Establishing a Life Course Approach to Cancer Prevention and Care

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No conflicts of interest related to this work

SITEMAN CANCER CENTER

BARNES-JEWISH Hospital BJC HealthCare | Washington University in St. Louis SCHOOL OF MEDICINE

Your Disease Risk™
THE SOURCE ON PREVENTION

- Funded by Breast Cancer Research Foundation - ongoing
- Funded by ACS as Clinical Research Professor (2002-2013) and by NCI through numerous mechanisms (1987-current)
- I have served as consultant to GRAIL, Inc. re their study design for marker validation
- Past legal consultant for plaintiffs on general causation in litigation: E+P and breast cancer, and talc and ovarian cancer

Importance of Youth & Teen Years in Lifelong Health

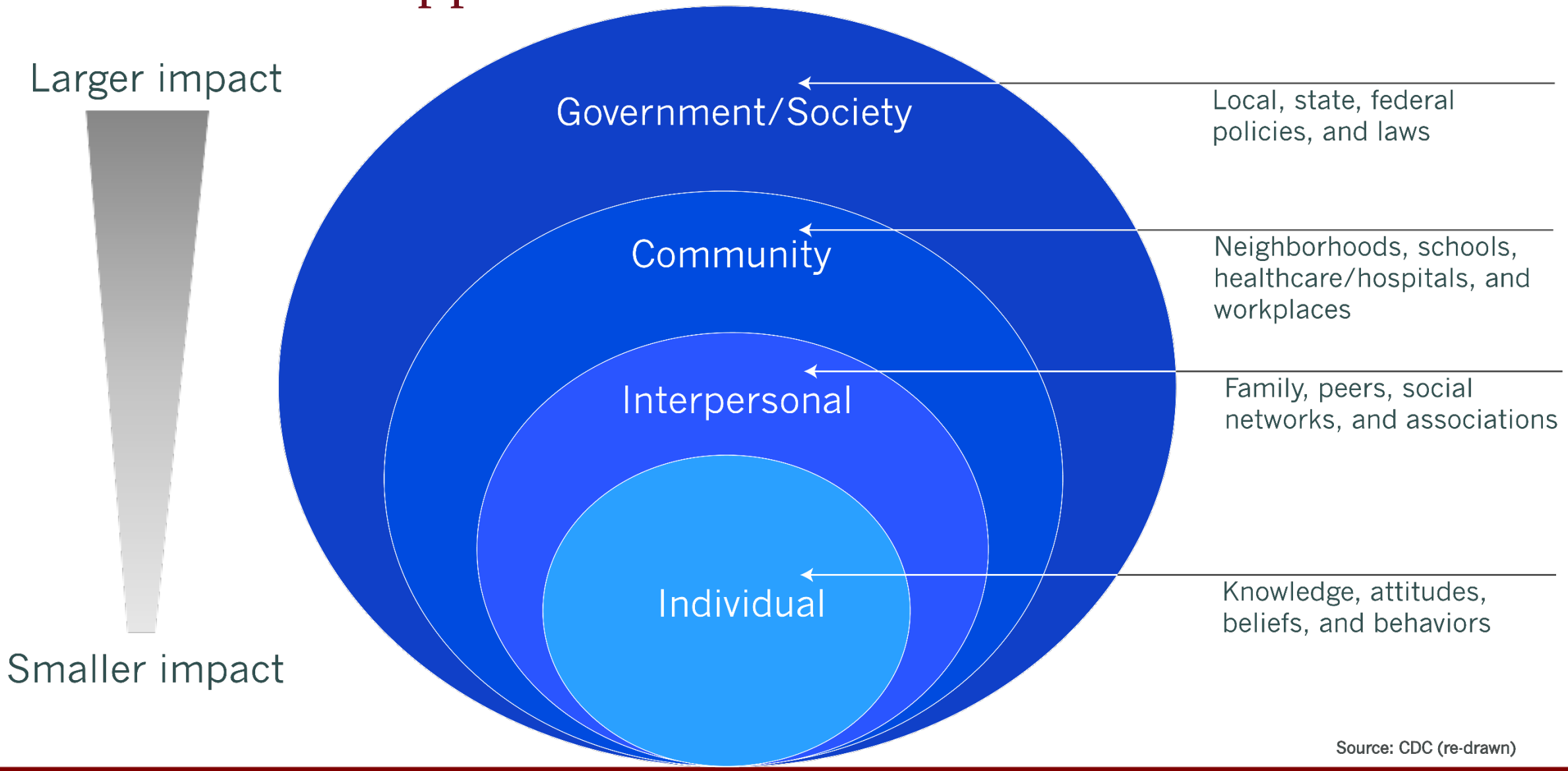
- Unique susceptibility (eg, alcohol and breast cancer)
- Establish long term risk-reducing behaviors/habits
- Establish long term knowledge and attitudes that feed broader interpersonal and societal support for prevention (e.g., family, school, workplace, policy)

Youth/Teen Behaviors Important to Cancer Risk

- Alcohol
- Tobacco
- HPV vaccination
- Sun/UV exposure
- Physical activity/inactivity
- Weight
- Diet (eg, plants, SSB, total energy)

Health & Economic Disparities

Multi-Level Approaches to Prevention



Source: CDC (re-drawn)

Alcohol

A known breast carcinogen

IARC
2007

Global

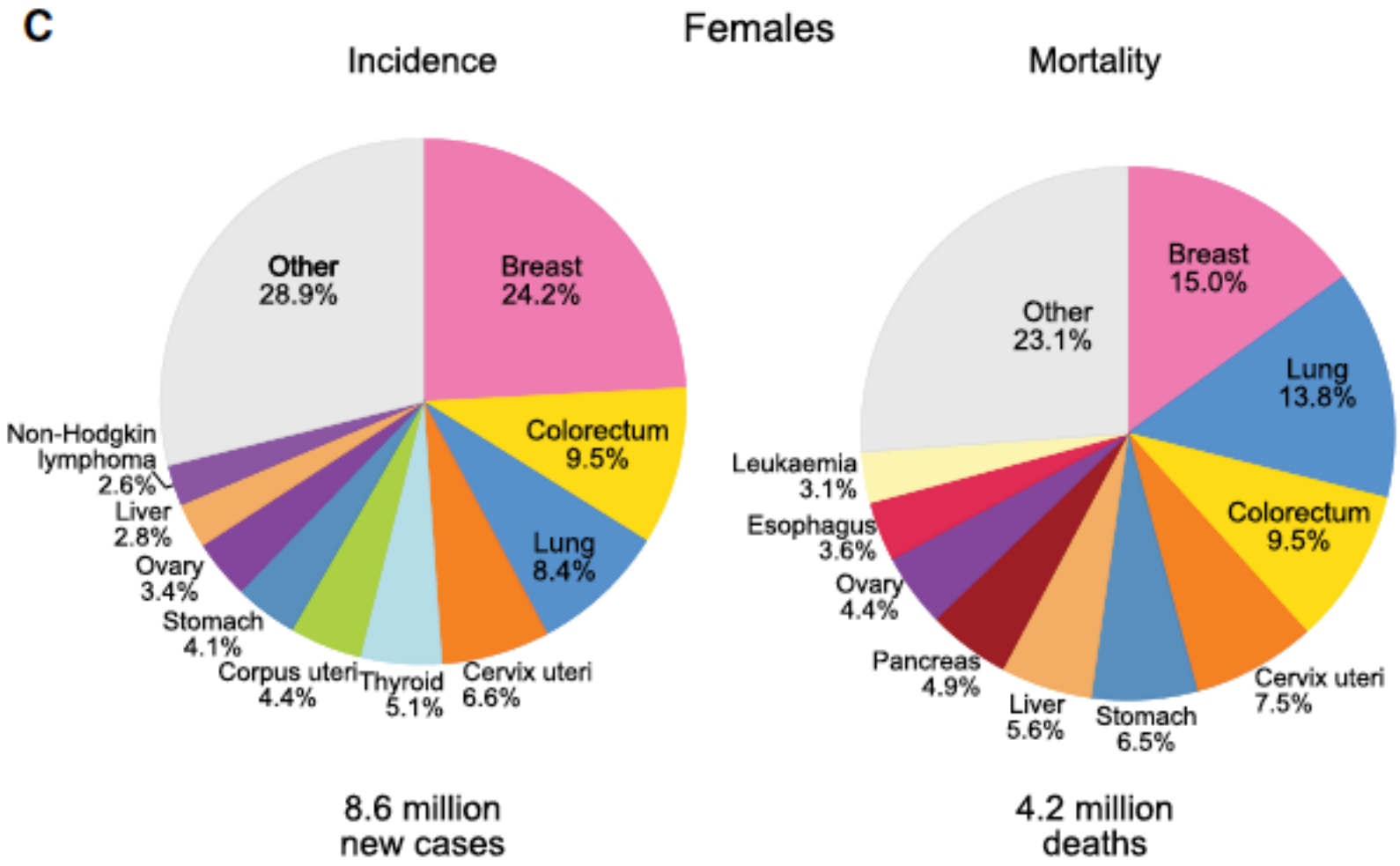
18.1 r

9.4

2.1 m

In

No.

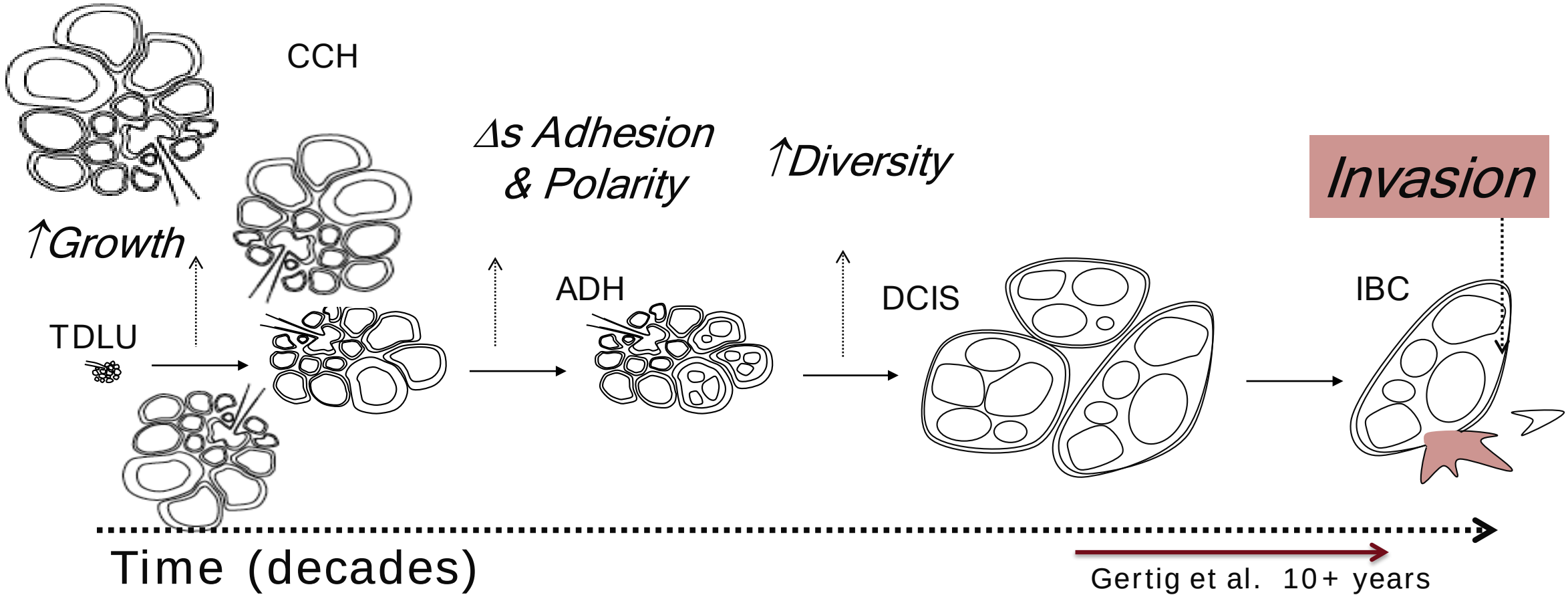


Globocan 2018 http://gco.iarc.fr/
https://www.iarc.fr/en/media-centre/pr/2018/pdfs/pr263_E.pdf
Bray et al, CA: A Cancer Journal for Clinicians 2018

Model of breast cancer development

Wellings-Jensen Model (JNCI 55:231, 1975)

Adapted from Allred



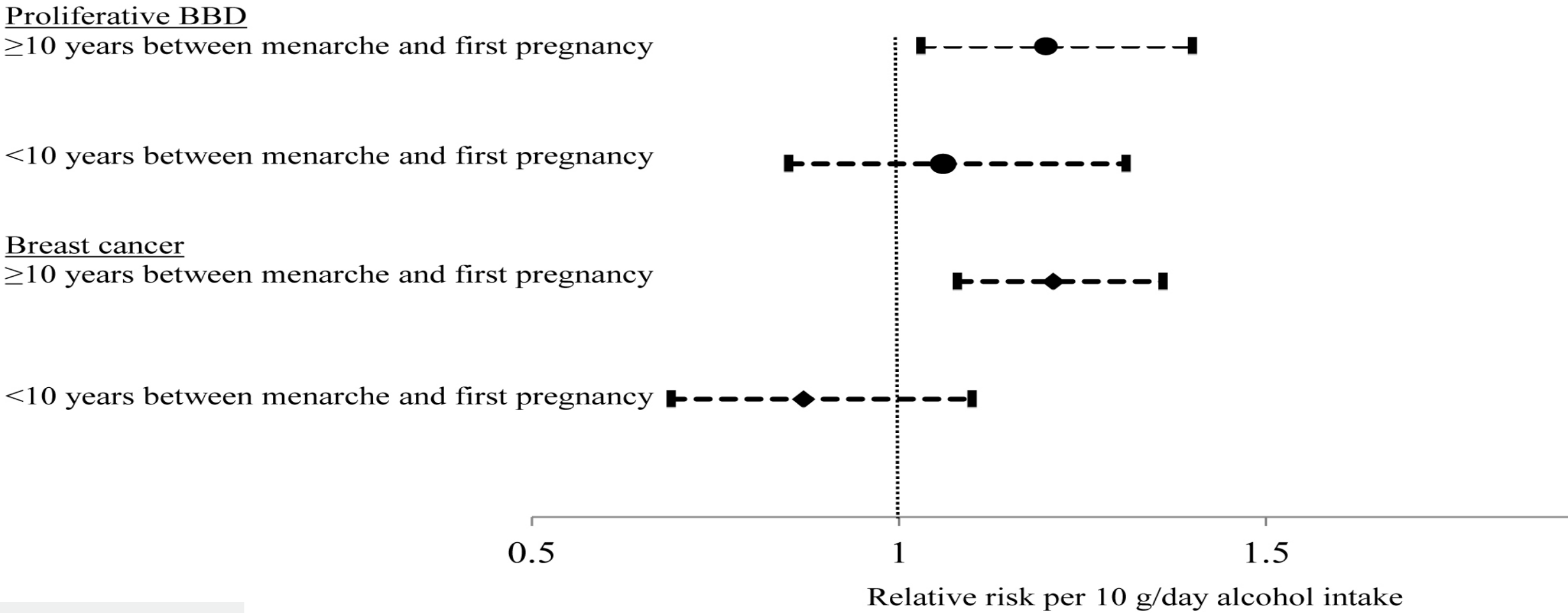
Alcohol intake, ages 18-22, incident proliferative benign breast disease (BBD), NHSII

Alcohol intake (g/day)	Cases (678)	Person-year	RR (95% CI)
None	155	64,827	1.0 reference
0.1-4.9	193	78,365	1.11 (0.89, 1.38)
5.0-14.9	236	88,310	1.36 (1.09, 1.69)
≥15	30	9519	1.35 (1.01, 1.81)
			$p_{,\ trend}$ <0.01

Parallel results in the GUTS cohort (daughters of NHSII)

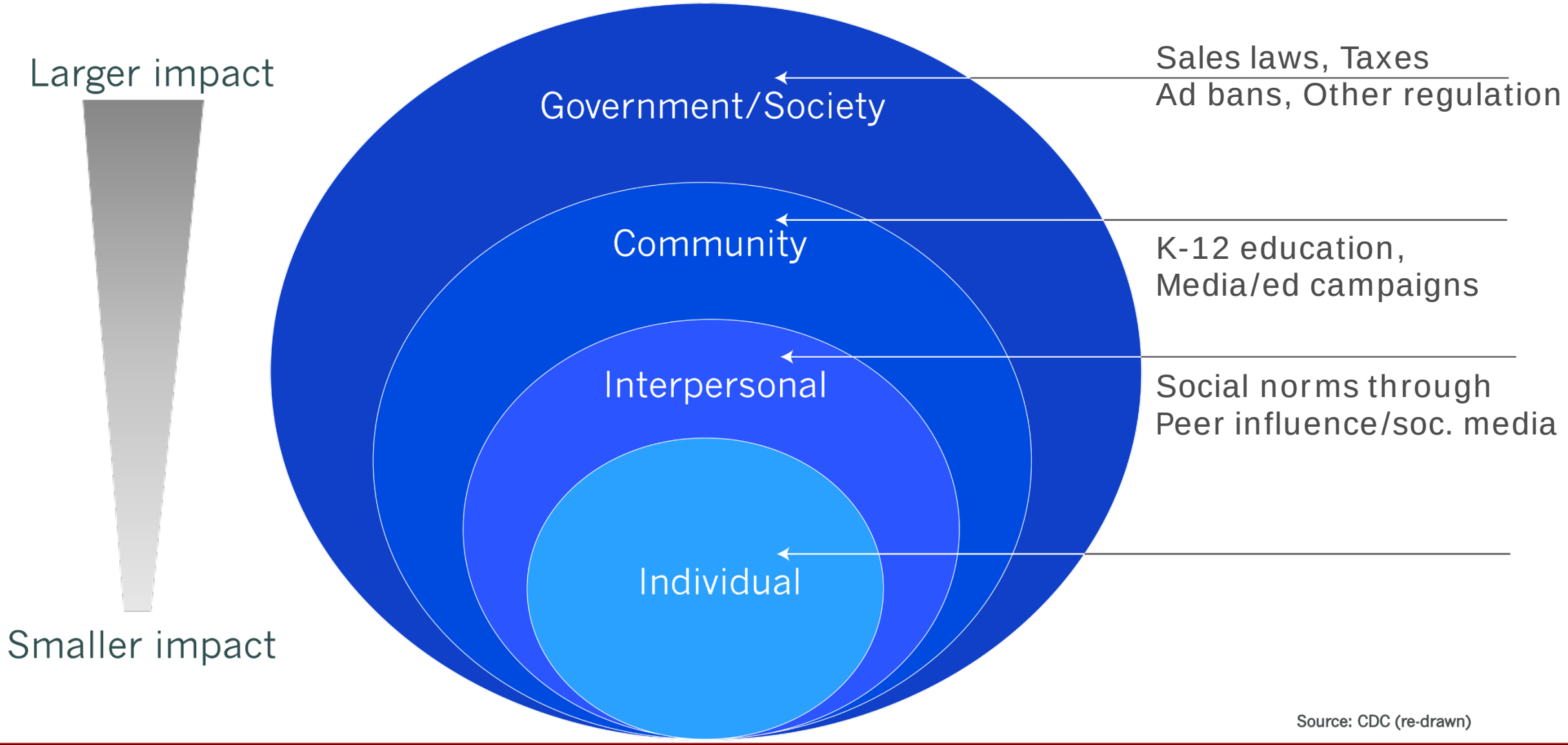
Liu et al. Pediatrics, 2012

Alcohol intake before first pregnancy, *NHSII*



Liu et al. J Natl Cancer Inst, 2013

Decreasing adolescent and adult alcohol intake



Source: CDC (re-drawn)

OBESITY AND CANCER

IARC 2002

"Sufficient evidence in humans for cancer-preventive effect of avoidance of weight gain for cancers of the colon, esophagus (adenocarcinoma), kidney (renal cell), breast (postmenopausal), and corpus uteri"

Translate: Obesity causes cancer

IACR Handbooks of Cancer Prevention Vol 6, 2002

The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL REPORT

Body Fatness and Cancer — Viewpoint of the IARC Working Group

Workgroup reviewed measures of adiposity; animal models; mechanisms; and epidemiologic evidence. Concluded lack of body fatness lowers risk, or obesity causes cancer.

NEJM August 25, 2016

Table 2. Strength of the Evidence for a Cancer-Preventive Effect of the Absence of Excess Body Fatness, According to Cancer Site or Type.*

Cancer Site or Type	Strength of the Evidence in Humans†	Relative Risk of the Highest BMI Category Evaluated versus Normal BMI (95% CI)‡
Esophagus: adenocarcinoma	Sufficient	4.8 (3.0–7.7)
Gastric cardia	Sufficient	1.8 (1.3–2.5)
Colon and rectum	Sufficient	1.3 (1.3–1.4)
Liver	Sufficient	1.8 (1.6–2.1)
Gallbladder	Sufficient	1.3 (1.2–1.4)
Pancreas	Sufficient	1.5 (1.2–1.8)
Breast: postmenopausal	Sufficient	1.1 (1.1–1.2)§
Corpus uteri	Sufficient	7.1 (6.3–8.1)
Ovary	Sufficient	1.1 (1.1–1.2)
Kidney: renal-cell	Sufficient	1.8 (1.7–1.9)
Meningioma	Sufficient	1.5 (1.3–1.8)
Thyroid	Sufficient	1.1 (1.0–1.1)§
Multiple myeloma	Sufficient	1.5 (1.2–2.0)
Male breast cancer	Limited	NA
Fatal prostate cancer	Limited	NA
Diffuse large B-cell lymphoma	Limited	NA
Esophagus: squamous-cell carcinoma	Inadequate	NA
Gastric noncardia	Inadequate	NA
Extrahepatic biliary tract	Inadequate	NA
Lung	Inadequate	NA
Skin: cutaneous melanoma	Inadequate	NA
Testis	Inadequate	NA
Urinary bladder	Inadequate	NA
Brain or spinal cord: glioma	Inadequate	NA

* BMI denotes body-mass index, CI confidence interval, and NA not applicable.
† Sufficient evidence indicates that the International Agency for Research on Cancer Handbook Working Group considers that a preventive relationship has been established between the intervention (in this case, the absence of excess body fatness) and the risk of cancer in humans — that is, a preventive association has been observed in studies in which

Evidence evolving

From only a couple of prospective cohorts in 2002, adding ACS mortality in 2003

- Now evidence from 30 to 50 or more prospective cohorts
- Pooled analysis of individual participant data from studies addressing BMI and less common cancers
  - Common cut points
  - Common approach to analysis
  - Common classification of potential confounders

Individual participant data – pooled analysis

IPD meta-analyses can improve the quality of data and the type of analyses that can be done and produce more reliable results (Stewart and Tierney 2002). For this reason they are considered to be a 'gold standard' of systematic review.

In fact, IPD meta-analyses have produced definitive answers to clinical questions, which might not have been obtained from summary data.

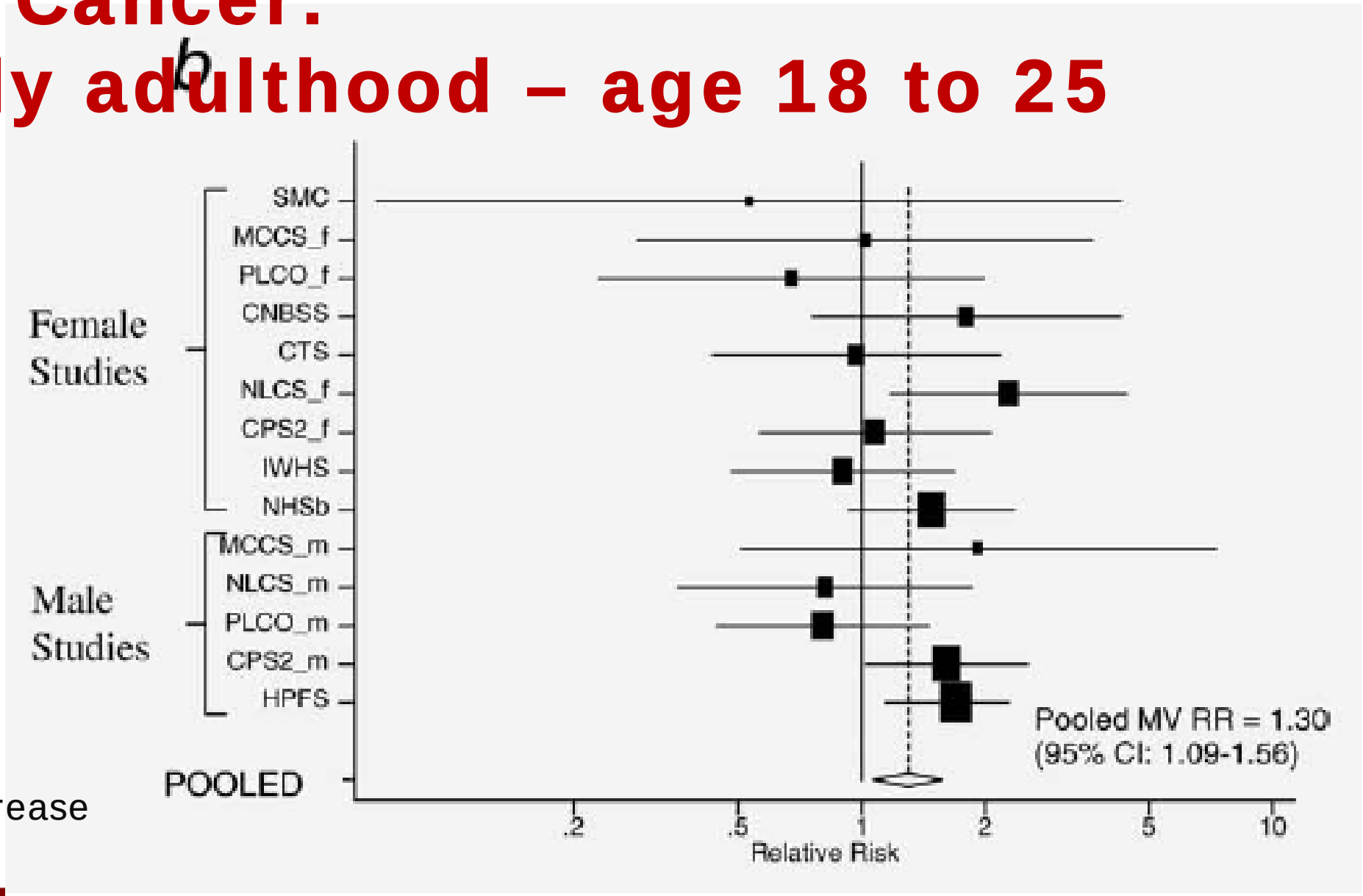
Cochrane Handbook Ch 18 and IPD methods

Pancreatic cancer

More than 20 prospective studies and case-control studies indicating a positive dose-response relation. Observed in the large majority of studies and in both genders.

Compared to normal weight, the RR for overweight was 1.18 (1.03-1.36) and for obesity 1.47 (1.23-1.75), estimated from pooled analysis of 14 cohorts [Genkinger 2011].

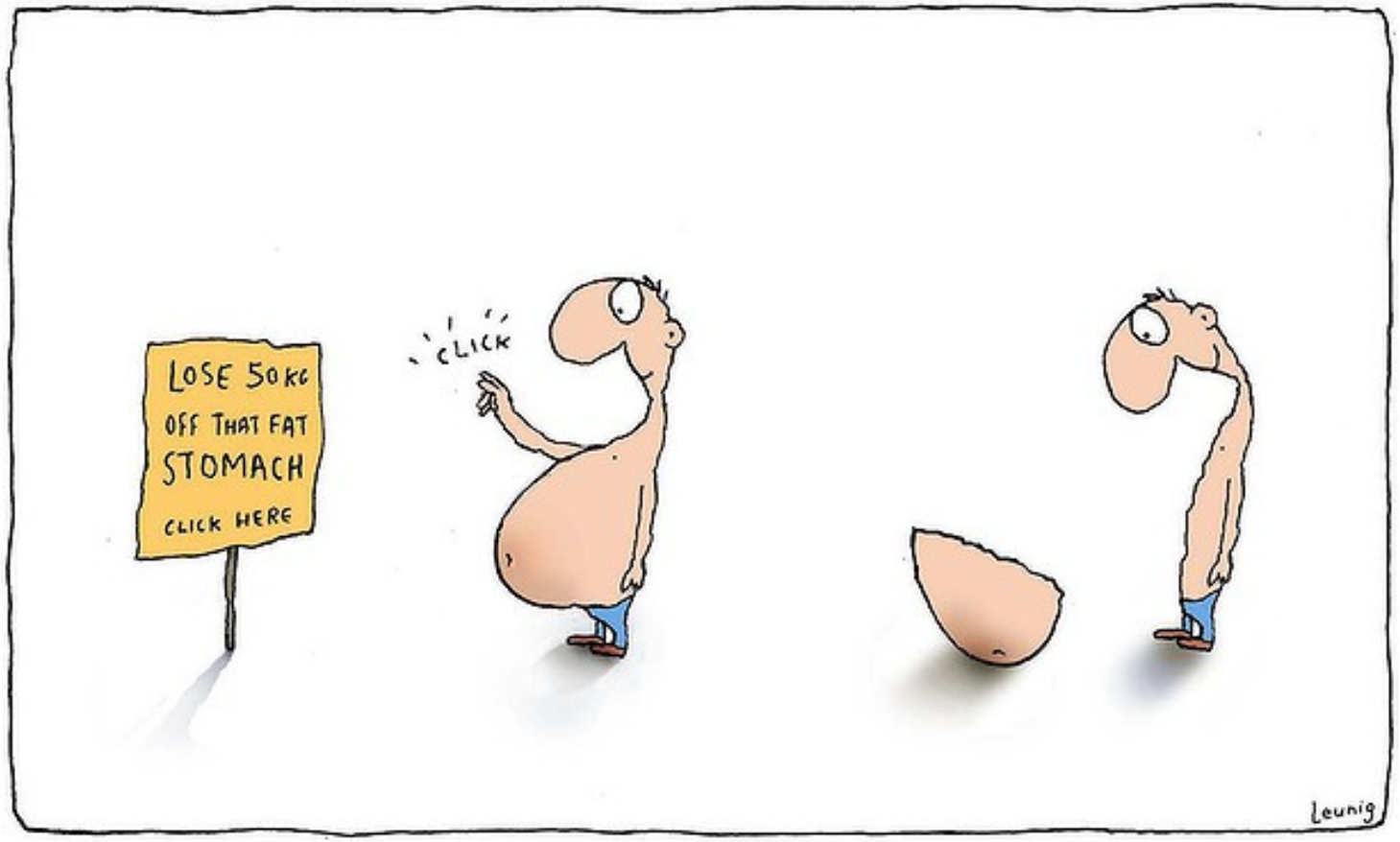
Pancreatic Cancer: BMI in early adulthood – age 18 to 25



BMI >25 vs BMI 21-22.9
MV RR 1.3 (1.1-1.6)

MVRR 1.2 per 5kg/m^2 increase

Obesity: Complex but Conquerable



Sugar-Sweetened Beverages

Soda Consumption in 9 – 12th Graders (Daily)

2007: 33.8%

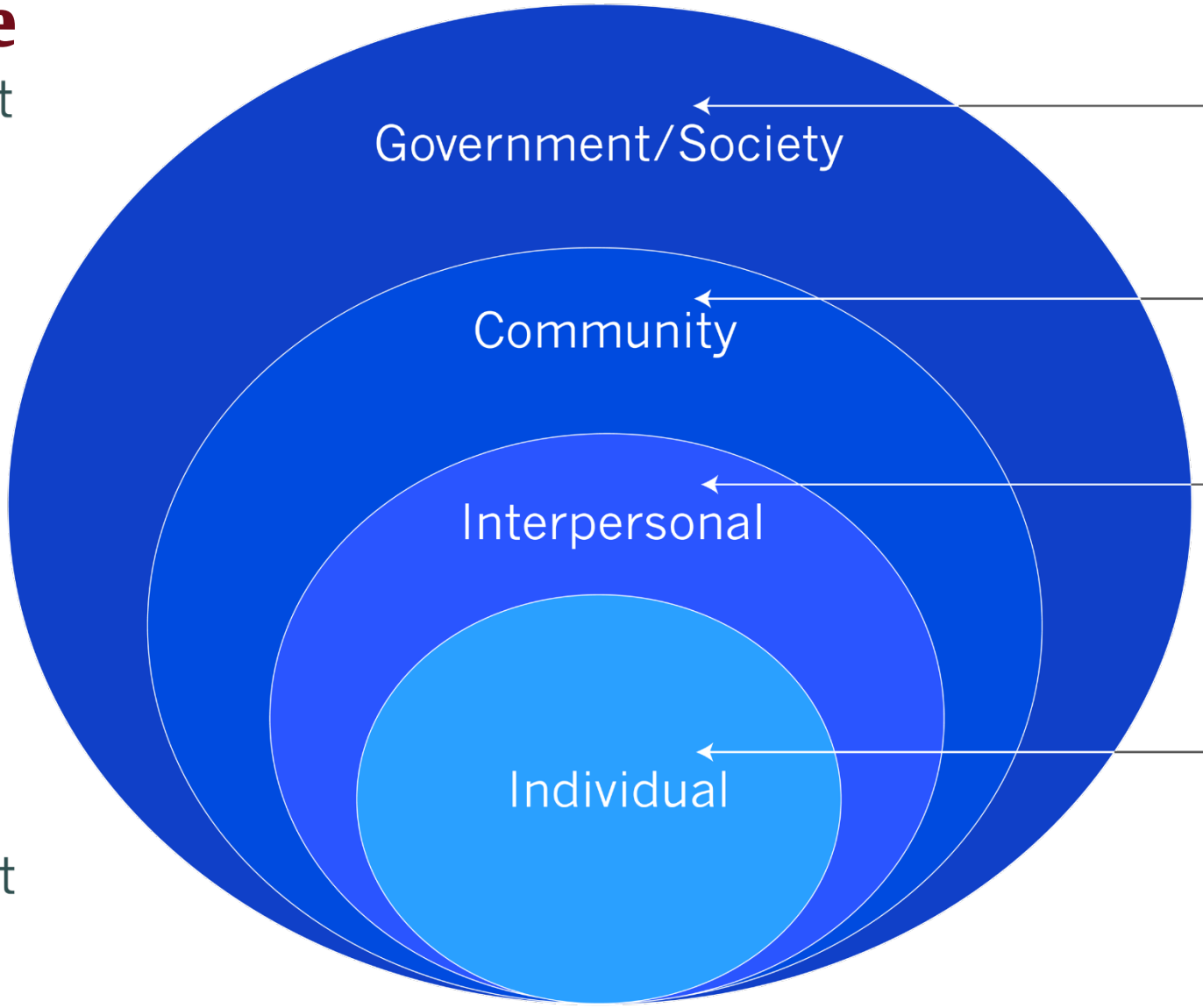
2015: 20.4%

Boston Public Health strategies replace SSB with water at all facilities/funded agencies

Miller et al, 2017 https://tinyurl.com/y2h33u7n

Sugar-Sweetened Beverages – one aspect of energy balance

Larger impact



Smaller impact

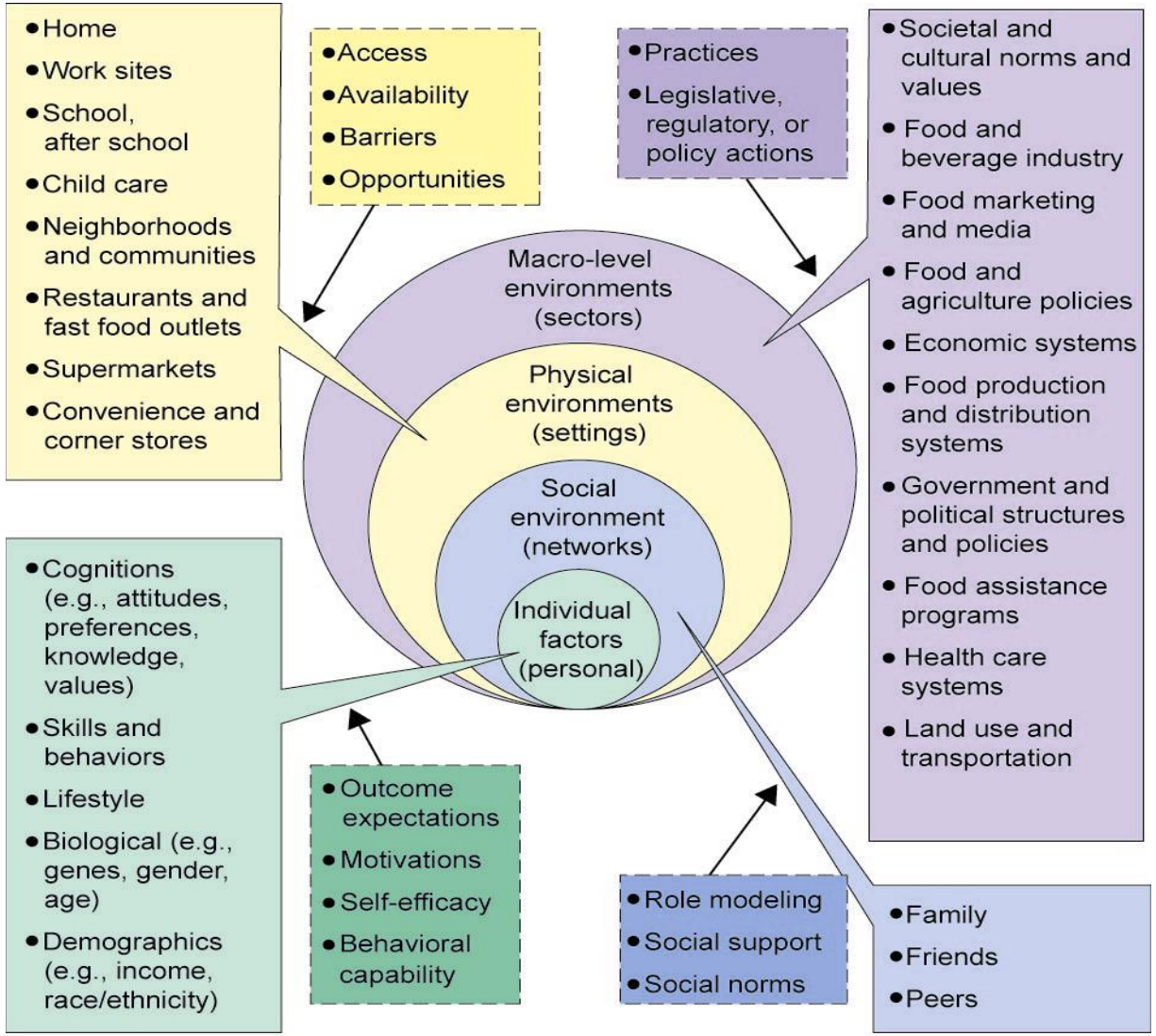
Taxes, Federal school nutrition standards

School healthy food/bev policies/options, Media campaigns

SSB-free households
Peer influence/soc. media

Source: CDC (re-drawn)

Multi-sector challenges for obesity prevention

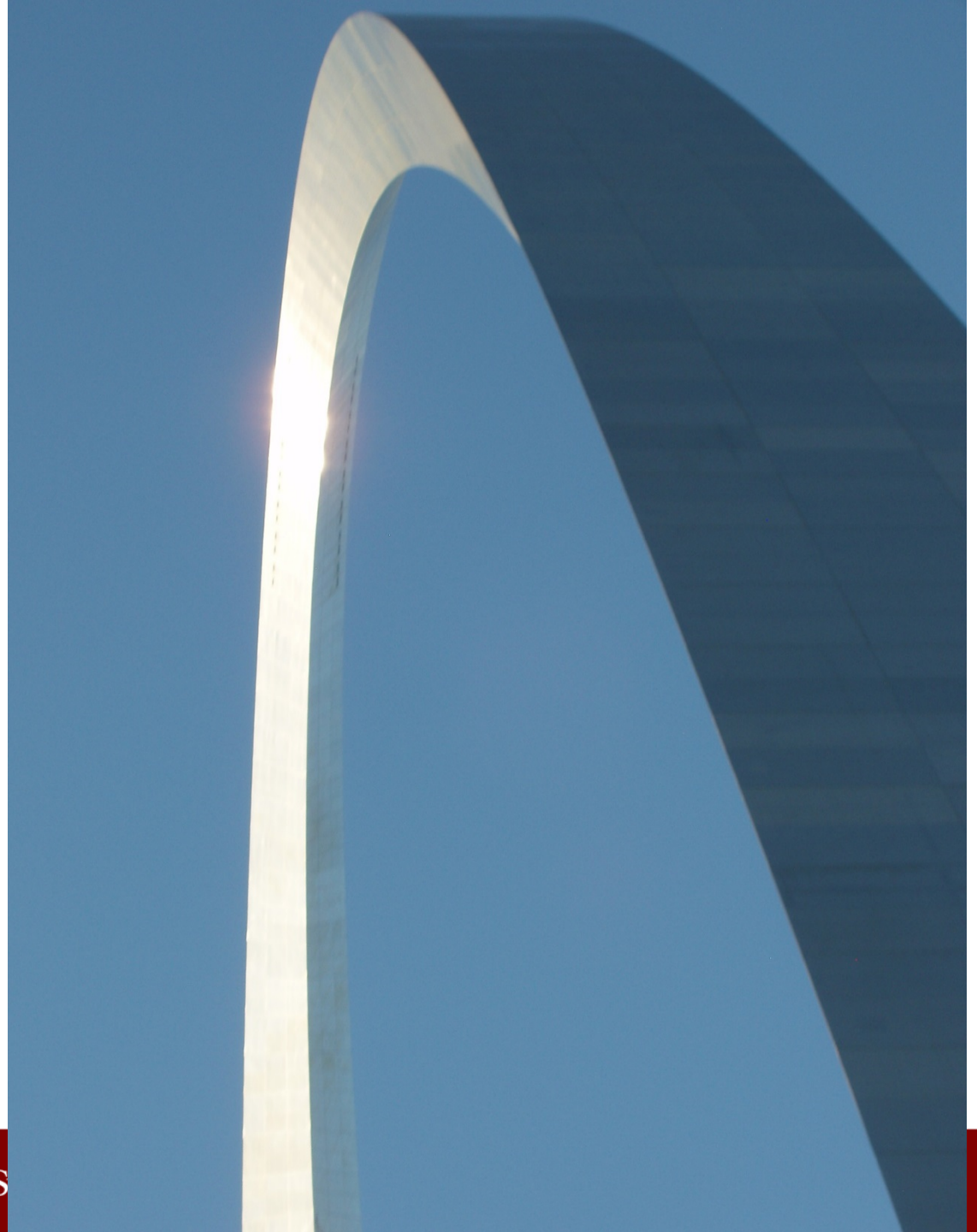


Story M, et al. 2008.
Annu. Rev. Public Health. 29:253–72

Annual Reviews

Future Directions

1. Further research assessing effective approaches for addressing specific behaviors in youth/teens
2. Further research on effectively and efficiently disseminating research findings into real world settings
3. Better integrate approaches across strategies to drive wellness
4. Greater attention on addressing broad-based structural inequalities that impact nearly all risk factors at all levels



Thank you

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