

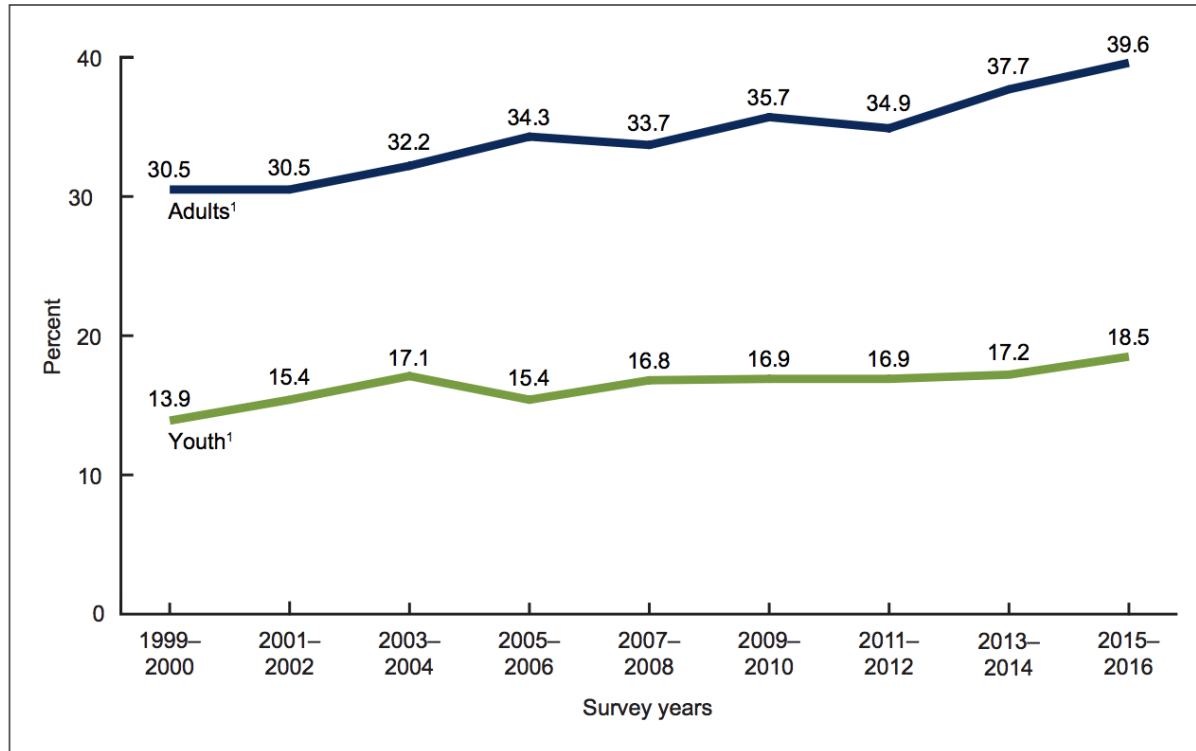
# HCC and Metabolic Syndrome; A New Paradigm

M. Shadab Siddiqui, MD

Associate Professor of Medicine

Virginia Commonwealth University

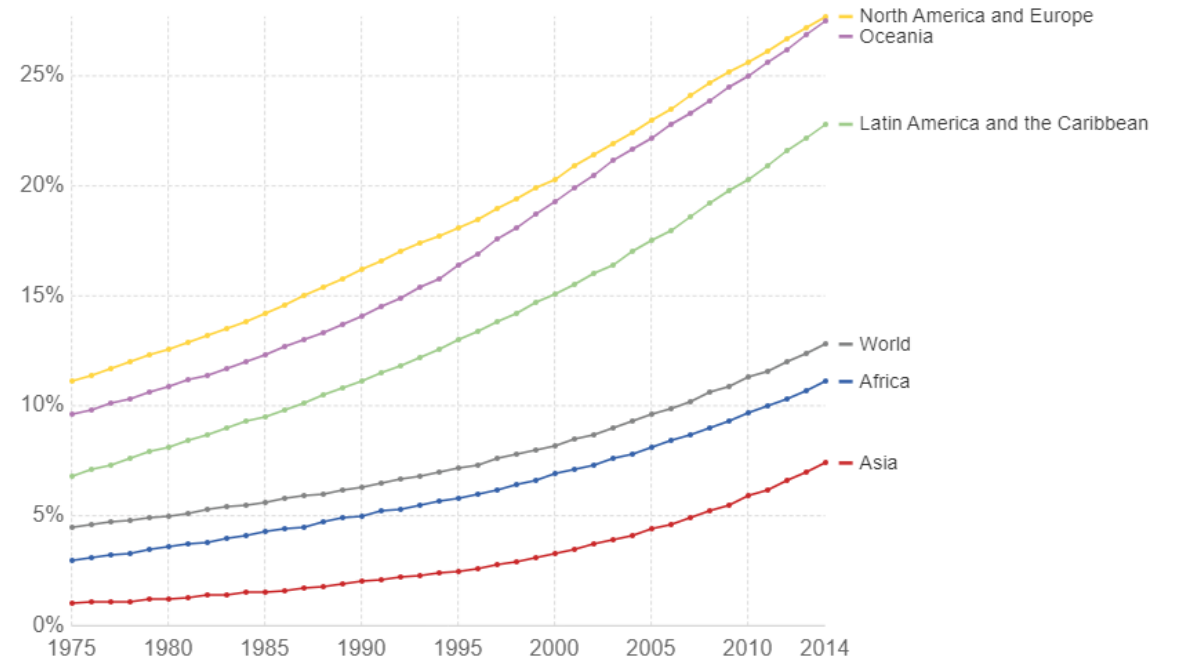
# Obesity is on the Rise



National Health & Nutrition Examination Survey, 1999-2016

## Prevalence of obesity in adults by region

The prevalence of obesity in adults, measured as the percentage of adults aged 18 years and older (both male and female) with a body-mass index (BMI) greater than 30 kilograms per metre squared.

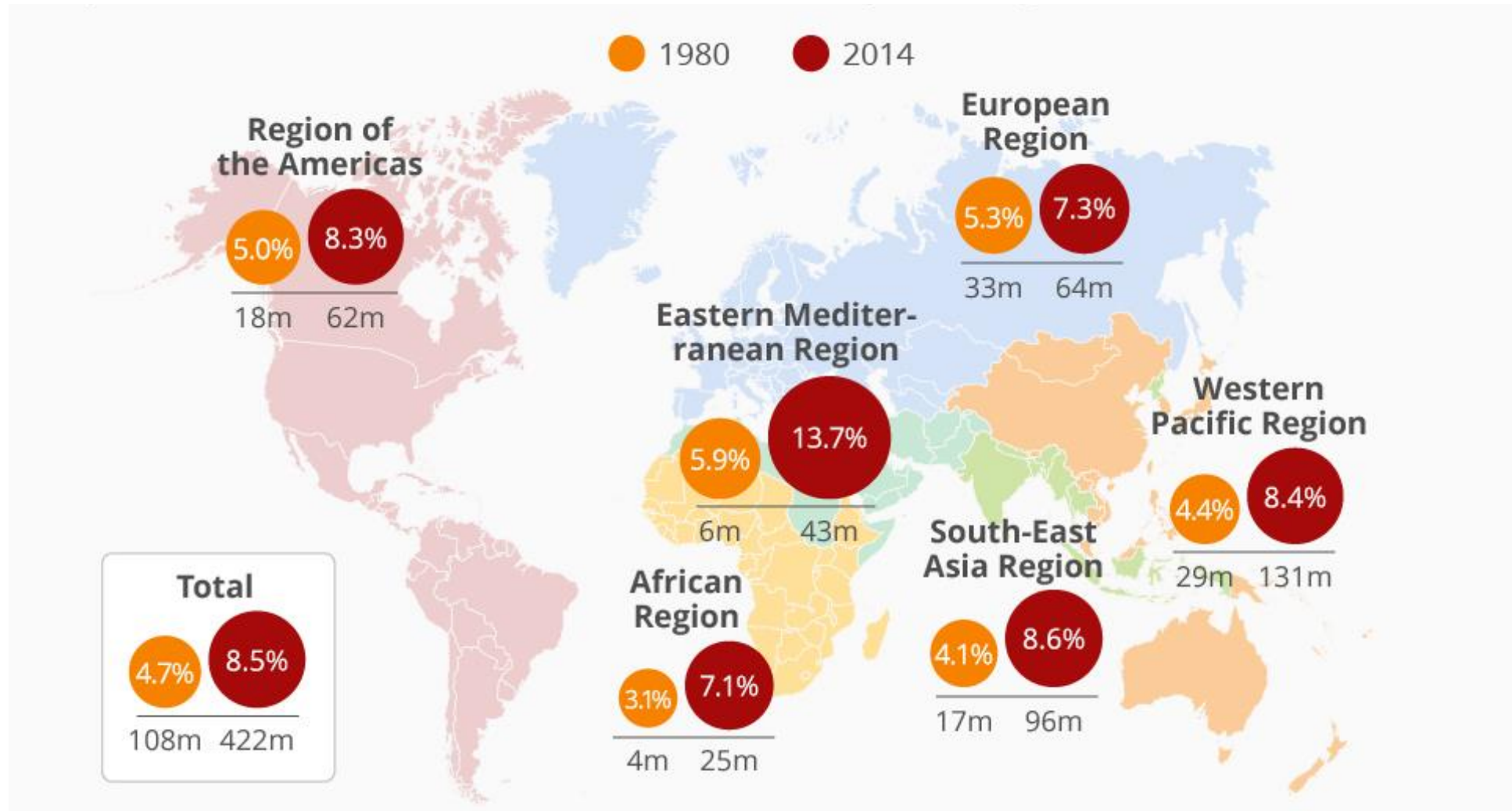


Source: UN Food and Agricultural Organization/WHO

OurWorldInData.org/obesity/ • CC BY-SA

WHO. Global Database on Body Mass Index. 2016

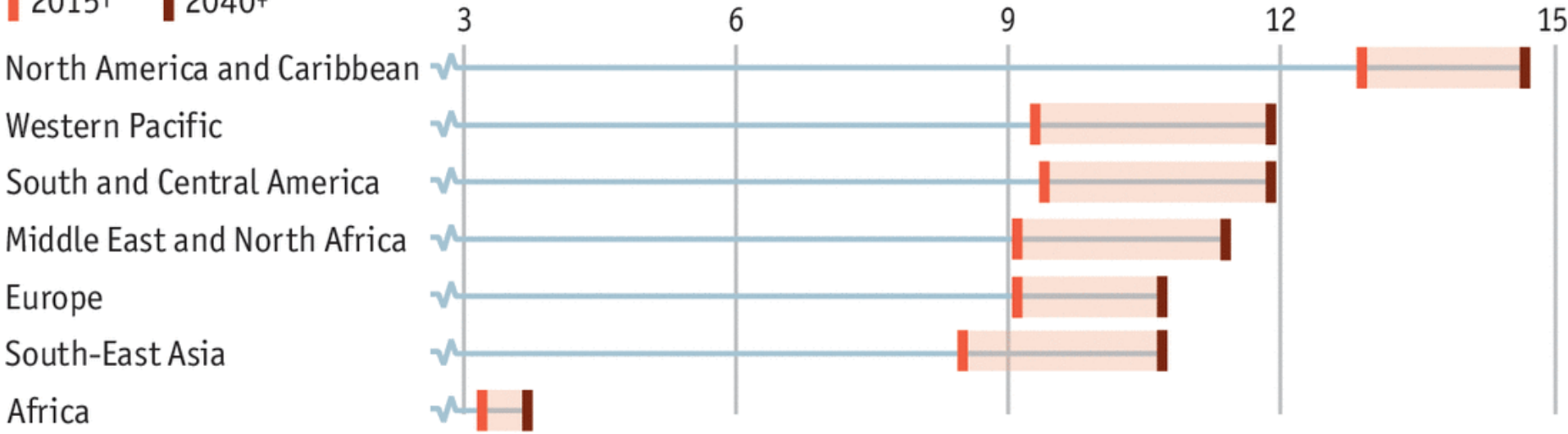
# Increasing Rates of Diabetes



# Prevalence of Diabetes Will Continue To Increase

Regional prevalence, as % of adult population

2015† 2040‡



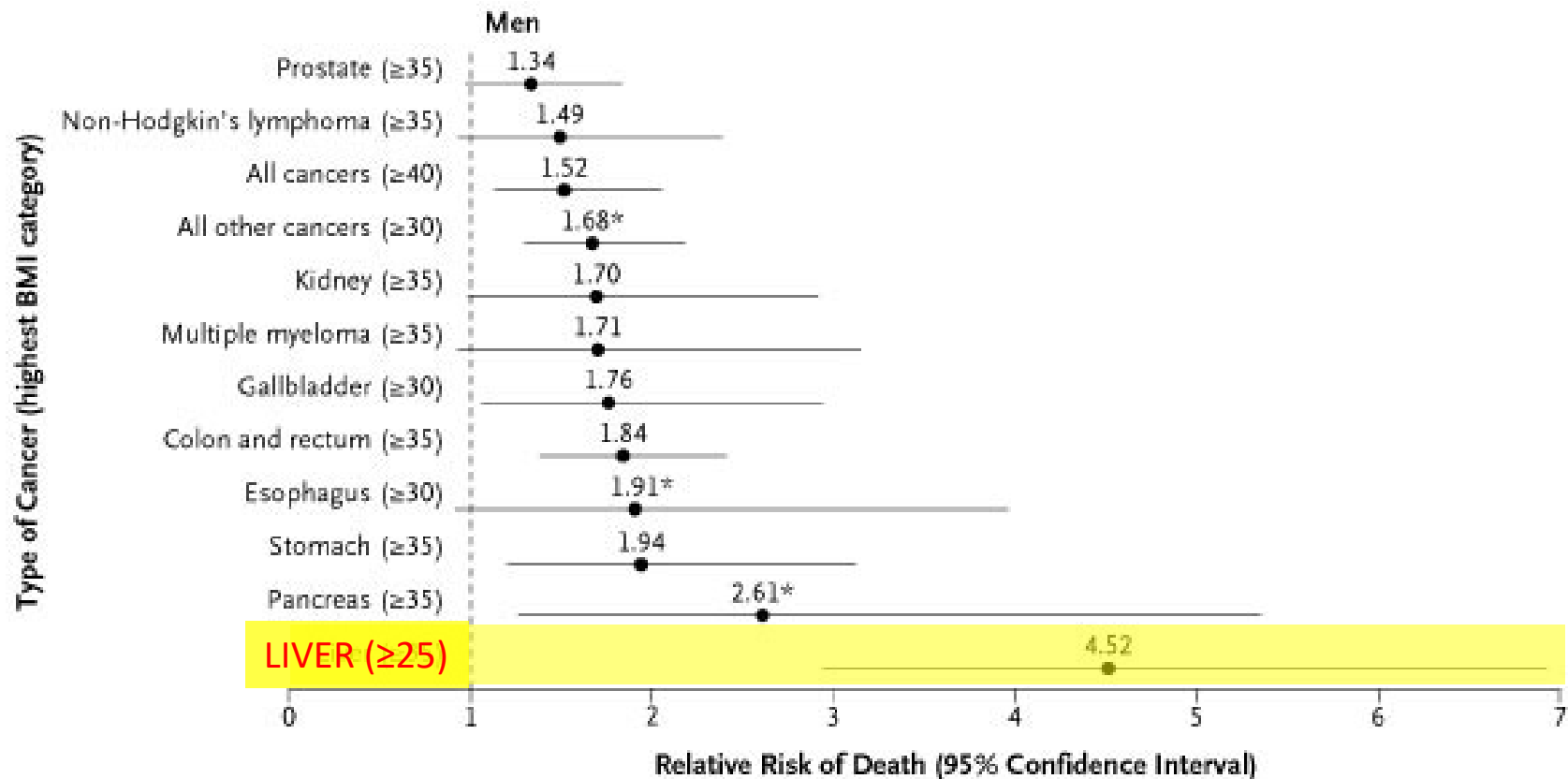
Sources: World Bank; IDF Diabetes Atlas, 2016

\*Aged 20- to -79-year-olds

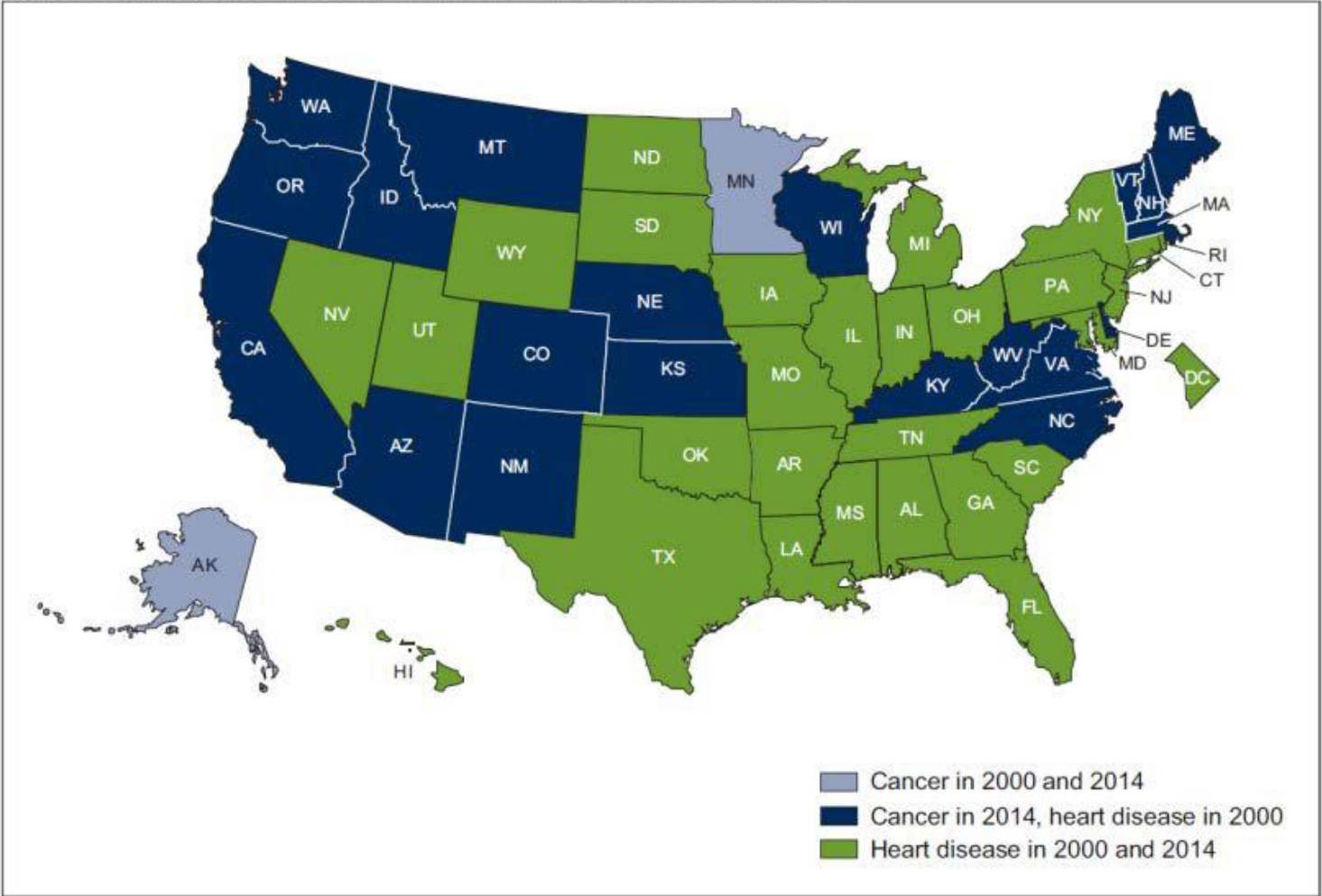
†Estimate

‡Forecast

# Higher Weight is Associated with Increased Death Rates

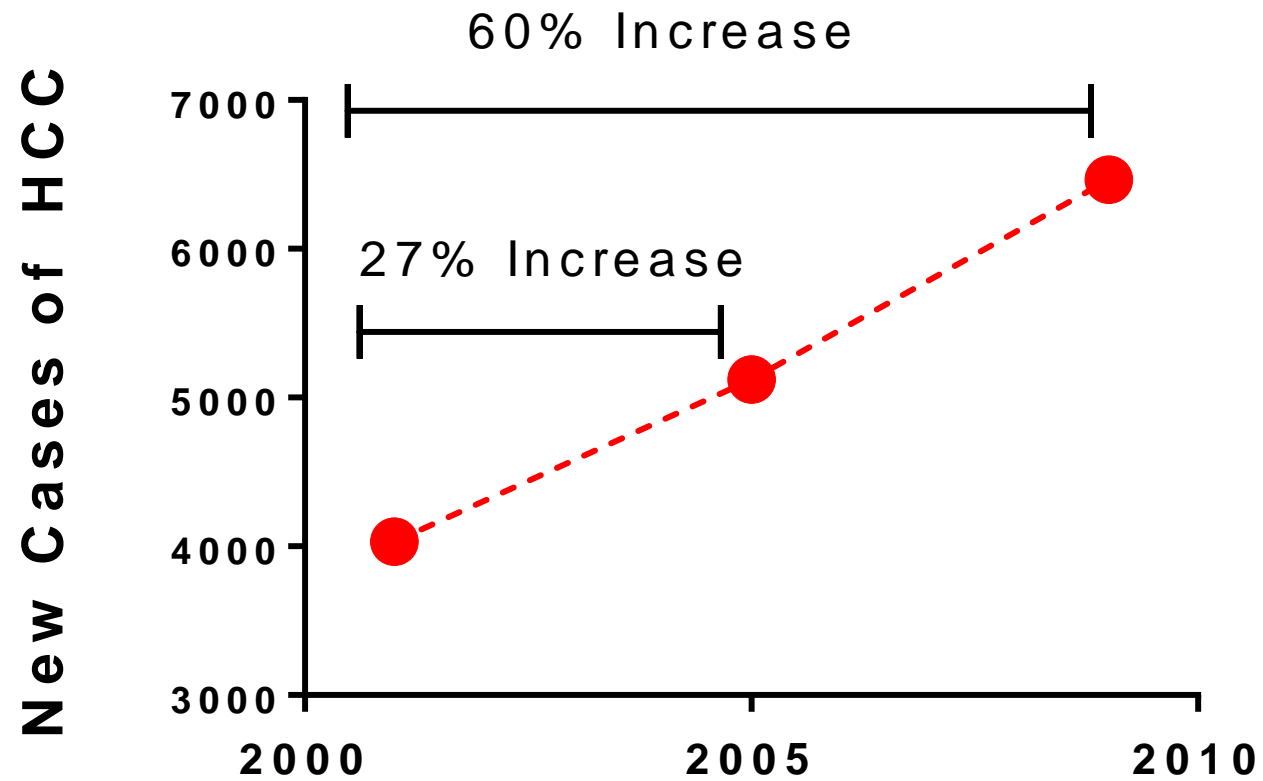


# Recent Changes in Cancer and Heart Disease Related Mortality in The US (2000 and 2014)

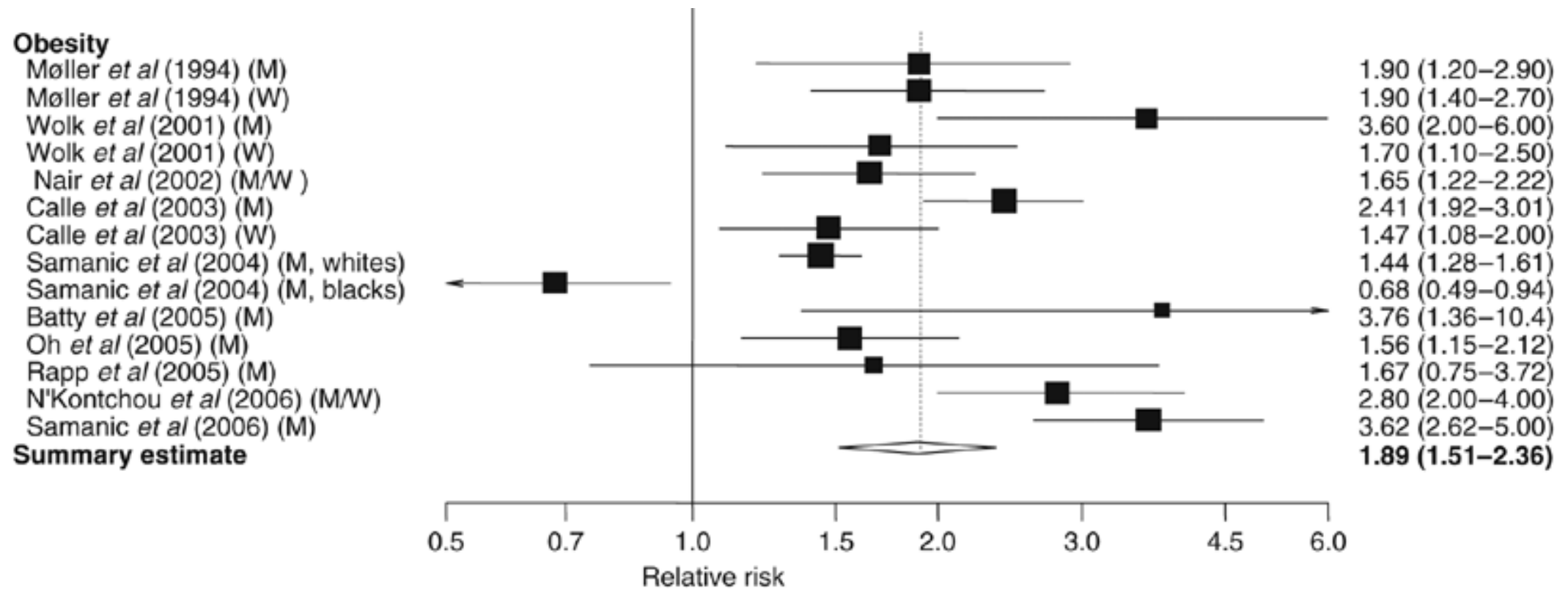


# Incident Rates of HCC are Increasing

---



# Excess Body Weight is Associated with Increased Risk of Liver Cancers

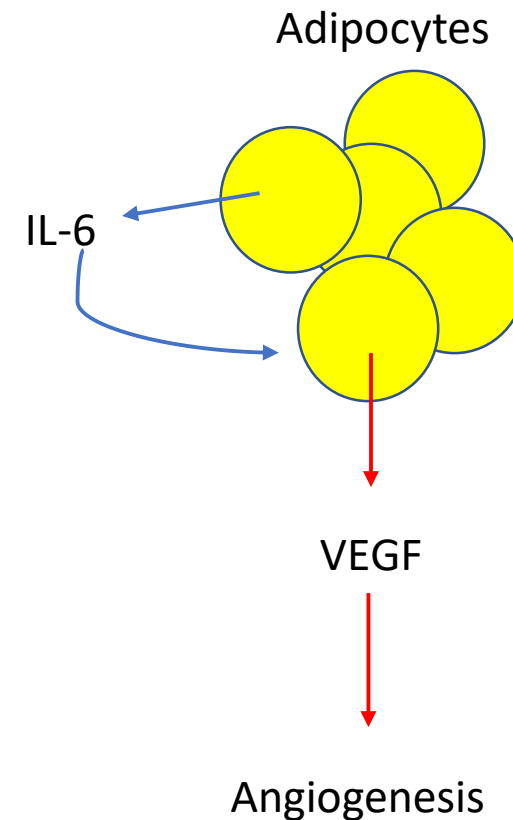




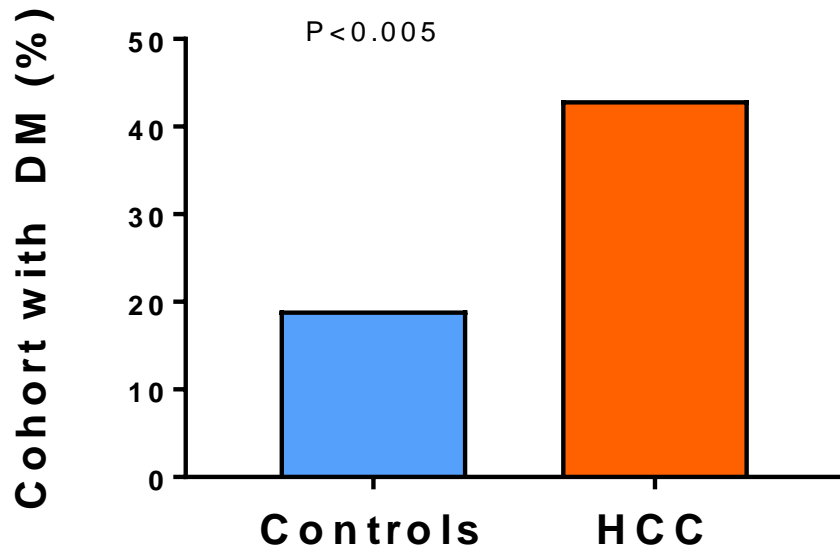
# Obesity Increases Recurrence of HCC After LT

---

- Retrospective study (N=342) of patients transplanted for HCC
- Obesity a strong predictor of HCC recurrence (HR=1.9,  $p < 0.05$ )
- Obesity associated with microvascular invasion seen on explant (P=0.04)

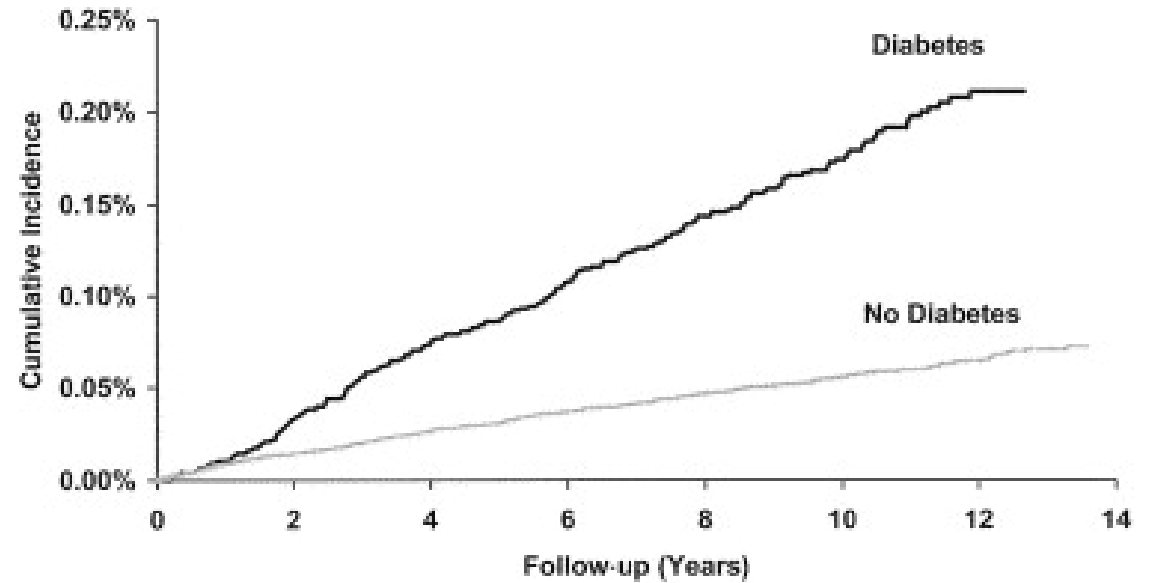


# Diabetes is a Risk Factor for HCC



In multivariate analysis, diabetes remained significantly associated with HCC with HR of 3.18 (2.85-3.54)

Davila et. al. Gut 2005



Diabetes had hazard rate ratio 2.16 (1.86-2.52) for development of HCC

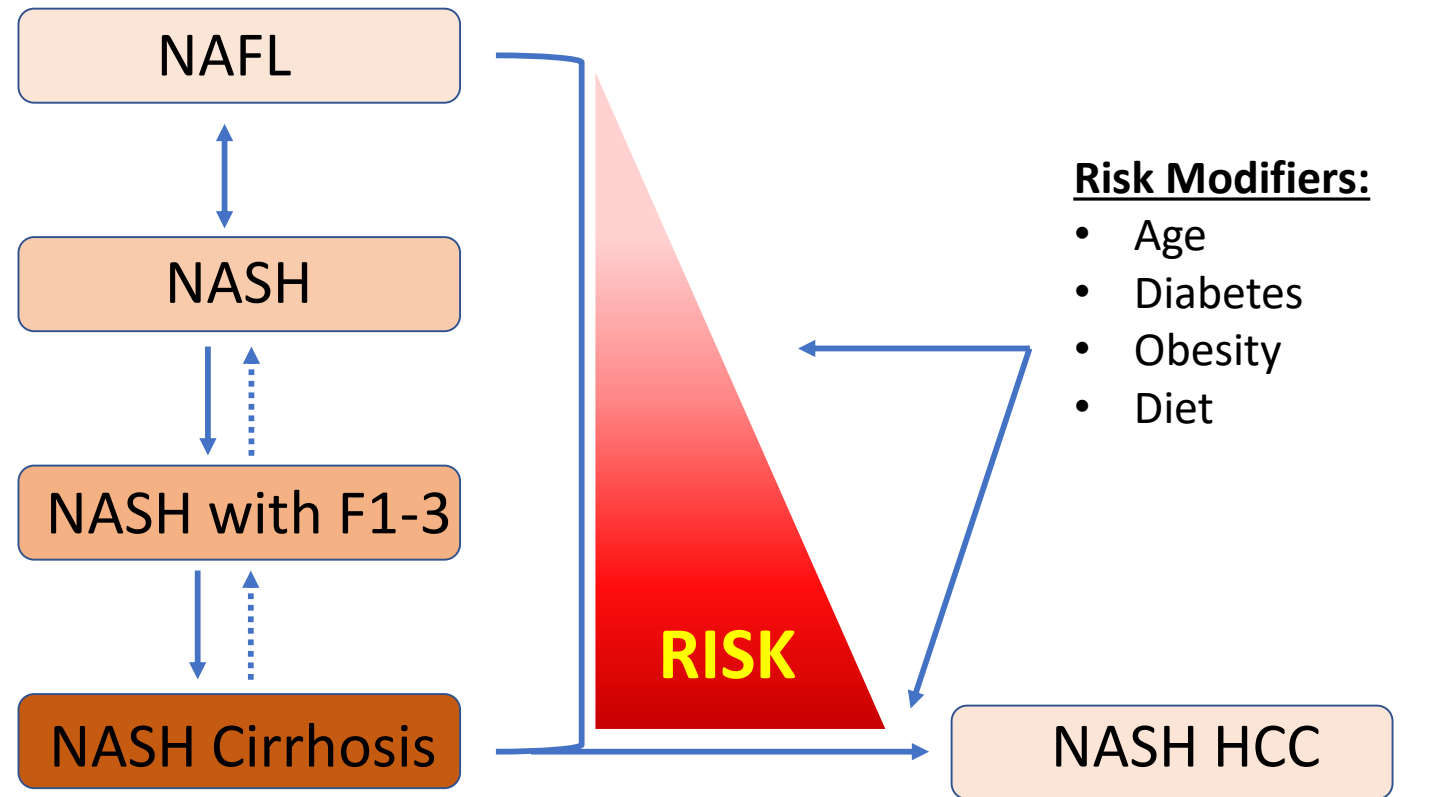
El-Serag et. al. Gastro 2004

# Dyslipidemia and Hypertension Increase Risk of HCC

---

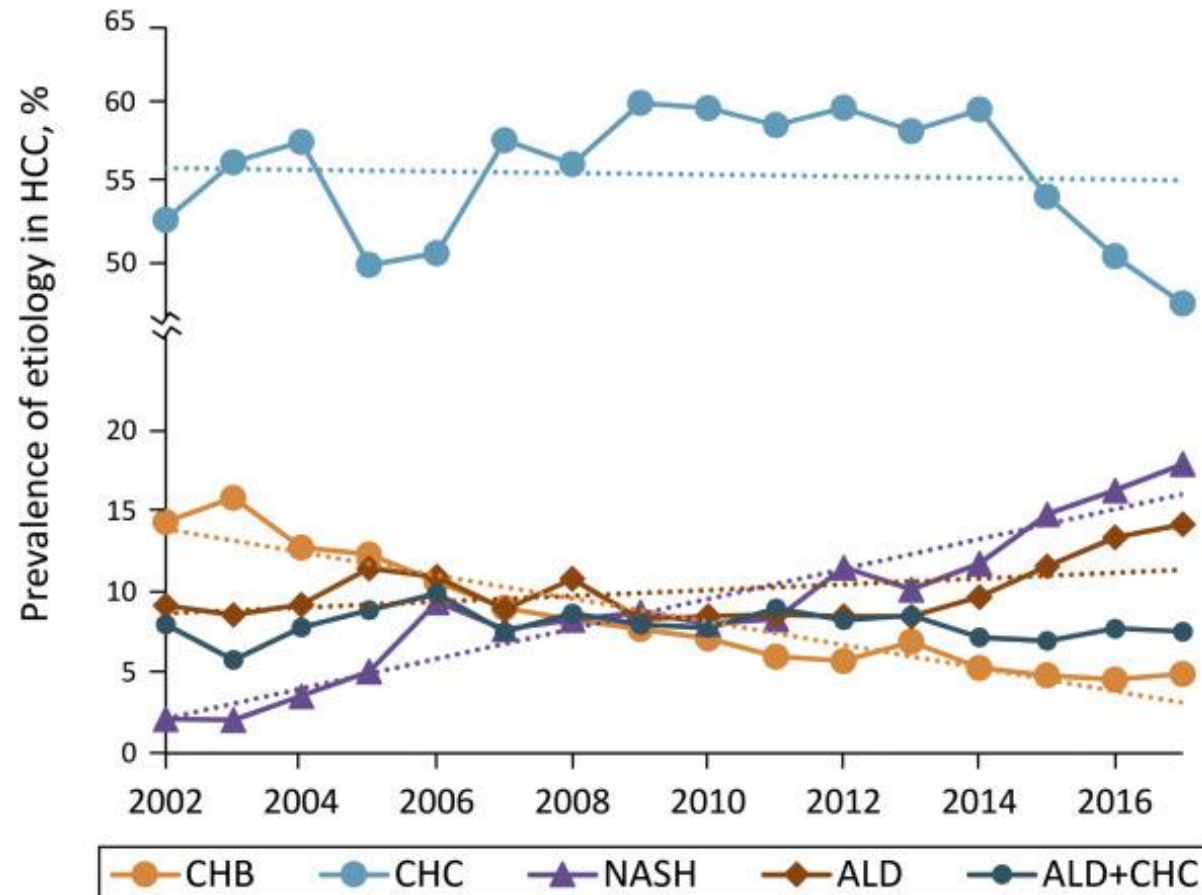
Metabolic Conditions	Adjusted OR	95% CI	P-value
Impaired glucose tolerance/Diabetes	2.90	2.71, 3.10	<0.001
Dyslipidemia	1.35	1.26, 1.45	<0.001
Obesity	1.93	1.71, 2.18	<0.001
Hypertension	2.22	2.04, 2.42	<0.001
Metabolic syndrome	2.58	2.40, 2.76	<0.001

# The Risk of NAFLD on HCC

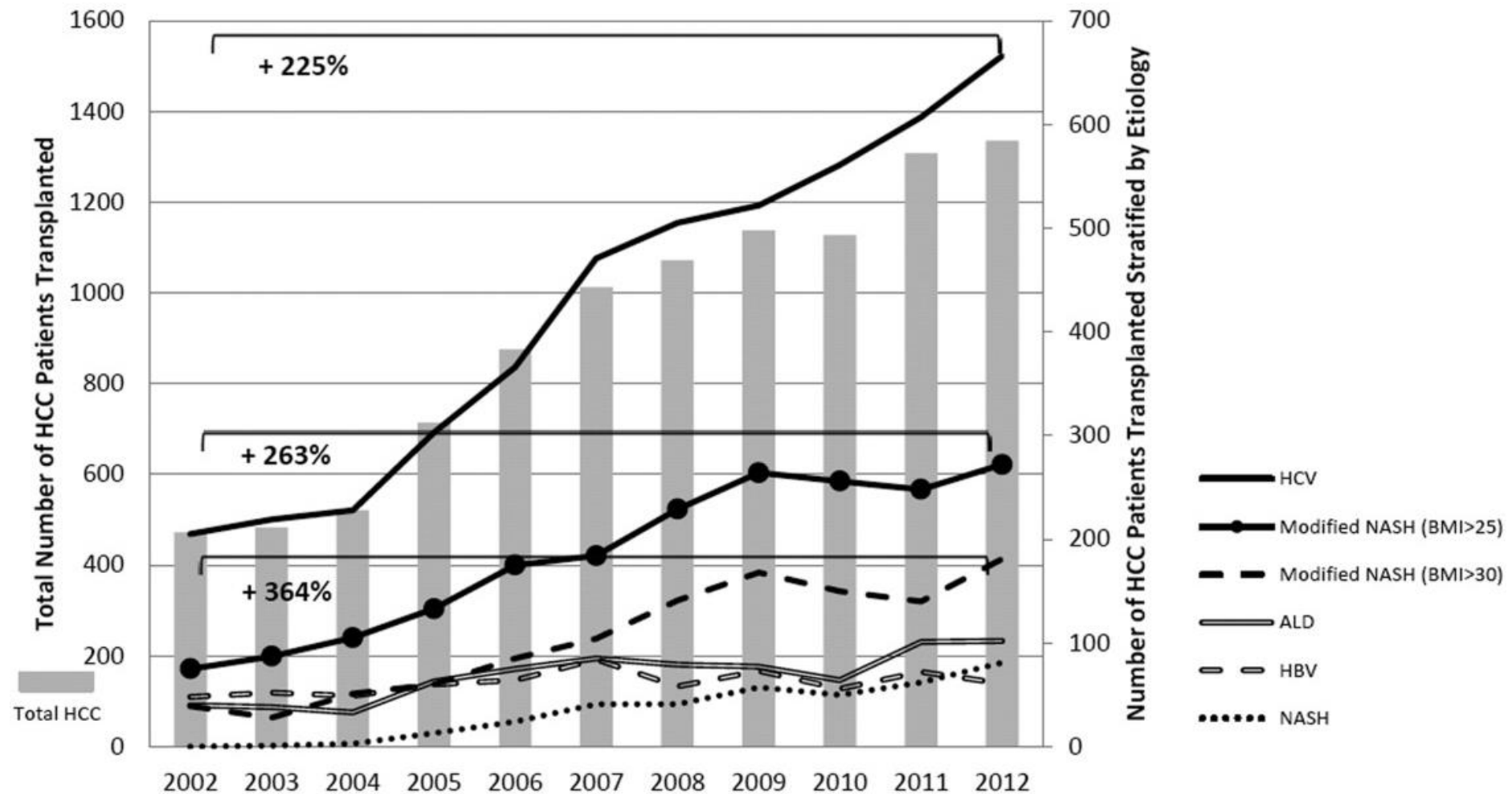


Annual incidence 2.4-12.8%

# NASH is the Most Rapidly Growing Cause of HCC Among Patients Listed for LT

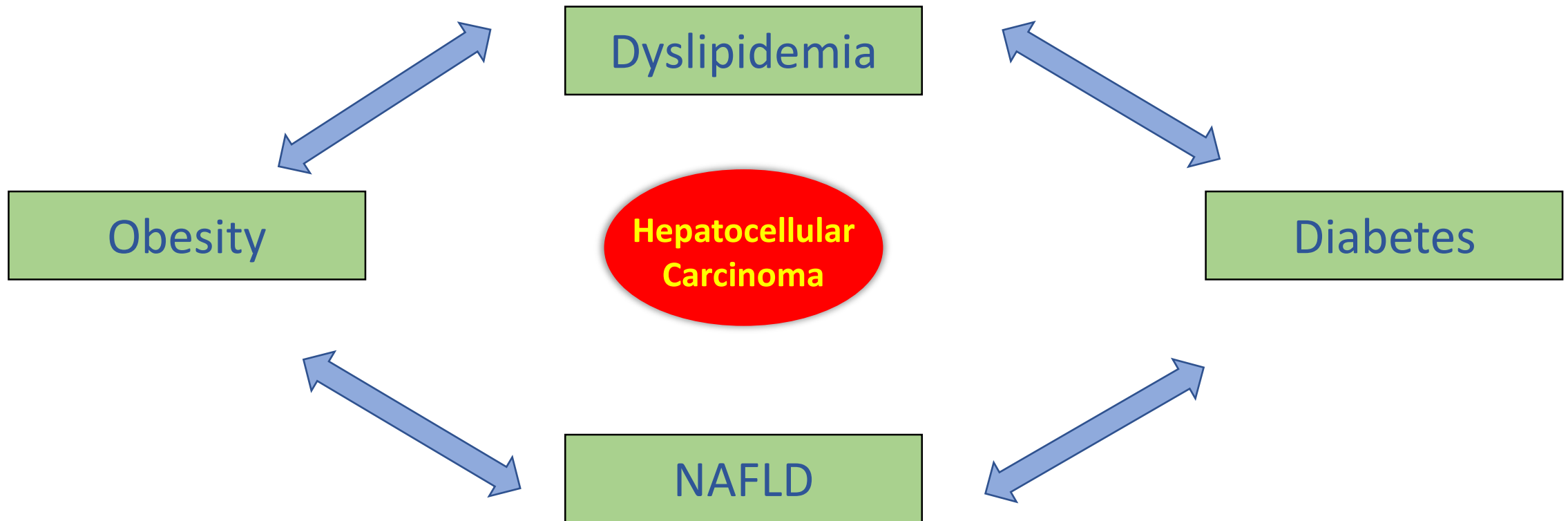


# NASH Related HCC is the Fastest Growing Indication for HCC-Related LT



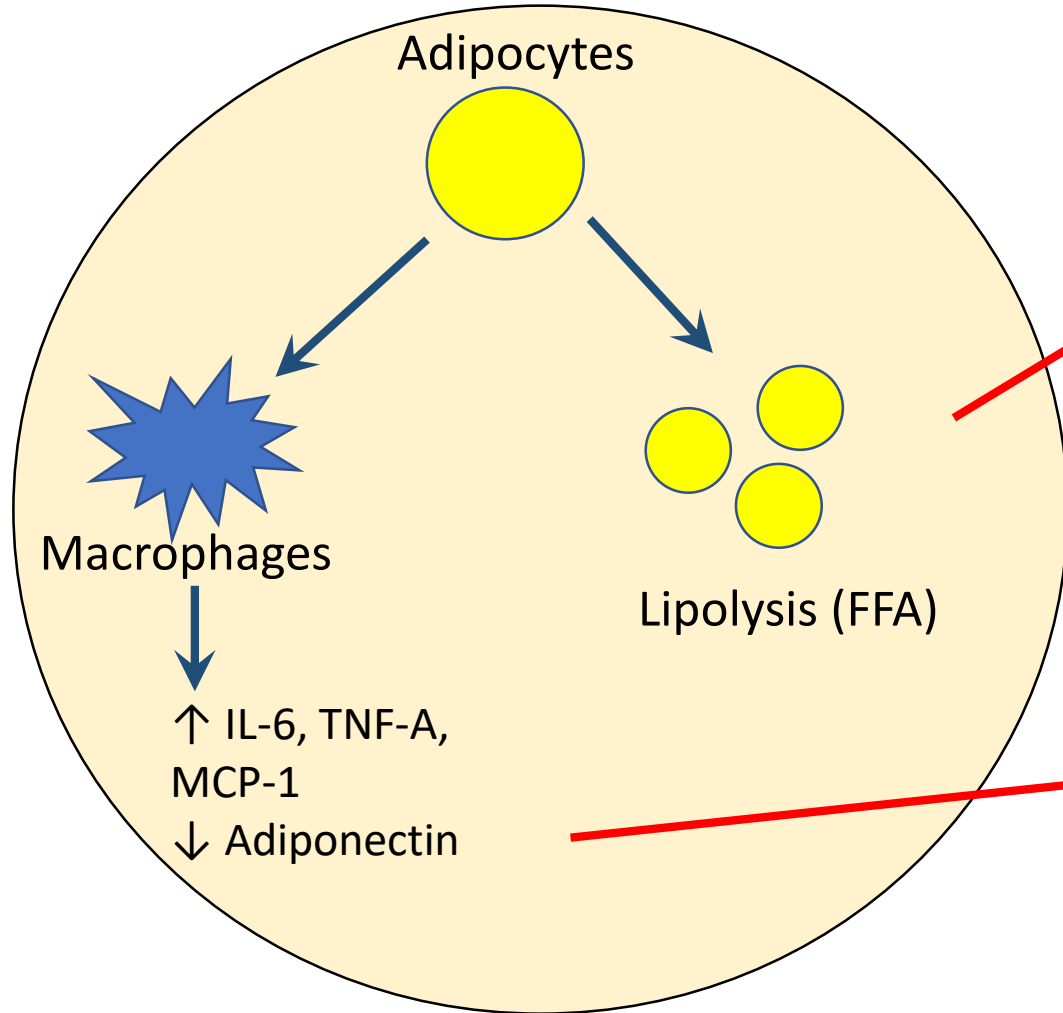
# The Crosstalk Between Metabolic Syndrome & HCC

---

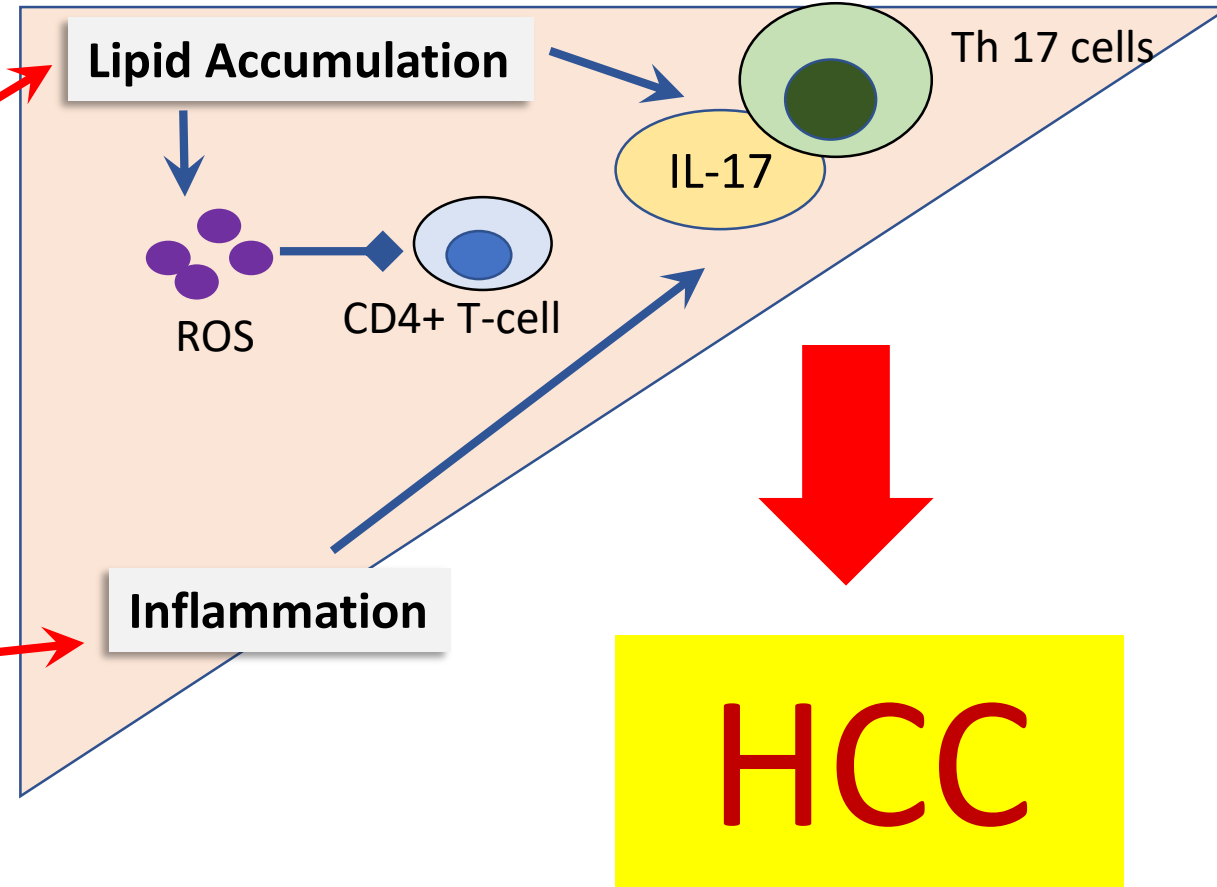


# Mechanism Linking Obesity to HCC

## ADIPOSE TISSUE



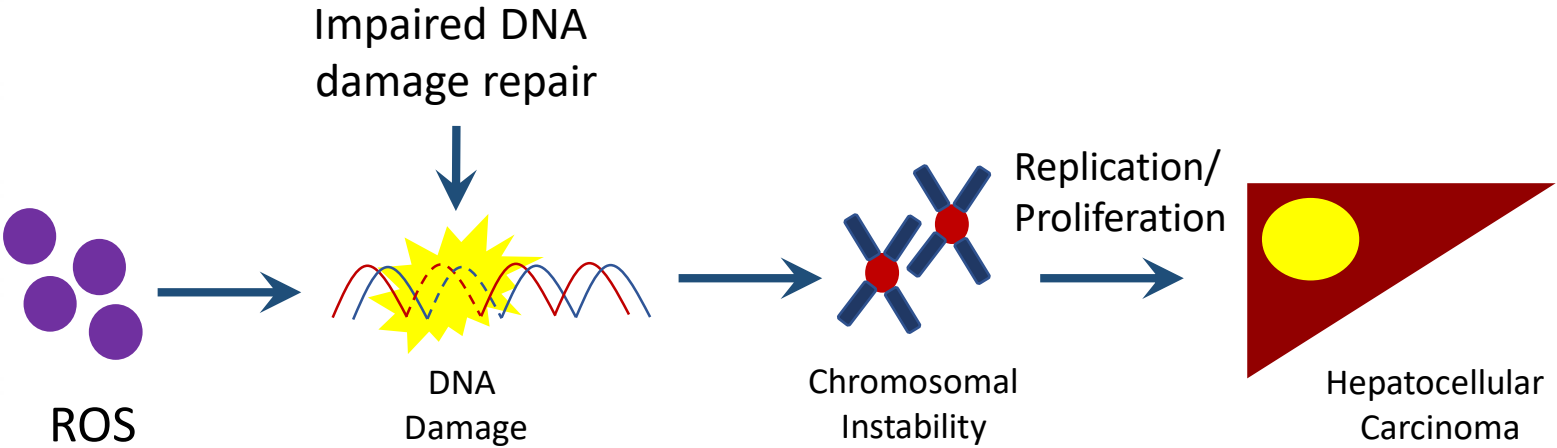
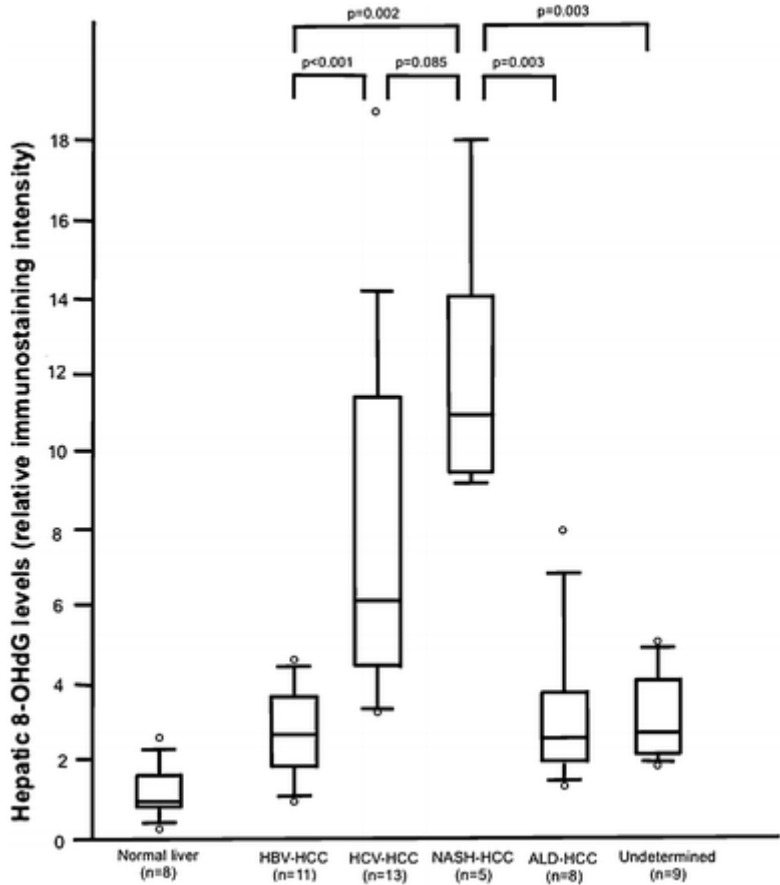
## LIVER



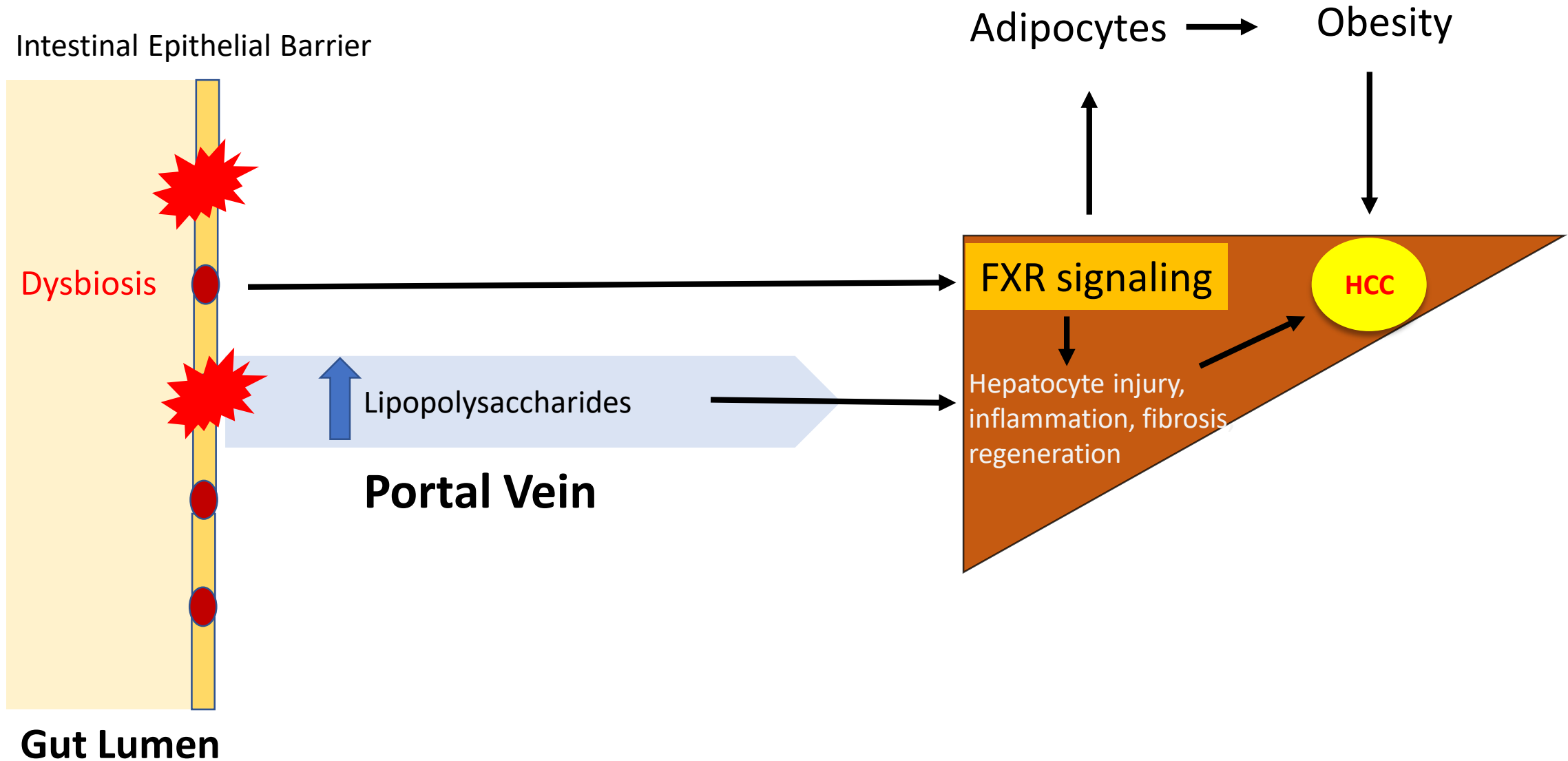


# Oxidative DNA Damage is Higher in NASH-Cirrhosis

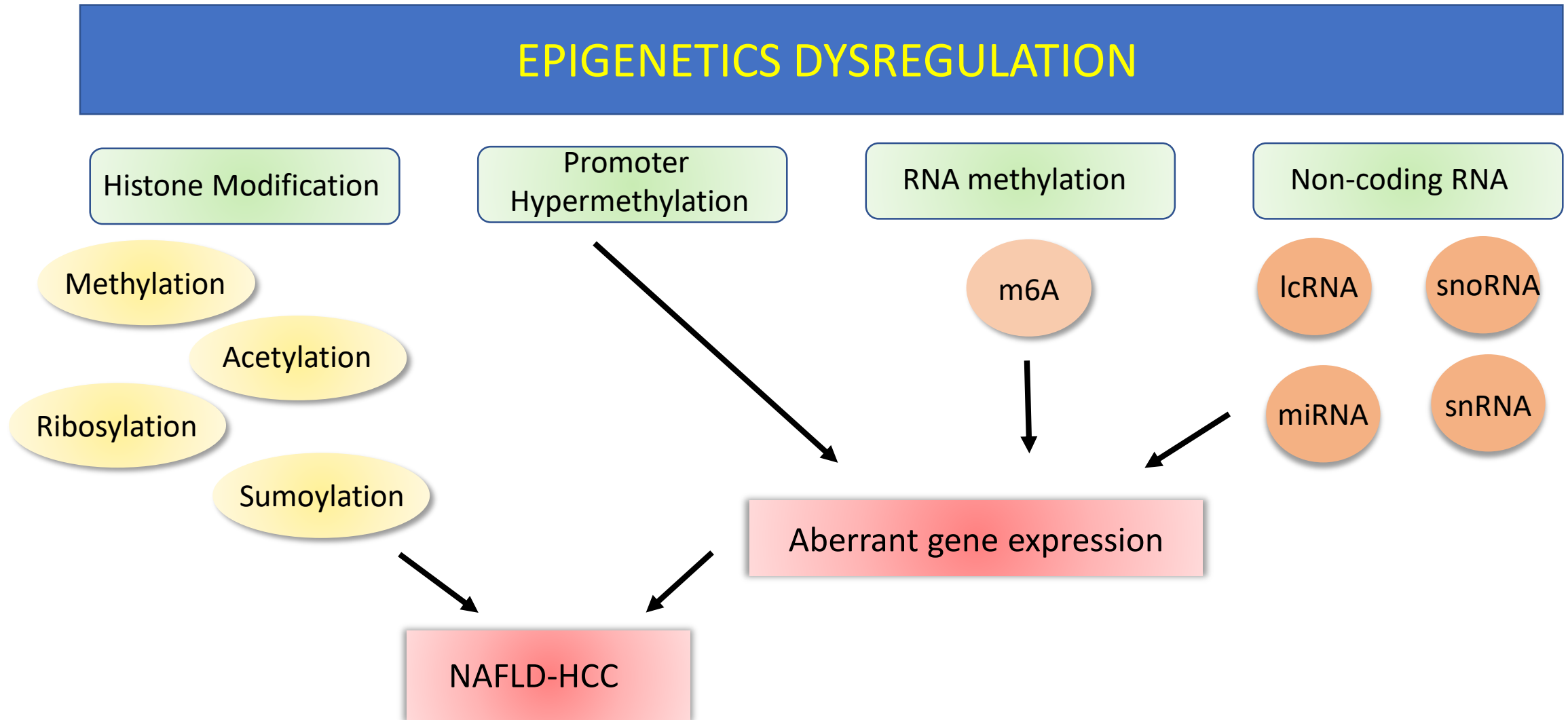
Marker of Oxidative DNA damage



# Role of Dysbiosis and Microbiome in HCC

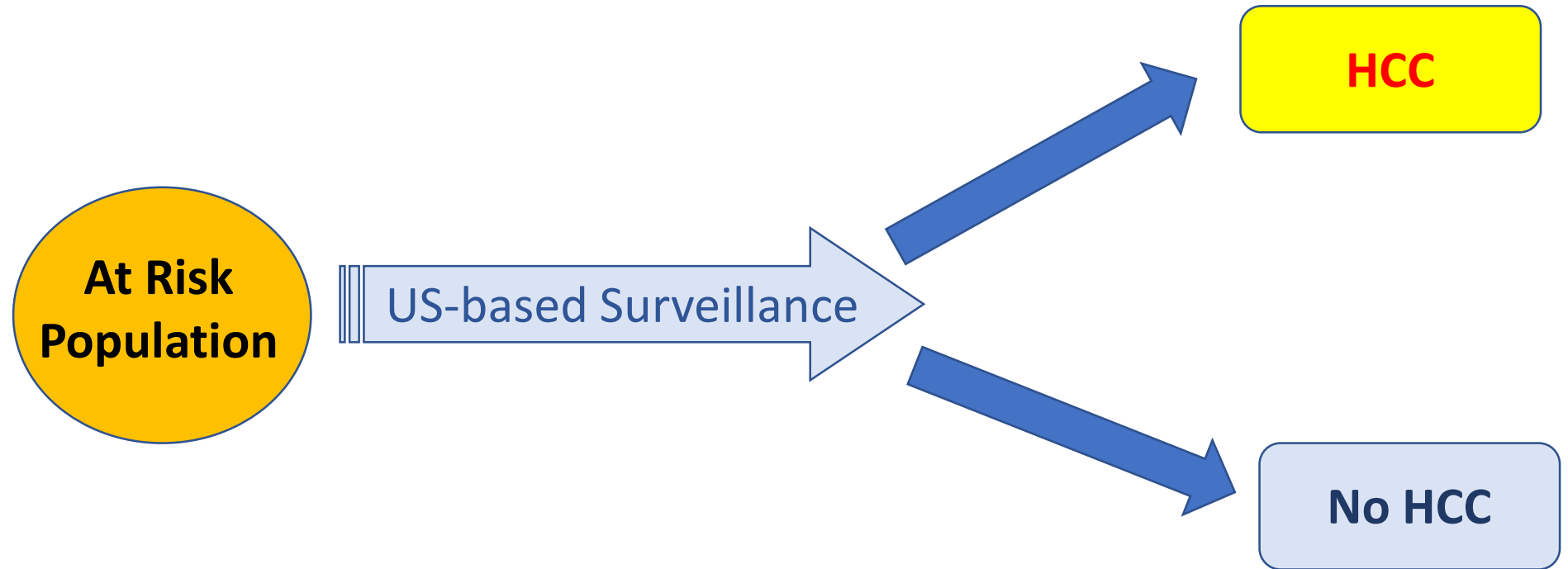


# Role of Epigenetics in Promoting HCC



# HCC Surveillance in Patients with NASH

---



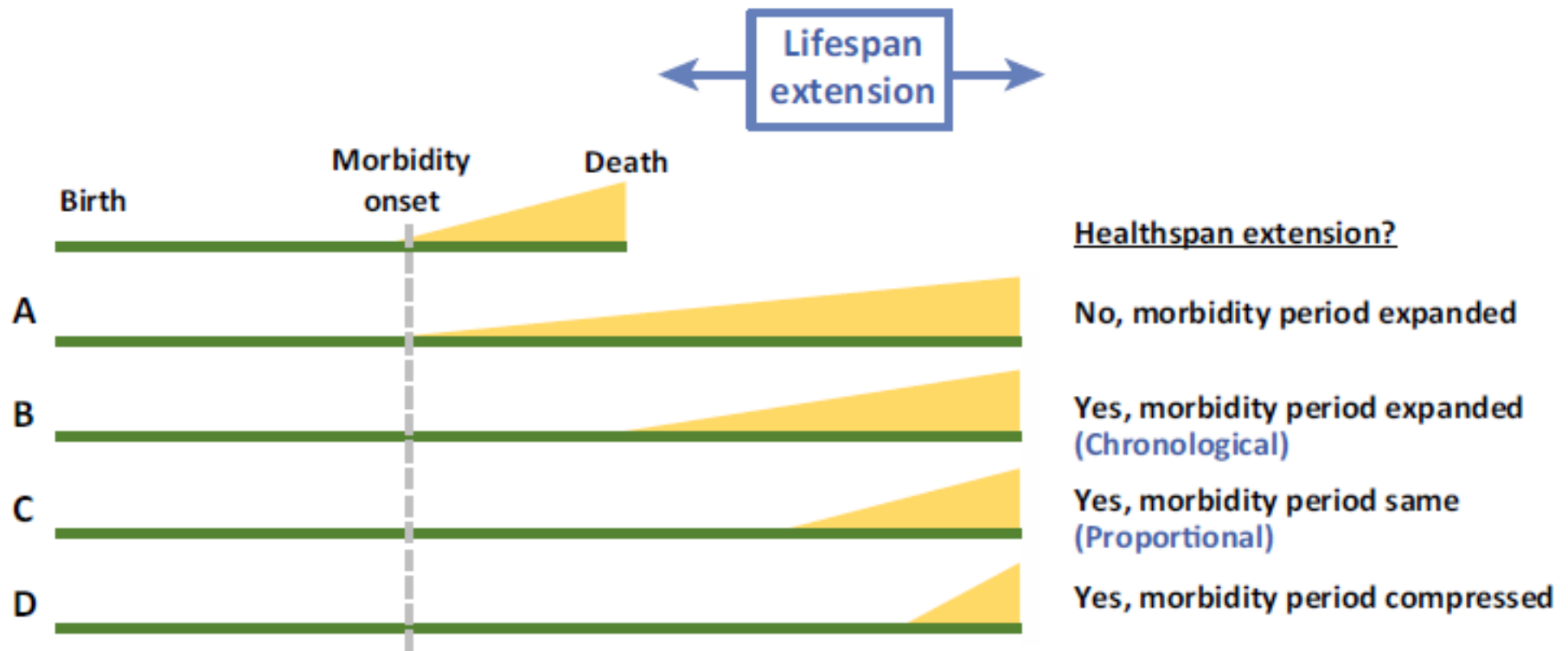
## Identification of at-Risk Population

- Cirrhosis vs. Non-Cirrhotics
- Undiagnosed patients

## Robust Surveillance Tools

- US-operator dependent
- Technically difficult (obesity)
- Heterogenous liver

# Improving Healthspan Not Only Lifespan



# Concluding Remarks

---

- Metabolic syndrome and its component are associated with increased risk of HCC
- NASH associated HCC is rising rapidly
- The molecular pathways leading to HCC are multi-factorial and likely different in different patients
- More research regarding optimal surveillance strategies are needed