Dynamism: Identifying Key Time Periods for Cancer Control

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US National Cancer Institute
Outline

- What is meant by dynamism?
- Why is it important?
- What are the key questions?
- What are some examples?
What is meant by dynamism?
Dynamism

- Refers to a process or system characterized by constant change
Multi-dimensionality vs dynamism

Multidimensional, static diet  Dynamism
Dynamism

- Refers to a process or system characterized by constant change
- Diet fits this criterion
  - Long-term dynamism: over years
  - Short-term dynamism: day-to-day
Why is this important?
Cancer has a long latency

DNA damage to cells
Abnormal cell growth
Lesion
Metastasis
Diagnosis
Treatment
Cellular processes are influenced by diurnal variations

What are the key questions?
Do specific time periods represent heightened risk?

<table>
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# Life transitions and diet change

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<td>Breast/formula fed?</td>
<td>Food preferences established</td>
<td>Food intake independent of parents</td>
<td>Partner, children influence food choices</td>
<td>Dietary change explored or necessary</td>
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“Overall, the IOM finds that major advances have been made in understanding breast cancer and its risk factors, but more needs to be learned about its causes and how to prevent it. The report urges a life-course approach to studying breast cancer because new information suggests that women and girls might be more susceptible to some risk factors during certain life stages.”
Atomic bomb radiation and breast cancer


The graph shows the relative risk (RR) of breast cancer in relation to age at radiation exposure. The x-axis represents age at radiation exposure in years (0 <10 10-20 20-30 30-40 40-50 50-60), and the y-axis represents relative risk (RR). The data indicates a decreasing relative risk with increasing age at exposure, with RR >4 for exposures before the age of 10, and RR <1.5 for exposures after the age of 60.
## Selected breast cancer risk factors

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<th>Comparison</th>
<th>RR</th>
<th>95% CI</th>
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<td>Age at menarche</td>
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*Analysis includes 322,647 women followed for 5-7 years, with 4,827 incident cases of breast cancer.

Hunter et al., *Cancer Cause. Control*, 1997
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Hunter et al., *Cancer Cause. Control*, 1997
Estrogen levels throughout life

Most breast cancer studies

Kushi, Workshop: Extending Methods in Dietary Patterns Research, 2016
Risk of early puberty by infant feeding practice*

![Bar chart showing hazard ratios for Thelarche and Pubarche with different feeding practices.

Thelarche:
- Formula fed: 1
- Mixed fed: 0.9
- Breastfed: 0.74

Pubarche:
- Formula fed: 1
- Mixed fed: 0.95
- Breastfed: 0.84

*BCERP studies

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Does risk or benefit accumulate over time?
Uauy and Solomons, *J Nutr.*, 2005
Does a change in diet alter the course of the risk profile?

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Healthy diet

Unhealthy diet

- **Foods**
  - Potato chips
  - Potatoes or fries
  - Processed meats
  - Unprocessed red meats
  - Butter
  - Sweets and desserts
  - Refined grains
  - Cheese
  - Vegetables
  - Nuts
  - Whole grains
  - Fruits
  - Yogurt

- **Beverages**
  - Sugar-sweetened beverages
  - 100% Fruit juice
  - Low-fat or skim milk
  - Whole milk
  - Diet (zero-calorie) soda

**Weight Change Associated with Each Increased Daily Serving, per 4-Year Period (lb)**
What are the patterns of eating frequency?
Examples of eating frequency patterns

A. 3 meals and snacks
B. 3 meals consumed during the day
C. 2 meals no breakfast
D. 3 small meals
E. Complete fast

Common Diet
TRF
5:2 diet
Alternate day fast
Alternate day ER

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If we alter eating frequency, does it modify the biology?
Short-term metabolic effects

Downstream effects on health

What are some examples?
Carbohydrate intake and breast cancer

Postmenopausal women*

Carbohydrate intake (quintiles)

Glycemic index (p trend=0.02)  Fiber (p trend=0.35)  Total CHO (p trend=0.82)

Relative Risk

1.0 1.0 1.0 0.99 0.97 0.99 1.02 0.99 1.05 0.93 1.02 1.15 0.96 0.96

1 (low) 2 3 4 5 (high)

*Nurses Health Study, 1980-1998

Holmes et al., Am. J. Epidemiol., 2004
Carbohydrate intake and breast cancer

Adolescent girls*

![Bar graph showing Relative Risk for carbohydrate intake quintiles]

- **Glycemic index** (p trend=0.01)
- **Fiber** (p trend=0.11)
- **Total CHO** (p trend=0.59)

Carbohydrate intake (quintiles)

*Nurses Health Study II, 1989-1998

- Frazier et al., *Cancer Cause. Control*, 2004
Risk of pancreatic cancer by alcohol dose, duration, and pattern of consumption, in men

- Highest lifetime alcohol consumption conferred > twofold increased risk which...
  - ... was elevated regardless of when in the past the heavy consumption occurred
  - ... increased with increasing decades of heavy consumption

- History of binge drinking increased risk ...
  - ... regardless of when binging first occurred
  - ... most dramatically for those whose last episode occurred 6-10 years before diagnosis (6-fold increase)
  - ... and years duration was positively associated with risk

Gupta et al., *Cancer Cause. Control*, 2010
Mortality in male Seventh-day Adventists, by age at entry to church and duration of membership

MRR

Mortality rate by age at entry, relative to those <20 y

Mortality rate by duration in church, for those entering at different age decades

Heuch et al., J. Clin. Epidemiol., 2005
Frequency and circadian timing of eating may influence biomarkers of inflammation

Marinac et al., *PLOS ONE*, 2015

10% increase in kcal/d resulted in ~3% increase in CRP

One more meal/d resulted in ~8% lower CRP
Frequency and circadian timing of eating may influence biomarkers of inflammation

- Systemic inflammation may be lowered by
  - eating more frequently
  - reducing evening energy intake
  - fasting for longer nightly intervals

This may reduce breast cancer risk in the long run

An increase of 1 hour in fasting duration resulted in ~8% lower CRP, but only among women who ate <30% of kcal in evening.

Marinac et al., *PLOS ONE*, 2015
Summary

- Diets are dynamic in both the short-term and long-term
- Patterns of long- and short-term dynamism may be critical to cancer control
- There are many questions worth exploring in this area
Acknowledgements

- Jill Reedy
- Angela Liese
- Stephanie George
- Larry Kushi
- Jennifer Lerman
- Marian Neuhouser