Public Health Ontario | Santé publique Ontario

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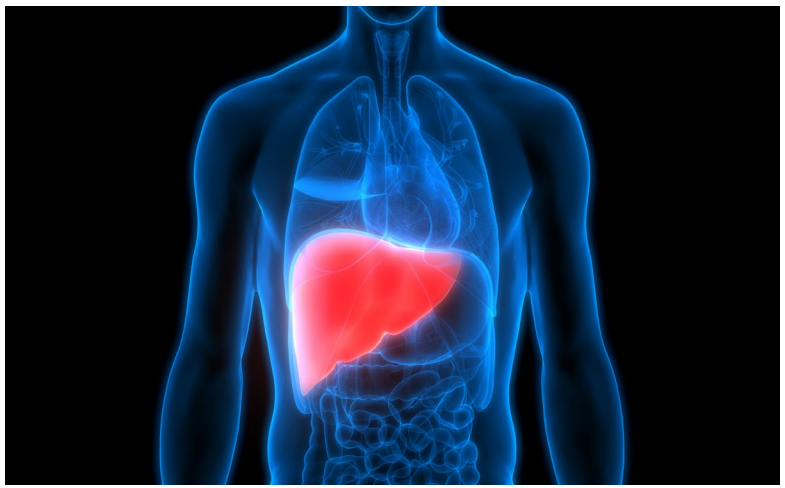
https://www.youtube.com/watch?v=HoQ514-snhw

Please scroll down this file to view a copy of the slides from the session.

Epidemiology and Outcomes of Alcohol Associated Liver Disease in Young Adults



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Hepatologist / Clinician Scientist
Queen's University

Conflicts of Interest for Jennifer Flemming: *None*

Learning Objectives

1) Understand the differences between high-risk alcohol consumption and alcohol use disorder

2) Describe the effects alcohol has on the liver

3) Appreciate the diverse spectrum of alcohol associated liver disease and approach to the treatment

4) Review data from Ontario describing epidemiology and outcomes of alcohol-associated hepatitis among adolescents and young adults in relation to changes in alcohol policy and COVID-19

5) Discuss potential policy implications related to alcohol in our population

ALCOHOL-ASSOCIATED LIVER DISEASE (ALD)

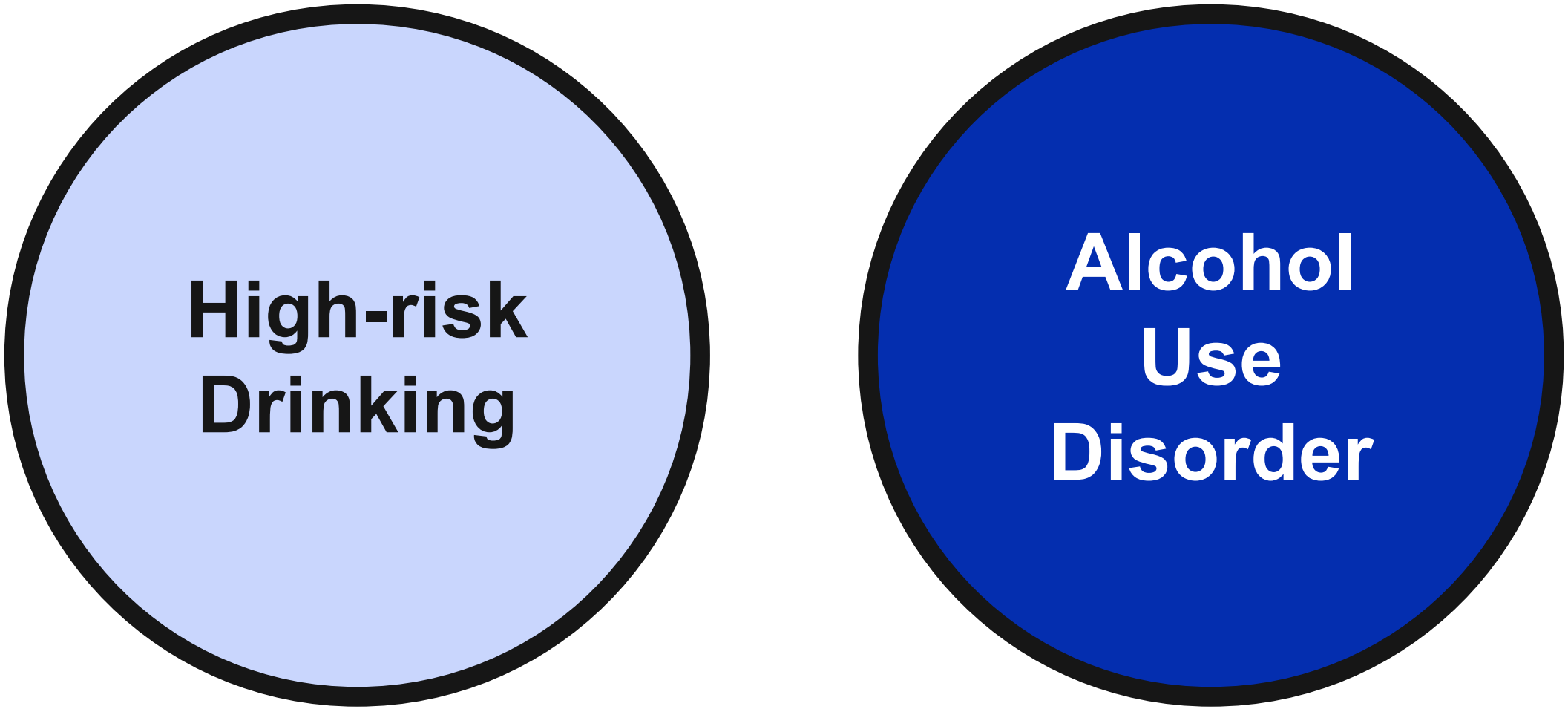
SECTION 1:
EPIDEMIOLOGY AND TERMINOLOGY

Alcohol is associated with MANY adverse health effects

- WHO has identified alcohol misuse as a leading **global cause of morbidity and mortality**
- Alcohol is attributed to **3 million deaths annually** across the world in addition to substantially morbidity
- Is the **LEADING cause** of premature mortality and disability in those **15-49 years of age**
- **Disadvantaged and vulnerable populations** carry the highest burden of alcohol associated death and hospitalization

WHO 2022

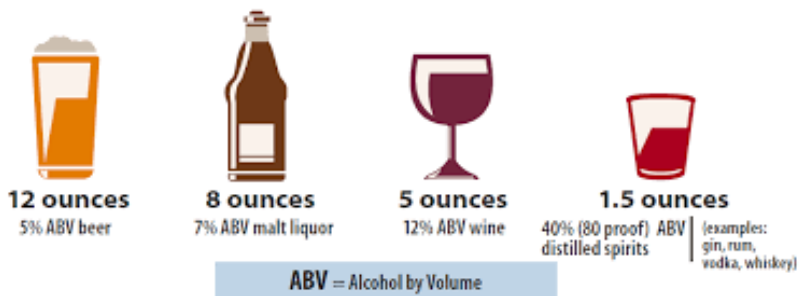
Distinct but related conditions



High-Risk Drinking

There is no labeling of alcohol content in Canada

1 standard drink = 10g alcohol

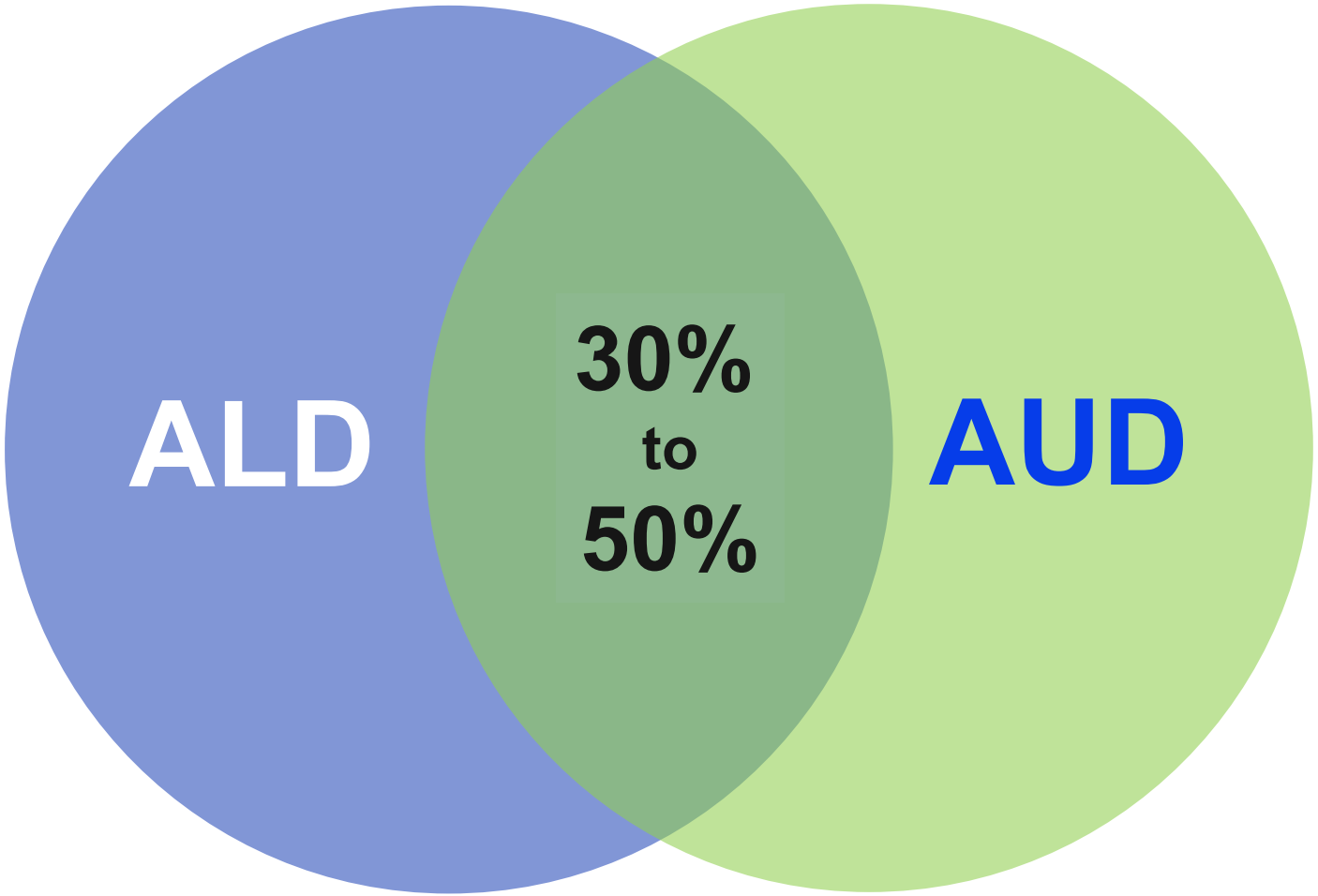


Alcohol Use Disorder

- Defined based on the ***behaviors and consequences of alcohol use***
- Diagnosed by presence of 2+ of the DSM-V criteria in the past year
  - Mild: 2-3
  - Moderate: 4-5
  - Severe: >=6

DSM-5 diagnosis criteria for alcohol use disorder*
1. Alcohol is often taken in larger amounts or over a longer period than was intended
2. There is a persistent desire or unsuccessful efforts to cut down or control alcohol use
3. A great deal of time is spent in activities necessary to obtain alcohol, use alcohol, or recover from its effects
4. Craving or strong desire, or urge to use alcohol
5. Recurrent alcohol use resulting in a failure to fulfill major role obligations at work, school, or home
6. Continued alcohol use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of alcohol
7. Important social, occupational, or recreational activities are given up or reduced because of alcohol use
8. Recurrent alcohol use in situations in which it is physically hazardous
9. Alcohol use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by alcohol
10. Tolerance, as defined by either of the following:
a. A need for markedly increased amounts of alcohol to achieve intoxication or desired effect
b. A markedly diminished effect with continued use of the same amount of alcohol
11. Withdrawal or taking alcohol to relieve withdrawal
**(At least of 2 symptoms in past 1 year; mild disorder:2-3; moderate:4-5; severe disorder≥6)*

Among those with alcohol-associated liver disease…



Canadian Community Health Survey
Past year alcohol use in Canada: 2017

Any alcohol use

~75%

High risk drinking

~20%

Alcohol use disorder

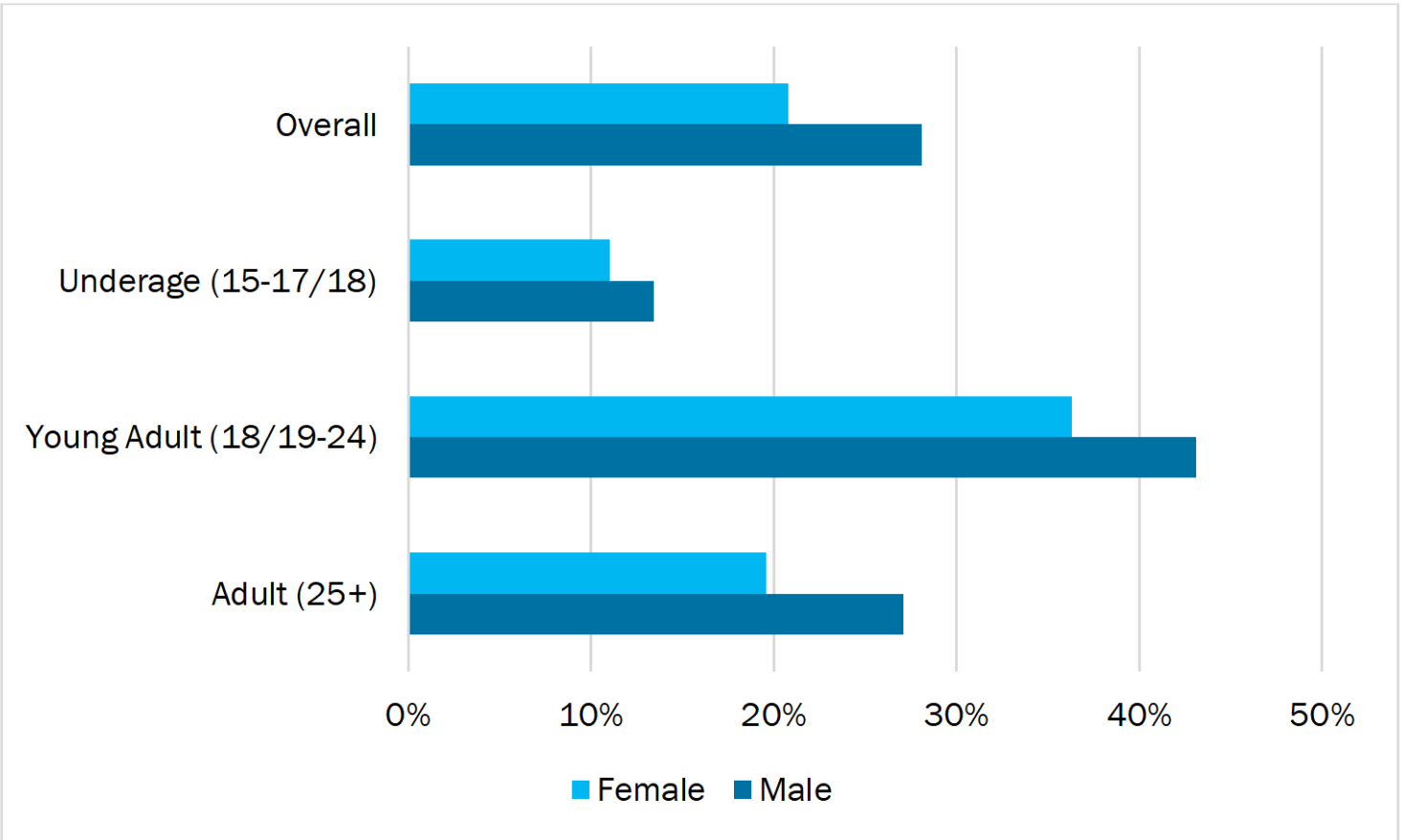
?~5%

* Not in the CCHS

Canadian Community Health Survey
Past year high-risk alcohol use in Canada: 2017

Between 2008-2017:

High risk drinking decreased by 10% in males but ***increased by 30% in females***



Canadian community health survey; www.Canada.ca

The liver is the most common end organ affected by high levels of alcohol consumption

ALCOHOL-ASSOCIATED LIVER DISEASE (ALD)

SECTION 2:
CLINICAL SPECTRUM OF ALD

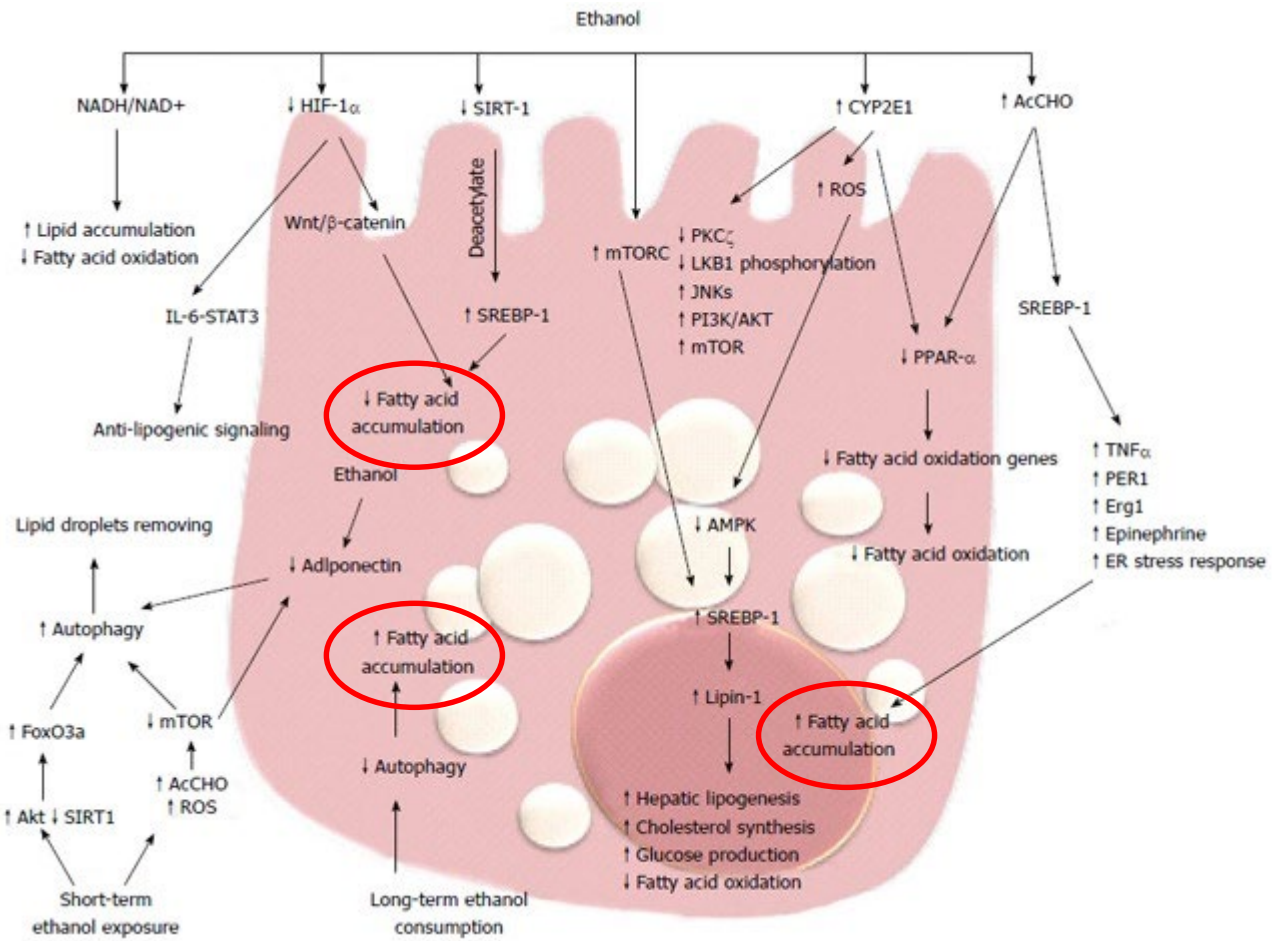
Its not just the quantity of alcohol consumed

Factors that increase the risk of ALD

- Genetics – PNPLA3
- Female sex
- Co-morbid liver disease (ie: Hepatitis B and C etc.)
- Type of alcohol and pattern
  - less likely with wine vs. beer/spirits
  - worse if drinking outside of mealtime or binge drinking
- Obesity
- Bariatric surgery
- Smoking

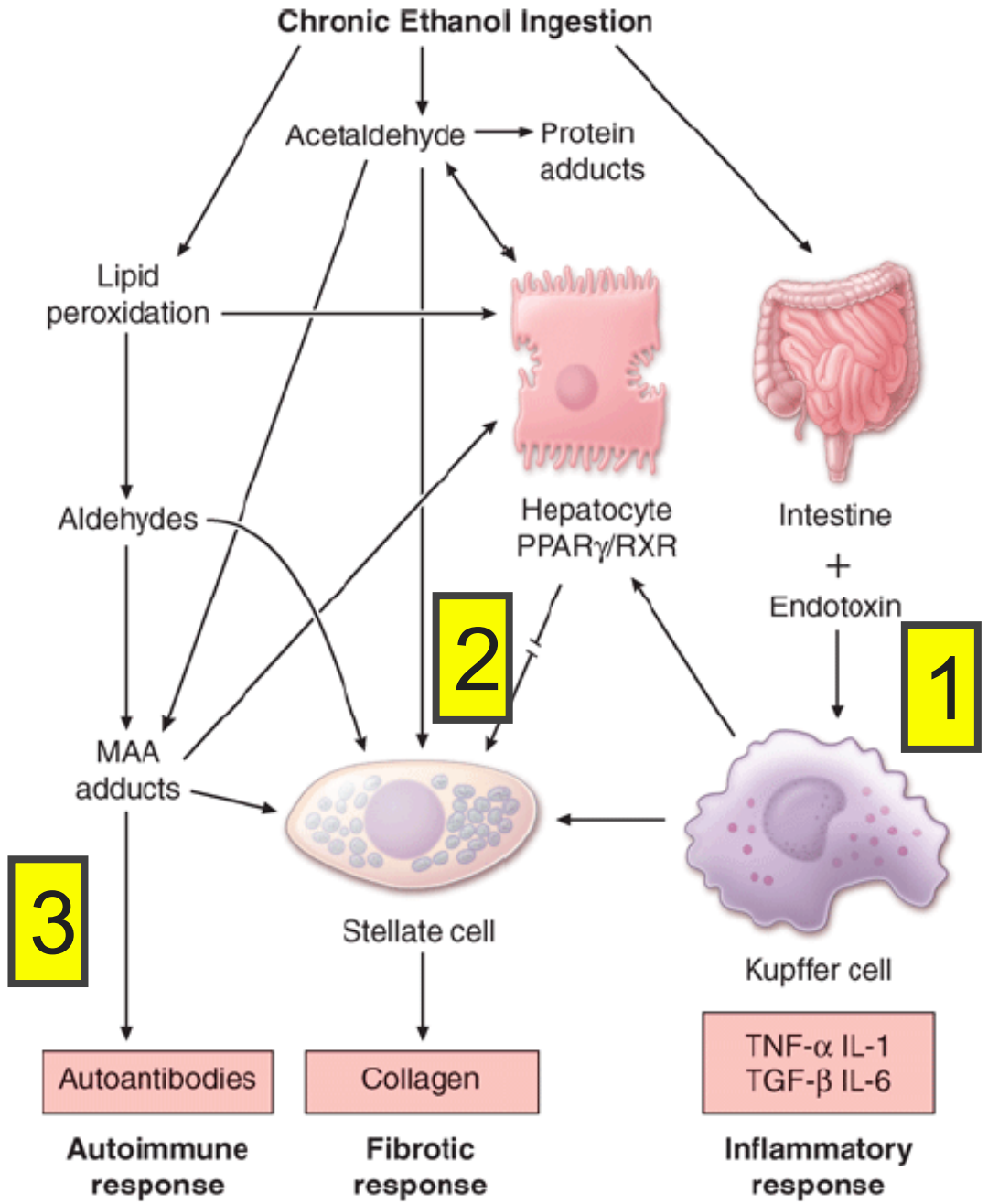
Alcohol consumption leads to:

increased fatty acid accumulation and deposition in the liver

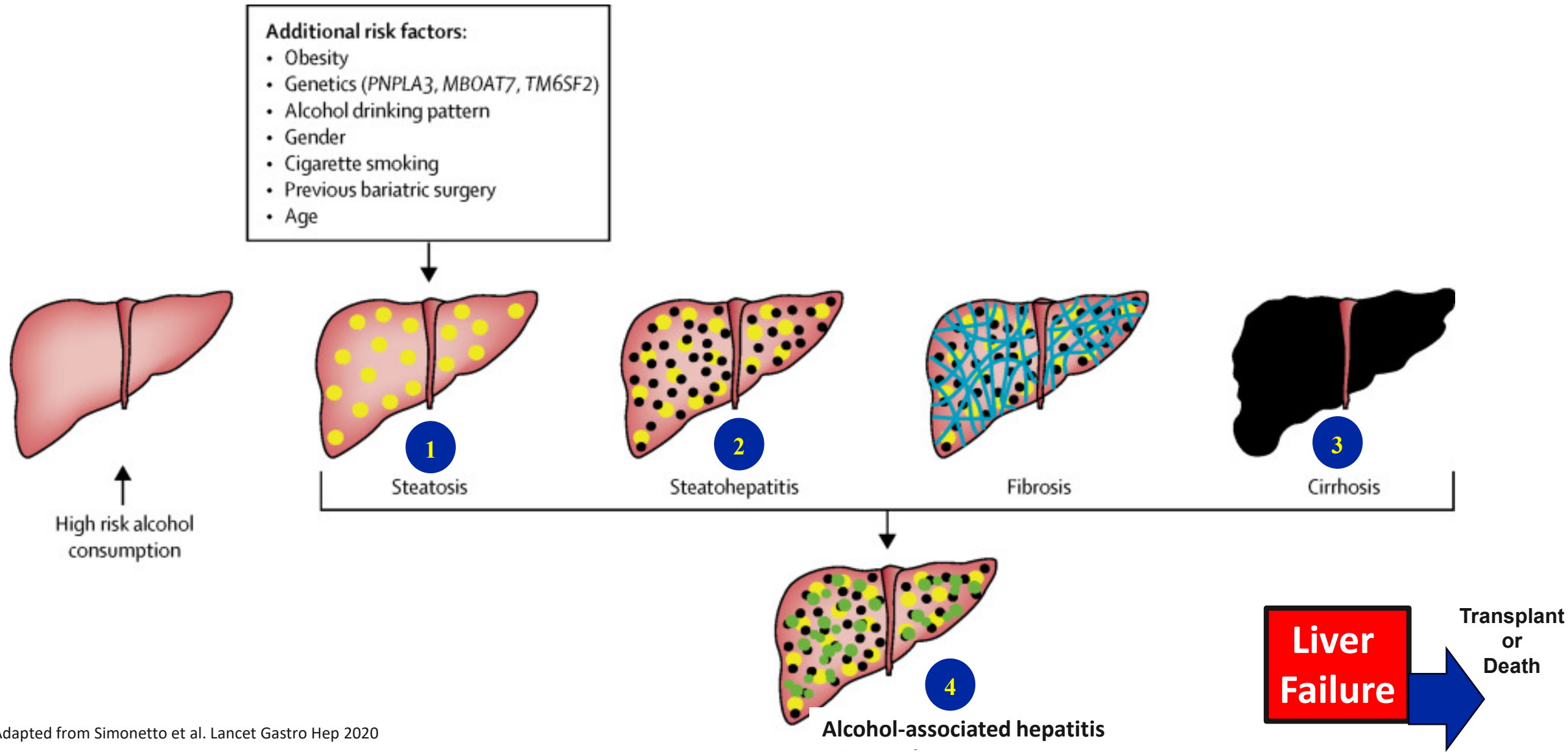


Once hepatic steatosis is established, damage occurs by:

1) **Kupffer Cells**
   - **Inflammation**
2) **Stellate Cells**
   - **Fibrosis**
3) **Autoimmune response**



Spectrum of alcohol-associated liver disease



Adapted from Simonetto et al. Lancet Gastro Hep 2020

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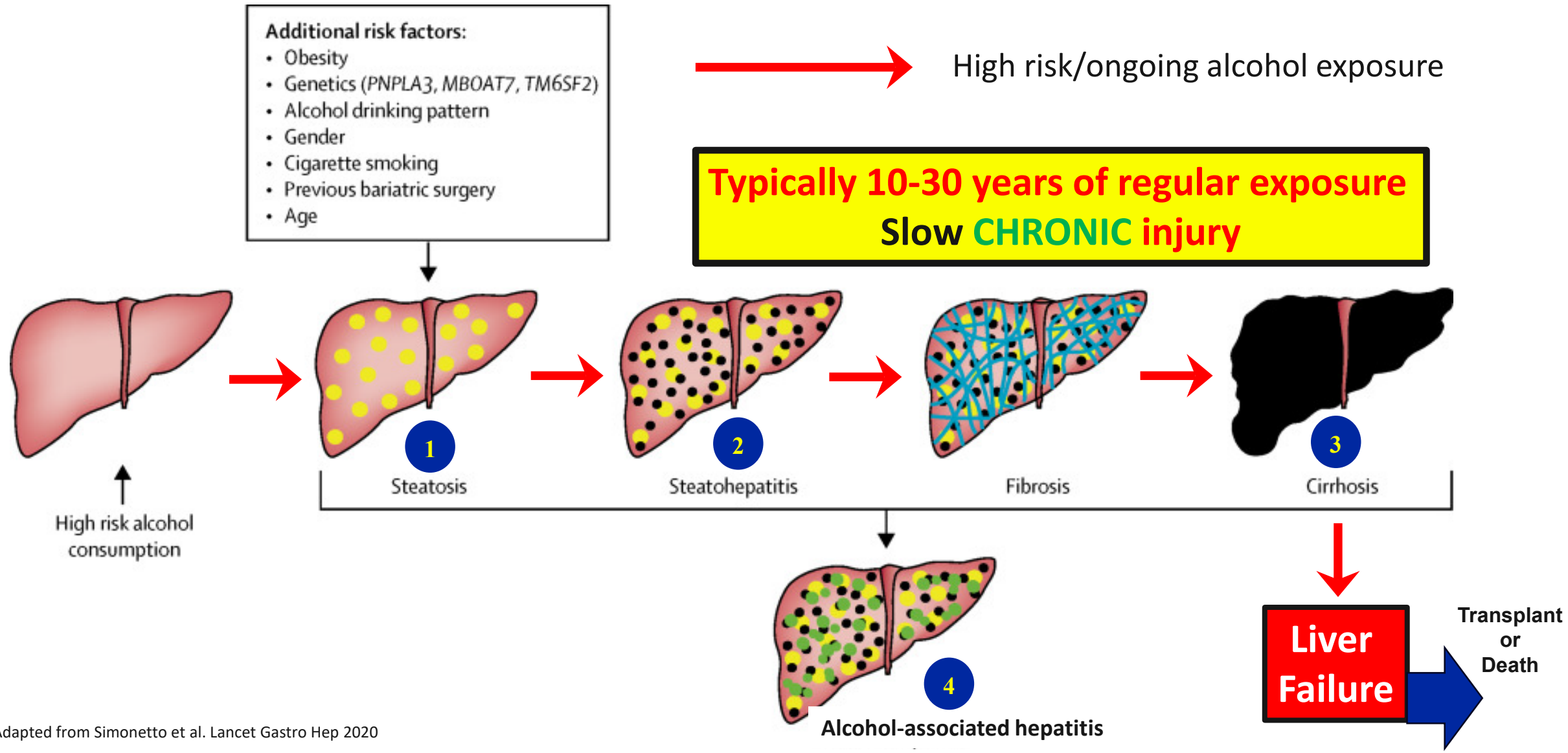

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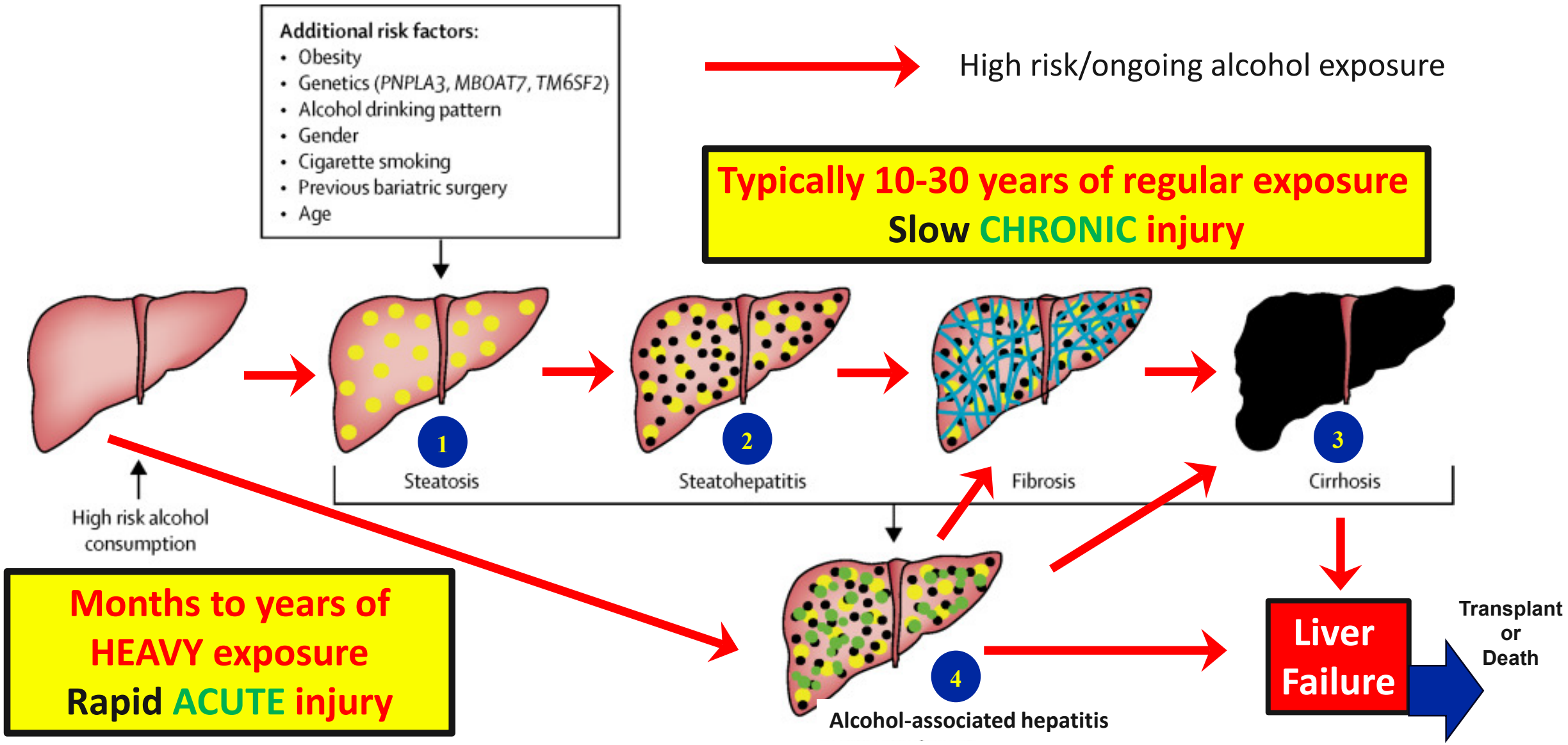

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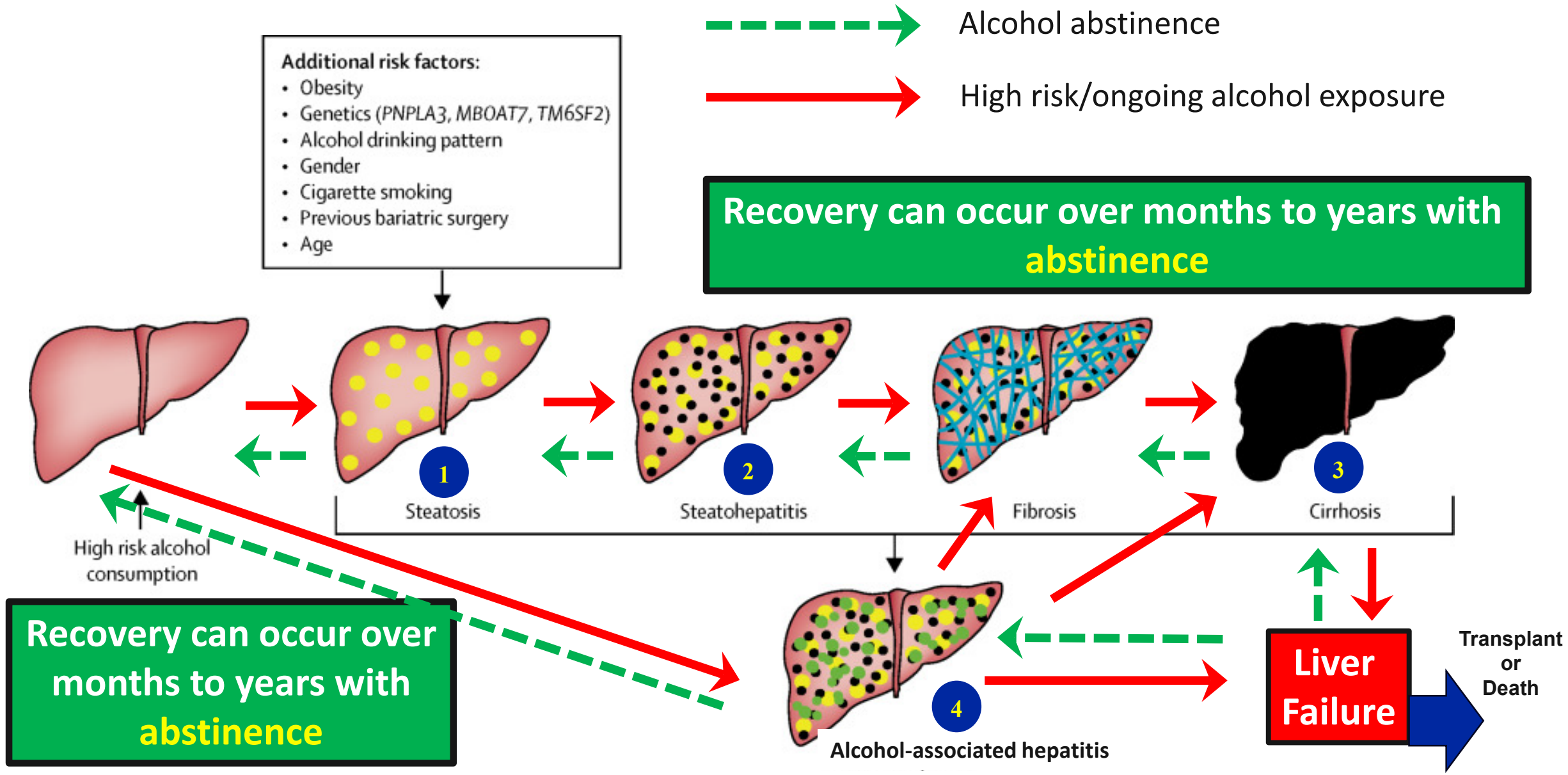


1 Alcohol-associated hepatic steatosis

No long term damage

Easily fixed

Car still works

2 Alcohol-associated steatohepatitis

More severe injury

Can be fixed

Car still works

3 Alcohol associated cirrhosis

Chronic long-term damage

Car may still be able to function

At high risk of breaking down or needed a new one

4 Alcohol-associated hepatitis

Acute
severe injury

Car is not functioning

Might be fixable, might need a new car

ALCOHOL-ASSOCIATED LIVER DISEASE (ALD)

SECTION 3:

Treatment of Alcohol-associated Liver Disease

General Principles: All forms of ALD

1) Abstinence

2) Abstinence

3) Abstinence

The single most important predictor of long-term outcomes in patients with alcohol-associated liver disease is whether long term abstinence is maintained

General Principles: All forms of ALD

Recidivism

- 1-year relapse rates as **high as 80%**
- Little data on predictors or relapse
  - High alcohol consumption, severe liver disease, unmarried, smoking, short length of abstinence

Arun AC et al. J Family Med Pri Care 2020.

Treatment of AUD

Behavioral Therapy + Medical Therapy

Very few studies have evaluated treatment efficacy or outcomes of AUD among individuals with advanced alcohol-associated liver disease

Treatment of AUD

Behavioral Therapy + Medical Therapy

Among patients with alcohol-associated cirrhosis, <15% ever received AUD treatment

Those who did receive treatment had lower rates of liver complications

Mellinger at al. Alcohol Clin Exp Res 2019

Pharmacotherapy

- **Options for medical therapy of AUD in patients with ALD**

1) **Acamprosate**: Renal clearance
2) **Baclofen**: Studied in advanced ALD
3) **Naltrexone**: Hepatic clearance, use with caution in advanced ALD but studies are suggesting safety
4) **Gabapentin**: renal clearance
5) **Disulfiram**: **DO NOT USE**

Alcohol-associated Hepatitis

Mild

Abstinence

Short term Recovery in >90%

Transplant

Death

No response ~40%

Severe

Abstinence + steroids + hospitalization

Short term Recovery in~60%

ALCOHOL-ASSOCIATED LIVER DISEASE (ALD)

SECTION 4:

Alcohol-associated Hepatitis in Adolescents and Young Adults

Ontario women and young adults experiencing greatest rise in ED visits for alcohol use

Researchers say interventions may be necessary to reduce harmful alcohol use, particularly in women and young adults.

Researchers looked at data for more than 765,000 emergency department (ED) visits in Ontario due to alcohol use between 2003 and 2016.

Overall, the increase in ED visits due to alcohol was 4.4x greater than the increase in ED visits due to all other causes combined.

AMONG WOMEN

ED visits due to alcohol **increased by 86%**, compared to 53% in men.

AMONG YOUNG ADULTS

ED visits due to alcohol **increased by 175%**, the largest change observed.

Myran DT et al. *CMAJ*. 2019.

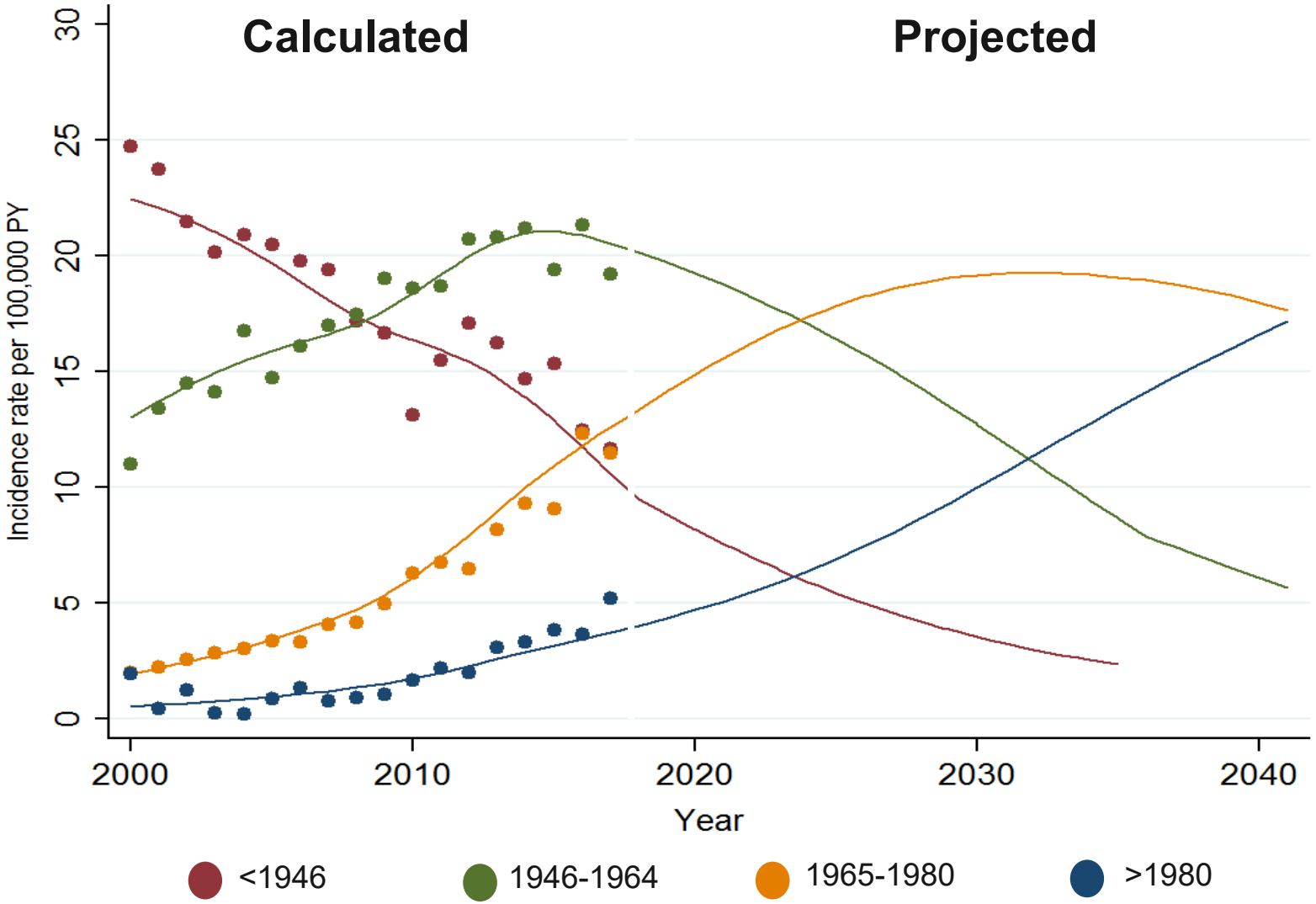
ICES *Data. Discovery. Better Health.*
ices.on.ca

uOttawa

The Ottawa Hospital | L'Hôpital d'Ottawa

INSTITUT DE RECHERCHE Bruyère RESEARCH INSTITUTE

Increase in cirrhosis incidence in young birth cohorts driven by alcohol associated liver disease



ALD
Cirrhosis

ALD

Calculations based on pre-pandemic patterns….

Flemming JA et al. Hepatology 2021

Impact of COVID-19 pandemic on alcohol use in the general population

JAMA Network | Open

Research Letter | Substance Use and Addiction

Changes in Adult Alcohol Use and Consequences During the COVID-19 Pandemic in the US

Michael S. Pollard, PhD; Joan S. Tucker, PhD; Harold D. Green Jr, PhD

HEPATOLOGY AASLD

Special Article

Coronavirus Disease 2019 Hangover: A Rising Tide of Alcohol Use Disorder and Alcohol-Associated Liver Disease

Text

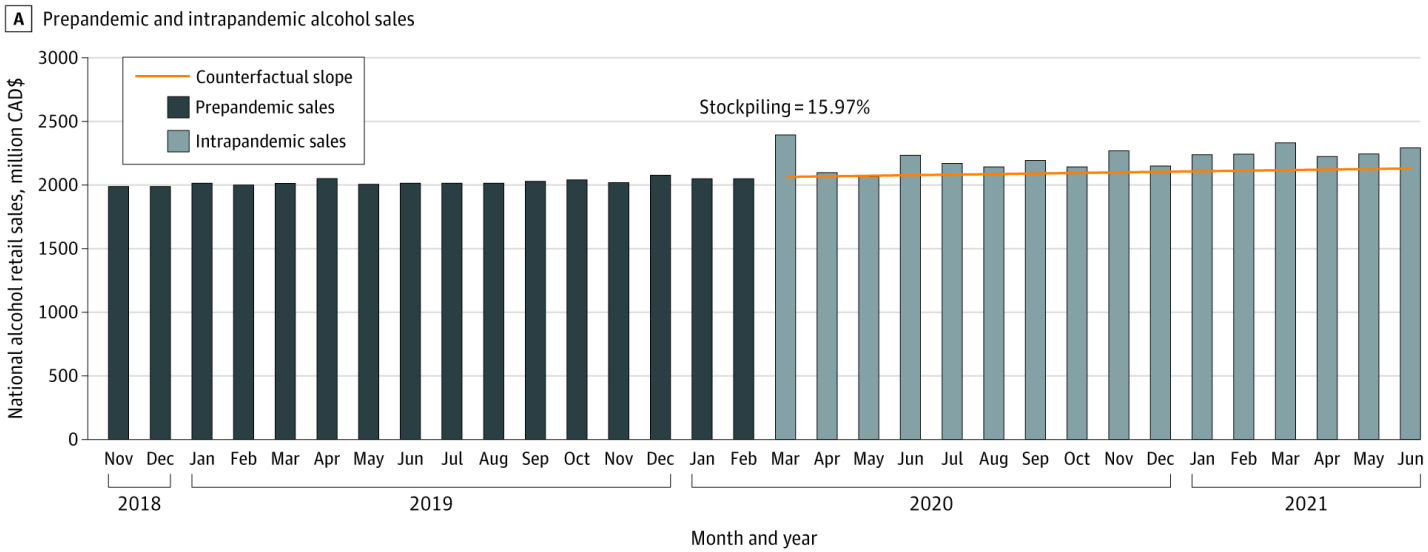
Ben L. Da, Gene Y. Im, Thomas D. Schiano

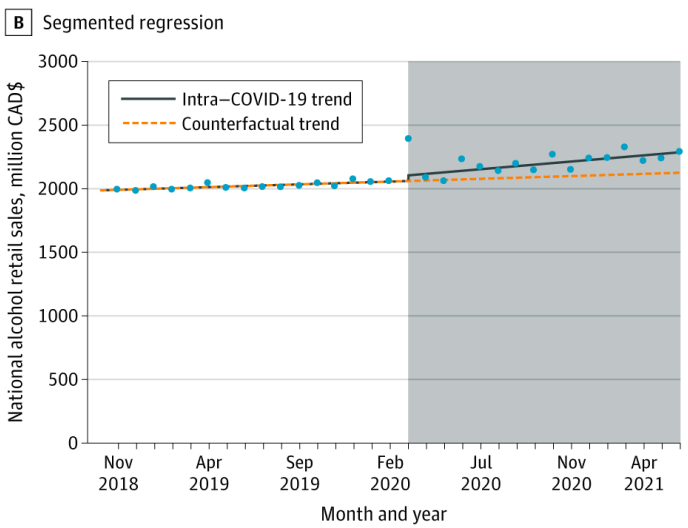
POLICY NEWS

Canada: COVID-19 Has Led to Alcohol Use Increase

Posted on **August 3, 2020** in **Alcohol Industry**, **Alcohol Norm**, **Corporate Consumption Complex**, **Human Rights**, **Policy**

Increased alcohol sales in Canada during COVID-19 March 2020 – June 2021



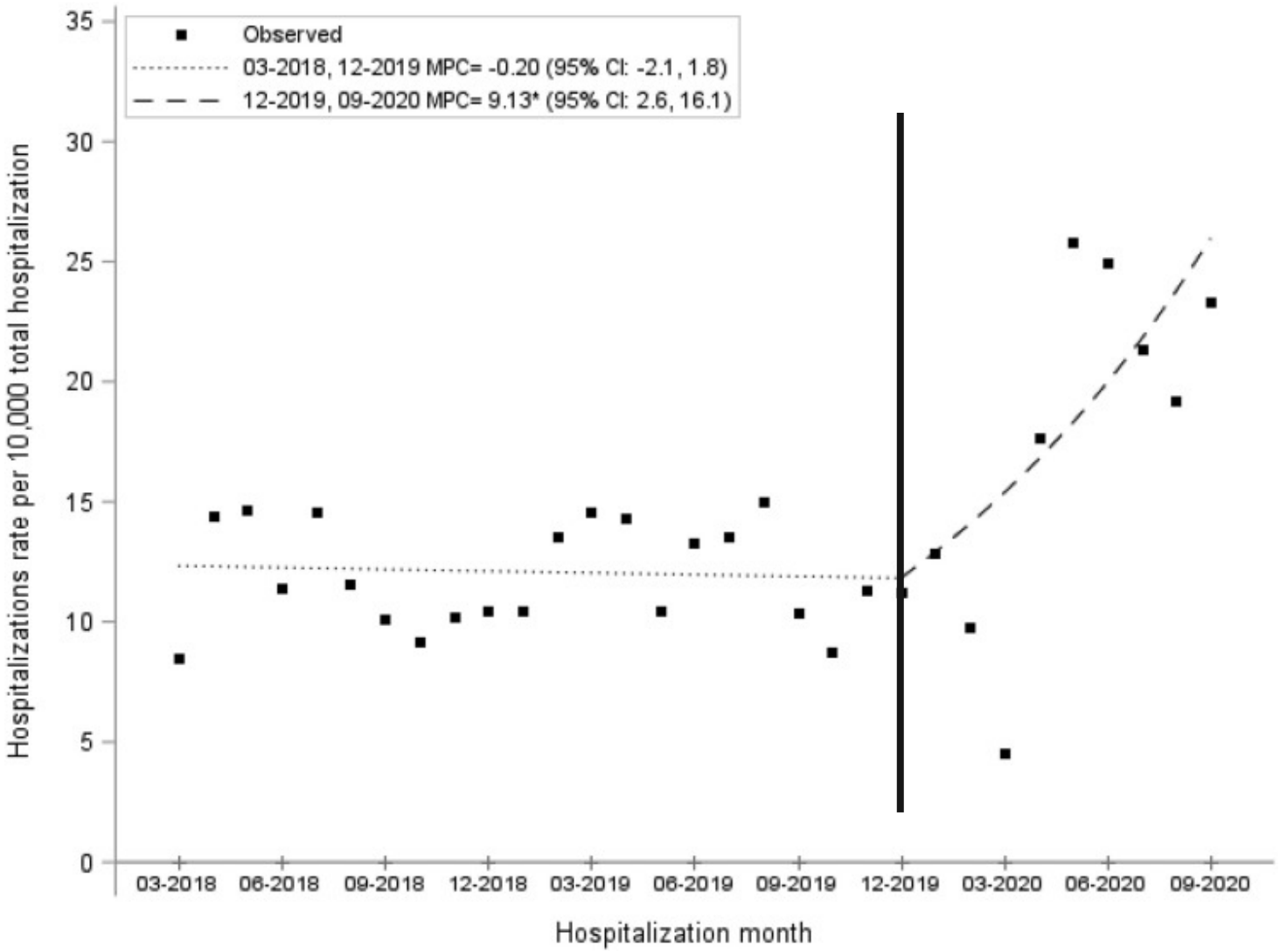


Alcohol sales increased by 5.5% per month during COVID-19

MacKillop et al. JAMA Open 2021

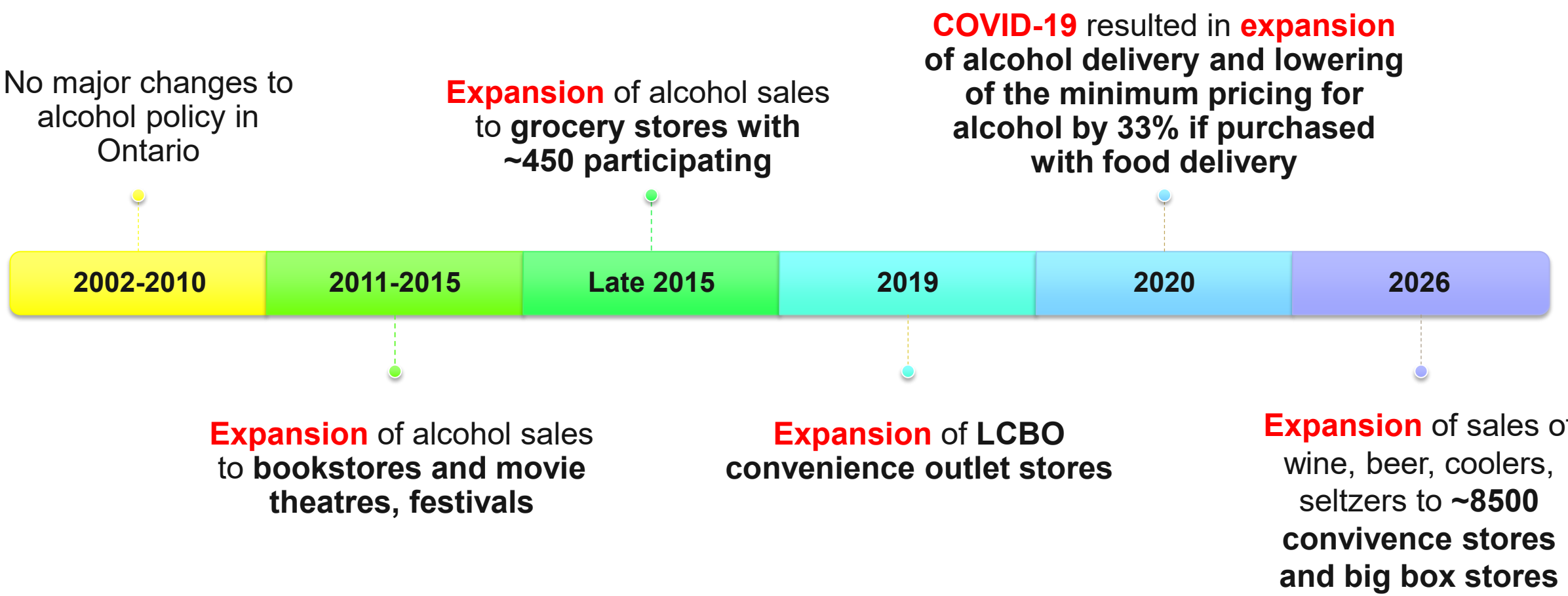
During the early COVID-19 pandemic, **hospitalizations for alcohol-associated hepatitis increased in Alberta by 10% per month**

More often among **younger aged** individuals and those **living rurally**



Shaheen A et al. Clin Gastro Hep 2021

Increasing availability of alcohol in Ontario



STUDY OBJECTIVES

1) To define the contemporary epidemiology and demographics of AYAs with AH from a diverse population during changes to governmental alcohol policy and the COVID-19 pandemic
2) To define the association between sex and long-term mortality and development of liver-related complications among AYAs surviving their first presentation of AH

STUDY DESIGN, DATABASES and COHORT

- Retrospective population-based cohort study from Ontario, Canada (population ~14 million, 20% immigrant/refugees)
- AYAs with first presentation of AH (emergency department [ED] or inpatient) from 2002 – 2021 were identified and followed to 2022
- AH – defined based on ICD-10 code K70.1 as **primary diagnosis**
  - Positive predictive value 90% (95% CI 78-96) Ornloft et al 2014
- Exclusions
  - History of cirrhosis or decompensation, liver transplant, lack of unique identifier

EXPOSURE AND OUTCOMES

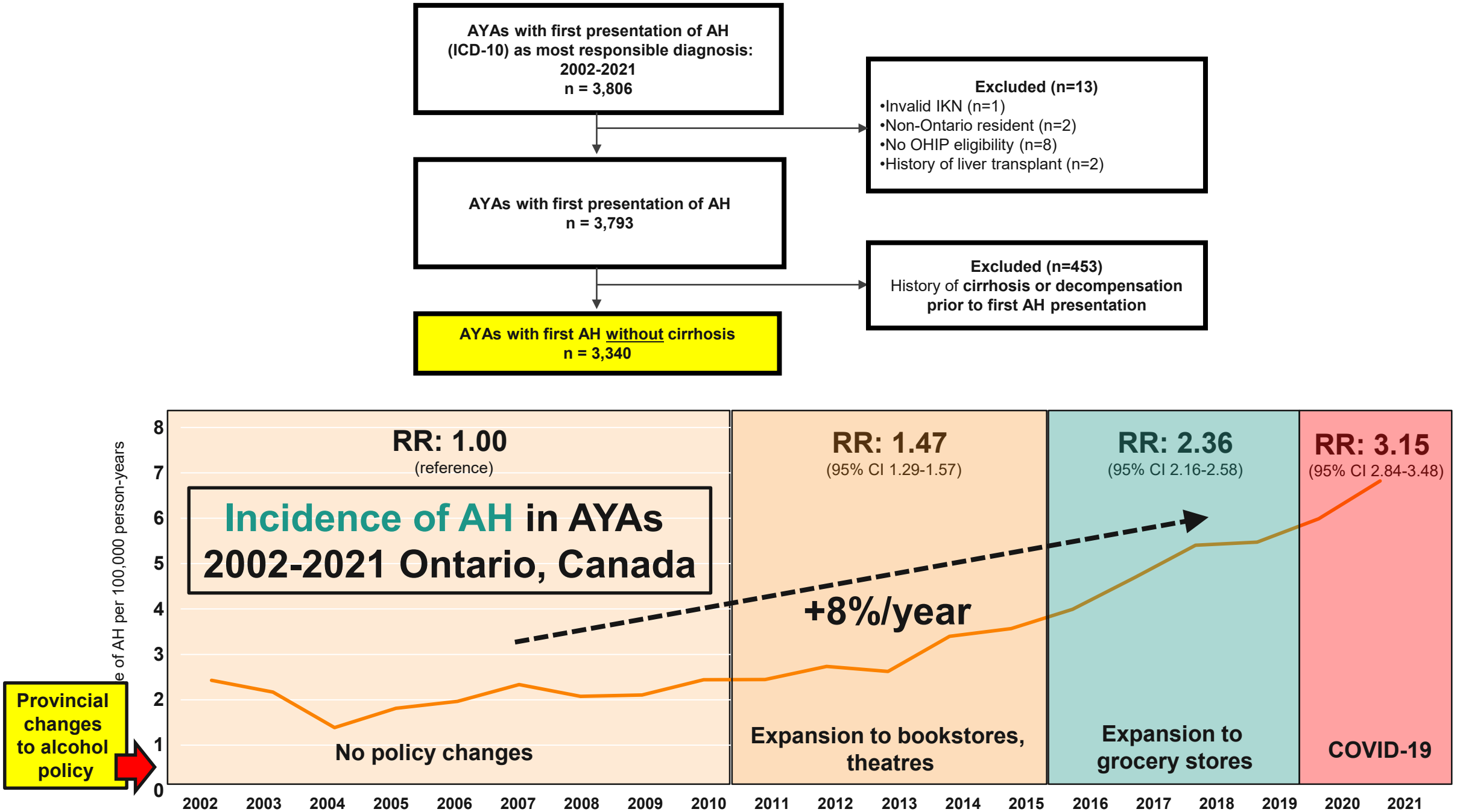
- **Sex (♀ female vs.♂male)**
  - From the Registered Persons Database (RPDB)
- **Overall mortality**
  - From the RPDB updated to **2022**
- **Cause-specific mortality**
  - From the Ontario Registers General Database updated to **2018**
- **Cirrhosis +/- decompensation**
  - Based on validated algorithms in ICES data
- **Liver transplant (LT)**
  - Deceased and live donor from billing codes and Tx database

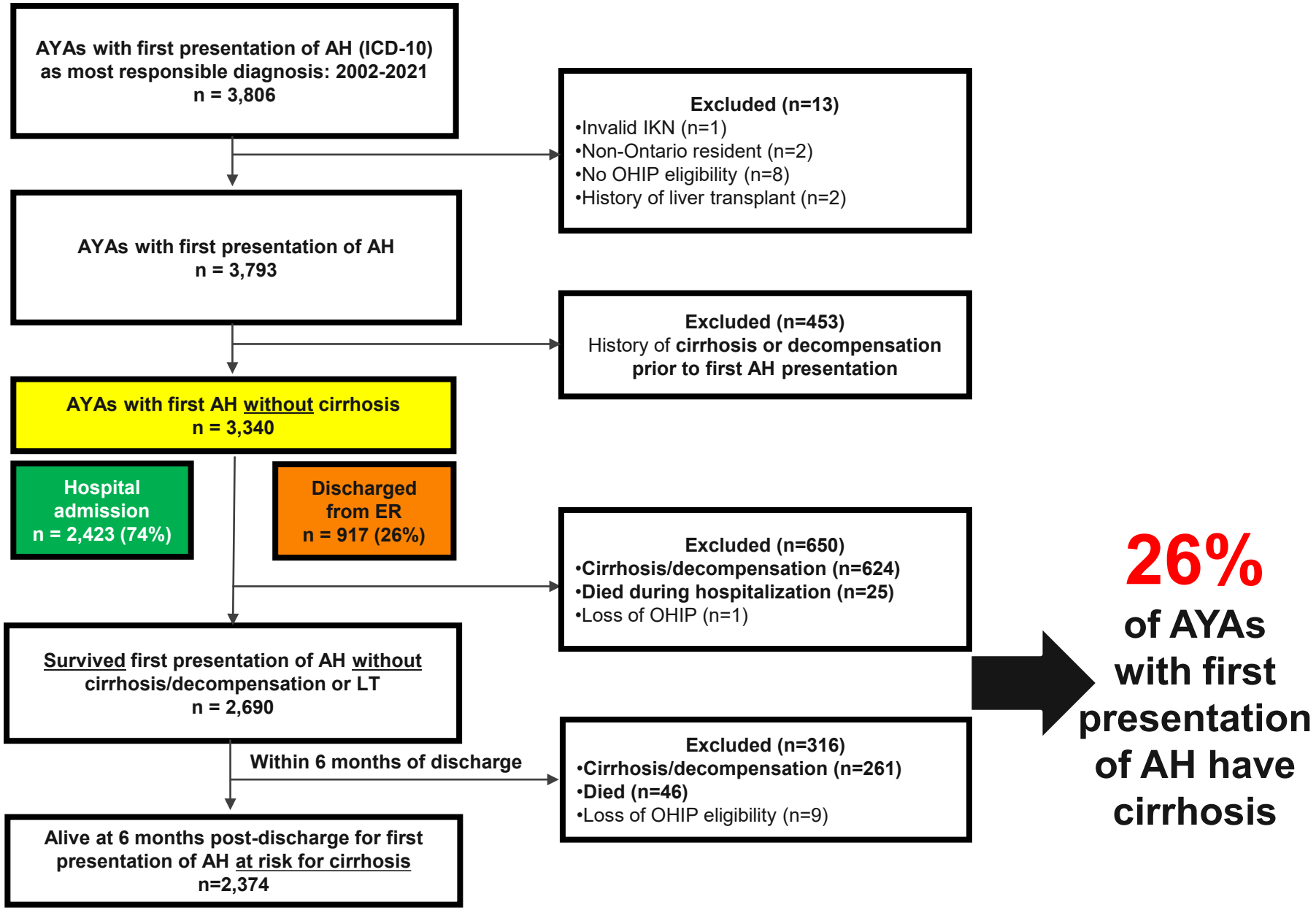
DEMOGRAPHICS AND SOCIAL DETERMINANTS OF HEALTH

- **Co-morbidity**
  - Elixhauser co-morbidity index
- **History of healthcare encounters 2-year prior to index**
  - Alcohol, substance use, mental health
- **Rural vs. urban residence**
  - Based on inhabitants +/- 10,000
- **Immigrant or refugee status**
  - Since 1985 using Canadian Immigration and Citizenship (CIC) database
- **Neighborhood-level Social Determinants of Health Quintiles**
  - Income, Ethnic Diversity, Housing Instability

STATISTICAL APPROACH

- **Incidence of AH in AYAs** calculated and compared over the study period using Poisson regression and rate ratios (RR)
- Multivariate competing risks regression to examine the association between **female sex** and:
  - **Overall mortality** (competing event: LT)
  - **Cirrhosis +/- decompensation** (competing events: death + LT)


AYAs with first presentation of AH (ICD-10) as most responsible diagnosis: 2002-2021 n = 3,806
Excluded (n=13)
•Invalid IKN (n=1)
•Non-Ontario resident (n=2)
•No OHIP eligibility (n=8)
•History of liver transplant (n=2)
AYAs with first presentation of AH n = 3,793
Excluded (n=453)
History of cirrhosis or decompensation prior to first AH presentation
AYAs with first AH without cirrhosis n = 3,340
Incidence of AH in AYAs 2002-2021 Ontario, Canada
RR: 1.00
(reference)
RR: 1.47
(95% CI 1.29-1.57)
RR: 2.36
(95% CI 2.16-2.58)
RR: 3.15
(95% CI 2.84-3.48)
+8%/year
No policy changes
Expansion to bookstores, theatres
Expansion to grocery stores
COVID-19
Provincial changes to alcohol policy
e of AH per 100,000 person-years
0
1
2
3
4
5
6
7
8
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020
2021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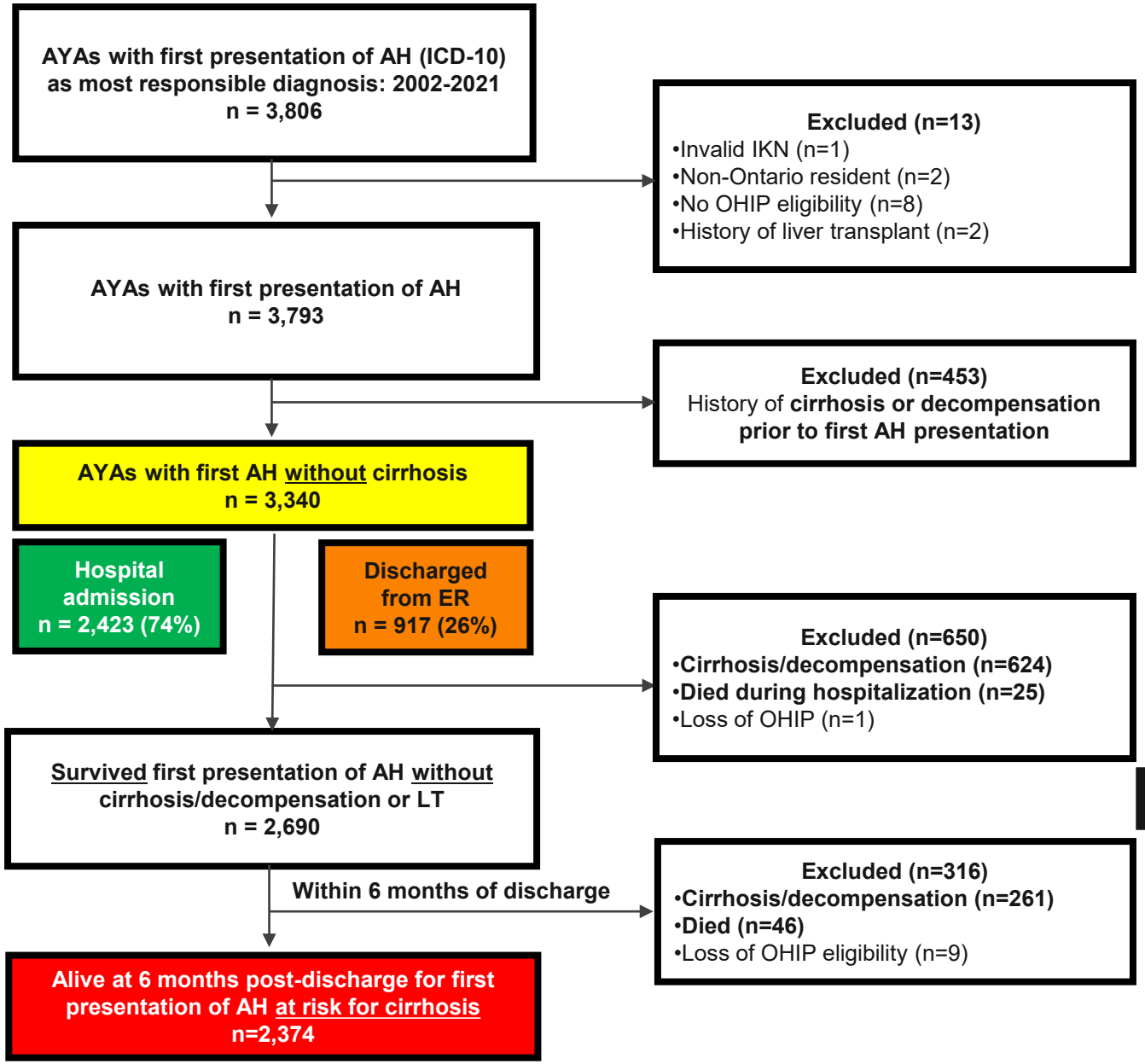
Hospital admission
n = 2,423 (74%)
Discharged from ER
n = 917 (26%)
Excluded (n=650)
•Cirrhosis/decompensation (n=624)
•Died during hospitalization (n=25)
•Loss of OHIP (n=1)
Survived first presentation of AH without cirrhosis/decompensation or LT
n = 2,690
Within 6 months of discharge
Excluded (n=316)
•Cirrhosis/decompensation (n=261)
•Died (n=46)
•Loss of OHIP eligibility (n=9)
Alive at 6 months post-discharge for first presentation of AH at risk for cirrhosis
n=2,374
26%
of AYAs with first presentation of AH have cirrhosis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OUTCOMES

MORTALITY

CIRRHOSIS +/- DECOMPENSATION

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of AYAs with first presentation of AH have cirrhosis

DEMOGRAPHICS OF THE OVERALL COHORT

n = 3,340

♀ **Female**
36%
n = 1,190

♂ **Male**
64%
n = 2,150

Age at presentation: 33 years
(IQR: 28-36, range: **14**-39)

Majority had <u>minimal</u> underlying co-morbidities
Elixhauser Co-morbidity Index 0-2: **92%**

Within <u>2-years</u> before AH presentation

- ED/inpatient stay for alcohol: **71%**
- History of mental illness: **57%**
- History of substance abuse: **34%**

<u>Social Determinants of Health</u>

Rural residence: 18%
(**22%** ♀ **vs.** 15% ♂)

Lowest Income quintile: 32%
(**37%** ♀ **vs.** 30% ♂)

Recent immigrant or refugee: 13%
(7% ♀ **vs. 16%** ♂)

Highest Ethnic Diversity quintile: 23%
(17% ♀ **vs. 26%** ♂)

Highest Housing Instability quintile: **30%**
(31% ♀ **vs.** 30% ♂)

Overall mortality

OVERALL MORTALITY

AYAs with first presentation AH without cirrhosis

n = 3,340

Median Follow-up

5 years

IQR 2-8 years

25%

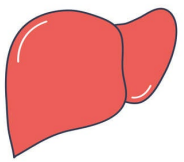
n = 844

Females: 25%

Males: 25%

Competing event

Liver Transplant



<1%

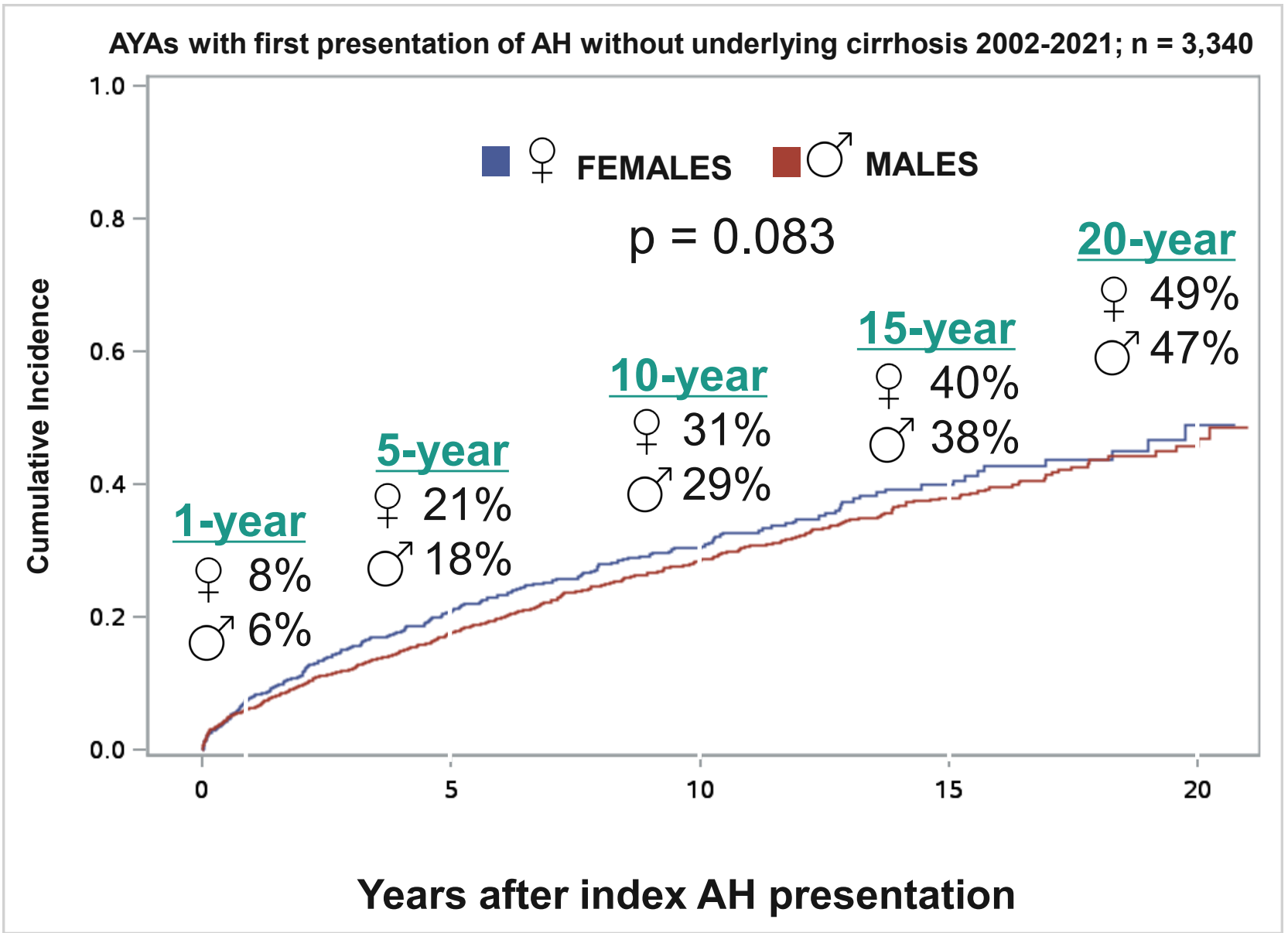
n = 23

Females: 0.1%-0.3%**

Males: **0.9%-1.1%****

**Ranges given due to need to suppress small cells

OVERALL MORTALITY



Adjusted* Competing Risks Analysis for Factors Associated with OVERALL MORTALITY

Female Sex
sHR 1.19 (0.95-1.27)

Age (per year)
sHR 1.03 (1.02-1.05)

Hospitalization at index
sHR 1.40 (1.19-1.65)

Cirrhosis or decompensation at index
sHR 1.75 (1.48-2.07)

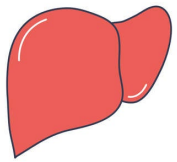
Rural residence
sHR 1.24 (1.03-1.49)

Elixhauser Co-morbidity Index 3+
sHR 1.99 (1.62-2.44)

*Also adjusted for income quintile and immigration status

CAUSES OF DEATH*

*available to the end of 2018 (n=590)



#1 LIVER-RELATED

25% (n=149)

28% ♀ vs. 23% ♂

#2 EXTERNAL

(ie. injury, accident, poisoning, suicide)

19% (n=113)

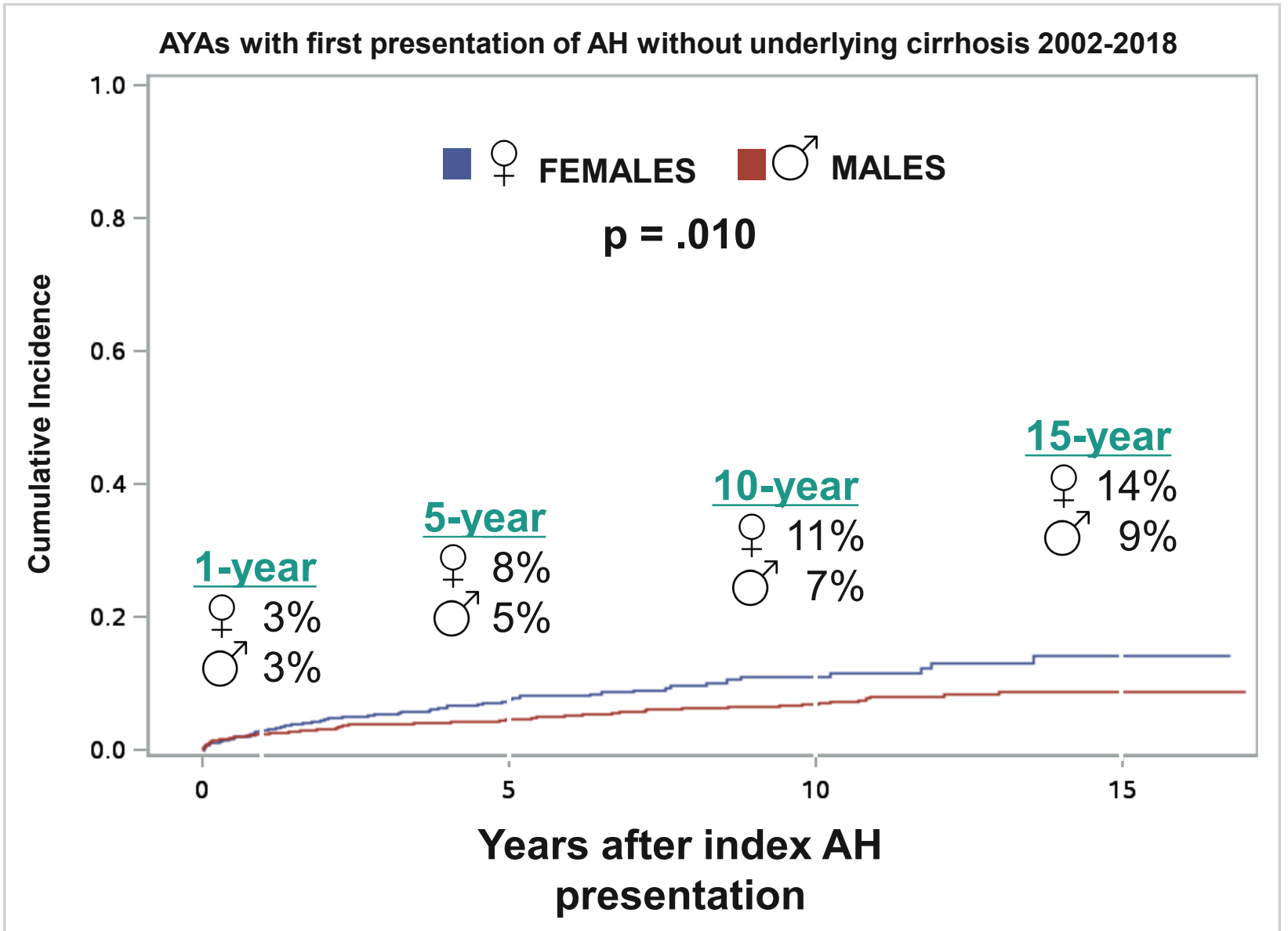
17% ♀ vs. **21%** ♂

#3 MENTAL HEALTH

13% (n=77)

14% ♀ vs. 13% ♂

LIVER-RELATED MORTALITY



Cirrhosis
+/- decompensation

CIRRHOSIS +/- DECOMPENSATION

AYAs who survived first presentation AH without cirrhosis or decompensation and alive at 6 months

n = 2,374

Median Follow-up

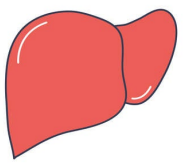
4 years

IQR 2-9 years

Competing events

DEATH

LT



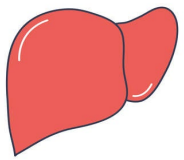
31%

n = 747
median 24 months (IQR 9-50)
30% decompensated

Females: **37%**
Males: 28%

20%

n = 466
Females: 18%
Males: 21%

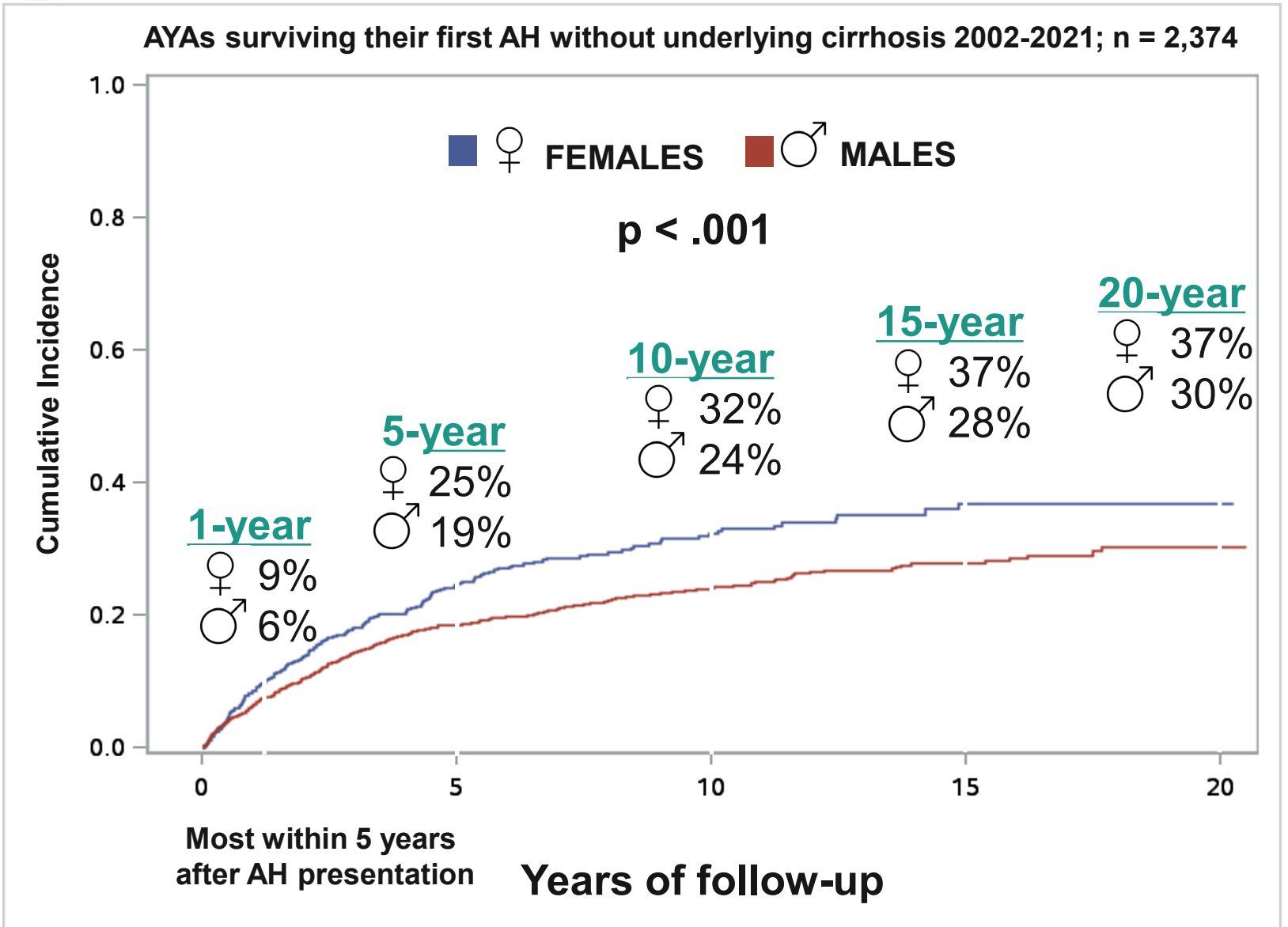


<1%

n = <6*

**Unable to report cells <6 for re-identification purposes

CIRRHOSIS +/- DECOMPENSATION



Adjusted* Competing Risks Analysis for Factors Associated with CIRRHOSIS

Female Sex
sHR 1.47 (1.23-1.76)

Age (per year)
sHR 1.04 (1.03-1.06)

Urban residence
sHR 1.29 (1.02-1.65)

Elixhauser Index 3+
sHR 1.36 (1.01-1.82)

*Also adjusted for income quintile, immigration status, and **type of AH presentation (ED vs. hospital)**

SUMMARY OF RESULTS

- The incidence of AH is rising among AYAs with death occurring in 25% after a median of 5-years of follow-up
- The young AH population is vulnerable in their SDOH and sex differences in underlying sociodemographic factors are present
- Although overall mortality after a first presentation of AH is similar between sexes – females have higher rates of liver-related mortality than males
- Female sex is associated with a ~50% higher risk of cirrhosis and decompensation among those surviving their first AH presentation

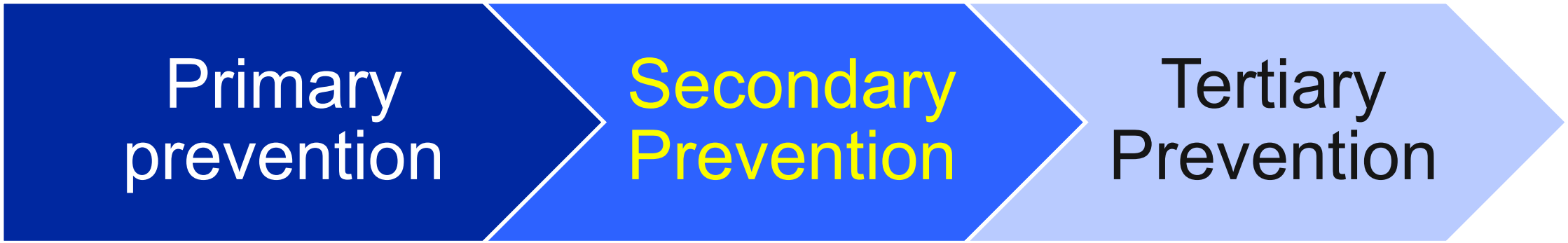
IMPLICATIONS

- This should be considered a public health crisis
- Unless efforts for early identification of AUD and ALD in AYAs is prioritized, there will be considerable ongoing premature mortality in this young vulnerable population
- Efforts to reverse these trends will require a sex-specific approach

ALCOHOL-ASSOCIATED LIVER DISEASE (ALD)

SECTION 5:
HEALTH POLICY IMPLICATIONS

Public Health Approach to Impact Alcohol Associated Harms to Adolescents and Young Adults

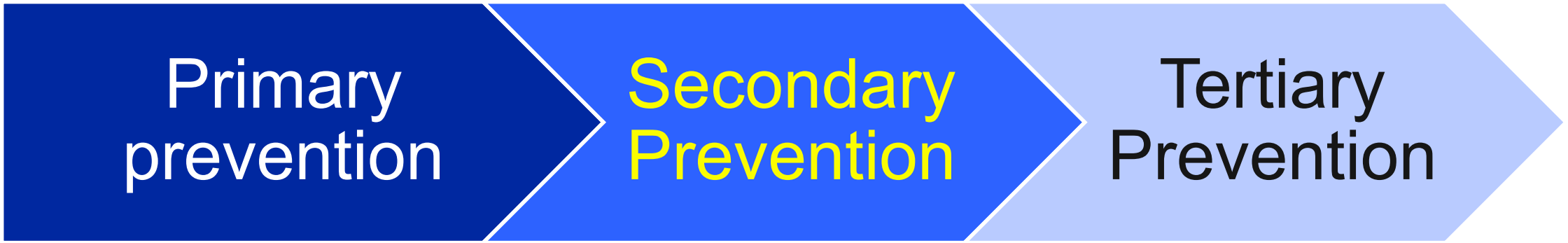


Limit the exposure of alcohol to our population

Early identification and treatment of heavy drinking, AUD, ALD

Treatment of end-stage liver disease from alcohol

Public Health Approach to Impact Alcohol Associated Harms to Adolescents and Young Adults



- Governmental Policy
- Marketing/Labelling
- Public education
- Access to mental health services
- Social determinants of health

- Screening for high-risk alcohol use, AUD and ALD
- Access to AUD treatment
- Hepatology + Addictions clinics

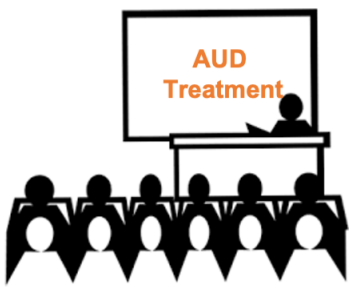
- Equitable access to liver transplant
- Relapse prevention services
- AUD treatment trials in advanced liver disease

Addressing Disparities in AUD Treatment in Individuals with ALD

PROVIDER

Systematic use of AUD screening tools in clinic

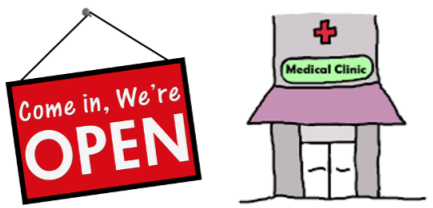
Education of hepatology providers in AUD treatment



HOSPITAL

Provide access to language and transportation services for AUD behavioral therapy

Timely and equitable access to addiction medicine, social work and psychiatry



RESEARCH

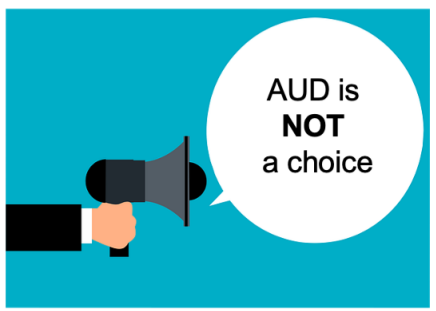
Design high quality studies to evaluate AUD treatment in those with ALD

Prioritize inclusion of study participants diverse in age, sex, race, gender, and culture

SOCIETY

Reduce the stigma associated with AUD and ALD

Public education on AUD and outcomes of AUD treatment



Sedaros and Flemming, CLD, 2023

Conclusions

- Alcohol associated liver disease is a significant health threat especially to our adolescents and young adults
- AYAs with the most severe form of ALD are at high risk of dying or developing cirrhosis within 5 years of their first presentation
- Governmental policy change and public health interventions should be strongly considered to reverse these trends for future generations

THANK YOU FOR YOUR ATTENTION

Special Thanks:
Maya Djerboua