



Diet and Cancer

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Outline

- How do we know whether/how diet is related to cancer?
- What more do we need to know?
- Why is multidimensionality important, and what are the key questions?
- Why is dynamism important, and what are the key questions?
- Wrap-up

How do we know whether/how diet is related to cancer?

Hierarchy of evidence



Systematic evidence review criteria

Is the review based on a focused question that is adequately formulated and described?

Were eligibility criteria for included and excluded studies predefined and specified?

Did the literature search strategy use a comprehensive, systematic approach?

Were titles, abstracts, and full-text articles dually and independently reviewed for inclusion and exclusion to minimize bias?

Was the quality of each included study rated independently by two or more reviewers using a standard method to appraise its internal validity?

Were the included studies listed along with important characteristics and results of each study?

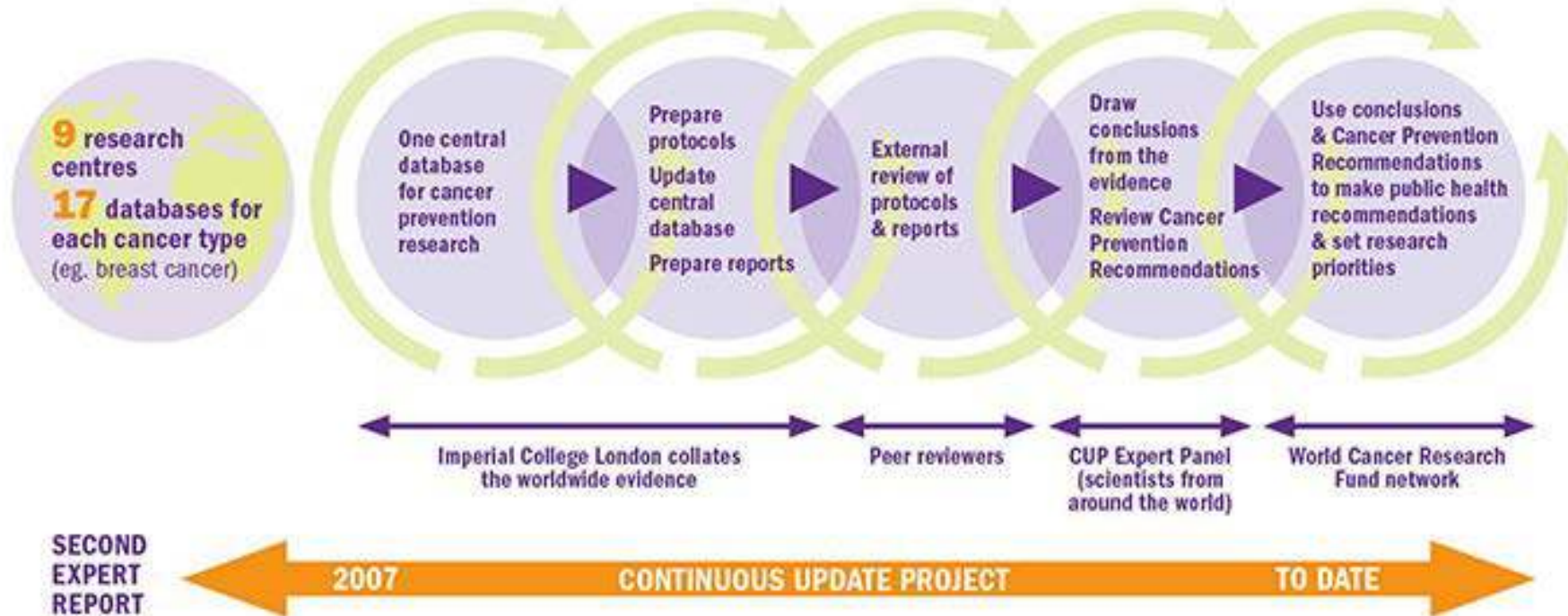
Was publication bias assessed?

Was heterogeneity assessed?

WCRF/AICR follows established criteria

Continuous Update Project

The process we use to analyse worldwide research

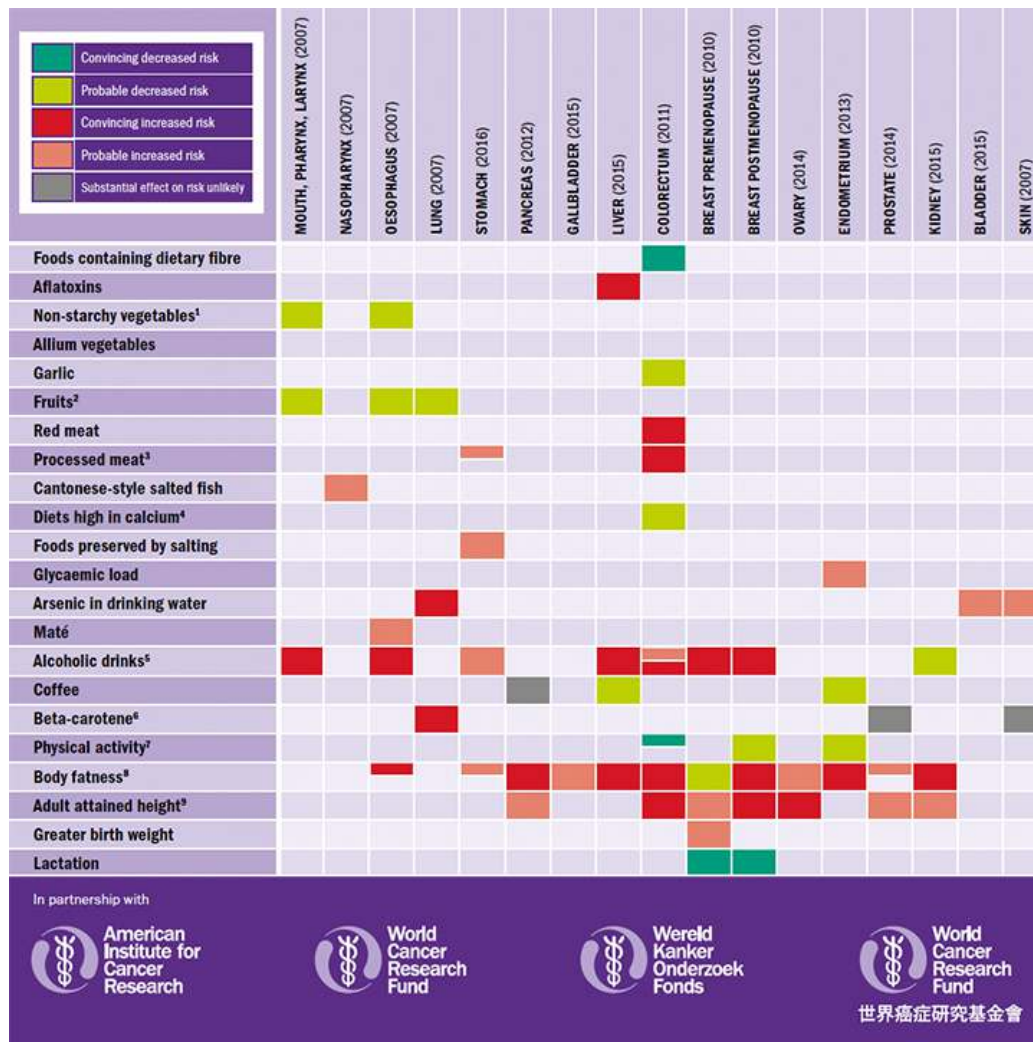


WCRF/AICR cancer prevention recommendations



WCRF/AICR cancer prevention recommendations





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	<table border="1"> <tr><td>Convincing decreased risk</td></tr> <tr><td>Probable decreased risk</td></tr> <tr><td>Convincing increased risk</td></tr> <tr><td>Probable increased risk</td></tr> <tr><td>Substantial effect on risk unlikely</td></tr> </table>	Convincing decreased risk	Probable decreased risk	Convincing increased risk	Probable increased risk	Substantial effect on risk unlikely	
Convincing decreased risk							
Probable decreased risk							
Convincing increased risk							
Probable increased risk							
Substantial effect on risk unlikely							
Foods containing dietary fibre		MOUTH, PHARYNX, LARYNX (2007)					
Aflatoxins		NASOPHARYNX (2007)					
Non-starchy vegetables¹		OESOPHAGUS (2007)					
Allium vegetables		LUNG (2007)					
Garlic		STOMACH (2016)					
Fruits²		PANCREAS (2012)					
Red meat		GALLBLADDER (2015)					
Processed meat³		LIVER (2015)					
Cantonese-style salted fish		COLORECTUM (2011)					
Diets high in calcium⁴		BREAST PREMENOPAUSE (2010)					
Foods preserved by salting		BREAST POSTMENOPAUSE (2010)					
Glycaemic load		OVARY (2014)					
Arsenic in drinking water		ENDOMETRIUM (2013)					
Maté		PROSTATE (2014)					
Alcoholic drinks⁵		KIDNEY (2015)					
Coffee		BLADDER (2015)					
Beta-carotene⁶		SKIN (2007)					
Physical activity⁷							
Body fatness⁸							
Adult attained height⁹							
Greater birth weight							
Lactation							

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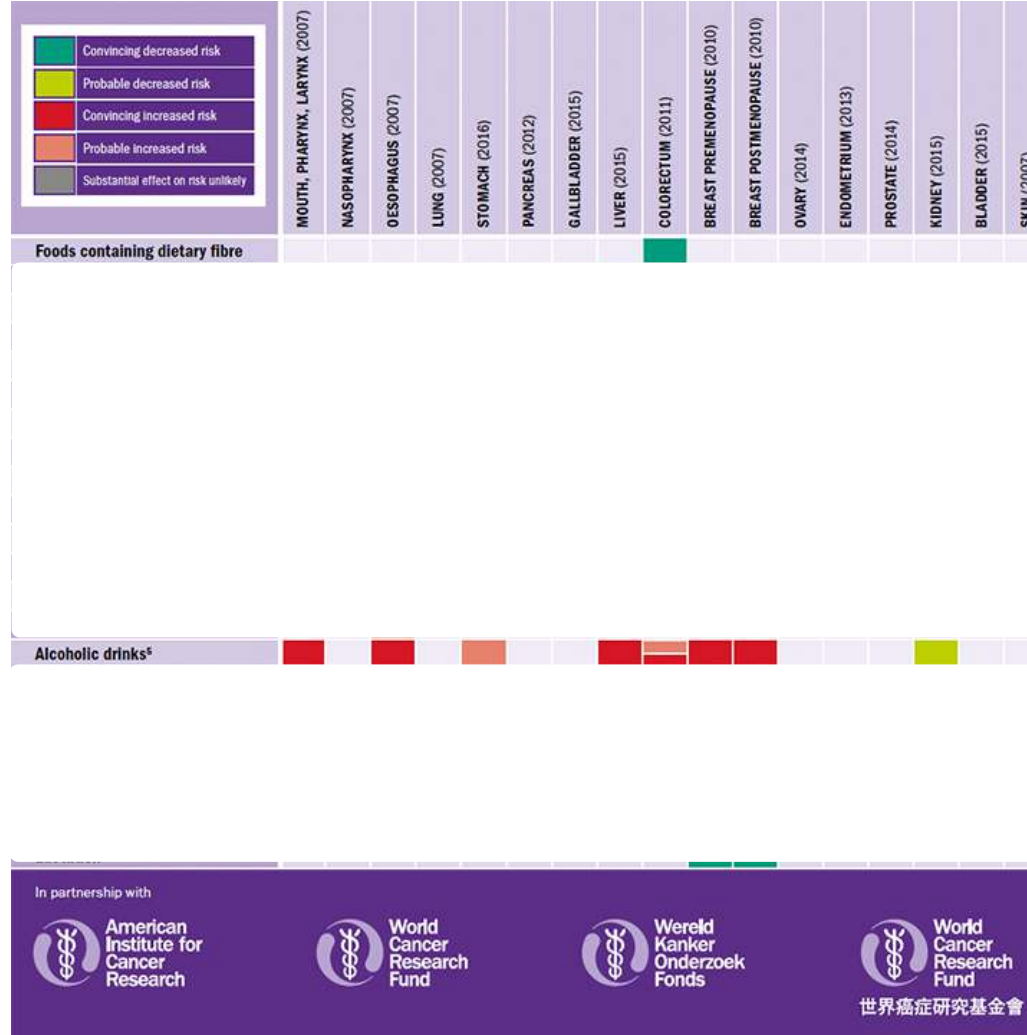
世界癌症研究基金會

	MOUTH, PHARYNX, LARYNX (2007)	NASOPHARYNX (2007)	ESOPHAGUS (2007)	LUNG (2007)	STOMACH (2016)	PANCREAS (2012)	GALLBLADDER (2015)	LIVER (2015)	COLORECTUM (2011)	BREAST PREMENOPAUSE (2010)	BREAST POSTMENOPAUSE (2010)	OVARY (2014)	ENDOMETRIUM (2013)	PROSTATE (2014)	KIDNEY (2015)	BLADDER (2015)	SKIN (2007)
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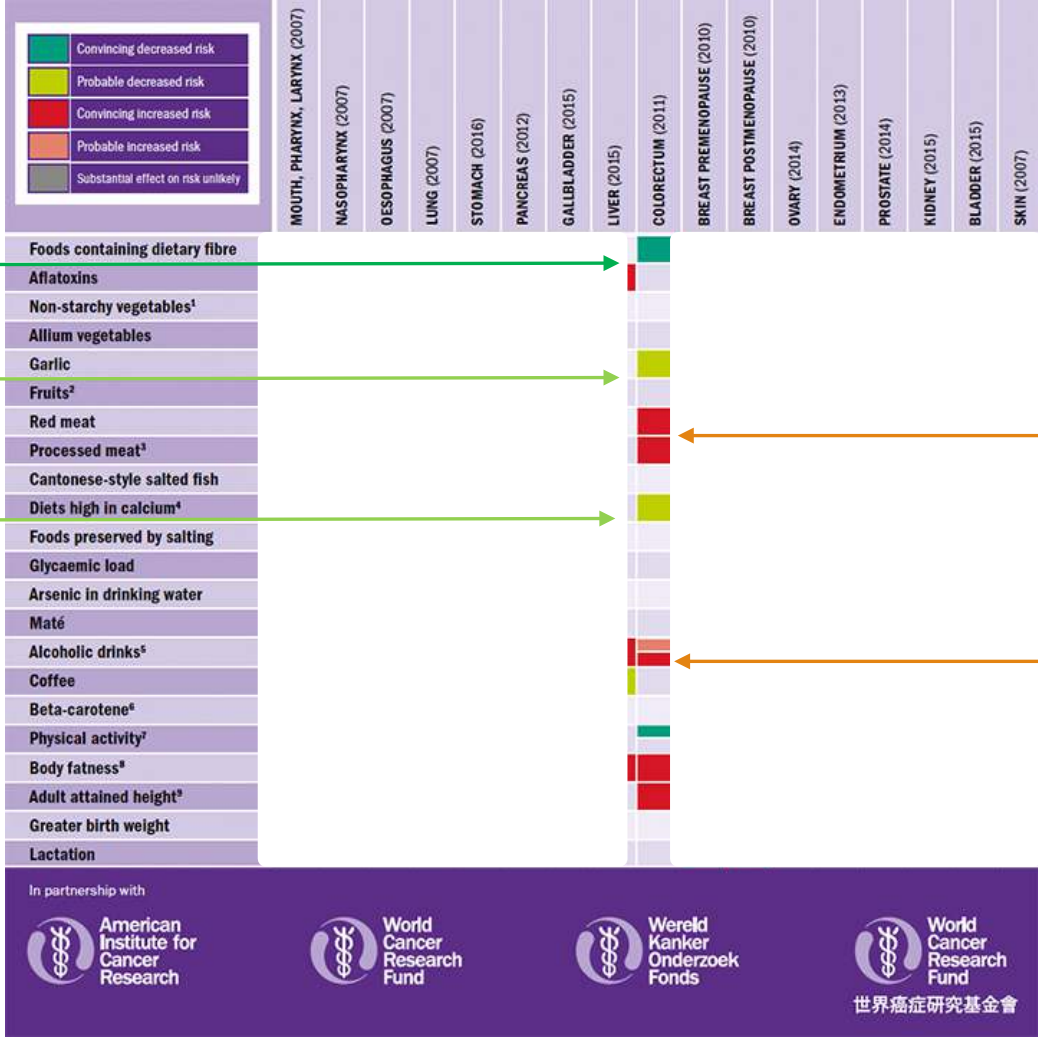
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Fiber reduces risk

Garlic probably reduces risk

Calcium probably reduces risk



Red meat and processed meat increase risk

Alcohol increases risk

What more do we need to know?



“...even a small insect is much more complicated than a star, and... everything about humans is very complicated...”

*Considering the confusion about diet, “It’s not that the people working in those fields are less competent, it’s that anything to do with humans and their behavior ... is **far more complicated than the cosmos...**”*

Definition of “dietary patterns”

“ . . . the quantities, proportions, variety, or combination of different foods, drinks, and nutrients (when available) in diets, and the frequency with which they are habitually consumed”

Further extend this definition to include:

Multidimensionality

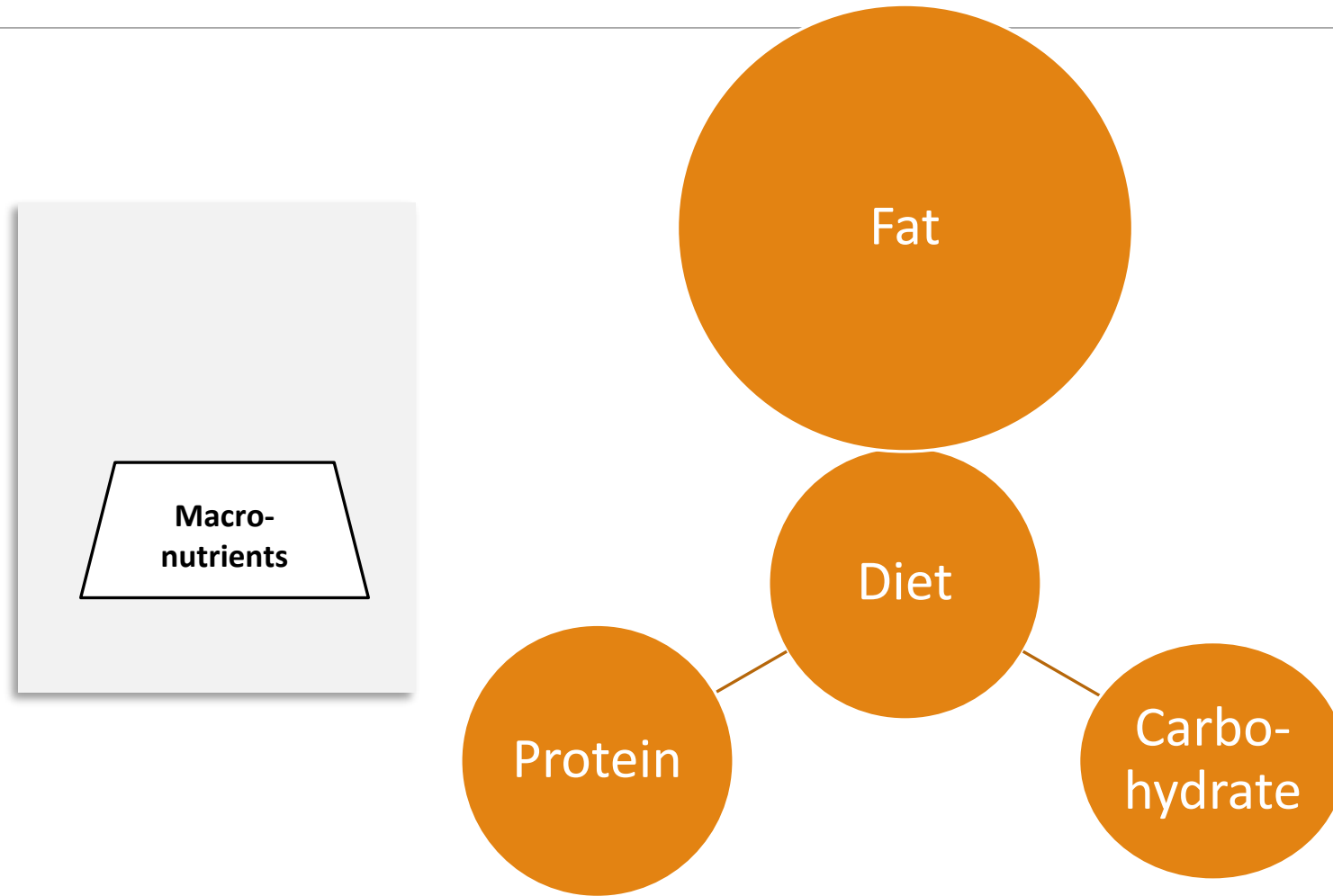
- Diet is a complex exposure: it is multilayered and multidimensional

Dynamism

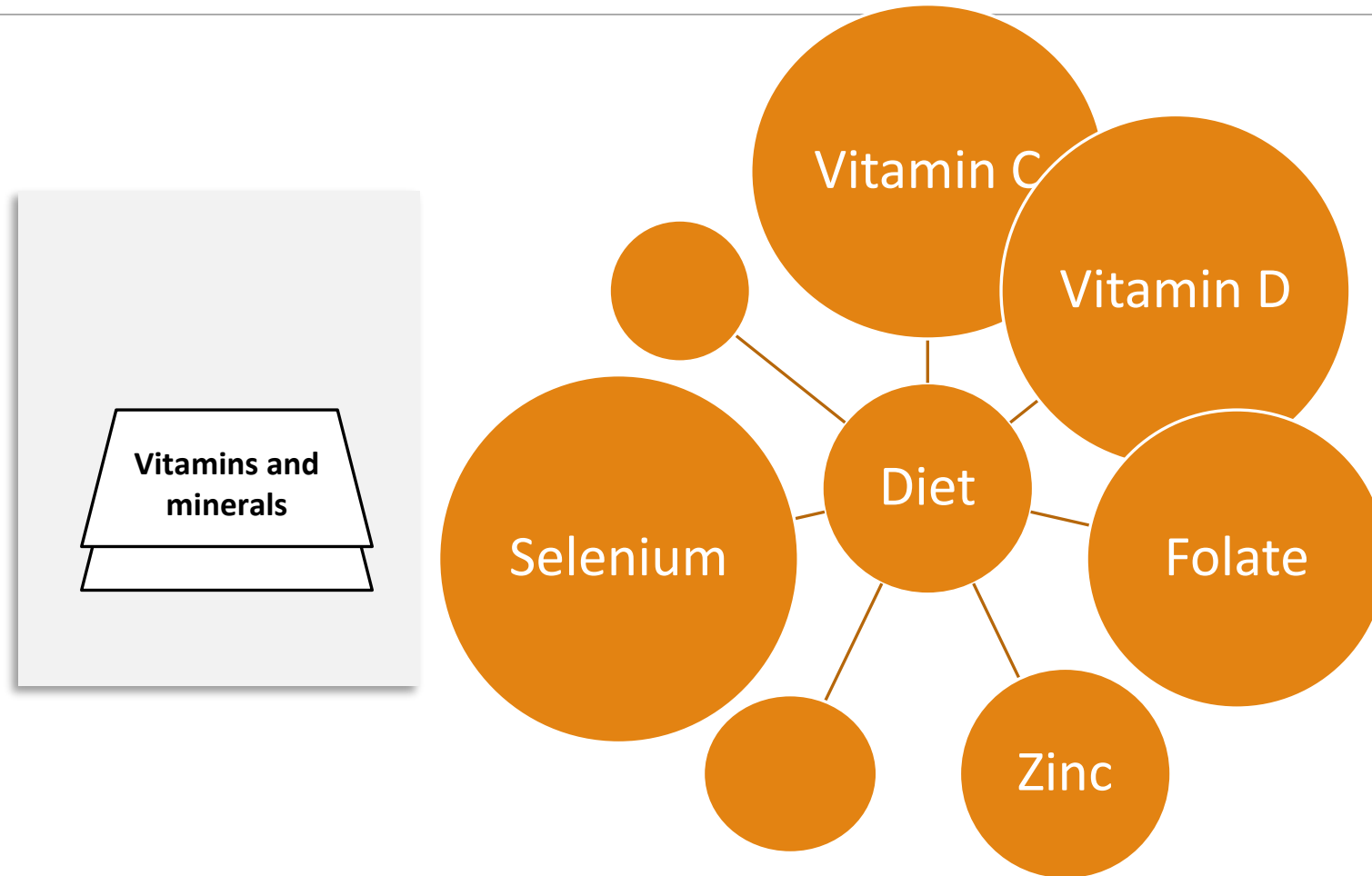
- Diet is a dynamic exposure : it varies over time, at both shorter and longer intervals

Why is multidimensionality important?

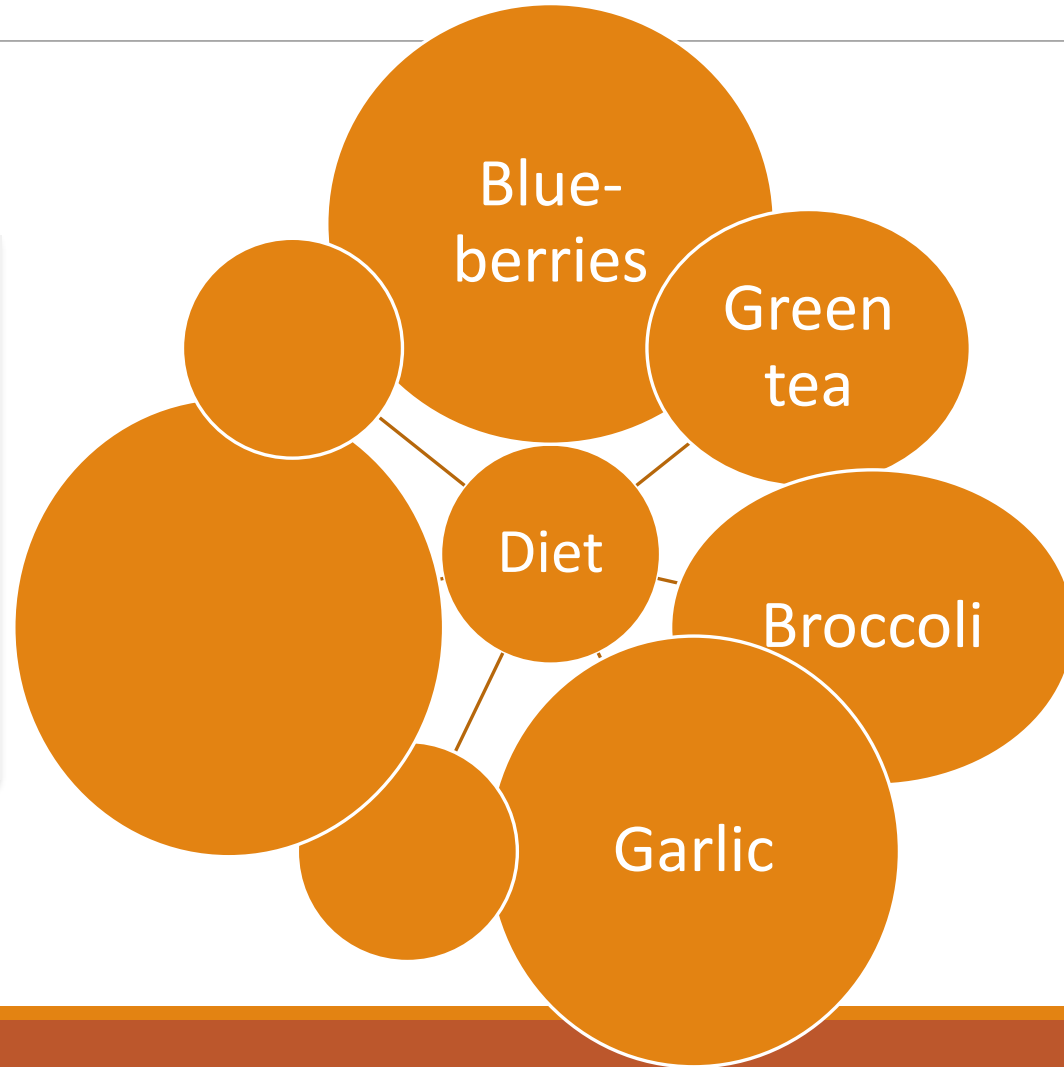
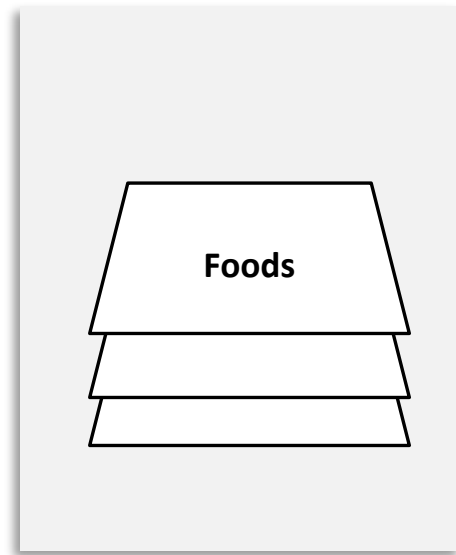
Diet is multidimensional



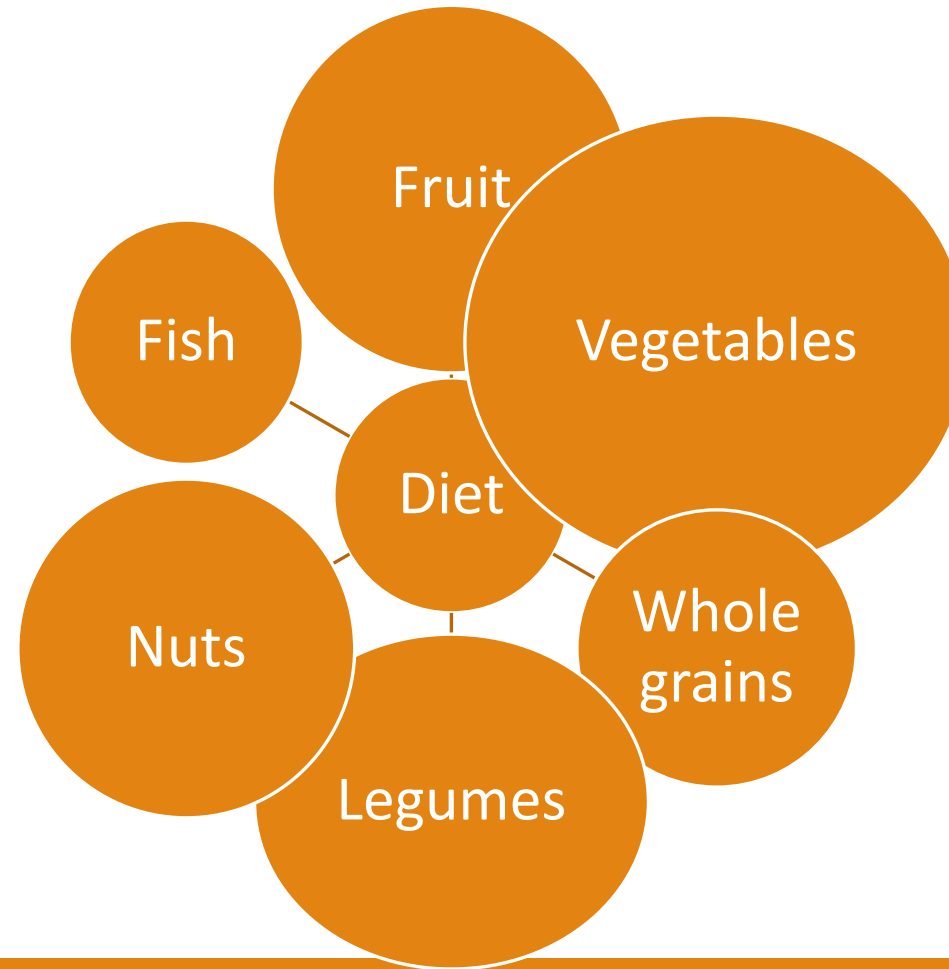
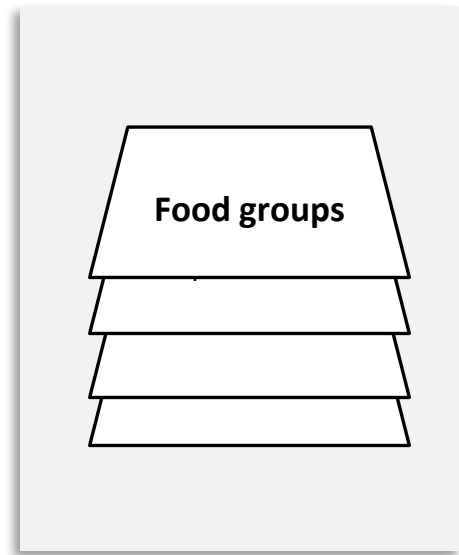
Diet is multidimensional



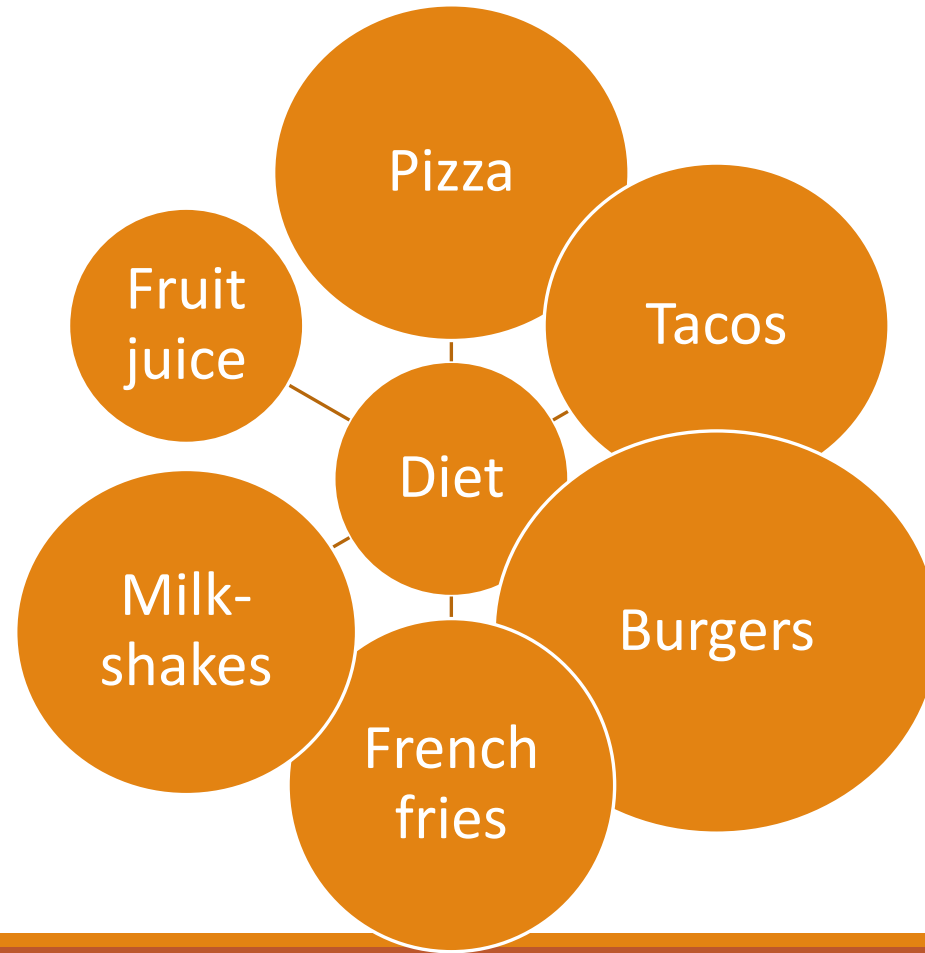
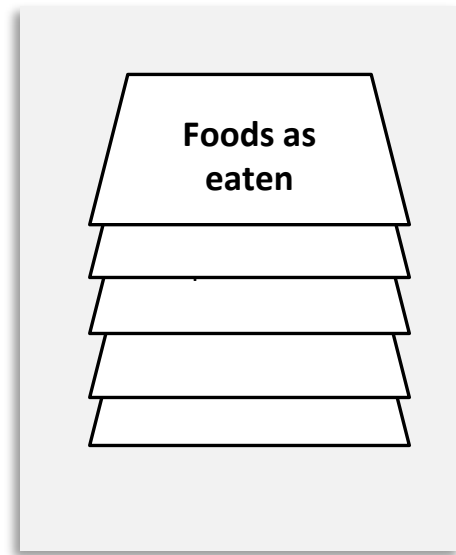
Diet is multidimensional



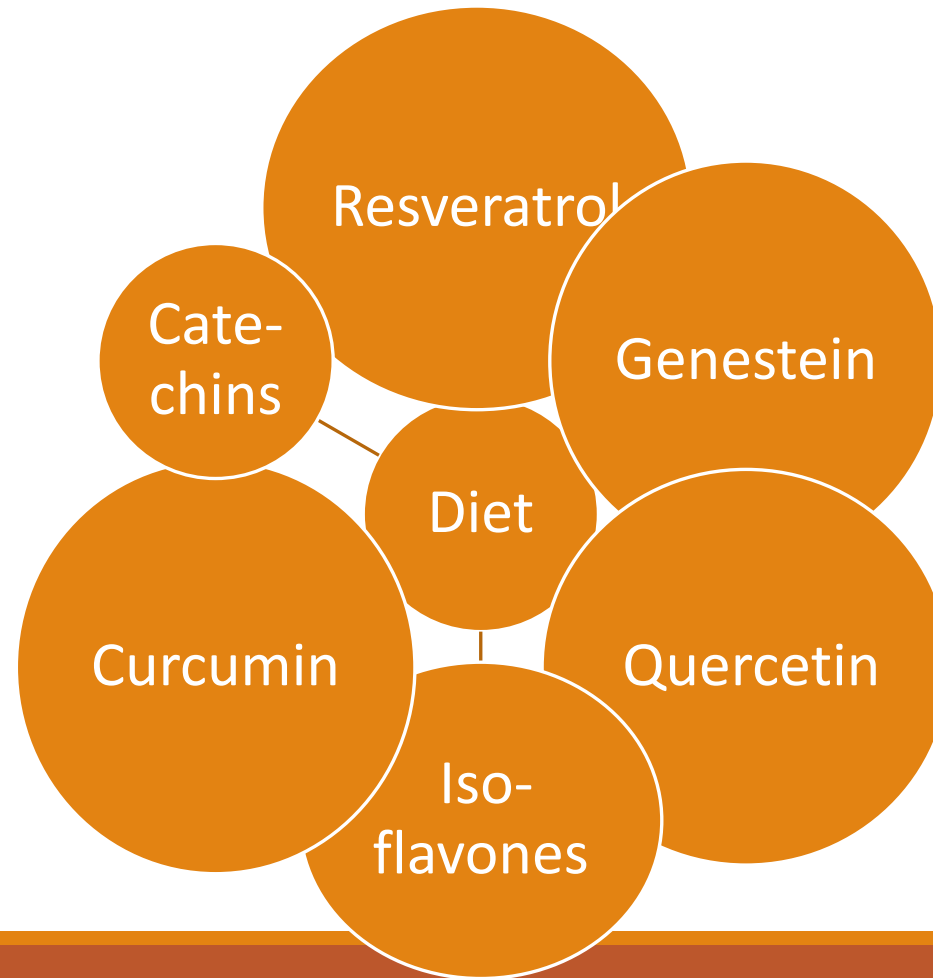
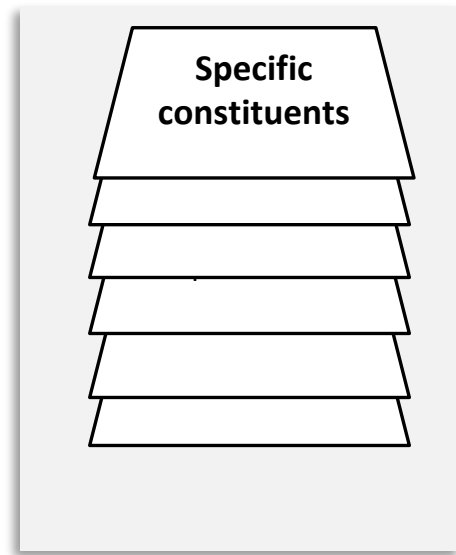
Diet is multidimensional



Diet is multidimensional



Diet is multidimensional

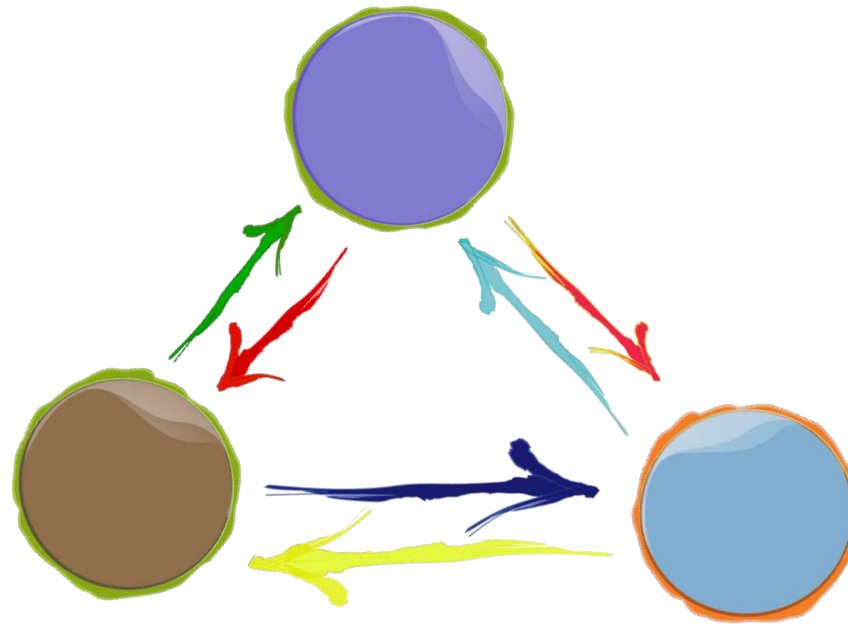


Multiple dimensions compound complexity

SYNERGY



INTERACTIONS



What are the key questions regarding multidimensionality?

Selective Diets

(e.g., Vegetarian)

Who are the vegetarians?



I am!

Exclude

- Meat
- Fish
- Poultry
- (Eggs)
- (Milk)

Include

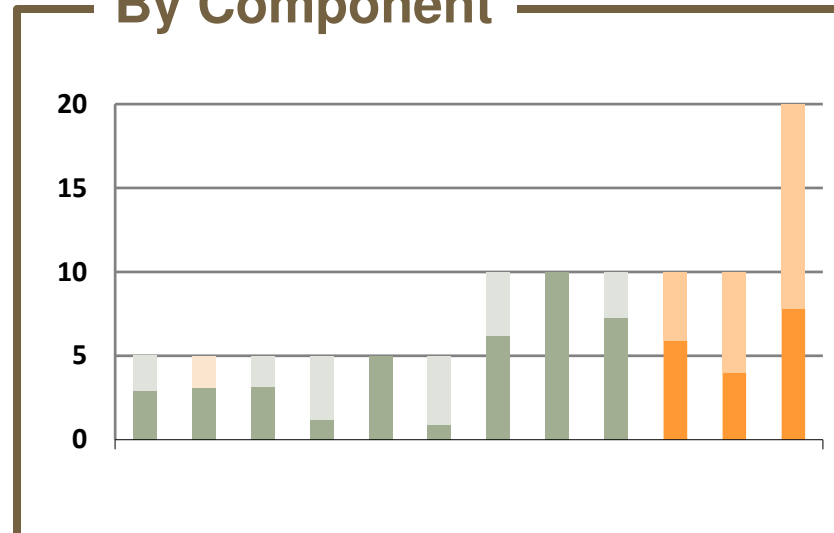
- Fruits?
- Vegetables?
- Whole grains?
- Refined grains?
- Added sugars?
- Solid fats?

Indexes/Scores

How close is the population to meeting a set of dietary recommendations?

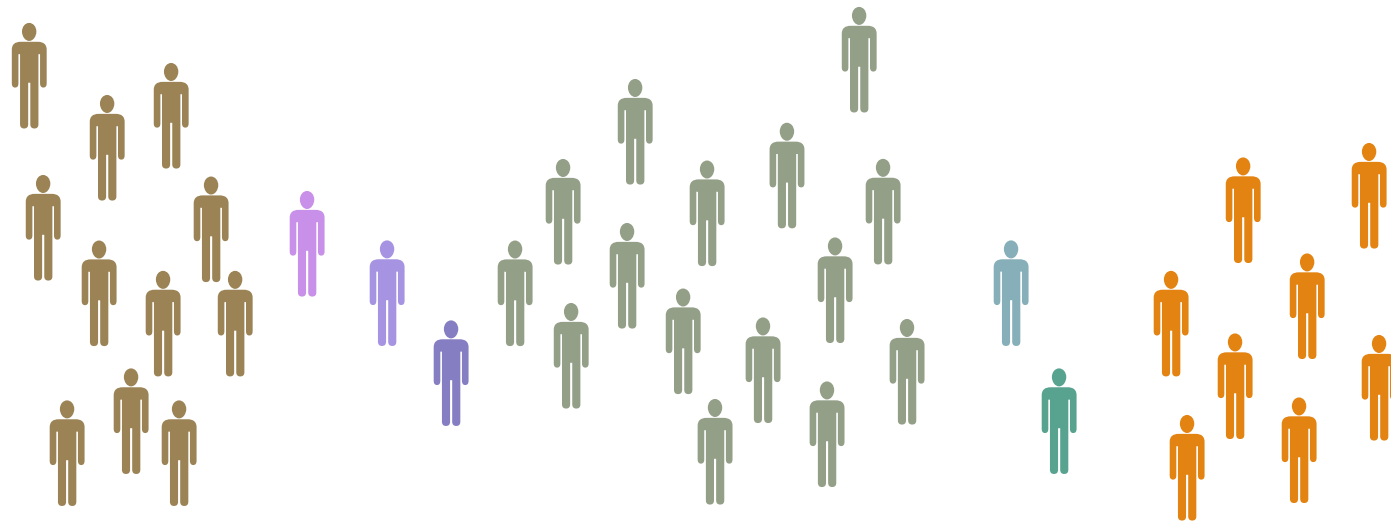
**Overall Diet Quality:
Total score = 58/100**

By Component



Cluster Analysis

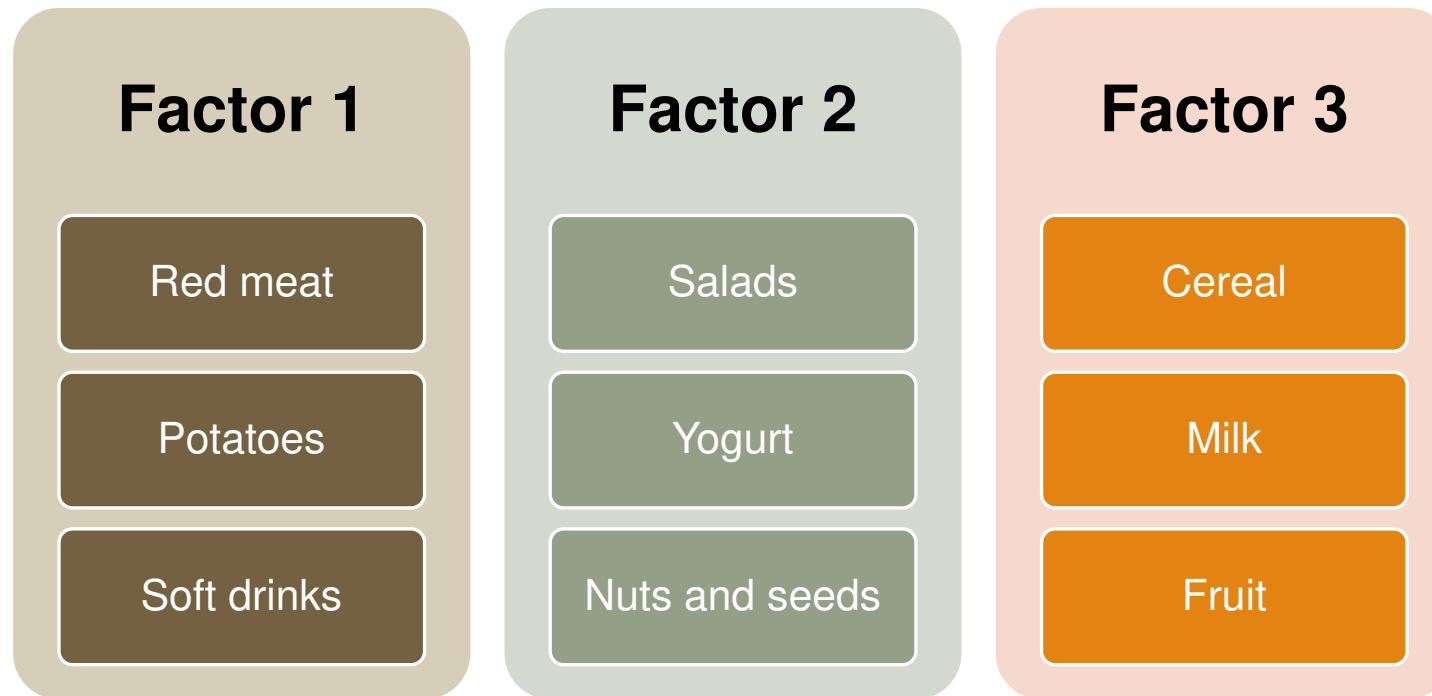
Are there groups of people with distinct eating patterns?



Groups **people** according to their dietary patterns

Factor Analysis

What elements of the diet track together in explaining variation in diets?



Identifies **elements of the diet** that track together

Hypothesis Testing

How do dietary patterns relate to health outcome?

Selective Diets

People who meet/don't meet criteria

Indexes/ Scores

Individuals' scores on quality and its components

Cluster Analysis

Groups of individuals and their diet patterns

Factor Analysis

Factors explaining variation in individuals' scores

Regression Model

Nutrition Evidence Library

What is the relationship between dietary patterns and risk of colorectal cancer?

Findings This systematic review included 21 articles from prospective cohort studies and one article from an RCT published since 2000 that examined the relationship between dietary patterns and risk of colorectal cancer

The **articles used diverse methodology** to assess dietary patterns. Nine articles used indices and scores to assess dietary patterns, 10 articles used data-driven methods and three used other approaches.

The **dietary patterns** examined in this systematic review were **defined in various ways, making comparisons between articles difficult**. However, despite general heterogeneity in this body of evidence, some **protective dietary patterns emerged**, particularly in articles **where patterns were defined by index or score**; articles using **data-driven methods were less consistent**.

- Patterns emphasizing vegetables, fruits, fish and seafood, legumes, low-fat dairy, and whole grains were generally associated with reduced risk of colorectal cancer
- Patterns higher in red and processed meats; potatoes and French fries; and sodas, sweets, added sugars were generally associated with increased risk of colorectal cancer.

The relationship between dietary patterns and colorectal cancer risk often varied by sex and tumor location. Results based on analysis by sex were mixed, while analysis in tumor subgroups seemed to indicate that dietary patterns may be more strongly associated with tumor development in distal regions of the colon and rectum.

Dietary Patterns Methods Project

a systematic
comparison of
diet quality
indices with
mortality

FACTS ABOUT
The DASH Eating Plan

Research has found that diet affects the development of high blood pressure, or hypertension (the medical term). Recently, even studies showed that blood pressure can be lowered by following a particular eating plan—called the Dietary Approaches to Stop Hypertension (DASH) eating plan—and reducing the amount of sodium consumed.

While each step alone lowers blood pressure, the combination of the eating plan and a reduced sodium intake gives the biggest benefit and may help prevent the development of high blood pressure.

This fact sheet, based on the DASH research findings, tells about high blood pressure, and how to follow the DASH eating plan and reduce the amount of sodium you consume. It offers tips on how to start and stay on the eating plan, as well as a table of sodium and some recipes. The amount and recipe are given for two levels of sodium consumption—2,300 milligrams (the upper limit by the Federal Government's National High Blood Cholesterol Education Program) and the amount used to figure food labels (1,500 milligrams).

Those with high blood pressure may especially benefit and reducing their sodium intake. But the guidelines include can follow.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health
National Heart, Lung, and Blood Institute

Examine indices

Healthy Eating Index

Mediterranean diet

- Red meat: 4 servings
- Sweets: 3 servings
- Eggs: 3 servings
- Potatoes: 3 servings
- Olive, pulses, nuts: 3-4 servings
- Poultry: 4 servings
- Fish: 5-6 servings
- Dairy products: 2 servings
- Olive oil as the main added lipid
- Fruit: 2 servings
- Vegetables (including wild greens): 6 servings
- Non-refined cereals and products (whole grain bread, whole grain pasta, brown rice, etc.): 8 servings

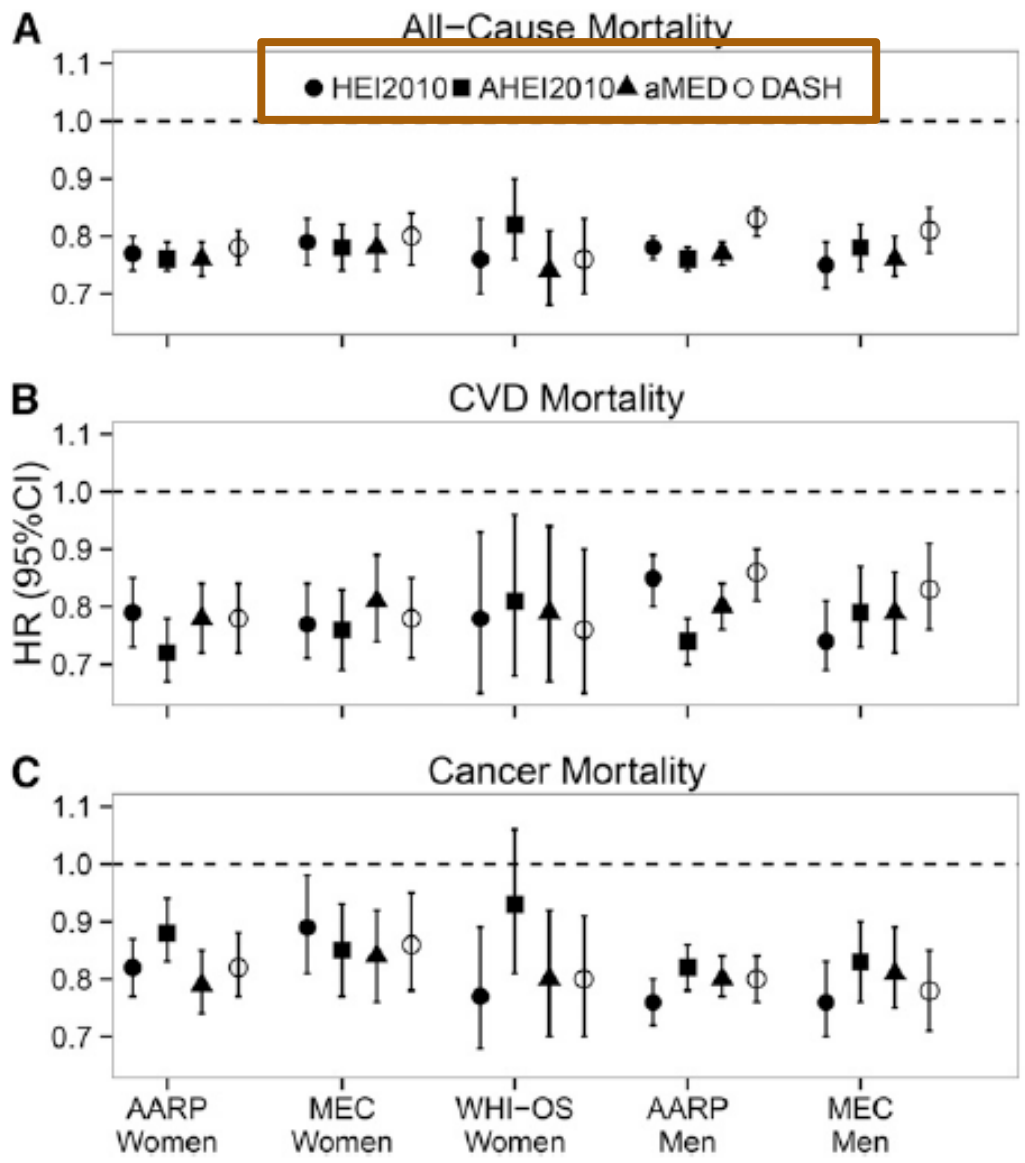
Wine in moderation

One serving equals approximately half of the portions as defined in the greek market regulations (portions served in restaurants)

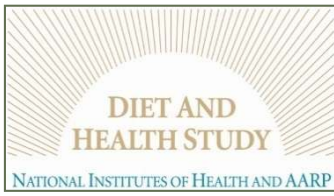
Also remember to:

- Drink plenty of water
- Avoid salt and replace it by herbs (e.g. oregano, basil, thyme, etc)

Source: Supreme Scientific Health Council, Hellenic Ministry of Health, available at: www.nut.uns.gr/dietaryENG.html



NIH-AARP



Multiethnic Cohort



Women's Health Initiative

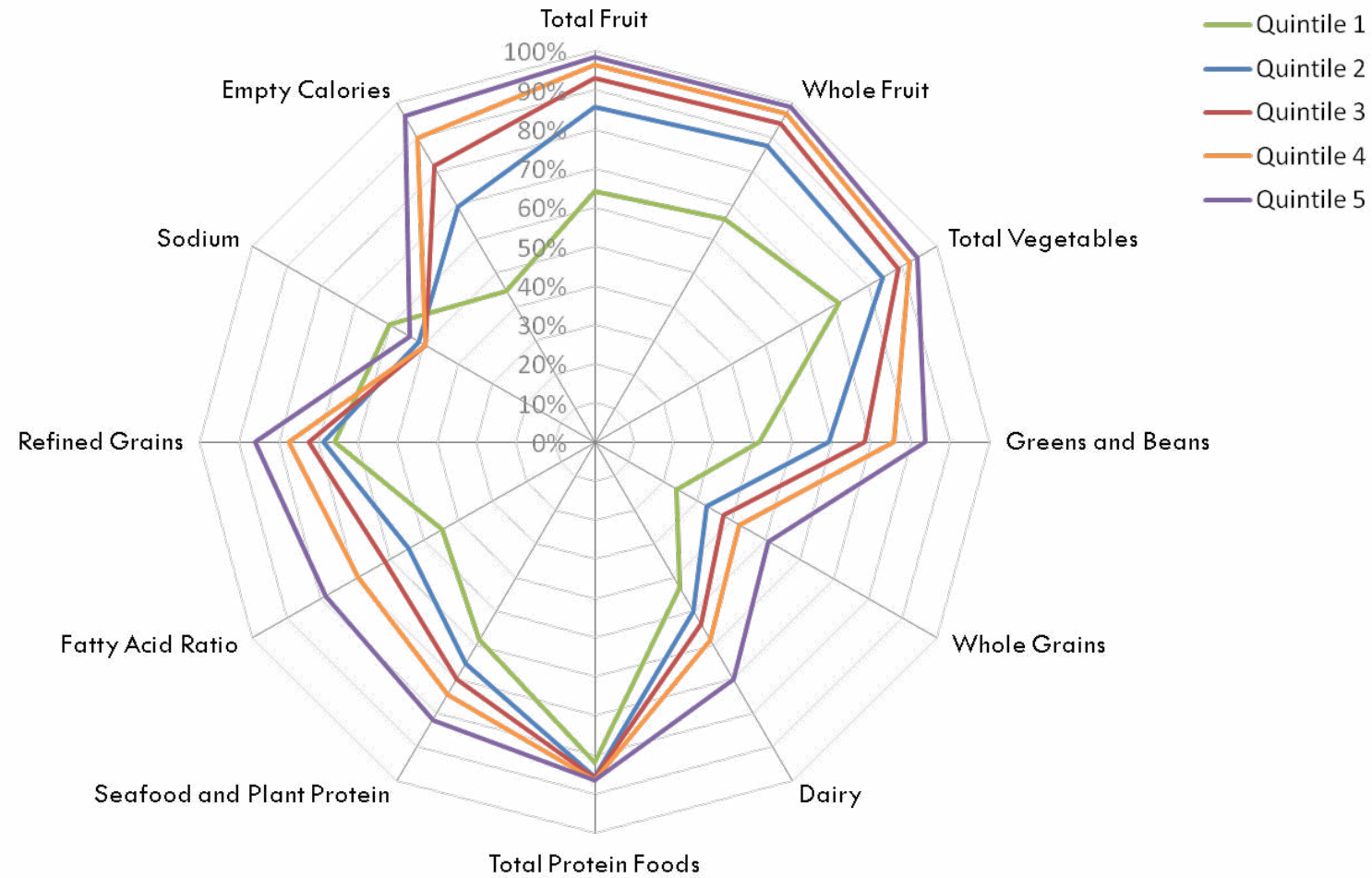


Adjusted for age, race/ethnicity, education, marital status, physical activity, smoking, energy, BMI, diabetes, alcohol (HEI & DASH), HRT (women only).

Perfect HEI score

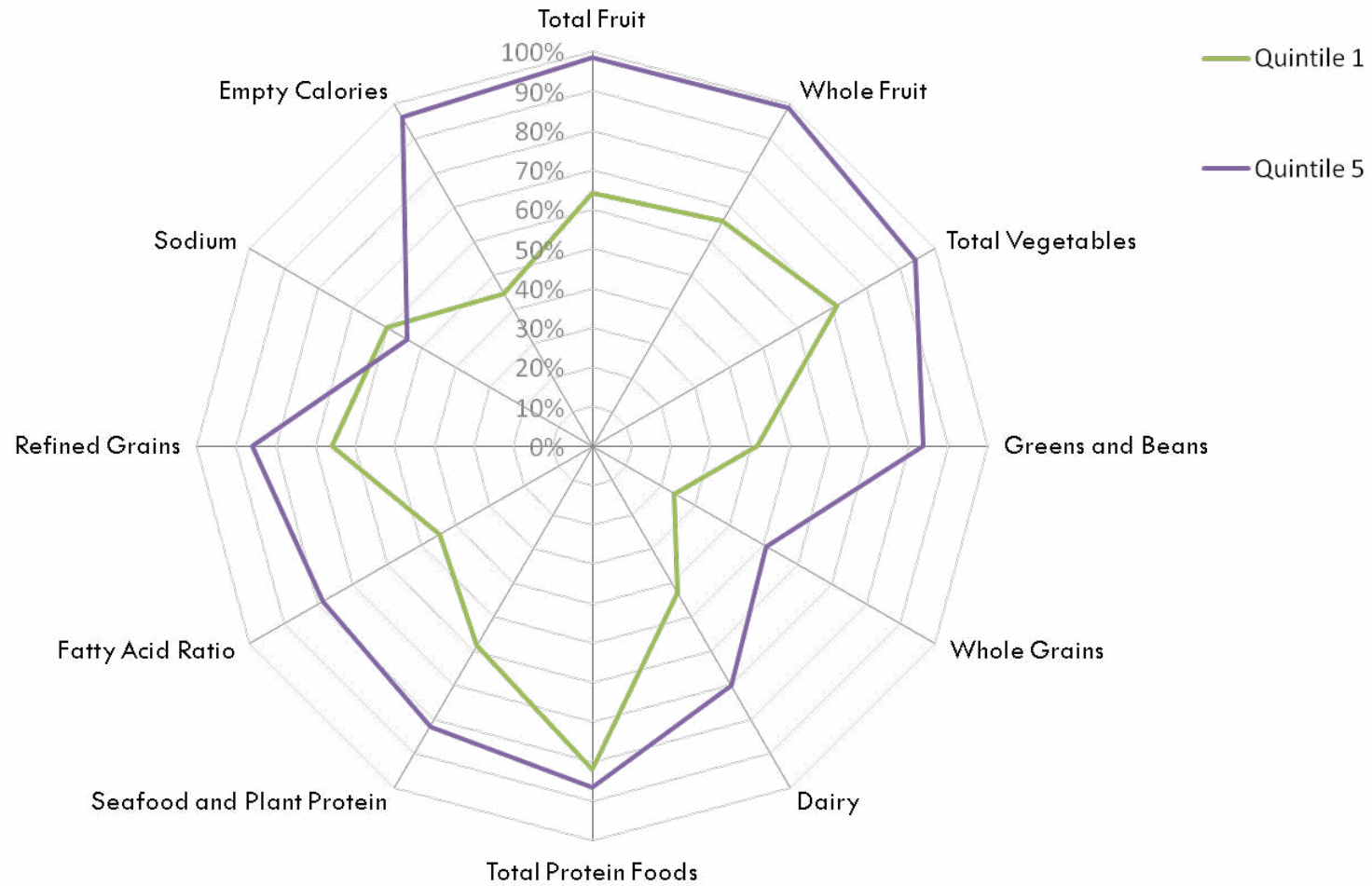


Average HEI-2010 component scores, by quintile of total score



Data Source: AARP study, FFQ, total scores = 52, 63, 69, 74 and 80

Average HEI-2010 component scores, by quintile of total score

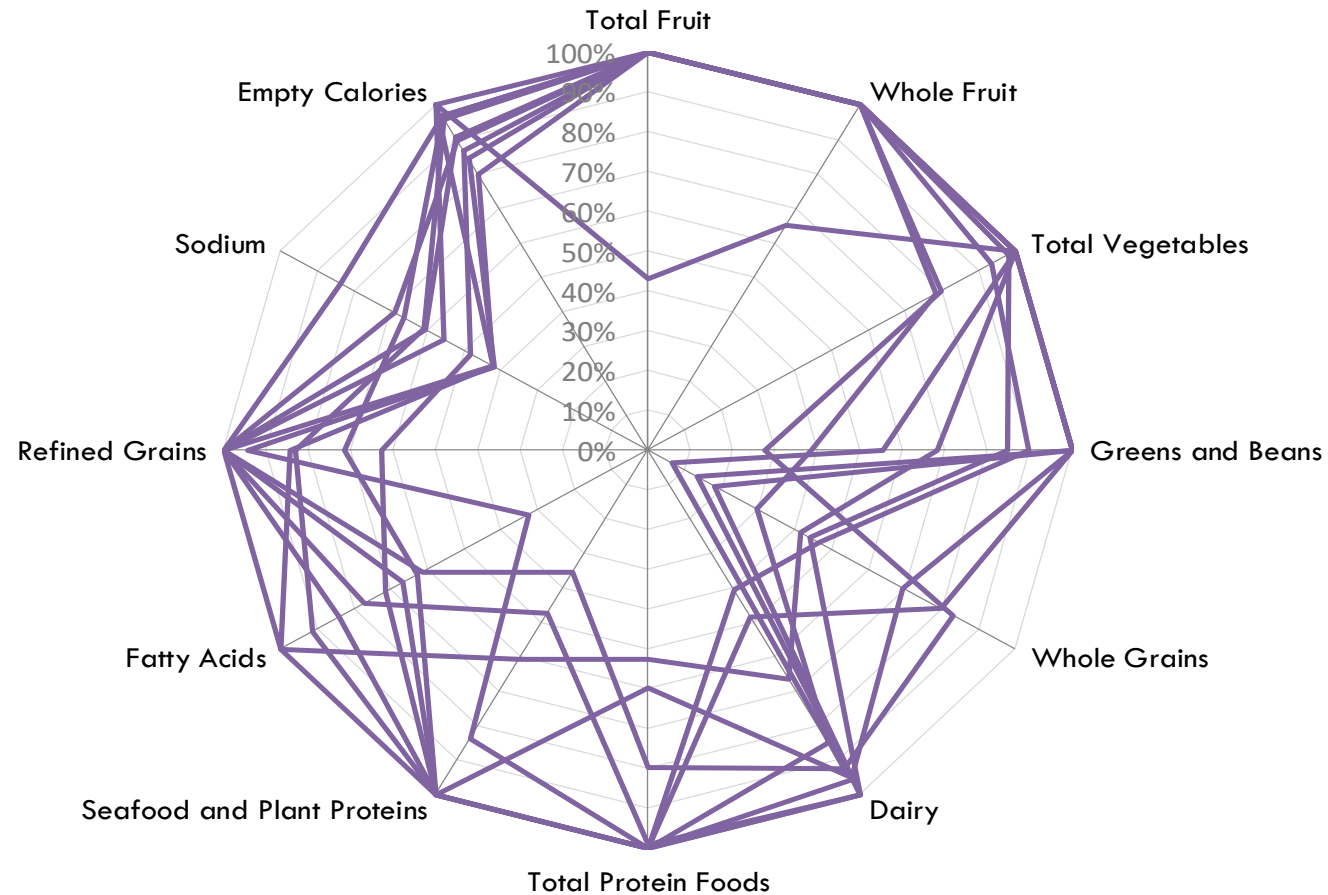


Data Source: AARP study, FFQ, total scores = 52 and 80

10 randomly selected females within quintile 1 of total HEI-2010 score



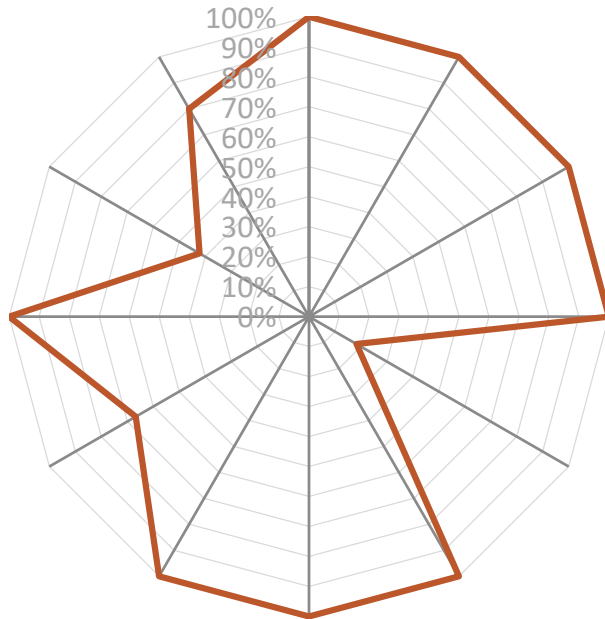
10 randomly selected females within quintile 5 of total HEI-2010 score



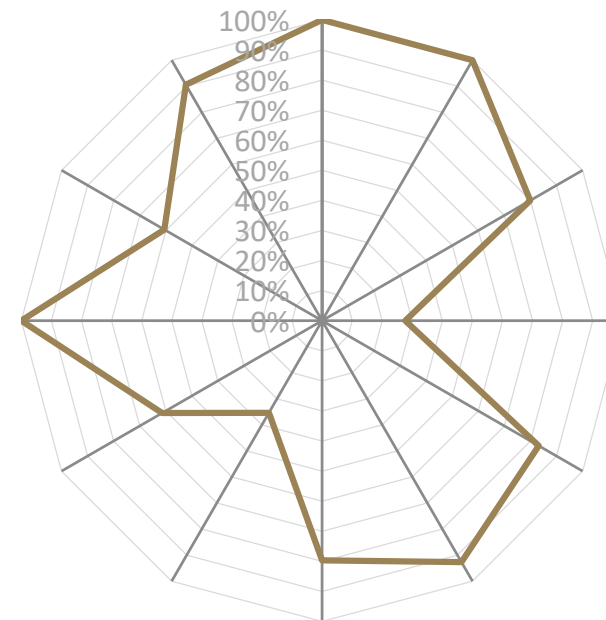
Patterning of indexes and hypothesis testing

Are different patterns of overall high quality equally protective?

Overall score=79



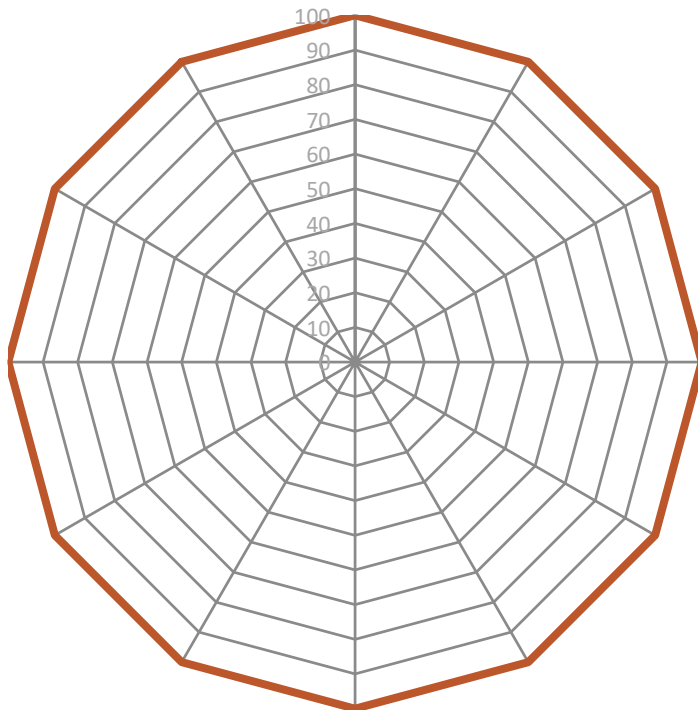
Overall score=79



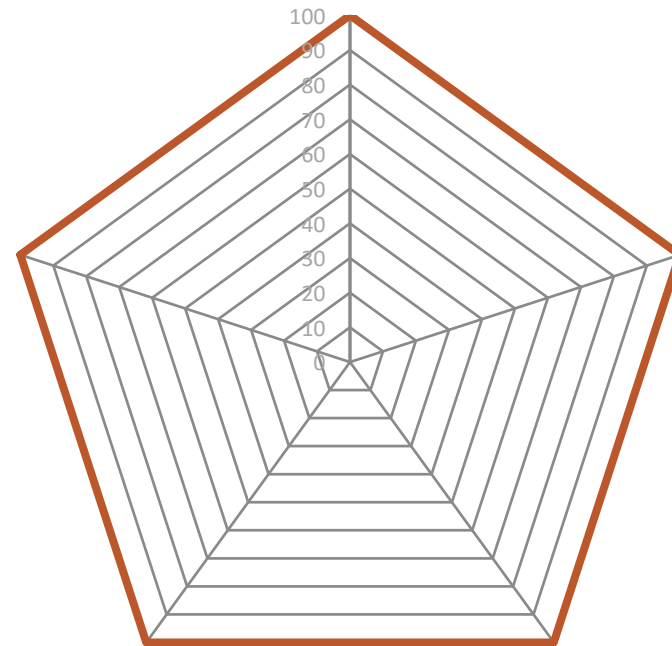
Indexes, modifications and hypothesis testing

Are all components of pattern necessary or is a subset sufficient?

Necessary?



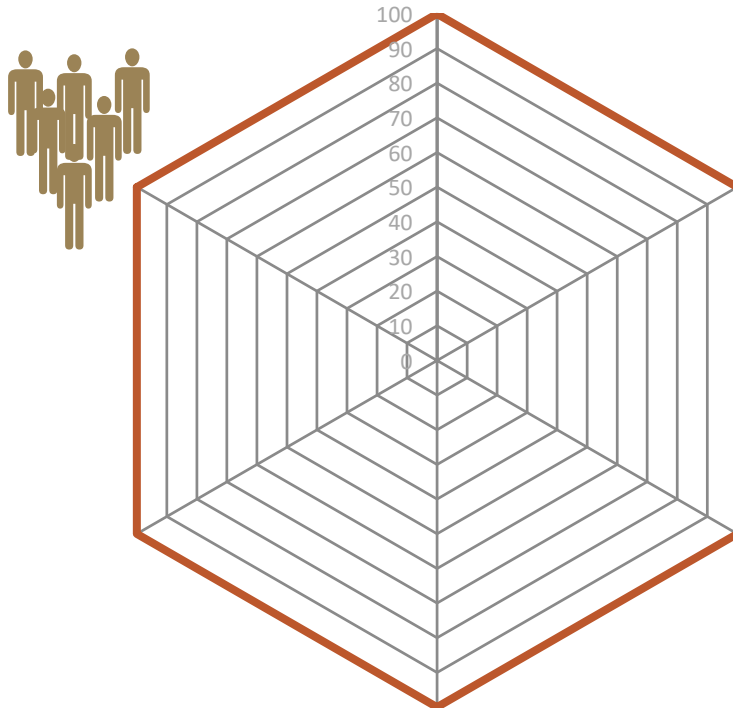
Sufficient?



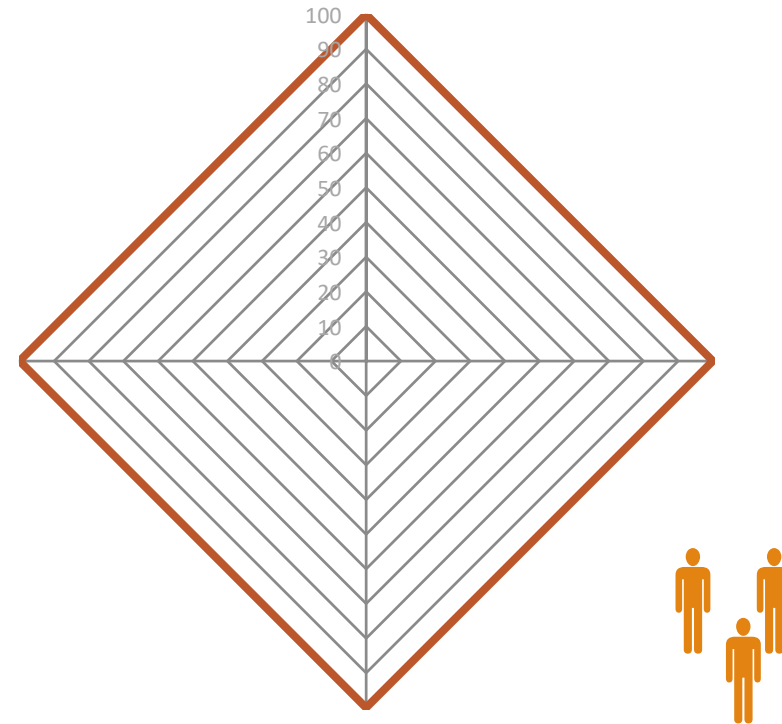
Sorting of population, indexes,
and hypothesis testing

Is recommended
pattern of eating
optimal/necessary/
sufficient for
everyone?

Ideal for some?



Ideal for others?

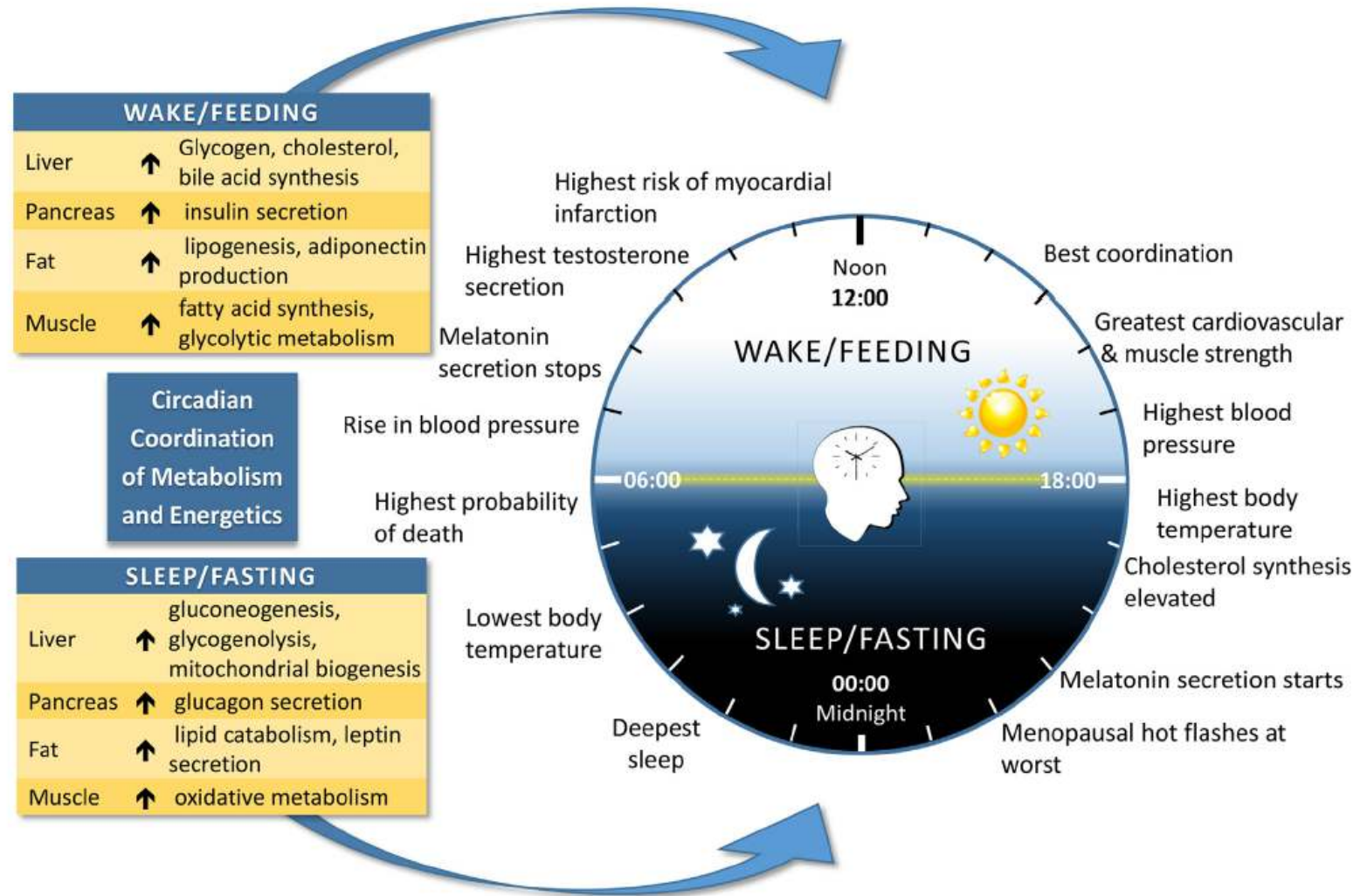


Why is dynamism important?

Cancer has a long latency



Cellular processes are influenced by diurnal variations



What are the key questions regarding dynamism?

Long-term

Do specific time periods represent heightened risk?



Life transitions and diet change

Reflects
maternal diet

Food intake
independent of
parents

Dietary change
explored or necessary

In Utero	Infancy and Childhood	Adolescence	Adulthood	Older Adulthood
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Breast/formula fed?
Food preferences
established

Partner, children
influence food
choices



BREAST CANCER AND THE ENVIRONMENT

A LIFE COURSE APPROACH

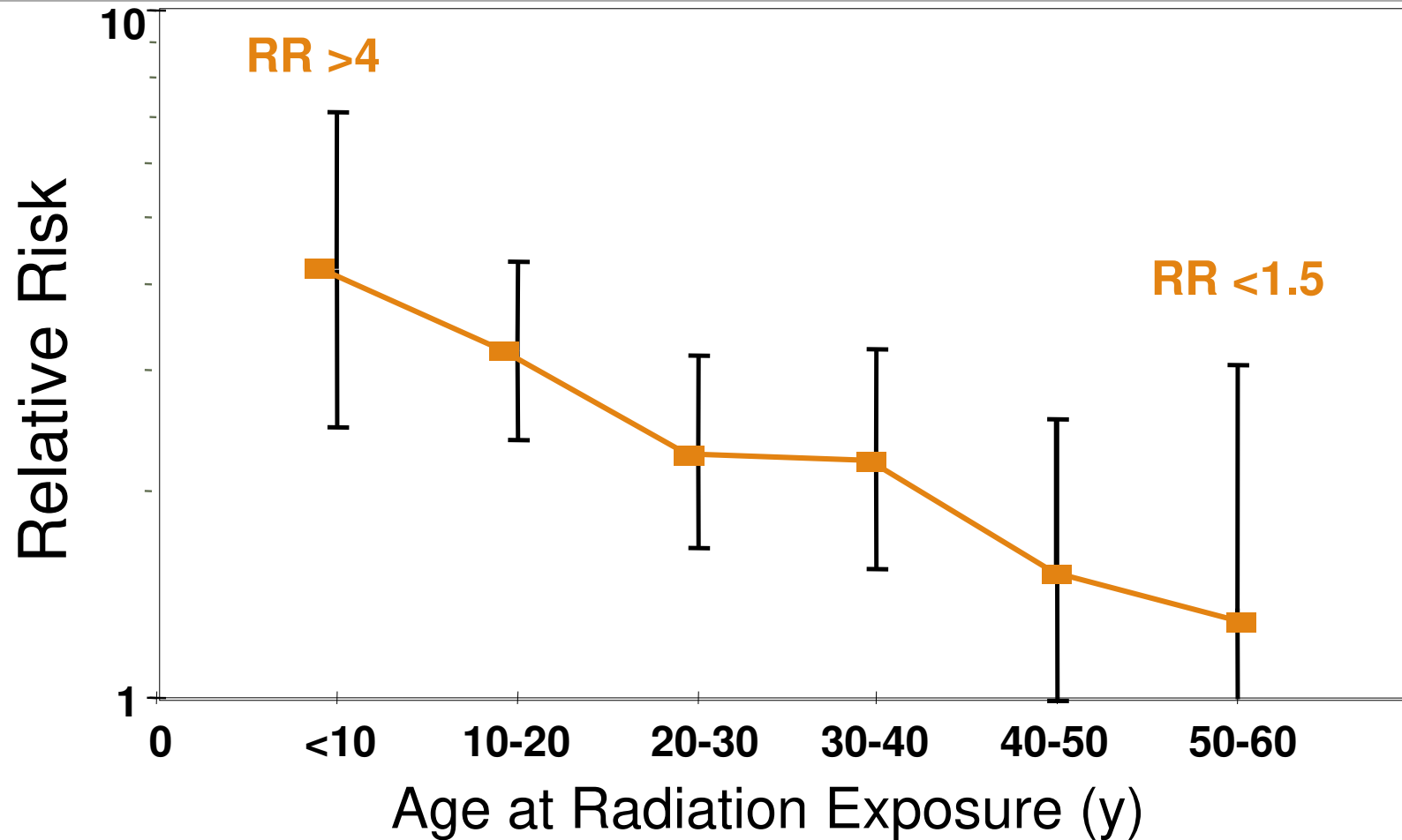
INSTITUTE OF MEDICINE
NATIONAL ACADEMIES PRESS

Institute of Medicine,
Board on Health Care Services, Board
on Health Sciences Policy
published December 7, 2011

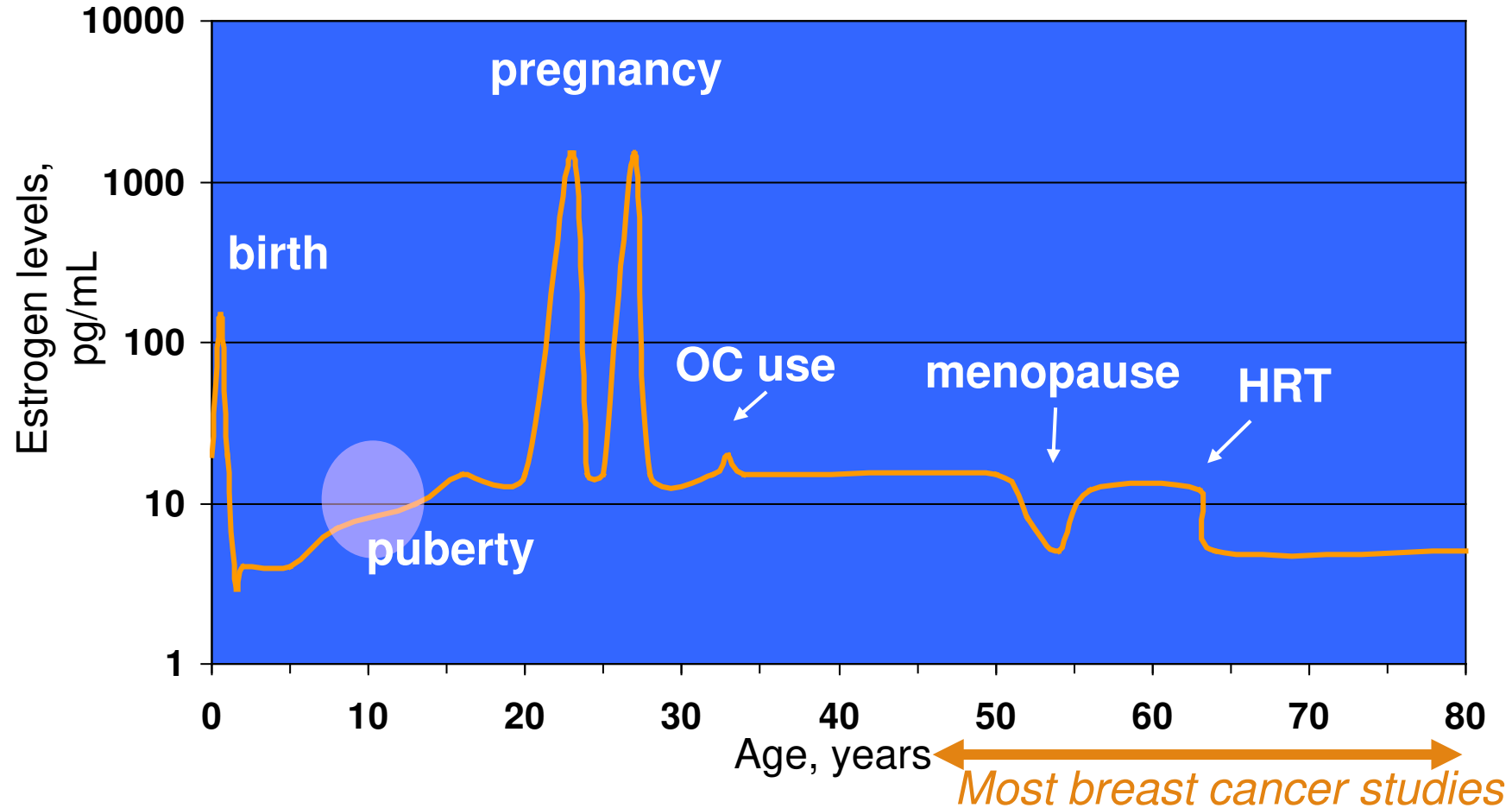
“Overall, the IOM finds that major advances have been made in understanding breast cancer and its risk factors, but more needs to be learned about its causes and how to prevent it.

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.”

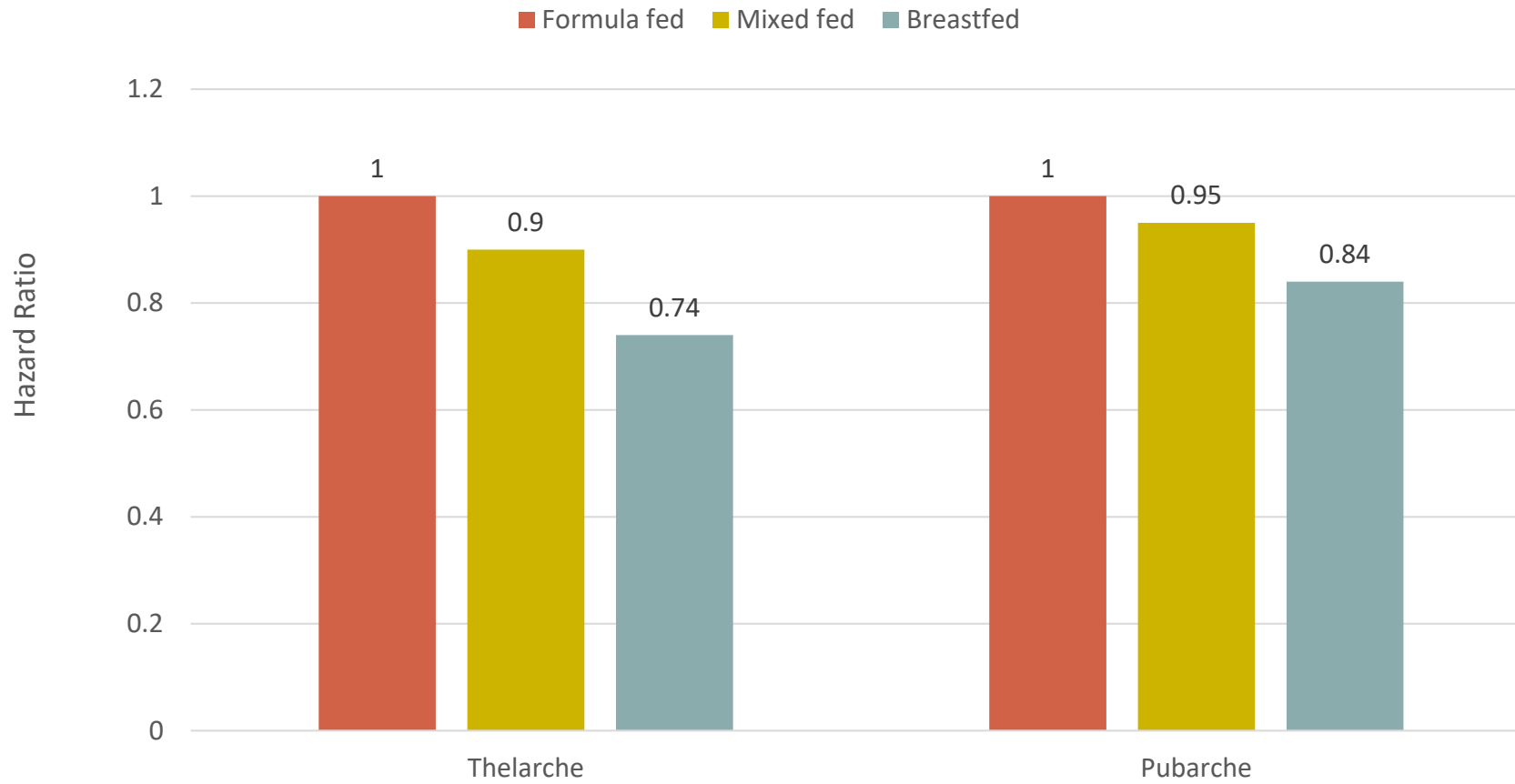
Atomic bomb radiation and breast cancer



Estrogen levels throughout life



Risk of early puberty by infant feeding practice*



*BCERP studies

Long-term

Does risk or benefit
accumulate over
time?

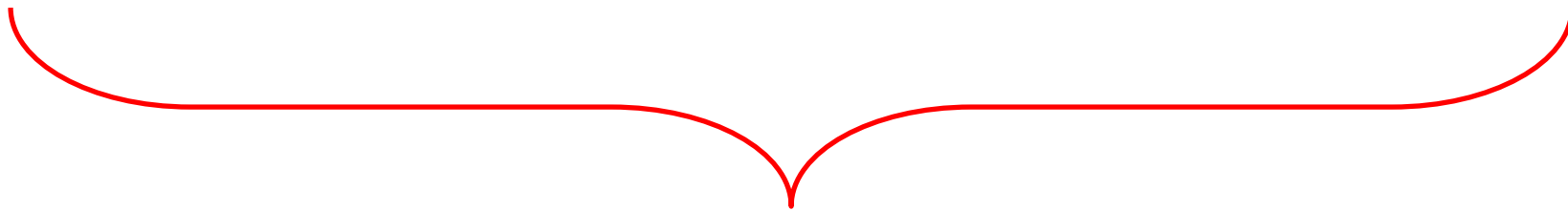
In Utero

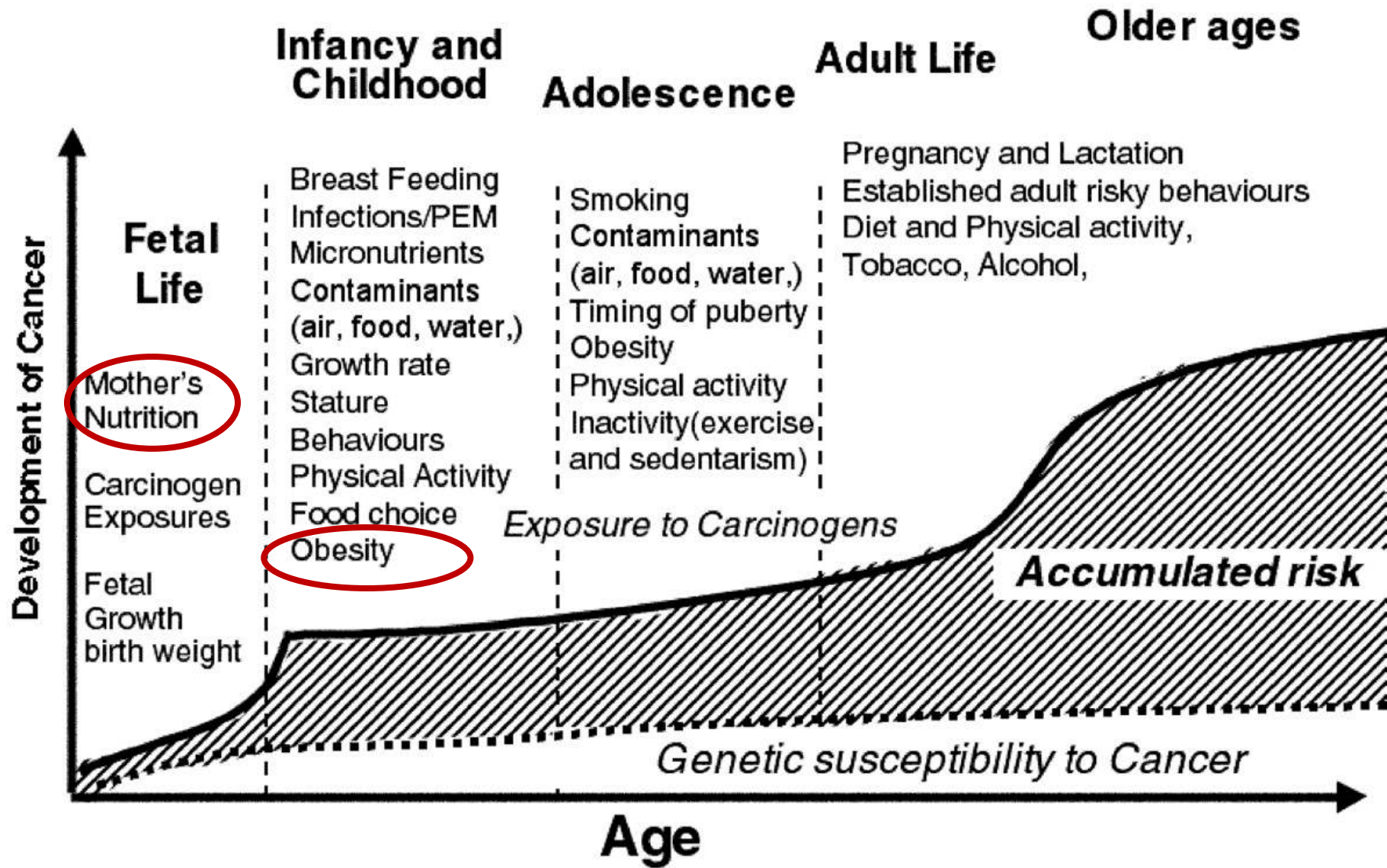
Infancy and
Childhood

Adolescence

Adulthood

Older
Adulthood





Long-term

Does a change in diet alter the course of the risk profile?



Healthy diet



Unhealthy diet

In Utero

Infancy and
Childhood

Adolescence

Adulthood

Older
Adulthood

■ NHS (women)
■ NHS II (women)
■ HPFS (men)

Foods

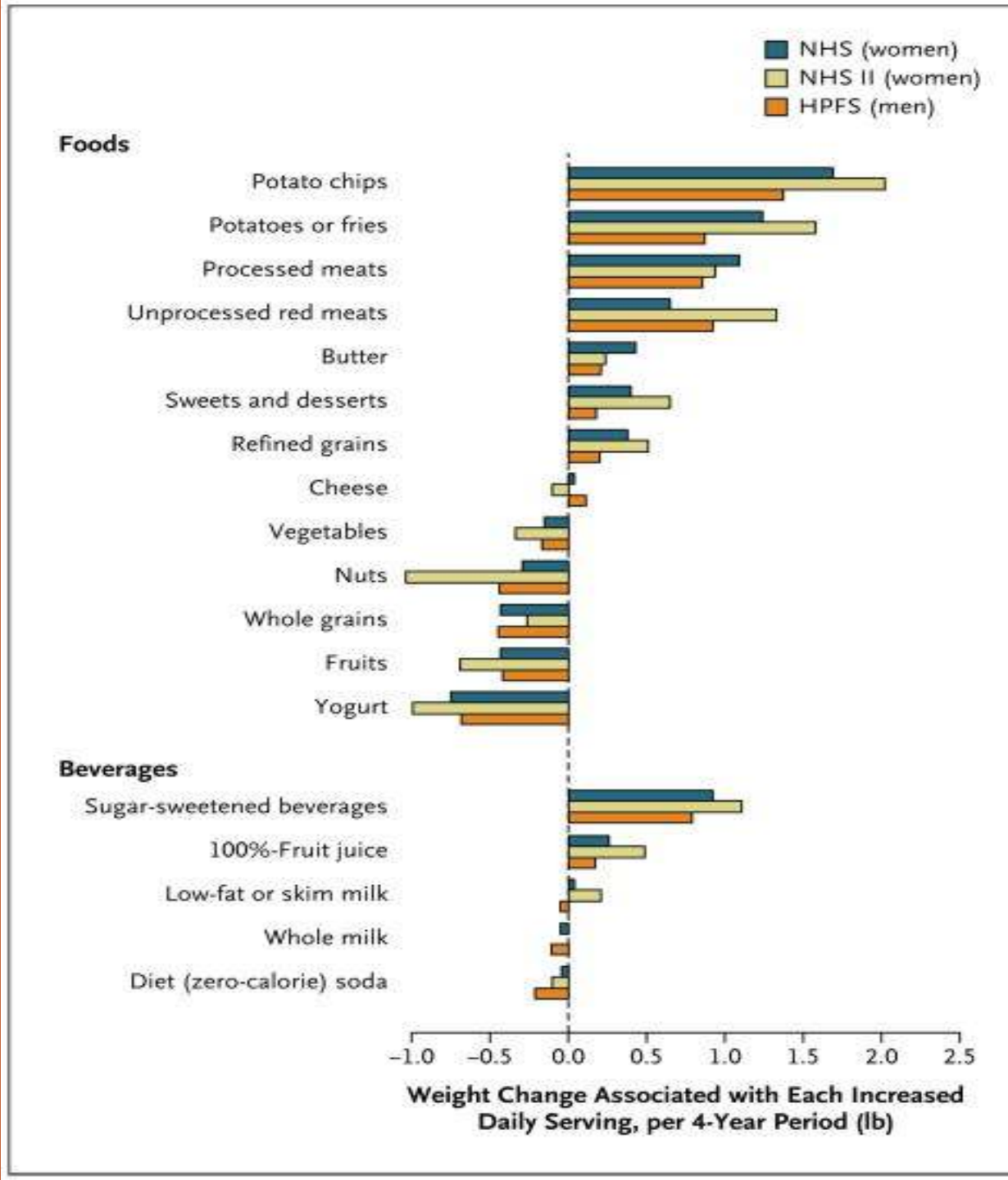
- Potato chips
- Potatoes or fries
- Processed meats
- Unprocessed red meats
- Butter
- Sweets and desserts
- Refined grains
- Cheese
- Vegetables
- Nuts
- Whole grains
- Fruits
- Yogurt

Beverages

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

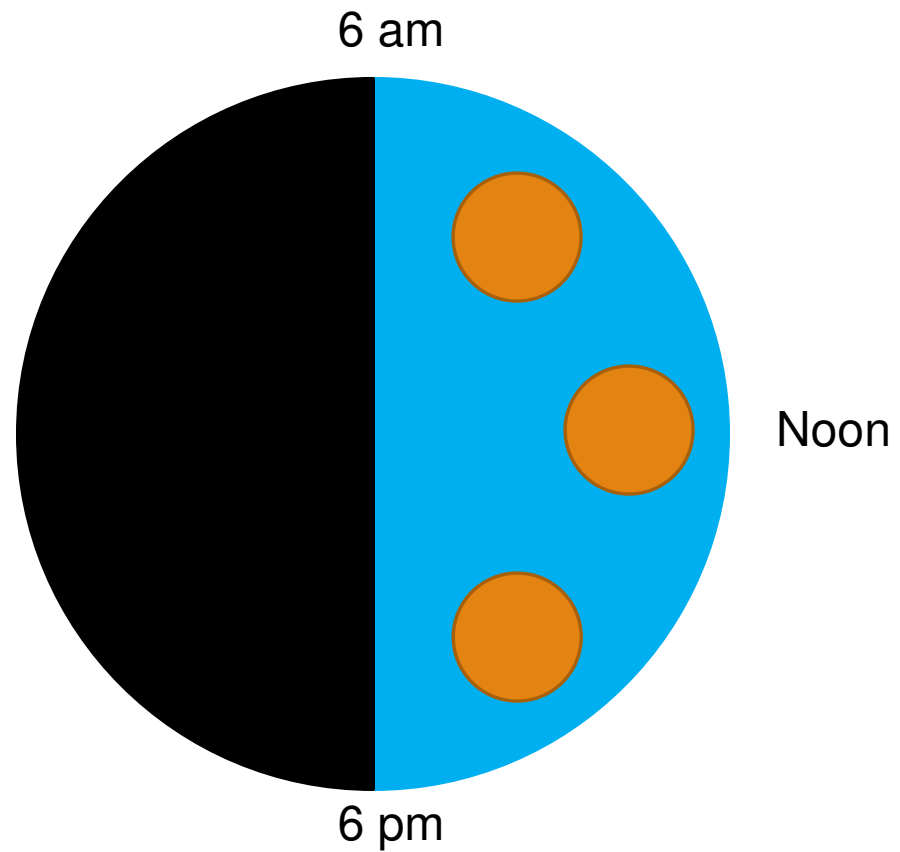
-1.0 -0.5 0.0 0.5 1.0 1.5 2.0 2.5
Weight Change Associated with Each Increased Daily Serving, per 4-Year Period (lb)

Mozaffarian et al., *N. Engl. J. Med.*, 2011.

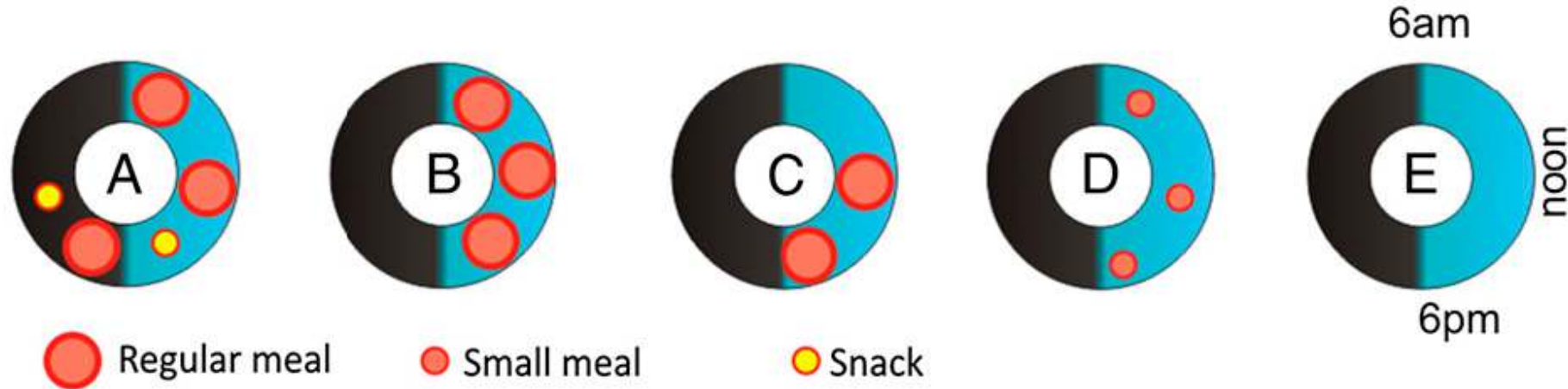


Short-term

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

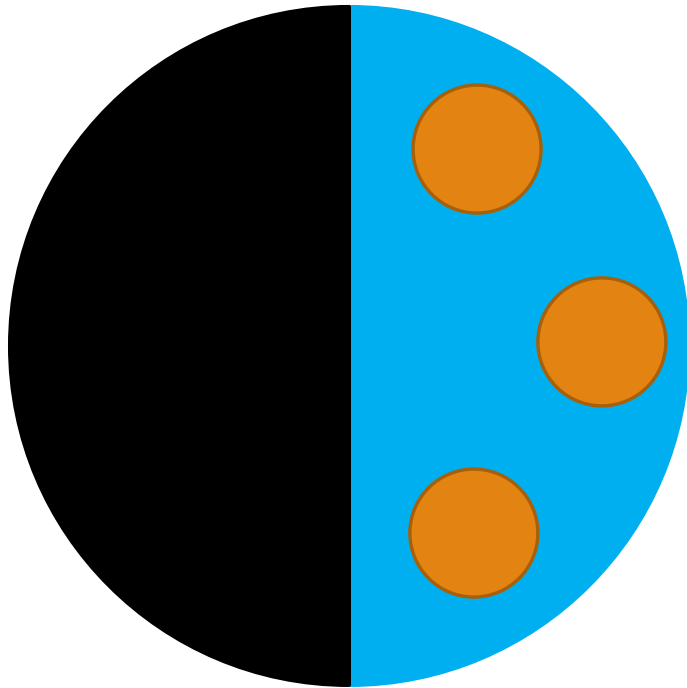
Alternate day fast

Alternate day ER

M	T	W	Th	F	S	Su
A	A	A	A	A	A	A
B	B	B	B	B	B	B
D	D	B	B	B	B	B
A	E	A	E	A	E	A
A	D	A	D	A	D	A

Short-term

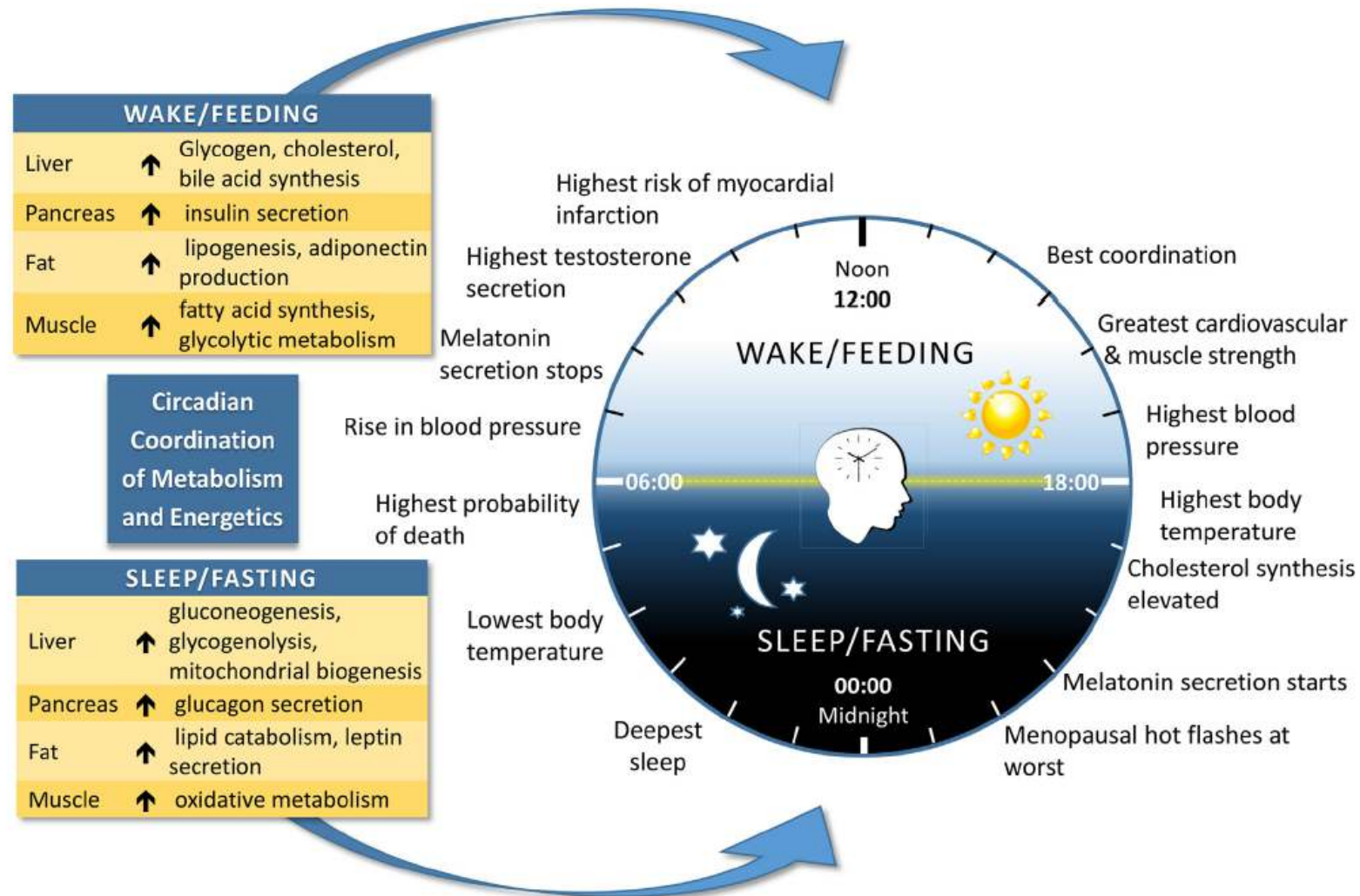
If we alter eating frequency, does it modify the biology?



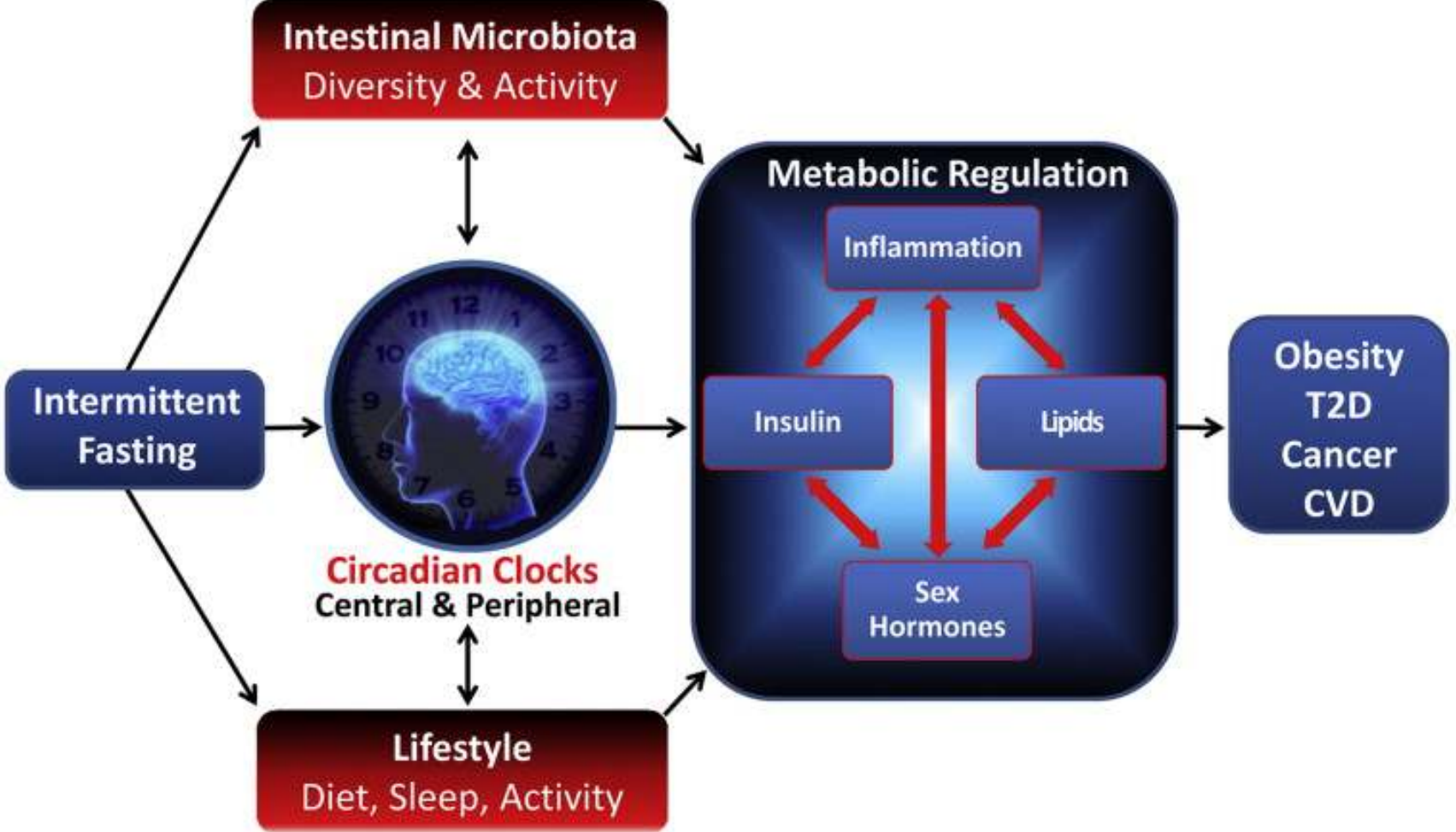
Calendar for the month of _____

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday

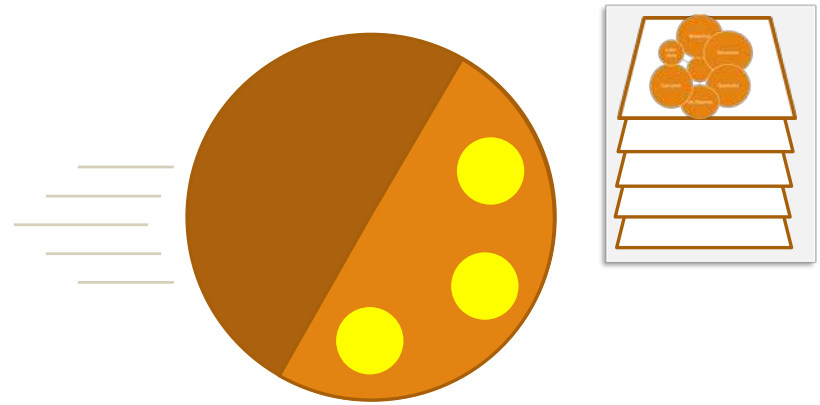
Short-term metabolic effects



Downstream effects on health



Putting it all together...



In Utero	Infancy and Childhood	Adolescence	Adulthood	Older Adulthood
Prevention	Screening	Diagnosis	Treatment	Survivorship through end of life

Key takeaways

Evidence-based reviews that follow strict criteria represent the pinnacle of research quality.

The WCRF/AICR recommendations are based on reviews which follow such criteria.

Diet is extraordinarily complex, involving both multidimensionality and dynamism.

Diets are multi-dimensional on a number of layers and dynamic in both the short-term and long-term

Patterns of multidimensionality and long- and short-term dynamism may be critical to cancer control

Further research into patterns of multidimensionality and dynamism may help elucidate better understanding of relationship between diet and cancer risk.

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Larry Kushi

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TusaRebecca Schap

Amy Subar