

Epidemiology (study design)

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Ecological studies

Design Concepts in Nutritional Epidemiology

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Introduction

- Ecological study– focus on
 - characteristics of population groups
 - rather than their individual members.
- The unit of analysis
 - not an individual
 - but a group: defined by
 - time (calendar period, birth cohort)
 - geography (country, province, or city)
 - social-demographic characteristics (e.g. ethnicity, religion, or socio-economic status)
- Provide the first look of relations for hypothesis generation

- To expand and **support** the conclusions drawn from individual-level investigations
- To complement individual-level data in the development of **multi-level models** to describe the combined effects of social factors and individual behaviors on health and disease.
- A well designed ecological study:
ex: EPIC (Fig 12.2)

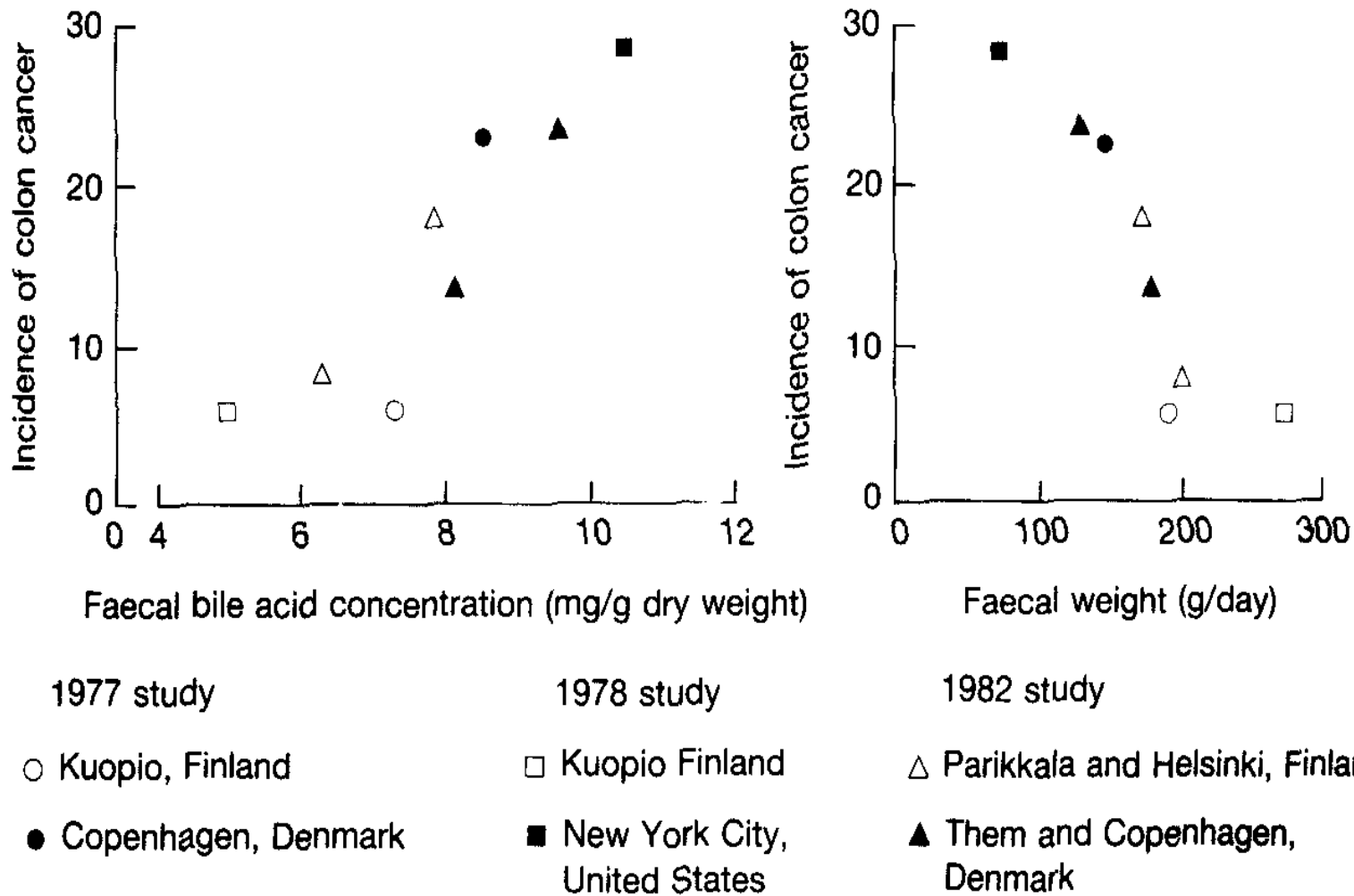


Fig. 12.2 The relationship between faecal bile acid concentration and faecal weight and the incidence of colon cancer in three studies, made in 1977, 1978, and 1982. (Source: Muir¹²)

➤ An example

➤ correlations over time—

- the standardized mortality rate from coronary heart disease, which has decreased in United States since the mid-1960s,
- the increase in the per capital alcohol consumption over the same period (Fig. 12.1).

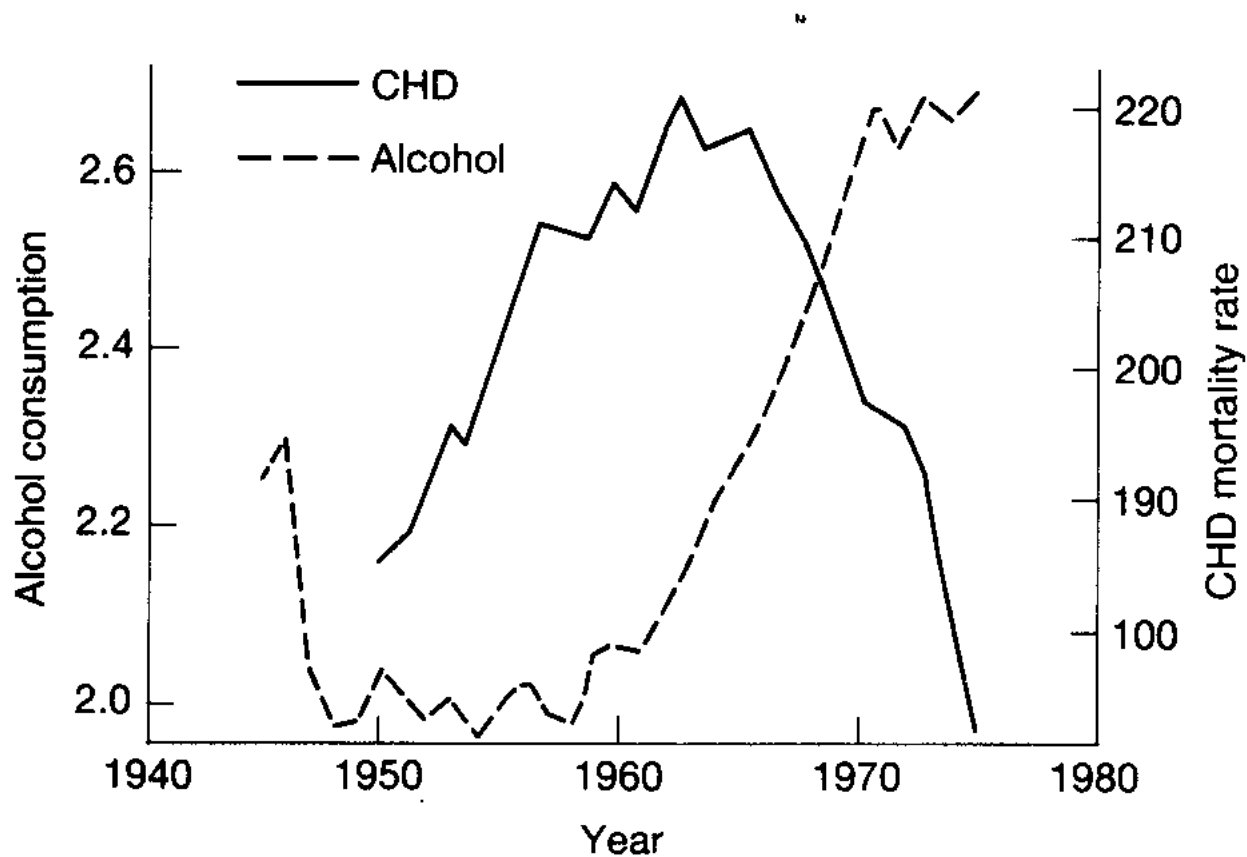


Fig. 12.1 Time trends in the age-standardized coronary heart disease (CHD) mortality rate (per 10⁵ population) and per capita alcohol consumption (gal/yr), US, 1945–1975 (Source: Kuller *et al.*²)

- Ecological analyses are only of value when the groups or **communities being compared are relatively heterogeneous** in their mean levels of exposure to dietary factors.
- For this reason, they have been used **most extensively for between-country** rather than within--country comparisons.
- Within--country comparisons:
ex: The People's Republic of China
-- because there are **wide variations** in **disease rates** from one region to another, accompanying substantial differences in culture, behavior and lifestyle.

Indices of dietary intake

➤ Average consumption

Estimates of average individual intake can be made from **pre-existing data** or from **population survey data** collected de novo —Table 12.1

Table 12.1 Estimates of per capita consumption.

Parts of the food chain surveyed	Type of data published	Scope and limitation of survey data
National food supply	Food balance data collected by agriculture ministries, collated by FAO	Allows for home production, imports and exports, changing food stocks
Market distribution	Industrial data	Limited to specific sectors
Household budget	Economic statistics	Limited to financial outlay of whole households on food: costs do not relate to nutritional value of purchases
Household consumption	Household food survey	Often fails to allow for food eaten elsewhere; food waste assumed
Individual nutrition	Individual food and nutrition intake	Numerous methods available of varying reliability

From James *et al.* *Healthy nutrition*.¹⁴

1. National food supply or food 'disappearance statistics'

The Food and Agricultural Organization (FAO) publishes food balance sheets for 146 countries

- Food 'disappearance' statistics --calculated by
 - estimating the quantity of food produced in a given country
 - added to the quantity of food imported
 - subtracting the food exported, lost in storage, fed to animals, or used for non-dietary purposes.
 - The resulting figure is converted to an estimate of per capita consumption by dividing by the total population

- Between-country comparisons that include both rich and poor nations may be subject to
 - biases in the quality of data collected at national levels

2. Household or population survey data

- dietary intake data from different countries can be collected by food frequency questionnaires, weighed inventories, diet histories, 24-hour recall, two-day recall, household food surveys, and other methods.
- When analysing the health status of different subgroups in the population, indirect methods of estimating per capita consumption derived from aggregate data for the population as a whole must be interpreted with caution.
- The United States Health and Nutrition Survey (HANES) is an exception, as intake estimated for various age-, gender-, and ethnic-group-specific populations.

3. In-depth surveys of population subgroups

Ecological analyses of cross-cultural variations in mortality have used detailed nutritional analysis of the diets of small samples of individuals from those countries.

For example, in an ecological analysis of the Seven Countries Study.

➤ National indirect indicators of consumption

In the absence of direct measures of dietary consumption, various **indirect markers** have been used. For example, **sales or tax records** have been used to estimate per capita consumption of alcohol.(Fig 12.3)

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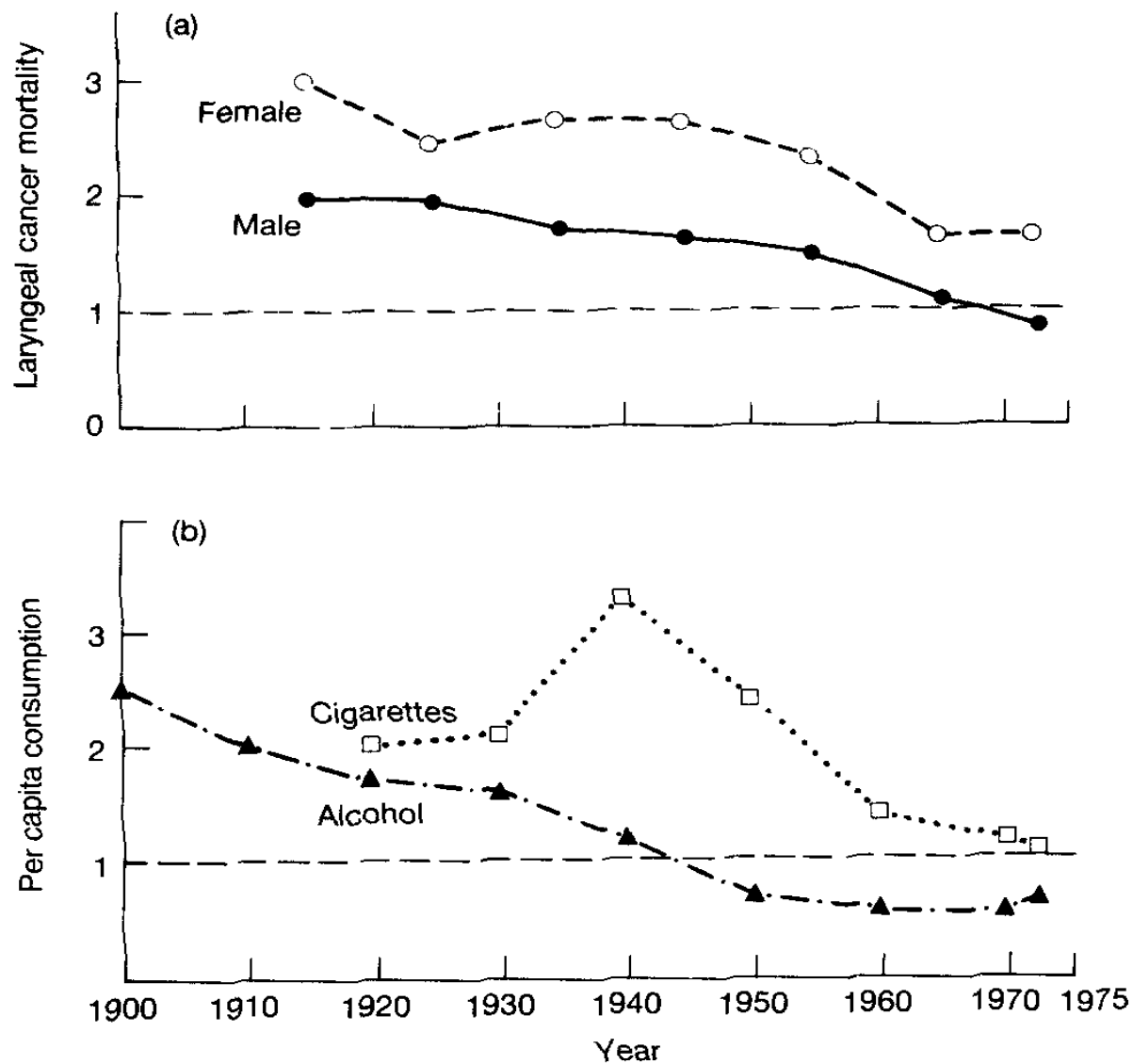


Fig. 12.3 Time trends in ratios of British versus Australian age-standardized laryngeal cancer mortality, by gender; and of British versus Australian consumption of alcohol and cigarettes. (Source: McMichael²³)

➤ Community-level indirect indicators of exposure

Community-level indicators of nutritional intake have been developed as part of community trials. For example, [grocery shop shelf space](#) has been used to estimate changes in individual diets following the introduction of community nutrition programs.

Recent theoretical work on ecological studies, however, highlights that community level measures of the social environment in which individuals live may reflect combinations of effects that are not apparent when individuals are measured separately.

➤ ‘Macroscopic generalization’

Occasionally, statements are made about dietary patterns in populations, based on observations of subgroups that have not been specifically sampled for the purpose. Thus, generalizations about dietary intake in the population are global statements not founded in sampling procedures.

➤ Average food/soil concentrations of micronutrients

The intake of various micronutrients may be inferred from **known deficiencies or excesses in the food or soil of a particular region**. This estimate of intake is particularly appropriate when most food sources for a region are local.

For example, in China, ecological analyses have demonstrated that areas with low soil levels of molybdenum (and low nitrate uptake) have higher rates of oesophagicancer.

The concentration of **trace elements in drinking water** has been linked with cardiovascular disease rates in ecological studies that are between- and within-country.

➤ Average food/water concentrations of toxins

Variation in the amount of toxins in the local diet can be correlated with variations in disease occurrence in a group of communities.

--such an analysis is only valuable in communities that do not consume food stuffs that are grown elsewhere in any significant quantity.

Ex.

The motor-neuron disease, lytico, that occurs commonly in Guam, has been associated with the consumption of the cycad, a palm-like plant that is the source of edible starch.

ex. liver cancer & aflatoxin contamination of
peanuts

--In fact, chronic HBV infection was determined to be of far greater importance than aflatoxin - highlighting the importance of considering the potential effect of confounding variables when interpreting the findings of ecological studies.

There have been limited investigations of the consequences of heavy metal contamination of soils and their uptake into vegetables and grasses and hence into the food chain.

➤ Biological indices of dietary intake or nutritional status

The analysis of blood, urine, faeces, toe-nail clippings, saliva, and breast-milk, has provided useful information about presumed dietary intake of a range of foods and toxins. In particular, these biological specimens appear to provide useful measures of micronutrient intake.

Since some disturbances of biological indices may reflect an aspect of the disease process itself, and not merely the causal pathway, ecological studies have an advantage over case-control studies in the way in which biological indices can be interpreted.

Some biological indices are particularly suited for ecological studies rather than for individual-level studies. For example, serum vitamin A concentration is not an accurate measure of an individual's nutritional status. In populations, however, the frequency of very low or very high serum concentrations of vitamin A is a useful measure of the average nutritional status of that community.

➤ Collection and analytical methods

The determination of mean values for indicators of dietary intake could theoretically involve the handling and analysis of many separate food samples or biological specimens from a particular geographic region.

A less expensive approach is to use pooled samples to derive estimates of intake for each geographic region.

The large Chinese ecological study used pooled biological samples, to derive estimates of nutrient intake for given communes.

Blood and specimens were combined into either gender-specific pools or age-gender-specific for each commune and then analysed.

An additional disadvantage is incurred if there is a non-linear association between the dietary component being estimated and disease risk. In such circumstances, pooled estimates of intake would not correlate with disease rates and the true association would be obscured.

A further problem occurs if the intention is to use a standardized value (e.g. urine metabolite from casual specimens expressed per mg creatinine).

Differences between groups may be obscured if there is large variation in the concentration of the standard between individual specimens (i.e. the denominator) which is not taken into account.

Calibration studies can be used to enhance the quality of the exposure data used in ecological research.

Biases in population level analyses can be corrected by using detailed dietary intake data collected on individual members of the populations being compared or biomarkers assessed in subgroups.

Indices of health status

➤ Routine measures of **mortality and morbidity**

The measures of mortality or morbidity most frequently used in ecological studies include international, national, and small-area data usually available through World Health Organization publications or from special reports from national governments.

Age- and gender-specific disease rates or summary statistics (adjusted for age and, less frequently, gender) such as **summary mortality rates** or **standardized mortality ratios** can be used.

--various measures of morbidity typically exist within developed countries for a variety of disorders

Ex. (DMFT) (Fig 12.4)

Accurate measures of disease incidence are not universally available, thus mortality data frequently are used as a proxy measure of disease risk.

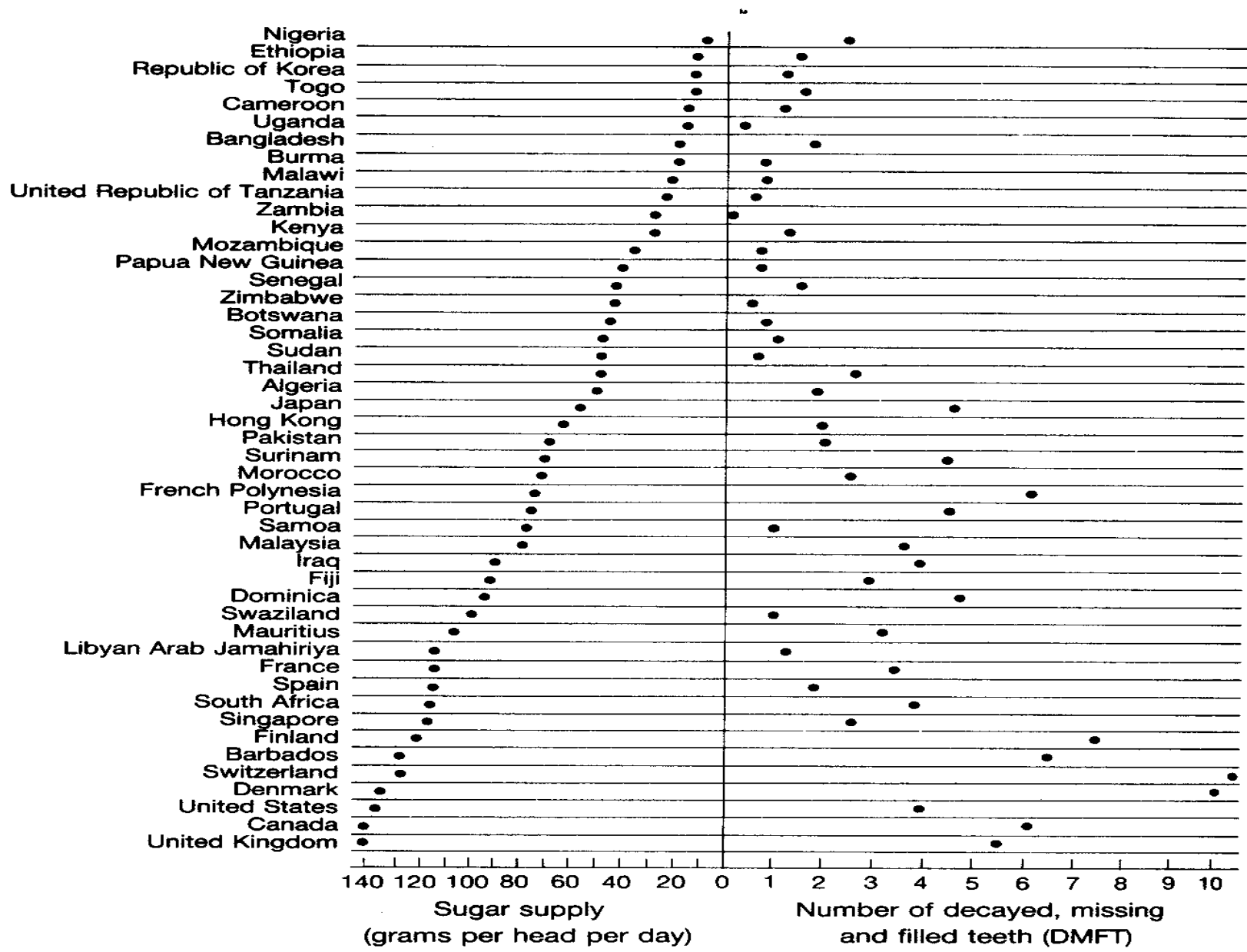


Fig. 12.4 Prevalence of dental decay, expressed as decayed, missing, and filled teeth (DMFT) children aged 12 years, and per capita daily sugar supply in 47 countries. (Source: Sreebny)

➤ Biological indices as (presumptive) disease-mediating processes

Biological specimens such as blood, urine, or faeces can be used as markers of stages in the disease process, or as direct measures of the presence of disease (for example, diabetes)

Populations or groups studied

- Migrants
- Religious groups
- Groups with distinct behavior
- Groups in cultural transition
- Groups in social upheaval
- Sub-populations displaying sharp cultural or behavioural differences

➤ Migrants

The exploration of the relative effect of genetic predisposition and environmental exposures on disease.

More definitive studies of the effect of acculturation and passage of time on diet in migrant populations have provided direct evidence of the gradual cultural adaptation to dietary patterns of the host population.

Comparisons between cancer sites of the generations taken for a migrant group to assume the disease profile of the host population may provides clues to carcinogenic processes.

(Fig. 12.5)

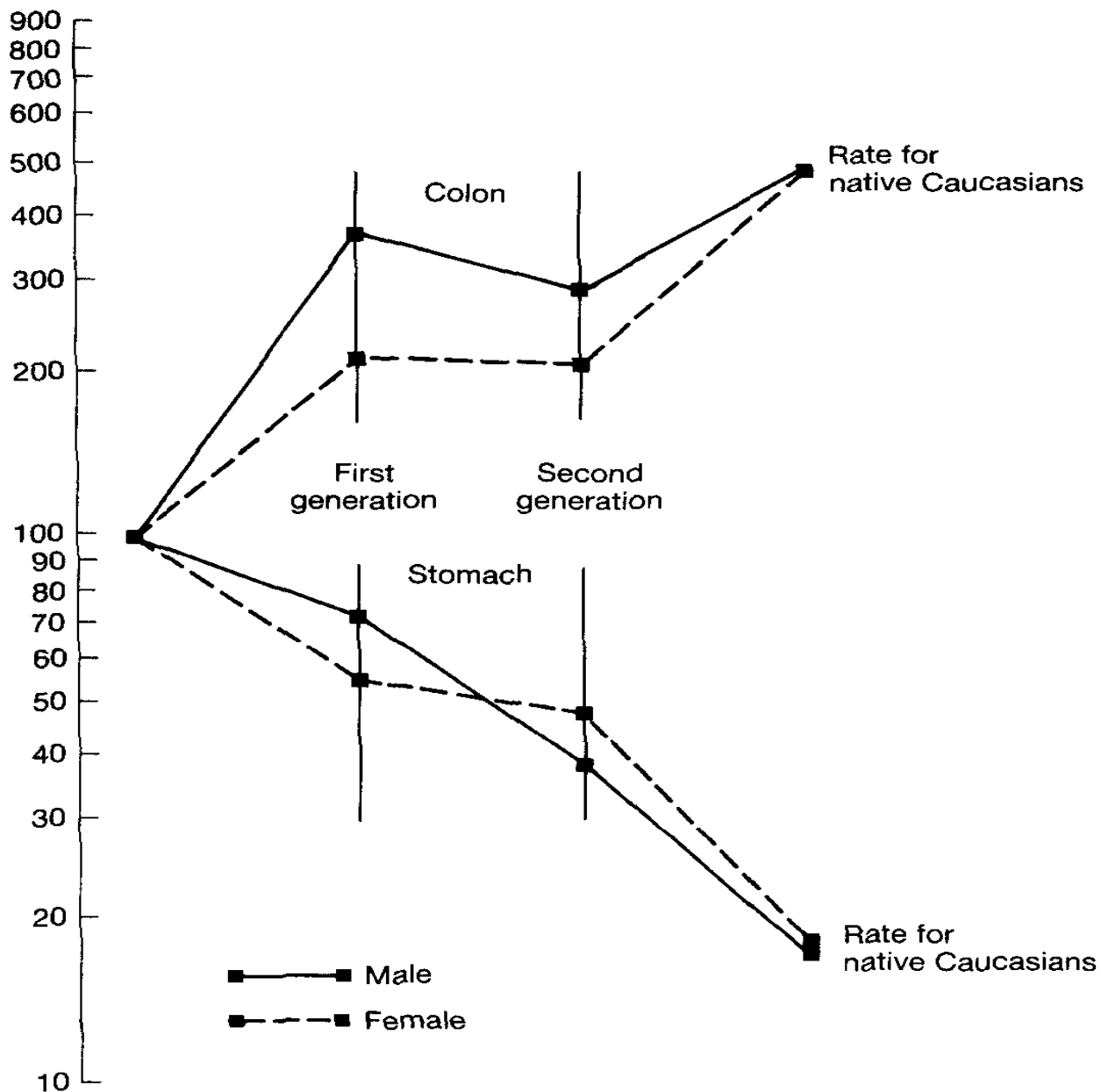


Fig. 12.5 Mortality from cancer of the stomach and colon in Japanese immigrants to the United States. (Source: Wynder *et al.*⁶¹)

➤ Religious groups

There have been many ecological studies of Seventh-Day Adventists, who frequently follow a lacto-ovo vegetarian diet.

➤ Groups with distinct behaviour

Other sub-populations with distinctive dietary patterns have been investigated to determine whether these patterns are associated with similarly distinctive disease patterns.

Ex.

low rates of coronary heart disease &
omega-3 fatty acid in Eskimo populations

➤ Groups in cultural transition

Omran coined the term 'epidemiologic transition' to describe the changes, over time, in patterns of disease and health in different cultures.

Westernization has frequently been accompanied by dramatic increases in the rates of non-insulin dependent diabetes mellitus (NIDDM) and other chronic disease.

Recent work has noted a subsequent pattern, particularly in some industrialized countries, characterized by behavioural change leading to increased take of fruits, vegetables, and complex carbohydrates and decreased intake of refined foods and dietary fats

➤ Groups in social upheaval

Ecological studies have been used to examine the association between nutritional status and widespread social change that is known to affect dietary patterns.

Ex. The Third World debt crisis of the 1980s,

➤ Sub-populations displaying sharp cultural or behavioral differences

An ecological study examining possible explanations for the higher incidence of childhood coeliac disease in Sweden compared with Denmark, neighbouring countries with similar health care systems and ethnicity, highlighted differences in infant feeding practices as an explanation for the different pattern in incidence rates.

This study demonstrates the advantages of ecological studies in examining the effect of different dietary patterns between groups that are similar in many respects other than dietary differences.

Techniques in examining relationships

- Disease mapping, simple regression, and correlations
- Time-lagging
- Cohort analysis
- Adjusting for confounders
- Multi-level analysis

Criteria of ‘proof’ in ecological associations between diet and disease

- Particular attention should be paid to the **biological plausibility** of association identified from ecological studies and the overall coherence of data.
- The **specificity of association** is a criterion that can be readily tested. Is the association specific to the dietary component of interest and the disease of interest, or is there a variety of unconnected associations that may reflect the quality of data rather than true associations?

- The calculation of correlation and regression coefficients, and the use of time series analysis to test co-variation, incorporate the notion of the dose-response criterion.
- Temporal relationships can be evaluated by investigating disease rate changes in exposures.

Limitations

- Beyond the logical problem of the ecological fallacy, there are methodological difficulties in ecological studies, particularly when used **to draw inferences at the level of individual**.
- **Confounding** is a particular problem in ecological studies of diet and diseases associated with industrialization.
- Between-country comparisons may be restricted by **the absence of comparable data**, usually on dietary intake .

- Within-country comparisons may yet be restricted by the **limited size of the population** in each region and the consequent **instability in rates**, as well as by homogeneity of exposures within the country as a whole.
- Inferences are limited by the **details and quality of the data**.
- Unless some time lag analysis is used, there must be an assumption that **current consumption patterns reflect past consumption**.
- The **population unit being used for analysis of morbidity or mortality** is often inappropriate for the analysis of exposure to diet.

- One must ensure that **the same geographical boundaries** are used for all analyses.
- Mortality and incidence data may be available for different age, race, and gender groupings while **dietary data may only be available for much larger aggregates.**
- **Interactions** between a variety of dietary exposures and a disease outcome or between diet and other exposure factors and disease **cannot be assessed** in ecological studies because data are not available about joint probabilities of exposure at the level of individual.

When are ecological studies the method of choice?

- Ecological studies are ideal for examining newly-proposed hypotheses.
- They have been particularly useful in situations where it is possible subsequently to study causal relationships at an individual level.
- the ecological approach is frequently the only one available for the examination of hypotheses when exposure cannot be defined meaningfully on an individual level.

- Ecological studies may be more appropriate **when there is great variability at the individual level** in the measure of exposure (regression dilution bias).
- Because of **the innate (and/or acquired) variability in individual response to diet intake**, the dietary risk factors for some diseases may be **more evident for groups/populations** than for individuals.

Ex. The INTERSALT study

- Instruments assessing dietary intake on an individual level are subject to measurement error (as are instruments measuring population levels of dietary intake). Narrow gradient of exposure combined with the inherent limitations of measuring instruments reduce the power of cohort and case-control studies to detect an increase in risk. (Fig. 12.7)

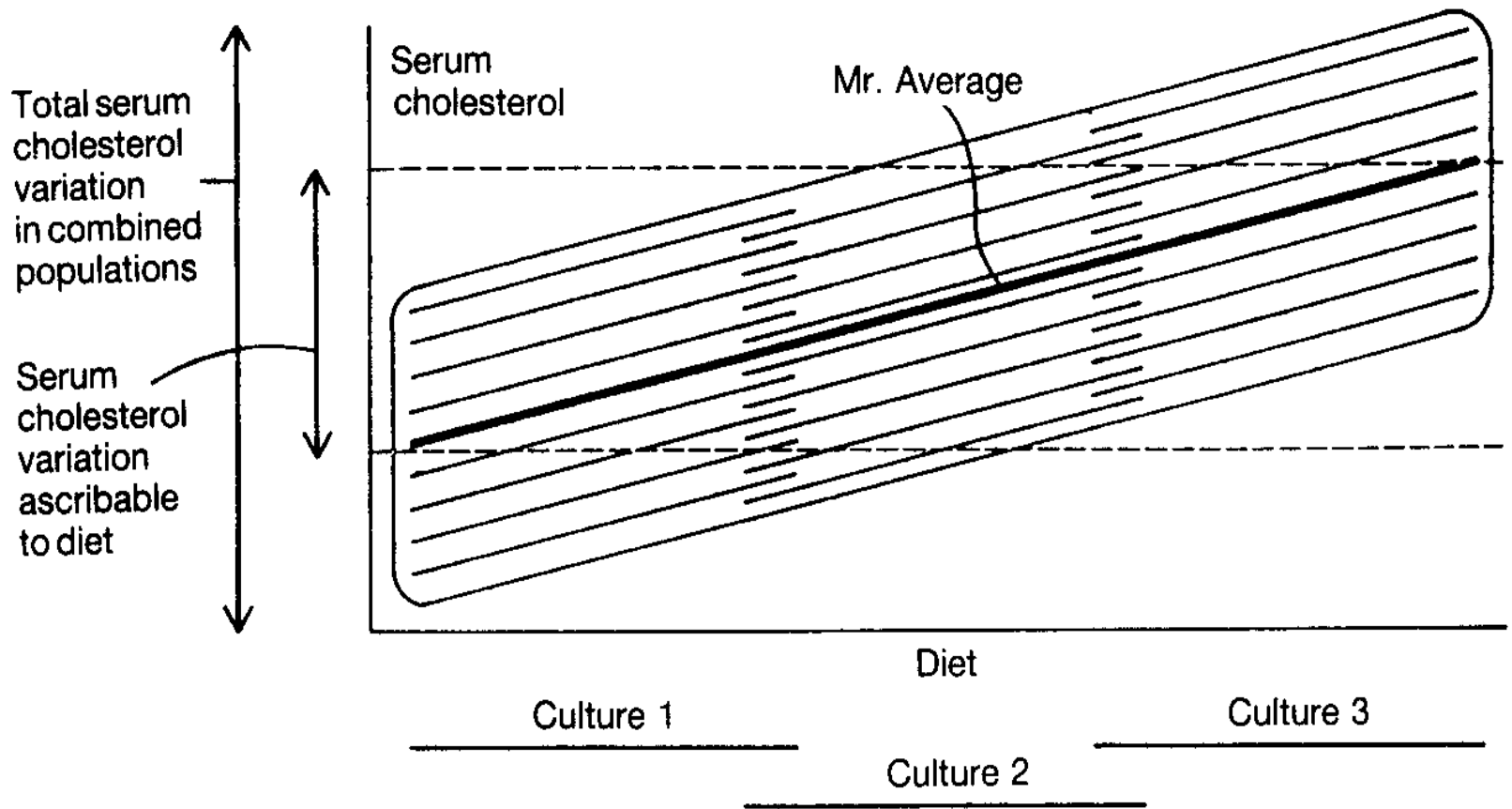


Fig. 12.7 A schematic representation of the variation of serum cholesterol ascribable to diet across three communities representing different cultures. (Source: Fraser⁹⁵)

- Ecological studies use average measures of intake, or blood nutrient analyses based on large numbers individuals, are less likely to be affected by the attenuation of effect estimate that could be found in individual-level studies.

Home work

- 找一個有關ecological study的文章
- 寫出
 - 假說
 - 研究單位
 - 因（暴露變項）、果（疾病變項）的測量
 - 分析方法
 - 結論
 - 可能的解釋結果的alternative hypothesis