

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

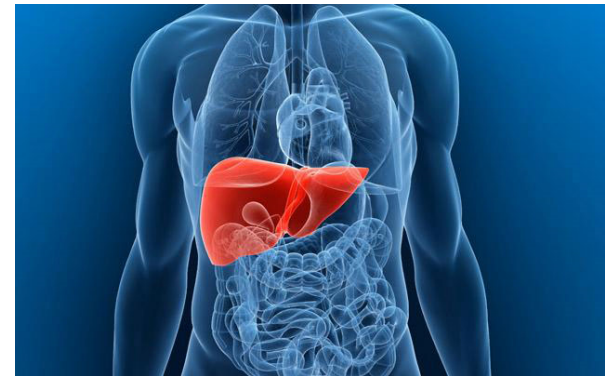
Energy storage (glycogen)

Cholesterol regulation

Blood clotting

Immune system

Produces sex hormones, thyroid hormones



Liver Cirrhosis

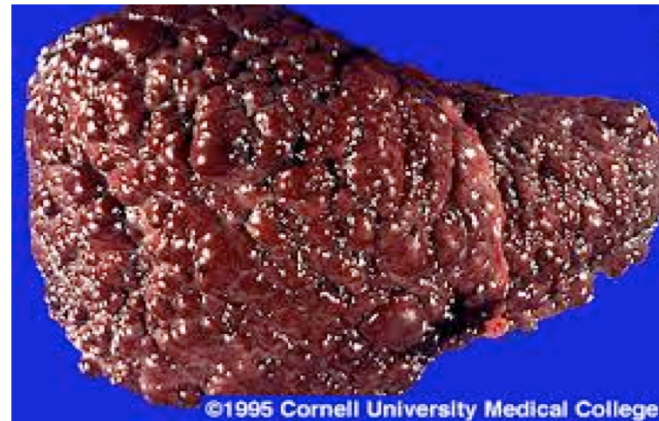
- End-stage scarring of the liver from many different causes
- Majority of causes related to environmental and lifestyle exposures
- Not just a disease related to alcohol use

Cirrhosis:

A final common pathway



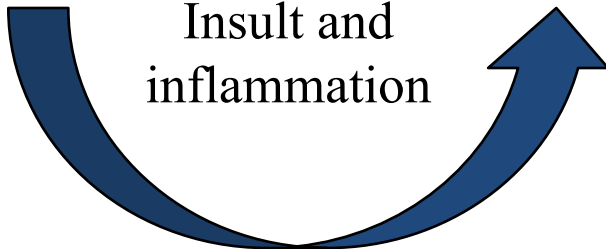
Normal Liver
No Fibrosis



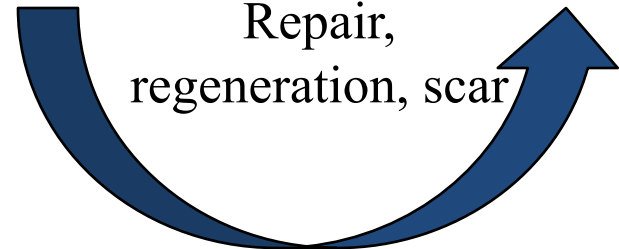
Cirrhosis
End-stage fibrosis

10-20 years

Insult and
inflammation



Repair,
regeneration, scar



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

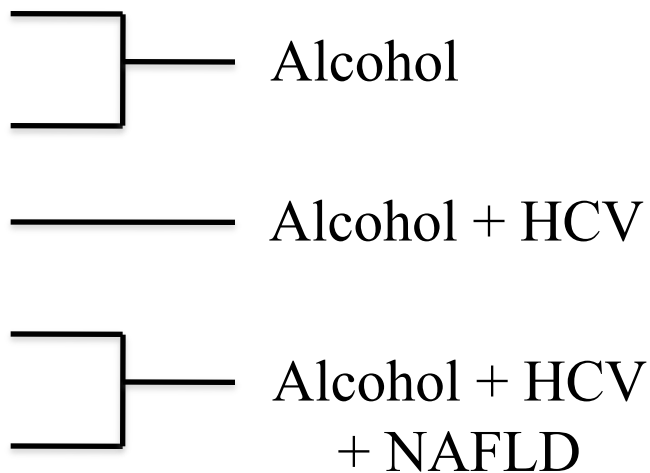
3) Alcohol-related disease

- Majority not in those considered to be ‘alcoholics’

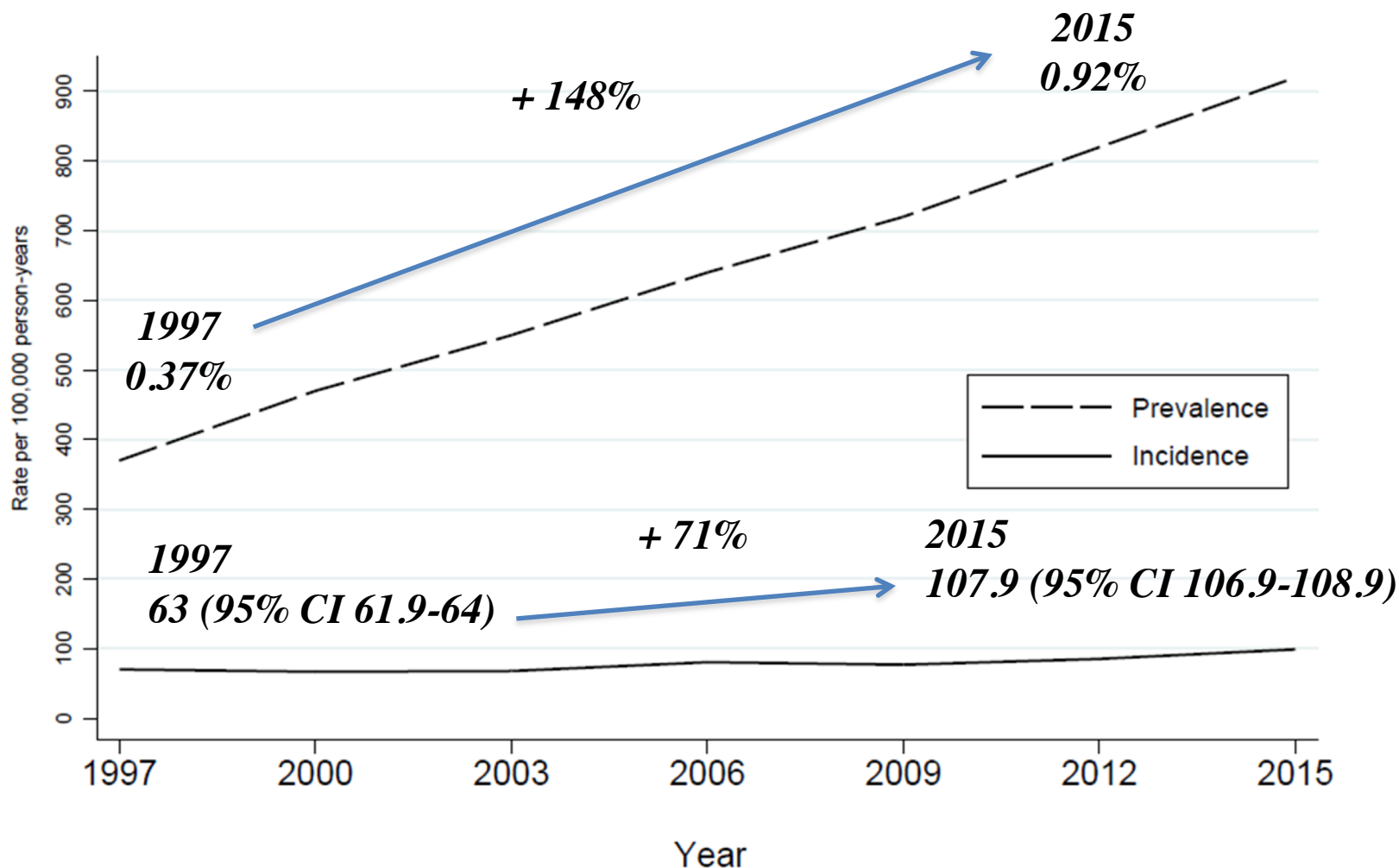
Liver Cirrhosis

- 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

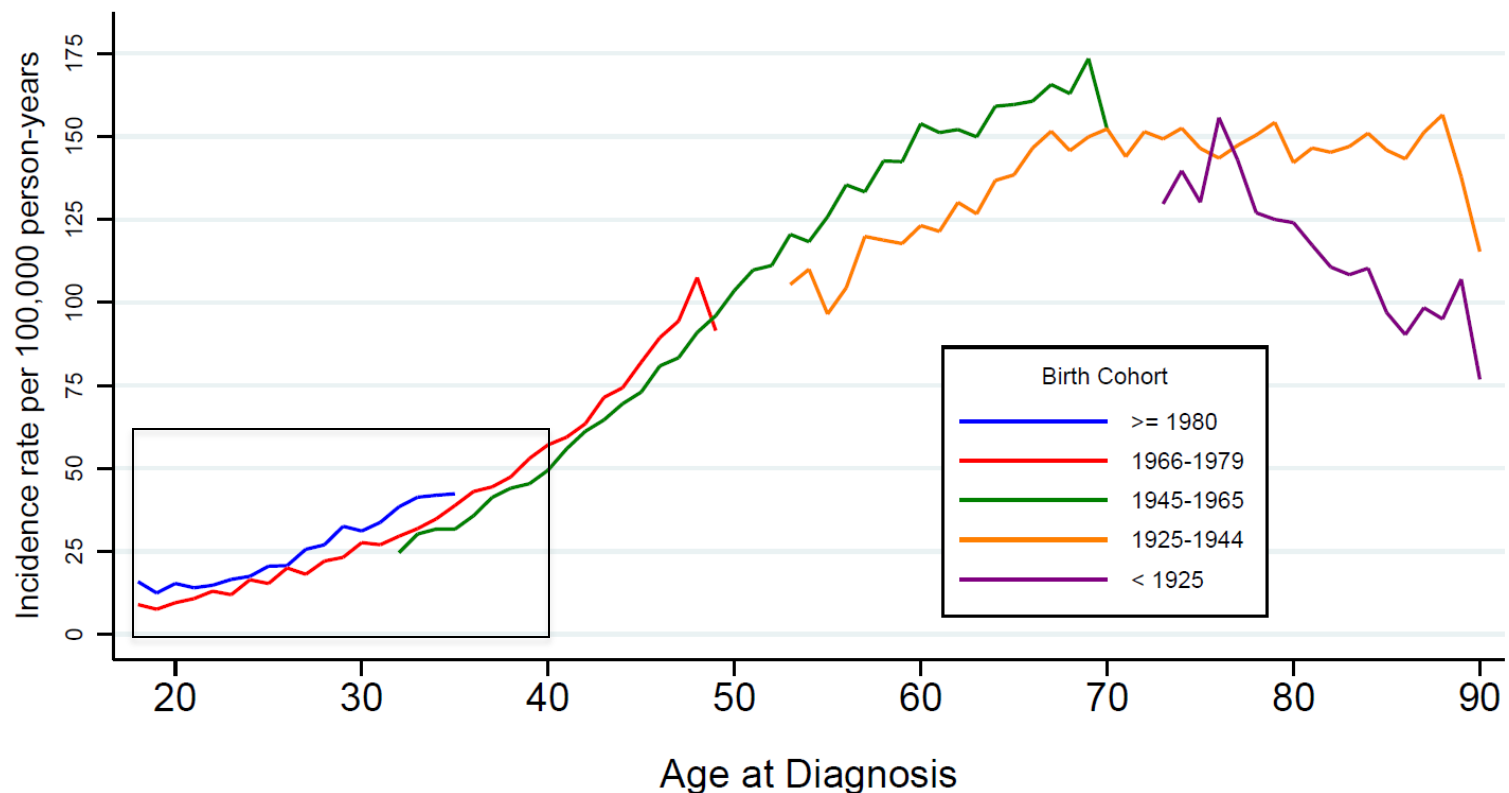
Cirrhosis Incidence - Ontario

- 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
- 
- ```
graph LR; G1["<1925: Greatest Generation"] --- E1["Alcohol"]; G2["1925-1944: Silent Generation"] --- E1; G3["1945-1965: Baby-boomers"] --- E2["Alcohol + HCV"]; G4["1966-1979: Generation X"] --- E3["Alcohol + HCV + NAFLD"]; G5[">1980: Millennials"] --- E3;
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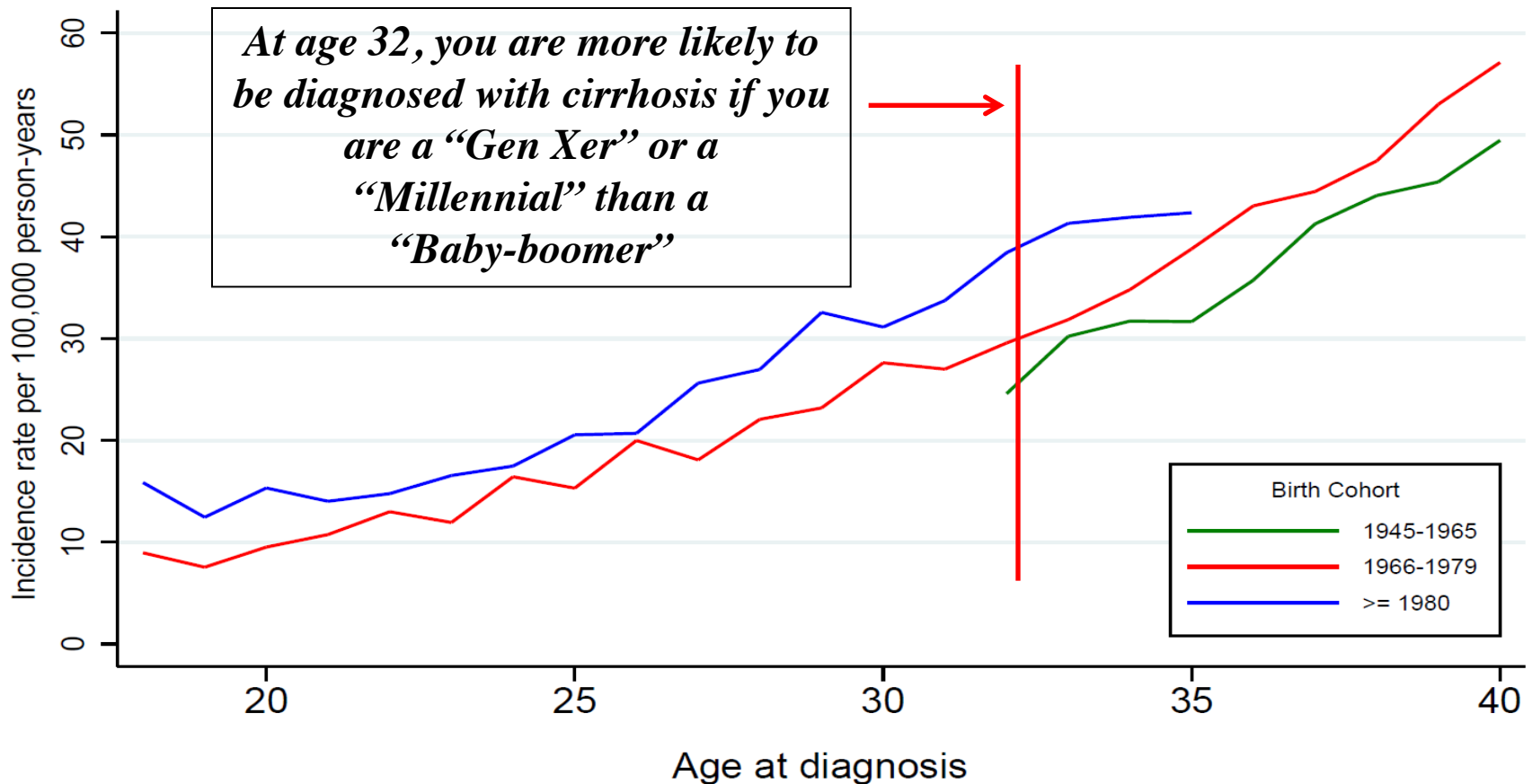
# Cirrhosis Epidemiology - Ontario



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- *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)*



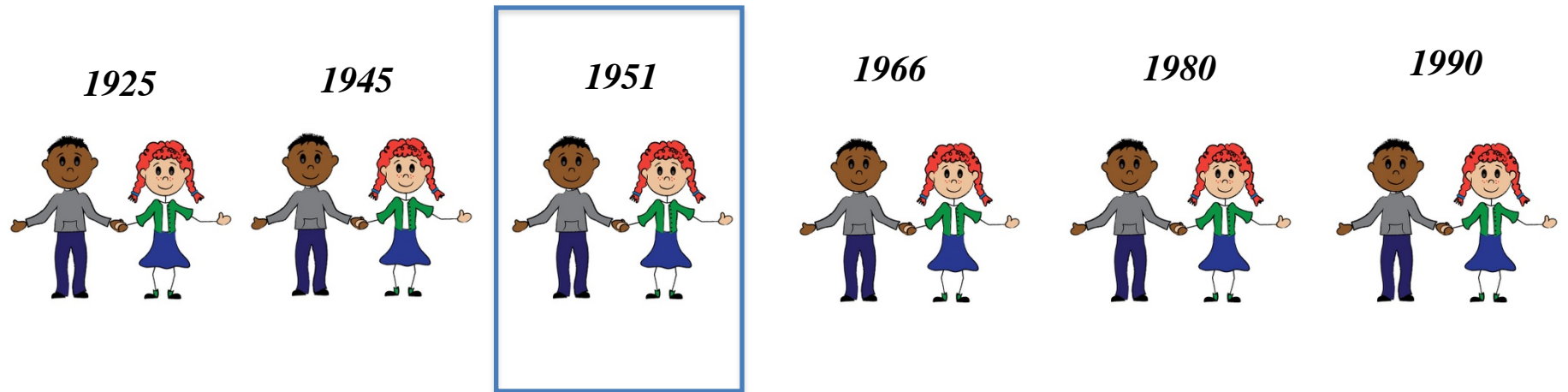
*Born in 1951*

*Same Age  
Same access to  
fibrosis assessment*



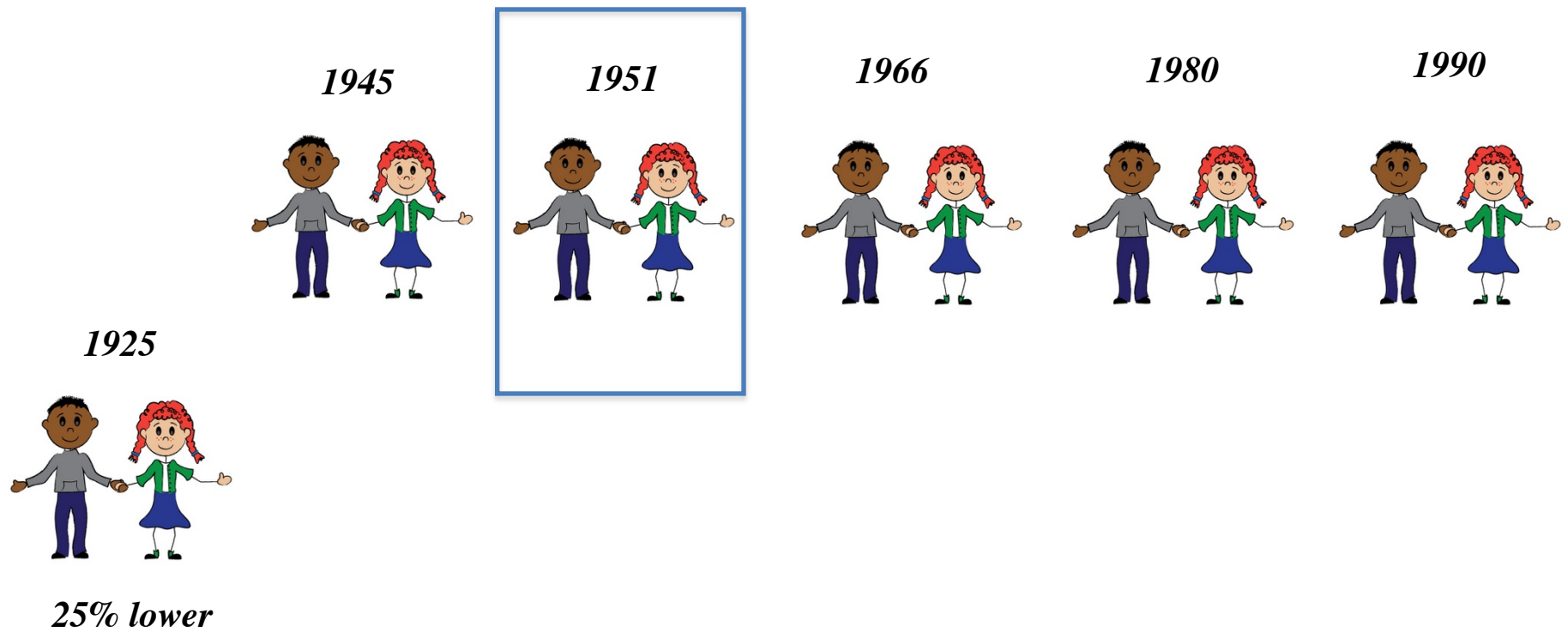
*Born in 1990*

# Risk of Cirrhosis

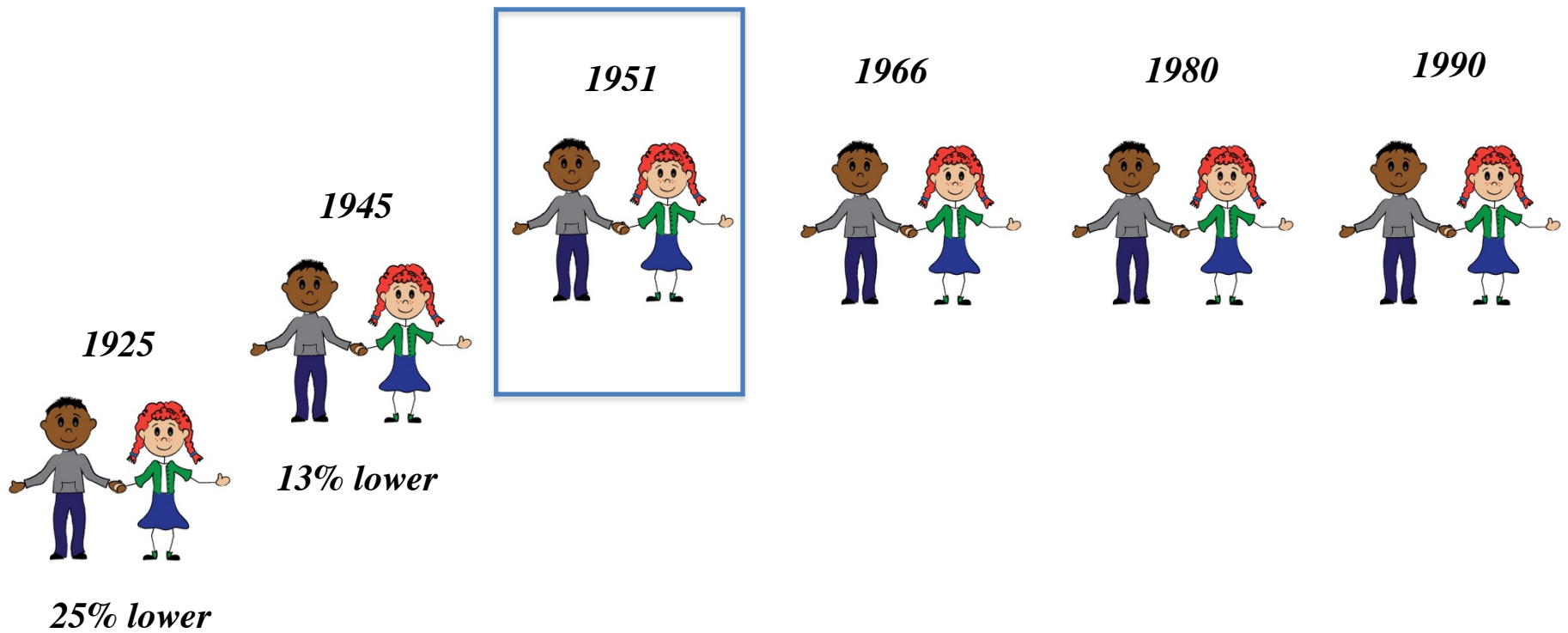




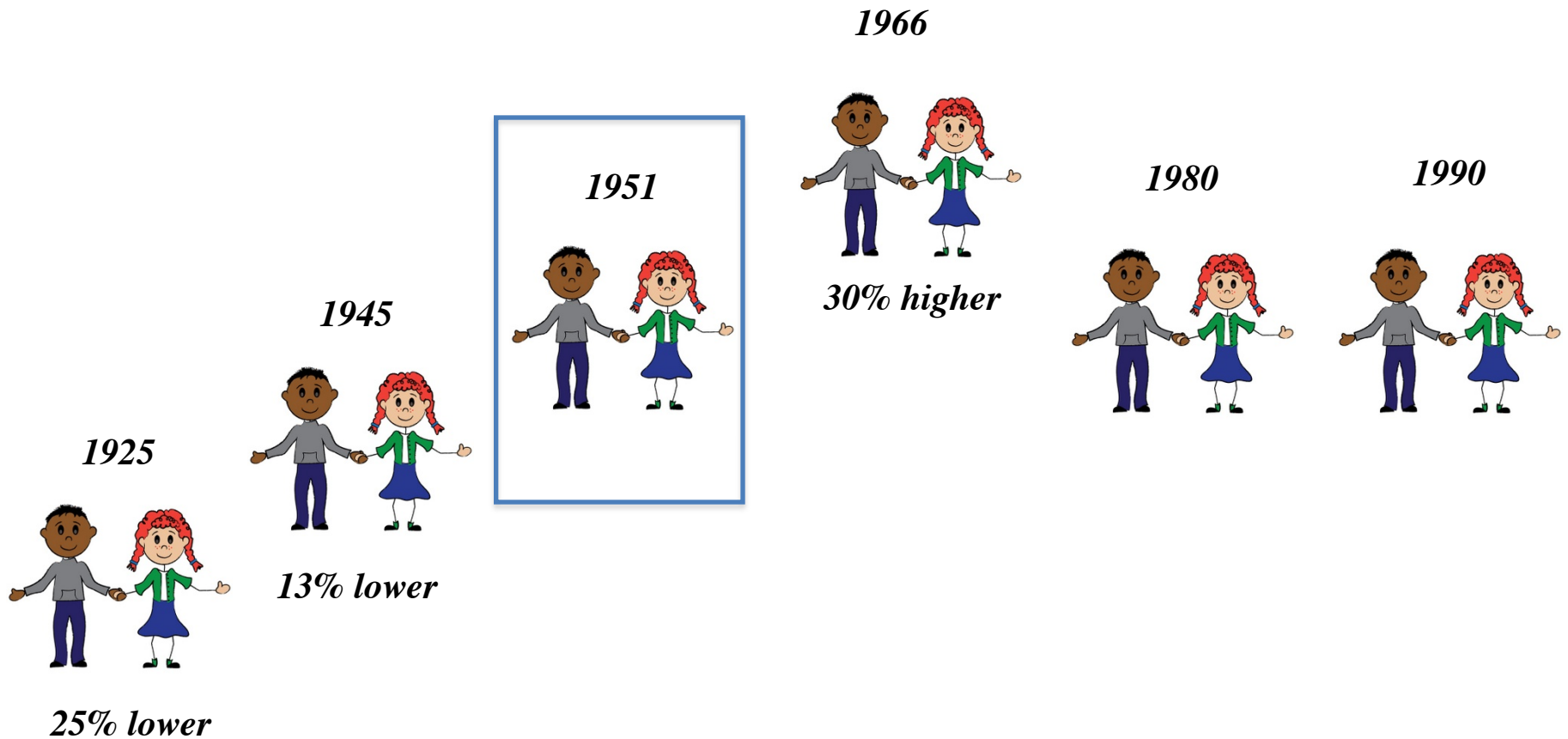
# Risk of Cirrhosis



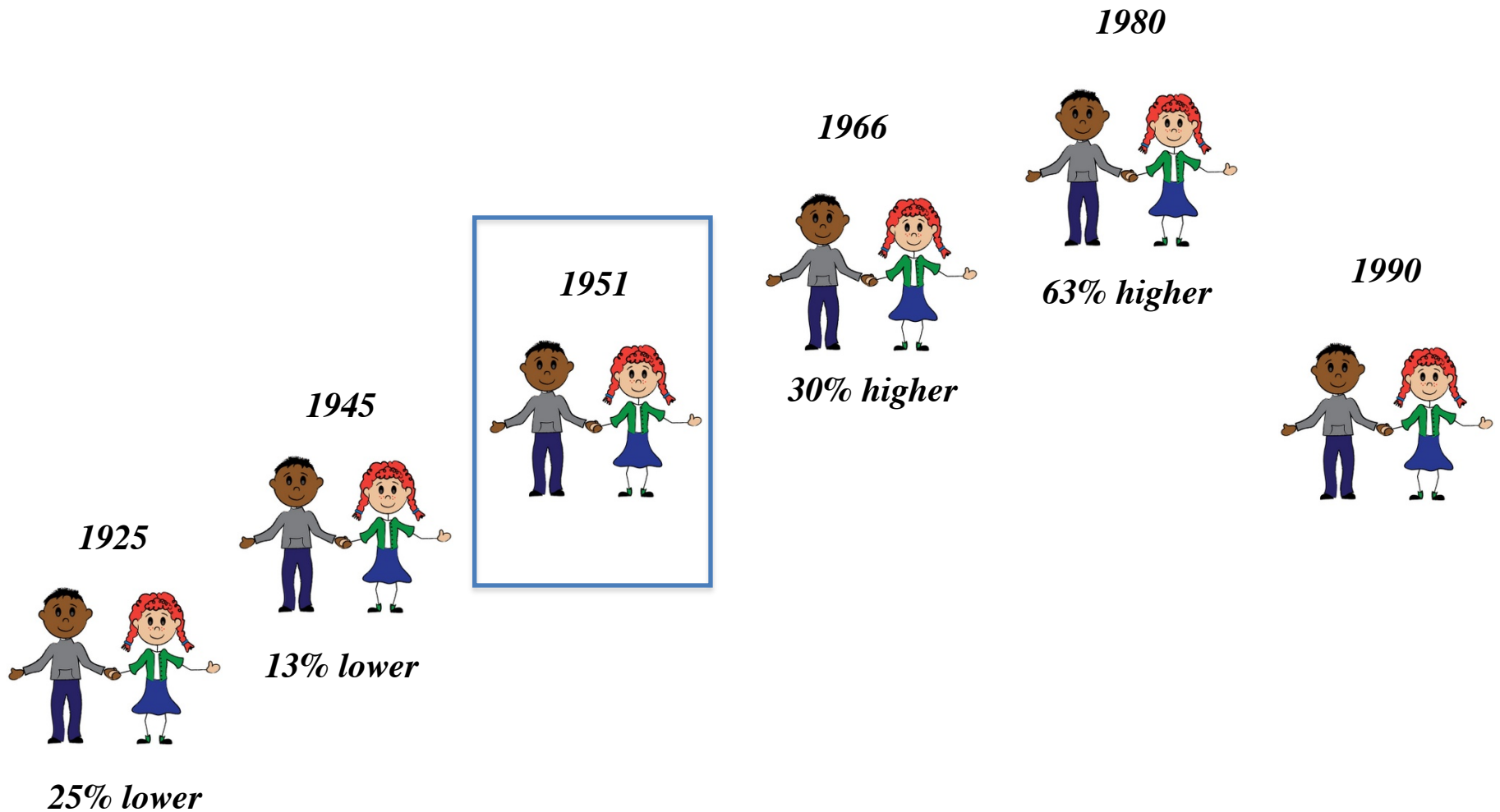
# Risk of Cirrhosis



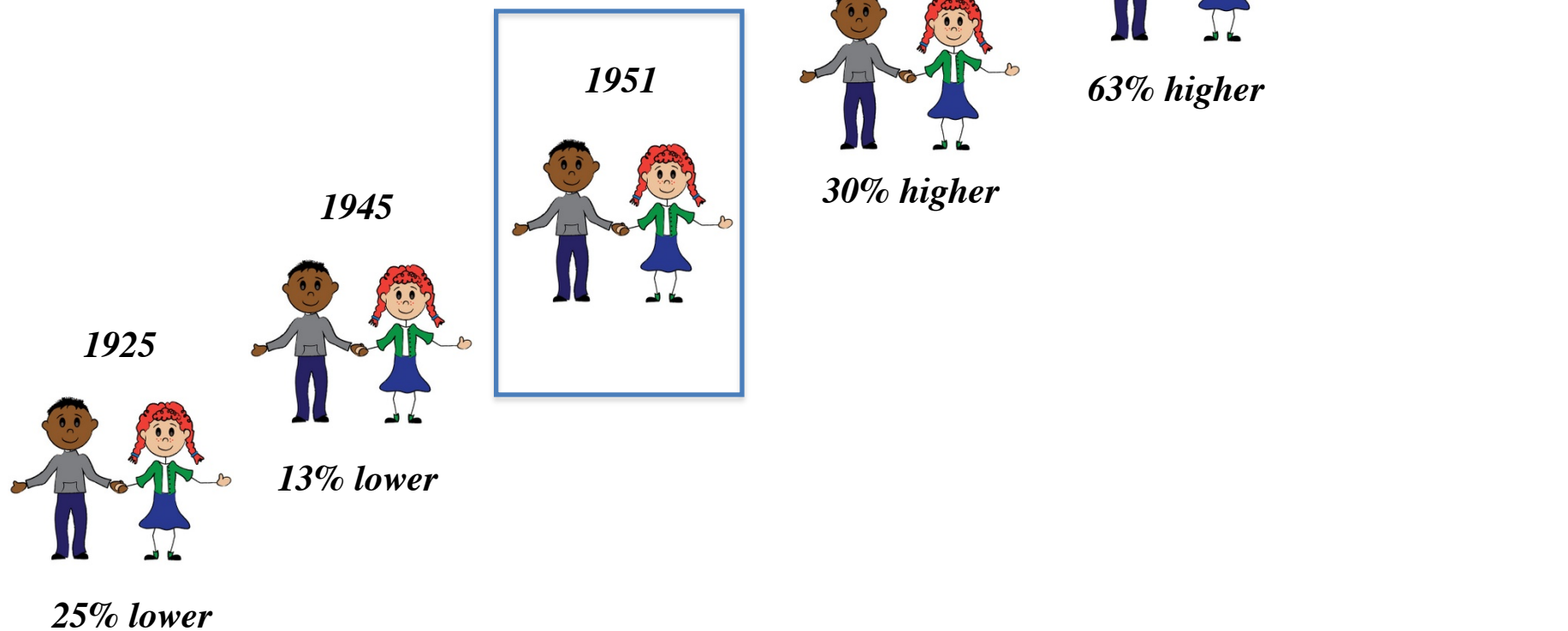
# Risk of Cirrhosis



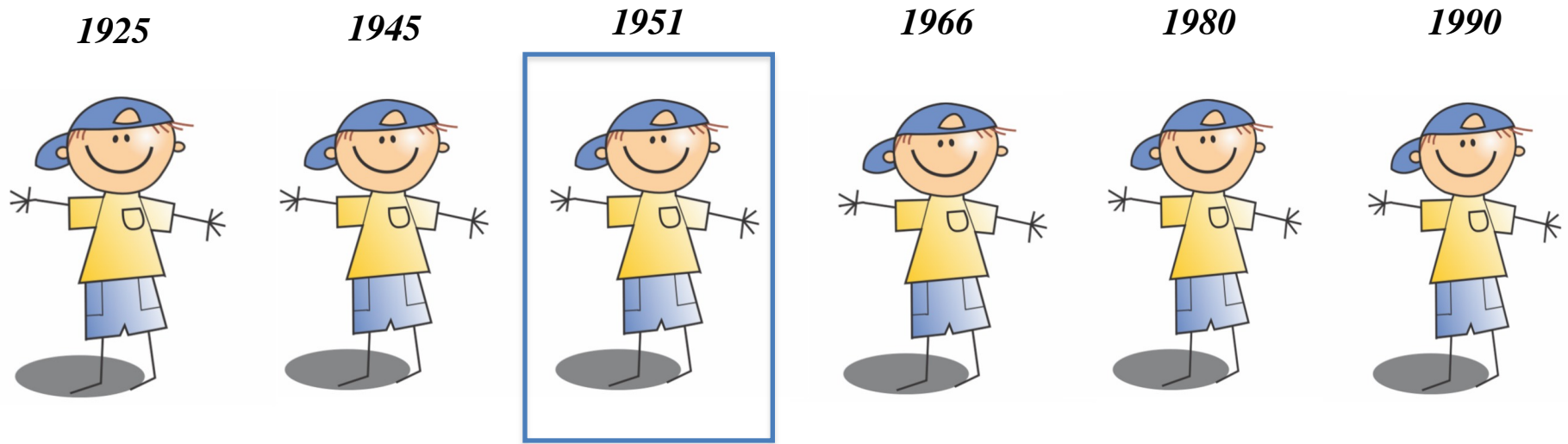
# Risk of Cirrhosis



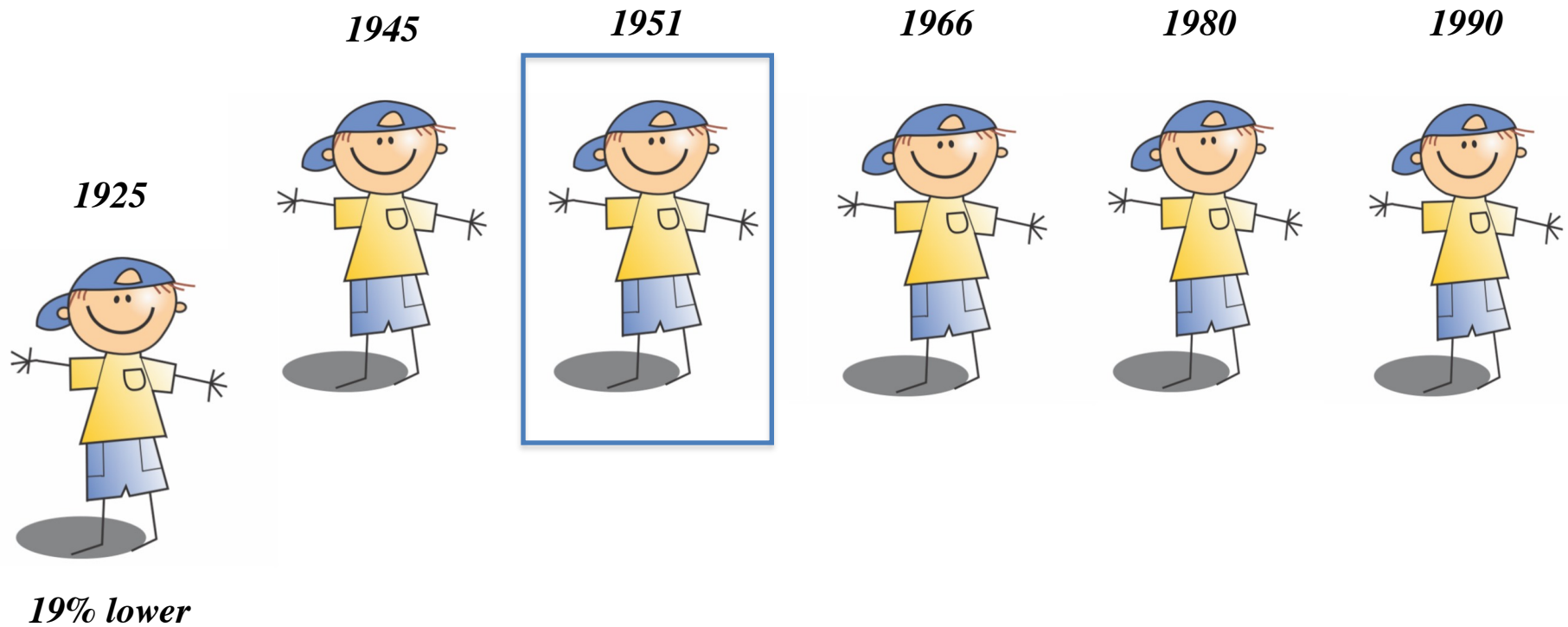
# Risk of Cirrhosis



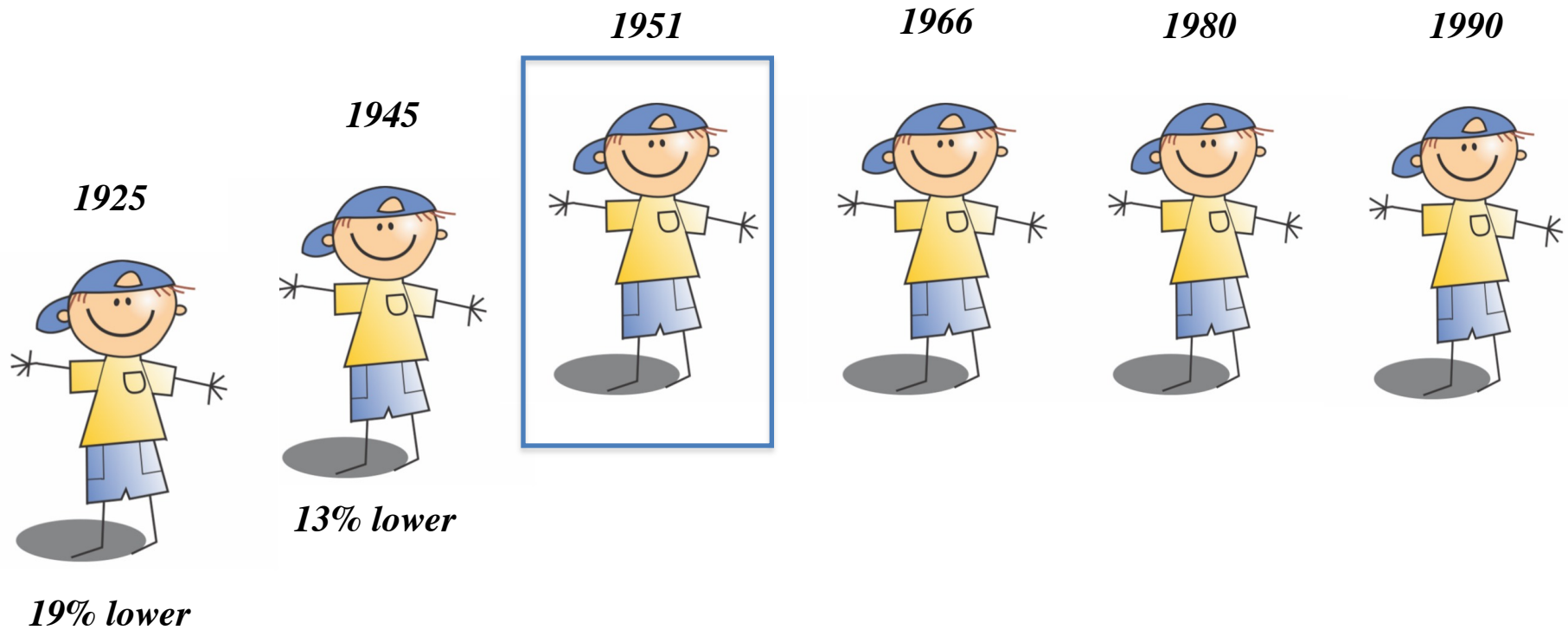
# Risk of Cirrhosis - Males



# Risk of Cirrhosis - Males

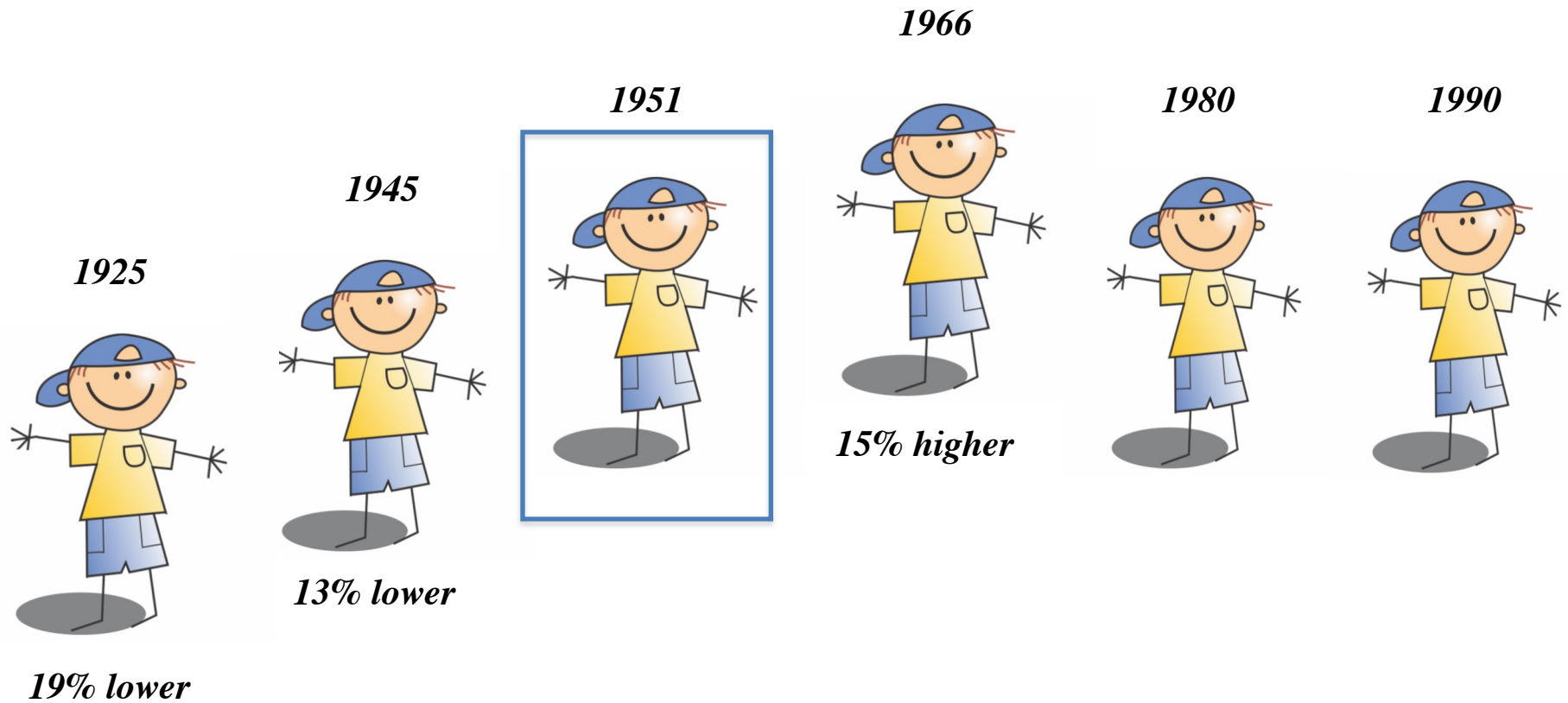


# Risk of Cirrhosis - Males

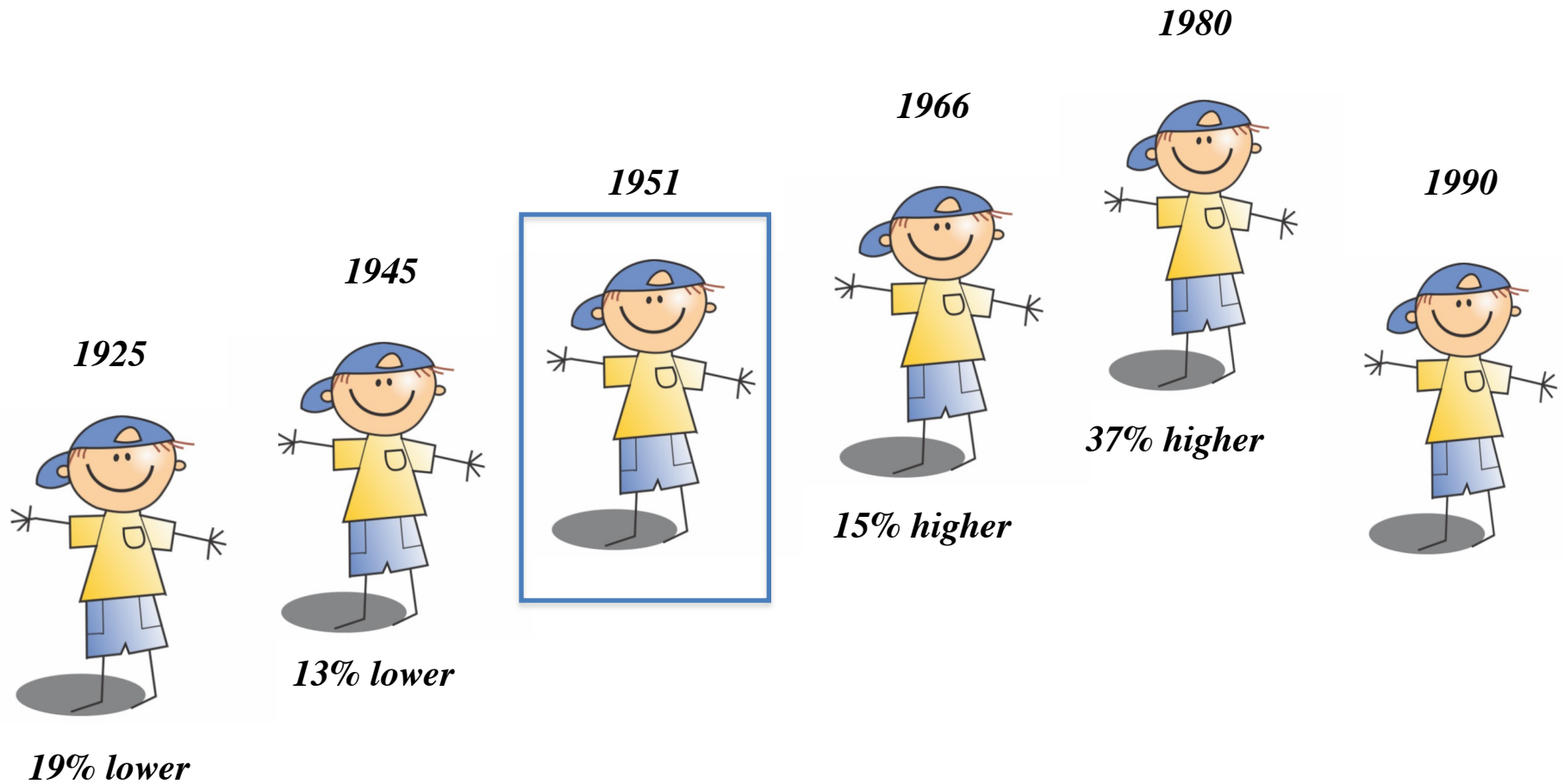




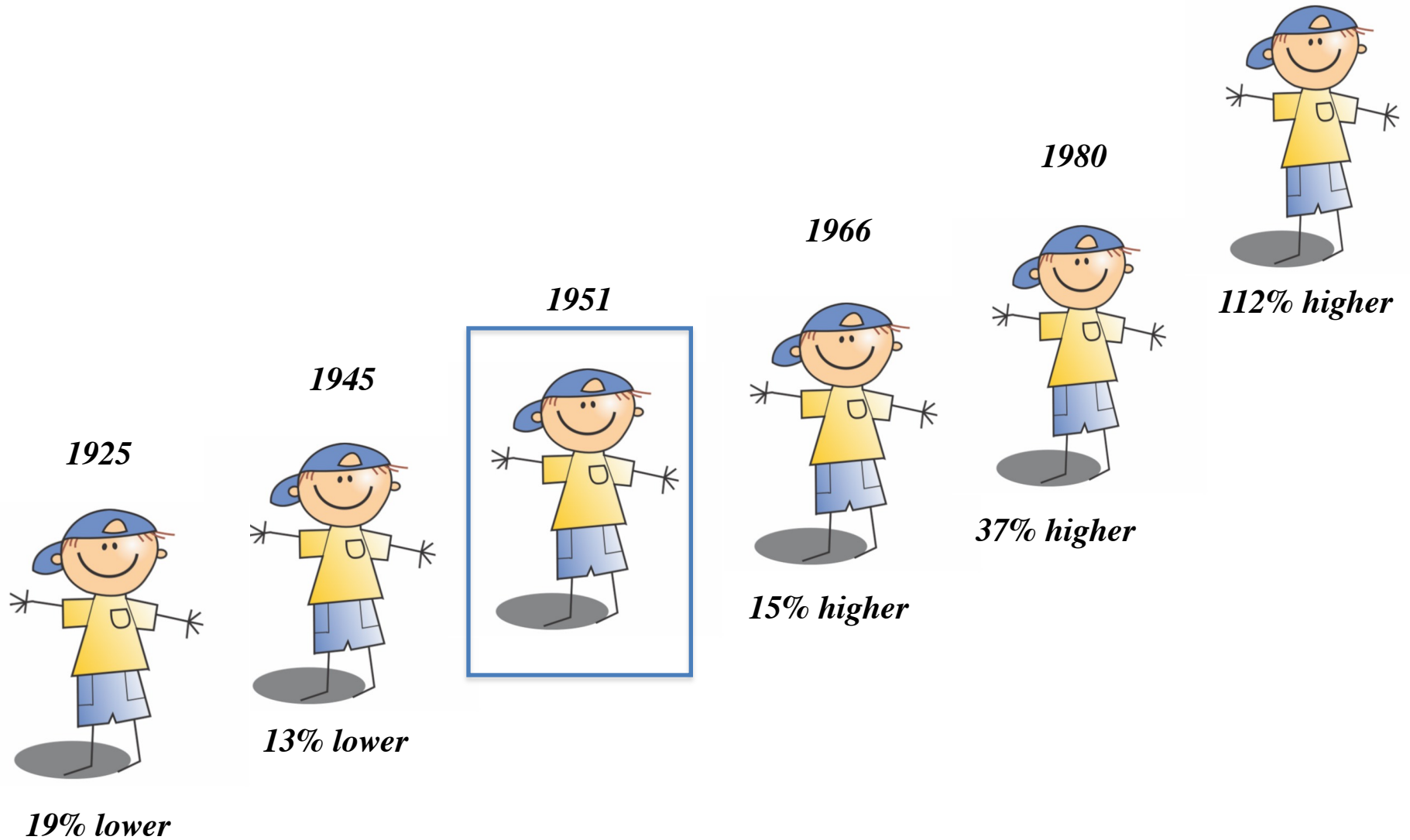
# Risk of Cirrhosis - Males



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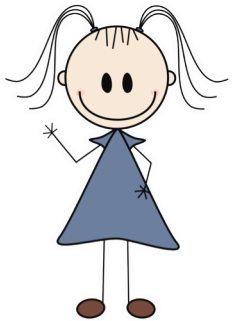


# Risk of Cirrhosis - Males

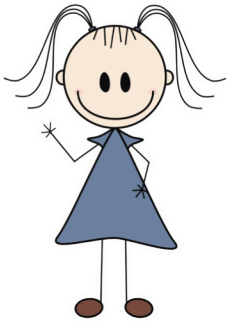


# Risk of Cirrhosis - Females

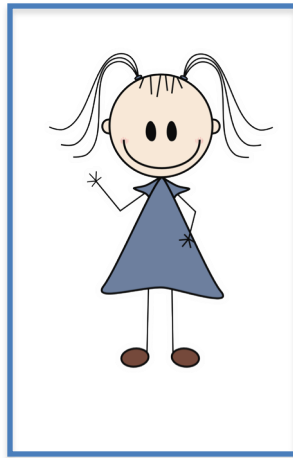
*1925*



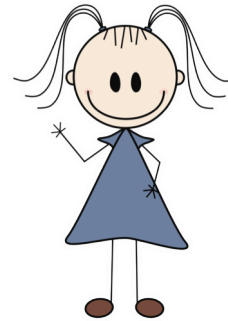
*1945*



*1951*



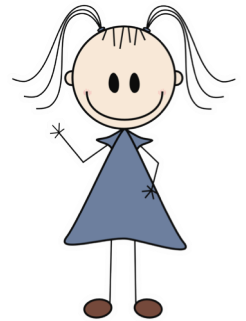
*1966*



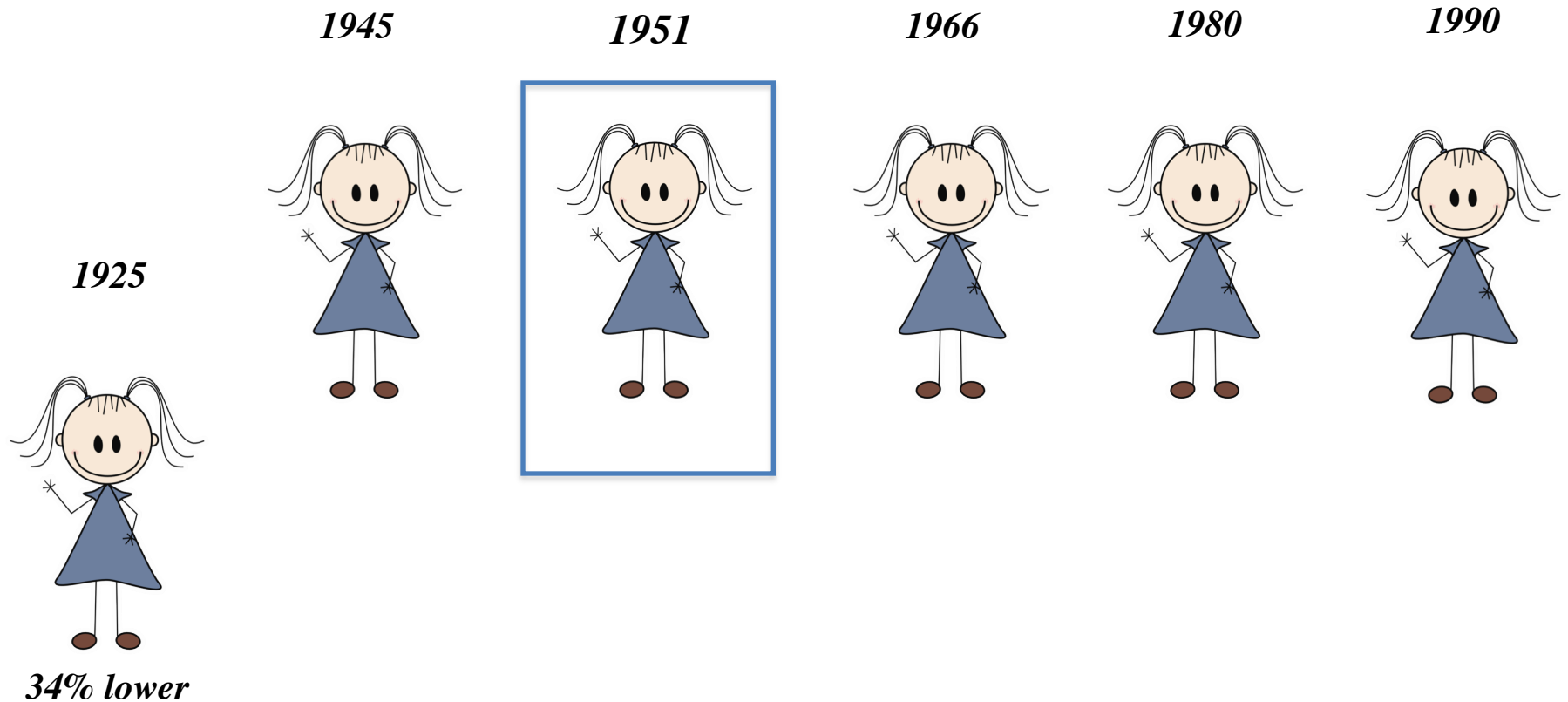
*1980*



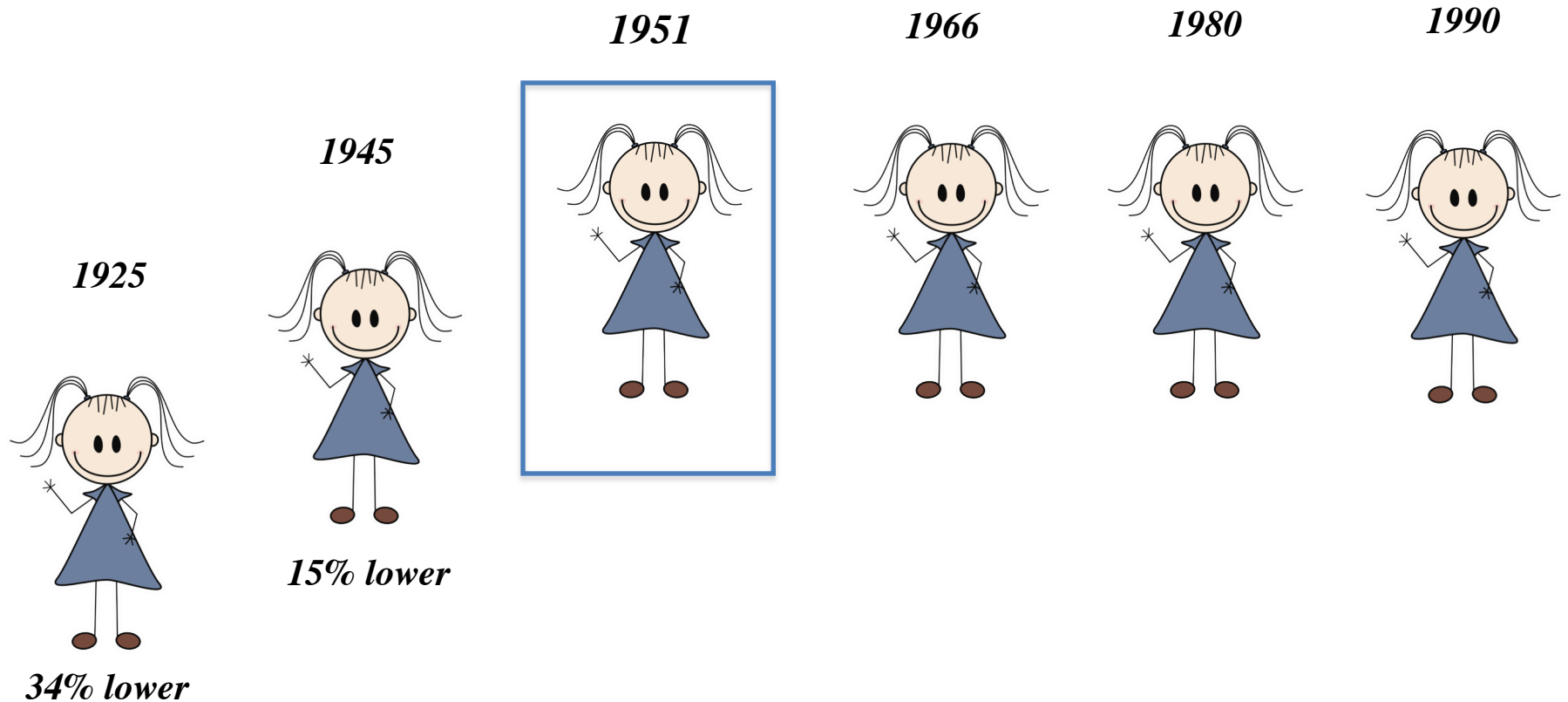
*1990*



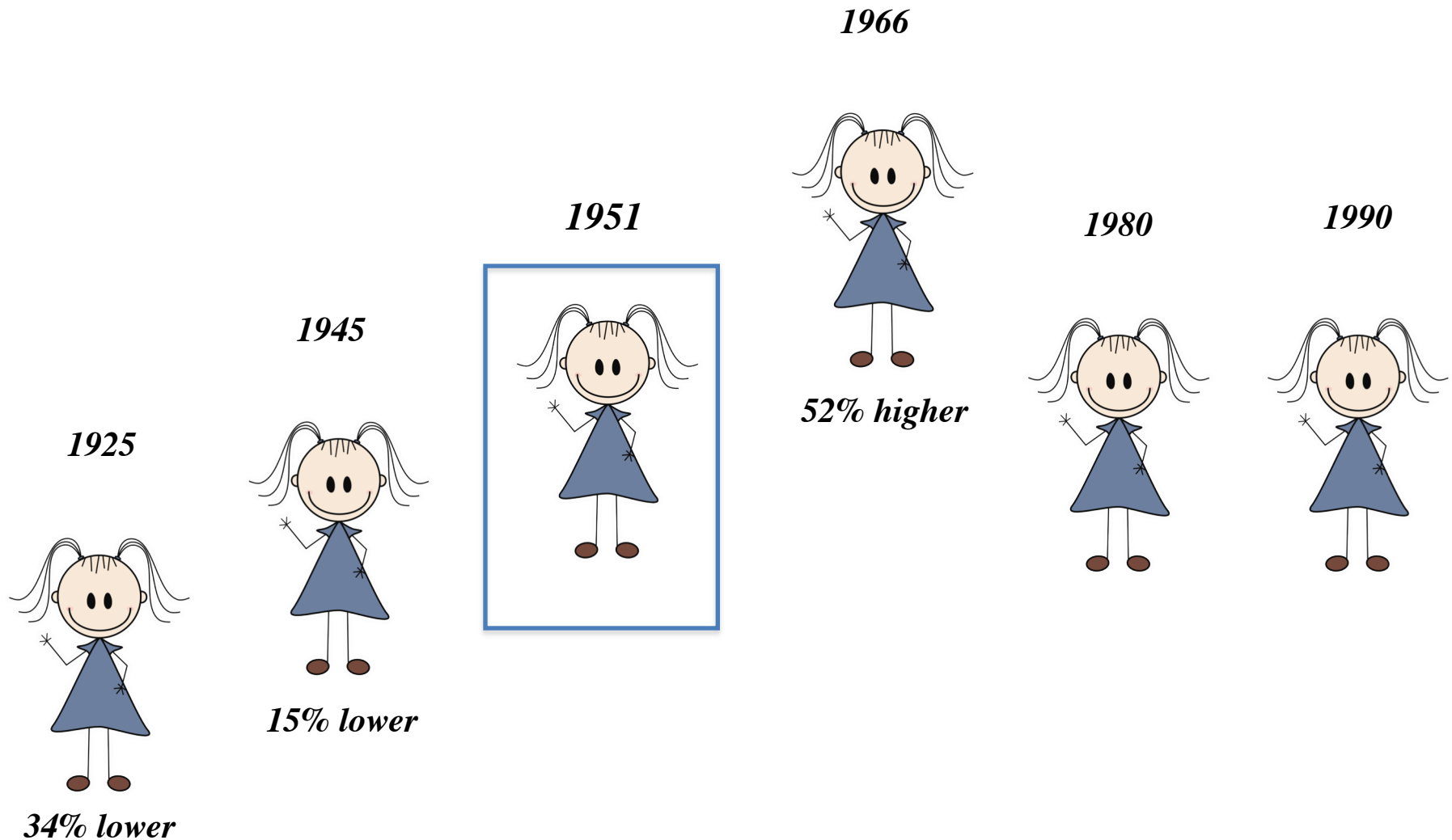
# Risk of Cirrhosis - Females



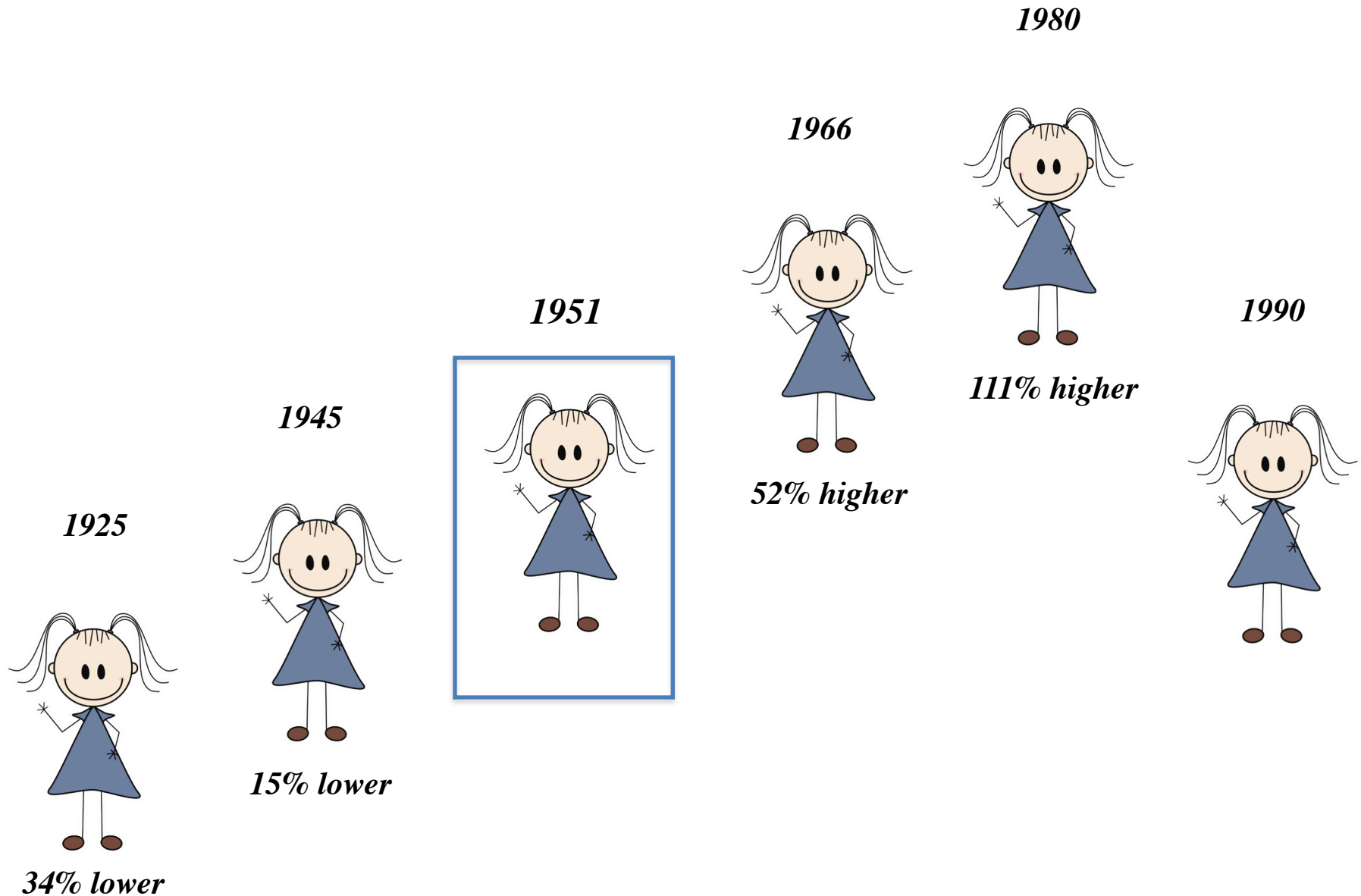
# Risk of Cirrhosis - Females



# Risk of Cirrhosis - Females

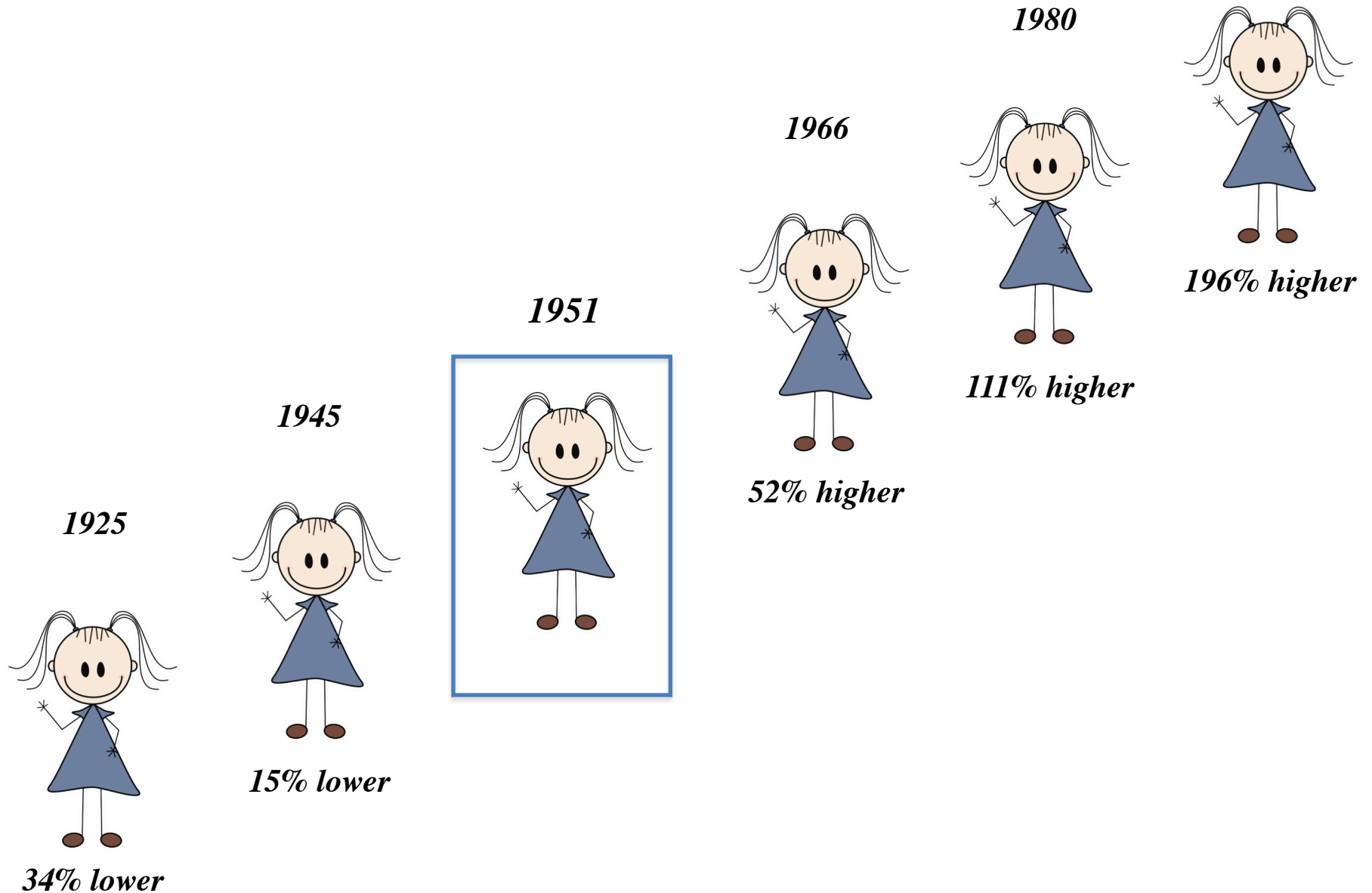


# Risk of Cirrhosis - Females

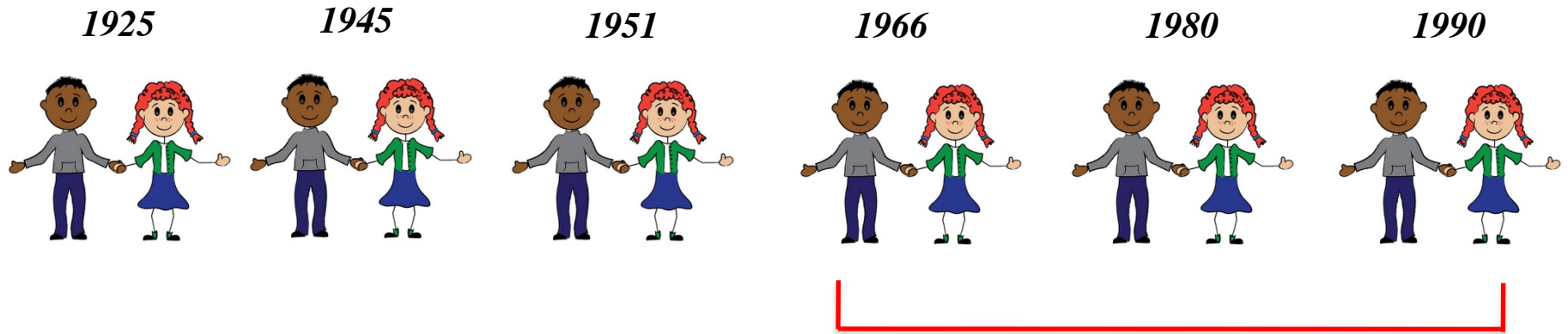




# Risk of Cirrhosis - Females



# 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

| <u>Table 1</u> : Cirrhosis cohort ≤ 40 years at diagnosis from 2007-2017 (N = 12,715) |                |
|---------------------------------------------------------------------------------------|----------------|
| Age at diagnosis (mean, sd)                                                           | 31.7 ± 6.4     |
| Male sex (n, %)                                                                       | 6,958 (55.3)   |
| Follow-up time (mean, sd)                                                             | 4.5 ± 2.9      |
| Death during follow-up (n, %)                                                         | 729 (5.8)      |
| Hospitalizations, total (mean)                                                        | 13,844 (1.09)  |
| Same-day surgery visits, total (mean)                                                 | 10,964 (0.86)  |
| Emergency room visits, total (mean)                                                   | 61,064 (4.8)   |
| Outpatient visits, total (mean)                                                       | 148,772 (11.7) |
| Liver transplants                                                                     | 166            |
| Total OHIP billing claims                                                             | 1,881,653      |

# 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

