

IUMFE - Université de Genève
Télémeeting du 12 février 2025

Diagnostic différentiel et investigation de tests hépatiques perturbés

Darius Moradpour

Service de Gastroenterologie et d'Hépatologie
Centre Hospitalier Universitaire Vaudois
Université de Lausanne

Unil

Darius.Moradpour@chuv.ch
www.gastro-hepato.ch



Liver Function Tests

- **Hepatocellular integrity**
AST, ALT
- **Cholestasis**
AP, γ -GT
- **Synthetic and excretory function**
PT/INR, albumin, bilirubin

Liver Function Test Elevation

Diagnostic Approach

- **History**
- **Physical examination**
- **Laboratory tests (LFTs - specific tests)**
- **Imaging: US (Doppler, CEUS), CT, MRI/MRCP, EUS, ERCP, angiography**
- **Liver biopsy (percutaneous, transjugular, EUS-guided, laparoscopic)**

DD of Chronic LFT Elevation

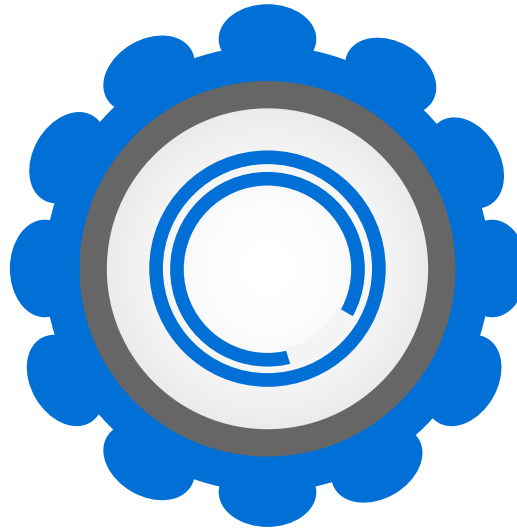
● Chronic viral hepatitis	HBsAg, anti-HCV
● Alcoholic liver disease	History
● MASLD/MASH	Associated conditions
● Drug toxicity	History
● Autoimmune liver disease	ANA, SMA; AMA; MRCP
● Hereditary hemochromatosis	Ferritin, transferrin saturation
● Wilson disease	Coeruloplasmin
● α 1-Antitrypsin deficiency	α 1-antitrypsin
● Celiac sprue	Anti-tTG
● Thyroid dysfunction	TSH

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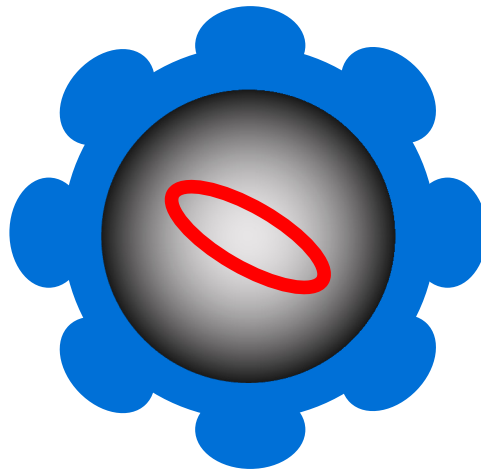
HAV



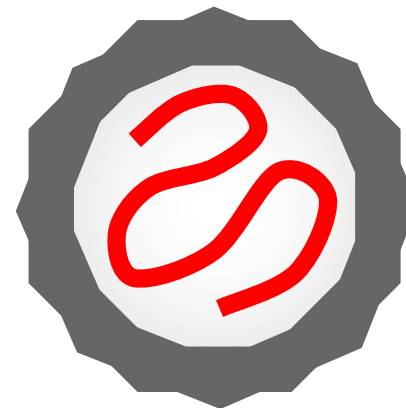
HBV



HCV



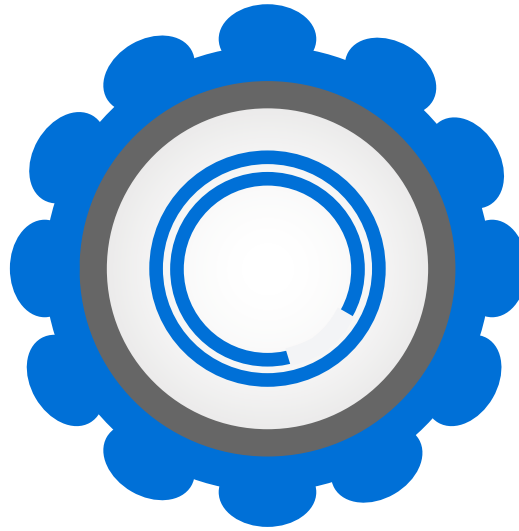
HDV



HEV



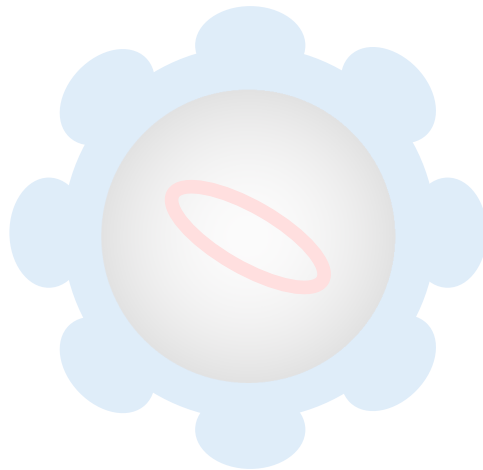
HAV



HBV



HCV

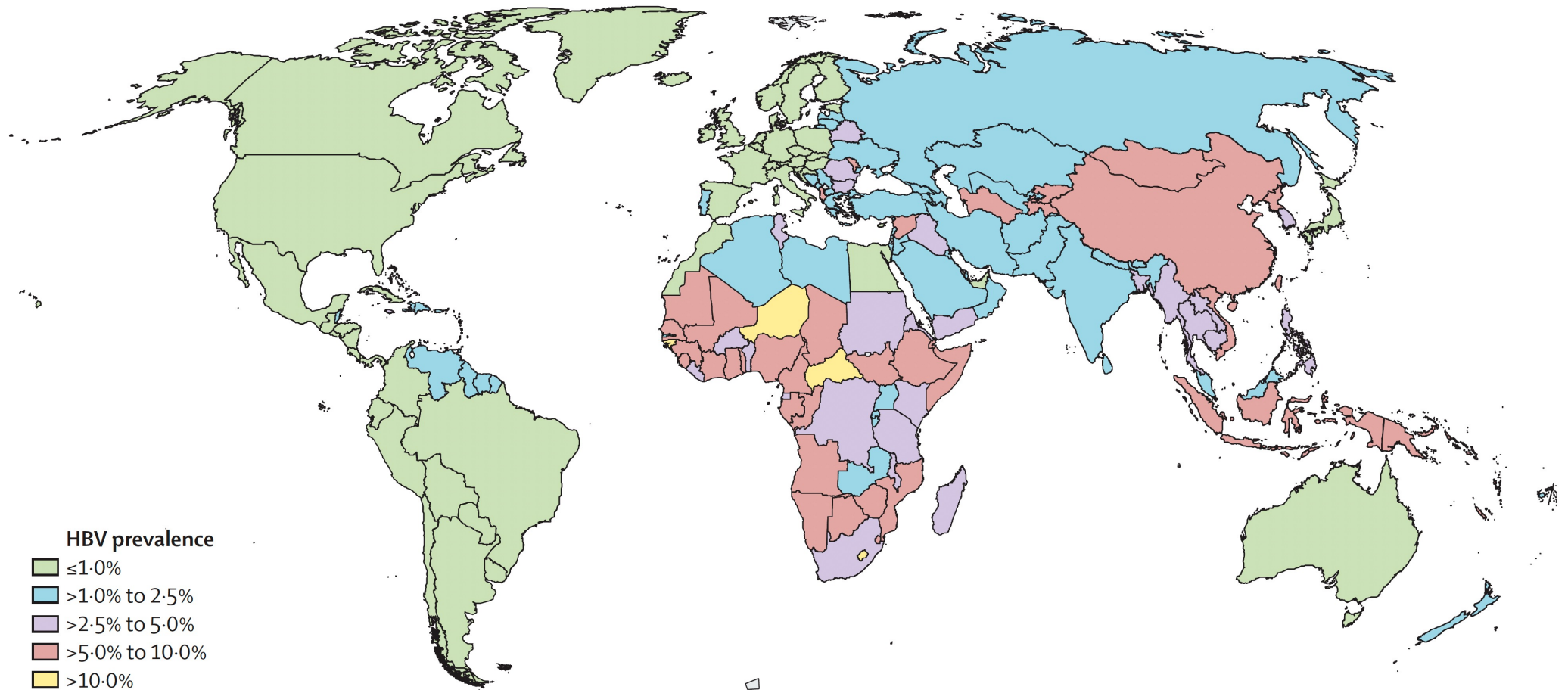


HDV



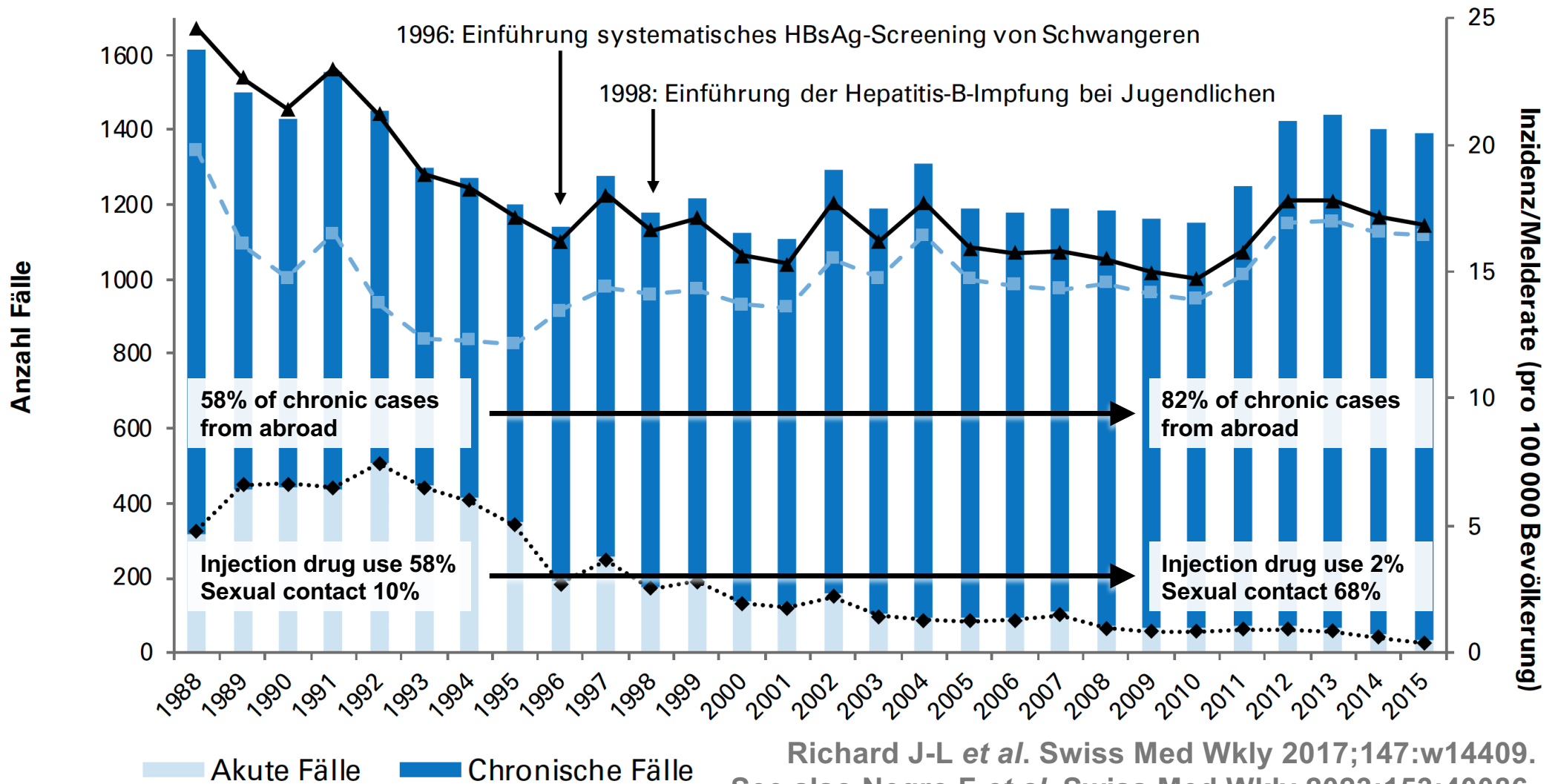
HEV

Current Epidemiology of Hepatitis B



The Polaris Observatory Collaborators. Lancet Gastroenterol Hepatol 2023;8:879-907.

Acute and Chronic HBV Infection in Switzerland



Richard J-L *et al.* Swiss Med Wkly 2017;147:w14409.
 See also Negro F *et al.* Swiss Med Wkly 2023;153:40086.

VIRAL HEPATITIS SUSPECTS



Health Care Provider-Initiated Testing for Chronic HBV Infection

A. Clinical signs or symptoms of hepatitis

B. Risk factors

- **Medical** (chronic liver disease, hemodialysis, persons with HIV infection or other STD, patients before immunosuppressive therapy, ...)
- **Demographic**
- **Behavioural** (family and household members, sexual partners, MSM, injecting drug use, ...)
- **Occupational**
- **Others** (newborns of HBV-infected mothers, institutionalized persons, imprisonment, ...)

SEVHep - SFOPH | Fretz R *et al.* Swiss Med Wkly 2013;143:w13793.
See also Tan R *et al.* Rev Med Suisse 2025;21:231-236.

Classification of Chronic HBV Infection

	HBsAg	HBeAg	HBV DNA ¹⁾	ALT
HBeAg-pos. chron. hepatitis B	+	+	10⁴-10⁷	↑
HBeAg-neg. chron. hepatitis B	+	-	> 2 x 10³	↑
HBeAg-neg. chron. HBV infection	+	-	< 2 x 10³	=
HBeAg-pos. chron. HBV infection	+	+	> 10⁷	=
Resolved hepatitis B	- (anti-HBs)	-	-	=

■ **Antiviral treatment**
■ **Monitoring (ALT ± AFP/US)**
■ **Attn ISDT!²⁾**

¹⁾IU/ml

²⁾Immunosuppressive drug therapy → preemptive or prophylactic antiviral therapy

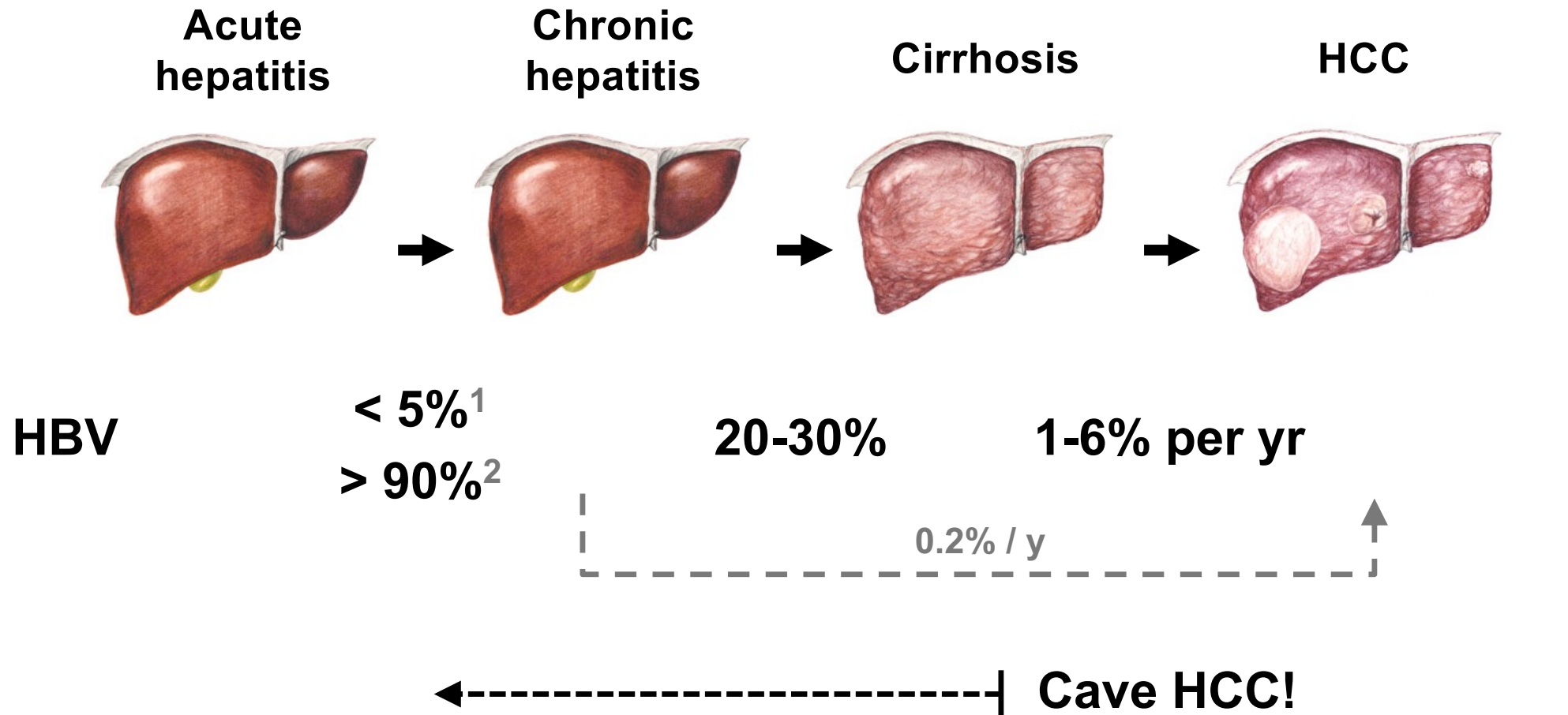
Adapted from Hoofnagle JH *et al.* Hepatology 2007;45:1056-1075 and EASL CPG. J Hepatol 2017;67:370-398.
See also Terrault NA *et al.* AASLD. Hepatology 2018;67:1560-1599 and WHO Guidelines of Mar 30, 2024 (www.who.int).

Chronic Hepatitis B Therapy 2025

PEG-IFN-α2a		Pegasys[®]	approved
Lamivudine	LAM	Zeffix[®]	approved
Telbivudine	L-dT	Sebivo[®]	approved
Entecavir	ETV	Baraclude[®] *	approved
Tenofovir	TDF	Viread[®] *	approved
" alafenamide	TAF	Vemlidy[®]	approved
Emtricitabine	FTC	+ TDF = Truvada[®] *	approved for HIV

* Also available as generic drugs

Natural History of Hepatitis B

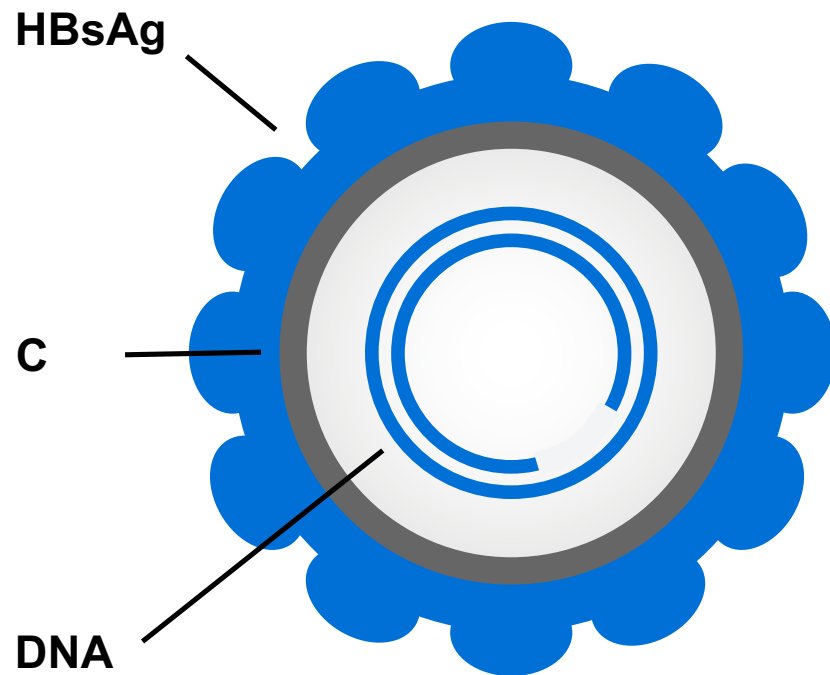


See Marcellin P *et al.* Lancet 2013;381:468-475.

¹Adult ²Newborn

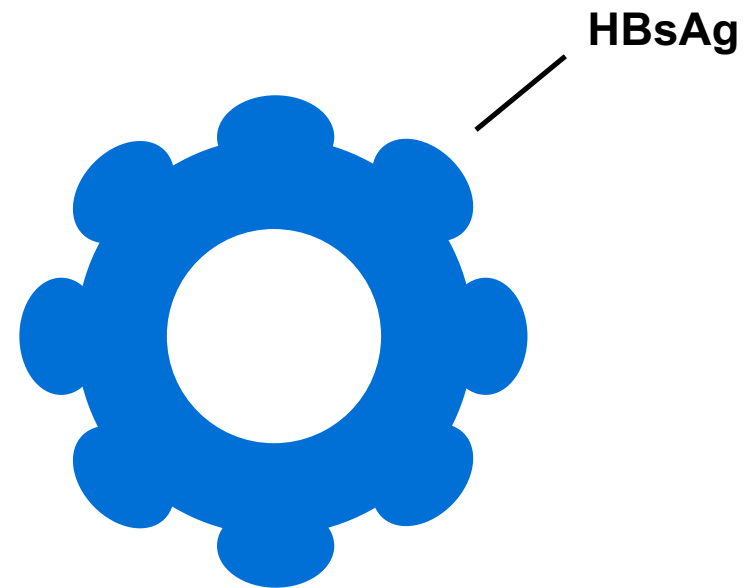
HBV Vaccination

HBV



→ anti-HBc
→ anti-HBs

HBV Vaccine



→ anti-HBs



Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra

Département fédéral de l'intérieur DFI
Office fédéral de la santé publique OFSP

Directives et recommandations

Recommandations pour la prévention de l'hépatite B

Office fédéral de la santé publique (OFSP), Commission fédérale pour les vaccinations (CFV)

Mars 2019

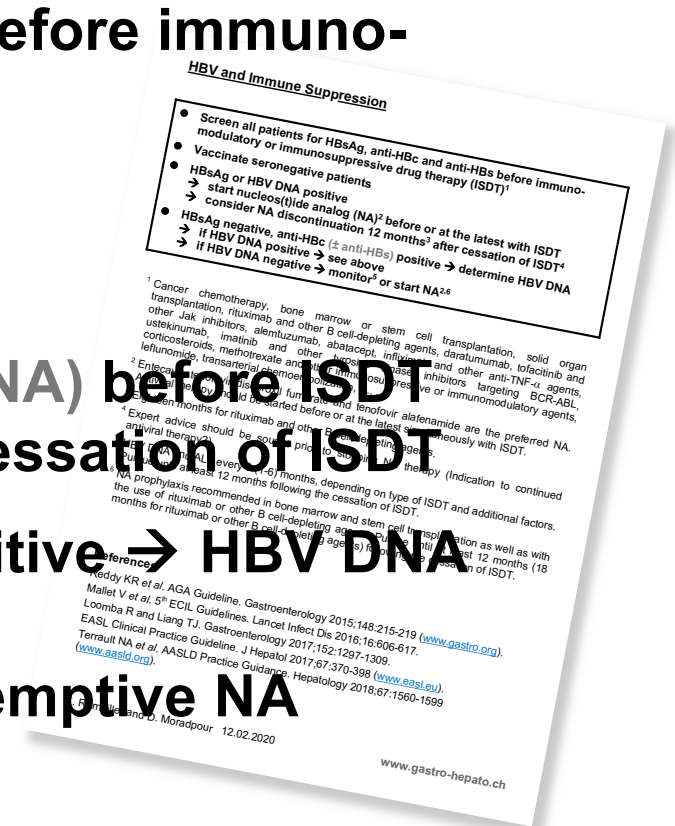
- Vaccination des nourissons, avec vaccin combiné hexavalent, à l'âge de 2, 4 et 12 mois
- Dépistage durant la grossesse → immunisation active et passive ; traitement antiviral dès 24^e - 28^e sem si HBV DNA > 2 x 10⁵ UI/ml
- Contrôle sérologique après vaccination de personnes à risque

www.bag.admin.ch

HBV Reactivation

HBV and Immune Suppression

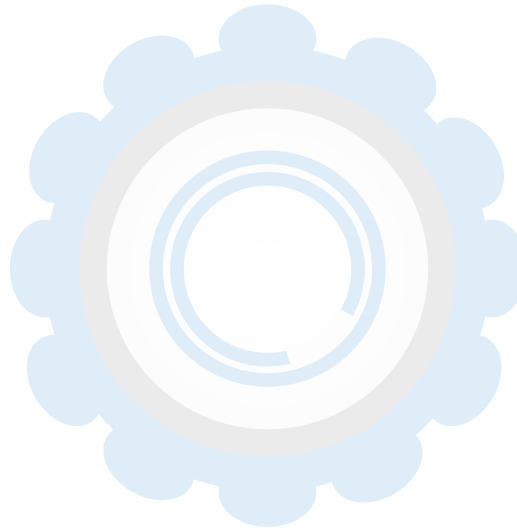
- Screen for HBsAg, anti-HBc and anti-HBs before immunosuppressive drug therapy (ISDT)
- Vaccinate seronegative patients
- HBsAg or HBV DNA positive
 - start prophylactic nucleos(t)ide analog (NA) before ISDT
 - continue for ≥ 12 (18 for RTX) mo after cessation of ISDT
- HBsAg negative, anti-HBc ($\pm$ anti-HBs) positive → HBV DNA
 - if HBV DNA pos → see above
 - if HBV DNA neg → monitor HBV DNA/preemptive NA or start prophylactic NA (RTX, BMT)



Based on Hwang JP and Lok ASF. NRGH 2014;11:209, Reddy KR *et al.* Gastroenterology 2015;148:215, Mallet V *et al.* Lancet Infect Dis 2016;16:606, EASL Clinical Practice Guidelines. J Hepatol 2017;67:370, Loomba R and Liang TJ. Gastroenterology 2017;152:1297, Terrault NA *et al.* Hepatology 2018;67:1560,



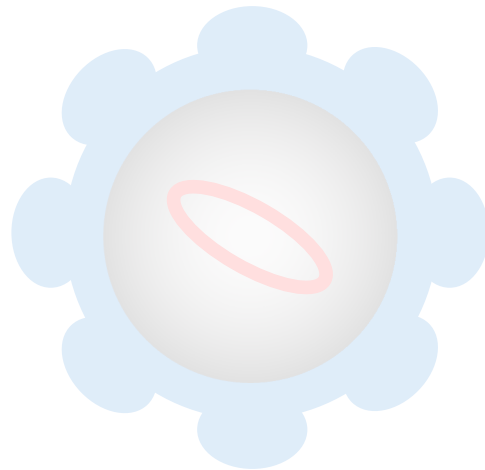
HAV



HBV



HCV



HDV



HEV

Health Care Provider-Initiated Testing for Chronic HCV Infection

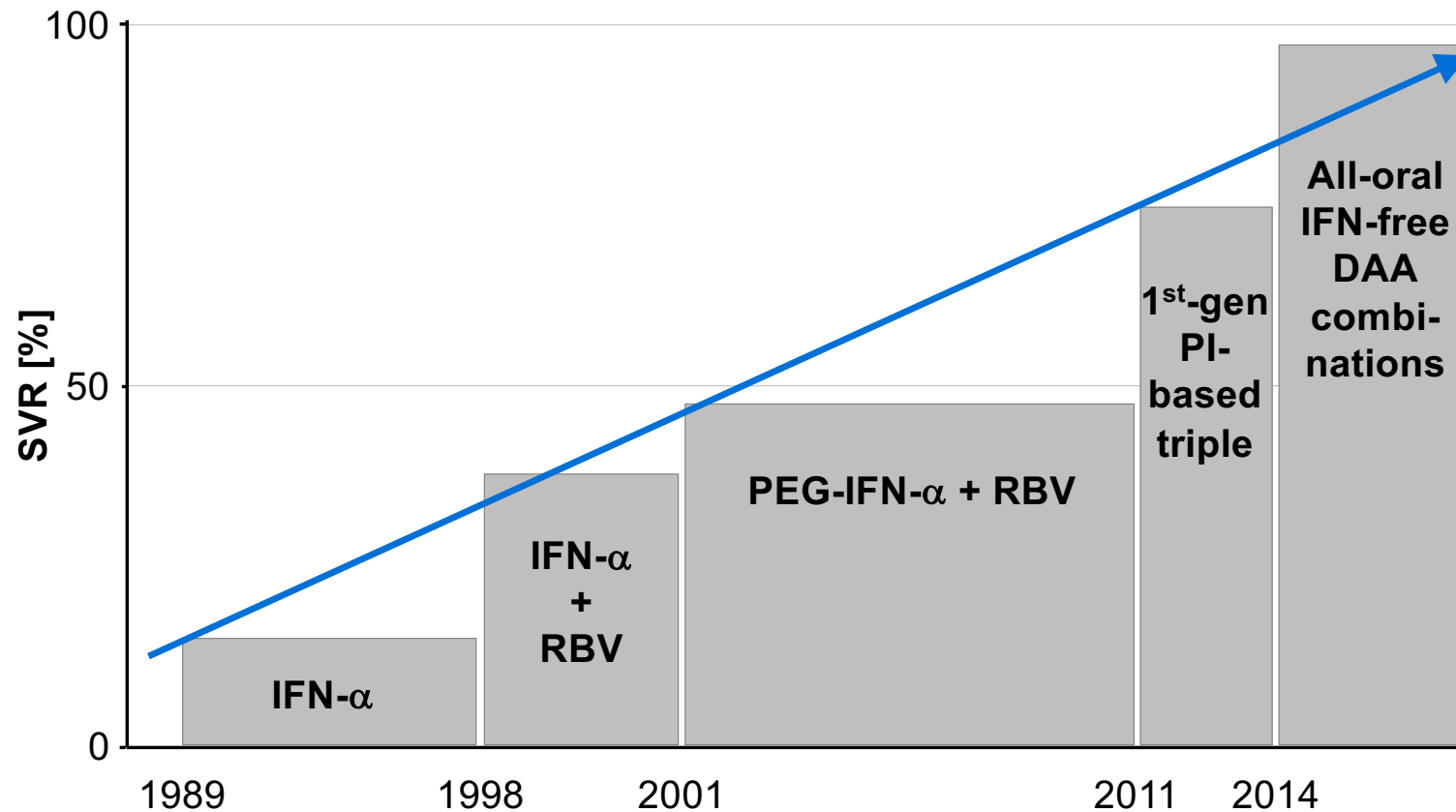
A. Clinical signs or symptoms of hepatitis

B. Risk factors

- **Medical** (recipients of blood products or solid organs before 1992, hemodialysis, persons with HBV or HIV infection, ...)
- **Demographic**
- **Behavioural** (injecting or intranasal drug use, MSM, sexual partners)
- **Occupational**
- **Others** (imprisonement, piercing or tattoos, children of HCV-infected mothers, ...)

SEVHep - SFOPH | Fretz R *et al.* Swiss Med Wkly 2013;143:w13793.
See also Tan R *et al.* Rev Med Suisse 2025;21:231-236.

A Success Story of Modern Medicine



Heim MH. Nat Rev Immunol 2013;13:535-542 | Moradpour D and Müllhaupt B. Swiss Med Forum 2015;15:366-370.
Lasker Award 2016 to Ralf Bartenschlager, Charles M. Rice and Michael J. Sofia (see e.g. JAMA 2016;316:1254-1255).
Nobel Prize 2020 to Harvey J. Alter, Michael Houghton and Charles M. Rice (see e.g. NEJM 2020;383:2297-2299).
Martinello M et al. Lancet 2023;402:1085-1096.

Treatment of Chronic Hepatitis C in 2025

Class	Generic name	Abbrev.	Fixed-dose combinations
Protease inhibitors	Glecaprevir Voxilaprevir	GLE VOX	Epclusa® Maviret® Vosevi®
NS5A inhibitors	Velpatasvir Pibrentasvir	VEL PIB	
Polymerase inhib.	Sofosbuvir	SOF	

Adapted from SASL-SSG-SSI Expert Opinion Statement (www.sasl.ch, www.sggssg.ch, www.sginf.ch).
 Sarrazin C *et al.* Z Gastroenterol 2020;58:1110-1131.
 EASL Recommendations. J Hepatol 2020;73:1170-1218 (www.easl.eu).
 AASLD-IDSA Hepatitis C Guidance. Hepatology 2020;71:686-720 (hcvguidelines.org).
 Martinello M *et al.* Lancet 2023;402:1085-1096.



Treatment of Chronic Hepatitis C

Expert Opinion Statement by SASL, SSG and SSI



Table 2. Recommended treatment options for patients with chronic hepatitis C.

A. Treatment-naïve patients.

Genotype	Non-cirrhotic	Cirrhotic (Child-Pugh A)
1a	VEL/SOF for 12 wks GLE/PIB for 8 wks	VEL/SOF for 12 wks GLE/PIB for 8 wks ¹
1b	VEL/SOF for 12 wks GLE/PIB for 8 wks	VEL/SOF for 12 wks GLE/PIB for 8 wks ¹
2	VEL/SOF for 12 wks GLE/PIB for 8 wks	VEL/SOF for 12 wks GLE/PIB for 8 wks ¹
3	VEL/SOF for 12 wks GLE/PIB for 8 wks	VEL/SOF ± RBV for 12(-24) wks ² GLE/PIB for 8 wks ¹ VOX/VEL/SOF for 12 wks ²
4	VEL/SOF for 12 wks GLE/PIB for 8 wks	VEL/SOF for 12 wks GLE/PIB for 8 wks ¹
5 and 6	VEL/SOF for 12 wks GLE/PIB for 8 wks	VEL/SOF for 12 wks GLE/PIB for 8 wks ¹

B. Treatment-experienced patients.*

Genotype	Non-cirrhotic	Cirrhotic (Child-Pugh A)
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3	VEL/SOF ± RBV for 12(-24) wks ² GLE/PIB for 16 wks	VEL/SOF ± RBV for 12(-24) wks ³ GLE/PIB for 16 wks VOX/VEL/SOF for 12 wks ³
4	VEL/SOF for 12 wks GLE/PIB for 8 wks	VEL/SOF for 12 wks GLE/PIB for 12 wks
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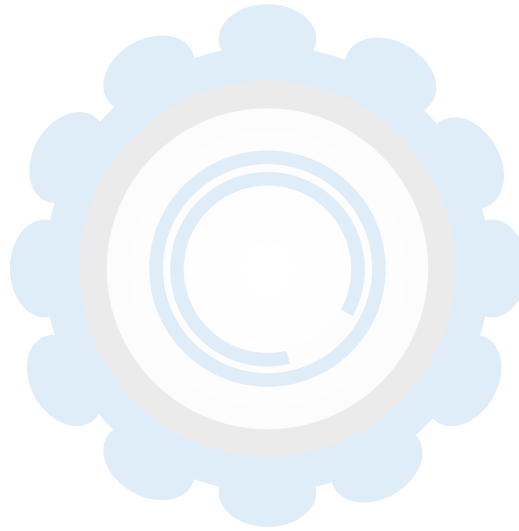
* Defined as patients who were previously treated with PEG-IFN- α and RBV; SOF, PEG-IFN- α and RBV; or SOF and RBV.

Adapted from latest update written by D. Moradpour, J. Fehr, D. Semela, A. Rauch as well as B. Müllhaupt and published in January 2021.

www.sasl.ch, www.sggssg.ch, www.sginf.ch



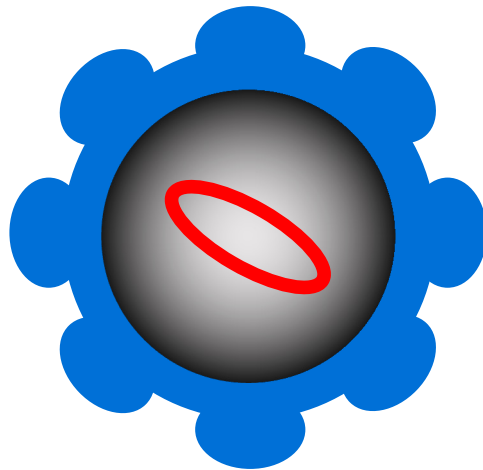
HAV



HBV



HCV

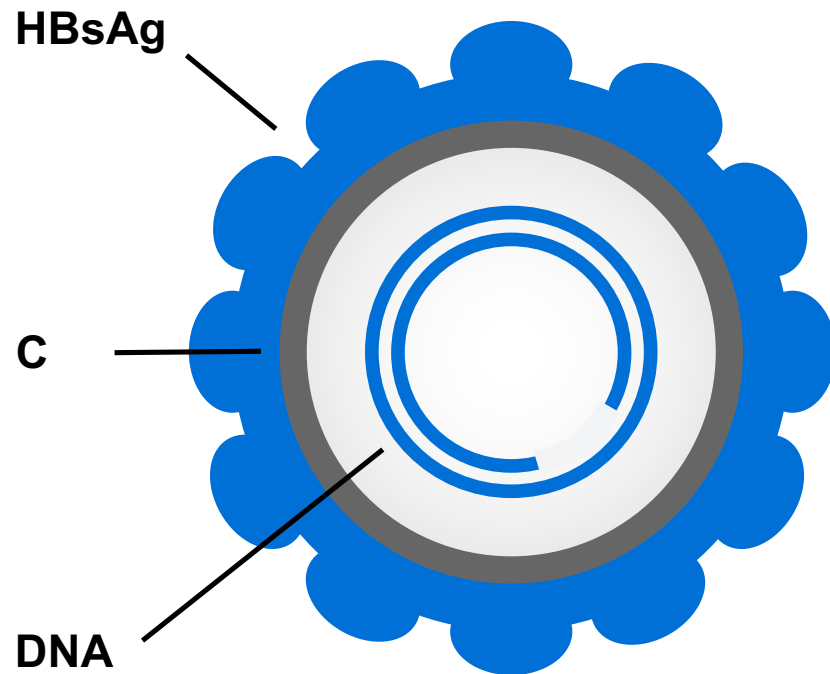


HDV

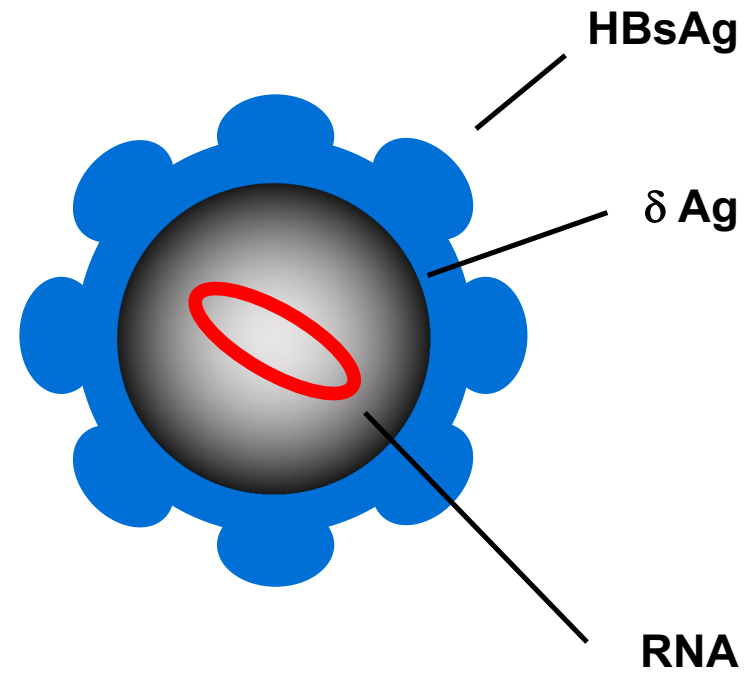


HEV

HBV

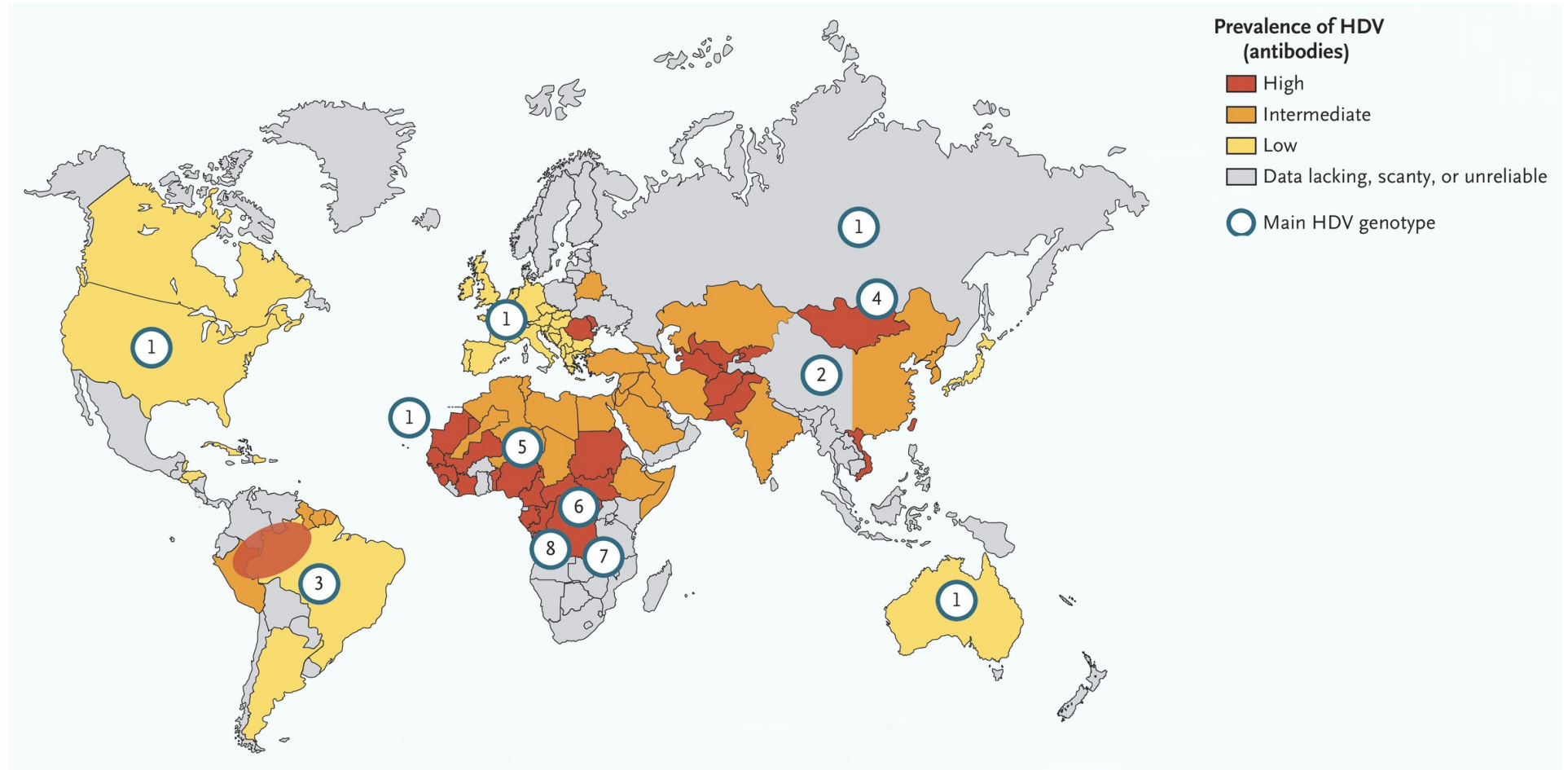


HDV



For recent reviews, see Rizzetto M *et al.* J Hepatol 2021;74:1200-1211, Urban S *et al.* Gut 2021;70:1782-1794, Asselah T and Rizzetto M. N Engl J Med 2023;389:58-70, EASL CGP. J Hepatol 2023;79:433-460 and Negro F and Lok AS. JAMA 2023;330:2376-2387.

Current Epidemiology of Hepatitis D



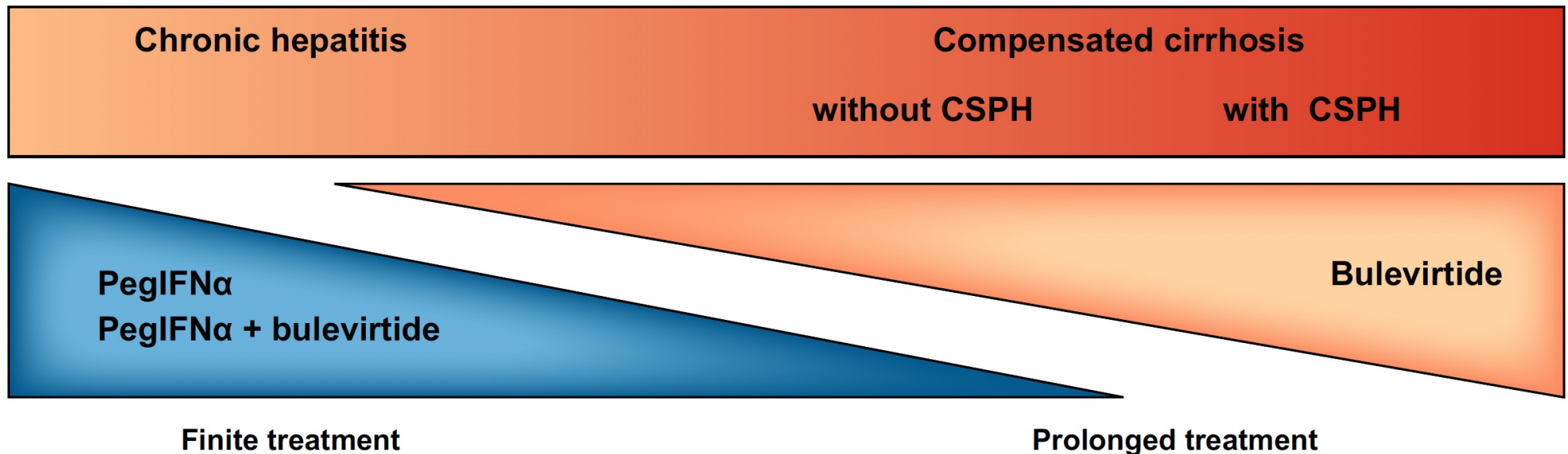
Asselah T and Rizzetto M. N Engl J Med 2023;389:58-70.
See also The Polaris Observatory Collaborators. J Hepatol 2024;80:232-242.

Hepatitis D

- Parenteral transmission
- Co-infection vs. superinfection; frequent and rapid development of cirrhosis and HCC
- Resurgence in Western Europe
- Screening: anti-HDV (all HBsAg-positive patients!)
- Diagnosis: HDV RNA
- Prevention: HBV vaccine
- Therapy: PEG-IFN- α , bulevirtide

Rizzetto M *et al.* J Hepatol 2021;74:1200-1211, Urban S *et al.* Gut 2021;70:1782-1794, Asselah T and Rizzetto M. N Engl J Med 2023;389:58-70, EASL CGP. J Hepatol 2023;79:433-460.

Treatment of Chronic Hepatitis D



Additional factors that influence the choice of antiviral treatment:

- phase of HBV infection
- tolerability or contraindications to PEG-IFN-alpha
- patient preference and treatment adherence

EASL Clinical Practice Guidelines. J Hepatol 2023;79:433-460.
Wedemeyer H *et al.* NEJM 2023;389:22-32 and J Hepatol 2024;81:621-629.
Asselah T *et al.* N Engl J Med 2024;391:133-143.

DD of Chronic LFT Elevation

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● Thyroid dysfunction	TSH

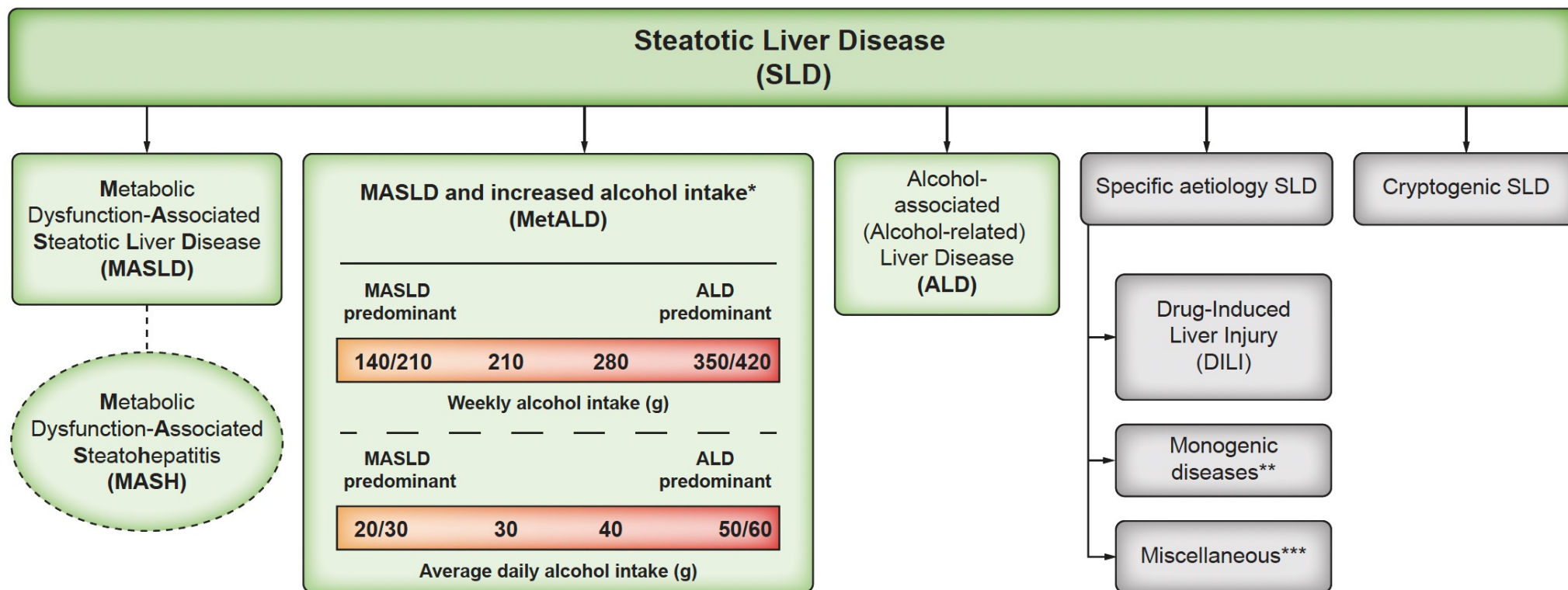


Recommended reading: Haber PS. N Engl J Med 2025;392:258-266.

DD of Chronic LFT Elevation

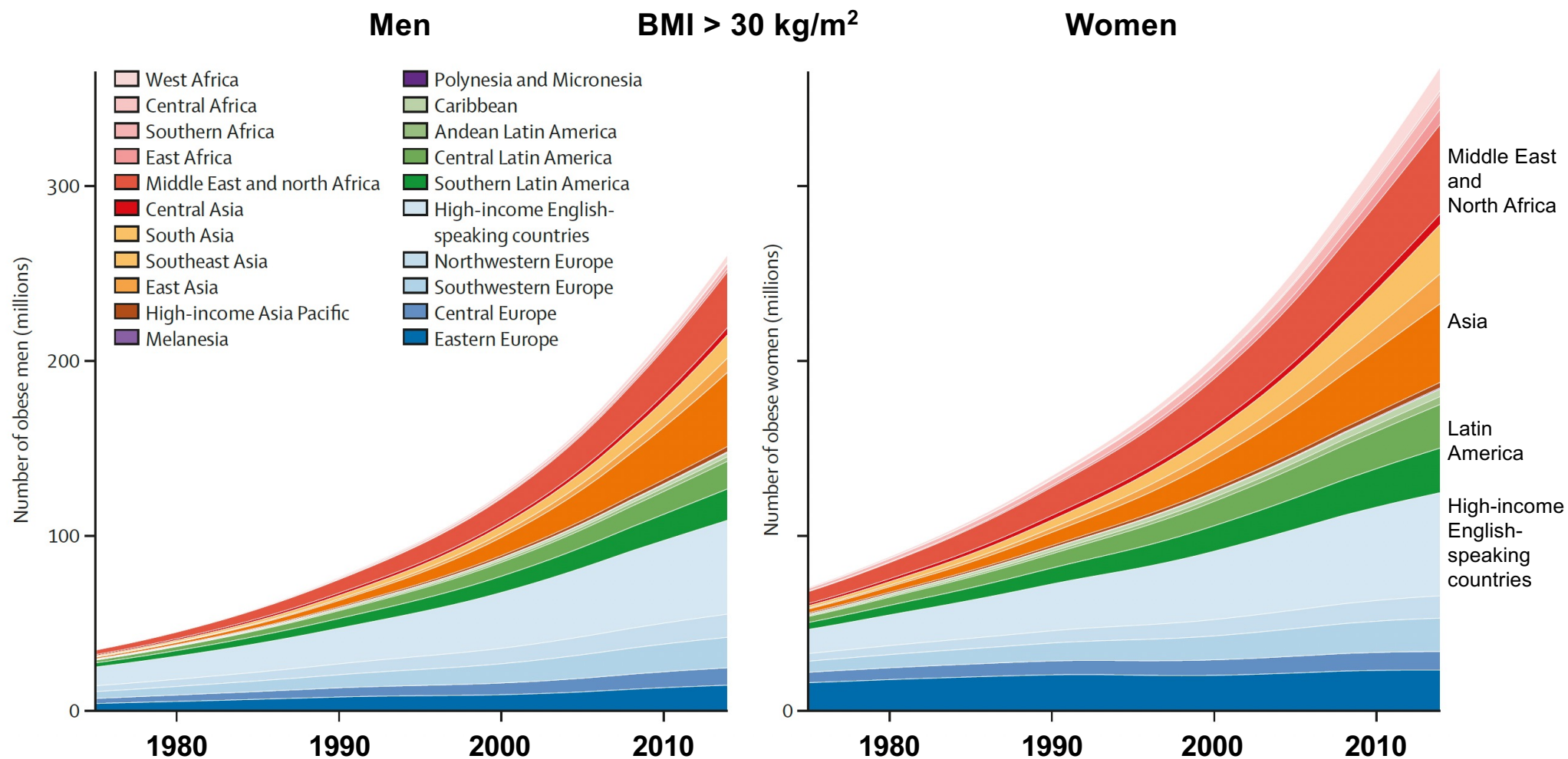
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NAFLD/NASH Becomes MASLD/MASH



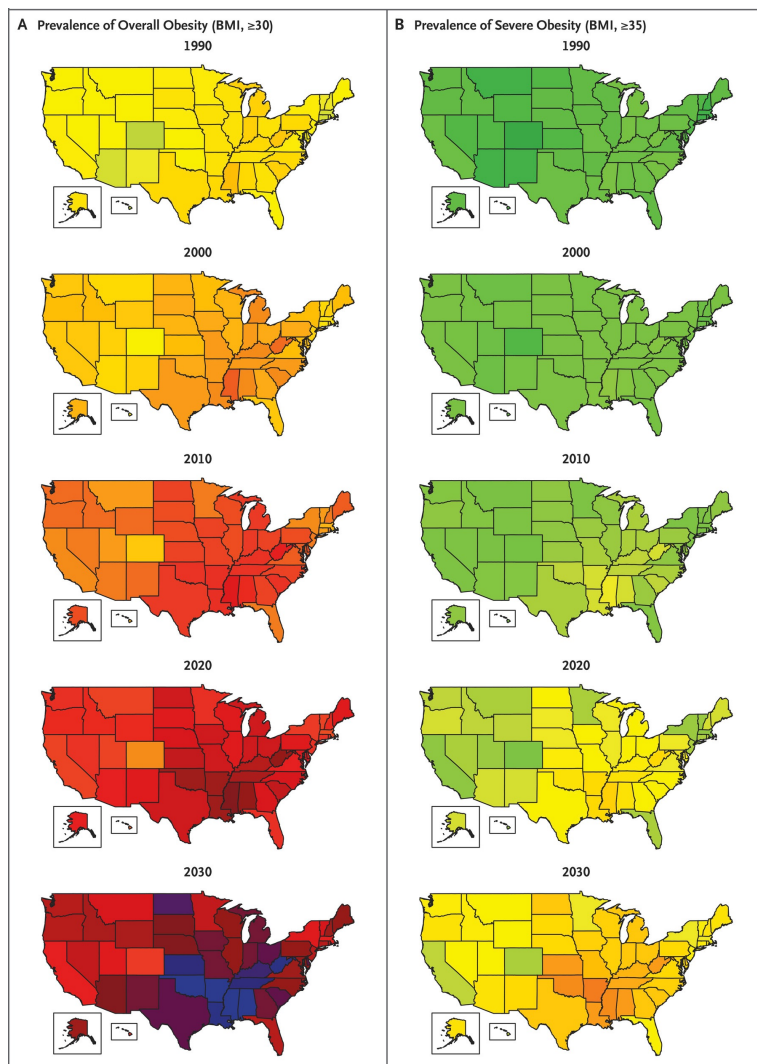
Rinella ME et al. J Hepatol 2023;79:1542-1556.

Trends in BMI in 200 Countries 1975-2014

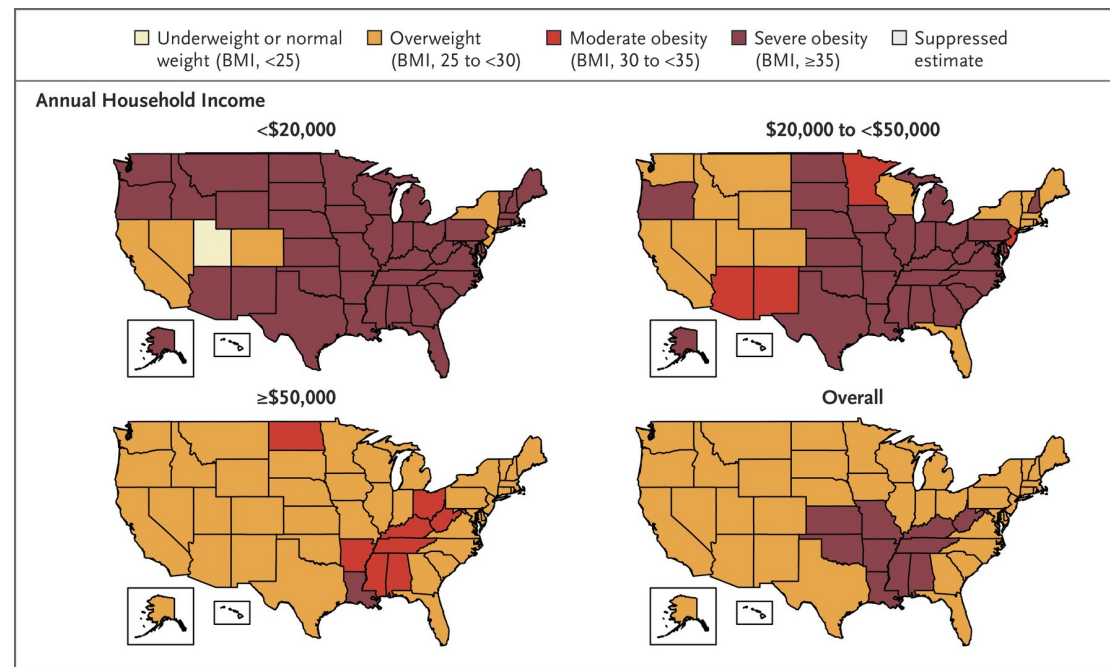


NCD Risk Factor Collaboration. Lancet 2016;387:1377-1396.

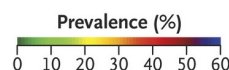
Projected Prevalence of Obesity in the US



Projected most common BMI category in 2030



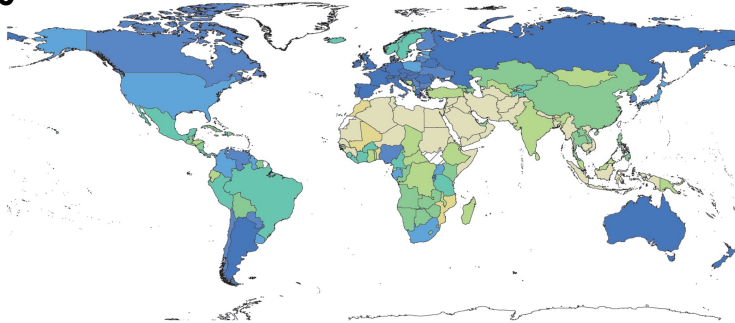
← Estimated prevalence of overall (BMI ≥ 30 kg/m²) and severe obesity (BMI ≥ 35 kg/m²) 1990-2030



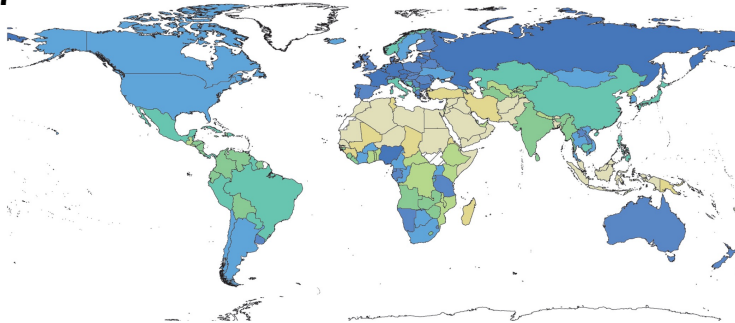
Ward ZJ *et al.* N Engl J Med 2019;381:2440-2450.

Global Alcohol Consumption 1990-2030

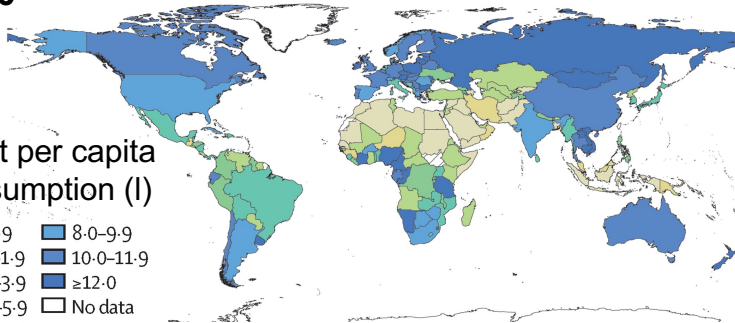
1990



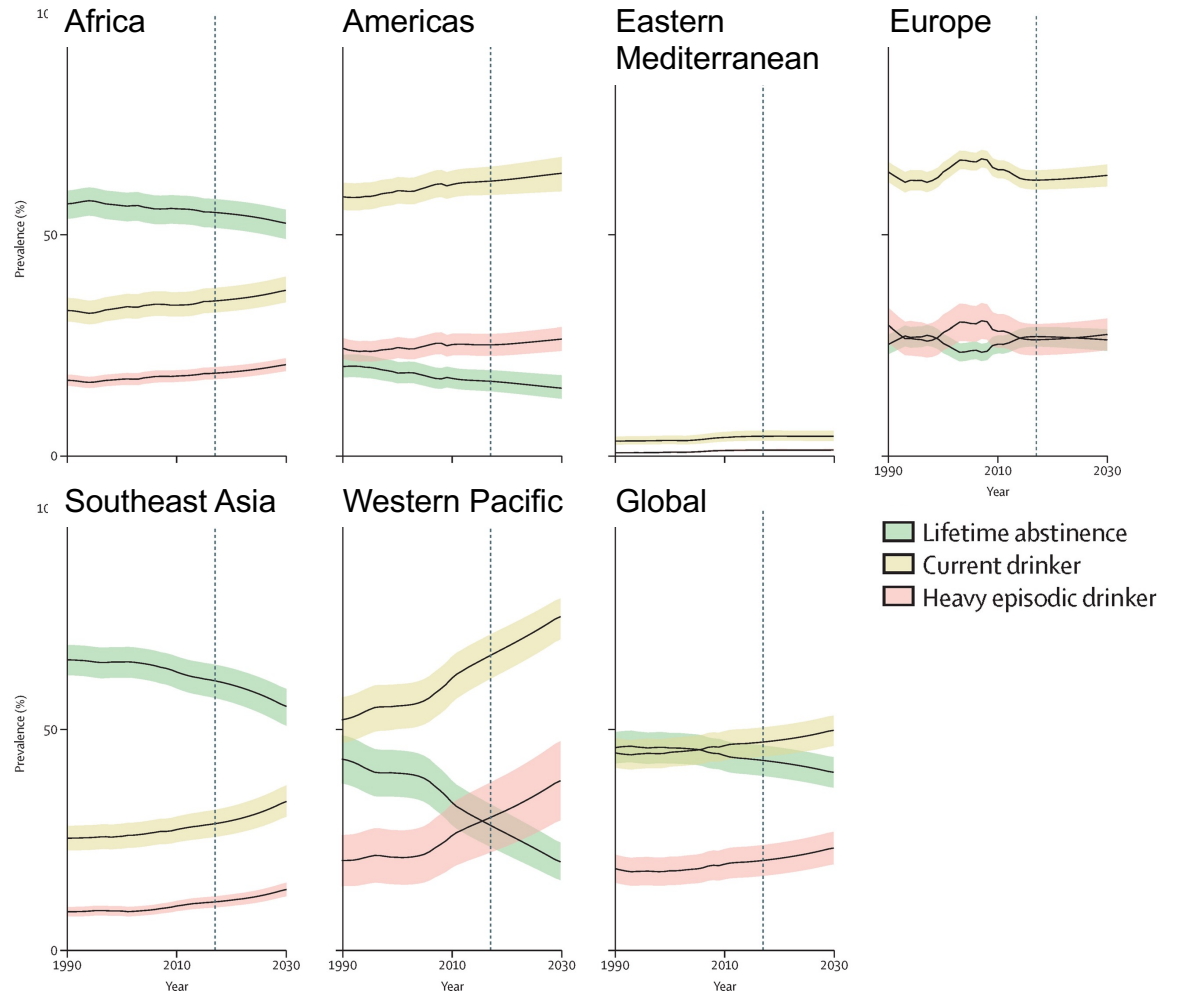
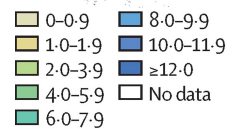
2017



2030



Adult per capita
consumption (l)

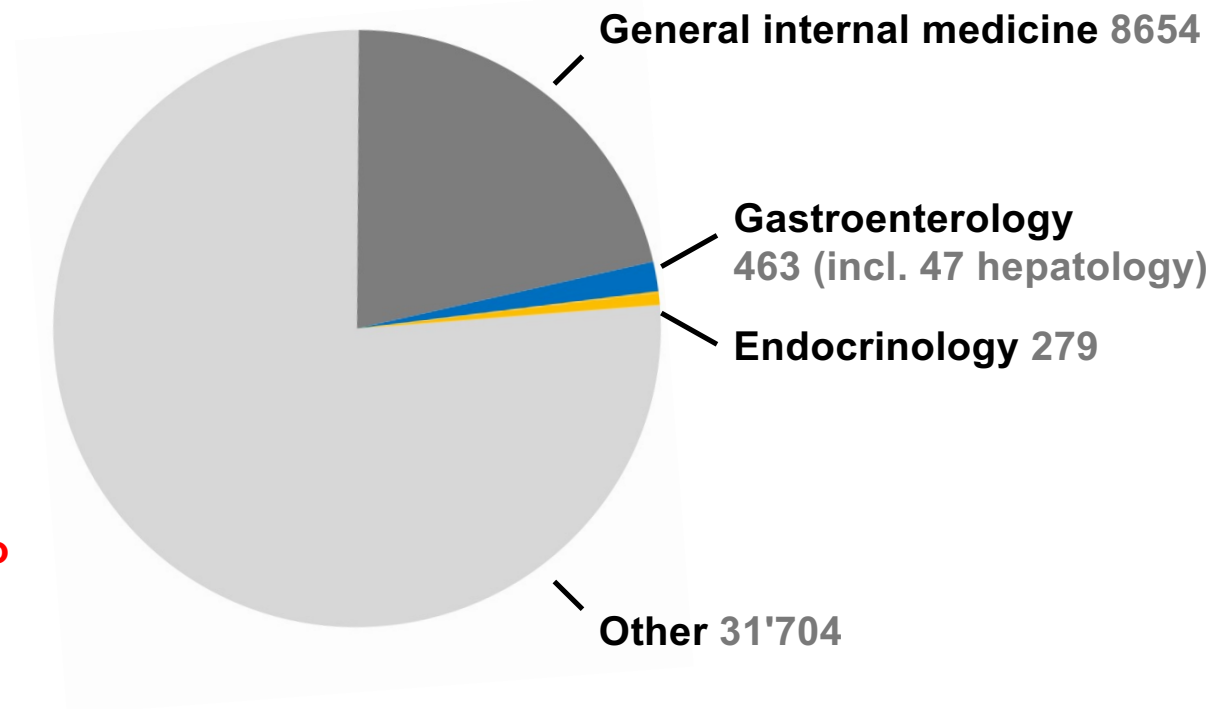
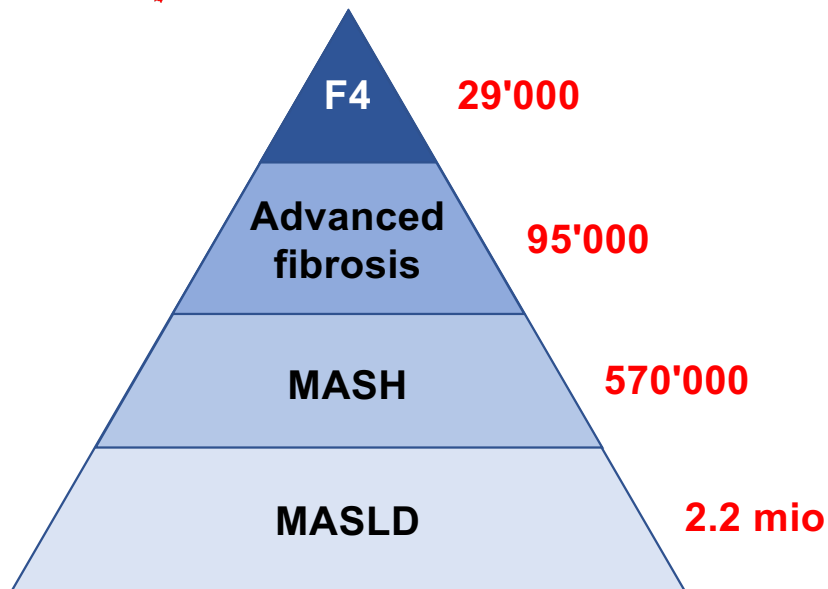


Manthey J *et al.* Lancet 2019;393:2493-2502.

THE PERFECT STORM



Projections for MASLD in Switzerland 2030

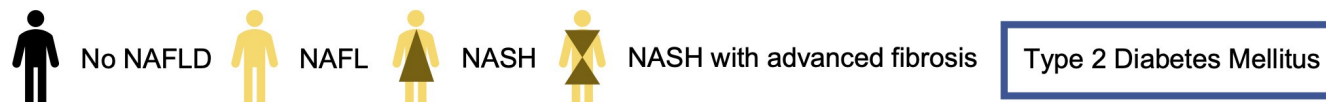
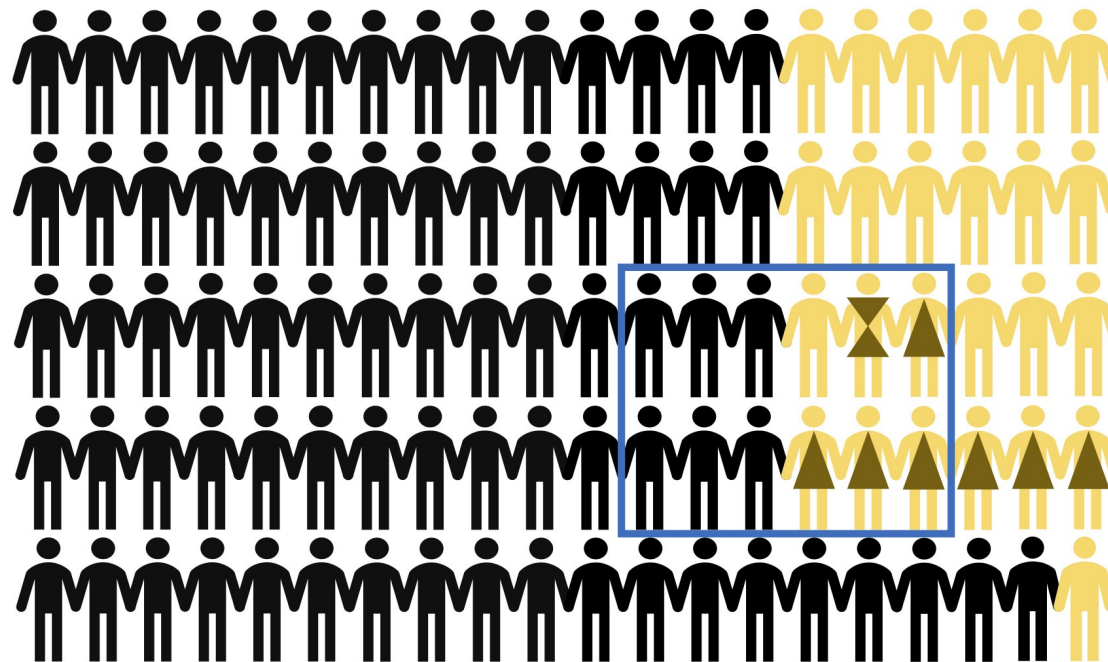


Courtesy of Nicolas Goossens

Adapted from Goossens N *et al.* Swiss Med Wkly 2019;149:w20152 and FMH-Ärztstatistik 2023.

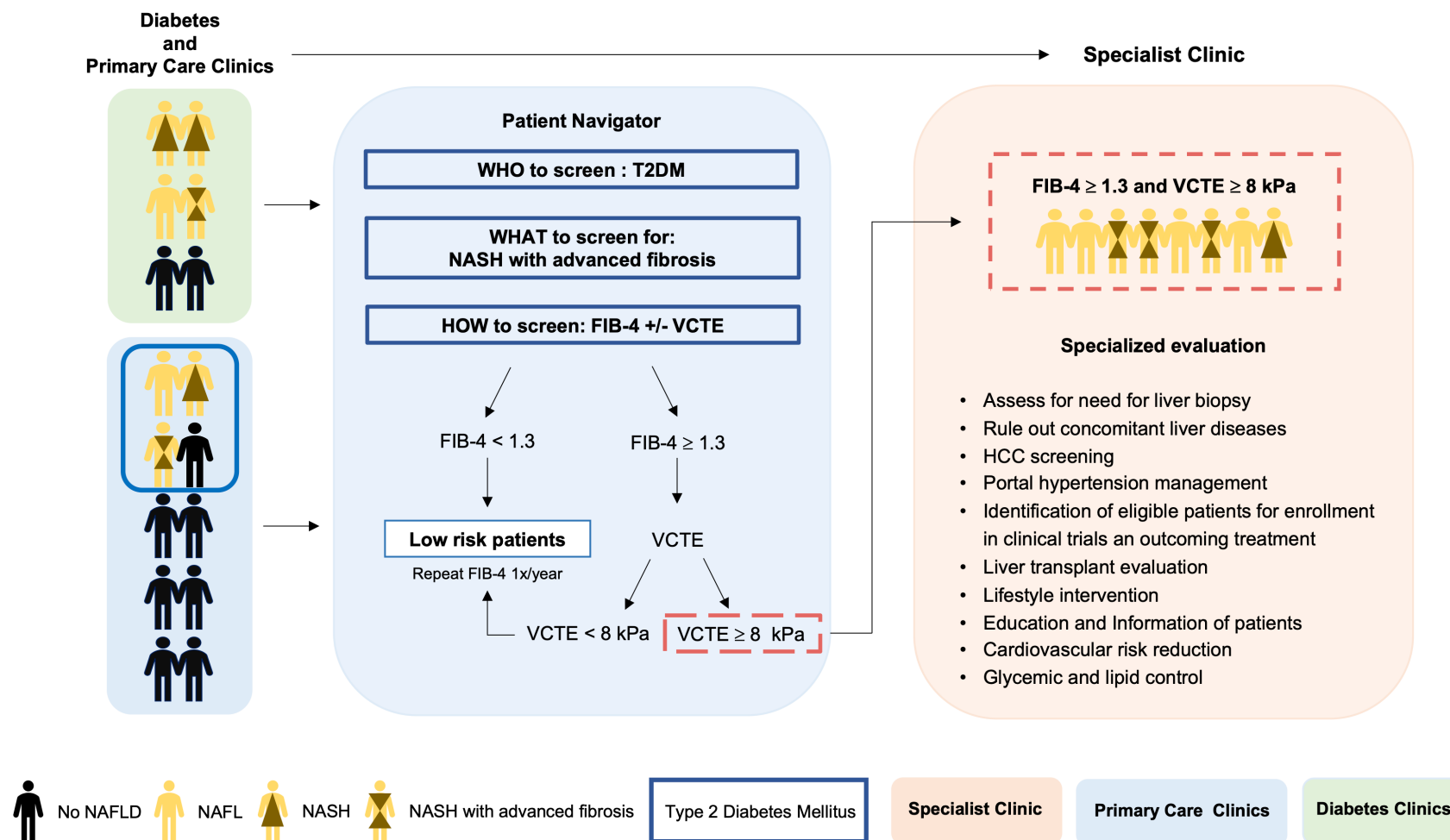
NAFLD Screening in the Primary Care Setting

General Population



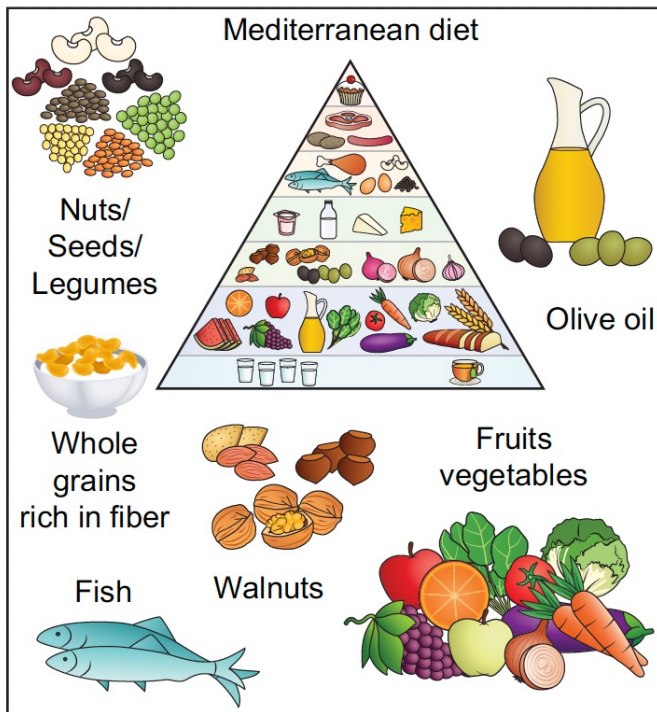
Vieira Barbosa J and Lai M. Hepatol Commun 2020;5:158-167.

NAFLD Screening in the Primary Care Setting

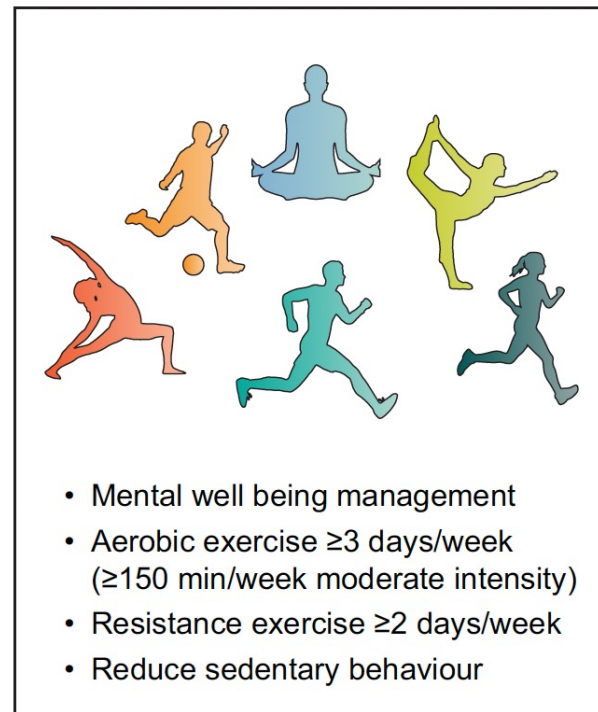


Lifestyle Advice for All Persons with MASLD

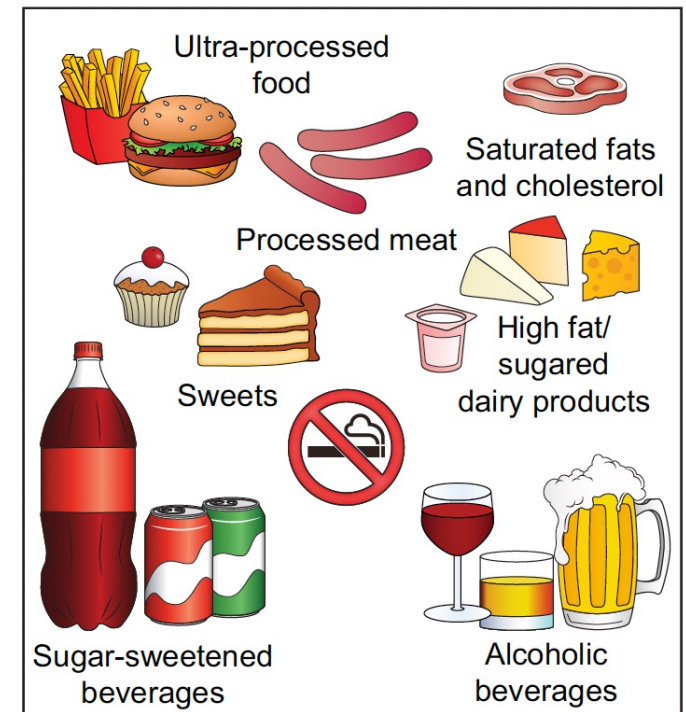
Recommended foods



Recommended activity



Non-recommended foods/
Minimize consumption



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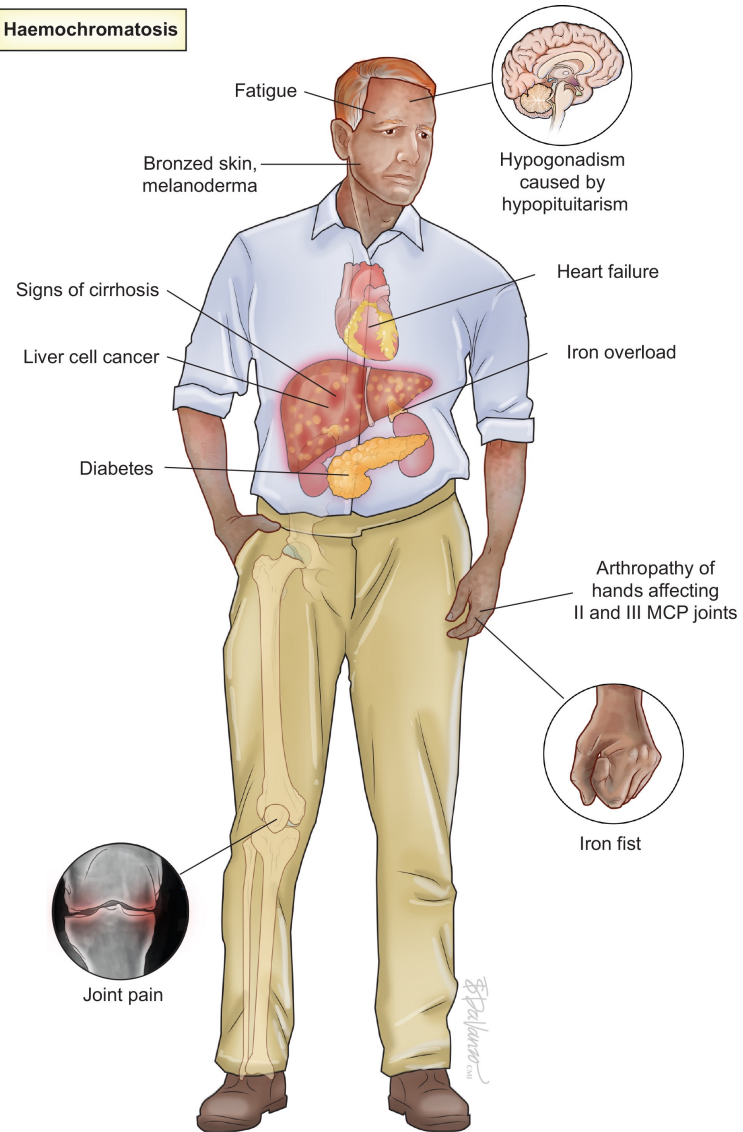
Autoimmune Liver Disease

- **Autoimmune hepatitis**
- **Primary biliary cholangitis**
- **Primary sclerosing cholangitis**
- **Overlap syndromes**
- **IgG4-associated cholangitis**

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Haemochromatosis



DD of Chronic LFT Elevation

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- **Wilson disease** Coeruloplasmin
- α 1-Antitrypsin deficiency α 1-antitrypsin
- Celiac sprue Anti-tTG
- Thyroid dysfunction TSH

DD of Chronic LFT Elevation

- Chronic viral hepatitis HBsAg, anti-HCV
- Alcoholic liver disease History
- MASLD/MASH Associated conditions
- Drug toxicity History
- Autoimmune liver disease ANA, SMA; AMA; MRCP
- Hereditary hemochromatosis Ferritin, transferrin saturation
- Wilson disease Coeruloplasmin
- **α 1-Antitrypsin deficiency** **α 1-antitrypsin**
- Celiac sprue Anti-tTG
- Thyroid dysfunction TSH

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Diagnostic différentiel et investigation d'une perturbation chronique des tests hépatiques

Cause	Diagnostic primaire	Diagnostic complémentaire
Hépatopathie alcoolique	Anamnèse	PBF
Hépatite médicamenteuse	Anamnèse	PBF
Hépatite virale chronique	HBsAg ; anti-HCV	HBeAg/anti-HBe, HBV-DNA ; anti-HDV, HDV-RNA ; HCV-RNA, génotype HCV ; HEV-RNA chez patient immunosupprimé ; PBF
Stéatohepatite non-alcoolique (MASH)	Syndrome métabolique, excl. d'autres causes	PBF
Hépatite auto-immune	Auto-ac anti-nucléaires et anti-muscle lisse, électrophorèse ou IgG	Exclusion d'autres causes, IgG, anti-actine, anti-LKM1, év. anti-SLA/LP et anti-LC1, PBF
Cholangite biliaire primitive (CBP) et cholangite sclérosante primaire (CSP)	Auto-anticorps anti-mitochondries (CBP) ; cholangio-IRM (CSP)	anti-M2, IgM, év. PBF (CBP) ; coloscopie, IgG4 (→ cholangite à IgG4), év. ERCP (CSP)
Hémochromatose héréditaire	Ferritine, CST	Test génétique (gène <i>HFE</i>), év. PBF
Maladie de Wilson	Céruloplasmine	Cuprurie de 24 h, examen ophtalmologique (anneau de Kayser-Fleischer), PBF avec dosage du cuivre, test génétique
Déficit en α 1-antitrypsine	α 1-antitrypsine	Focalisation iso-électrique ou test génétique
Hépatopathie vasculaire	Examen clinique (congestion cardiaque D), US-Doppler (syndrome de Budd-Chiari)	Examen cardiologique (échocardiographie), examen hématologique et d'hémostase, év. PBF
Maladie coeliaque	anti-tTG (avec IgA totaux)	Biopsie duodénale
Dysfonction thyroïdienne	TSH	Examen endocrinologique