Mojca Matičič

SLOVENIA

University Medical Centre Ljubljana

Faculty of Medicine, University of Ljubljana

Head of Unit for Viral Hepatitis

Full professor of Infectious Diseases and Epidemiology

Main expertise:

- **A clinician managing patients with HBV/HCV infections**
- **Chair of the National Viral Hepatitis Expert Board**

The European Code Against Cancer

The need for updating EU Council Recommendations for public and policy makers to prevent HCC

Hepatitis C

Prof. Mojca Matičič, MD, PhD

University Medical Centre Ljubljana
Faculty of Medicine, University of Ljubljana
Slovenia

VHPB Technical Meeting: Antwerp, 27 March 2025

Disclosure

Within the last 36 months:

- Lecturer: Abbvie, Bayer, Gilead, Lenis, Medicopharmacia, Merck, Sandoz, Roche

No conflict of interest regarding this presentation

IARC classification of carcinogens

International Agency for Research on Cancer
World Health Organization

IARC MONOGRAPHS ON THE IDENTIFICATION OF CARCINOGENIC HAZARDS TO HUMANS

HOME | NEWS | MEETINGS | **CLASSIFICATIONS** | PUBLICATIONS | PRIORITIES | PREAMBLE | STAFF | CONTACT

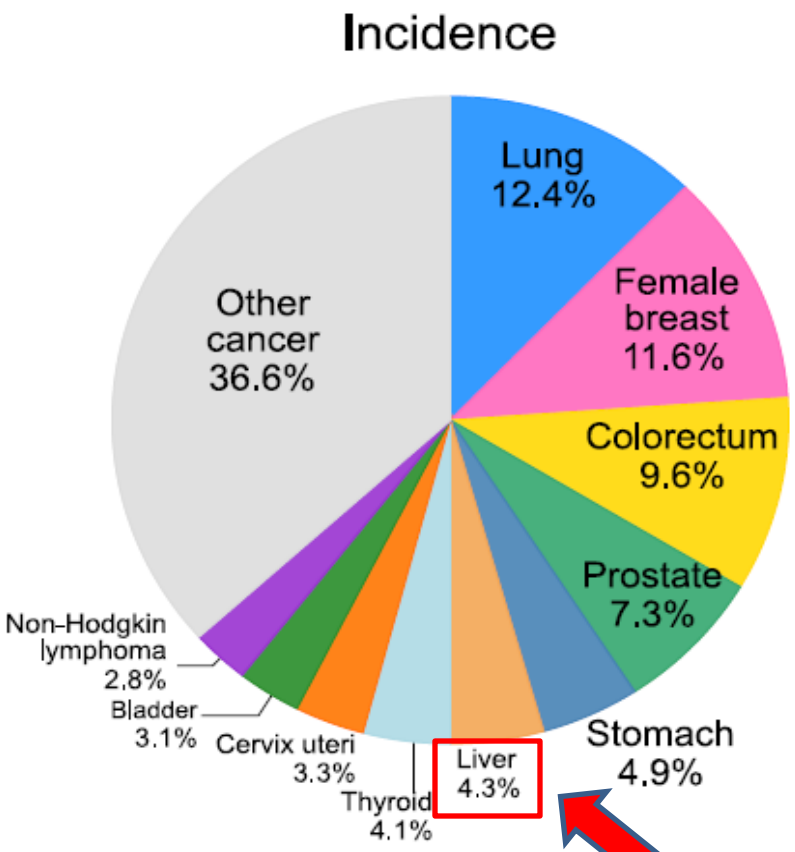
CAS No.	Agent	Group	Volume	Volume publication year	Evaluation year
	Hepatitis C virus (chronic infection with)	1	59, 100B	2012	2009

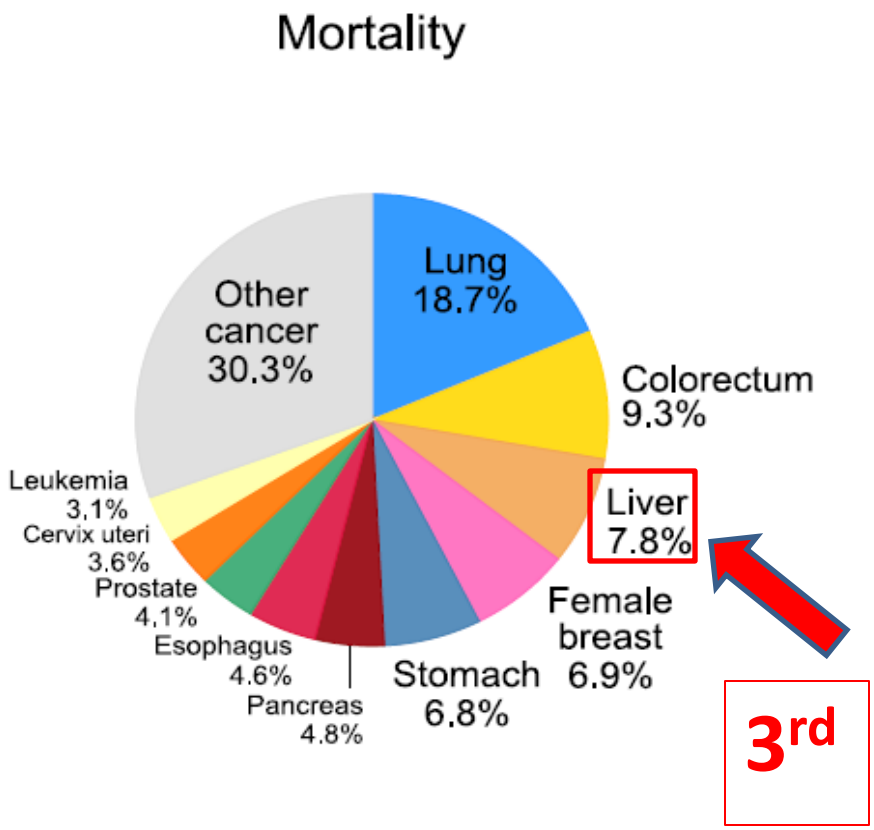
Agents Classified by the *IARC Monographs*, Volumes 1–137

Group 1	Carcinogenic to humans	132 agents
Group 2A	Probably carcinogenic to humans	96 agents
Group 2B	Possibly carcinogenic to humans	320 agents
Group 3	Not classifiable as to its carcinogenicity to humans	499 agents

IARC. https://monographs.iarc.who.int/agents-classified-by-the-iarc/

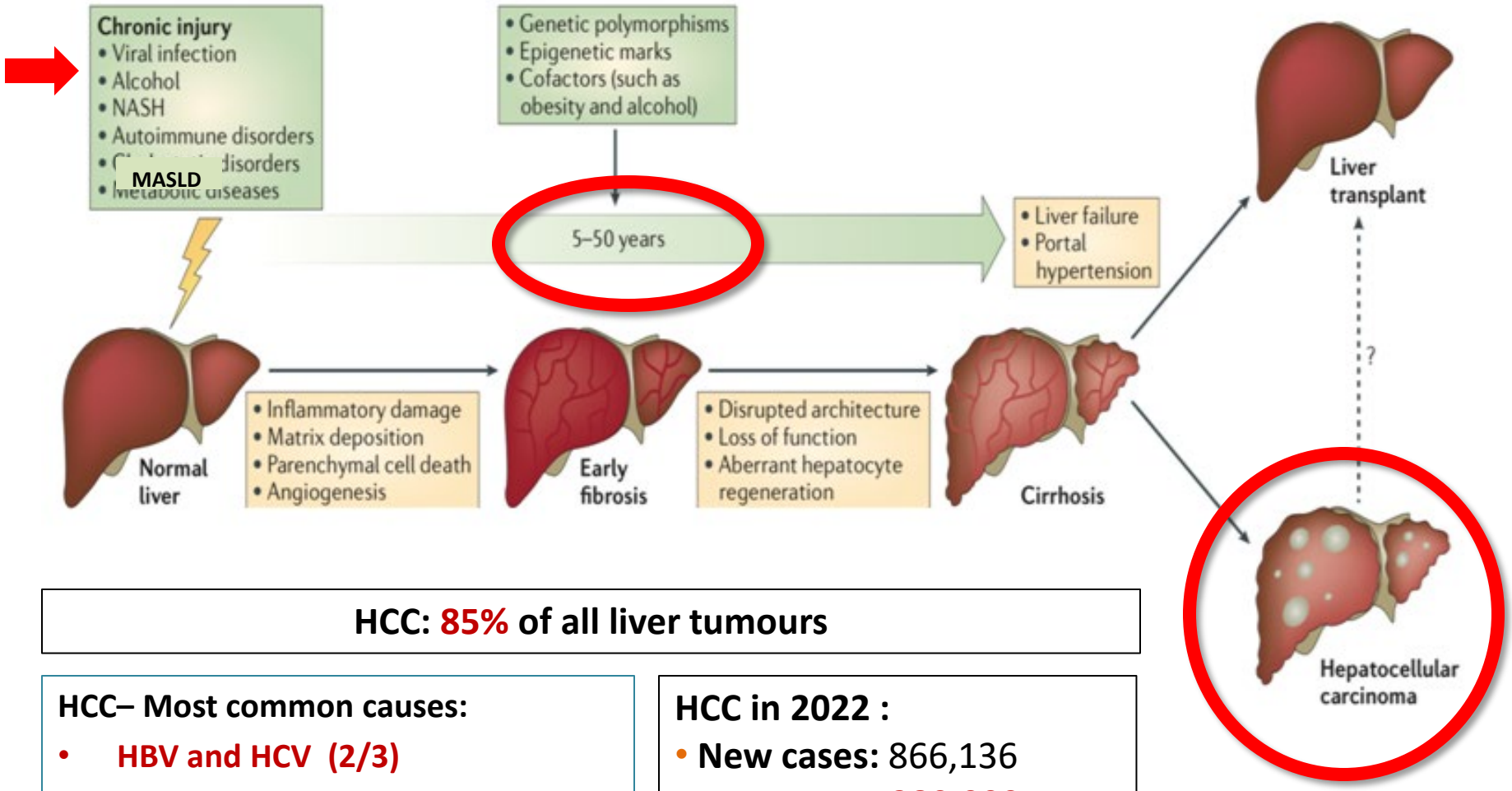
The global distribution of cases and deaths for the top six cancers in 2022





Bray F, et al. CA Cancer J Clin 2024; 74: 229-63.

The global burden and ethiology of HCC



HCC: 85% of all liver tumours

HCC– Most common causes:

- **HBV and HCV (2/3)**
- Alcohol
- MASLD

HCC in 2022 :

- **New cases:** 866,136
  HBV: 380,000
  HCV: 170,000

Pellicoro et al. Nature Reviews 2014;14:181-94.

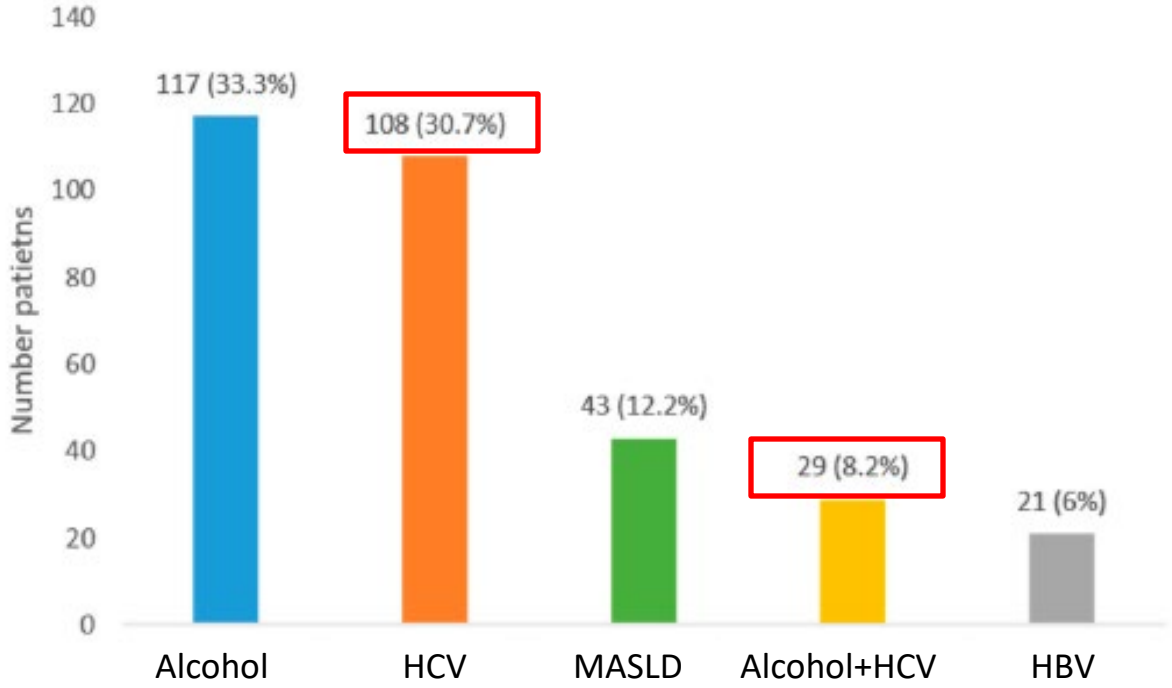
IARC. Global Cancer Observatory 2025. https://gco.iarc.who.int/en

EUROPE

Ethiology of HCC

Katalonia, period 2019-2022

N = 352



HCV

Vargas-Accarino E, et al. Cancers (Basel). 2024;16(8):1521.

European Comission

Tools supporting the member states in managing cancer

- **Europe's Beating Cancer Plan:** supports cancer screening, prevention, treatment
- **European Cancer Information System (ECIS):** supports systematic cancer burden monitoring
- **European Cancer Inequalities Registry (ECIR):** reports disparities
- **The New Council Recommendation on Vaccine Preventable Cancers:** suports increasing of vaccination coverage (since 2024)
- **European Code Against Cancer (ECAC):** informs individuals on how to reduce their risk of cancer

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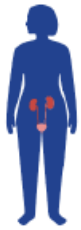
“Europe's Beating Cancer Plan”

Cancer Screening (since 2003) : Breast, Cervix, Colon

BREAST CANCER



CERVICAL CANCER

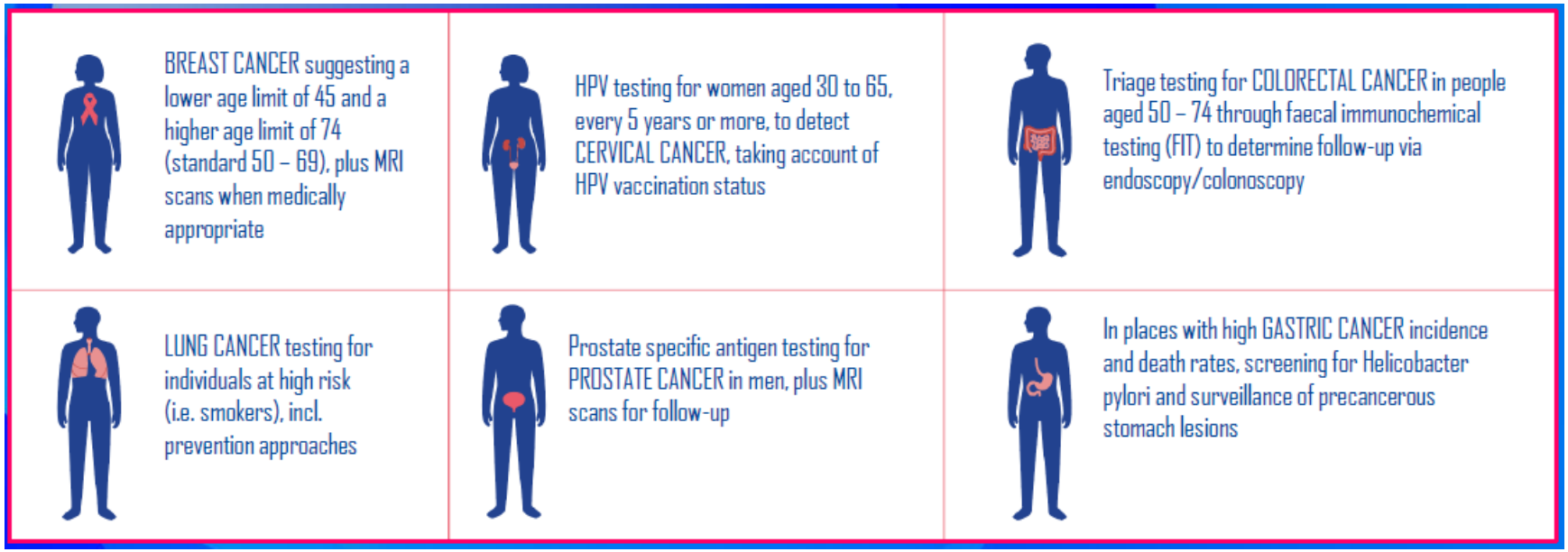
COLORECTAL CANCER

https://eur-lex.europa.eu/legal-content/SL/TXT/PDF/?uri=CELEX:52021DC004

“Europe's Beating Cancer Plan”

European Health Union: A new EU approach on cancer detection – screening more and screening better

Cancer Screening (since 2003) : Breast, Cervix, Colon



Additional Cancer Screening (since 2023) : Lungs, Prostate, Gastric

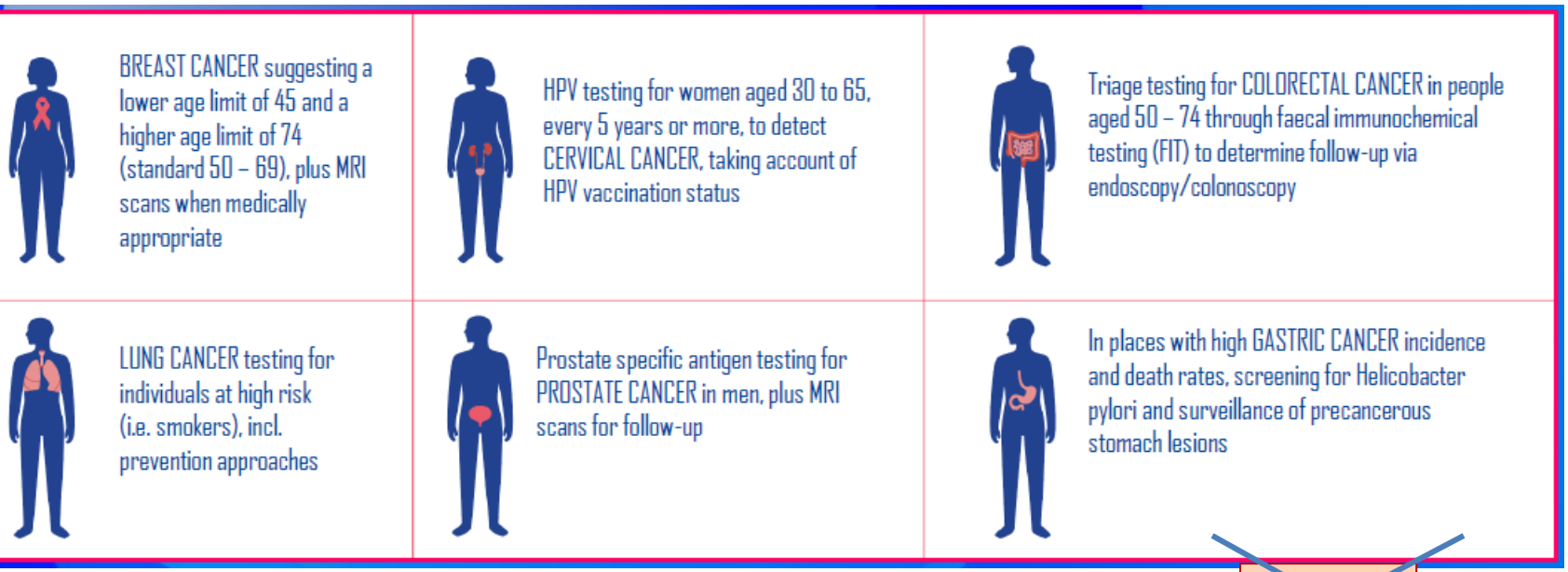
https://eur-lex.europa.eu/legal-content/SL/TXT/PDF/?uri=CELEX:52021DC004

https://ec.europa.eu/commission/presscorner/detail/en/ip_22_5562

“Europe's Beating Cancer Plan”

European Health Union: A new EU approach on cancer detection – screening more and screening better

Cancer Screening (since 2003) : Breast, Cervix, Colon



Additional Cancer Screening (since 2023) : Lungs, Prostate, Gastric ~~Liver~~

https://eur-lex.europa.eu/legal-content/SL/TXT/PDF/?uri=CELEX:52021DC004

https://ec.europa.eu/commission/presscorner/detail/en/ip_22_5562

European Comission

Tools supporting the member states regarding cancer

- **Europe's Beating Cancer Plan:** supports cancer prevention, screening, early detection, treatment
- **European Cancer Information System (ECIS):** supports systematic cancer burden monitoring
- **European Cancer Inequalities Registry (ECIR):** reports disparities
- **The New Council Recommendation on Vaccine Preventable Cancers:** suports increasing of vaccination coverage (since 2024)
- **European Code Against Cancer (ECAC)**: informs individuals in lay language on how to reduce their risk of cancer

What is ECAC ?

European Code Against Cancer

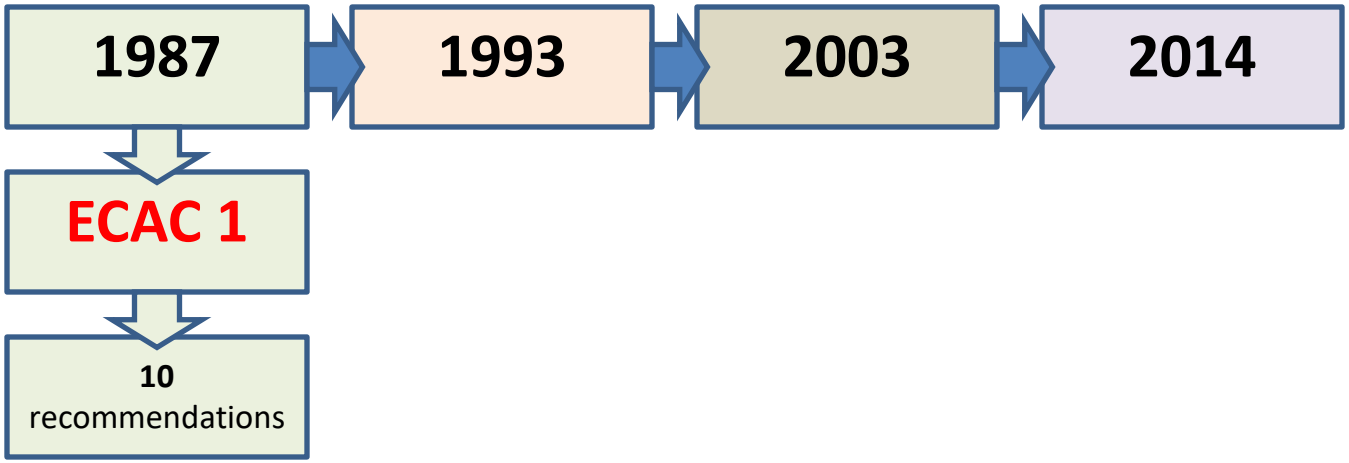
- **Intended for**:
  - the **general** population in the EU

  - **not s**pecifically targeted for:
    - people at high risk for a distinct cancer type
    - subpopulations with distinctive risks that require specific preventive measures

If everyone followed the recommendations:
est. 40% of deaths due to cancer in Europe **could be avoided**

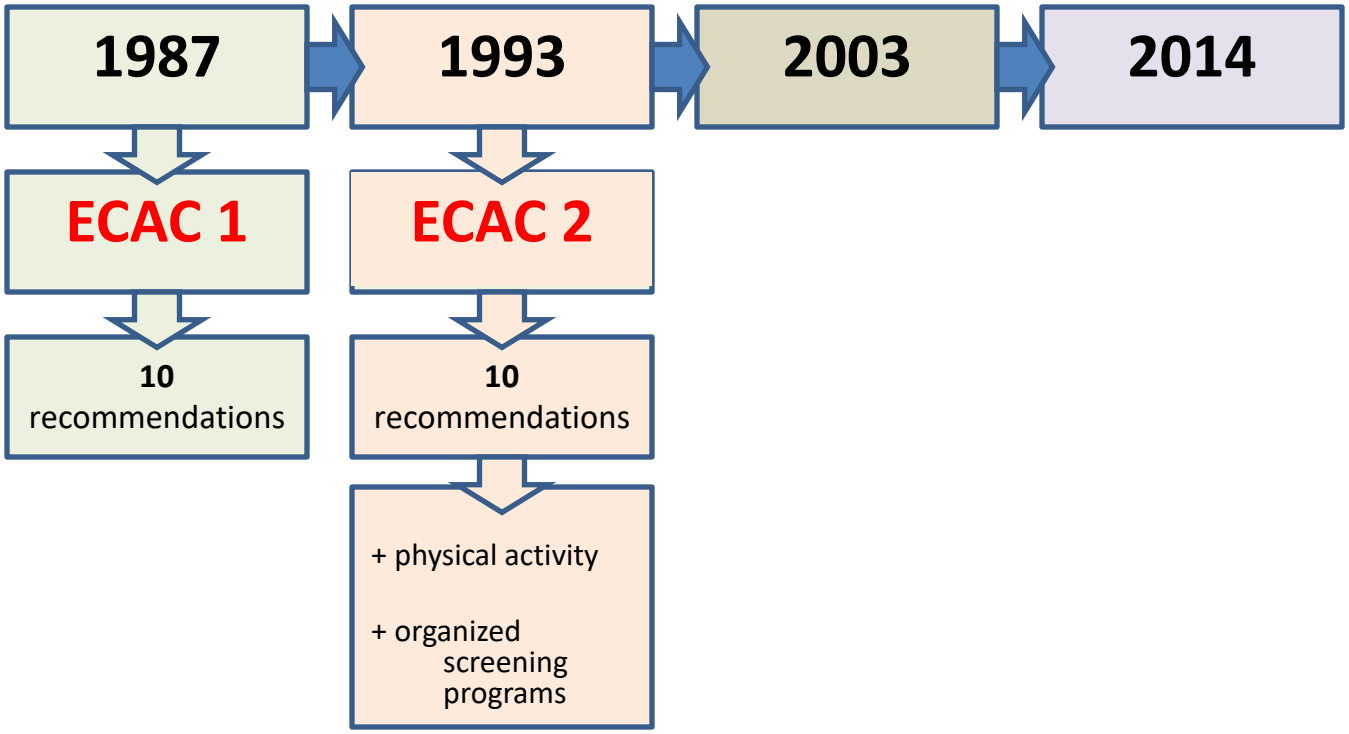
Ritchie D, et al. Cancer Epidemiology 2021; 7: 101898.
EC. https://health.ec.europa.eu/non-communicable-diseases/cancer/europes-beating-cancer-plan-eu4health-financed-projects/projects/ecac5_en

ECAC: A timeline

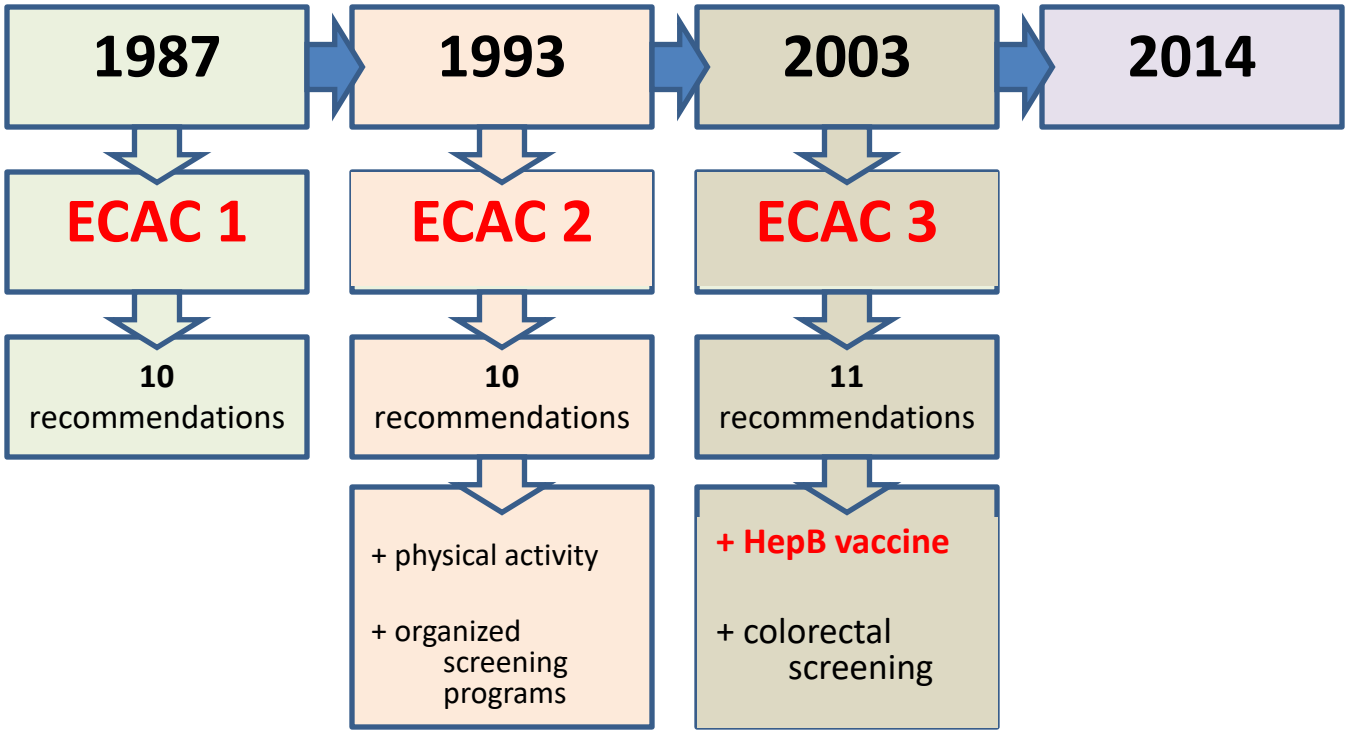


- First ECAC launched in **1987**
- So far **4 editions**
- Each edition of the ECAC **builds on the previous editions**, maintaining consistency whilst **reflecting the current developments** in the body of evidence as they **occur between each edition**

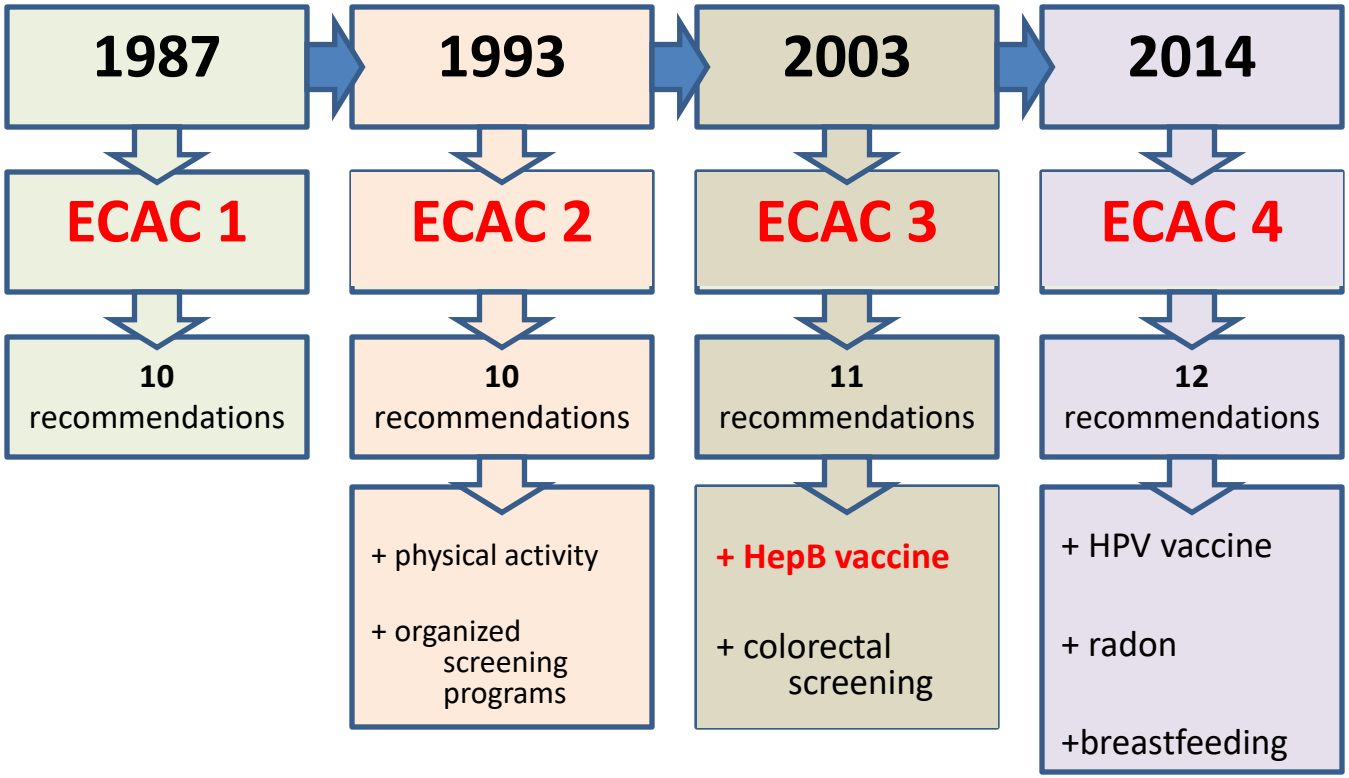
ECAC: A timeline



ECAC: A timeline



ECAC: A timeline

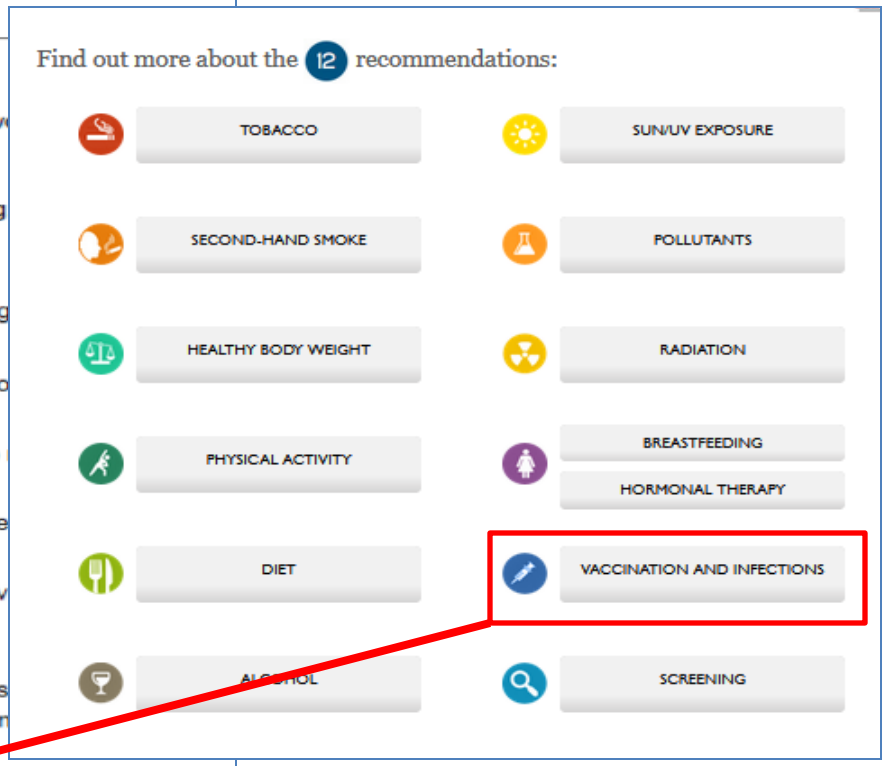


ECAC #4 (2014)

EUROPEAN CODE AGAINST CANCER

12 ways to reduce your cancer risk

1. Do not smoke. Do not use any form of tobacco.
2. Make your home smoke free. Support smoke-free policies in your w
3. Take action to be a healthy body weight.
4. Be physically active in everyday life. Limit the time you spend sitting
5. Have a healthy diet:
   - Eat plenty of whole grains, pulses, vegetables and fruits.
   - Limit high-calorie foods (foods high in sugar or fat) and avoid sug
   - Avoid processed meat; limit red meat and foods high in salt.
6. If you drink alcohol of any type, limit your intake. Not drinking alcoho for cancer prevention.
7. Avoid too much sun, especially for children. Use sun protection. Do sunbeds.
8. In the workplace, protect yourself against cancer-causing substance health and safety instructions.
9. Find out if you are exposed to radiation from naturally high radon le home. Take action to reduce high radon levels.
10. For women:
    - Breastfeeding reduces the mother's cancer risk. If you can, breas
    - Hormone replacement therapy (HRT) increases the risk of certain Limit use of HRT.
11. Ensure your children take part in vaccination programmes for:
    - Hepatitis B (for newborns)
    - Human papillomavirus (HPV) (for girls).
12. Take part in organized cancer screening programmes for:
    - Bowel cancer (men and women)
    - Breast cancer (women)
    - Cervical cancer (women).



IARC/WHO. https://cancer-code-europe.iarc.fr/index.php/en/ecac-12-ways

ECAC #4 (2014)

Contents lists available at ScienceDirect

Cancer Epidemiology

The International Journal of Cancer Epidemiology, Detection, and Prevention

journal homepage: www.cancerepidemiology.net

European Code against Cancer 4th Edition: Infections and Cancer☆

Patricia Villain[a], Paula Gonzalez[a,1], Maribel Almonte[a], Silvia Franceschi[a], Joakim Dillner[b,c], Ahti Anttila[d], Jin Young Park[a], Hugo De Vuyst[a], Rolando Herrero[a,*]

In the Q&A section:

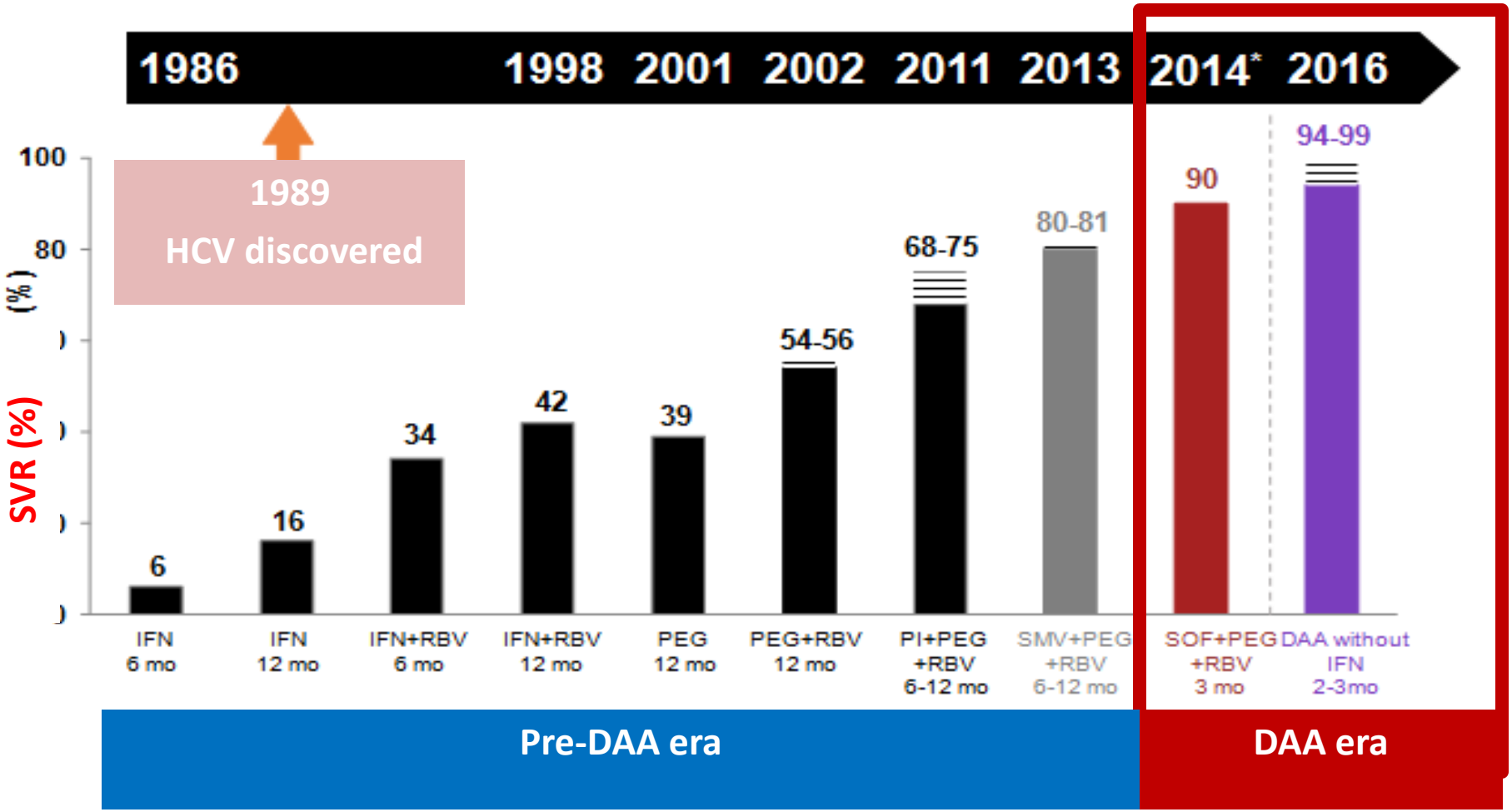
- **Individuals in high-risk groups for chronic HBV/HCV infection:**
  - advised to seek medical advice about testing and obtaining treatment when appropriate.

- **To prevent HCV transmission:**
  - to avoid injections and use oral treatments, especially when traveling to countries in which medical care is suboptimal.
  - to avoid body piercing, tattooing or acupuncture, if there is any doubt about the safety/ hygiene of the procedure.

Villain P, et al. Cancer Epidemiol 2015; 395: S120-38.

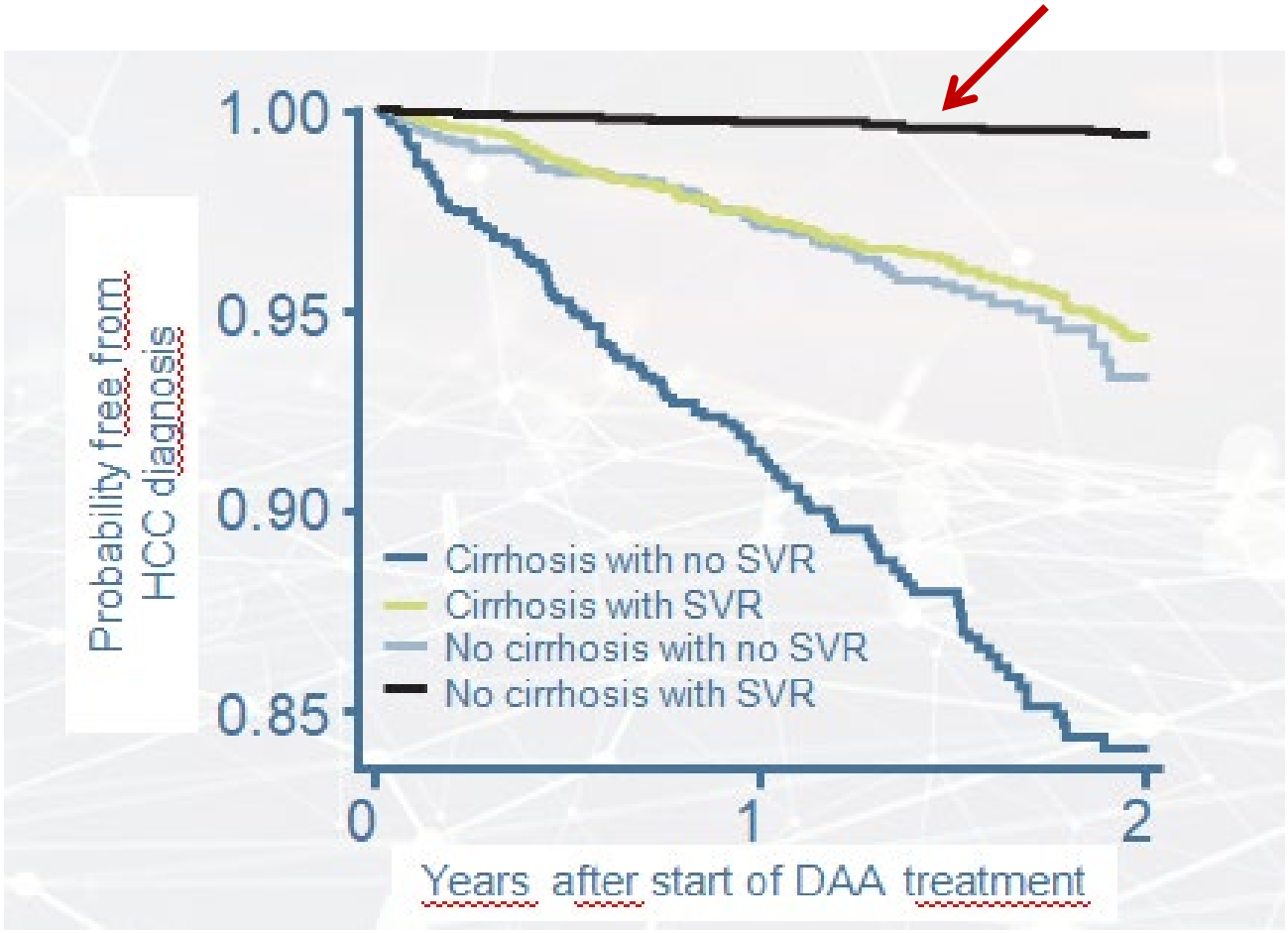
2014-2025: WHAT IS NEW?

HCC in the era of DAA treatment



Strader DB, et al. Hepatology 2004;39:1147-71.. Jacobson I, et al. EASL 2013. Amsterdam. The Netherlands. Poster #1425. Manns M, et al. EASL 2013. Amsterdam. The Netherlands. Oral #1413. Lawitz E, et al. APASL 2013. Singapore. Oral #LB-02. Afdhal N, et al. N Engl J Med 2014; 370: 1889-98. Kowdley K, et al. N Engl J Med 2014; 370: 1879-88. Manns M, Maasoumy B. Nature Perspect Gastrenterol Hepatol 2022; 19: 533-50.

Residual risk of HCC after HCV eradication (SVR)

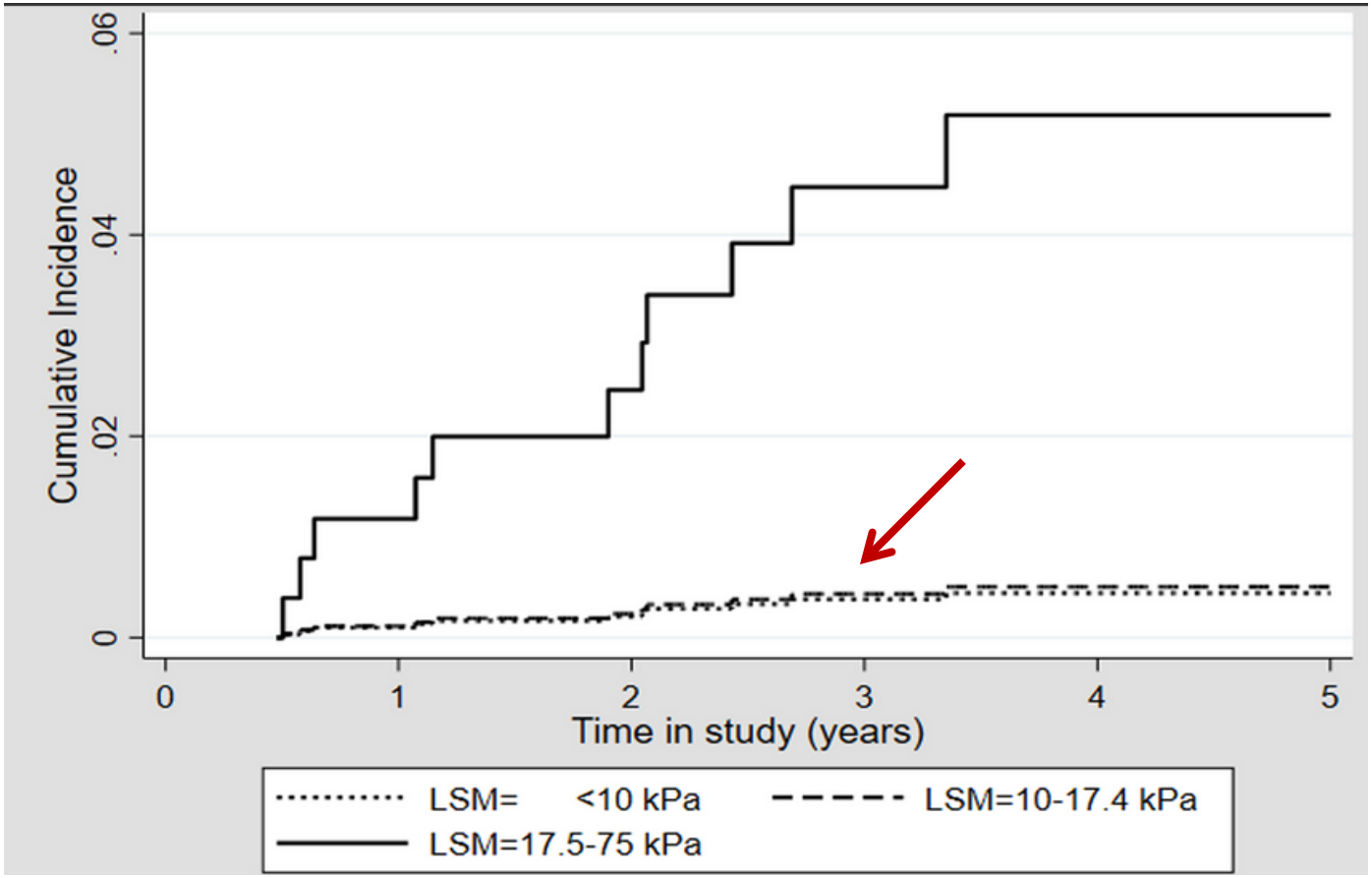


HCC Risk in DAA-Treated Veterans (N = 25,424)

DAA-induced SVR is associated with a 71% reduction in HCC risk

Ioannou GN, et al. J Hepatol. 2017; S0168-8278(17)32273-0.

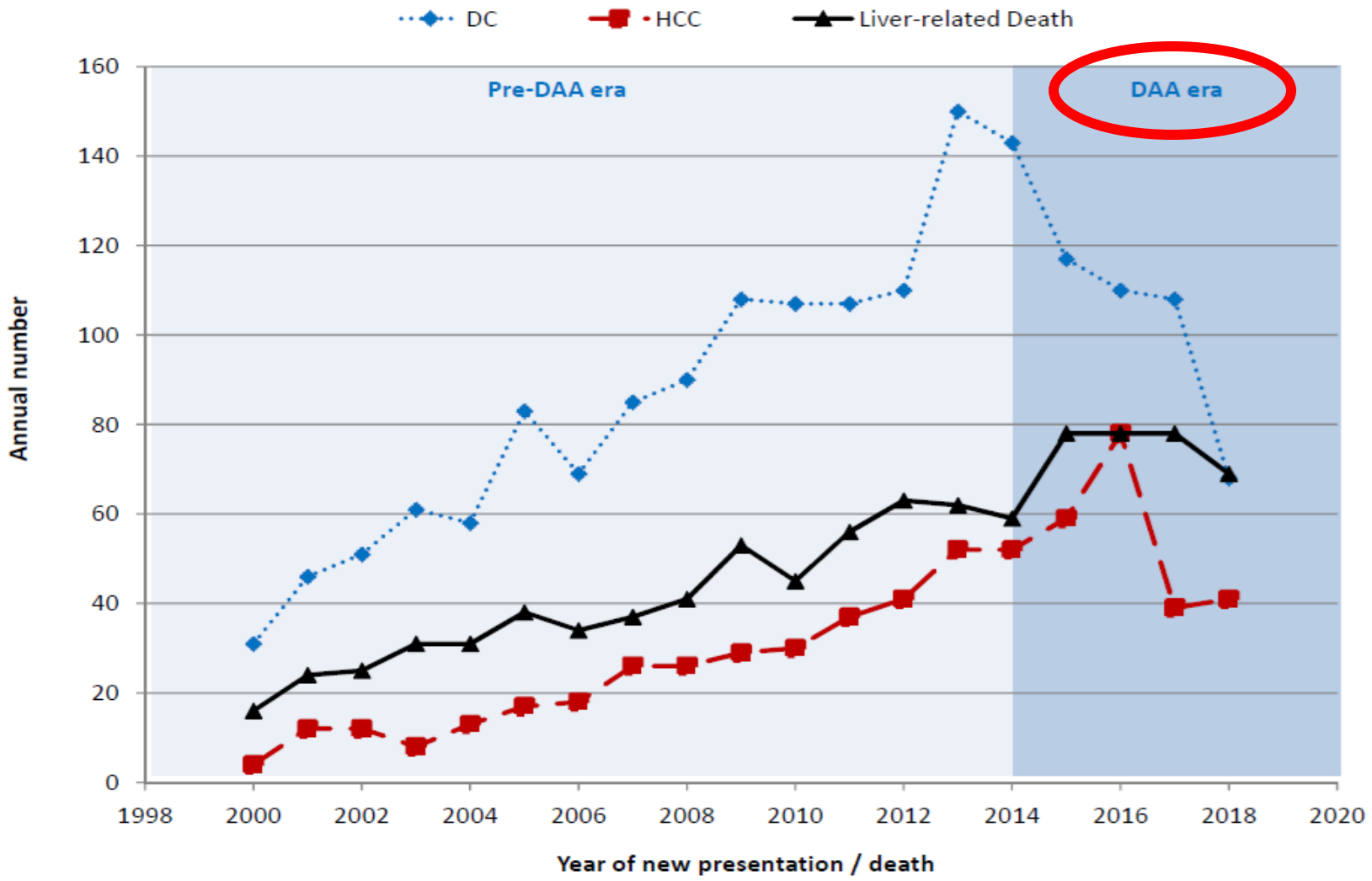
Incidence of HCC for patients achieving SVR after DAA treatment



Low incidence of HCC in HCV patients with pretreatment liver stiffness <17.5 kPa who achieve SVR following DAAs (N=773)

Søholm J, et al. PLOS ONE 2020:15(12): e0243725.

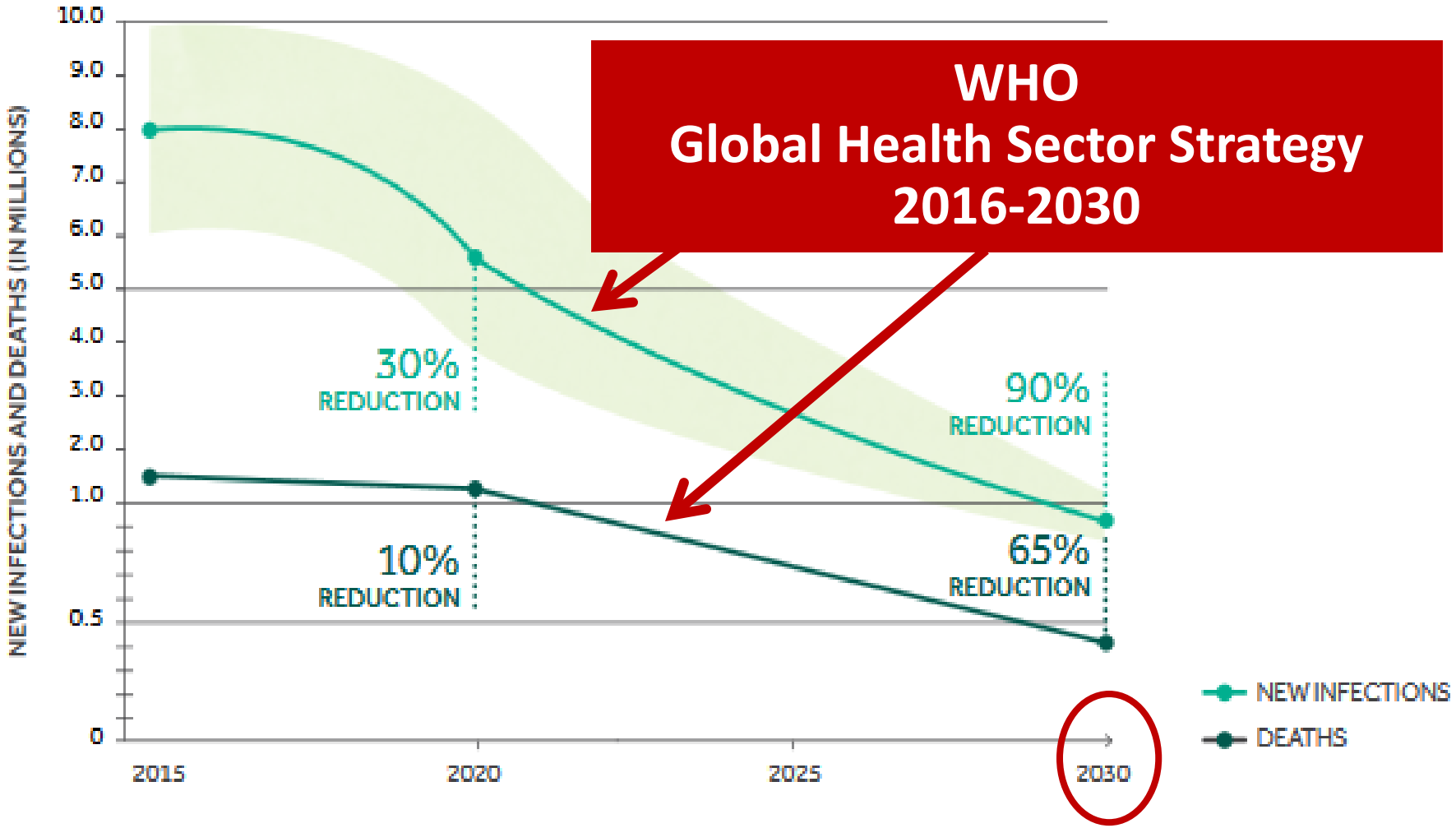
Population impact of DAAs
a national record-linkage study (N=11,000)



Hutchinson, SJ, et al. Gut 2020;, 69: 2223-31.

2014-2025: WHAT IS NEW?

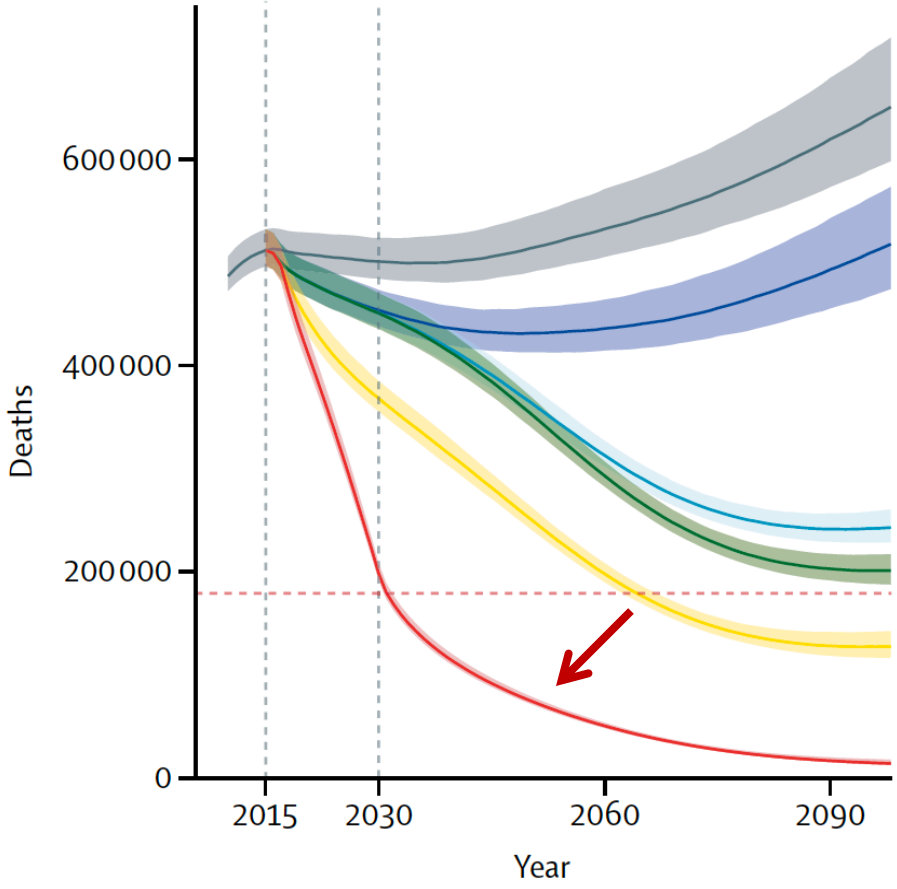
HCC in the era of HCV elimination



WHO. Global Health Sector on Viral Hepatitis. Available at: http//apps.who.int/gb/ebwha/pdf_files/WHA69/A69_32-en.pdf?ua=1

Global intervention results towards the elimination of hepatitis C

A global mathematical model: Scaling up prevention, testing and treatment



No DAA - **Status quo** scenarios

Blood safety and infection control – interventions reduce mortality in long term

PWID harm reduction

DAAs at the time of diagnosis – improves long-term outlook

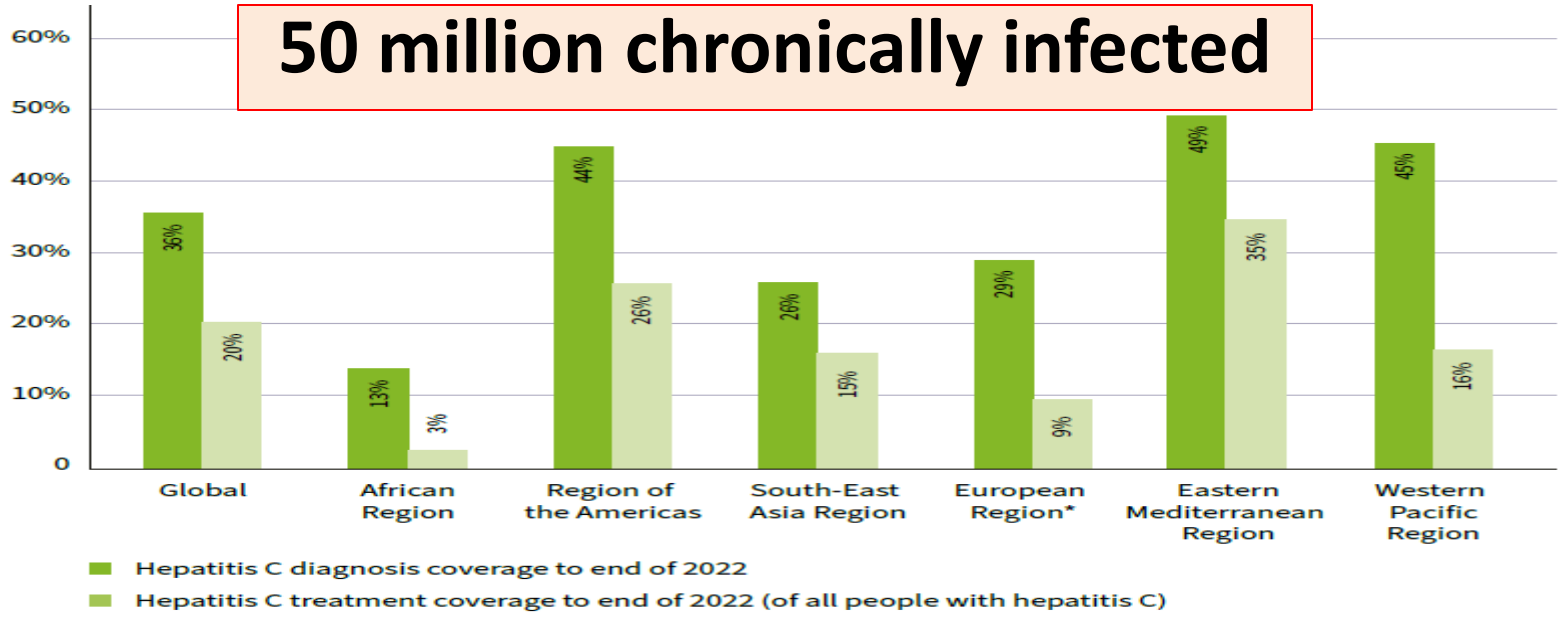
HCV testing & treatment scale-up

Heffernan A, Lancet 2019; 393: 1319-29.

Progress towards global hepatitis C targets, 2022

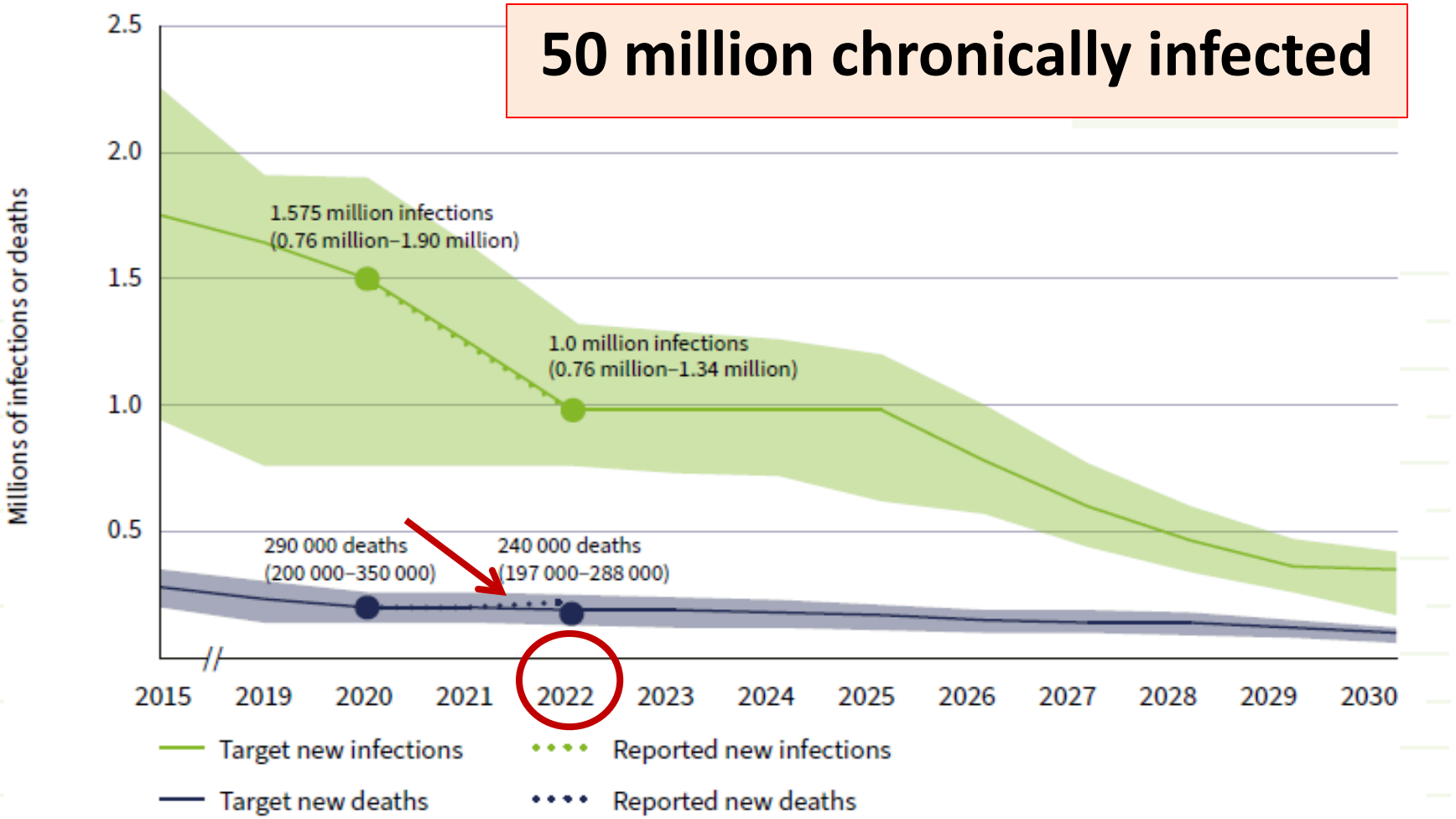
Indicator	Baseline – 2020	Progress – 2022	Targets – 2025	Targets – 2030
		Coverage		
Hepatitis C: percentage of people living with hepatitis C diagnosed	21% against a target of 30%	36.4%	60%	90%
Percentage of people living with hepatitis C treated	13% against a target of 30%	20%	50%	80%

50 million chronically infected



WHO. Global hepatitis report 2024. 9 April 2024. https://www.who.int/publications/i/item/9789240091672

Global trends in incidence and mortality of HCV



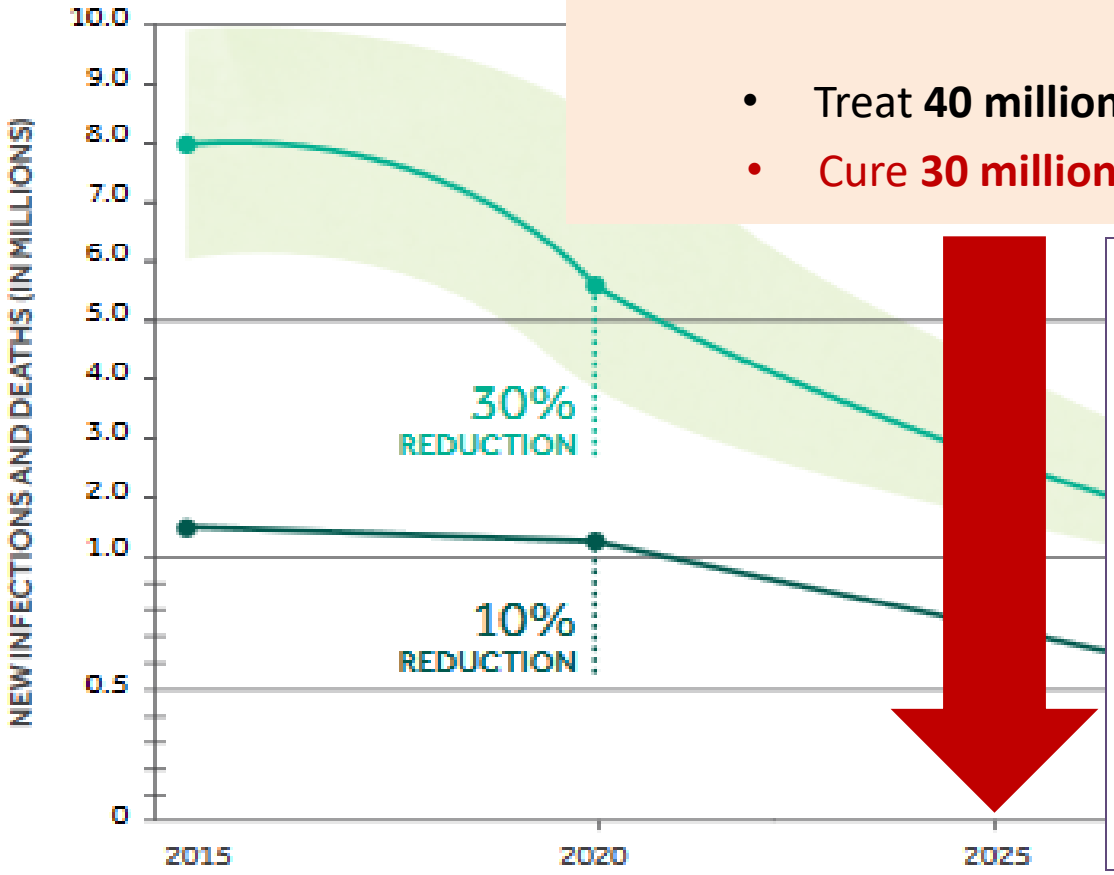
*WHO. Global hepatitis report 2024. **9 April 2024.** https://www.who.int/publications/i/item/9789240091672*

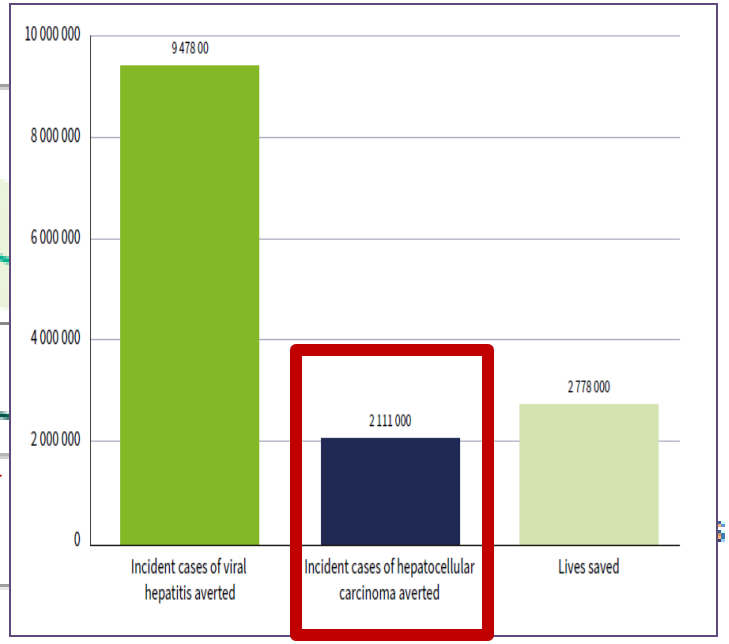
2014-2025: WHAT IS NEW?

HCC in the era of HCV elimination

Period 2024-2026:

- Treat **40 million HBV**
- Cure **30 million HCV**



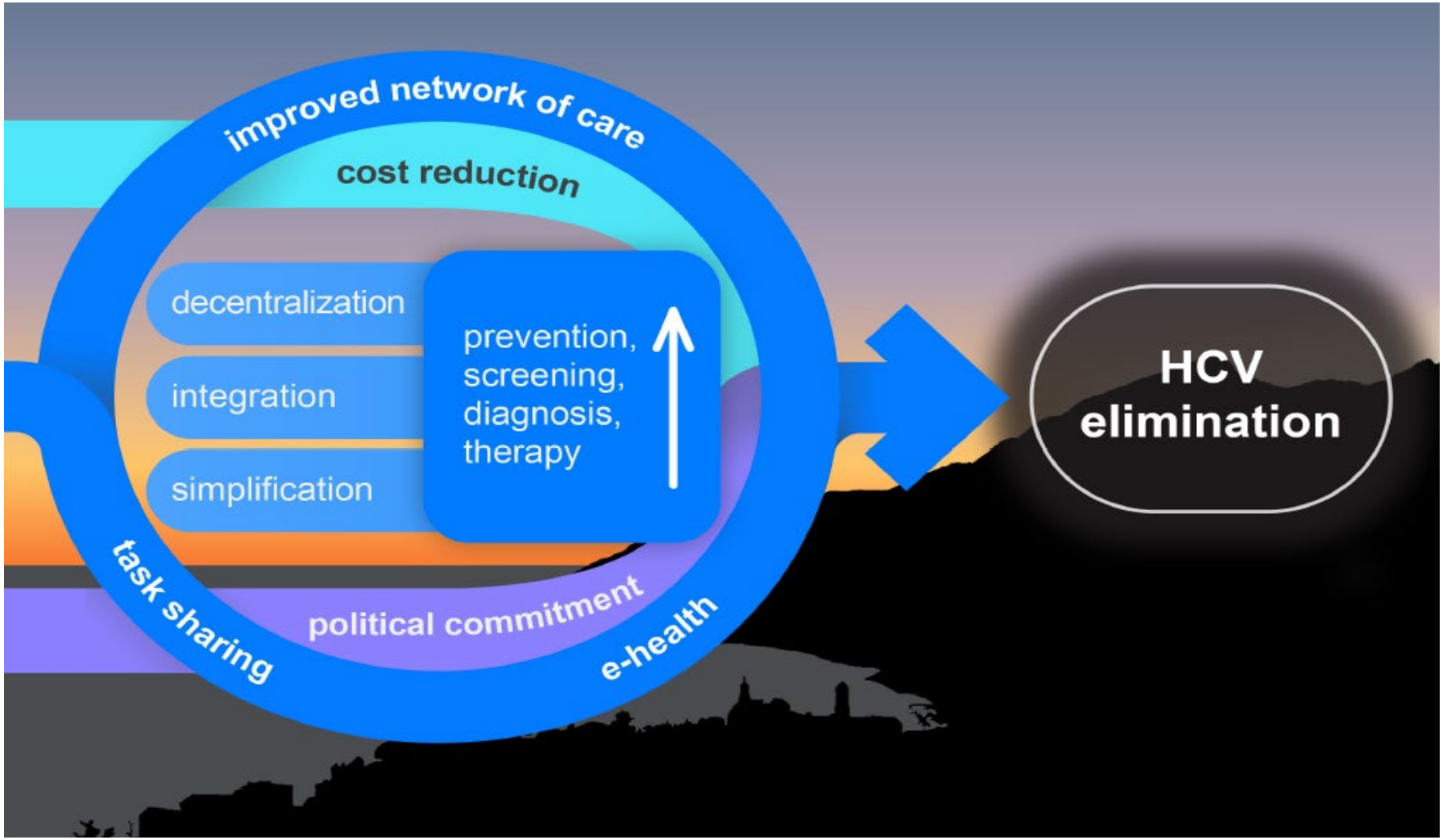


Prevent **2.8 million deaths** by l. 2030

*WHO. Global hepatitis report 2024. **9 April 2024.** https://www.who.int/publications/i/item/9789240091672*

HOW to find the missing HCV infected?

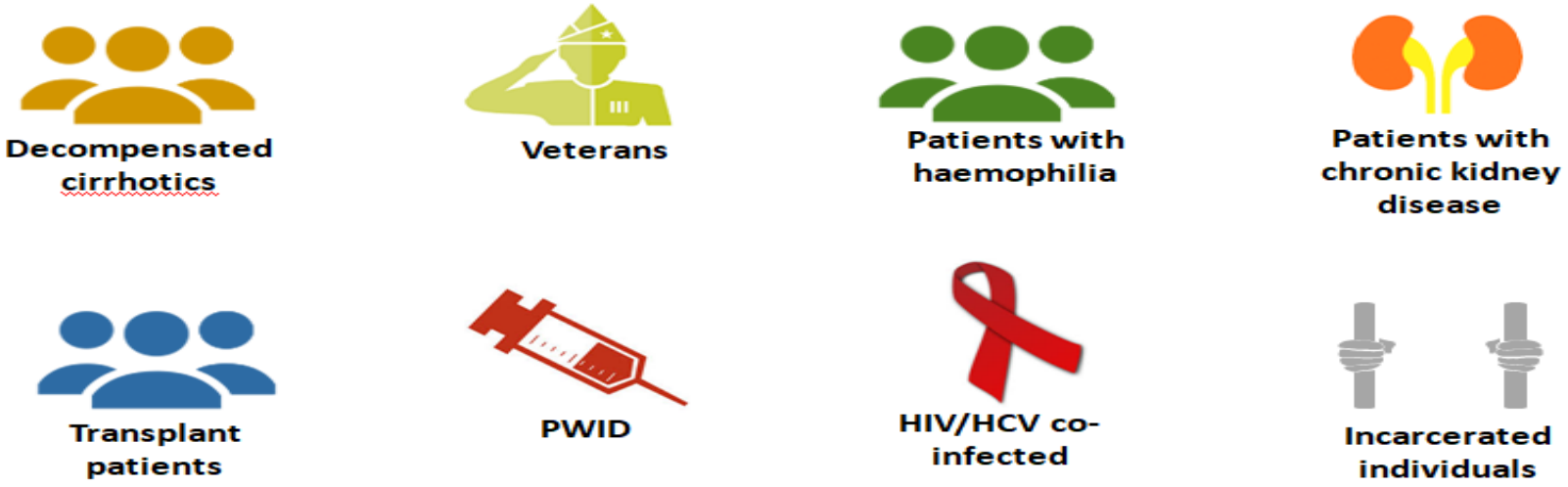
The process requires a paradigm shift to make HCV care **widely accessible**



Torre P, et al. Viruses 2024; 16: 1792.

RISK-BASED HCV screening

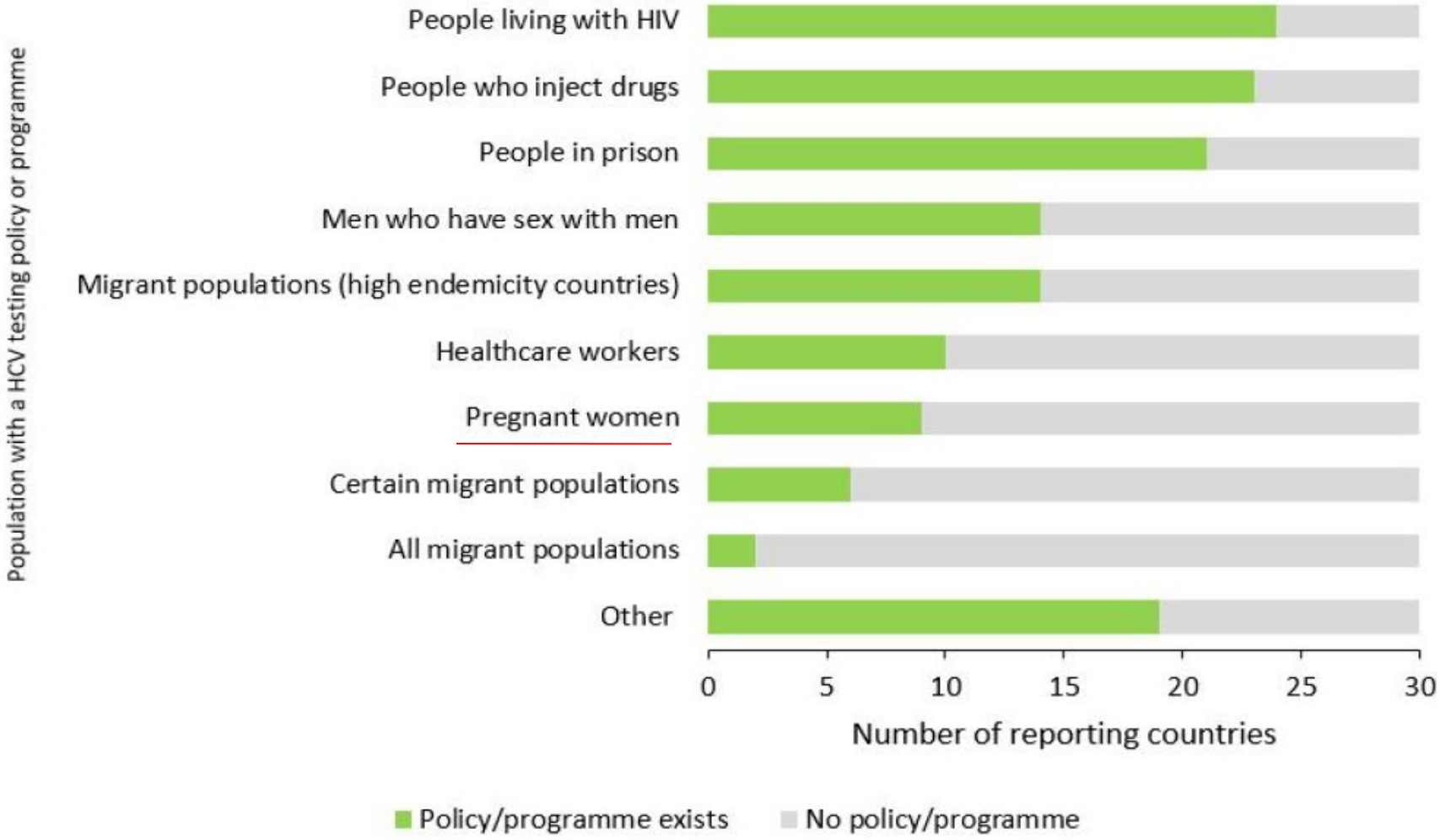
- Screening within groups/regions **with higher risk** for HCV
  → immediate treatment of HCV RNA infected



Risk-based screening strategies:
failed to identify the majority of HCV infected
even in high income countries

Lazarus JV et al. J Hepatol. 2017;67: 665-6.
Schillie S, et al. MMWR Recomm Rep 2020; 69(No. RR-2): 1–17.

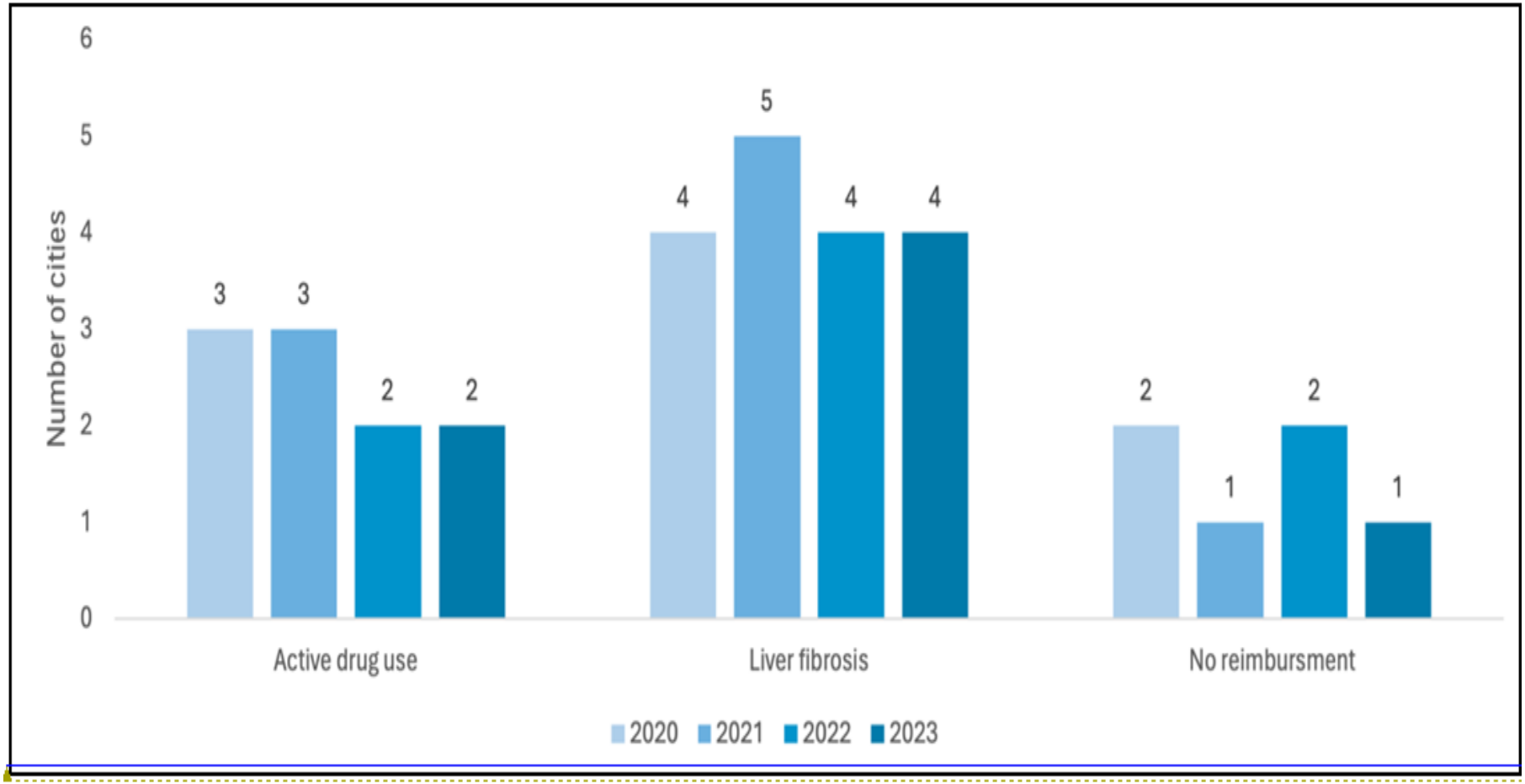
EU/EEA 2023
Existence of HCV screening policy in key populations



ECDC. Monitoring of the responses to the hepatitis B and C epidemics in EU/EEA countries, 2023. Stockholm: 2024.

Barriers to HCV treatment

25 European countries, period 2020-2023



Maticic M, et al. Harm Reduct J 2024: 21: 203-12.

UNIVERSAL HCV screening

- **Massive** population HCV **screening**
  → immediate **treatment** of HCV RNA infected

EGYPT:

Before 2014:

HCV prevalence 10% (6 million)

In 2015:

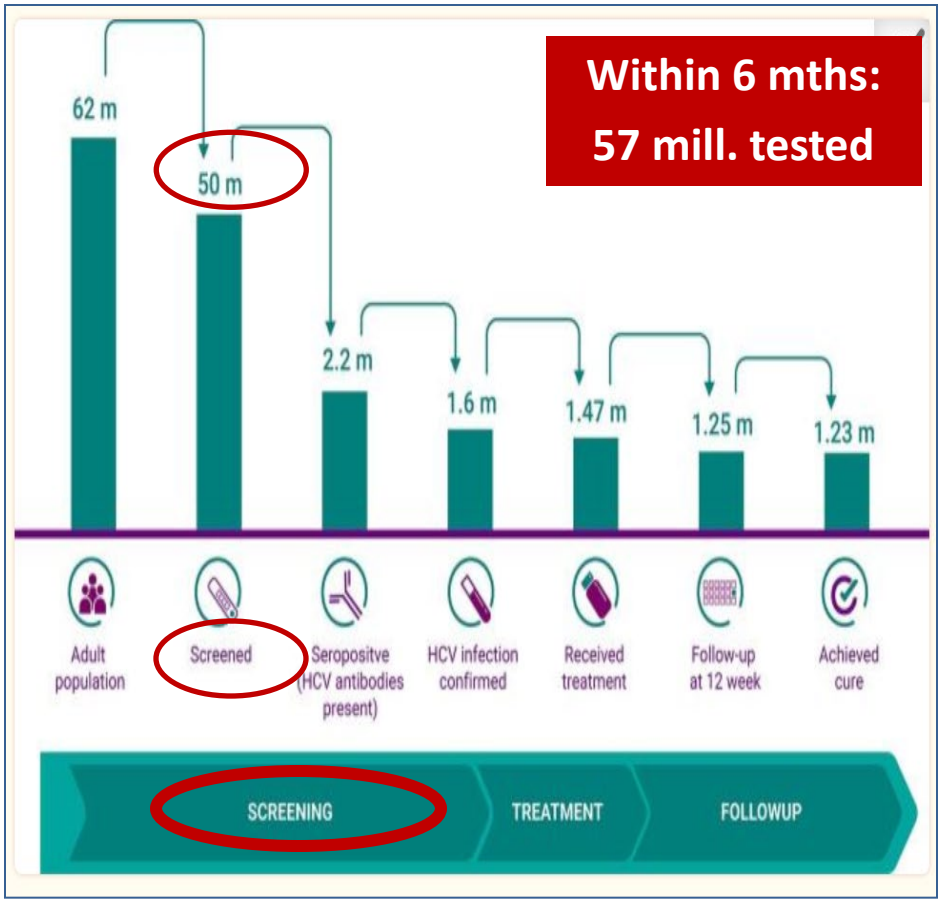
Introduction of generic DAAs

In 2018:

National screening program – test&treat

HCV prevalence, period 2015-2020:

10.5 % → <0.5 %



Hassanin A, et al. Glob Health Sci Pract 2021; 9: 187-200.

UNIVERSAL HCV SCREENING?
WHO

- Promote HCV testing **of all people during clinical visits** via reminders to practitioners

7.3.1 Clinician reminders to prompt HCV testing during clinical visits

Unlike interventions to increase HBV testing, which were primarily delivered in community settings, all 11 of the interventions to increase HCV testing either targeted health care providers or took place at established health care facilities *(191, 200-209)*. Reminder stickers attached to patient charts or in an electronic medical records system prompted providers to order HCV tests if patients belonged to a high-risk birth cohort *(204)*, reported risk behaviour *(207)* or both *(203)*. These studies found that clinician reminders to prompt HCV screening during clinical visits substantially increased HCV testing rates compared with no clinician reminders (RR = 3.70 [95% CI: 1.81–7.57]). The certainty of evidence was rated as very low.

WHO 2024. ://iris.who.int/bitstream/handle/10665/363590/9789240052734-eng.pdf?sequence=1

UNIVERSAL HCV SCREENING?

EASL

Recommendations 2018	Grade of evidence	Grade of recommendation
Screening strategies		
• Screening according to local epidemiology and within framework of national plans	A	1
• May include at-risk populations, birth cohort testing and general population testing in areas of intermediate to high seroprevalence (≥2–5%)	B	2

EASL . J Hepatol 2018;69:461–511.

Recommendation 2020:

Screening strategies

- Should be defined **according to the local epidemiology of HCV infection**, ideally within the framework of local, regional or national action plans (A1).

EASL. J Hepatol 2020; 73: 1170-218.

UNIVERSAL HCV SCREENING?

APASL

Due to the few clinical manifestations of chronic HCV infection, **screening is important based on the geographical region and risk population.**

It would be more helpful to identify HCV infection earlier than to reduce transmission and the infection pool by initiating treatment.

Omata M, et al. Hepatol Int 2016; 10: 681-701.

BIRTH COHORT HCV SCREENING (since 2013)
USA

CDC & US Preventive Services Task Force

- **Rationale for the birth-cohort 1945-1965 screening:**
  - risk based testing is unsuccessful (45-85% remain undiagnosed)
  - prevalence among birth cohort estimated **4-5%**
  - approach would identify 808,580 cases – is cost-effective at $35,700 per QUALY

- **Model assumed:**
  - 91% screening uptake
  - 41% of HCV-positive start HCV treatment
  - **birth cohort screening detects 3x more cases than risk-based strategy**

Moyer VA. U.S. Preventive Services Task Force recommendation statement. Ann Intern Med 2013;159:349-57.

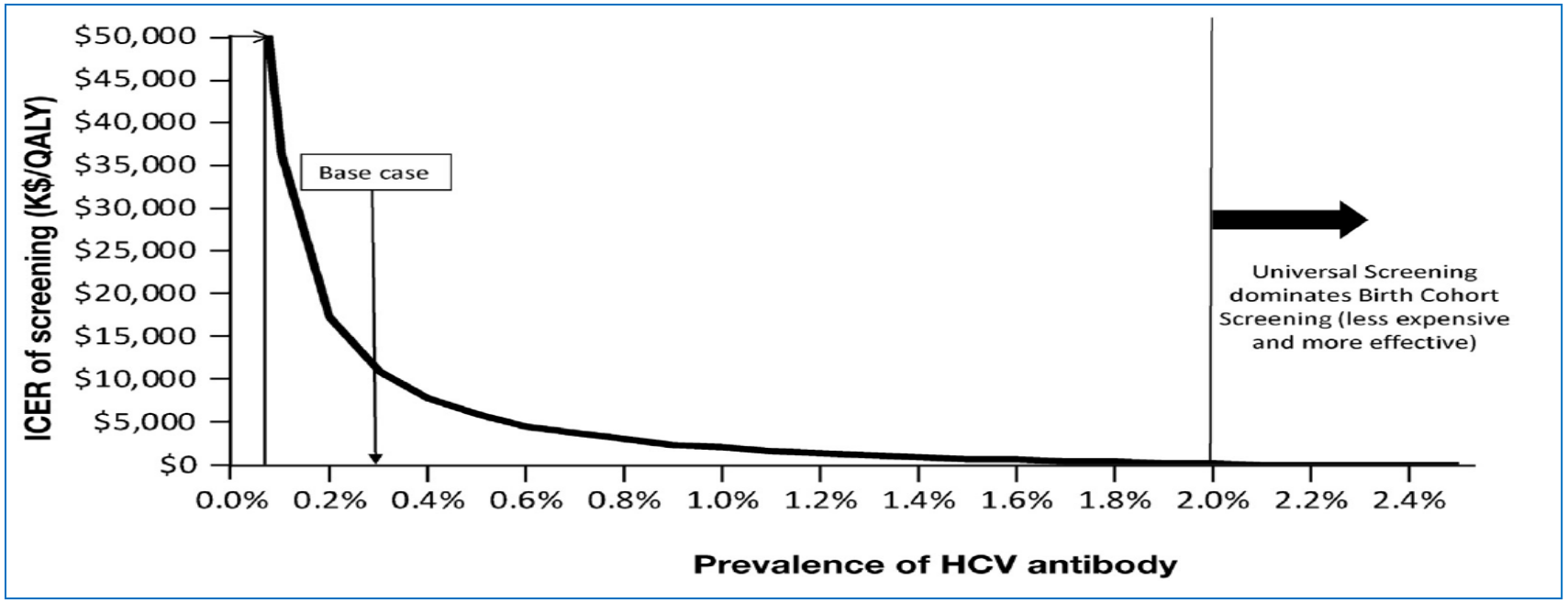
UNIVERSAL HCV SCREENING?
USA

Cost-effectiveness analysis (Markov state transition model) :

- a strategy of universal 1-time HCV screening **of all adults ≥18 years**

  is cost-effective compared with either no screening or **birth cohort-based** screening born between 1945-1965, provided that the

  HCV sero-prevalence is >0.07%.



Eckman MH, et al. Clin Gastroenterol Hepatol 2019; 17: 930-9.

UNIVERSAL HCV SCREENING?

USA

HCV screening in asymptomatic Adolescents and Adults and effect of DAA treatment

A Systematic Review Update for the U.S. Preventive Services Task Force
(49 studies, adjusted for potential confounders)

Treatment induced SVR was associated with a consistent **reduction of**:

- all-cause mortality (13 studies
- liver-related mortality (4 studies)
- **the incidence of HCC:** 20 studies (pooled HR, 0.29 [95% CI, 0.23-0.38])

Chou R, et al. Evidence Synthesis No. 188. AHRQ Publication No. 19-05256-EF-1.

UNIVERSAL HCV SCREENING
USA

Clinicians should universally screen:

- All adults 18 and older at least once in their lifetime, except in settings where the prevalence of hepatitis C virus (HCV) infection (HCV RNA-positivity) is under 0.1%.
- All pregnant women during each pregnancy, except in settings where the prevalence of HCV infection (HCV RNA-positivity) is under 0.1%.

CDC recommends one-time hepatitis C testing for people with recognized risk factors or exposures, including:

- People who currently or have previously injected drugs and shared needles, syringes, or other drug preparation equipment.
- People with human immunodeficiency virus (HIV).
- People with selected medical conditions, including people who have ever received maintenance hemodialysis and persons with persistently abnormal alanine aminotransferase (ALT) levels.

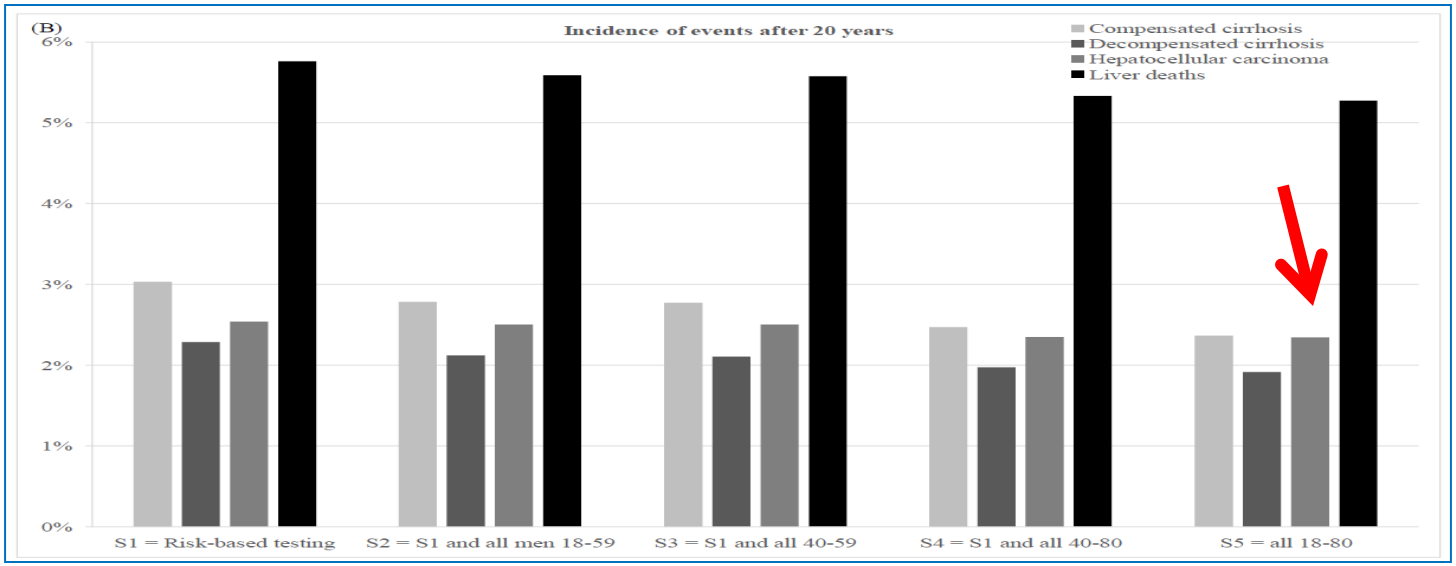
CDC 2025. https://www.cdc.gov/hepatitis-c/hcp/diagnosis-testing/index.html

UNIVERSAL HCV SCREENING?
FRANCE

- France: one of the countries with the highest HCV screening level –
  yet 40% still undiagnosed
  screening targets people at high risk of infection
- **Cost-effectiveness analysis** (Markov model):

  UNIVERSAL SCREENING is **the most effective** strategy and **is cost-effective** when treatment is initiated regardless of fibrosis stage.

→ after 20 years: ↓**HCC** incidence from **2.54% to 2.34%**



Deuffic-Burban S, et al. J Hepatol 2018; 69: 785-92.

UNIVERSAL HCV SCREENING?
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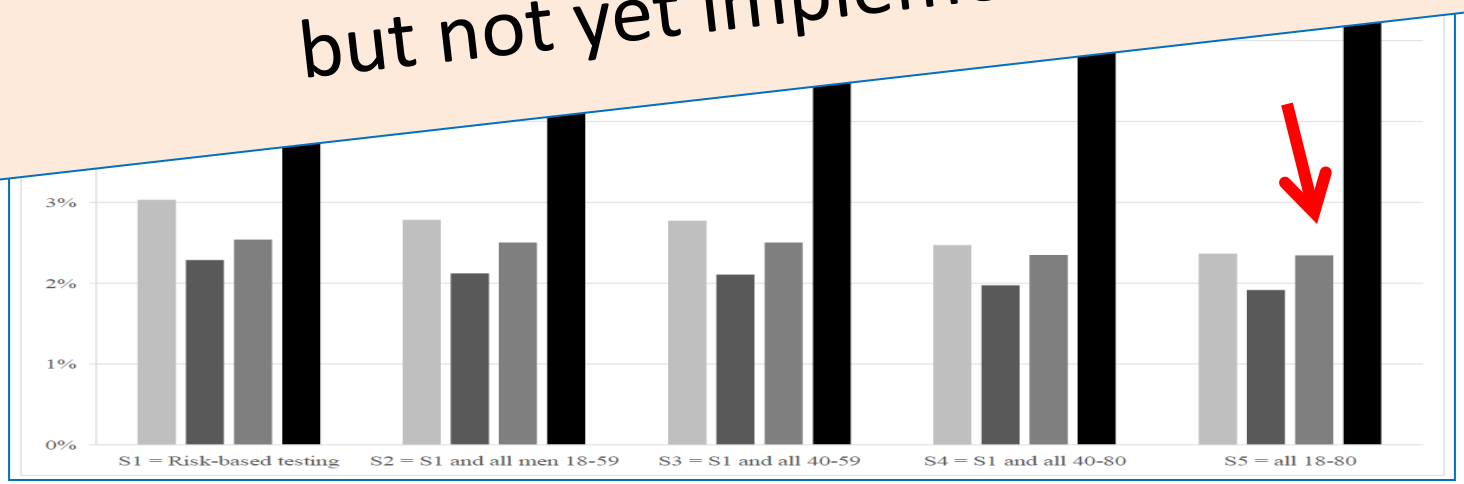
  when treatment is initiated regardless of fi

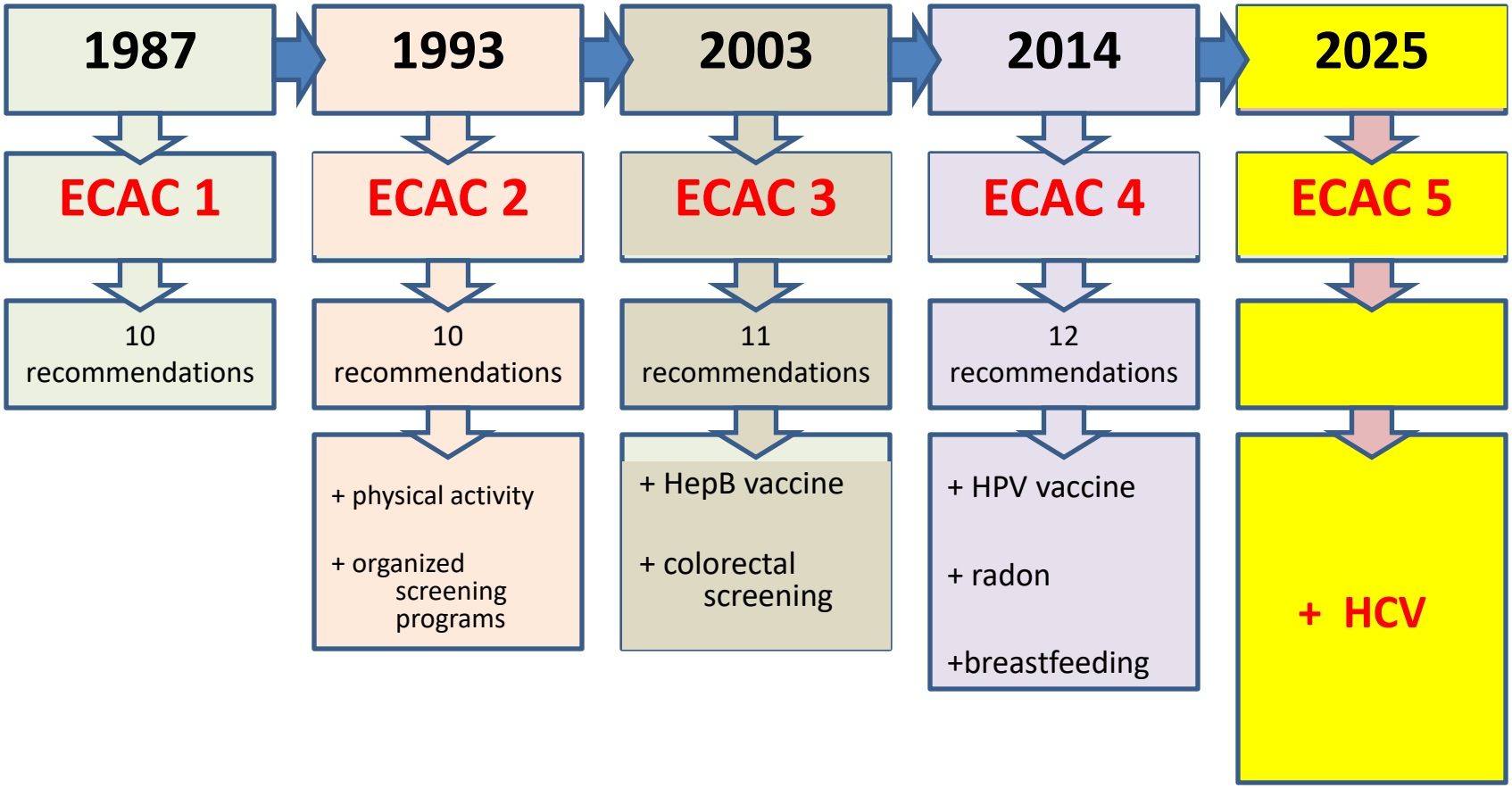
→ after 20 ye

UNIVERSAL SCREENING recommended,
but not yet implemented



Deuffic-Burban S, et al. J Hepatol 2018; 69: 785-92.

It is time for ECAC #5

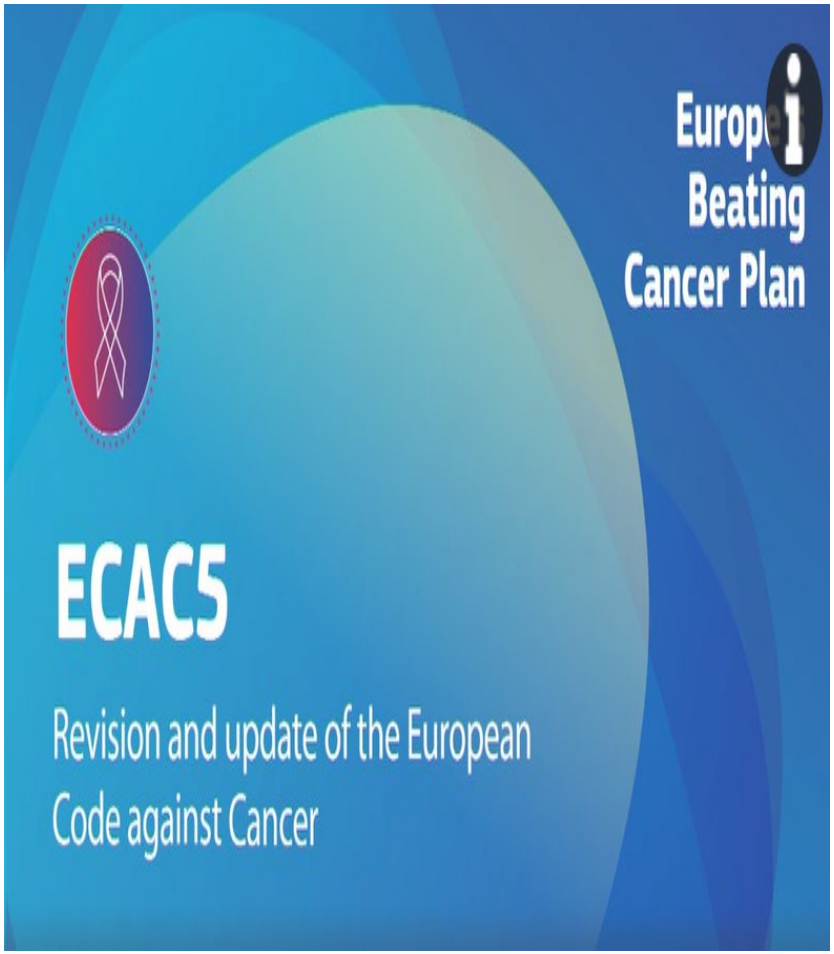


Project ECAC #5

Project duration:
1 Jul 2022 - **30 Jun 2026**

The project will produce a **revised and updated** ECSC (5th edition) with:

- recommendations to **individuals and policymakers**
- supporting material on the Code and putting the recommendations into context
- scientific justification for the Code, published in scientific literature



EC. https://health.ec.europa.eu/non-communicable-diseases/cancer/europes-beating-cancer-plan-eu4health-financed-projects/projects/ecac5_en

ECAC #5

Prevention of liver cancer by early HCV testing and treatment

Recommendations for:

- Affordable and accessible testing and medications

ECAC #5

Prevention of liver cancer by early HCV testing and treatment

Recommendations for:

- Affordable and accessible testing and medications
- Avoiding inequity in diagnosis and treatment

ECAC #5

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Recommendations for:

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- Fight stigma and discrimination

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ECAC #5

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ECAC #5

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- Monitoring the burden of HCV infection
- **UNIVERSAL HCV screening?**