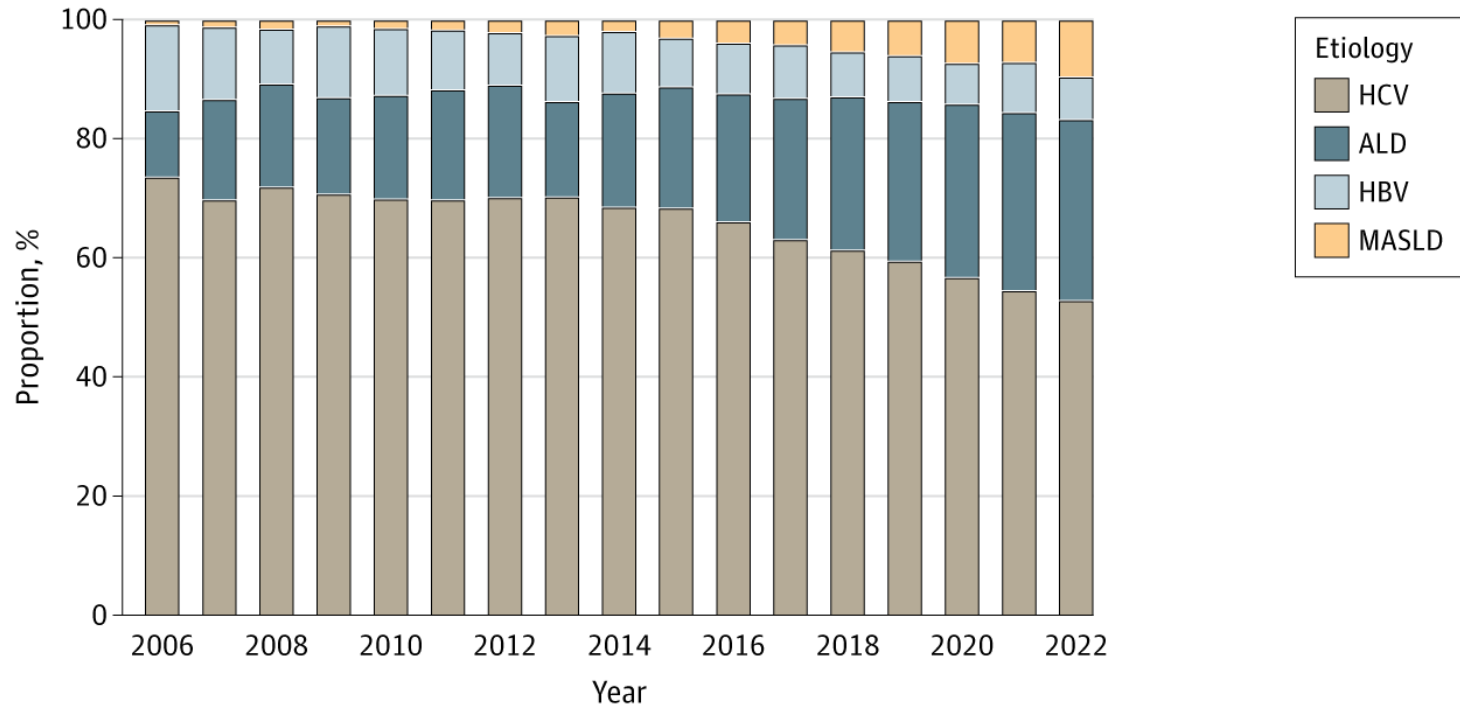
Cancer Causes Control. 2011 Mar;22(3):523-7.

### USA:

McMahon BJ, Bulkow LR, Singleton RJ, Williams J, Snowball M, Homan C, Parkinson AJ.

**Elimination of hepatocellular carcinoma** and acute hepatitis B in children 25 years **after a hepatitis B newborn and catch-up immunization program**. Hepatology. 2011 Sep 2;54(3):801-7.

## Trends in Hepatocellular Carcinoma Mortality Rates in the USA

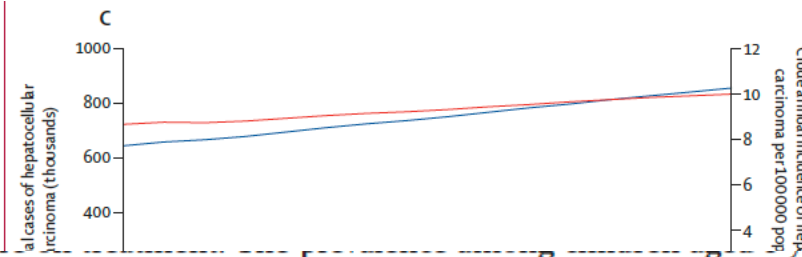




# Global prevalence, cascade of care, and prophylaxis coverage of hepatitis B in 2022: a modelling study

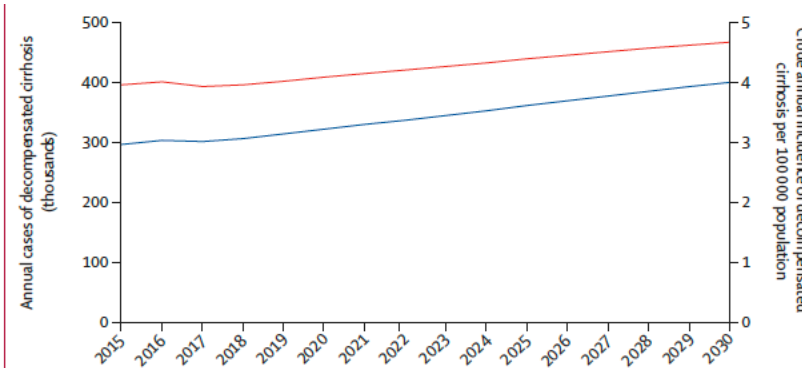
The Polaris Observatory Collaborators\*

HCC




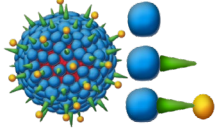

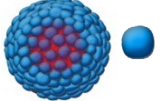

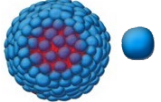

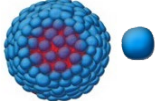

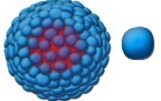
estimated to be 0.7% (0.6–1.0), corresponding to 5.6 million (4.5–7.8) children with HBV infection. Based on the most recent data, 85% of infants received three-dose HBV vaccination before 1 year of age, 46% had received a timely birth dose of vaccine, and 14% received hepatitis B immunoglobulin along with the full vaccination regimen.

decompensated  
cirrhosis



**HBV vaccines did not always work:  
How to induce protective immunity in all individuals?**

## EMA approved HBV vaccines

Manufacturer	Non-Proprietary Name	Brand Name	Effective HBV-Vaccine Antigen	Approved Adult Populations	Administration	Antigen Dose + Adjuvant
	Hepatitis B Vaccine (Recombinant)	<b>PreHevbri®</b>	 S + Pre-S2 + Pre-S1	• All, Age 18+	3 x 1ml	10µg + 500µg alum
	Hepatitis B Vaccine (Recombinant)	<b>Engerix-B®</b> <i>(also included in Twinrix®)</i>	 S	• All, Age 16+ • in CKD	3 x 1ml 4 x 2ml	20µg + 500µg alum 40µg + 1,000µg alum
	Hepatitis B Vaccine (Recombinant)	<b>HBVAXPRO®</b>	 S	• All, Age 16+ • in CKD	3 x 1ml 3 x 1ml	10µg + 500µg alum 40µg + 500µg alum
	Hepatitis B Vaccine (Recombinant) Adjuvanted	<b>Heplisav-B®</b>	 S	• All, Age 18+	2 x 0.5ml	20µg + 3,000µg CpG 1018
	Hepatitis B Vaccine (Recombinant) Adjuvanted	<b>FENDRIX®</b>	 S	• CKD only, Age 15+	4 x 0.5 ml	20µg + ASO4C + 500µg alum

Slide from Vesikari, Maubach et al. *GHS* 2023 (LB/O106)




NEW HBV Clinical Practice Guidelines  
to be released in Amsterdam May 2025



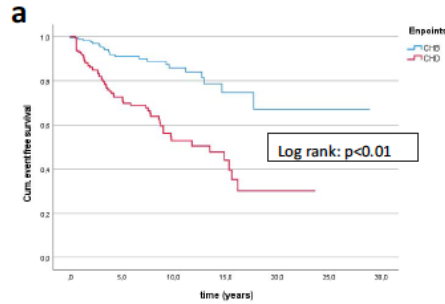
## Vaccination against hepatitis B

**... does also prevent from HDV infection!**

# Clinical long-term outcome of hepatitis D compared to hepatitis B monoinfection

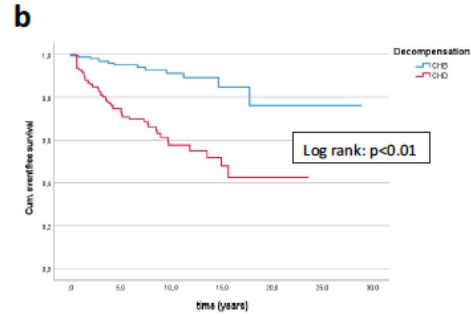
Anika Wranke<sup>1</sup> · Benjamin Heldrich<sup>1</sup> · Katja Deterding<sup>1</sup> · Katharina Lulse Hupa-Breler<sup>1</sup> · Janina Kirschner<sup>1</sup> · Birgit Bremer<sup>1</sup> · Markus Cornberg<sup>1,2,3</sup> · Heiner Wedemeyer<sup>1,2,3,4</sup> 

Event-free



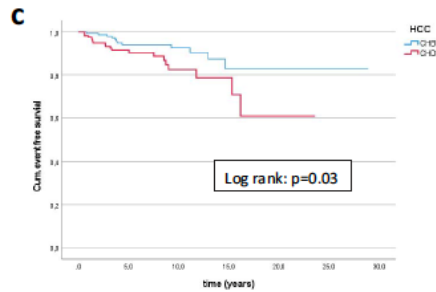
CHD	175	80	29	12	2	
CHB	175	108	56	16	4	1

Decompensation



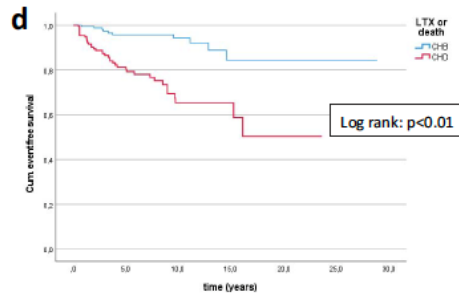
CHD	175	80	29	12	2	
CHB	175	108	56	16	4	1

HCC



CHD	175	80	29	12	2	
CHB	175	108	56	16	4	1

Death/LTx



CHD	175	80	29	12	2	
CHB	175	108	56	16	4	1



October 9 – 10, 2025  
Hannover, Germany



# DeltaCure

4<sup>th</sup> International Meeting

Chairs: Heiner Wedemeyer and Pietro Lampertico

# Vaccination against HBV to reduce HCC risk – some open questions

**... what is the effect on HCC prevention in different regions/populations?**

*E.g. Ndow, ..., Lemoine. Lancet GH Dec 2024; 9: 1133-46: Prolifica study in the Gambia, 6-11 years of follow-up: HCC cases: 0!*

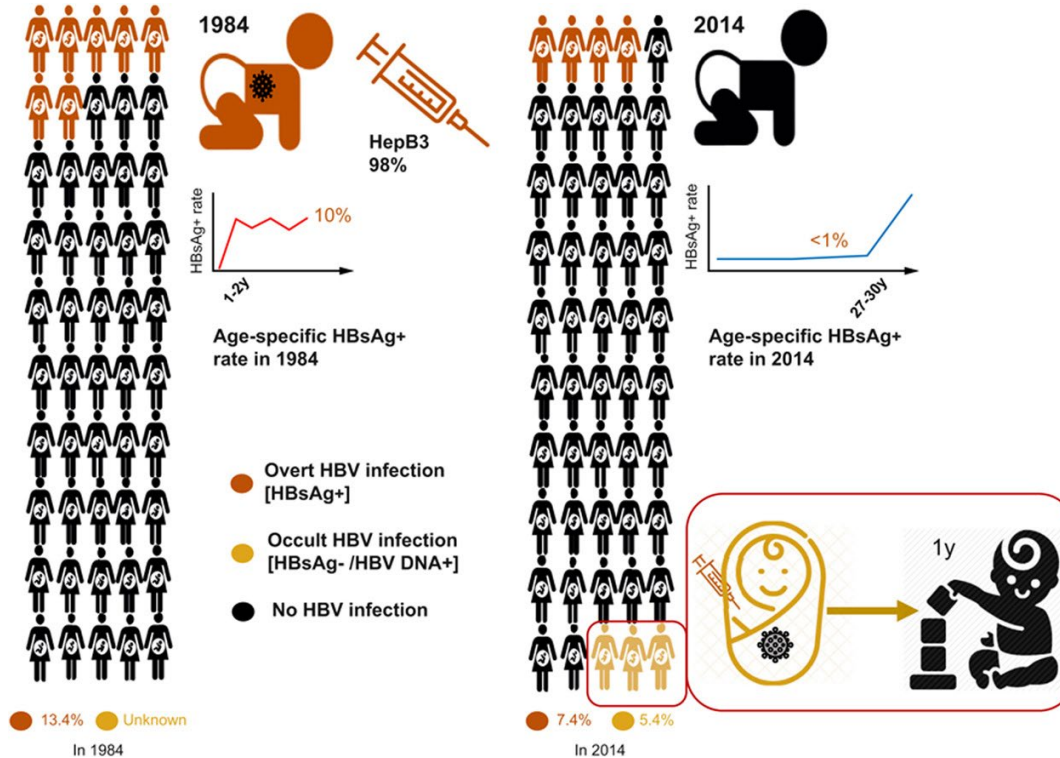
**... neonate/childhood vaccination works to reduce HCC risk, but what are the effects of universal vaccination or vaccination of adult risk groups?**

**... are booster vaccinations needed to reduce the risk of cancer?**

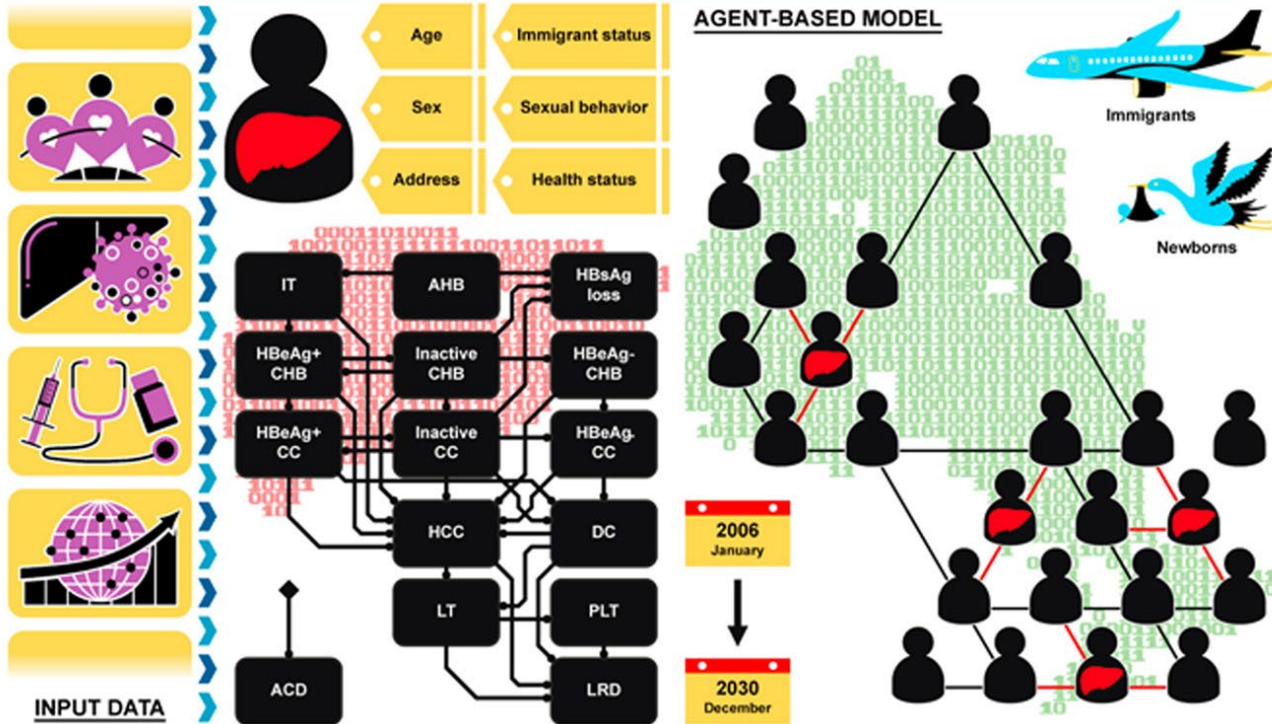
**... can mother with occult HBV infection transmit HBV and is vaccination effective in this context?**

**... Feasibility of hepatitis B elimination in high-income countries with ongoing immigration?**

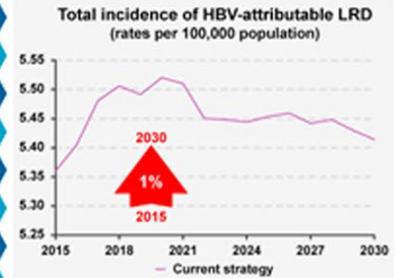
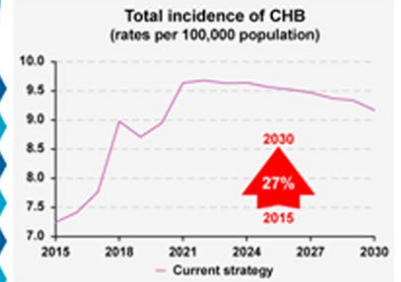
# Absence of chronicity in infants born to immunized mothers with occult HBV infection in Taiwan



An agent-based model was developed to determine which integrated strategies involving vaccination, screening, and treatment would achieve the WHO HBV elimination goals



**GENERATED PREDICTIONS**



**For immigrant-receiving countries, current and scaled-up intervention strategies are inadequate to achieve the WHO goals**





Deutsche  
-Leberstiftung

# NASH und HCC...



