PFAS and Liver Cancer: The mediating role of plant-based diet

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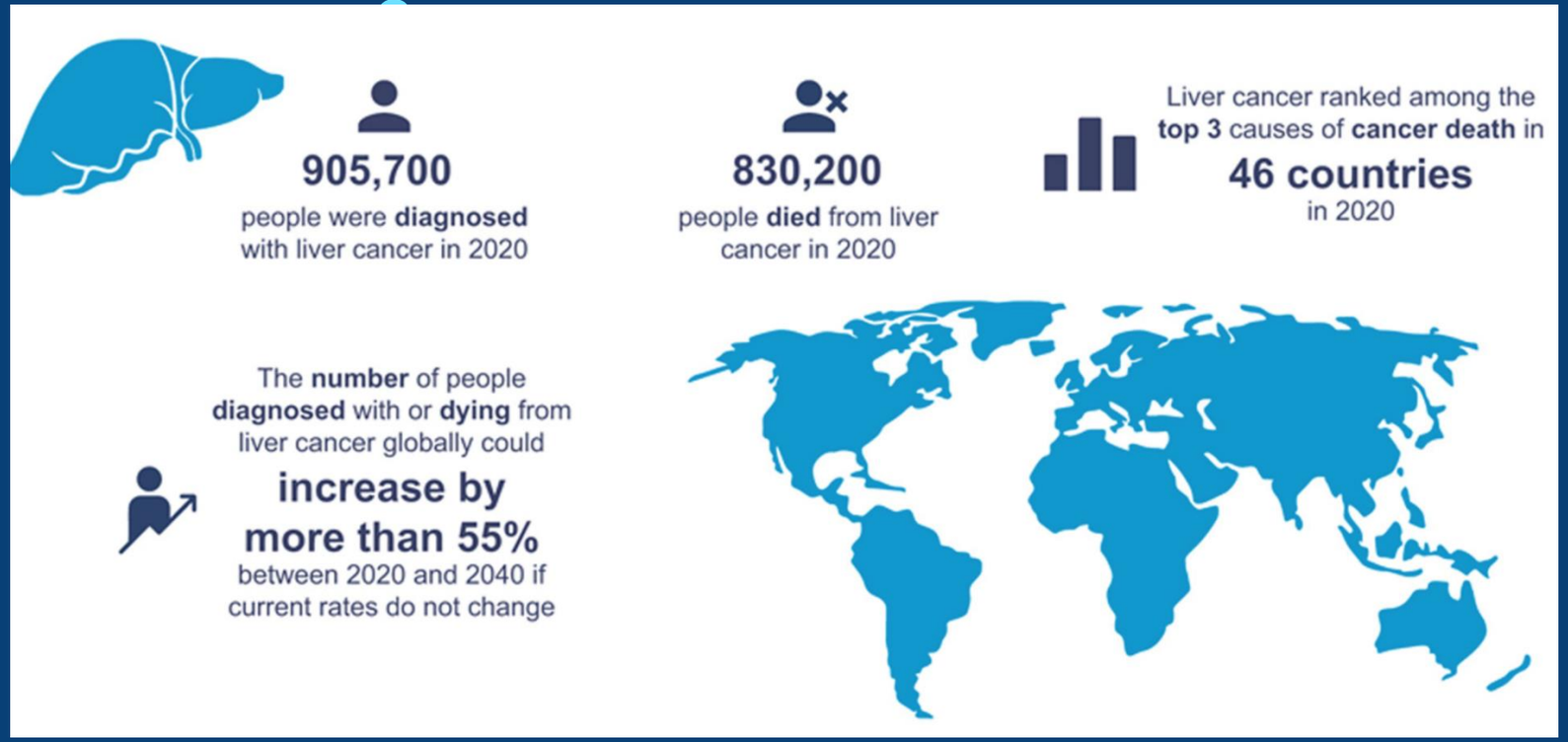
2nd Medical Conference on Plant-Based Nutrition
Athens, March 8, 2025

CTER

THE GROWING BURDEN OF LIVER CANCER

An epidemic

Global Burden of Liver

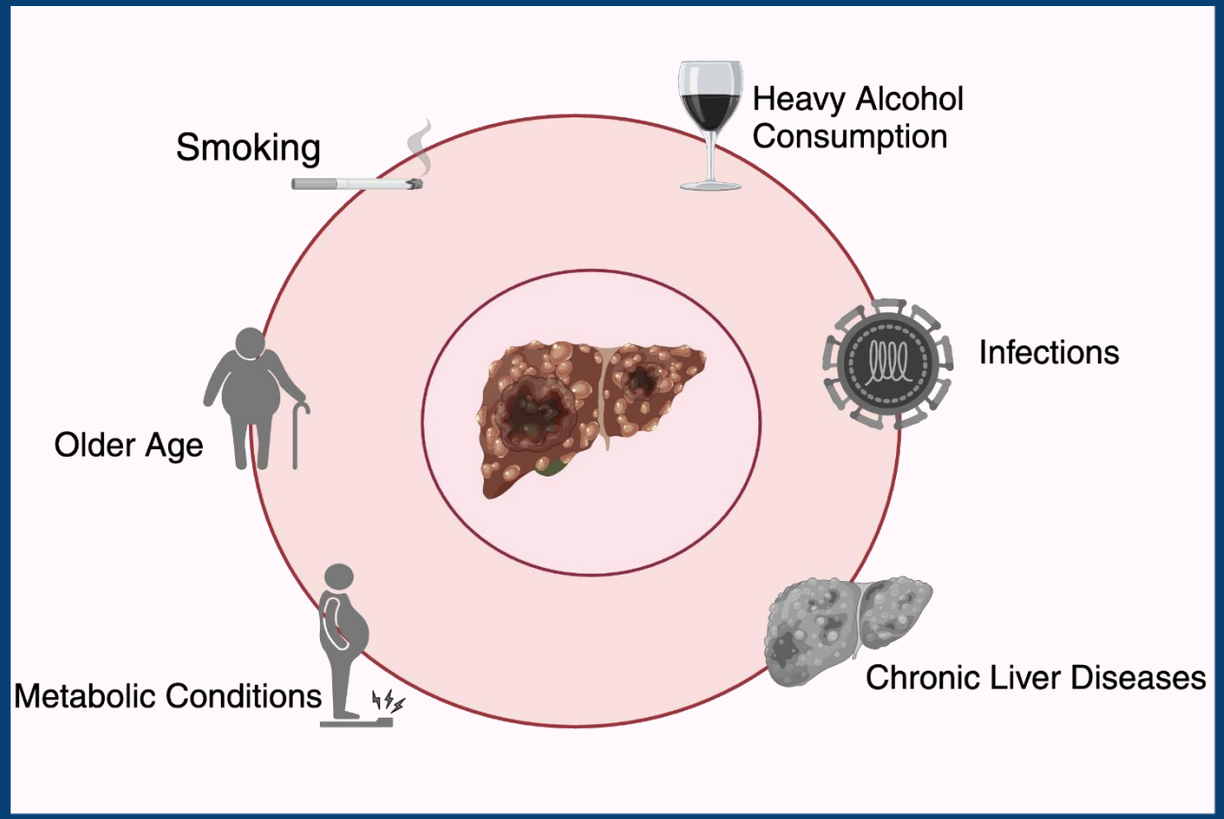


- HCC is the most common type of liver cancer
- Incidence and mortality rates have increased in the past four decades
- 5-year survival rate: 22%

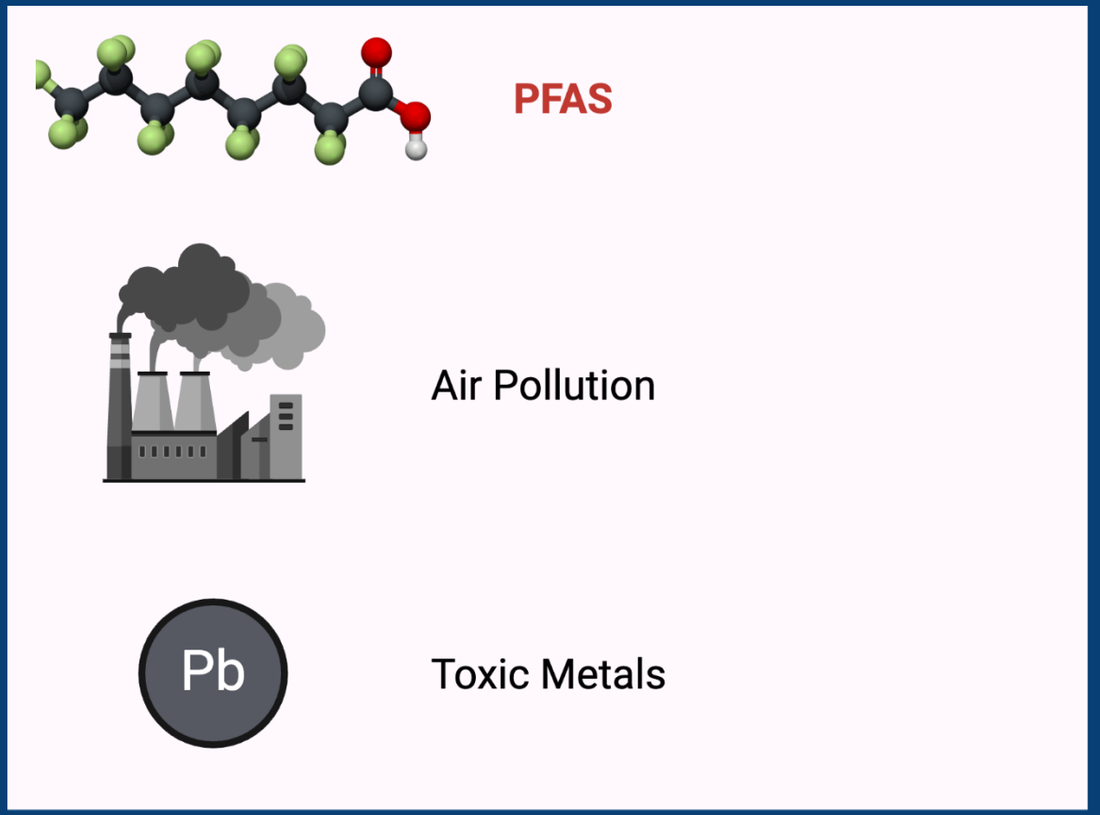
American Cancer Society, 2024; Ioannou, 2021, Journal of Hepatology; Rumgay et al., 2022, Journal of Hepatology

RISK FACTORS OF LIVER CANCER

KNOWN RISK FACTORS



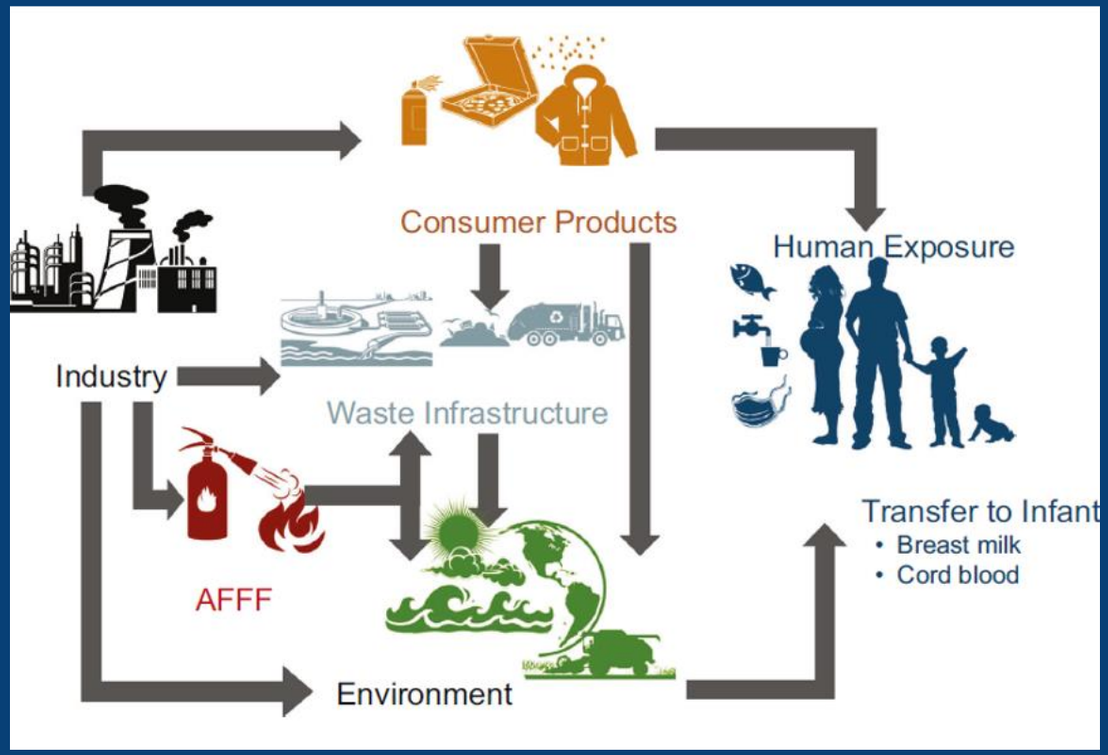
EMERGING ENVIRONMENTAL RISK FACTORS



Das KP et al., 2017; Wu X et al., 2018;
Lin CY et al., 2010; Gleason; JA et al., 2015

What are PFAS?

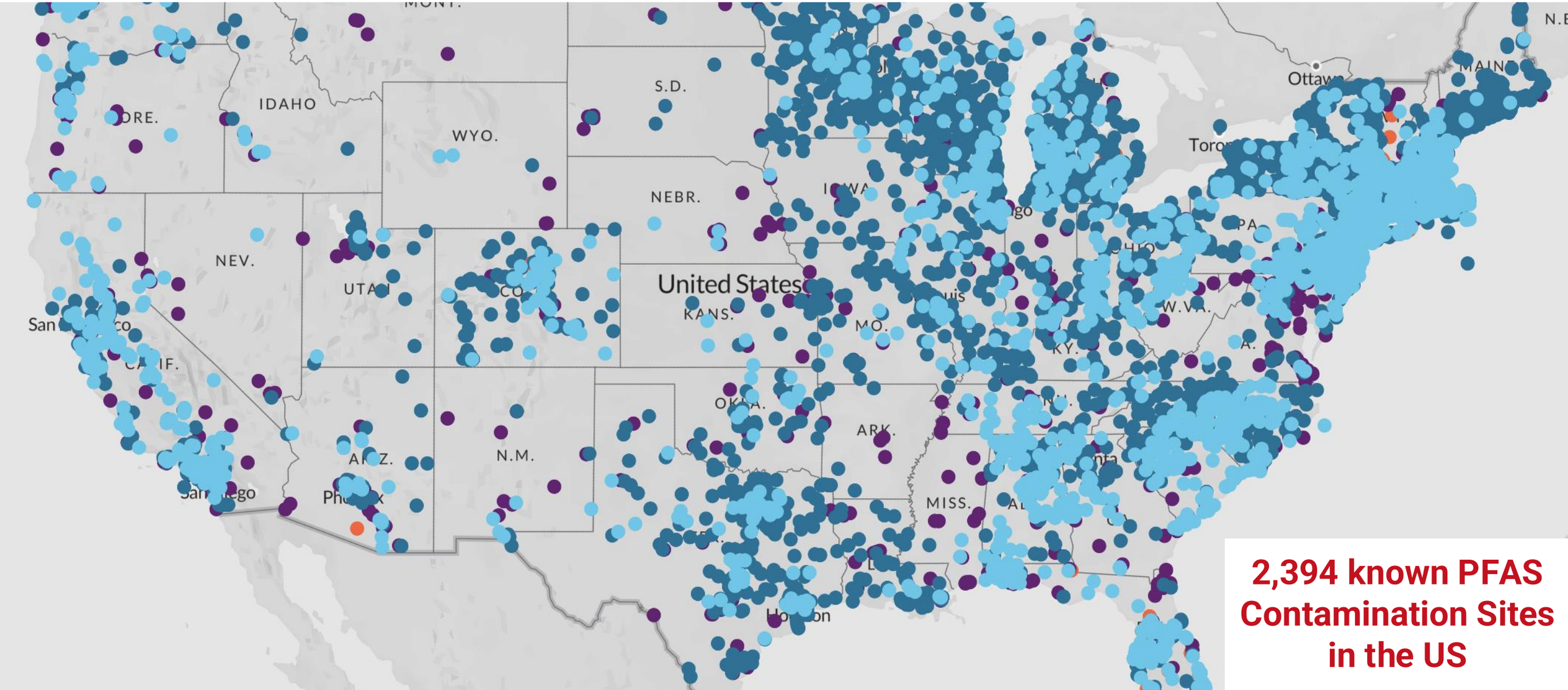
- > 7,000 chemicals
- PFAS have been widely used in industrial applications
- Resistant to degradation
- Detected in the blood of almost everyone in the U.S



Sunderland et al., J Expos Sci & Epidemiol, 2019

PFAS Water Contamination in the United States, November 20, 2024 (EWG)

Drinking water ~200 million Americans may be contaminated with PFAS (Andrews & Naidenko, 2020)



2,394 known PFAS Contamination Sites in the US

FIRST ECOLOGICAL STUDY EXAMINING PFAS EXPOSURE AND CANCER RISK

Article | Open access | Published: 09 January 2025

Associations between per-and polyfluoroalkyl substances (PFAS) and county-level cancer incidence between 2016 and 2021 and incident cancer burden attributable to PFAS in drinking water in the United States

Shiwen Li ✉, Paulina Oliva, Lu Zhang, Jesse A. Goodrich, Rob McConnell, David V. Conti, Lida Chatzi & Max Aung

Journal of Exposure Science & Environmental Epidemiology (2025) | Cite this article

Main finding: PFAS in drinking water is associated with cancers in the organ system including oral cavity/pharynx, lung, digestive system, brain, urinary system, soft tissue and thyroid

Sherlock Li, PhD
Postdoctoral Scholar, USC

Li et al., 2025,
Journal of Exposure Science & Environmental Epidemiology

FIRST SYSTEMATIC REVIEW ON HUMAN AND ANIMAL STUDIES ON PFAS AND LIVER CANCER

Title: Exposure to Per- and Polyfluoroalkyl Substances and Liver Cancer: A Systematic Review of Animal and Epidemiological Studies

Authors: Roselyn B. Tanghal[1*], Emily Beglarian[1], Arthur Stem[2], Max Aung[1], Tanya L. Alderete[3], Alan Ducatman[4], Vasilis Vasiliou[2], Rob McConnell[1], David Conti[1], Lida Chatzi[1]

Roselyn B. Tanghal, MPH
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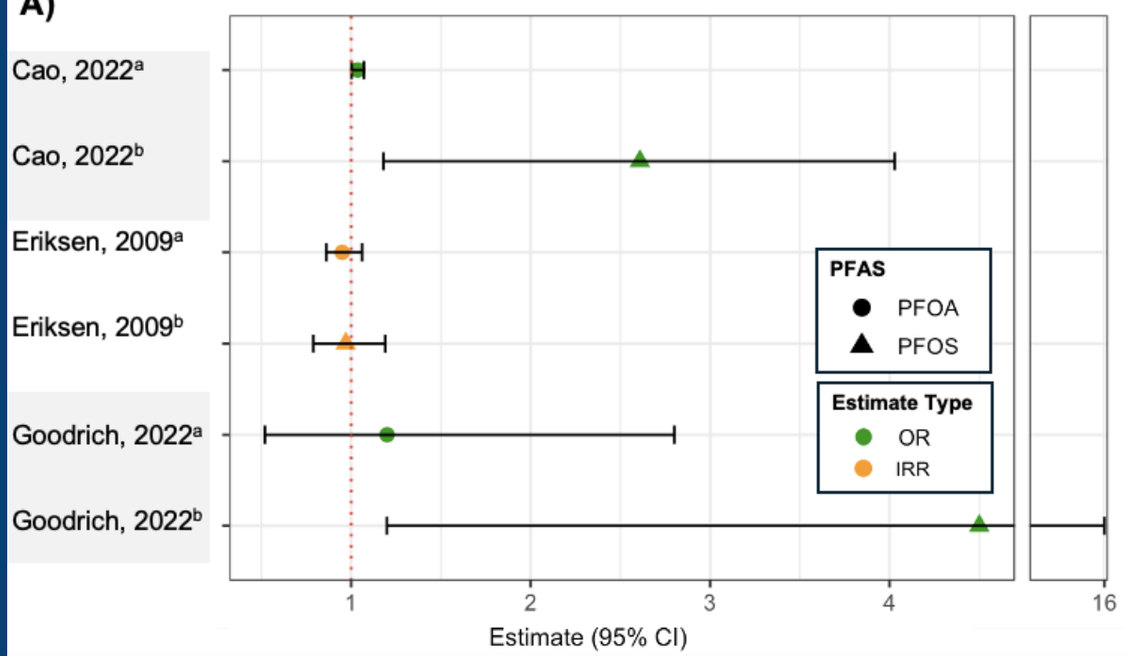
Methods and Results

- Evaluate and summarize all available **human** and **animal** studies examining exposure to PFAS and liver cancer risk and mortality
- PubMed and Embase were searched using a predefined set of keywords to identify relevant articles.
- Fourteen studies (11 human and 3 animal) met the inclusion criteria

Tanghal et al., 2025, Manuscript Under Review

ASSOCIATION BETWEEN PFOS EXPOSURE AND LIVER CANCER RISK: BIOMONITORING STUDIES

A)



B)

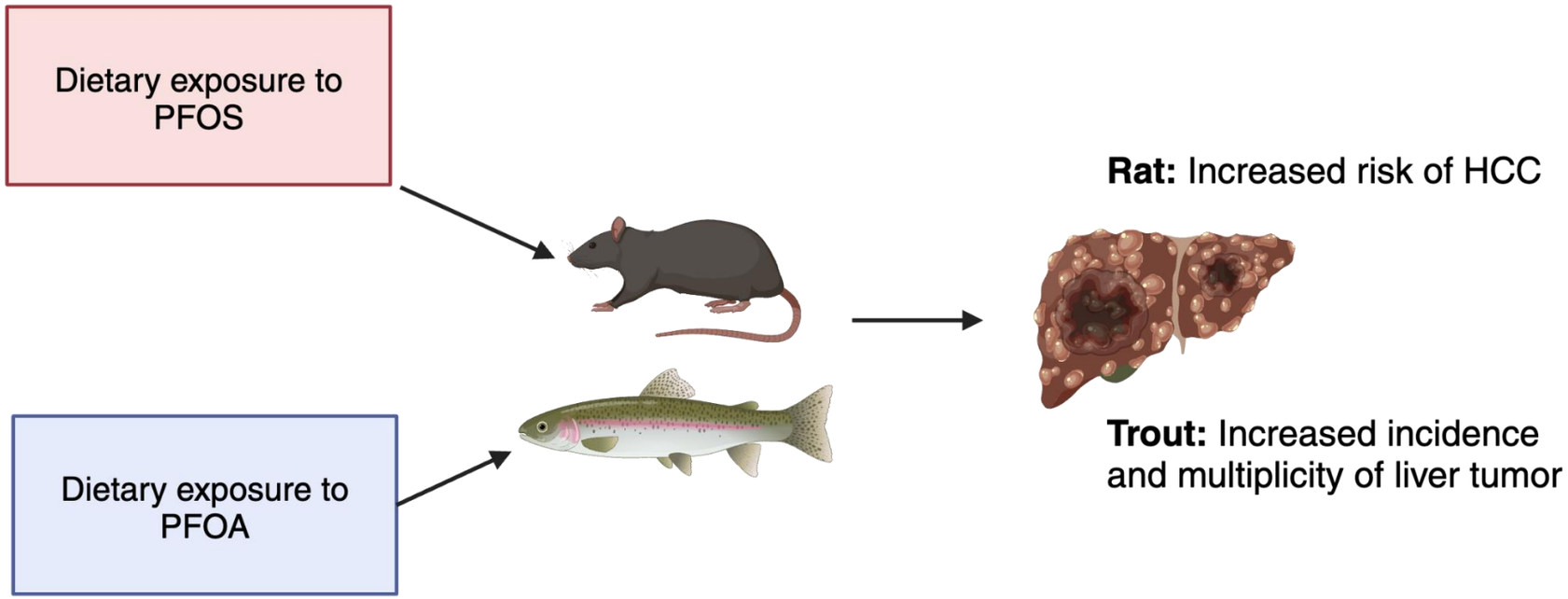
Study	Outcome[b]	Comparison
Cao, 2022[a]	LC	Per each incremental value of log-transformed PFOA
Cao, 2022[b]	LC	Per each incremental value of log-transformed PFOS
Eriksen, 2009[a]	LC	Per 1 ng/mL increase in PFOA
Eriksen, 2009[b]	LC	Per 10 ng/mL increase in PFOS
Goodrich, 2022[a]	HCC	PFOA above the 85th percentile (>8.5 µg/L) vs below
Goodrich, 2022[b]	HCC	PFOS above the 85th percentile (>54.9 µg/L) vs below

This figure displays the effect estimates from included human biomonitoring studies, two studies (Cao, 2022 and Goodrich, 2022) found positive associations with high PFOS levels and liver cancer risk.

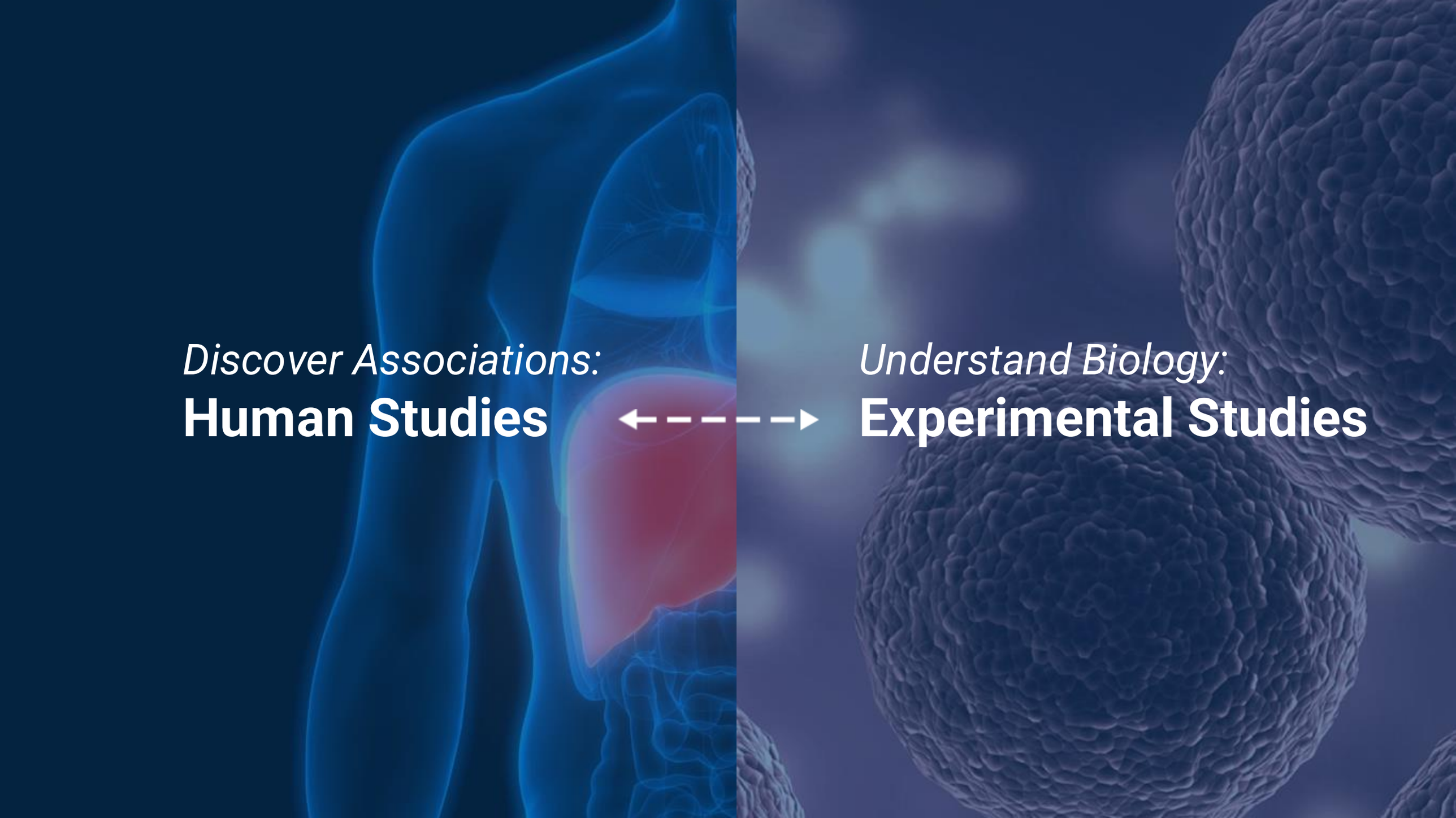
Tanghal et al., 2025, Manuscript Under Review

ASSOCIATION BETWEEN PFOS EXPOSURE AND LIVER CANCER RISK: ANIMAL STUDIES

- All three studies (one study in rat and two studies in rainbow trout) demonstrated a dose-dependent increase in liver tumor incidence following PFAS exposure.



Butenhoff et al., 2012, Toxicology
Benninghoff et al., 2012, Toxicological Sciences
Titlton et al., 2008, Environmental Health Perspectives


Discover Associations:
Human Studies
Understand Biology:
Experimental Studies

PFAS ALTER LIPID METABOLISM & INCREASES THE RISK OF CARCINOGENSIS: AN EXPERIMENTAL STUDY WITH LIVER SPHEROIDS

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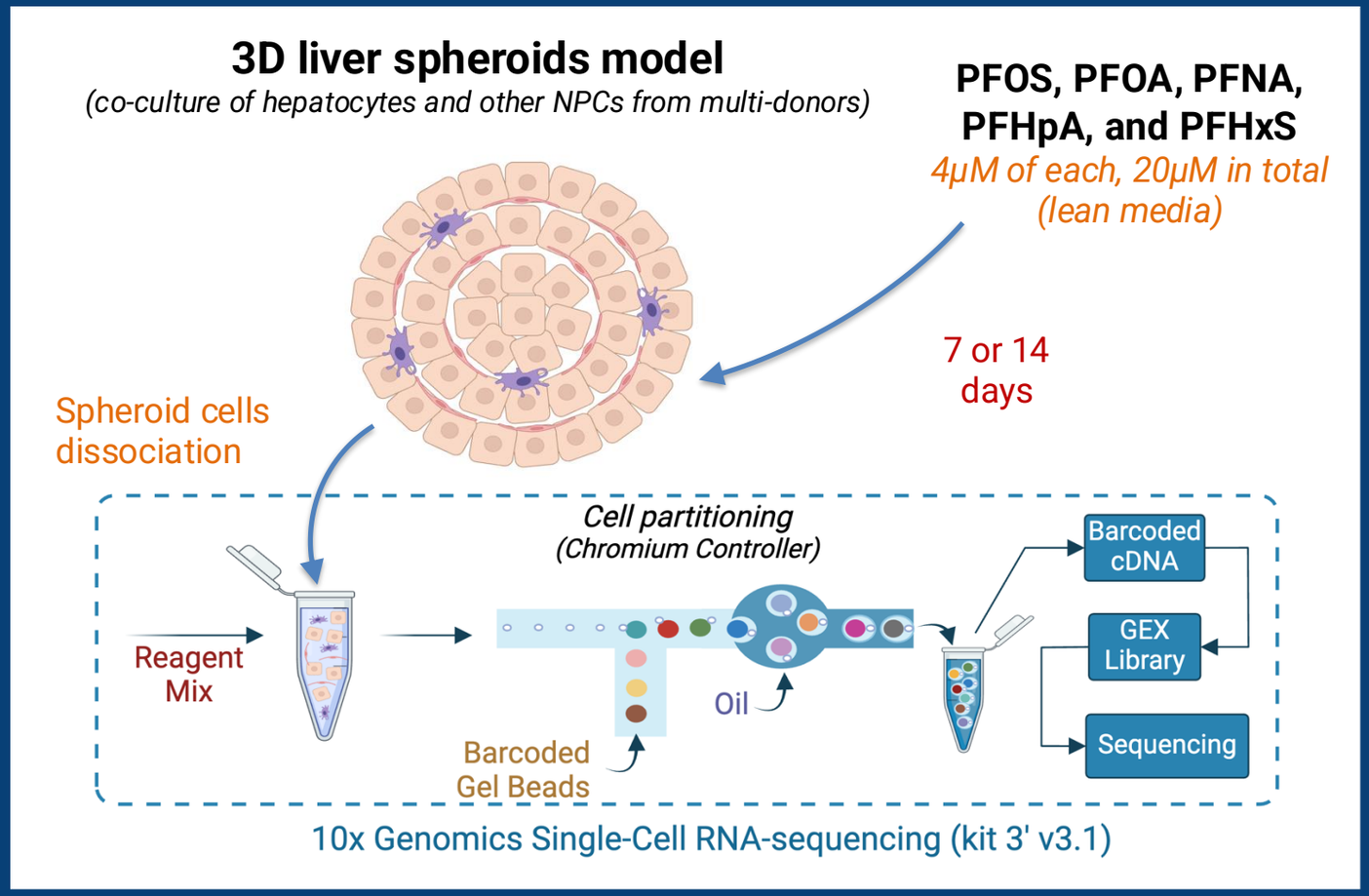
DISCOVER ASSOCIATIONS → UNDERSTAND BIOLOGY

R01ES030691,P30ES007048

EXPERIMENTAL STUDY DESIGN

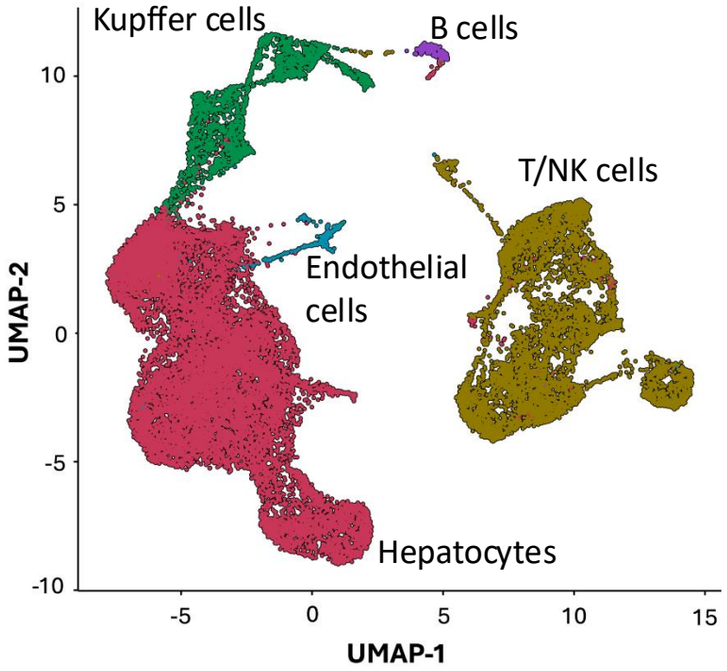


Aim 1: Identify the hepatic biological pathways impacted by short- and long-term exposure to individual PFAS and PFAS mixtures commonly found in human plasma and drinking water.

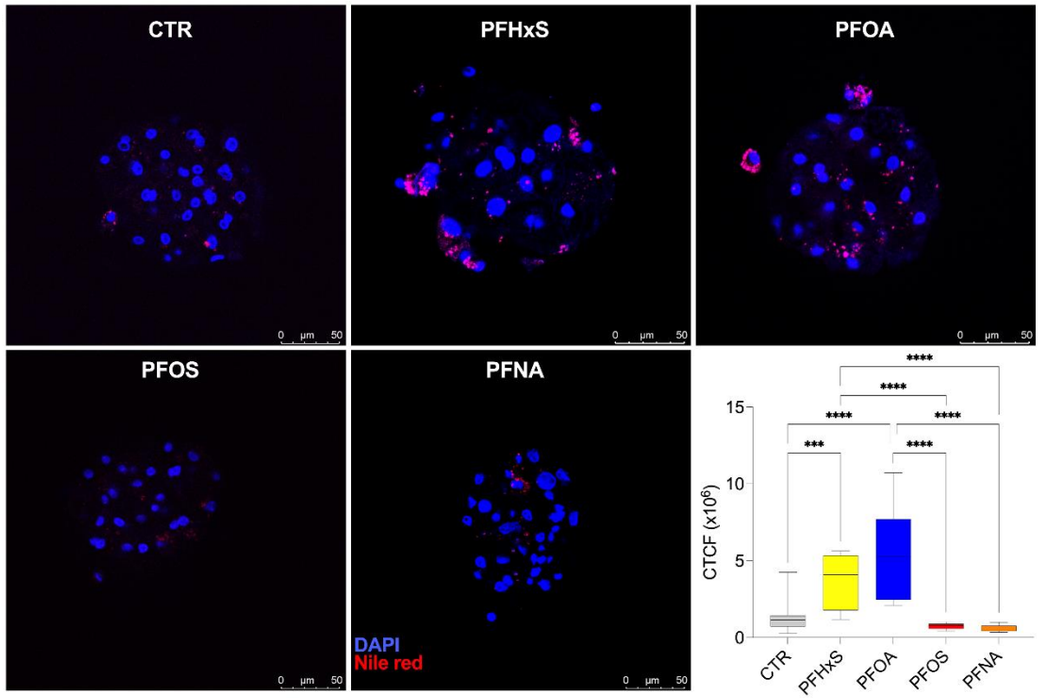
Aim 2: Test if PFAS removal can reverse or attenuate the harmful effects of PFAS exposure.

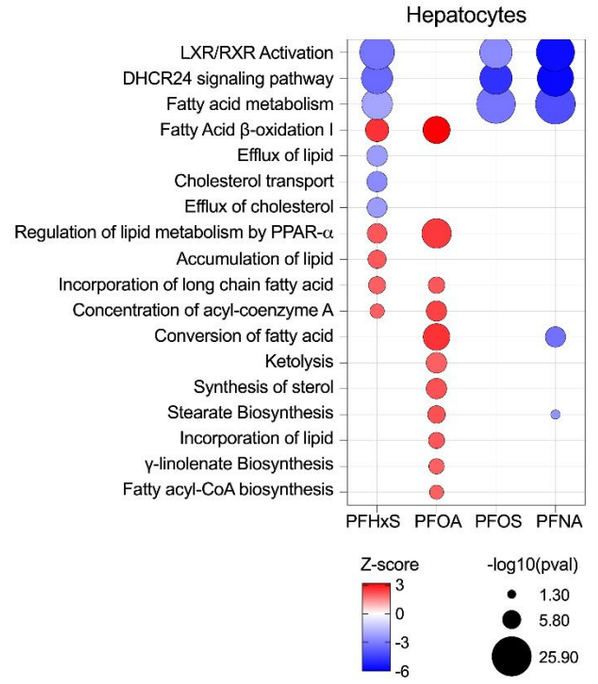
EXPERIMENTAL STUDY: STEATOGENIC EFFECTS

Cell Clusters



Steatogenic effect



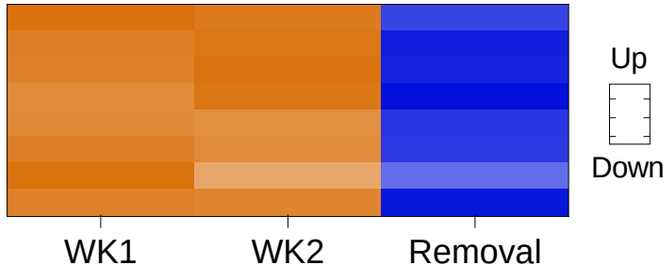


Golden-Mason & Salomon et al. EHP (under review) 2025

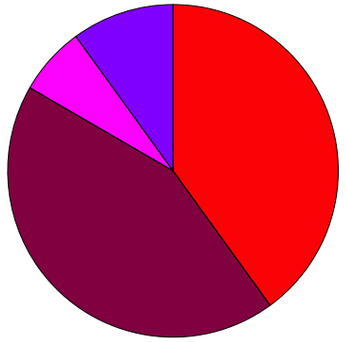
R01ES030691,P30ES007048

EXPERIMENTAL STUDY: PFAS MIXTURES AND REMOVAL

Gene Expression and Protein Translation



2 weeks of exposure



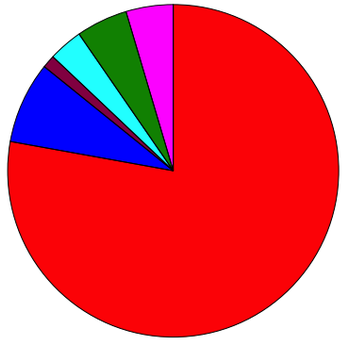
- Cancer
- Cell Death
- Cellular stress and injury
- Inflammatory Response

Hepatic effects

↑ Inflammation ↑ Necrosis
↑ Steatosis ↑ HCC

Adaptation to PFAS exposure

1 week of exposure

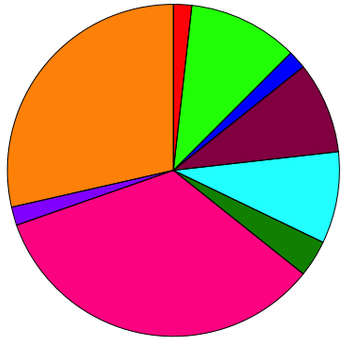


- Cancer
- Cell Cycle
- Cell Death
- Cell Survival
- Cellular Proliferation
- Cellular stress and injury

Hepatic effects

↑ Fibrosis ↑ Necrosis

1 week of exposure + 1 week of recovery



- Cancer
- Carbohydrate Metabolism
- Cell Cycle
- Cell Death
- Cell Survival
- Cellular Proliferation
- Cellular stress and injury
- Inflammatory Response
- Lipid Metabolism

Hepatic effects

↑ Cell proliferation ↑ Hepatotoxicity

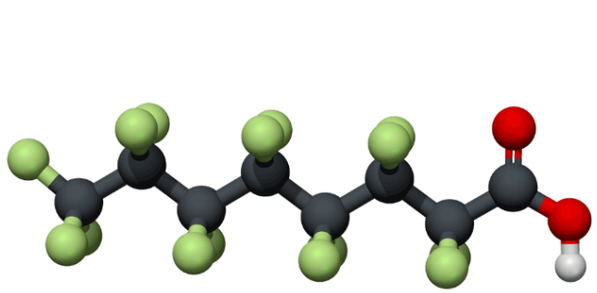
Normalization of liver functions

Diet is a mitigator between PFAS and Liver Cancer

March 9, 2025

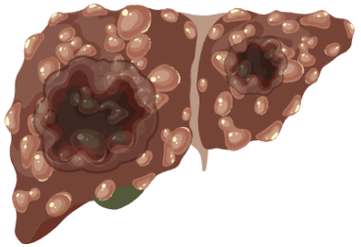
HYPOTHESIS

Diet is a mitigator between PFAS and Liver Cancer



PFAS

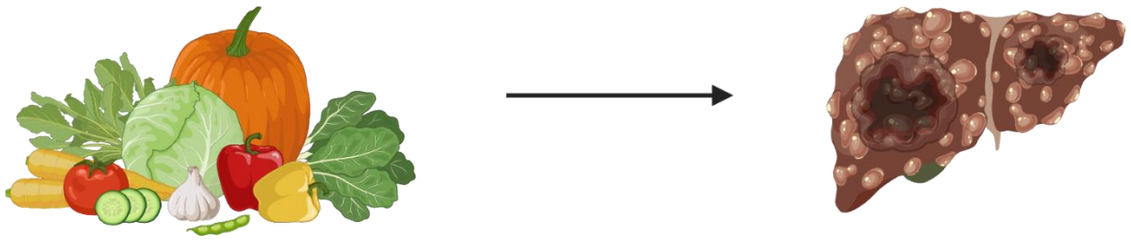
Diet



Liver Cancer

WHAT WE KNOW: PLANT BASED DIET AND LIVER CANCER

- Greater adherence to plant-based diets is associated with a reduced risk of HCC.
- Dietary fibers from whole grains, fruits, and vegetables have beneficial effects on liver cancer through reduction of liver fat content.
- A systematic review of 30 studies find that increased intake of vegetables, whole grains, and certain micronutrients were associated with a reduced risk of HCC.



Kim et al., 2023, The American Journal of Clinical Nutrition; George et al., 2020, Nutrients

PLANETARY HEALTH DIET

Higher consumption of adequacy components **(whole grains, whole fruits, non-starchy vegetables, nuts and seeds, legumes, and unsaturated oils)**

- Developed by the EAT-Lancet Commission, a group of 37 scientists from 16 countries to promote health and protect the planet
- Optimal diet emphasizing plant-based foods with limited animal products for healthy diet and sustainable food production
- Limited animal products supports sustainable food production by lowering greenhouse gas emissions and reduce land and water use

EAT-Lancet Report, 2019

PLANETARY HEALTH DIET AND LIVER CANCER Ongoing Study

Evaluate the association between adherence to Planetary Health Diet Index and Liver Cancer

Aim

- Assess the relationship between adherence to PHD and liver cancer mortality in a large, population-based cohort.

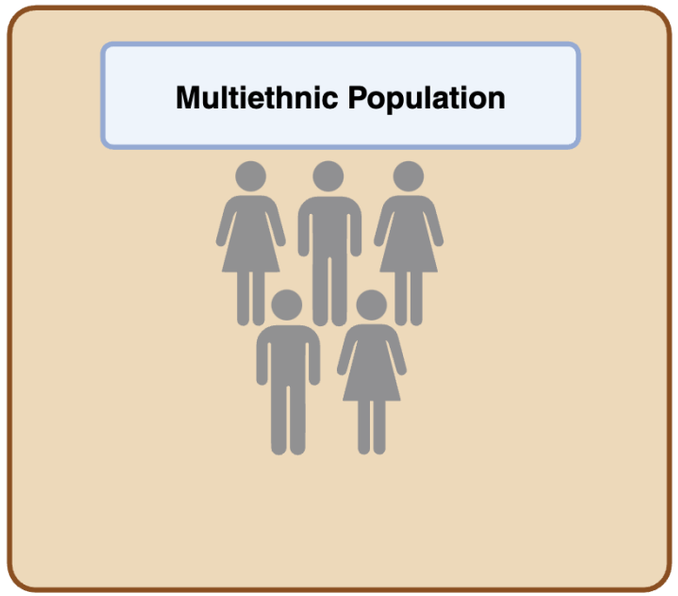
MEC

UNIVERSITY OF HAWAI'I CANCER CENTER

USC University of Southern California

The Multiethnic Cohort Study

Understanding ethnic differences in cancer to prevent it in all populations

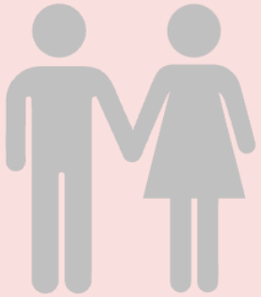


- **Prospective cohort study**
- **>200,000 participants from Los Angeles and Hawaii**
- **>20 years follow up time**

Kolonel et al., 2000, American Journal of Epidemiology
Stram et al., 2000, American Journal of Epidemiology

METHODS

Participant Recruitment



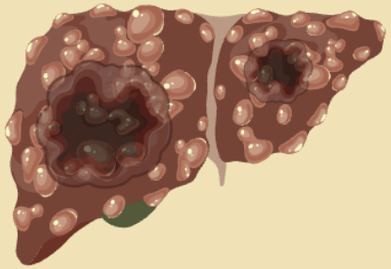
Los Angeles, CA and Hawaii

Diet

Baseline questionnaire

Between 1993 to 1996

Identification of Liver Cancer Cases



Linkage with SEER in Hawaii and California

DEMOGRAPHICS OF PARTICIPANTS

Demographics

Variables	Controls	Cases
	N (%) or Mean (SD)	N (%) or Mean (SD)
Age at cohort entry Mean(SD)	59.9 (8.84)	61.0 (7.82)
Area		
Hawaii	99285 (48.3%)	511 (45.7%)
Los Angeles	106173 (51.7%)	608 (54.3%)
Sex		
Male	92123 (44.8%)	720 (64.3%)
Female	113335 (55.2%)	399 (35.7%)
Ethnicity		
Black	33148 (16.1%)	130 (11.6%)
Native Hawaiian	13790 (6.7%)	76 (6.8%)
Japanese	54409 (26.5%)	344 (30.7%)
Latino	45151 (22.0%)	364 (32.5%)
Other	11630 (5.7%)	75 (6.7%)
Non-Hispanic White	47330 (23.0%)	130 (11.6%)
BMI (kg/m^2)	26.5 (5.08)	27.5 (4.76)

DIET AND HCC Preliminary Results

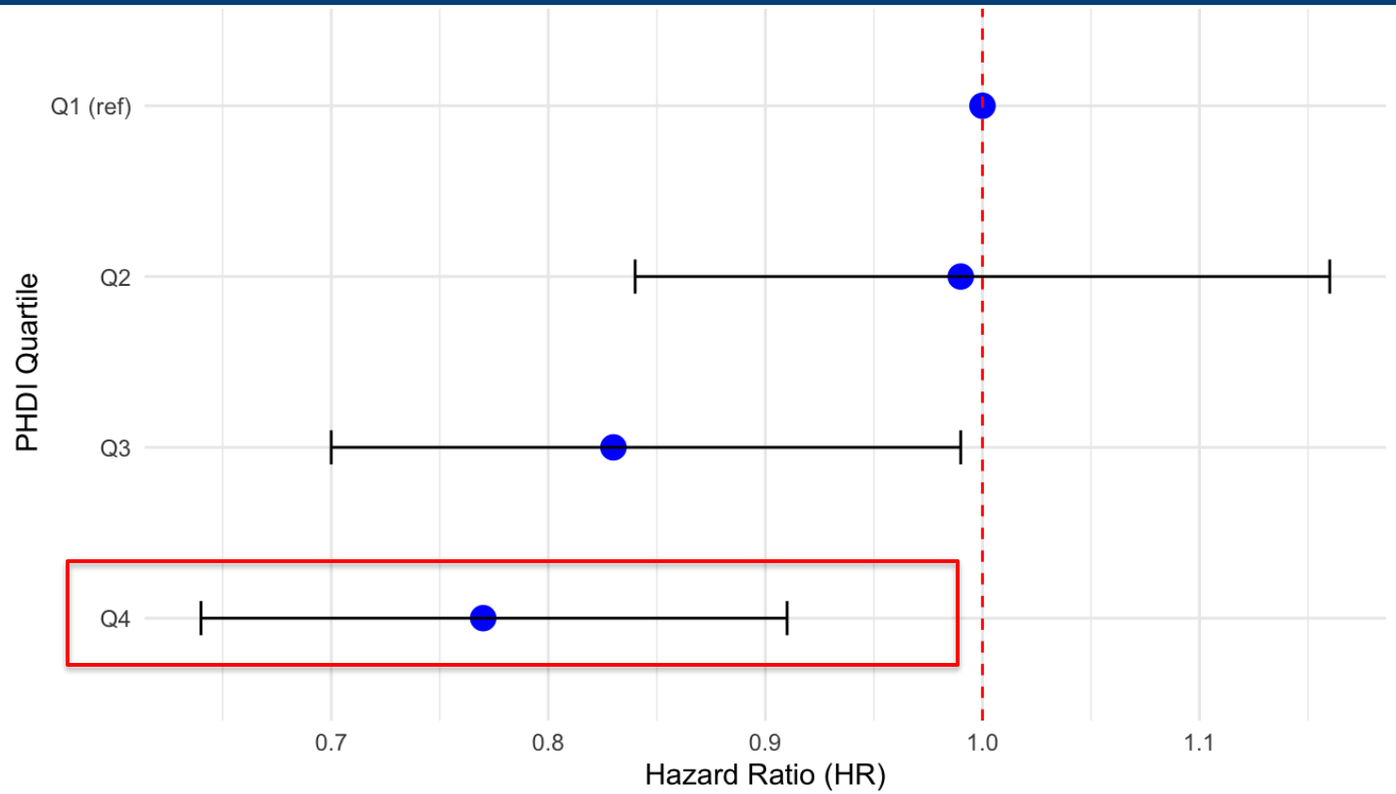
Table 2. Planetary Health Diet Index and Hepatocellular Carcinoma Risk in the Multiethnic Cohort Study

Quartile (range)	Cases	HR*	HR†
Q1 (3.7– 46.9)	293	1.0 (ref)	1.0 (ref)
Q2 (47.0–54.2)	307	0.99 (0.84,1.17)	0.99 (0.84,1.16)
Q3 (54.3–62.0)	269	0.84 (0.71, 0.99)	0.83 (0.70, 0.99)
Q4 (62.1–119.3)	250	0.78 (0.66, 0.93)	0.77 (0.64, 0.91)
P value for trend		0.001	0.001

*Adjusted for age at cohort entry, sex, and race and ethnicity.
†Additionally adjusted for BMI and diabetes history.

Compared to low adherence to Planetary Health Diet (PHD) in Q1, high adherence in Q4 is associated with a 23% lower risk for HCC.

POPULATION ATTRIBUTABLE FACTOR OF PHD FOR HCC RISK



PAF = 6.23% of HCC cases could be prevented if the entire population followed a high-PHD (Q4) diet rather than a low PHD (Q1) diet.

Model adjusted for age, sex, race and ethnicity, BMI, and diabetes status.

The Role of Plant-Based Diets in Reducing Chemical Exposures: A Pathway to Healthier Living

March 9, 2025

DIET AND EXPOSURE TO CHEMICALS

Chemical Exposures based on Diet	
Animal-based diet	**Plant-based diet**
✔ Per- and polyfluoroalkyl substances (PFAS)	✔ Pesticides in non-organic foods
✔ Dioxins and Polychlorinated biphenyls (PCBs)	
✔ Pesticides	
✔ Bisphenols (BPA)	
✔ Organochlorine Pesticides (DDE & DDT)	
✔ Polybrominated diphenyl ethers (PBDEs)	
✔ Phthalates	

- Animal-based diets contain many chemical contaminants compared to plant-based diets.

Guo et al., 2019, International Journal of Environmental Research and Public Health; Serrano et al., 2014, Environmental Health; Baudry et al. 2021, Food and Chemical Toxicology

WHAT WE KNOW ABOUT DIET and PFAS

environment INTERNATIONAL

Associations of dietary intake and longitudinal measures of per- and polyfluoroalkyl substances (PFAS) in predominantly Hispanic young Adults: A multicohort study

Hailey E. Hampson [a], Elizabeth Costello [a], Douglas I. Walker [b], Hongxu Wang [a], Brittney O. Baumert [a], Damaskini Valvi [b], Sarah Rock [a], Dean P. Jones [c], Michael I. Goran [d], Frank D. Gilliland [a], David V. Conti [a], Tanya L. Alderete [e], Zhanghua Chen [a], Leda Chatzi [a], Jesse A. Goodrich [a,*]

High Intake of Tea, Pork, Hot Dogs and Processed Meats associated with higher PFAS levels

Existing Evidence

- Diet is a source of PFAS exposure through the intake of contaminated foods
- Key sources of dietary PFAS:
  - Seafood
  - Meat
  - Dairy
- PFAS exposure can also indirectly occur from contaminated food packaging and cookware

Hampson et al., 2024, Environment International
Roth et al., 2020. Frontiers in Toxicology

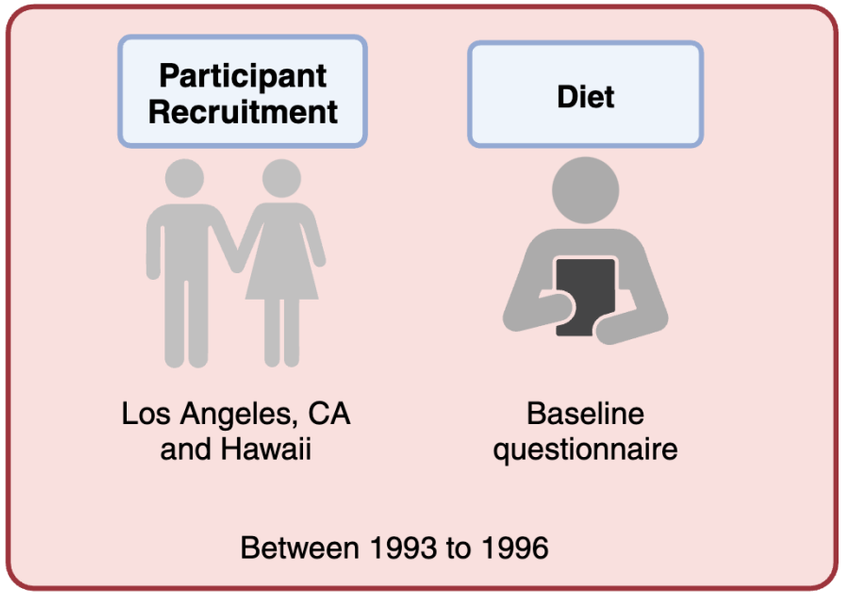
Planetary Health Diet and PFAS Ongoing Study

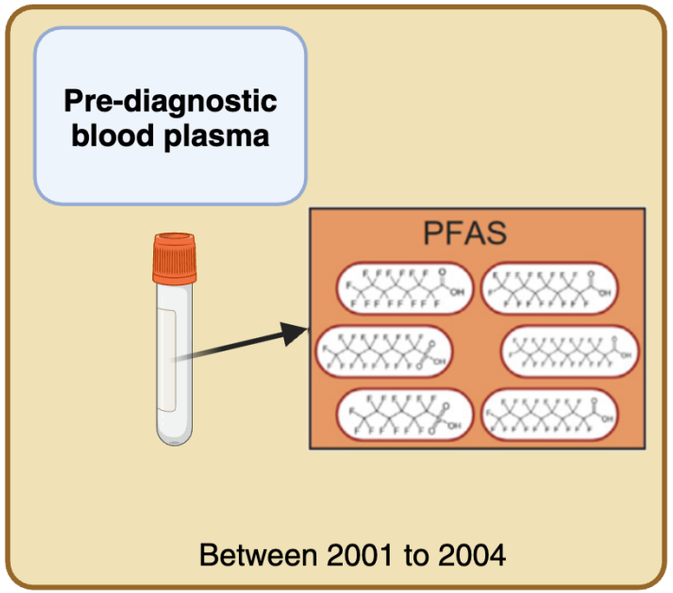
Evaluate the association between adherence to Planetary Health Diet and PFAS Levels.

Aim 1

- Assess the relationship between adherence to PHD and PFAS in a large, population-based cohort.

STUDY POPULATION AND METHODS: MULTIETHNIC COHORT



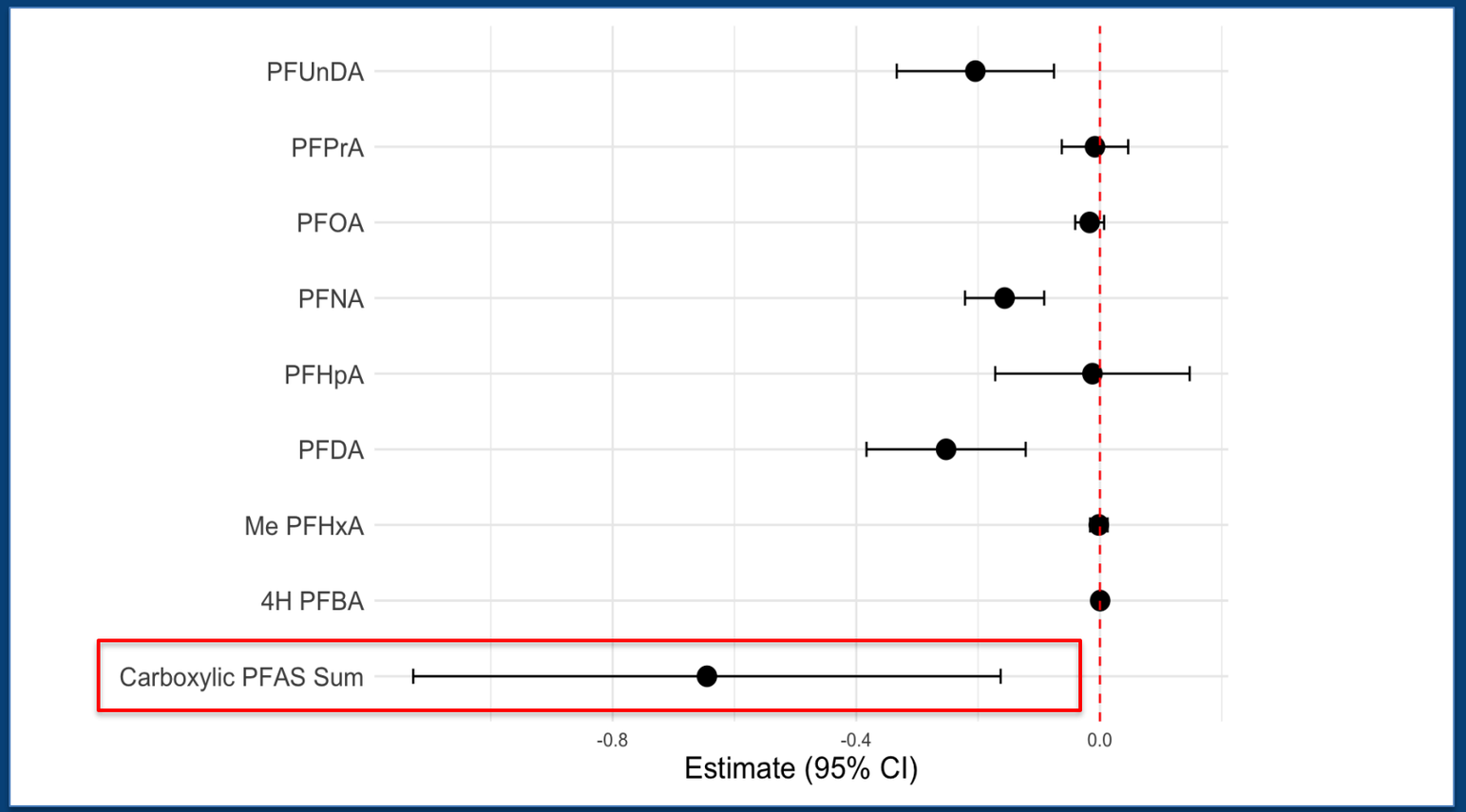


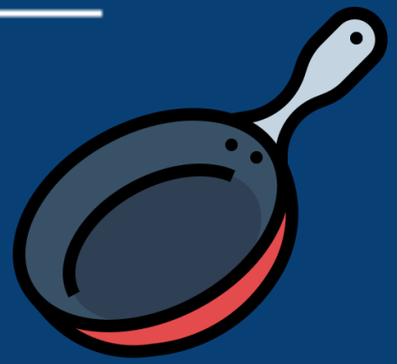
Nested case-control study design with 2,800 participants

Questionnaire collected information on food intake and dietary patterns.

PFAS were measured from blood samples collected from participants.

HIGHER ADHERENCE TO PHD IS ASSOCIATED WITH LOW EXPOSURE TO PFCAs.



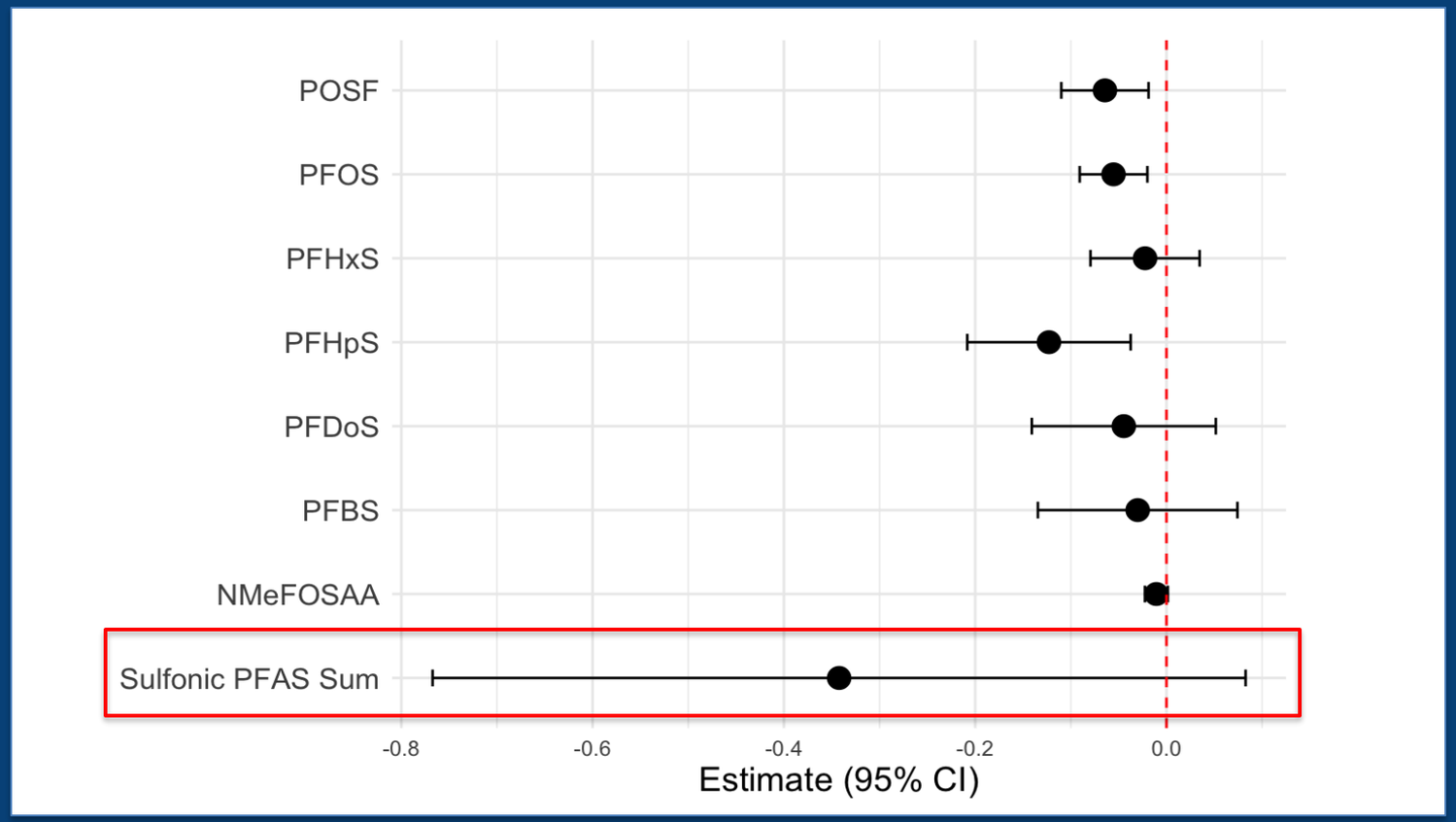


Carboxylic PFAS

- Subgroup of PFAS with a carboxyl functional group
- Found in non-stick coatings and water-resistant products

Higher PHDI score (1 unit increase in quintile) is associated with lower PFCAs.

HIGHER ADHERENCE TO PHD IS ASSOCIATED WITH LOW EXPOSURE TO PFSAs

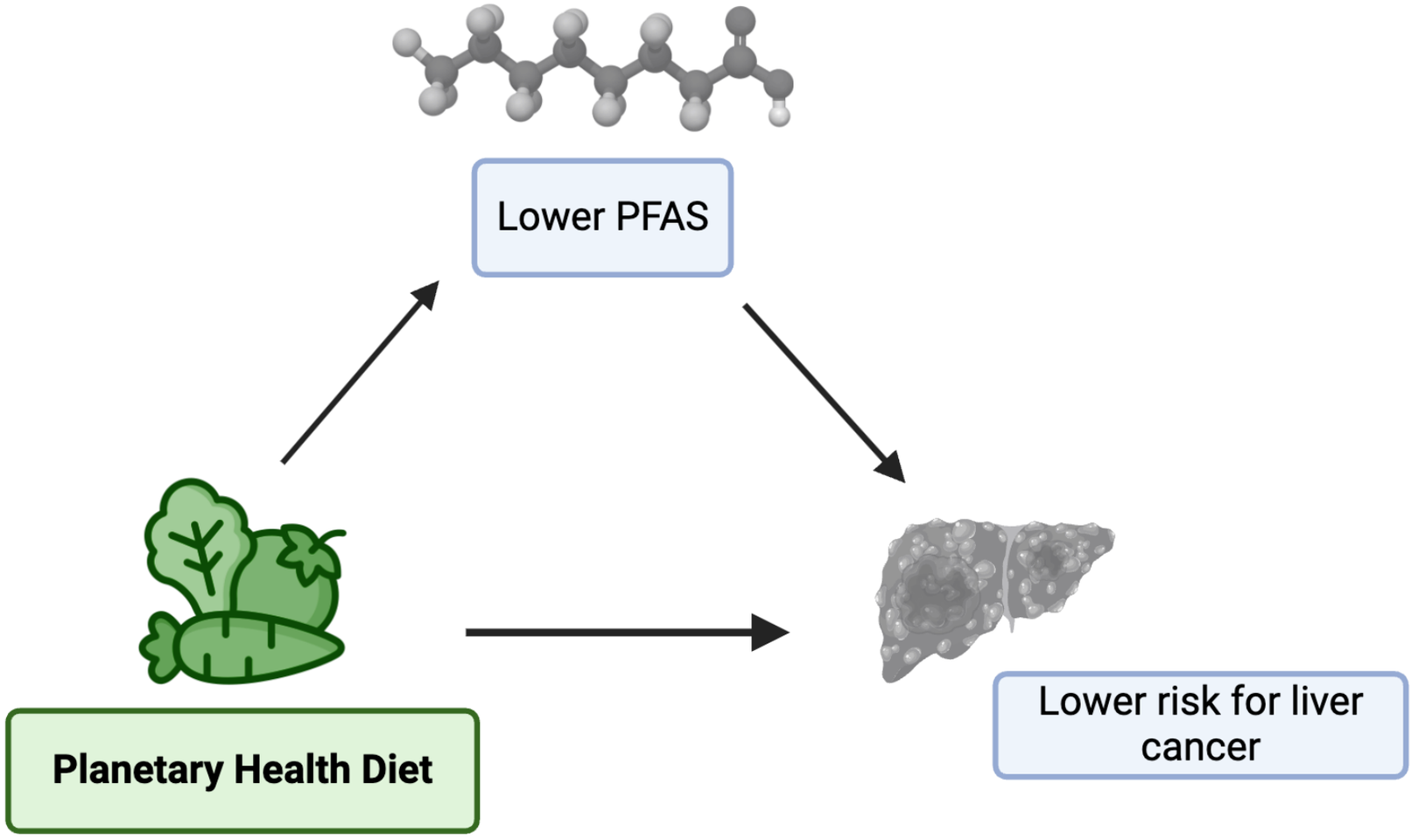


Higher PHDI score (1 unit increase in quintile) is associated with lower PFSAs.

Sulfonic PFAS

- Subgroup of PFAS with a sulfonic acid functional group
- Found in firefighting foams, water-repellent coatings, and industrial applications

CONCLUSION


Lower PFAS
Planetary Health Diet
Lower risk for liver cancer

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- Dean Jones, PhD

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Harvard University
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Mount Sinai
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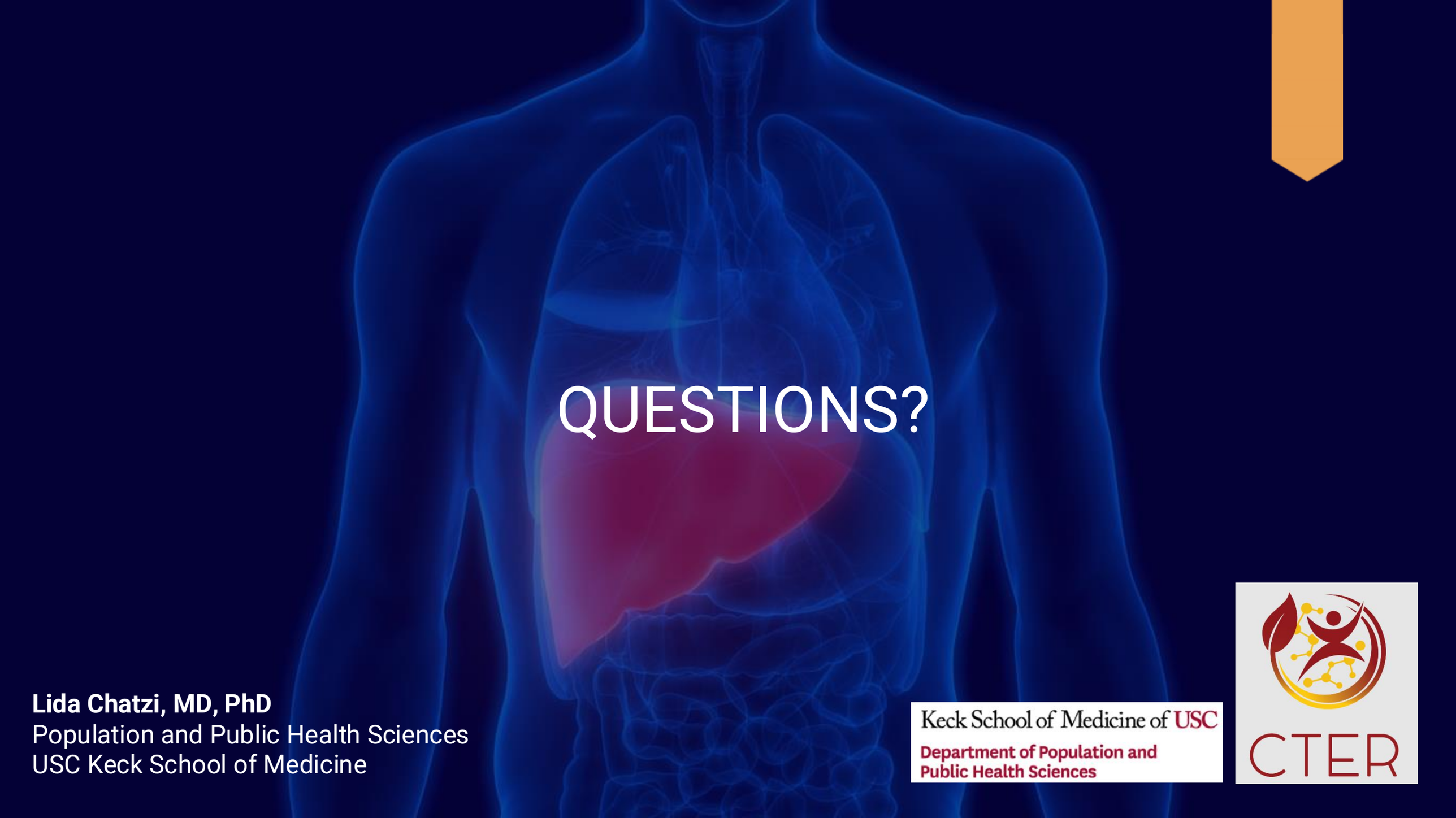
R01ES036253; U01HG013288
5P30ES007048-23; 5P30DK048522-24,
USC President's Sustainability Research Award



QUESTIONS?

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