Establishing a Life Course Approach to Cancer Prevention and Care

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No conflicts of interest related to this work

• 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. regarding 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
Alcohol

A known breast carcinogen

IARC
2007
Global

18.1 million new cases of cancer diagnosed
9.4 million men; 8.6 million women
2.1 million new cases of breast cancer
In women, No. 1 for incidence (24.2%) and No. 1 for mortality (15% of cancer deaths)

Globocan 2018  http://gco.iarc.fr/
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

1. TDLU
2. ADH
3. DCIS
4. IBC

↑ Growth

Δs Adhesion & Polarity

↑ Diversity

Invasion

Time (decades)

Gertig et al. 10+ years
## Alcohol intake, ages 18-22, incident proliferative benign breast disease (BBD), NHSII

<table>
<thead>
<tr>
<th>Alcohol intake (g/day)</th>
<th>Cases (678)</th>
<th>Person-year</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>155</td>
<td>64,827</td>
<td>1.0 reference</td>
</tr>
<tr>
<td>0.1-4.9</td>
<td>193</td>
<td>78,365</td>
<td>1.11 (0.89, 1.38)</td>
</tr>
<tr>
<td>5.0-14.9</td>
<td>236</td>
<td>88,310</td>
<td>1.36 (1.09, 1.69)</td>
</tr>
<tr>
<td>≥15</td>
<td>30</td>
<td>9519</td>
<td>1.35 (1.01, 1.81)</td>
</tr>
</tbody>
</table>

p, trend <0.01

Parallel results in the GUTS cohort (daughters of NHSII)

Alcohol intake before first pregnancy, *NHSII*

**Proliferative BBD**
≥10 years between menarche and first pregnancy

<10 years between menarche and first pregnancy

**Breast cancer**
≥10 years between menarche and first pregnancy

<10 years between menarche and first pregnancy

Relative risk per 10 g/day alcohol intake

Decreasing adolescent and adult alcohol intake

Sales laws, Taxes
Ad bans, Other regulation

K-12 education, Media/ed campaigns

Social norms through Peer influence/soc. media

Source: CDC (re-drawn)
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
Workgroup reviewed measures of adiposity; animal models; mechanisms; and epidemiologic evidence. Concluded lack of body fatness lowers risk, or obesity causes cancer.
<table>
<thead>
<tr>
<th>Cancer Site or Type</th>
<th>Strength of the Evidence in Humans†</th>
<th>Relative Risk of the Highest BMI Category Evaluated versus Normal BMI (95% CI)‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophageal adenocarcinoma</td>
<td>Sufficient</td>
<td>4.8 (3.0–7.7)</td>
</tr>
<tr>
<td>Gastric cardia</td>
<td>Sufficient</td>
<td>1.8 (1.3–2.5)</td>
</tr>
<tr>
<td>Colon and rectum</td>
<td>Sufficient</td>
<td>1.3 (1.3–1.4)</td>
</tr>
<tr>
<td>Liver</td>
<td>Sufficient</td>
<td>1.8 (1.6–2.1)</td>
</tr>
<tr>
<td>Gallbladder</td>
<td>Sufficient</td>
<td>1.3 (1.2–1.4)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>Sufficient</td>
<td>1.5 (1.2–1.8)</td>
</tr>
<tr>
<td>Breast: postmenopausal</td>
<td>Sufficient</td>
<td>1.1 (1.1–1.2) §</td>
</tr>
<tr>
<td>Corpus uteri</td>
<td>Sufficient</td>
<td>7.1 (6.3–8.1)</td>
</tr>
<tr>
<td>Ovary</td>
<td>Sufficient</td>
<td>1.1 (1.1–1.2)</td>
</tr>
<tr>
<td>Kidney: renal-cell</td>
<td>Sufficient</td>
<td>1.8 (1.7–1.9)</td>
</tr>
<tr>
<td>Meningioma</td>
<td>Sufficient</td>
<td>1.5 (1.3–1.8)</td>
</tr>
<tr>
<td>Thyroid</td>
<td>Sufficient</td>
<td>1.1 (1.0–1.1) §</td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td>Sufficient</td>
<td>1.5 (1.2–2.0)</td>
</tr>
<tr>
<td>Male breast cancer</td>
<td>Limited</td>
<td>NA</td>
</tr>
<tr>
<td>Fatal prostate cancer</td>
<td>Limited</td>
<td>NA</td>
</tr>
<tr>
<td>Diffuse large B-cell lymphoma</td>
<td>Limited</td>
<td>NA</td>
</tr>
<tr>
<td>Esophageal squamous-cell carcinoma</td>
<td>Inadequate</td>
<td>NA</td>
</tr>
<tr>
<td>Gastric noncardia</td>
<td>Inadequate</td>
<td>NA</td>
</tr>
<tr>
<td>Extrahepatic biliary tract</td>
<td>Inadequate</td>
<td>NA</td>
</tr>
<tr>
<td>Lung</td>
<td>Inadequate</td>
<td>NA</td>
</tr>
<tr>
<td>Skin: cutaneous melanoma</td>
<td>Inadequate</td>
<td>NA</td>
</tr>
<tr>
<td>Testis</td>
<td>Inadequate</td>
<td>NA</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>Inadequate</td>
<td>NA</td>
</tr>
<tr>
<td>Brain or spinal cord: glioma</td>
<td>Inadequate</td>
<td>NA</td>
</tr>
</tbody>
</table>

† 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/m² 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

- 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

- Home
- Work sites
- School, after school
- Child care
- Neighborhoods and communities
- Restaurants and fast food outlets
- Supermarkets
- Convenience and corner stores

- Access
- Availability
- Barriers
- Opportunities

- Societal and cultural norms and values
- Food and beverage industry
- Food marketing and media
- Food and agriculture policies
- Economic systems
- Food production and distribution systems
- Government and political structures and policies
- Food assistance programs
- Health care systems
- Land use and transportation

- Cognitions (e.g., attitudes, preferences, knowledge, values)
- Skills and behaviors
- Lifestyle
- Biological (e.g., genes, gender, age)
- Demographics (e.g., income, race/ethnicity)

- Outcome expectations
- Motivations
- Self-efficacy
- Behavioral capability

- Role modeling
- Social support
- Social norms

- Family
- Friends
- Peers

Annu. Rev. Public Health. 29:253–72
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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