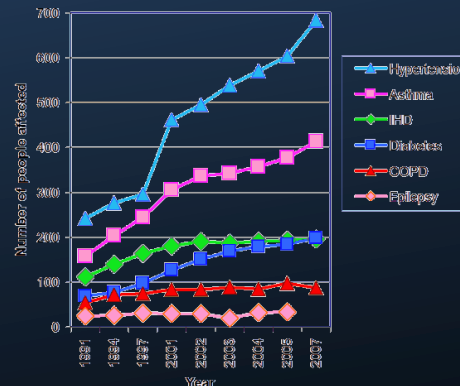


Nutritional epidemiology as a Public Health Science

studying nutritional determinants of disease

Anne-Claire Vergnaud, PhD

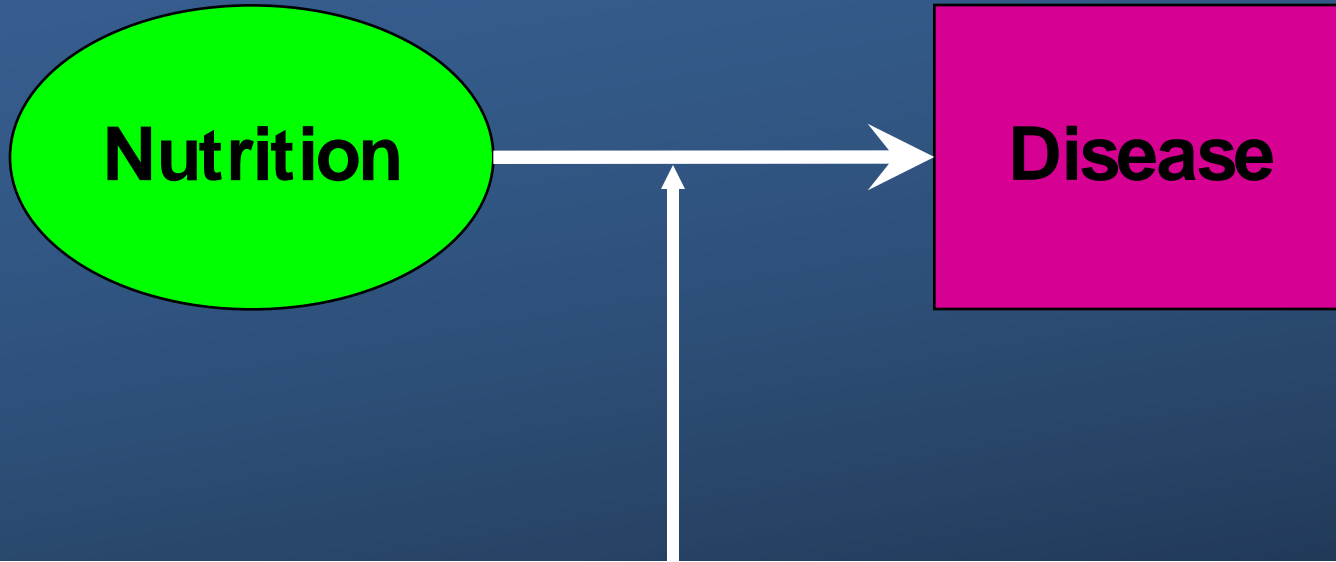
Global Health course, Imperial College



Today's session

- **9.30-10.20 am: Lecture:**
 - Goals of nutritional epidemiology
 - Nutrition transition
 - Exposure assessment methods
 - Methodology issues
 - Summary
 - **10.40-11.40 am: Seminar**
 - Discussion about dietary patterns in north India
 - **11.50-12.40 am: Practical**
 - Statistical analysis of a cohort study
- All the basic principles of epidemiology and statistics apply!

Goals of nutritional epidemiology



**What's the connection?
And how do we figure it out?**

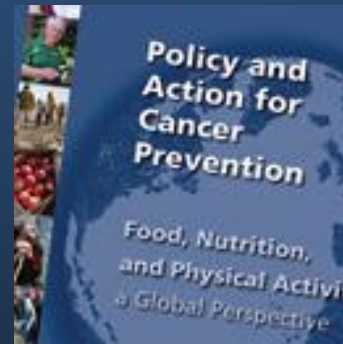
'Nutrition'



- Everybody eats, has some body size, some level of activity
- ▶ Major public health implications

(Minimal) Estimates of Cancer Preventability Through Diet, Body Fatness, Physical Activity

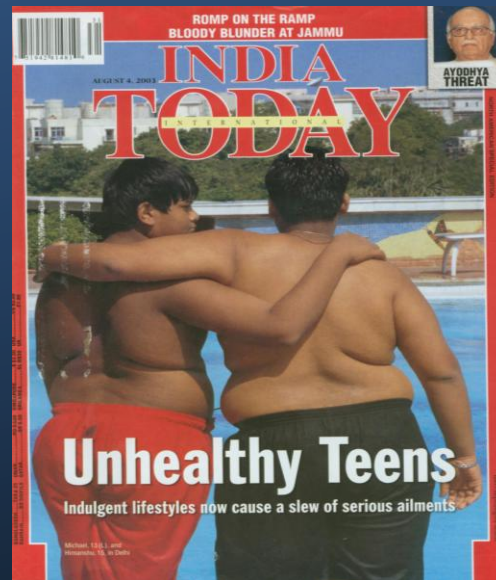
- UK 26%
- USA 24%
- Brazil 19%
- China 20%



More than 70% of all cancer deaths in 2005 occurred in low and middle income countries

Exposure assessment (1)

Anthropometry



Markers (1)

- Weight
- Height

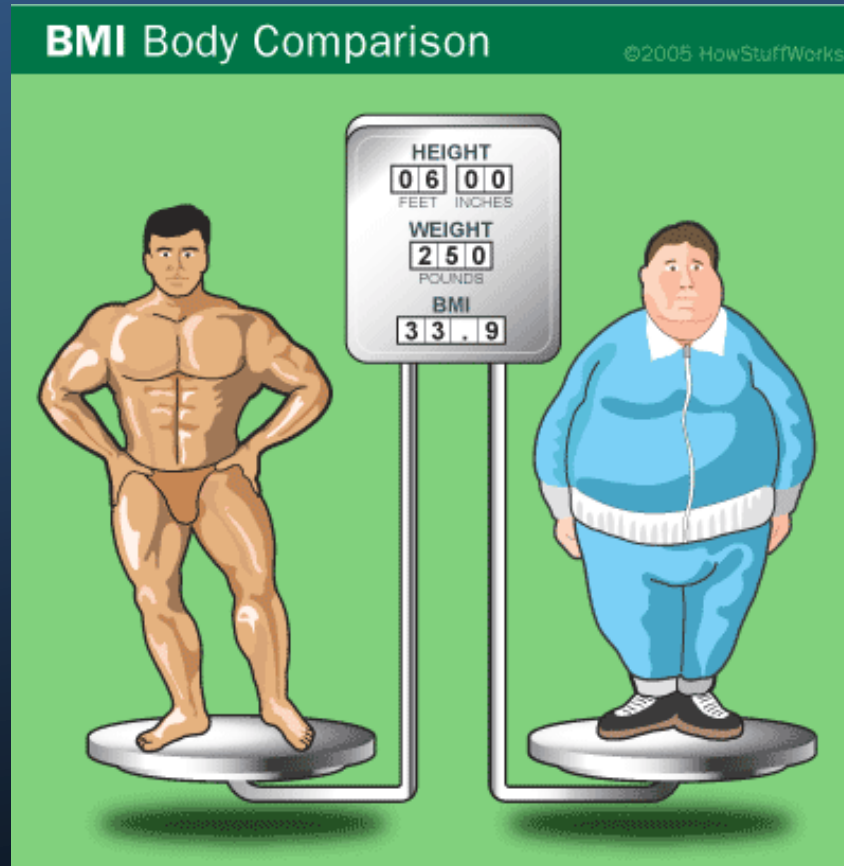
BMI

Normal weight: $< 25 \text{ kg/m}^2$

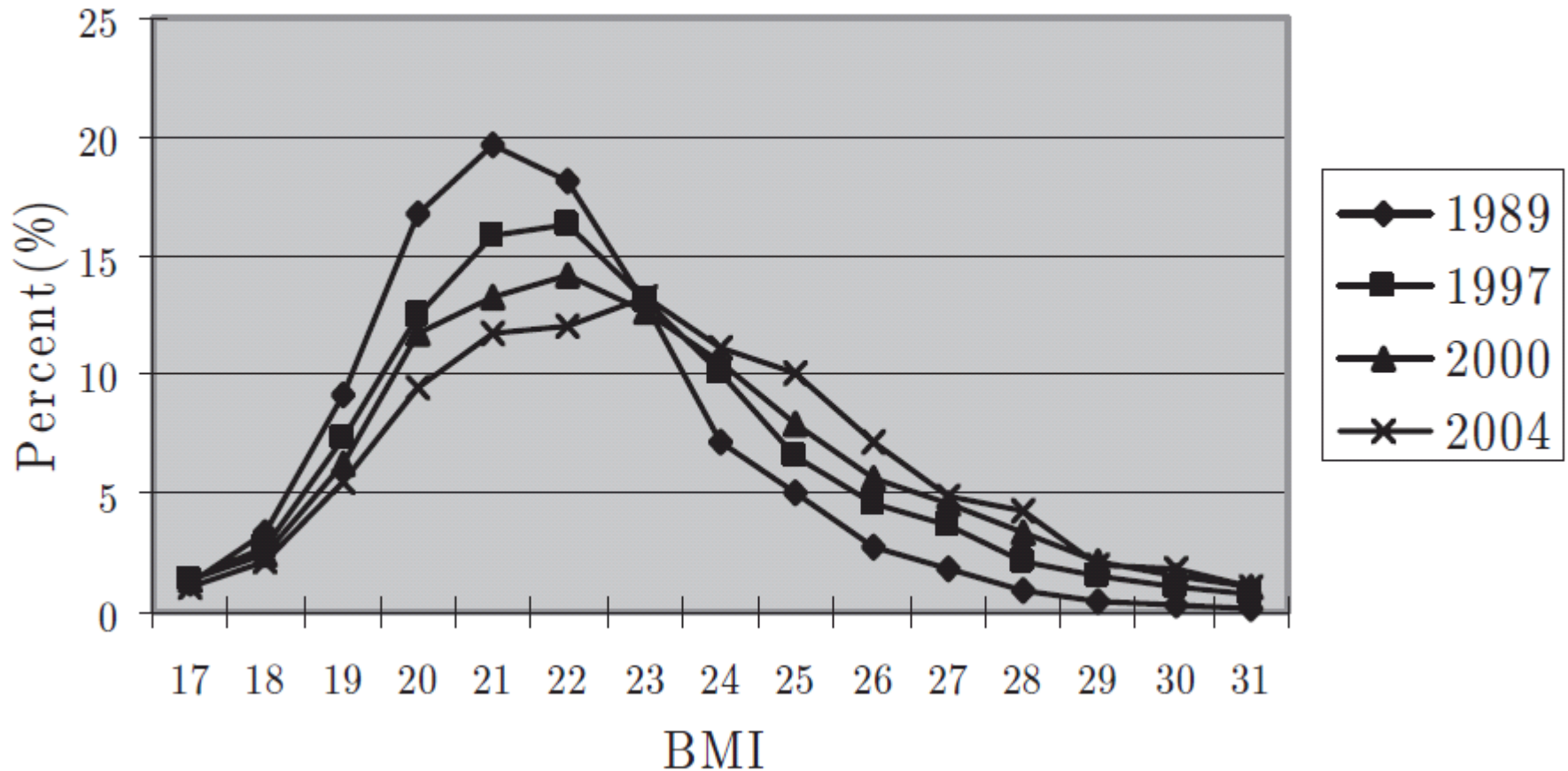
Overweight: $[25-30[\text{ kg/m}^2$

Obesity: $\geq 30 \text{ kg/m}^2$

Discrimination
of populations



Changes in distribution of adult male BMI in China



Markers (2)

- Waist circumference
- Hip circumference
- WHR

Visceral fat tissue?

- Frequency of diabetes mellitus according to BMI and waist circumference
- Skinfolds

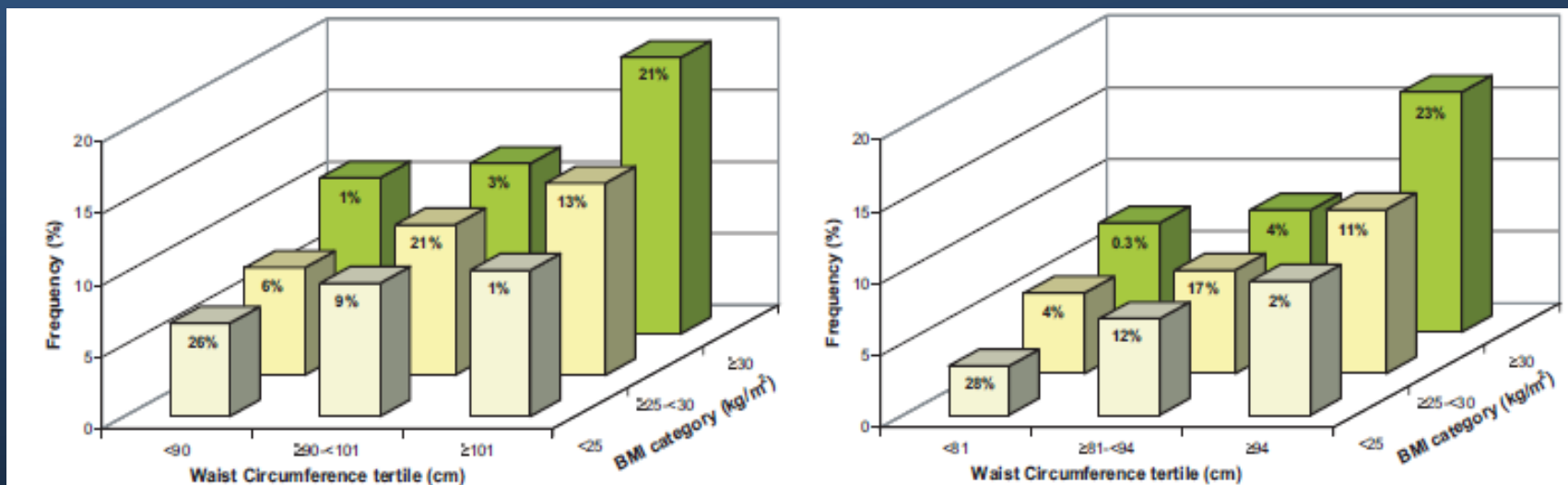
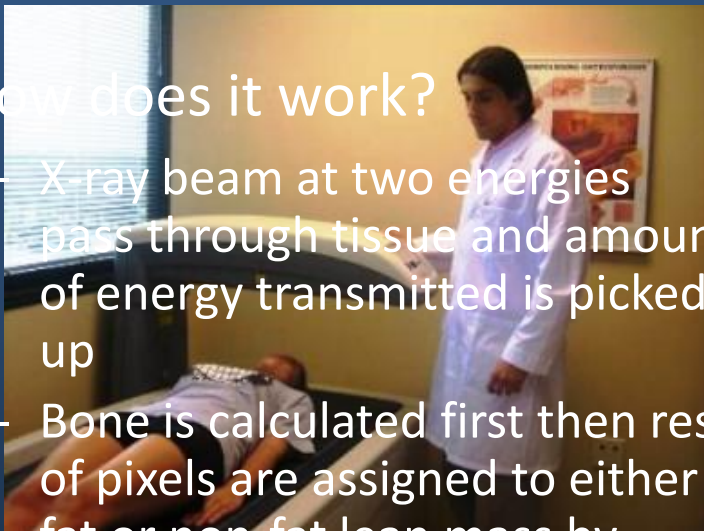


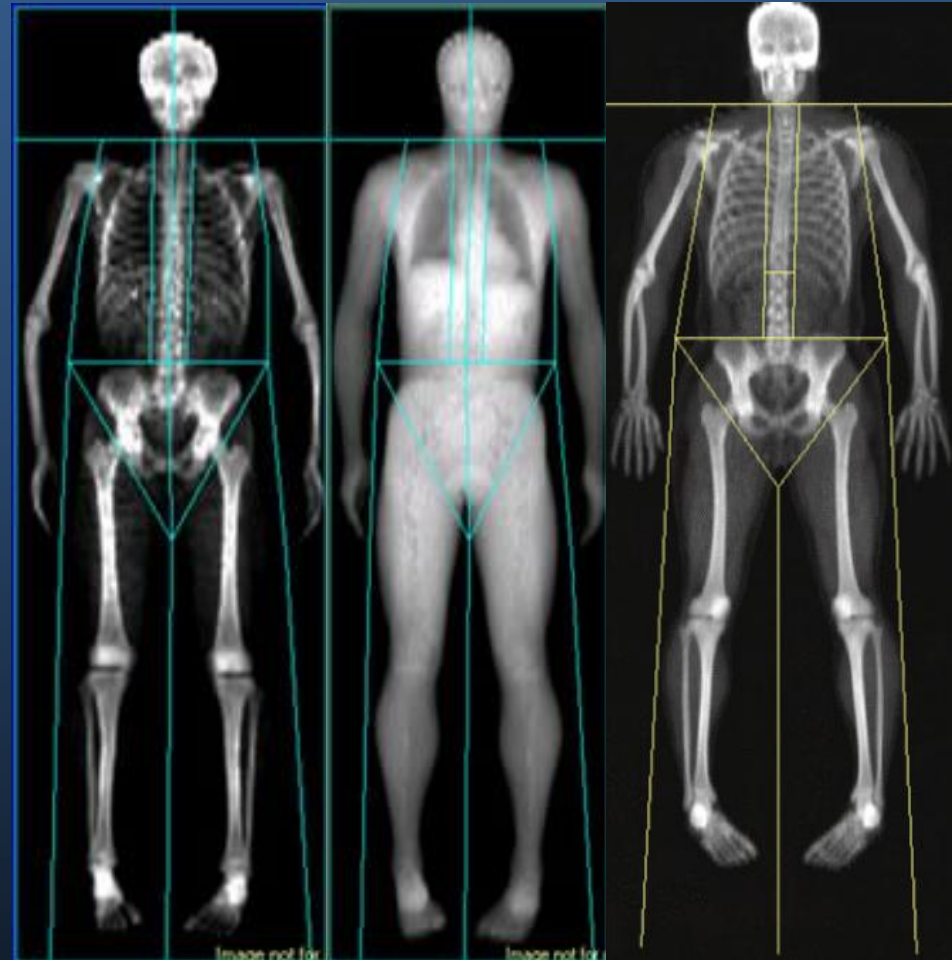
Figure 5. Frequency of known CVD for men (A) and women (B), and known diabetes mellitus for men (C) and women (D), adjusted for age, region, and smoking status, by gender-specific WC tertiles and BMI categories. The percentage of patients in each of the 9 groups is shown.

Dual energy x-ray absorptiometry

- Measure:
 - Bone, non-fat lean soft tissue, fat
 - Total and regional masses



- How does it work?
 - X-ray beam at two energies pass through tissue and amount of energy transmitted is picked up
 - Bone is calculated first then rest of pixels are assigned to either fat or non-fat lean mass by algorithms



Prevalence of pre-diabetes and mean fasting insulin, 2H-OGTT insulin and HOMA-1 by BMI and trunk fat% in 280 Chinese women with normal glucose tolerance

BMI	%TF	Fasting ln(insulin)	2H-OGTT ln(insulin)	HOMA-1	OR (95%CI) of pre-diabetes
<23	Low	1.6 ± 0.8	2.8 ± 0.9	1.3 ± 1.2	1
	High	1.7 ± 0.8 *	2.9 ± 0.9 *	1.4 ± 1.0 *	1.5 (1.2-2.0)
≥23	Low	1.6 ± 0.7	2.8 ± 0.9	1.3 ± 1.2	1.3 (1.0-1.6)
	High	1.8 ± 0.8 *	3.0 ± 0.9 *	1.6 ± 1.6 *	1.6 (1.3-2.0)

YunXian *et al.* *Metabolism* 2010

Exposure assessment (2)

Physical activity



Physical Activity Assessment Methods

Indirect

- **Physiologic measures**
 - Metabolic
 - Cardiorespiratory
 - Motor
 - Muscular
- **Health status**
- **Surveys**

Key parameters to describe Physical Activity

Intensity

Calories expended, power output, relative metabolic level (VO_2), relative to lactate threshold, relative to heart rate, multiples of resting metabolic rate (MET), rate of perceived exertion, can include sedentary

Frequency

Days, sessions, bouts

Duration

Minutes per session, minutes per (day, week)

Volume

METS-min per week, distance traveled, energy expenditure

Pattern

Usual, weekend, holiday, interrupted or not

Type

Specific activity, domain (occupation, household, transport, leisure), body position

Example: Diary or log

- 1-3 days of all or specific activities; activities and time spent

Activity Diary Page

Date: _____ Mon. Tues. Wed. Thurs. Fri. Sat. Sun.

TIME OF DAY	ACTIVITY	DURATION	LEVEL OF EXERTION	LEVEL OF ENJOYMENT

TOTAL Daily Activity Minutes: _____

Notes: _____

Defining “MET” Intensity of Physical Activity

- MET: Metabolic Equivalent Tasks
- MET= ratio of the metabolic rate of an activity divided by metabolic rate of an individual at rest (sitting quietly).
- Walking at 5 km/h requires 3 METs for a 60-kg person
- Final physical activity score (MET-h/wk).
 - The durations of each physical activity (h/wk) is multiplied by its metabolic cost (in MET) and summed

Physical Activity Assessment Methods

Direct

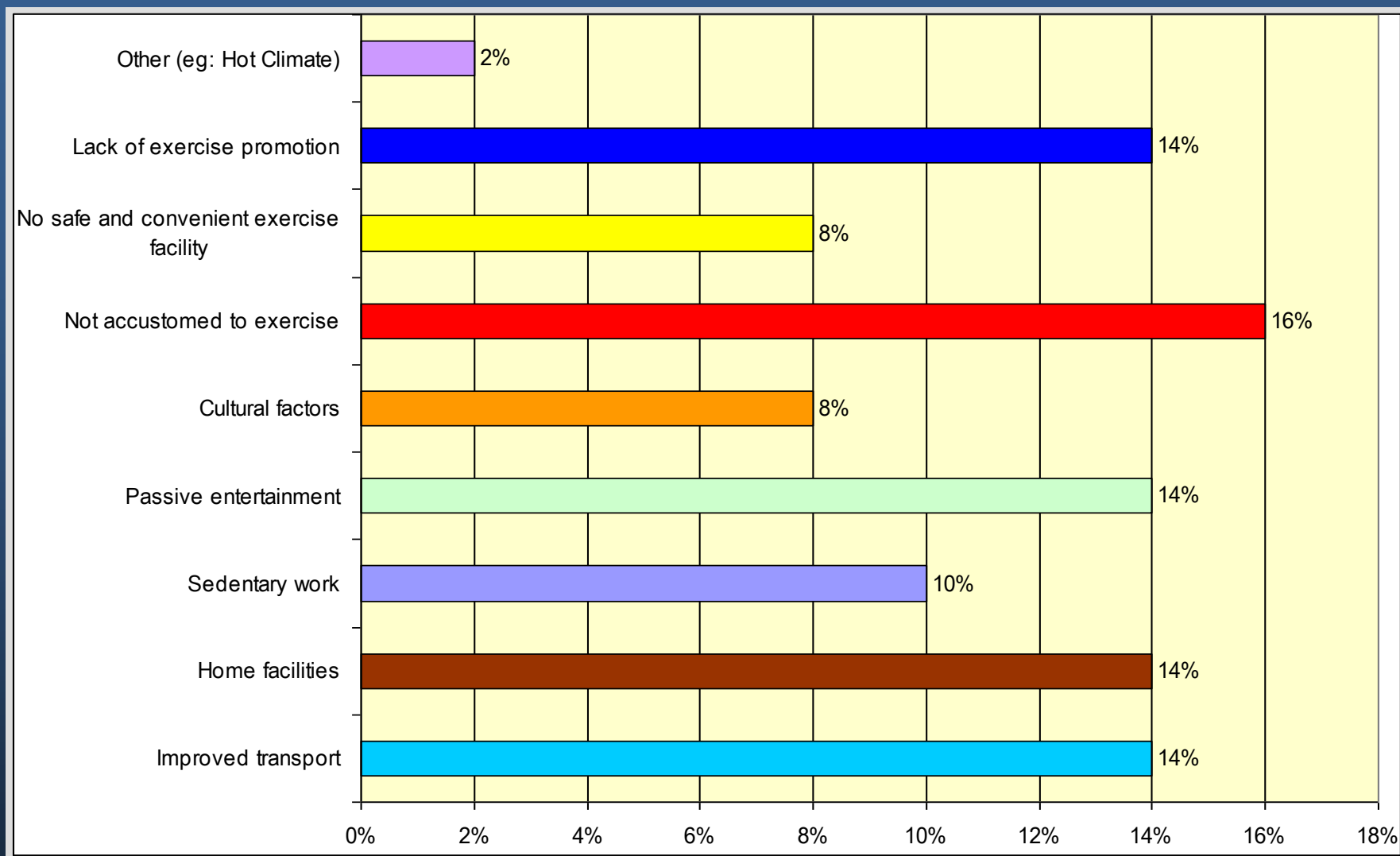
- Observation
- Direct calorimetry
- Doubly labeled water
- Accelerometers/
pedometers



Indirect

- Physiologic measures
 - Metabolic
 - Cardiorespiratory
 - Motor
 - Muscular
- Health status
- Surveys

Main Factors leading to reduced physical activity



Exposure assessment (3)

Diet



Example:

A posteriori Dietary patterns in indigenous population of the Andea North-Western region of Argentina

- Widespread poverty
- Stigmatization of local staple foods
- Globalization and urbanization
- Nutrition Transition
 - Chronic malnutrition in children (10.7%) and adolescents (12.4%)
 - Overweight and obesity in adults (50.6%)
- A random sample of 1048 subjects aged 2-86 years



Methods

Methodological issues	Methodological choices
1/ Measurement error in dietary assessment	



“Let’s see...number of cheeseburgers eaten in a typical month? three...no, I’ll put down four.”

Measurement error

- All methods measure diet with error
- Exposure measurement error leads to:
 - More difficult to compare studies
 - Loss of statistical power (attenuation of the diet-disease relationship)
 - observed relative risks closer from 1 than it should be, and SEs are larger

Methods

Methodological issues	Methodological choices
1/ Measurement error in dietary assessment	

Methods

Methodological issues	Methodological choices
1/ Measurement error in dietary assessment	Use of 2 different assessment tools <ul style="list-style-type: none">• A semi-quantitative FFQ• A 24 h recall

1/ Example of Food Frequency Questionnaire

Korea Genome Epidemiologic Study

- Generally self-administered

- Strengths

- Circumvents recent changes in diet

- Does not affect eating behavior

- Acceptable

- Cheap

- Weaknesses

- Lacks detail

- Finite food list

- Details of cooking methods

- Cognitively complex

- Prone to bias

The image shows a food frequency questionnaire form. It includes several photographs of food items: kimchi (photos 8-1, 8-2, 8-3), tofu (photos 6-1, 6-2, 6-3), and potato (photos 7-1, 7-2, 7-3). Below the photos is a table for data entry. The table has columns for 'average fq of intake during past year' (rare, 1, 2-3, 4-5, 6-7, 8-9) and 'Portion size' (1, 2, 3). The rows list various food items in Korean and English, such as 배추김치 (cabbage kimchi), 무우김치 (radish kimchi), 통치미 (watery radish kimchi), 기타 김치 (other kimchi), 장아찌 (salted cucumber), 계란 (egg), 두부 (tofu), 목 (jelly), 감자 (potato), and 잡채 (mixed dish).

	average fq of intake during past year									Portion size
	rare	1	2-3	4-5	6-7	8	9	10	11	
배추김치 cabbage kimchi										1 photo 8-1 (8pieces) 2 photo 8-2 (6pieces) 3 photo 8-3 (9pieces)
무우김치 radish kimchi										1 photo 8-1 (8pieces) 2 photo 8-2 (6pieces) 3 photo 8-3 (9pieces)
통치미 watery radish kimchi										1 1/2 bowl 2 1 bowl 3 1 1/2 bowl
기타 김치 other kimchi (갓김치 leaf mustard kimchi, 파김치 Green onion kimchi)										1 photo 8-1 2 photo 8-2 3 photo 8-3
장아찌 Salted Cucumber (마늘장아찌 garlic jiangajji, 마늘쫀, 무장아찌)										1 photo 9-1 2 photo 9-2 3 photo 9-3
계란 egg										1 egg 1/2 2 egg 1 3 egg 1 1/2
두부 tofu (순두부, 두부찌개, 된장찌개에 들어간 두부 포함)										1 photo 6-1 (1 slice) 2 photo 6-2 (2 slices) 3 photo 6-3 (3 slices)
목, jelly										1 photo 6-1 (1 slice) 2 photo 6-2 (2 slices) 3 photo 6-3 (3 slices)
감자, potato (찐감자, 감자튀김, 감자국, 감자찌개, 감자저림 등)										1 photo 7-1 2 photo 7-2 3 photo 7-3
고구마, sweet potato (찐고구마, 맛탕 등)										1 medium size 1/2 2 medium size 1 3 medium size 1 1/2
잡채(당면) a mixed dish of vegetables and sliced meat										1 photo 10-1 (1/2) 2 photo 10-2 (1) 3 photo 10-3 (1 1/2)

2/Example of 24h food recall

Nutrinet-Santé Study (France)

Journée de MARDI (10/02/2009) Aide ?

petit déjeuner ✖

08h30 - à domicile

Saisissez ici l'aliment recherché ou cliquez sur la famille de l'aliment ci-dessous Rechercher

- ▶ Eaux et autres boissons froides et chaudes
- ▼ Pains, biscottes, pains de mie et autres
 - ▶ tous types de baguettes et pains
 - ▼ pains de mie
 - pain de mie nature
 - pain de mie complet
 - pain viennois ou brioché
 - muffin anglais nature
 - muffin anglais complet
 - ▶ pains grillés, biscottes, pains suédois...
- ▶ Hors d'œuvre, salades diverses, entrées exotiques
- ▶ Charcuteries
- ▶ Produits apéritifs
- ▶ Soupes

- ▶ Viandes, poissons, oeufs
- ▶ Pâtes, riz, pommes de terre et légumes secs
- ▶ Légumes
- ▶ Plats cuisinés (faits maison ou du commerce)
- ▶ Fast food, pizzas, sandwichs, tartes et autres

- ▶ Produits laitiers (laits, yaourts, fromages)
- ▶ Aliments sucrés (petit déjeuner, goûter, dessert) ▼

Aliment non trouvé ?

Enregistrer en brouillon Annuler



2/Example of 24h food recall

Nutrinet-Santé Study (France)

Saisissez l'heure et le lieu de la prise alimentaire

Type de prise alimentaire : **Petit déjeuner**

Heure de la prise alimentaire : 08 h 30

Lieu de la prise alimentaire : Choisissez

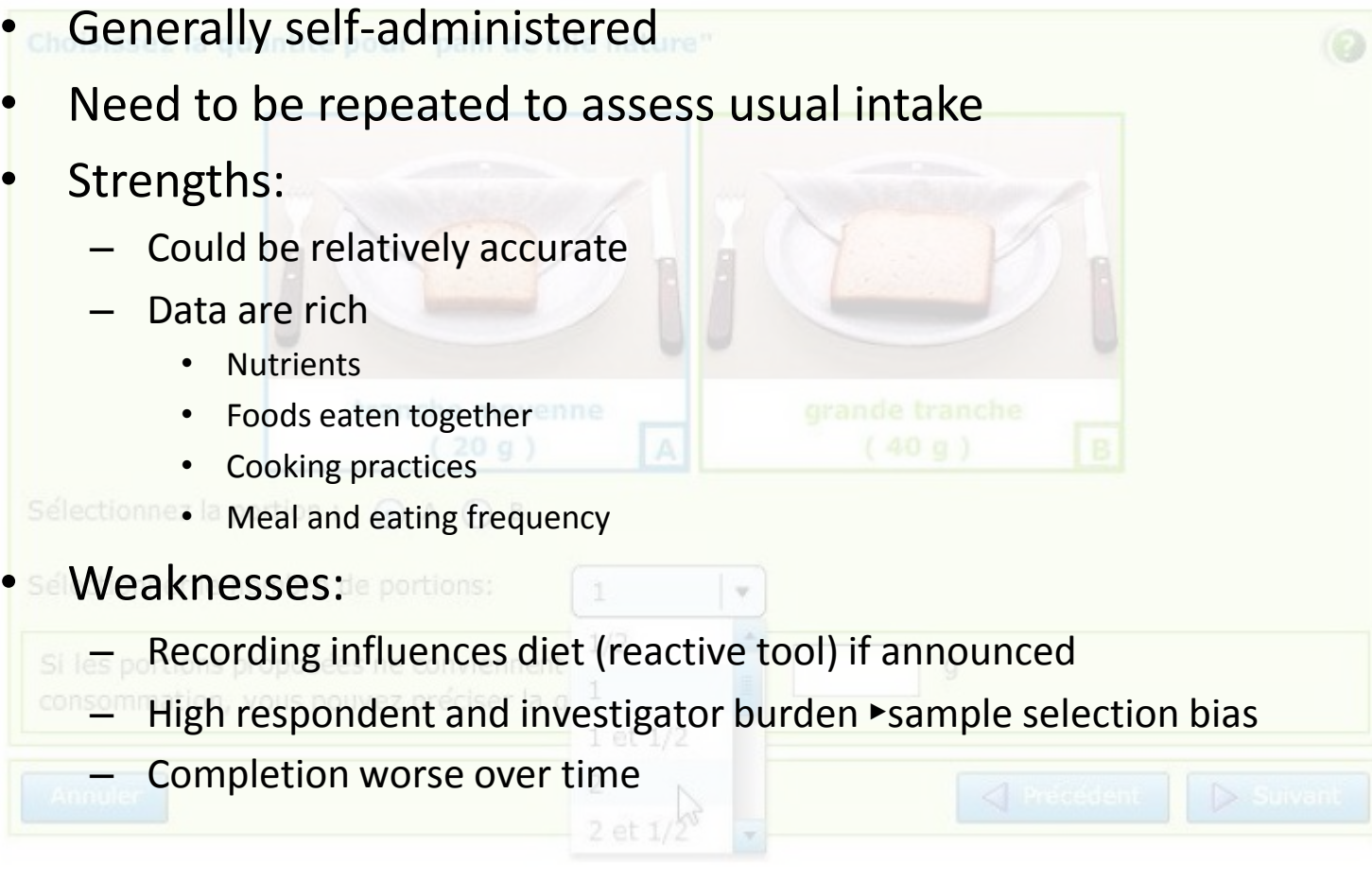
- à domicile
- chez des amis ou de la famille
- au self d'entreprise, à la cantine, sur mon lieu de travail
- au restaurant, au café, en restauration rapide sur place
- dehors, dans la rue, dans les transports



2/Example of 24h food recall

Nutrinet-Santé Study (France)

- Generally self-administered
- Need to be repeated to assess usual intake
- Strengths:
 - Could be relatively accurate
 - Data are rich
 - Nutrients
 - Foods eaten together
 - Cooking practices
 - Meal and eating frequency
- Weaknesses:
 - Recording influences diet (reactive tool) if announced
 - High respondent and investigator burden ► sample selection bias
 - Completion worse over time



Methods

Methodological issues	Methodological choices
1/ Measurement error in dietary assessment	Use of 2 different assessment tools <ul style="list-style-type: none"><li data-bbox="1083 448 1649 494">• A semi-quantitative FFQ<li data-bbox="1083 522 1387 568">• A 24 h recall

Methods

Methodological issues	Methodological choices
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2/ Change of food consumption <ul style="list-style-type: none"><li data-bbox="117 684 817 729">• Variations according to season<li data-bbox="117 758 488 803">• Daily variations	

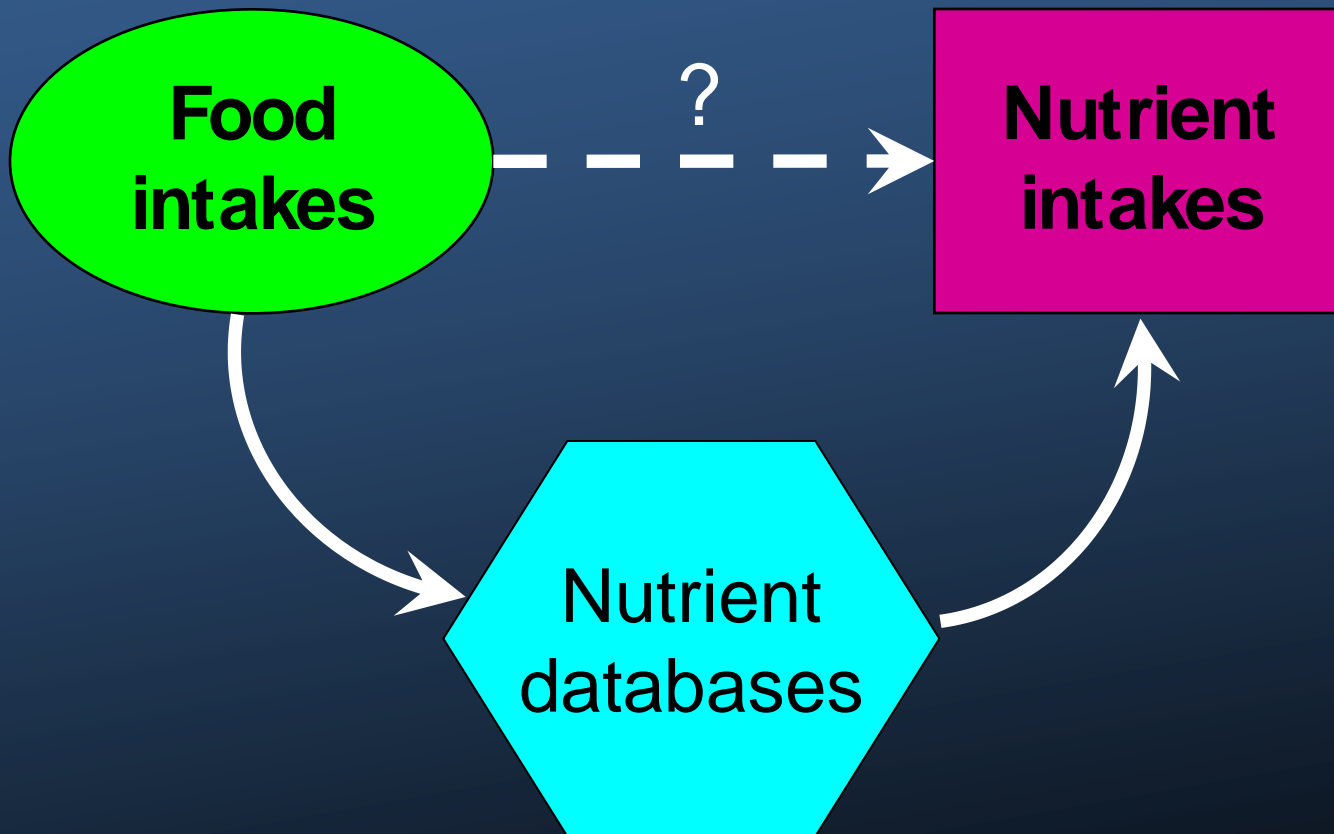
Methods

Methodological issues	Methodological choices
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2/ Change of food consumption <ul style="list-style-type: none">• Variations according to season• Daily variations	<ul style="list-style-type: none">• 2 waves: One post-harvest season and the second preharvest season• Questionnaires administered homogeneously from Monday to Sunday

Methods

Methodological issues	Methodological choices
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3/ Convert food consumption into nutrient	

Nutrient Databases



Nutrient Databases

- Source of error in all self-report dietary data
- Content of foods constantly changing
 - Database needs to match time period of study
 - Cultivars of produce vary by region

Methods

Methodological issues	Methodological choices
1/ Measurement error in dietary assessment	Use of 2 different assessment tools <ul style="list-style-type: none">• A semi-quantitative FFQ• A 24 h recall
2/ Change of food consumption <ul style="list-style-type: none">• Variations according to season• Daily variations	<ul style="list-style-type: none">• 2 waves: One post-harvest season and the second preharvest season• Questionnaires administered homogeneously from Monday to Sunday
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2/ Change of food consumption <ul style="list-style-type: none">• Variations according to season• Daily variations	<ul style="list-style-type: none">• 2 waves: One post-harvest season and the second preharvest season• Questionnaires administered homogeneously from Monday to Sunday
3/ Convert food consumption into nutrient	<ul style="list-style-type: none">• Use of Argentinean and Latin-American food composition tables• Use of Spanish food composition tables for foods not included in Latin-American tables• Estimation of portion sizes in the community

Methods

Methodological issues	Methodological choices
1/ Measurement error in dietary assessment	Use of 2 different assessment tools <ul style="list-style-type: none">• A semi-quantitative FFQ• A 24 h recall
2/ Change of food consumption <ul style="list-style-type: none">• Variations according to season• Daily variations	<ul style="list-style-type: none">• 2 waves: One post-harvest season and the second preharvest season• Questionnaires administered homogeneously from Monday to Sunday
3/ Convert food consumption into nutrient	<ul style="list-style-type: none">• Use of Argentinean and Latin-American food composition tables• Use of Spanish food composition tables for foods not included in Latin-American tables• Estimation of portion sizes in the community
4/ Colinearity of dietary intake	

Methods

Methodological issues	Methodological choices
1/ Measurement error in dietary assessment	Use of 2 different assessment tools <ul style="list-style-type: none">• A semi-quantitative FFQ• A 24 h recall
2/ Change of food consumption <ul style="list-style-type: none">• Variations according to season• Daily variations	<ul style="list-style-type: none">• 2 waves: One post-harvest season and the second preharvest season• Questionnaires administered homogeneously from Monday to Sunday
3/ Convert food consumption into nutrient	<ul style="list-style-type: none">• Use of Argentinean and Latin-American food composition tables• Use of Spanish food composition tables for foods not included in Latin-American tables• Estimation of portion sizes in the community
4/ Colinearity of dietary intake	Use of dietary patterns

Dietary patterns

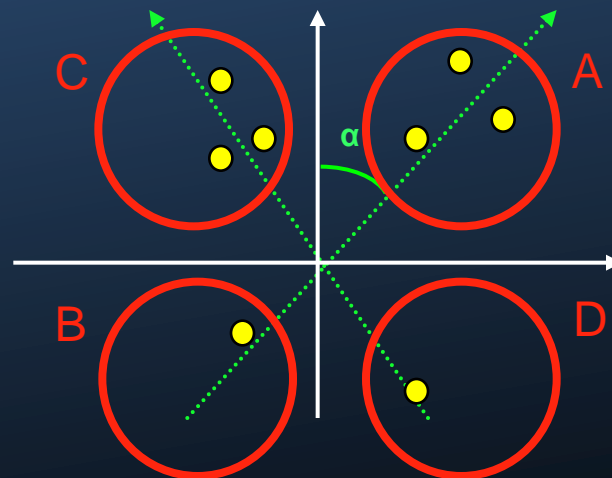
- Hypotheses-based scores
 - Based on literature
 - *A priori* decisions made by the investigators
 - Items included
 - Cut-off points...
 - Around 20 different scores
 - *Waijers PM et al. A critical review of predefined diet quality scores. Br J Nutr, 2007*
 - Ex: Mediterranean score, healthy eating index...
- Data driven scores
 - Goal: synthesizing all food consumption in few variables
 - Several statistical methods
 - Principal component analysis
 - Clusters...
 - Food classification influences results

Principal component analysis

- Find the linear combination of initial variables which discriminates subjects the most (using the variance-covariance matrix)

$$y_k = a_{k1}x_1 + a_{k2}x_2 + \dots + a_{kj}x_j + \dots + a_{kp}x_p$$

- Independant scores
 - No colinearity problem
- Reduction of the number of variables needed to estimate the whole diet



Identified Factors

Principal components (PC)	Positive scoring coefficients (≥ 0.20)	Negative scoring coefficients (≤ -0.20)	Variance explained (%)
PC1 "Not-Autochthon, Western-like diet"	Beef (0.51) Common bread (0.42) Chicken (0.42) Fruit (0.38) Sugary drinks (0.29) Common potato (0.25) Yogurt (0.25) Green beans (0.23) Sweet and milky desserts (0.21)	Lamb (-0.61) Bollo and Tortilla (-0.52) Animal fat (-0.46) Creole potato (-0.43) <i>Mote</i> (-0.30) Herbal teas (-0.32) Llama (-0.27) Vegetables (-0.20)	8.6
PC2 "Autochthon, Andean-like diet"	Herbal teas (0.60) Added sugar & sweets (0.58) Vegetables (0.42) Pasta, rice, polenta (0.41) Batata (0.40) Beans (0.39) Eggs (0.36) Fruit (0.29) Common bread (0.28) Creole potato (0.27) Cheese (0.25) Sugary drinks (0.24) <i>Mote</i> (0.22) Chickpeas (0.22) Beef (0.22)		6.7

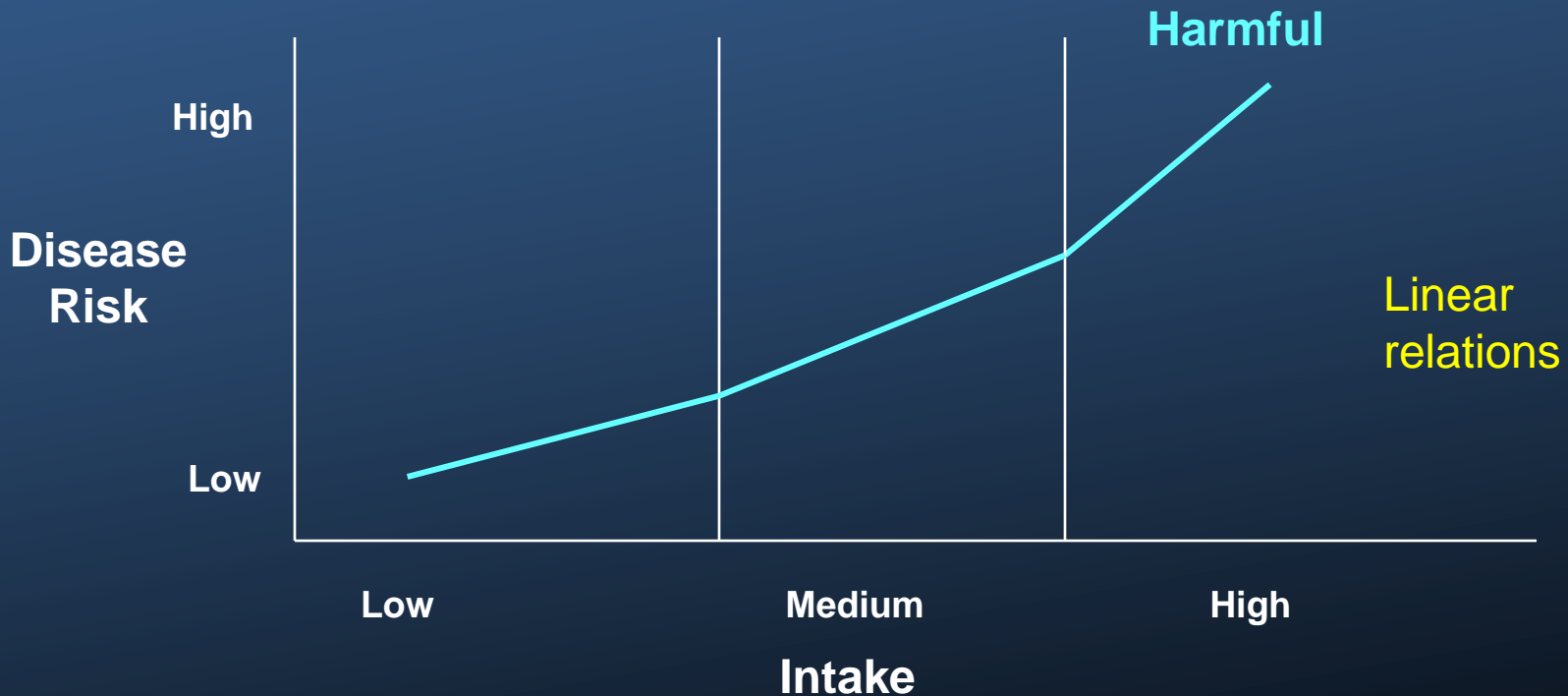
Results

- “Western-like” pattern
 - Worst diet quality
 - Consumed by young, urban inhabitants
 - Independent of seasonal availability of foods
 - Probably reflecting the nutrition transition
- “Authohton, andean-like”
 - Better diet quality
 - Consumed by individuals of all ages, in rural regions
 - When food availability is high

Challenges in nutritional epidemiology

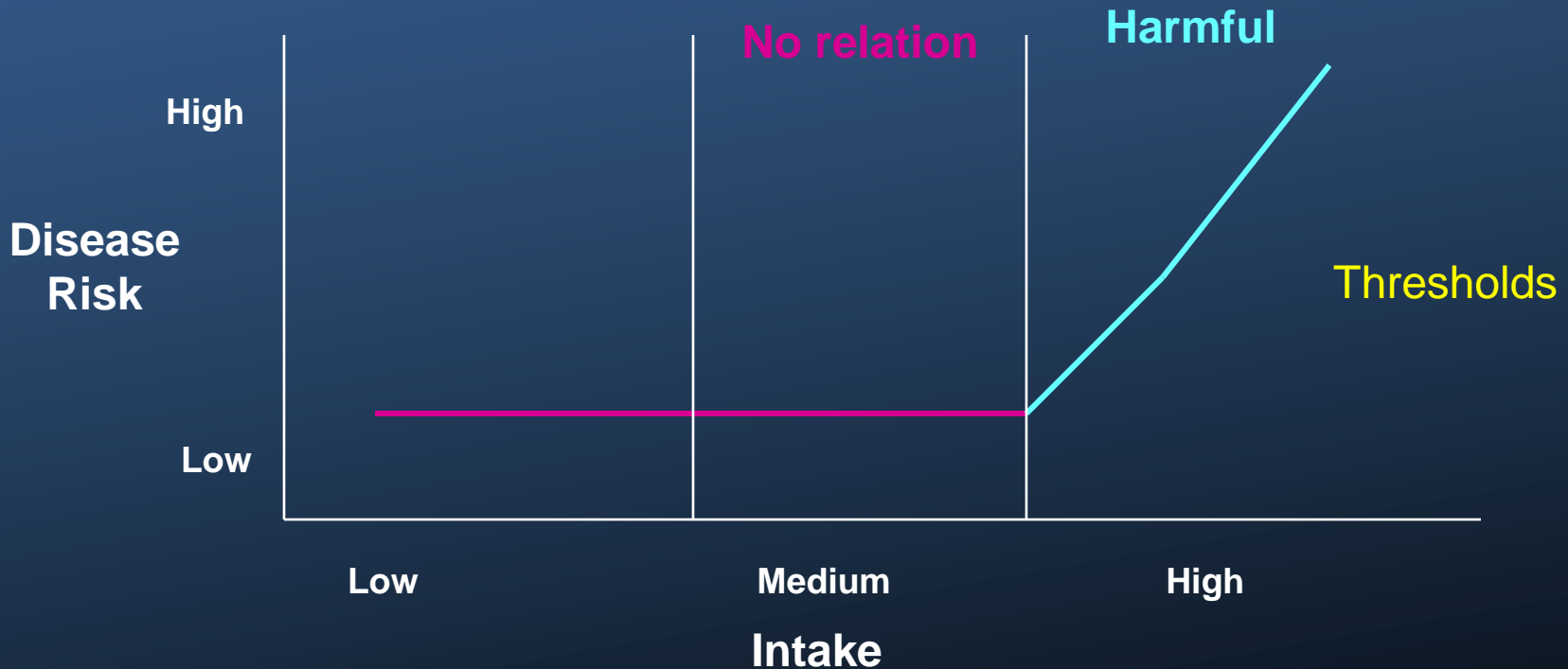
Elements which could dilute the true association (1)

- Range of exposure is important



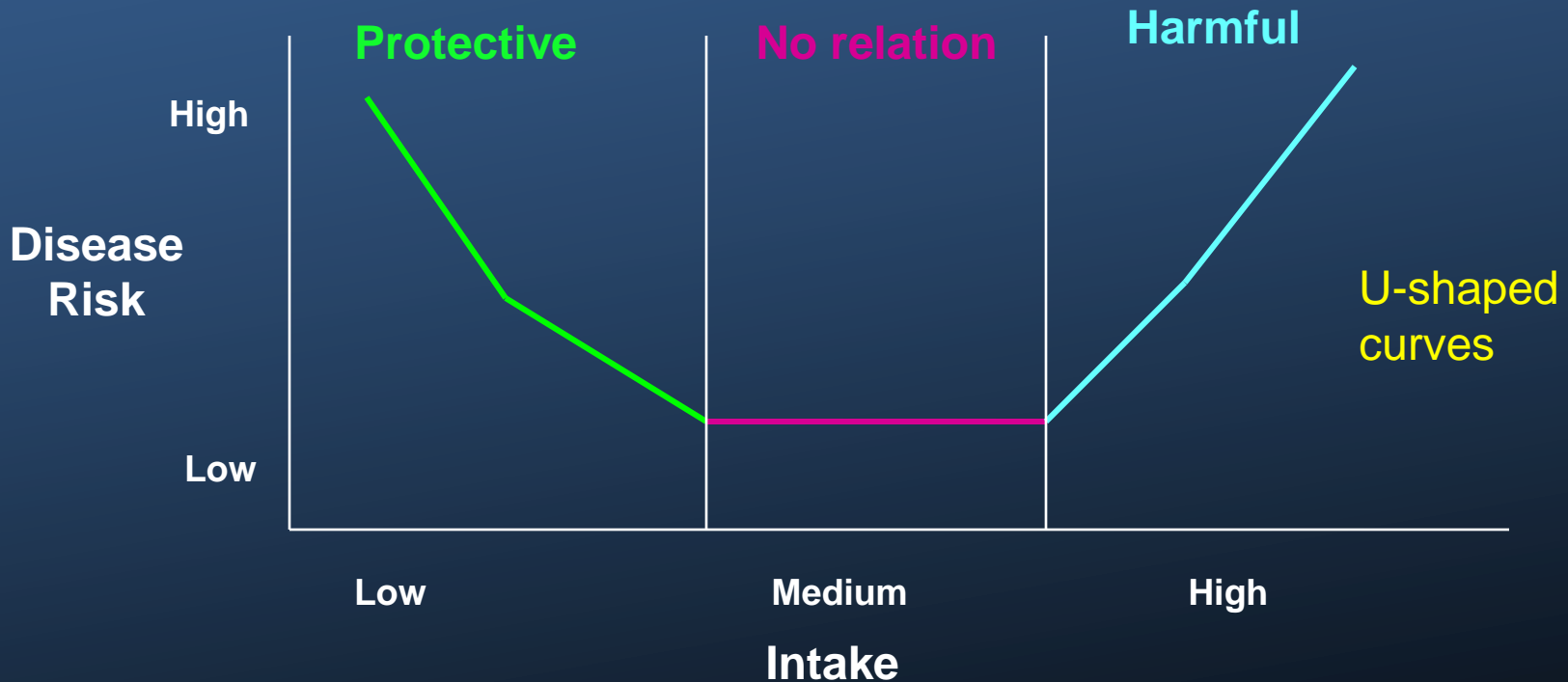
Elements which could dilute the true association (1)

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Elements which could dilute the true association (1)

- Range of exposure is important

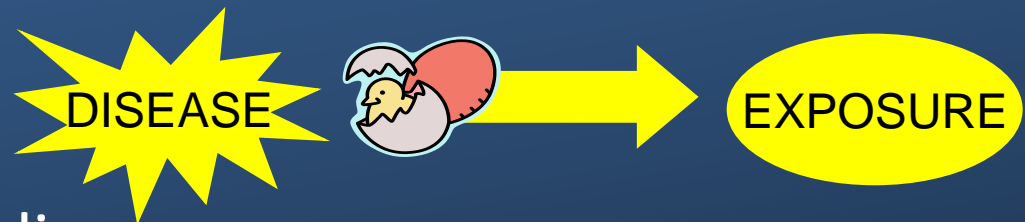


Elements which could dilute the true association (2)

- Interactions can be important
 - Nutritional factor x nutritional factor
 - Nutritional factor x other lifestyle factor
 - Nutritional factor x gene(s)
 - And various combinations
- Studying interactions can be HARD (e.g., big sample sizes)

Elements which could dilute the true association (3)

- Reverse causality
 - Less likely in cohort and intervention studies
- Long interval between diet and chronic disease occurrence
- Associations are relatively weak



“With epidemiology you can tell a little thing from a big thing. What’s very hard to do is tell a little thing from nothing at all”

Dr. M. Thun. American Cancer Society

Reducing measurement error

- Improvement and development of assessment methods.
 - Ex: Integrated controls in the computer-based 24h records of the Nutrinet-Santé cohort
- Energy adjustment
 - Several methods

Residual method



Figure 11-5. Calorie-adjusted intake = $a + b$, where a = residual for subject from regression model with nutrient intake as the dependent variable and total caloric intake as the independent

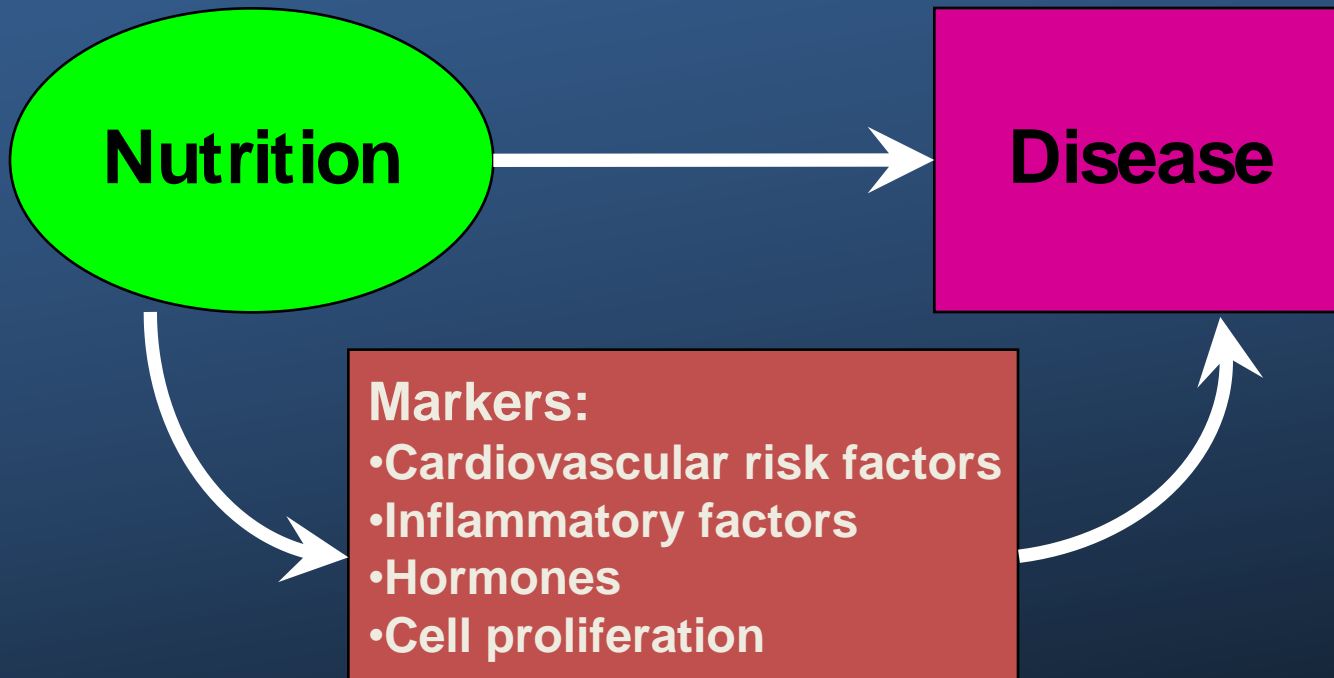
variable and b = the expected nutrient intake for a person with mean caloric intake. (From Willett and Stampfer, 1986; reproduced with permission.)

Reducing measurement error

- Improvement and development of assessment methods.
 - Ex: Integrated controls in the computer-based 24h records of the Nutrinet-Santé cohort
- Energy adjustment
 - Several methods
- Repeated measurements
 - Decrease variability intra-subjects
 - Take into account change of diet during follow-up
- Calibration
 - the process in which values from one method are related to the standard (better) method (ex: EPIC)

Increasing power

- Intermediate end points

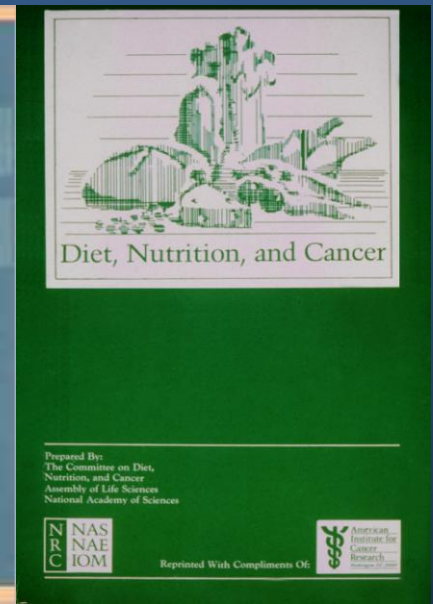
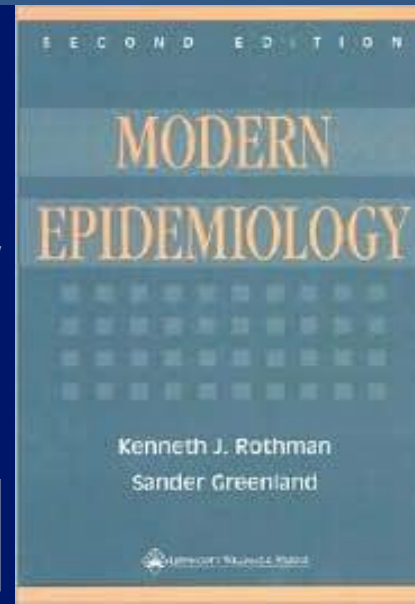
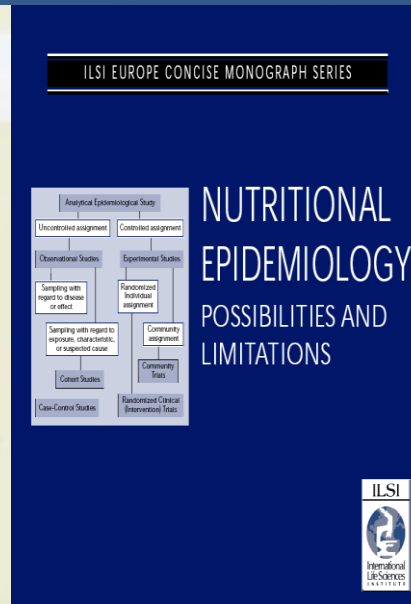


- **Increases power (continuous outcomes)**
- **Permits to understand the mechanisms**
- **Can enhance the evidence for causality**

Summary

- Important biases to worry about
 - Design
 - Measurement error
 - Confounding
- Associating diet-disease is complex:
 - Nature of diet (including strong correlations)
 - Long time interval between diet-chronic disease
 - Small RR (but attributable risk may be high)
 - Chronic diseases have multiple causes
- Consider results from many studies (not just epidemiological ones) before concluding an association

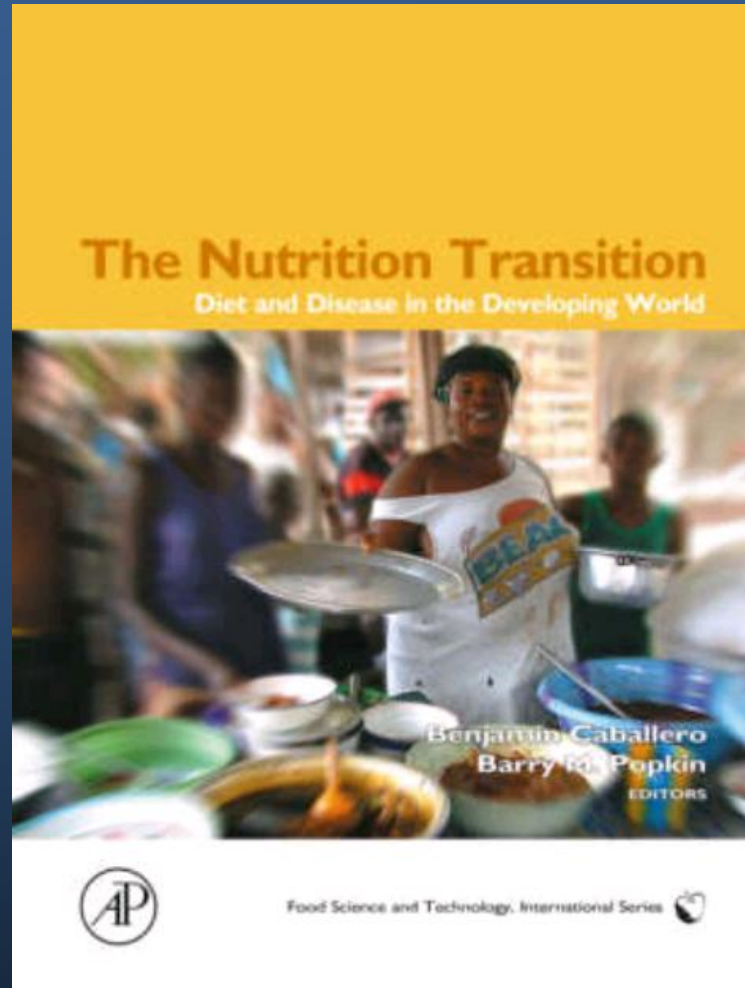
More about nutritional epidemiology:



Journals such as:

- American Journal of Clinical Nutrition
- American Journal of Epidemiology
- BMJ
- Cancer Epidemiology Biomarkers & Prevention
- JAMA

More about nutrition transition:



Benjamin Caballero,
Barry M. Popkin
Academic Press
(2002)

Thanks to the contribution of Professors of the International Course on Nutritional Epidemiology (Imperial College) for allowing the use of some slides