Birth Cohort Effects on Cirrhosis Incidence: A Population-based Study

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What Does My Liver Do?

Over 500 different functions!
- Produces bile for digestion
- Metabolizes all drugs and toxins
- Energy storage (glycogen)
- Cholesterol regulation
- Blood clotting
- Immune system
- Produces sex hormones, thyroid hormones
Liver Cirrhosis

- End-stage scarring of the liver from many different causes

- Majority of causes related to environmental and lifestyle exposures

- Not just a disease related to alcohol use
Cirrhosis: A final common pathway

- Normal Liver
  - No Fibrosis
  - Insult and inflammation

- Cirrhosis
  - End-stage fibrosis
  - Repair, regeneration, scar

10-20 years
Liver Cirrhosis

1) Non-alcoholic fatty liver disease (NAFLD)
   • Affects almost 1/3 of the general population
   • Up to 10% of children, 80% of obese children

2) Hepatitis C
   • Most common in those born 1945-1965

3) Alcohol-related disease
   • Majority not in those considered to be ‘alcoholics’
Liver Cirrhosis

- Because NAFLD is so common, the number of people with cirrhosis is thought to be increasing.

- No previous work has been able to describe the epidemiology of cirrhosis in the era of NAFLD.
Cirrhosis Incidence - Ontario

- Using linked databases from ICES, a cohort of ~200,000 patients with cirrhosis identified from 1997-2015
- 62% male, median age 57 years (IQR 46-67)
- Stratified based on birth cohort
  - <1925: Greatest Generation
  - 1925-1944: Silent Generation
  - 1945-1965: Baby-boomers
  - 1966-1979: Generation X
  - >1980: Millennials

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Cirrhosis Epidemiology - Ontario

**1997**
- Prevalence: 0.37%
- Incidence: 63 (95% CI 61.9-64)

**2015**
- Prevalence: 0.92%
- Incidence: 107.9 (95% CI 106.9-108.9)

+ 71%

+ 148%

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Cirrhosis Epidemiology - Ontario

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At age 32, you are more likely to be diagnosed with cirrhosis if you are a “Gen Xer” or a “Millennial” than a “Baby-boomer”

Cirrhosis Epidemiology - Ontario

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Cirrhosis Epidemiology - Ontario

- Age-Period-Cohort modeling was used to describe the independent risk of cirrhosis based on birth year after adjustment for age and the period of diagnosis (to account for changes in fibrosis assessment)

Born in 1951

Same Age
Same access to fibrosis assessment

Born in 1990

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Risk of Cirrhosis

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Risk of Cirrhosis

25% lower
Risk of Cirrhosis

25% lower

13% lower
Risk of Cirrhosis

- 1925: 25% lower
- 1945: 13% lower
- 1951: 30% higher
- 1966: 63% higher
- 1980
- 1990

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Risk of Cirrhosis

- 1925: 25% lower
- 1945: 13% lower
- 1951: 
- 1966: 30% higher
- 1980: 63% higher
- 1990: 142% higher

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Risk of Cirrhosis - Males

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Risk of Cirrhosis - Males


19% lower

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Risk of Cirrhosis - Males

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Risk of Cirrhosis - Males

1925: 19% lower
1945: 13% lower
1951: (frame)
1966: 15% higher
1980
1990

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Risk of Cirrhosis - Males

1925: 19% lower
1945: 13% lower
1951: (No change indicated)
1966: 15% higher
1980: 37% higher
1990: (No change indicated)

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Risk of Cirrhosis - Males

1925: 19% lower
1945: 13% lower
1951: 15% higher
1966: 37% higher
1980: 112% higher
1990:

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Risk of Cirrhosis - Females


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Risk of Cirrhosis - Females

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34% lower
Risk of Cirrhosis - Females

- 1925
- 1945: 15% lower
- 1951
- 1966
- 1980
- 1990

34% lower

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Risk of Cirrhosis - Females

1925: 34% lower
1945: 15% lower
1951: 52% higher
1966
1980
1990

Flemming JA et al. Manuscript under review.
Risk of Cirrhosis - Females

Flemming JA et al. Manuscript under review.
Risk of Cirrhosis - Females

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Cause of increased incidence?

‘Generation X’ and ‘Millennial Birth Cohorts’
- All under the age of 50 at diagnosis
- ? NAFLD
  - First described in 1980
  - NAFLD most common CLD in children
- ? Increase in HCV in people who inject drugs
- ? Alcohol consumption
The ENHAnCe Study

- American Association for the Study of Liver Disease
  - Clinical, Translational, and Outcomes Research Award
- Epidemiology, Natural History and Healthcare Utilization in Young Adults with Cirrhosis

<table>
<thead>
<tr>
<th>Table 1: Cirrhosis cohort ≤ 40 years at diagnosis from 2007-2017 (N = 12,715)</th>
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</thead>
<tbody>
<tr>
<td>Age at diagnosis (mean, sd)</td>
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<tr>
<td>Male sex (n, %)</td>
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<tr>
<td>Follow-up time (mean, sd)</td>
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<tr>
<td>Death during follow-up (n, %)</td>
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<tr>
<td>Hospitalizations, total (mean)</td>
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<tr>
<td>Same-day surgery visits, total (mean)</td>
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<td>Emergency room visits, total (mean)</td>
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<tr>
<td>Outpatient visits, total (mean)</td>
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<tr>
<td>Liver transplants</td>
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<td>Total OHIP billing claims</td>
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The ENHAnCe Study

• **Aim 1**: To elucidate the etiologic causes of cirrhosis in young adults and describe changes in the incidence of etiologies over time.

• **Aim 2**: To define the natural history of cirrhosis in young adults from decompensation to liver transplantation or death.

• **Aim 3**: To quantify the healthcare utilization in young adults with cirrhosis and compare costs based on etiology of disease.
Thank You