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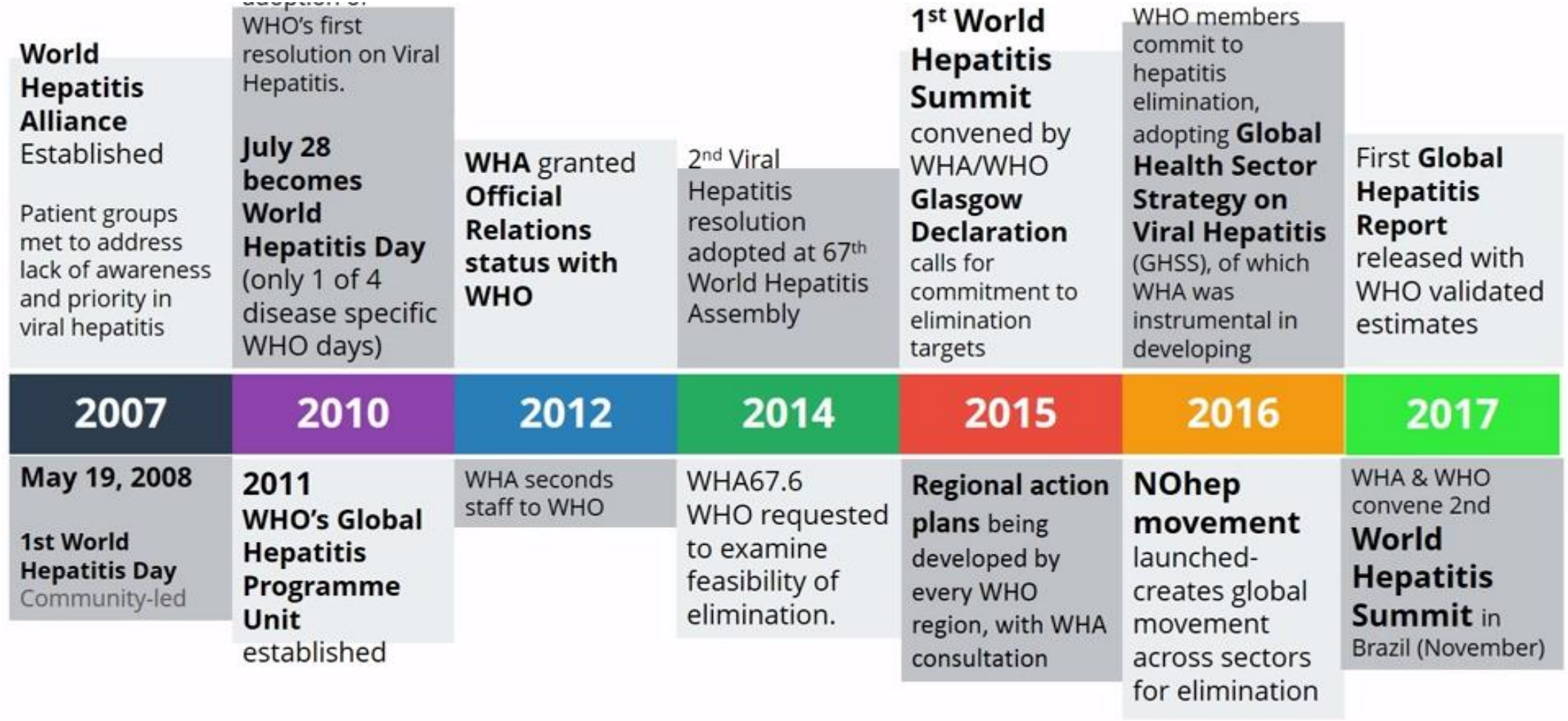
L'élimination de l'hépatite B est-elle réaliste ?

Victor de Lédinghen MD PhD

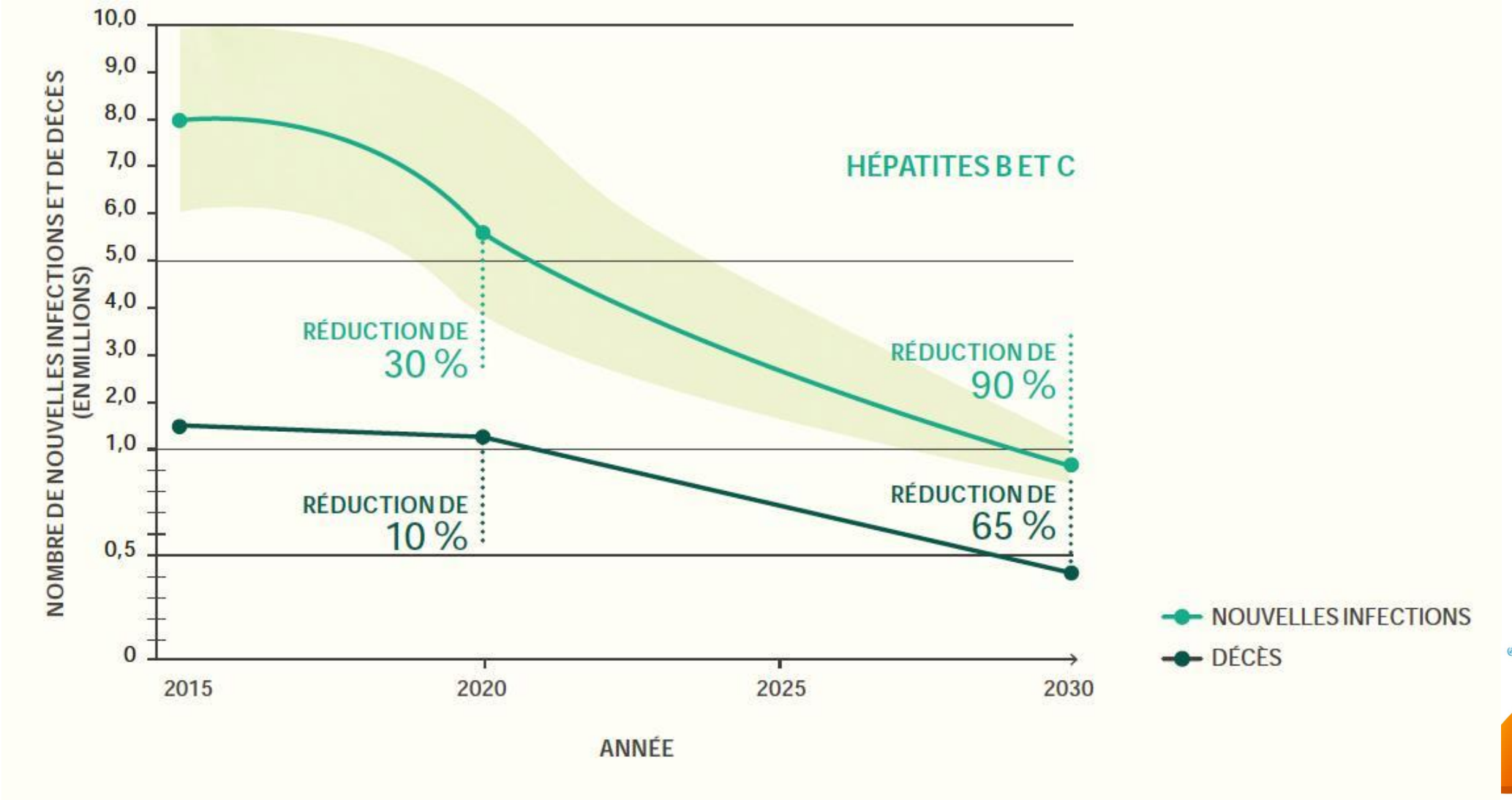
CHU Bordeaux
France

Hammamet, 20 novembre 2021

Elimination des hépatites virales. Une longue histoire…



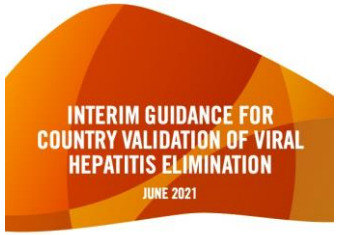
Définition de l’élimination des hépatites virales



INTERIM GUIDANCE FOR COUNTRY VALIDATION OF VIRAL HEPATITIS ELIMINATION
JUNE 2021

Objectifs pour l'élimination de l'hépatite B

- ✓Prévalence AgHBs ≤ 0,1% chez les enfants de moins de 5 ans
- ✓Mortalité annuelle < 4/100 000
- ✓Couverture vaccinale ≥ 90%



http://www.who.int/hiv/topics/hepatitis/en/

Pourquoi la route est-elle encore longue?

- ✓ Manque d'information de la population générale et des populations à risque
- ✓ Stigmatisation de l'infection
- ✓ Manque de données épidémiologiques
- ✓ Insuffisance de couverture vaccinale
- ✓ Insuffisance d'accès au diagnostic et au traitement
- ✓ Insuffisance d'investissements financiers en faveur de l'élimination
- ✓ Manque d'intégration de l'élimination de l'hépatite B dans les programmes de soins existants

Howell J et al. J Hepatol 2021;74:535-49

Où en est-on dans chaque pays? Observatoire Polaris.

Exemple : La Chine

China

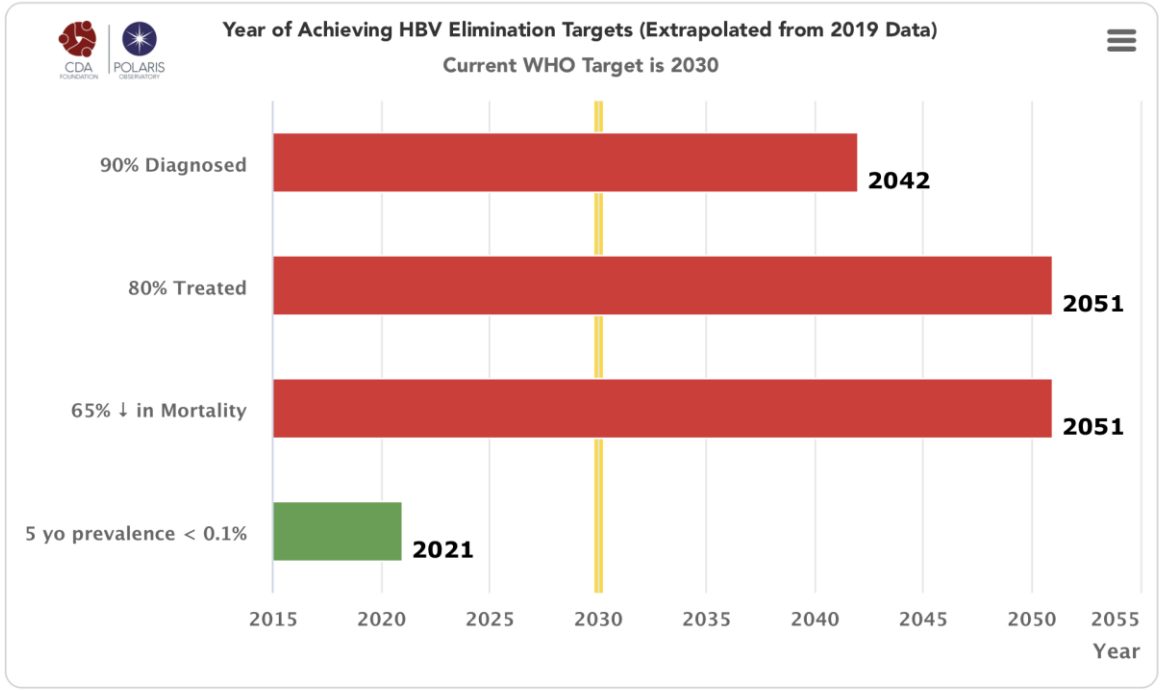
2019 Population: 1 433 784 000 | 2019 Adult Population: 1 129 233 000 | World Bank Classification: Upper Middle Income

HCV Status: ***Polaris Estimate*** **HBV Status**: ***Verified***

HCV Infections (2016)	**Diagnosed**	**Annual Treated**	**Annual Deaths**	**5 deaths per hour**
9,795,000 (0.7%)	**22%**	**2%**	**45,300**	
HBV Infections (2016)	**Diagnosed**	**Treated**	**Annual Deaths**	**46 deaths per hour**
87,267,000 (6.2%)	**19%**	**16%**	**401,000**	
	Birth Dose	**3+ Dose**	**HBIG**	**Tx Pregnant Women**
	96%	**99%**	**95%**	**26%**

Year of Achieving Elimination Targets (Extrapolated from 2019 Data)
Current WHO Target is 2030

Year of Achieving All Goals for HBV > Year 2051



https://cdafound.org/dashboard/polaris/dashboard.html

Volonté politique

Investissement financier

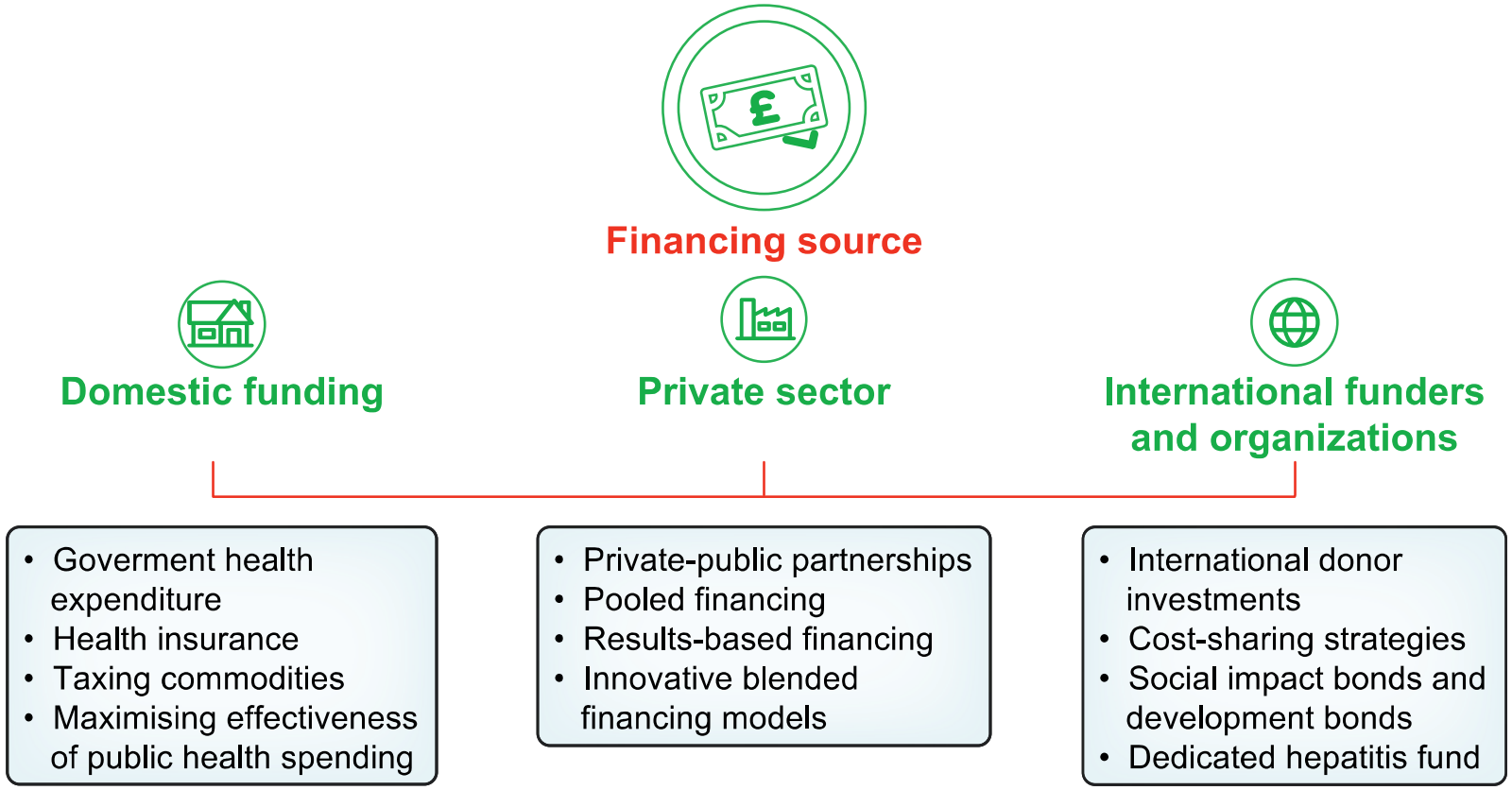


Fig. 1. Proposed Investment framework for hepatitis B and hepatitis C elimination. (Source: Pedrana A, Howell J, Scott N, *et al.* Global hepatitis C elimination: an investment case. Lancet Gastroenterology and Hepatology 2020[20]). (This figure appears in color on the web.)

Actions politiques

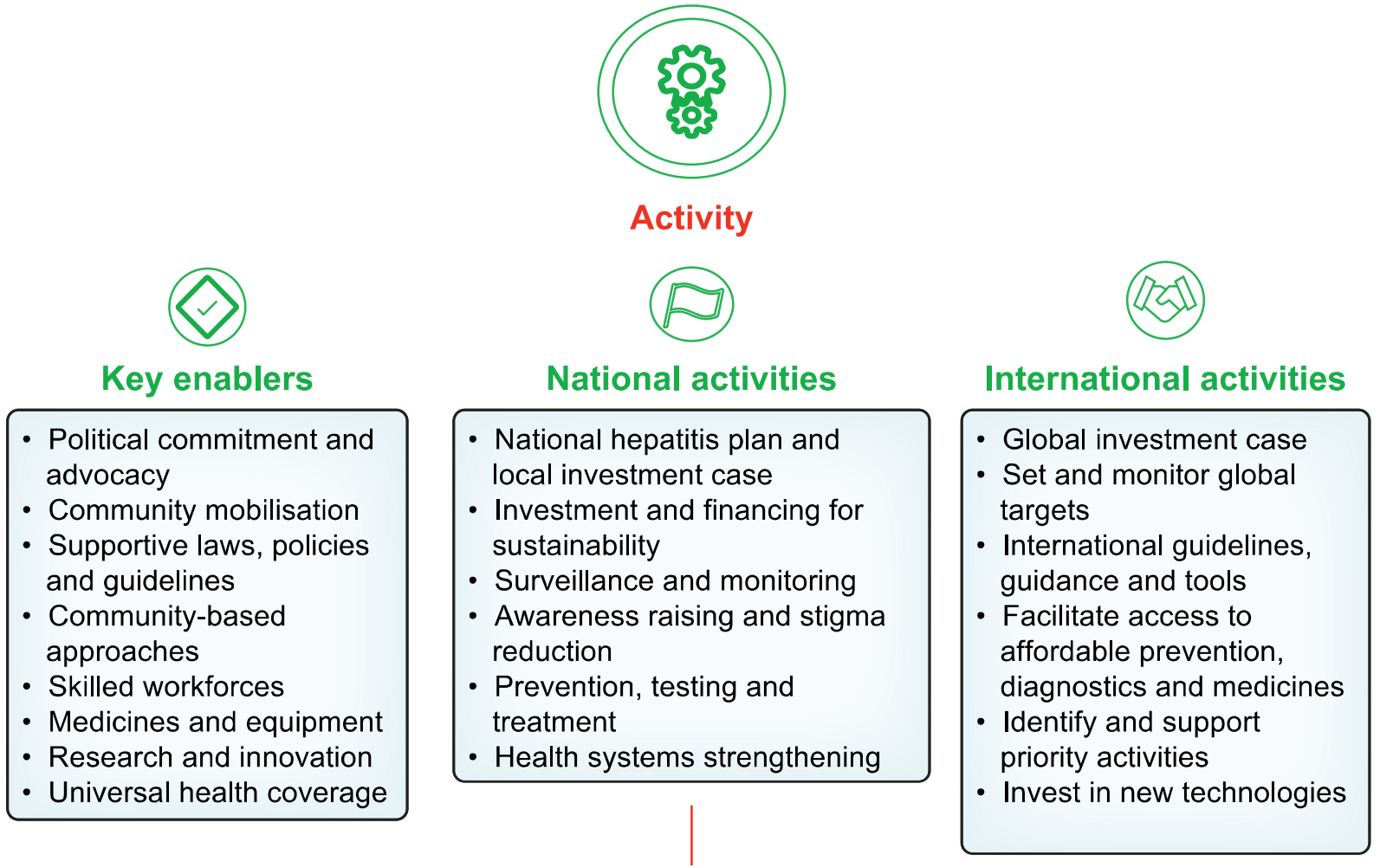


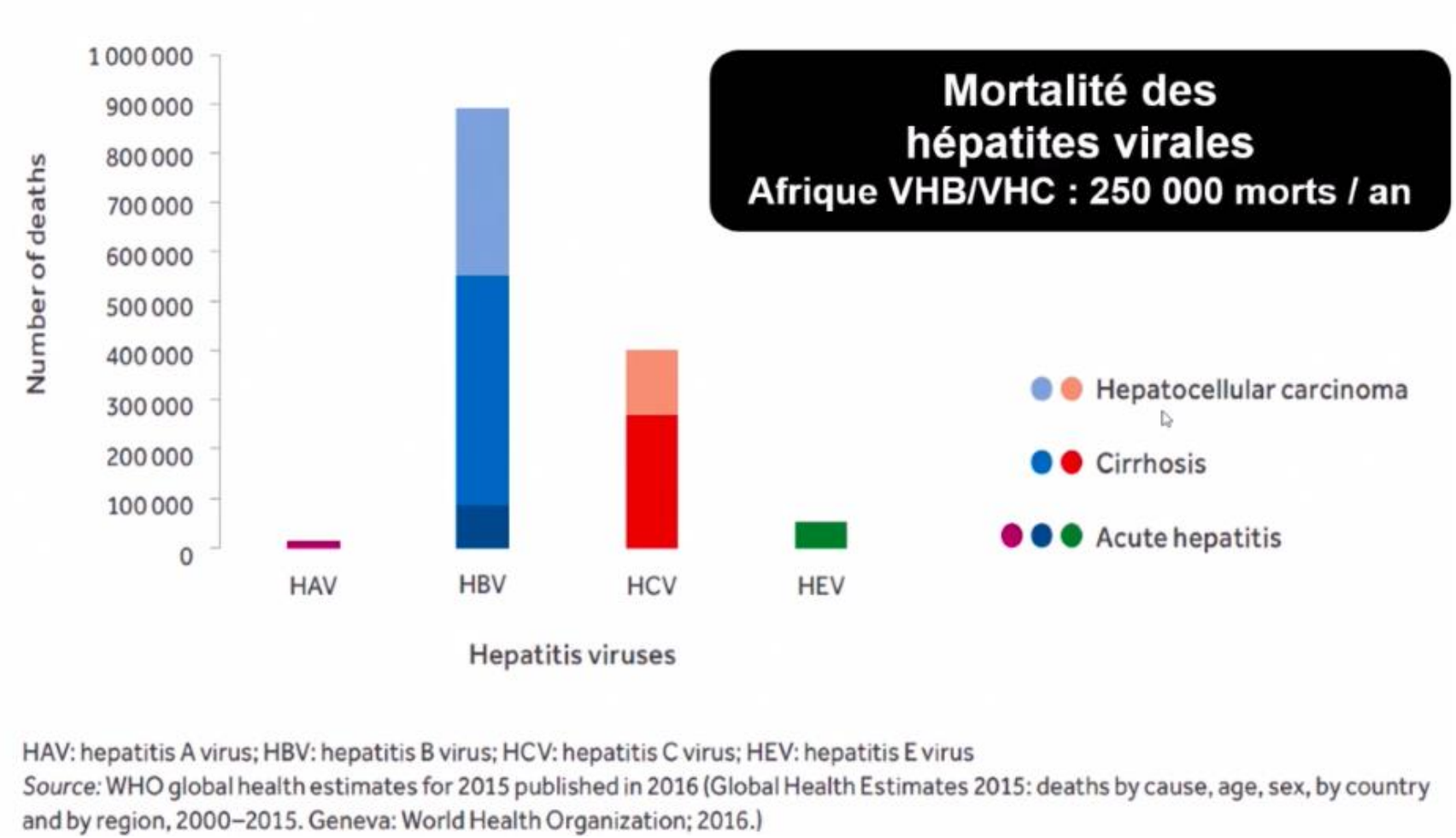
Fig. 1. Proposed Investment framework for hepatitis B and hepatitis C elimination. (Source: Pedrana A, Howell J, Scott N, *et al.* Global hepatitis C elimination: an investment case. Lancet Gastroenterology and Hepatology 2020[20]). (This figure appears in color on the web.)

Epidémiologie

Prévalence de l’hépatite B dans le monde en 2019 (AgHBs positif)

Prévalence AgHBs chez les enfants < 5 ans : 4,7% dans les années 90’ et 0,9% en 2019

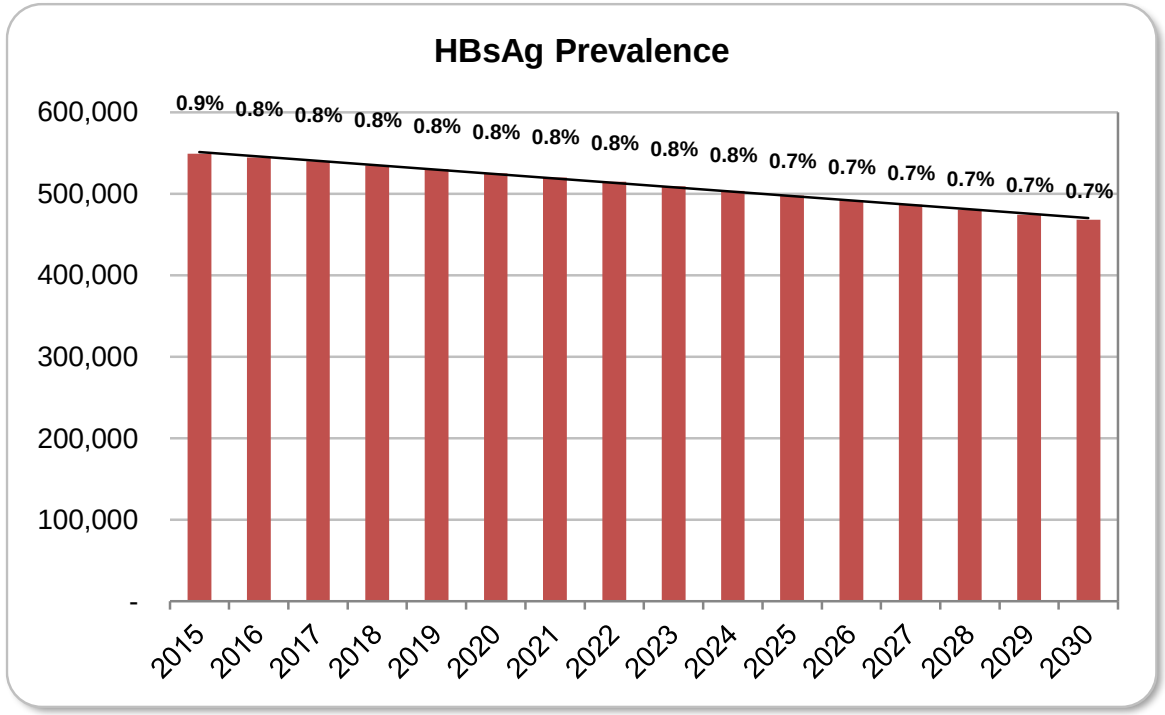
Mortalité annuelle des hépatites virales B



HAV: hepatitis A virus; HBV: hepatitis B virus; HCV: hepatitis C virus; HEV: hepatitis E virus
Source: WHO global health estimates for 2015 published in 2016 (Global Health Estimates 2015: deaths by cause, age, sex, by country and by region, 2000–2015. Geneva: World Health Organization; 2016.)

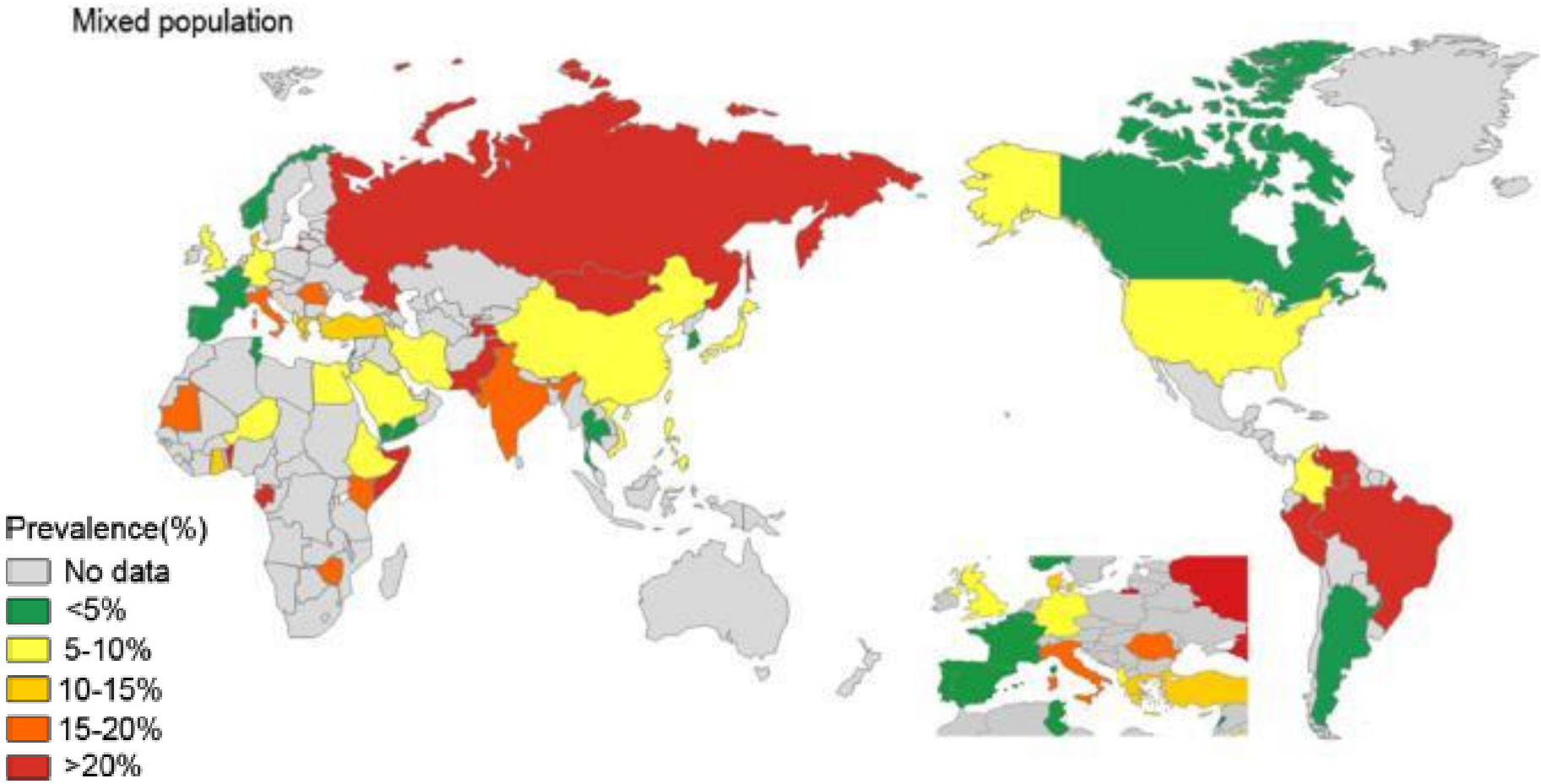
Makoni M et al. Lancet 2019

Prévalence de l'infection VHB en France



- With updated model inputs, in 2015, it is estimated that the prevalence of chronic HBV in France is 0.86%, representing ~ **550, 000** chronic infections, dropping to 0.70%, ~473,000 chronic infections by 2030
- With previous model inputs, in 2015, it was estimated that the prevalence of chronic HBV in France is 0.5%, representing ~ **348,820** chronic infections, dropping to 0.4%, 276,980 chronic infections by 2030

Séroprévalence de l'infection VHD chez les patients AgHBs+



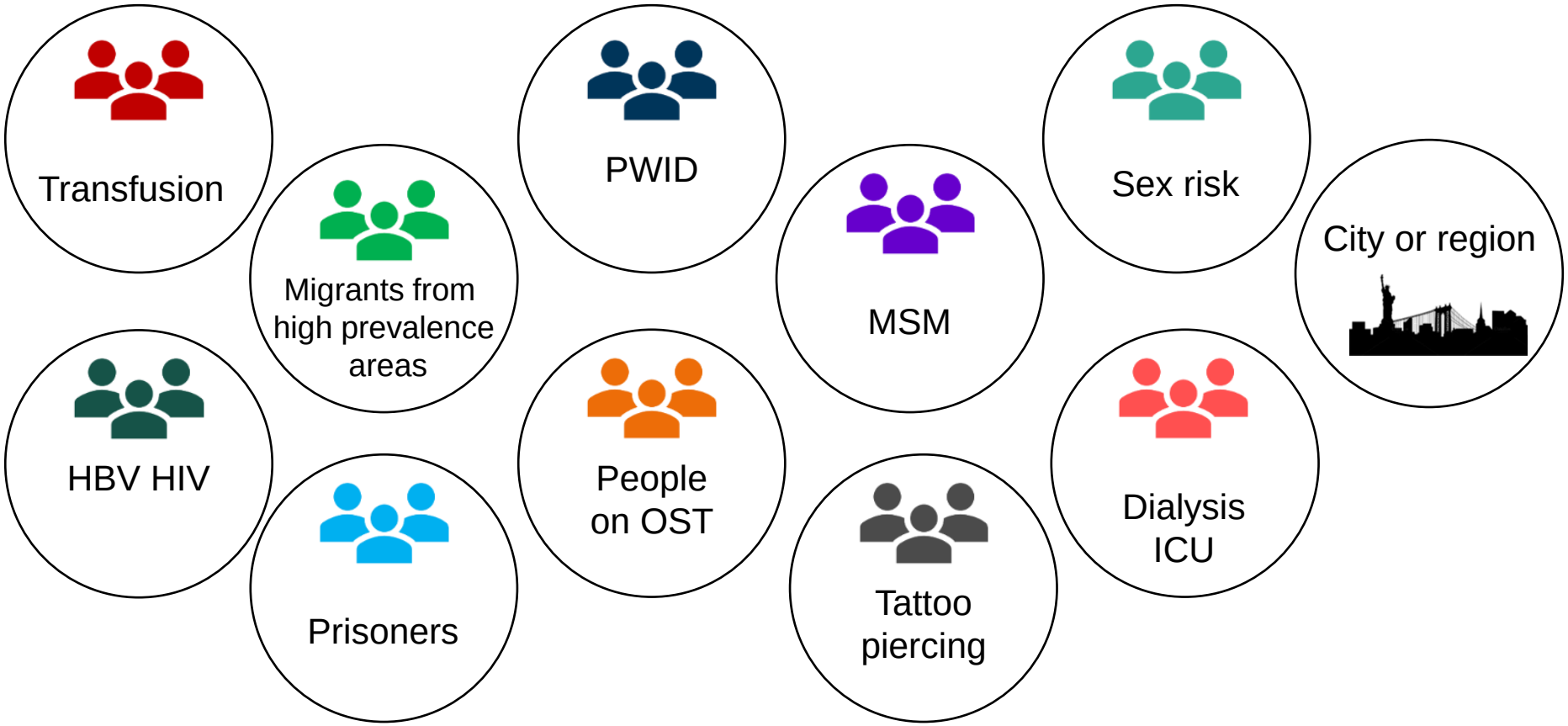
Chen HY et al. Gut 2018

Dépistage

Personnes exposées au risque de VHB

- ✓ Les personnes nées ou ayant résidé dans les régions de forte endémicité
- ✓ L'entourage proche et les partenaires sexuels d'une personne porteuse du VHB
- ✓ Les usagers de drogues par voie intraveineuse ou intranasale
- ✓ Les voyageurs et les personnes amenés à résider dans un pays de forte ou moyenne endémicité
- ✓ Les personnes séropositives pour le VIH, VHC ou ayant une IST en cours ou récente
- ✓ Les personnes ayant un tatouage ou un piercing
- ✓ Les personnes séjournant ou ayant séjourné en milieu carcéral
- ✓ Les personnes ayant des relations sexuelles avec des partenaires différents
- ✓ Les personnes ayant un risque d'exposition professionnelle

« Aller vers » le dépistage des personnes à risque



Rendre le dépistage plus accessible

Où	Comment	Qui
• Maisons de santé • Hôpital • Maternités • CSAPA • Migrants • SDF • Pharmacies	• AgHBs • TROD	• Généralistes • Pharmaciens • Personnel para-médical • Educateurs • Travailleurs sociaux

Le “comment” depend du “qui” et du “où”

QUELLE EST LA PLACE DES NOUVELLES MÉTHODES VIROLOGIQUES DE DÉPISTAGE DE L'INFECTION PAR LE VIRUS DE L'HÉPATITE B ?

1. **Le dépistage sérologique classique d'une infection par le virus de l'hépatite B repose sur la détection simultanée de l'antigène HBs, de l'anticorps anti-HBs et de l'anticorps anti-HBc (A1)**
2. **Les tests de diagnostic rapide de l'antigène HBs peuvent être utilisés dans les populations éloignées des structures de soins dans le cadre de programmes de prévention et de dépistage (B1)**
3. **Chez les patients éloignés des structures de soins ou sans abord veineux, le papier buvard (dried blood spot) est une alternative validée pour quantifier l'ADN du virus de l'hépatite B (B1)**

ACCORD FORT

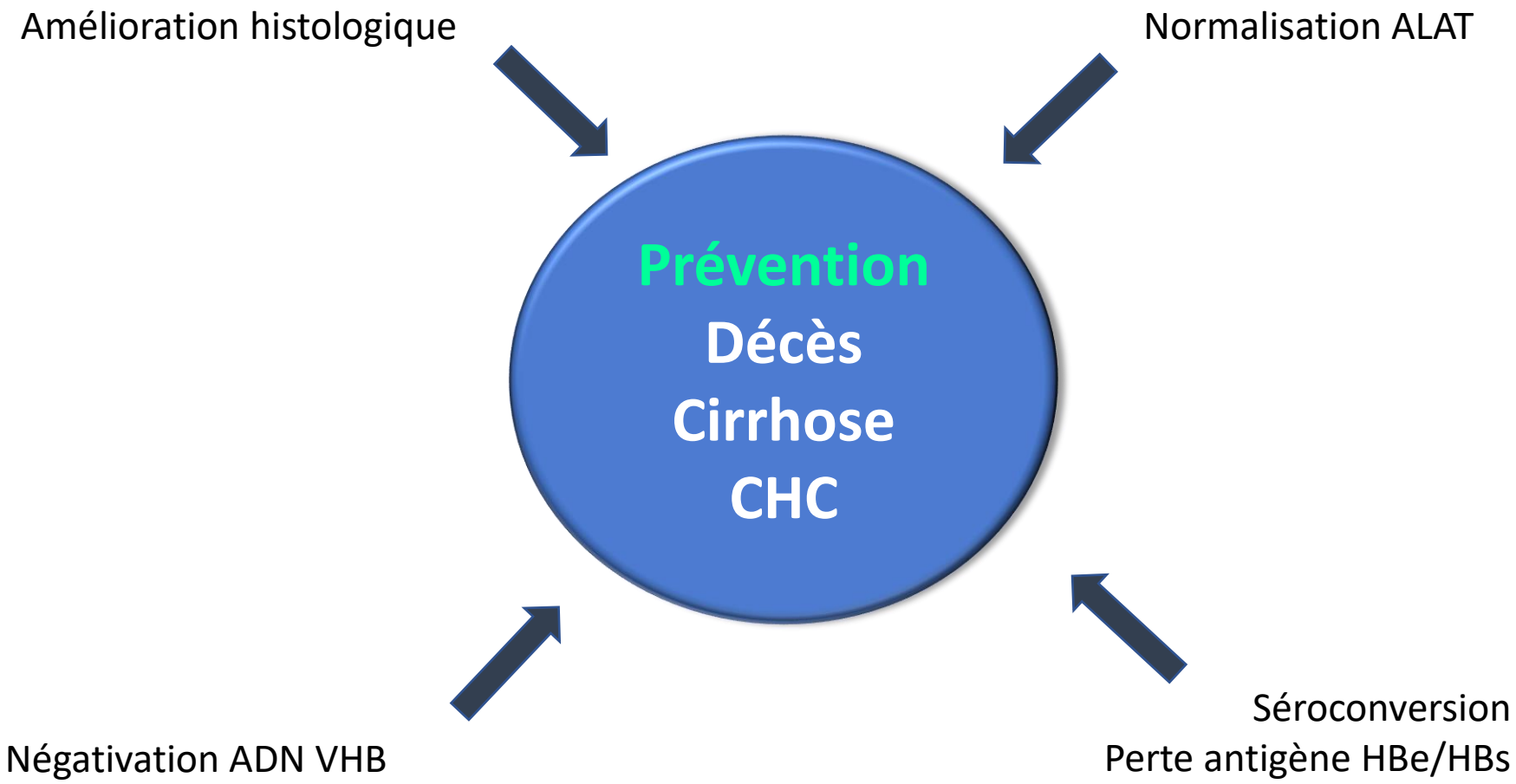
QUELLES SONT LES MÉTHODES NON-INVASIVES RECOMMANDÉES LORS DU BILAN INITIAL D'UNE INFECTION CHRONIQUE PAR LE VIRUS DE L'HÉPATITE B ? BILAN VIROLOGIQUE.

1. **Le bilan virologique initial d'une infection chronique par le virus de l'hépatite B doit comporter l'antigène HBe, l'anticorps anti-HBe et l'ADN du virus de l'hépatite B (A1)**
2. **Le génotypage du virus de l'hépatite B n'a pas d'intérêt et ne doit pas être effectué en dehors de programmes de recherche (B1)**
3. **Le dosage quantitatif de l'antigène HBs est utile pour définir le stade de la maladie et ajuster les modalités de surveillance (B1)**
4. **Des sérologies VIH, virus de l'hépatite C et virus de l'hépatite D doivent systématiquement être effectuées pour éliminer une co-infection virale (A1)**

ACCORD FORT

Traitement

Buts du traitement de l’hépatite B



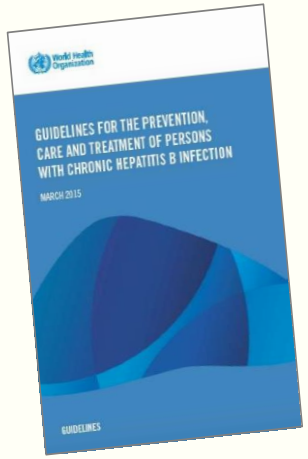
Objectifs thérapeutiques pour valider l'élimination de l'hépatite B

BOX 5.3 Programmatic targets for validating the elimination of HBV and HCV mortality

Countries should have achieved and maintained for at least 2 years the following programmatic targets for validating the elimination of HBV and HCV mortality:

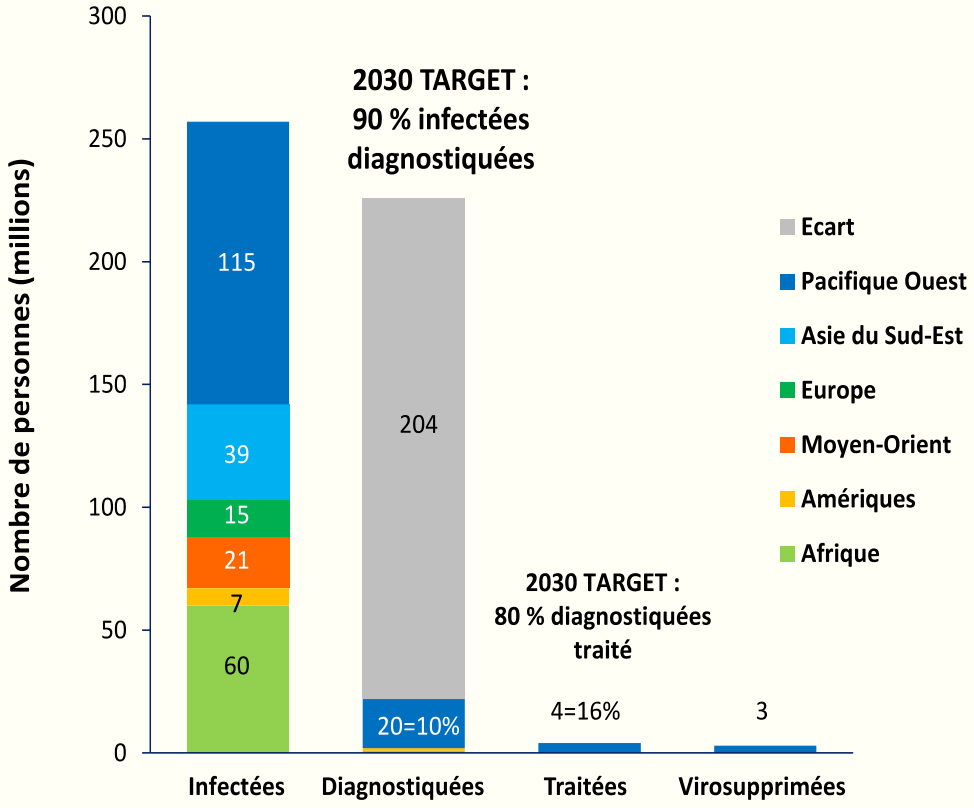
- ≥90% of persons with chronic hepatitis B or C virus infection diagnosed
- ≥80% of eligible persons diagnosed with chronic hepatitis B virus infection treated
- ≥80% of persons diagnosed with chronic hepatitis C virus infection treated

Cascade de soins de l'hépatite B



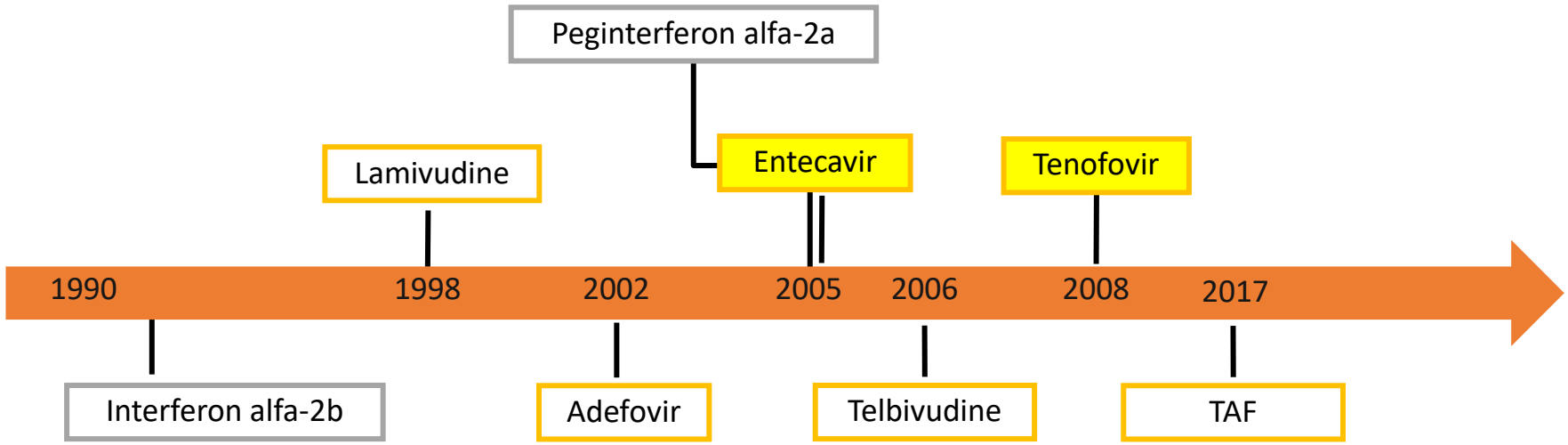
- ✓ **257 millions de personnes VHB+ dans le monde**
- ✓ **4,5 millions sous traitement**
- ✓ Combien de personnes nécessitent un traitement ?

Cascade de soins pour le VHB par région OMS 2016



Bhadoria A, Suisse, AASLD 2019, Abs. 925 actualisé

Traitements de l’hépatite B



Qui traiter en priorité? Critères OMS

- ✓ Cirrhose compensée ou décompensée
  - ✓ Quel que soit le statut HBe, la charge virale ou le taux de l'ALAT
- ✓ Patients avec élévation de l'ALAT et ADN VHB > 20000 UI/ml

  Quel que soir le statut HBe, surtout chez les sujets de moins de 30 ans
- ✓ Si ADN VHB non disponible, patients avec élévation de l'ALAT
  - ✓ Quel que soit le statut HBe
- ✓ Surveillance régulière des autres patients

Coût mensuel du traitement par Tenofovir

Pays	Ténofovir disoproxil fumarate	Entécavir
Maroc	27 €	250 €
Algérie	8 €	100 €
Bénin	12 €	ND
Burkina Faso	4 €	ND
Cameroun	3 €	ND
Congo	15 à 45 €	ND
Côte d'Ivoire	6 €	ND
Niger	11 à 15 €	ND
Sénégal	7 €	ND
Mali	8 €	ND
Gabon	235 €	186 €

Courtesy R Sombié

Définition du “HBV cure”

	Sterilising ‘cure’	Idealistic functional ‘cure’	Realistic functional ‘cure’	Attainable partial functional ‘cure’
Clinical scenario	Never infected	Recovery after acute HBV	Chronic HBV with HBsAg loss	Inactive carrier off treatment
HBsAg	Negative	Negative	Negative	Positive
Anti-HBs	Negative/Positive	Positive	Positive/negative	Negative
HBeAg	Negative	Negative	Negative	Negative
Serum HBV DNA	Not detected	Not detected	Not detected	Low level or not detected
Hepatic cccDNA, transcription	Not detected Not active	Detected Not active	Detected Not active	Detected Low level
Integrated HBV DNA	Not detected	Detected?	Detected	Detected
Liver disease	None	None	Inactive, fibrosis regress over time	Inactive
Risk of HCC	Not increased	Not increased	Declines with time	Risk lower *vs.* active hepatitis

Anti-HBs, antibody to HBsAg; cccDNA, covalently closed circular DNA; HCC, hepatocellular carcinoma.

Cornberg M et al. J Hepatol 2020;72:539-57

Traitements du futur. HBV cure

Table 2. Summary of new HBV antiviral therapies.

Compound	Phase of development	Comments / Data
HBV entry inhibitors		
NTCP inhibitor, Myrcludex B (Myr Pharmaceuticals)	Phase III (Hepatitis D) Phase I/II (Hepatitis B)	Strong effect on serum HDV RNA levels, induced ALT normalisation under monotherapy.[111]
Cyclosporine analogues	Preclinical	Several cyclosporine derivatives inhibited HBV infection with a sub-micromolar IC_{50} with no inhibition of bile acid uptake.[112]
Targeting cccDNA (Destabiliser, epigenetic regulators, endonucleases)		
cccDNA destabiliser, ccc_R08 (Roche)	Preclinical	First-in-class orally available HBV cccDNA destabiliser achieved sustained HBsAg and HBV DNA suppression in a mouse model.[64]
Targeted endonuclease, CRISPR/CAS9	Preclinical	Cleavage of cccDNA by Cas9 showed reduction in both cccDNA and other parameters of viral gene expression and replication *in vitro*[65]
Targeting HBx		
CRV431 (ContraVir)	Phase I	Cyclophilin inhibitor that prevents Cyclophilin A-HBx complex formation and HBV replication.[113]
Nitazoxanide (Romark)	Phase II	First-in-class thiazolide originally developed as antiprotozoal agent. Inhibits HBV transcription from cccDNA by targeting the HBx–DDB1 interaction.[70] A pilot trial showed antiviral efficacy.[114]
Inhibition of gene expression / gene silencing		
Antisense oligonucleotides and locked nucleic acids		
GSK3389404 (GlaxoSmith Kline)	Phase II	Methoxyethyl antisense oligonucleotide conjugated to N-acetylgalactosamine moieties. Acceptable safety and pharmacokinetic profile in phase I.[72]
Locked nucleic acid platform-based single-stranded oligonucleotides (Roche)	Preclinical	Liver-targeted single-stranded oligonucleotide therapeutics based on the locked nucleic acid platform. Rapid and long-lasting reduction of HBsAg in a mouse model.[71]
RNA interference		
ARC-520 (Arrowhead)	Development discontinued	Decrease in HBsAg level in HBeAg-positive but not in HBeAg-negative patients.[29]
JNJ-3989 (Janssen) formerly ARO-HBV-1001 (Arrowhead)	Phase I/II	HBsAg reduction in HBeAg-positive and HBeAg-negative patients. Majority of patients achieved HBsAg <100 IU/ml.[73]
AB-729 (Arbutus)	Preclinical	Activity *in vitro* and strong HBsAg reduction in mice.[115]
ALN-HBV (Alnylam)	Preclinical	Profound and durable HBsAg silencing *in vitro* and *in vivo*.[116]
Targeting the viral RNA post-transcriptional regulatory element		
Dihydroquinolizinone compounds RG7834 (Roche) AB-452 (Arbutus)	Preclinical	Specific blockage of the production of HBV DNA and viral antigens.[74,76,117]
Core protein (Capsid) assembly modulators (CpAMs)		
NVR 3-778 (Novira, Janssen Pharmaceutica)	Development discontinued	First in-class CpAM showed reduction of HBV DNA and HBV RNA, greater effect in combination with PEG-IFN.[79]
ABI-H0731 (Assembly Bioscience)	Phase IIa	CpAMs showed high antiviral efficacy in phase I and IIa studies with >2 log decline of HBV DNA. HBV RNA decline is stronger with CpAM (ABI-H0731) compared to NA therapy.[118–124]
RO7049389 (Roche)	Phase II	
JNJ-56136379 (Janssen)	Phase II	
AB-506 (Arbutus)	Phase I	
ABI-H2158 (Assembly Bioscience)	Phase I	
GLS4JHS (Jilin University)	Phase I/II	
EDP-514 (Enanta)	Preclinical	
GLP-26 (Emory University)	Preclinical	
ABI-H3733 (Assembly Bioscience)	Preclinical	
HBsAg release inhibitors		
Nucleic acid polymers (REP compound series) (Replicor)	Phase II	Small studies with REP compounds (i.v. application) in combination with TDF and PEG-IFN in HBV monoinfected and HBV/HDV co-infected patients show strong HBsAg decline.[81,82]

ALT, alanine aminotransferase; Anti-HBs, antibody to HBsAg; cccDNA, covalently closed circular DNA; CpAMs, core protein assembly (or allosteric) modulators; NA, nucleos(t)ide analogue.
*For drugs in preclinical development the list may not be complete.

Table 3. Summary of new immunomodulatory therapies targeting HBV.

Compound	Phase of development	Comments / Data
Targeting cell intrinsic and Innate Immune responses		
RO7020531 (Roche) TLR 7 agonist	Phase I	Combination with the CpAM RO7049389 achieved sustained HBV DNA suppression and HBsAg loss in a mouse model.[125]
Vesatolimod, GS-9620 (Gilead) TLR 7 agonist	Phase II	Dose-dependent pharmacodynamic induction of ISG15 and host NK and HBV-specific T cell responses but no HBsAg reduction in patients.[87,88] Lack of effect for cccDNA *in vitro*.[126]
JNJ-4964 (Janssen) TLR 7 agonist	Preclinical	Antiviral efficacy (HBV DNA, HBsAg, liver HBV DNA, HBV RNA) in a mouse model.[127]
GS-9688 (Gilead) TLR 8 agonist	Phase I	Induced IL-12 and IL-RA1 in humans. Short duration did not result in HBsAg decline.[128]
AIC649 (AiCuris) TLR 9 agonist	Phase I	Increased IL-1β, IL-6, IL-8 and IFN-γ and reductions in IL-10 levels.[129]
Inarigivir soproxil (Spring Bank) RIG-I agonist	Phase II	Dual mode of action: RIG-I Agonist and interference with the interaction of the viral polymerase and pgRNA. The ACHIEVE trial showed dose-dependent antiviral response on HBV DNA and HBV RNA.[92]
Targeting adaptive immune responses		
Checkpoint Inhibitors Nivolumab (Opdivo, Bristol-Myers Squibb)	Phase I	Single dose of Nivolumab (with or without GS4774) showed HBsAg reduction >0.5 log in some patients.[96]
TG1050/T101 (Transgene/Talsy) Non-replicative adenovirus serotype 5 encoding 3 HBV proteins (Therapeutic Vaccine)	Phase I	Induction of T cell responses in mouse models and reduction of viral parameters.[130] Dose-related immunogenicity in patients but so far only preliminary data on clinical effects.[131]
CPmutS (Vaccitech) Adjuvanted ChAd and MVA vectored therapeutic HBV vaccines	Phase I	Robust T cell and anti-HBs response in mice.[132]
HepTcell (Altimmune) HBV Peptide therapeutic vaccine with TLR9 adjuvant IC31	Phase I	Human T cell responses against HBV markedly increased over baseline compared to placebo but no effect on HBsAg.[133]
JNJ-64300535 (Janssen) Electroporation of DNA vaccine	Phase I	No clinical data (NCT03463369).
INO-1800 (Inovio) DNA plasmids encoding HBsAg and HBcAg) plus INO-9112 (DNA plasmid encoding human interleukin 12)	Phase I	Activated and expanded CD8+ killer T cells (www.inovio.com).
GS-4774 (Globeimmune, Gilead) Heat-inactivated, yeast-based, T cell vaccine	development discontinued	No significant reductions in serum HBsAg in phase II.[134]
Genetically engineered T cells / Monoclonal or bispecific antibodies	Preclinical	Reductions in HBsAg and HBV DNA in mouse models.[101,102]

cccDNA, covalently closed circular DNA; pgRNA, pregenomic RNA.
*For drugs in preclinical development the list may not be complete.

Cornberg M et al. J Hepatol 2020;72:539-57

Prévention

Objectifs de prévention pour valider l'élimination de l'hépatite B

BOX 3.1 Impact targets for validation of elimination of MTCT of HBV

Countries that provide **universal HepB-BD** to all neonates should have achieved the following **impact target** for validation of EMTCT of hepatitis B:

- ≤0.1% HBsAg prevalence among the ≤5-year-old birth cohort (and older children)[a]

Countries that provide targeted timely HepB-BD only should have achieved an additional **impact target** for validation of EMTCT of hepatitis B:[b]

- ≤0.1% HBsAg prevalence among the ≤5-year-old birth cohort (and older children)

AND

- Maternal–child transmission rate of ≤2%

a The ≤0.1% HBsAg prevalence can be measured among either 5 year olds, 1 year olds or those aged 1–5 years, according to existing country surveillance and data collection activities. For those regions and countries with a long history of high Hep B vaccination coverage (e.g. Region of the Americas), and that already conduct school-based serosurveys, there could be flexibility to conduct serosurveys in older children >5 years.

b Countries that provide targeted timely HepB-BD, and where vertical transmission continues due to specific populations of pregnant women with a high HBsAg prevalence, e.g. Indigenous populations or other higher-risk vulnerable populations, are required to show both ≤0.1% HBsAg prevalence among ≤5-year-old children *and* an MTCT rate of ≤2%.

EMTCT: elimination of mother-to-child transmission; HepB-BD: hepatitis B birth dose; HBsAg: hepatitis B surface antigen; MTCT: mother-to-child transmission

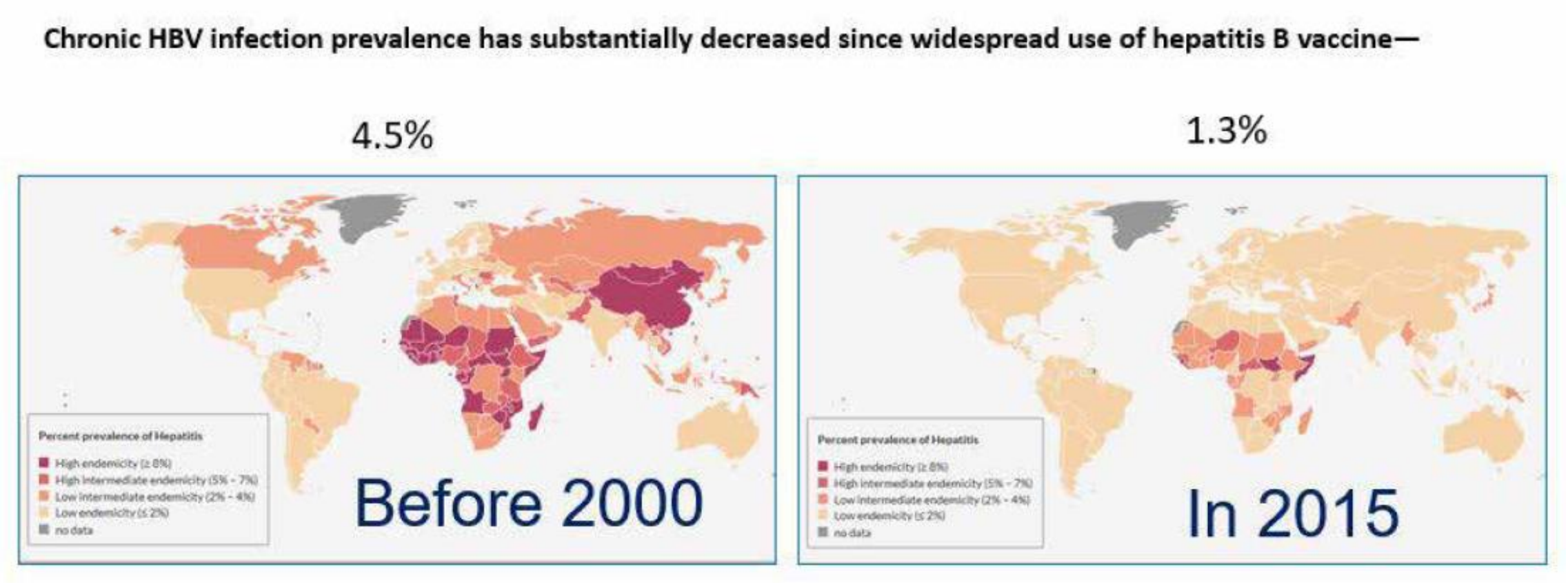
Recommandations OMS

- ✓ Prévention transmission materno-foetale
  - ✓ Prophylaxie par Tenofovir
  - ✓ Vaccination du bébé dès la naissance

- ✓ Vaccination des enfants avant l'âge de 5 ans

Since 2020, WHO has recommended that hepatitis B surface antigen (HBsAg)-positive pregnant women at high risk of transmitting the virus to their infants due to high HBV DNA level (≥200 000 IU/mL) receive peripartum antiviral tenofovir prophylaxis from the 28th week of pregnancy until at least delivery to prevent mother-to-child transmission (PMTCT) of HBV *(9).* This recommendation is in addition to the 3-dose hepatitis B vaccination in all infants (starting with timely HepB-BD). In a number of settings (mostly high-income countries), hepatitis B immunoglobulin (HBIg) may also be used to further reduce the risk of MTCT of HBV.

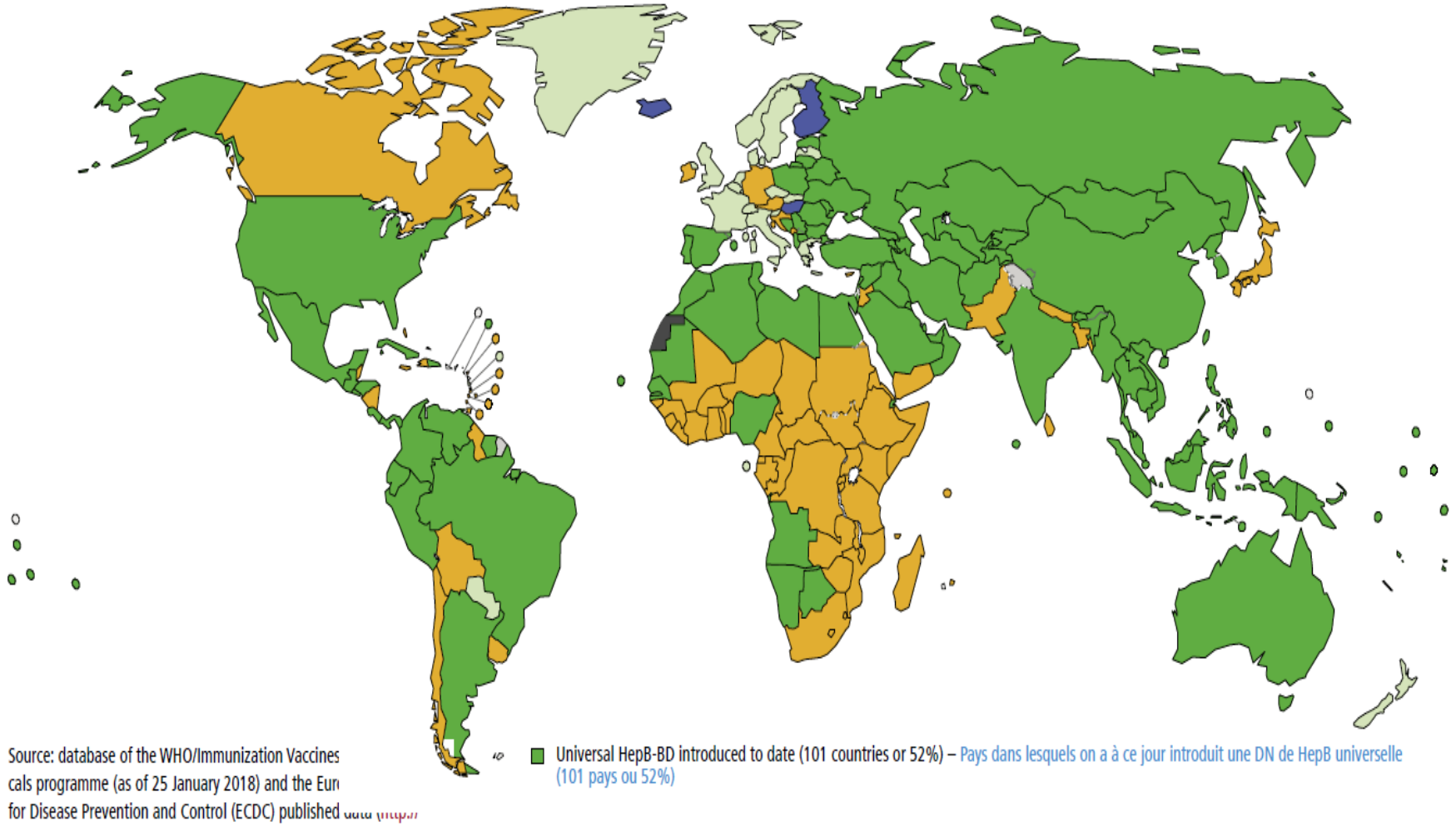
Prévalence des infections VHB chez l'enfant de moins de 5 ans



Région Afrique : 3 %
Objectif OMS 2030 : 0,1 %

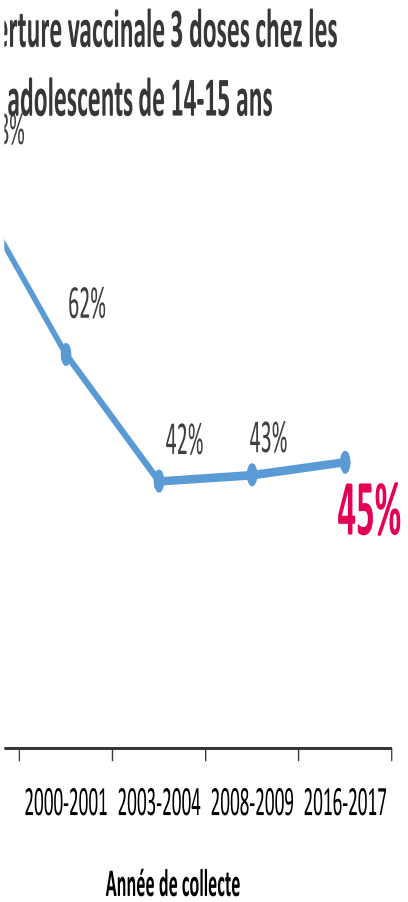
WHO, Global Hepatitis Report 2017

Pays avec une politique de vaccination selon les critères OMS



WHO, Wkly Epidemiol Rec, février 2018

UVERTURE VACCINALE ANTI-VHB



ad. Natle Méd., 2016 ; données
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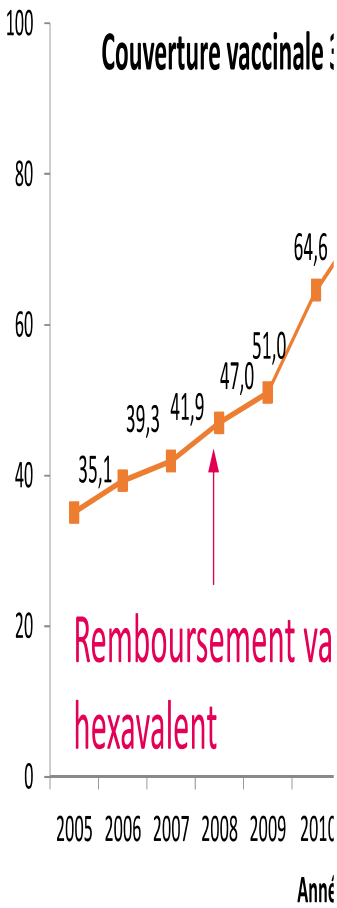


Drees, Remontées des services
mois. exploitation Santé publiqu

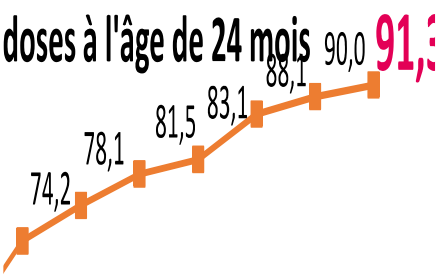
Obligation vaccinale pour les enfants nés à partir du 1

CV à 7 mois vaccin hexavalent :

- **98,6%** pour les nourrissons nés entre janvier et mai 20
- *vs.* **93,1%** pour ceux nés entre janvier et mai 2017

Couverture vaccinale en France

Santé publique France



cin

2011 2012 2013 2014 2015 2016 2017

de collecte

e PMI – Certificat de santé du 24e
France

janvier 2018

8 **+5,5 points**

8

SNDS, exploitation SpF

Couve

100%

88

NÉES DE COUVERTURE VACCINALE CHEZ LES HOMMES T DES RELATIONS SEXUELLES AVES LES HOMMES ET LE GERS DE DROGUE

Santé publique France

RMI 2645 HOMMES AYANT DES RELATIONS SEXUELLES AVEC S HOMMES (ÉTUDE ANRS PREVAGAY 2015)

' estimée à 63% (IC à 95%: 60,0 – 65,9)

' chez les PVVIH estimée à 65,2% (IC à 95% 57,6 – 72,1) chez les VIH et 90,1% (IC à 95% 74,5 – 97,0) chez celles infectées par le VHC

AGERS DE DROGUES (ÉTUDE ANRS COQUELICOT 2011-2013)

HBs Ag seroprevalence and self-reported HBV vaccination history according to the endemicity level of untry of birth, ANRS-Coquelicot Survey 2011–2013

	HBs Ag seroprevalence (95% CI)	Self-reported HBV vaccination history† (95% CI)
ic zone	0·7*** (0·3–1·5)	62·6 (57·6–67·4)
)	(*n* = 7)	(*n* = 686)
ndemic zone	2·2*** (0·8–5·7)	59·3 (48·8–68·9)
	(*n* = 7)	(*n* = 179)
mic zone	7·6*** (2·7–19·1)	47·4 (29·9–65·5)
	(*n* = 9)	(*n* = 60)
	1·4 (0·8–2·5)	60·9 (56·2–65·4)
)	(*n* = 23)	(*n* = 925)

15; Brouard, Epidemiol Infect 2017

Conclusion

Comment augmenter les financements?

Mechanism	Approaches*	Examples
Reduction in treatment costs	Price negotiations with pharmaceutical manufacturers for hepatitis treatment and diagnostics	Australia, Brazil, Thailand[16,26]
	Local production of generic medicines	China, India[26]
	Inclusion of diagnostics and medications under UHC, list on Essential medicines and Essential diagnostics list	Rwanda, Pakistan, Brazil[26]
	Utilisation of TRIPs flexibilities to access affordable medicines and diagnostics	Thailand (hepatitis C medications)[26]
Maximise effectiveness of public health spending	Integration of viral hepatitis into existing health services for HIV, maternal child health programmes, and non-communicable diseases	Hepatitis B: South Africa,[33] Brazil[26]; Hepatitis C: Egypt, Pakistan[16,20]
	Adopting an investment case approach to guide investments	South Africa,[33] China,[26,34] Senegal,[35] The Gambia[36]
	Leverage WHO regional technical and resource support for viral hepatitis and other disease elimination activities to improve efficiency and effectiveness	Russian Federation (strategic planning), Ethiopia (surveillance reporting), Pacific Islands and Territories (vaccination)[16]
Share costs with other strategies	Immunization and blood safety	Rwanda, Brazil, China[26]
	Co-infection with HIV and service delivery	Rwanda, Brazil, South Africa[26]
	Prevention of mother-to-child transmission including investment to increase in-hospital births through MDG funding pools	China,[26] Fiji,[37] Malaysia[16]
	Hepatitis C programmes	Myanmar, Mongolia[16]
	Non-communicable disease programmes	Egypt (hepatitis C)
Increase innovation to increase efficiencies over time	Dried blood sampling	The Gambia[36]
	Non-specialist care and telemedicine	Australia[37,38]
	PoC multi-disease diagnostic platforms (e.g. GenXpert) to increase hepatitis B testing capacity	Rwanda[16]
	Cross-sectoral government ministry partnerships	South Africa- Ministry of Health and Ministry of Finance[16]
International donor investment	Hepatitis B vaccination	GAVI Alliance hepatitis B vaccination program (birth dose soon to be added to global program)[39]; utilization of MDG4 and 5 funds to increase vaccination coverage including birth dose- Fiji, Brazil, Rwanda[26]
	Prevention of mother-to-child transmission including investment to increase in-hospital births	Public- private partnerships-China[26] (Zeshan Foundation and Rotary International with Ministry of Health) China-GAVI-MoH partnership Global Fund
	Provision of effective treatment	Rwanda – CHAI; NGO and pharma funding partnership with MoH, Fiji, Kiribati, Samoa and Tonga (Gilead, HepB Free) Universal health coverage and essential medicines list-China, Brazil, Rwanda[16]
	Low-cost diagnostics	China, India Unitaid is partnering with the Foundation for Innovative Diagnostics (FIND) through a US $38 million grant to support the development point-of-care diagnostics[40] Development and validation of in-house HBV DNA assays with international support–The Gambia[41]
	Regional strategy support	Colombia, Brazil, Chile–leveraging the PAHO Strategic Fund to cover cost of diagnostics and treatment to increase affordability[16]

- ✓ Négociation des prix
- ✓ Intégration de l'élimination de l'hépatite B dans les programmes existants déjà
- ✓ Renforcer l'innovation (télémédecine, tests rapides…)
- ✓ Aide internationale

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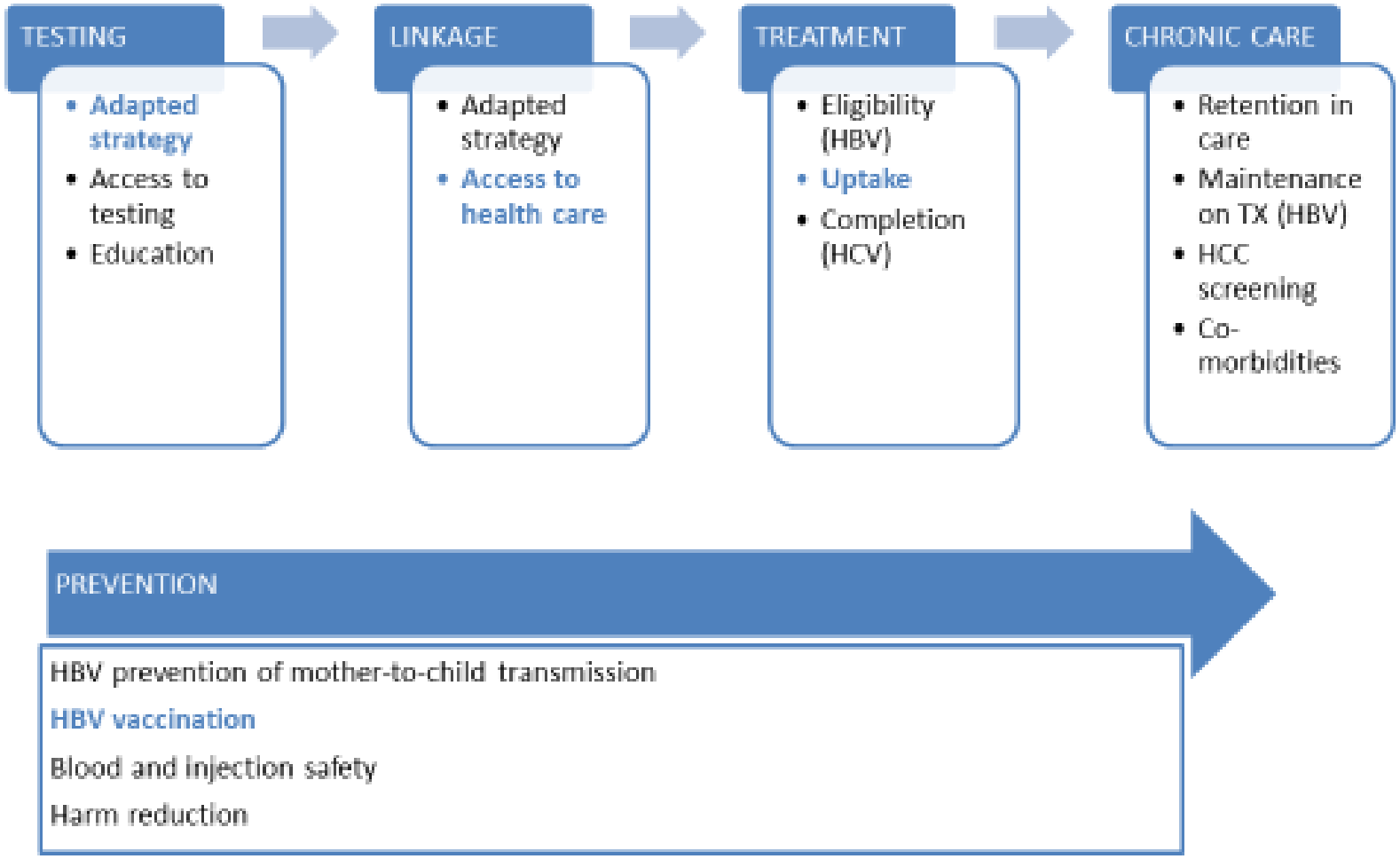
L’élimination nécessite d’agir à toutes les étapes de la cascade



Wandeler G. Public health issues of hepatitis in high-income countries

Actions essentielles pour l'élimination de l'hépatite B

1. **Raise awareness** among populations at risk, policymakers and politicians through population-level education campaigns, targeted outreach, advocacy and civil society activities
2. **Reduce stigma and discrimination** through population education, advocacy and changes in current policy and legislation frameworks to protect the rights of people living with hepatitis B
3. **Increase coverage of hepatitis B infant vaccination including birth dose** and catch up programmes for unvaccinated at-risk groups
4. **Increase coverage and access to affordable diagnosis, linkage to care and treatment** including expansion of hepatitis B diagnosis and monitoring programmes under Universal Health Coverage and inclusion of hepatitis B treatment in the Essential Medicines List
5. **Improve surveillance systems and epidemiologic data collection** to inform context of local epidemics and driving factors for transmission and provide feedback on progress towards achieving elimination goals
6. **Invest to improve quality, access, affordability and coverage of health services and infrastructure** to deliver hepatitis B elimination programs nested within existing public health programmes to allow rapid scale-up, facilitate cost-effective resource utilisation and limit up-front expenditure
7. **Support research and development of novel diagnostics and new therapeutics** to increase coverage of hepatitis B diagnosis and monitoring and achieve hepatitis B cure

- ✓ Sensibiliser les soignants et les politiques
- ✓ Lever les stigmatisations
- ✓ Vacciner
- ✓ Favoriser l'accès au diagnostic et au traitement
- ✓ Surveillance épidémiologique
- ✓ Renforcer les équipes existantes
- ✓ Encourager la recherche HBV cure

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L'élimination de l’hépatite B est-elle réaliste ?