Epidemiology in a changing world

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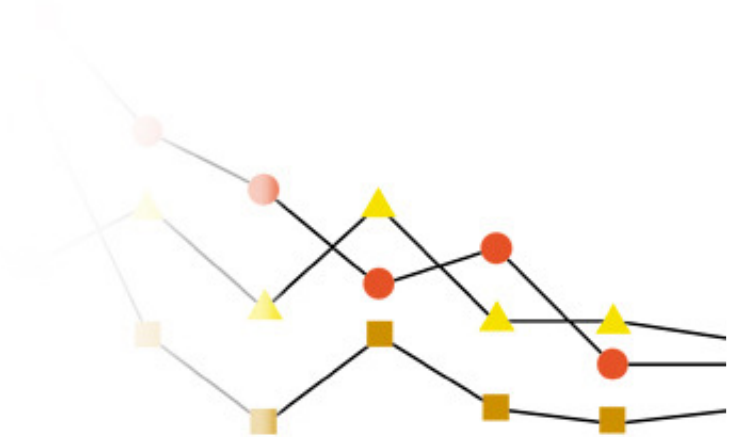
Traditional Epidemiology

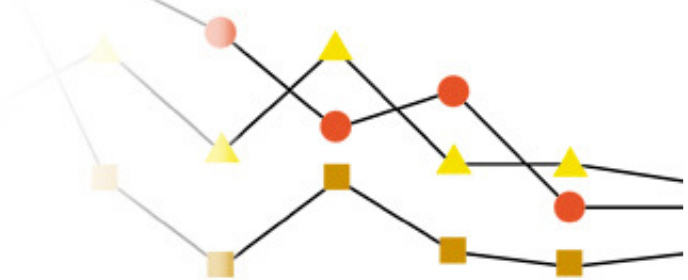
The study of the ***distribution*** and ***determinants*** of health-related states or events in specified ***populations***, and the application of this study to control of health problems

(Last, 1988)



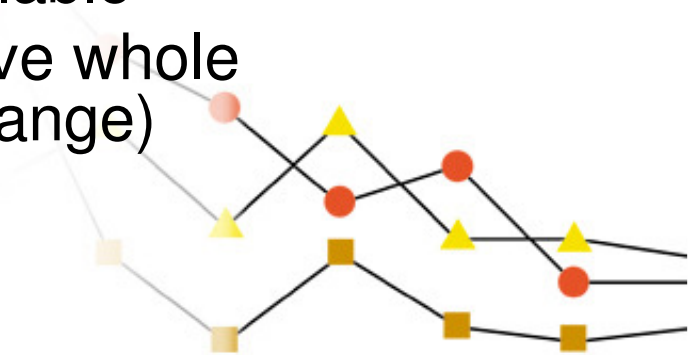
Epidemiology Is a Population Science

- “Traditional” epidemiology starts at the population level and the first step is to ascertain variations in the occurrence of disease within and between populations
- “Populations” include not only countries, but geographical regions, demographic groups, communities, extended families, etc



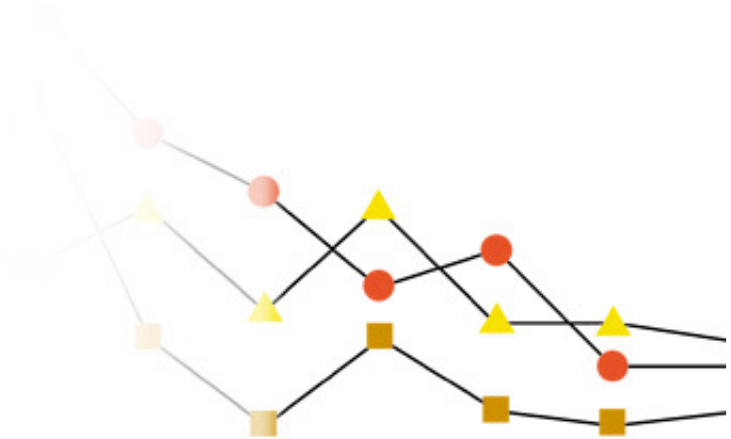
Epidemiology in the 21st century: challenges

- Epidemiology is struggling with problems of correlated exposures and small relative risks.
- The “easy” things (e.g. asbestos and lung cancer) have been discovered and we are now grappling with much more difficult problems.
- One response to these problems has been a stronger emphasis on using better technology (e.g. molecular biology and genetic research)
- Some issues are studied simply because a new methodology (or funding) has become available
- Major environmental health problems involve whole populations or ecosystems (e.g. climate change)



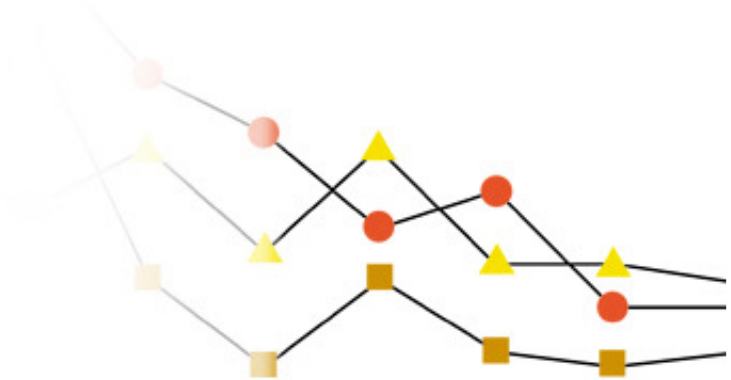
Levels of analysis in epidemiology

Ecosystems	Environmental science
Populations	Epidemiology
Individuals	Clinical research
Molecules	Molecular biology



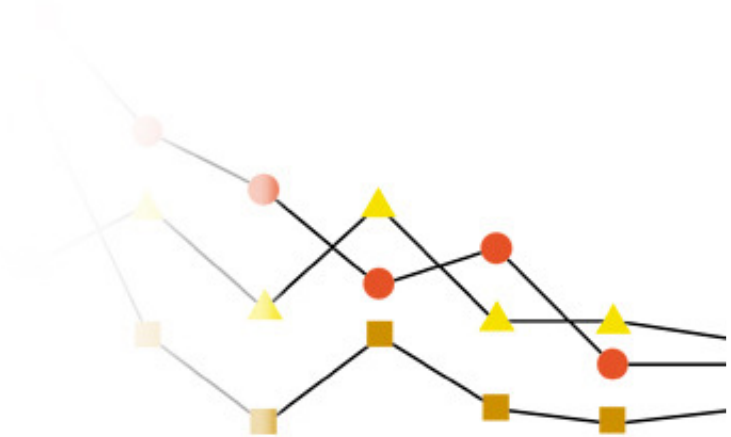
Epidemiology in a changing world:

- The molecular level
- The individual level
- The population level
- The ecosystem level
- The way forward



Epidemiology in a changing world: microlevel

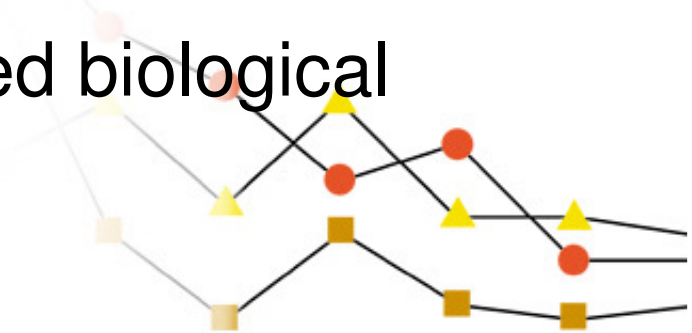
- Biomarkers of exposure
- Genetic factors



Successful uses of biomarkers

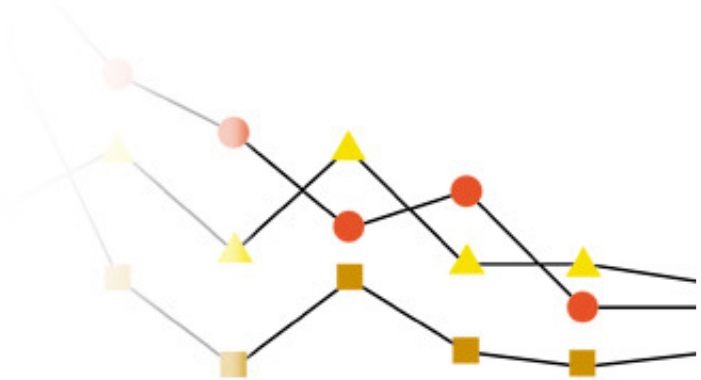
- Human papilloma virus and cervical cancer
- Hepatitis B virus and liver cancer
- Aflatoxins and liver cancer

The most successful uses historically have involved acute effects of exposures; successful uses in studies of chronic disease have primarily involved biological agents



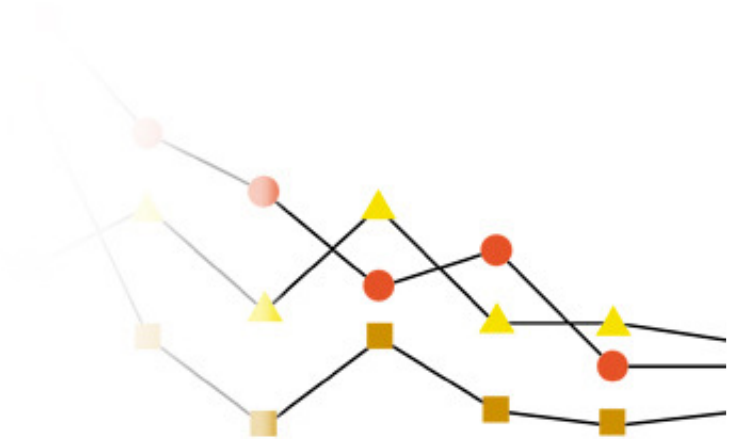
Current limitations of biomarkers

- Historical exposures
- Individual temporal variation
- Effects on precision and validity



Measuring historical exposures

- Most biomarkers of exposure provide poor (or no) estimates of historical exposures or cumulative exposures
- There are some exceptions to this (e.g. TCDD)



Individual temporal variation

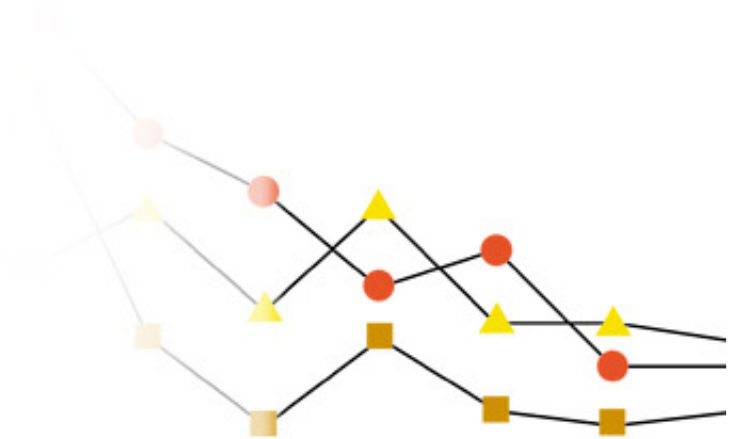
- The variation in exposure levels within an individual (because of day-to-day differences in exposure) may be greater than the variation between individuals
- Thus, a job-exposure matrix, combined with a work history, may provide a better estimate of a worker's long-term exposure than is provided by a single biomarker measurement

Precision and validity

- The use of biomarkers may severely limit the size of a study; thus, any gains in validity (from better exposure information) may be offset by losses in precision
- Even if the use of a biomarker reduces information bias, it may reduce response rates, thereby increasing selection bias

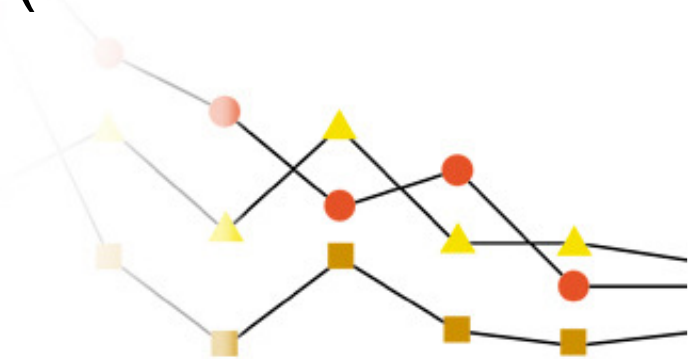
Inherent limitations of biomarkers

- What does a biomarker measure?
- Increased likelihood of confounding
- Public health implications



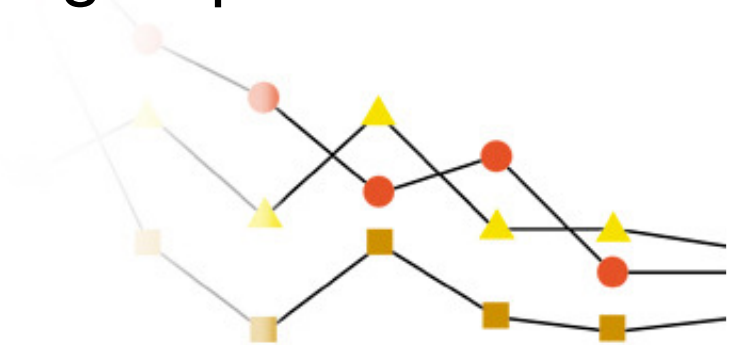
What does a biomarker measure?

- Exposure or biological response (or disease process)?
- One biological response to one chemical
- Individual response to exposure (individual metabolism)

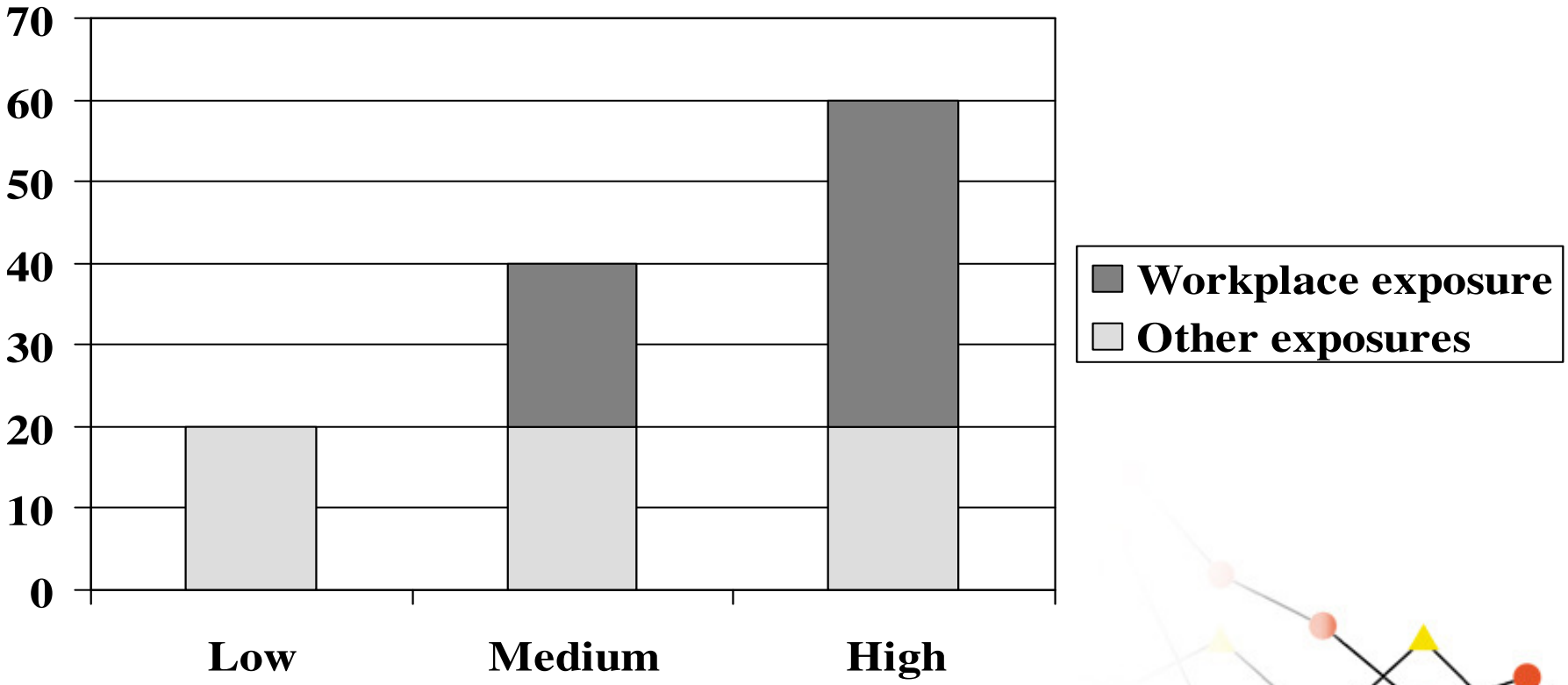


Problems of the reductionist approach: beta carotene and cancer

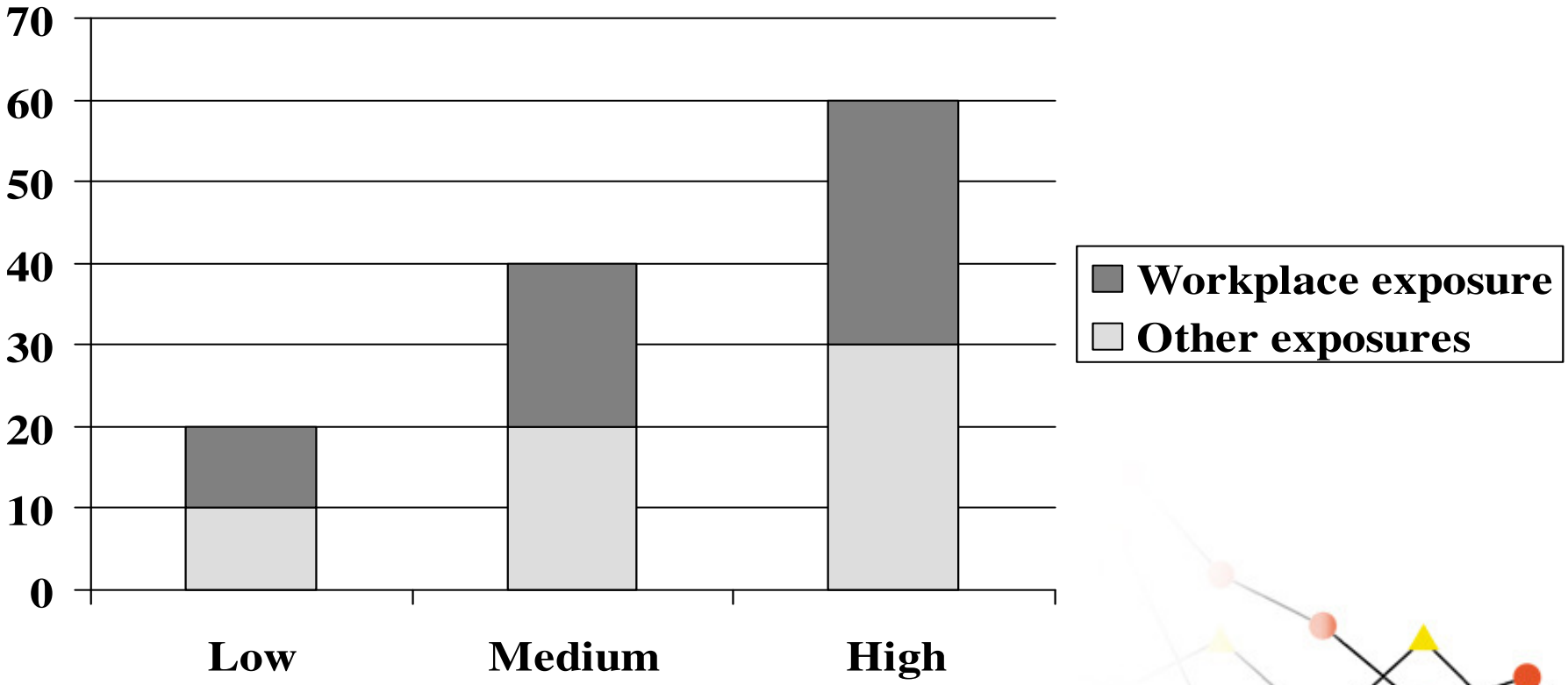
- Epidemiological studies have shown that consumption of green and yellow vegetables reduces the risk of some cancers
- Intervention studies were carried out using beta carotene
- Two out of three large trials showed an increased risk of lung cancer in the intervention group



Classification based on environmental levels in the workplace

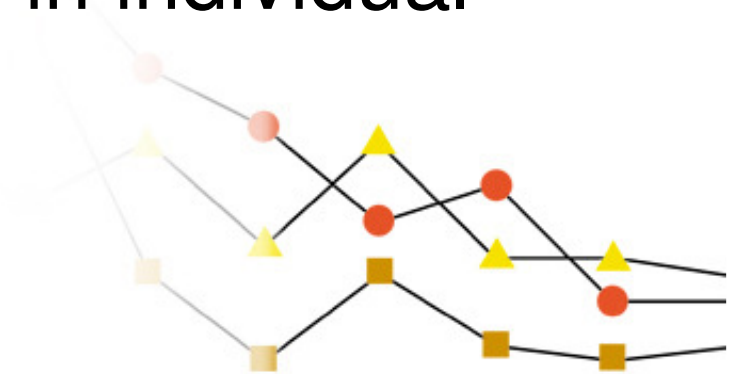


Classification based on PAH-DNA adducts



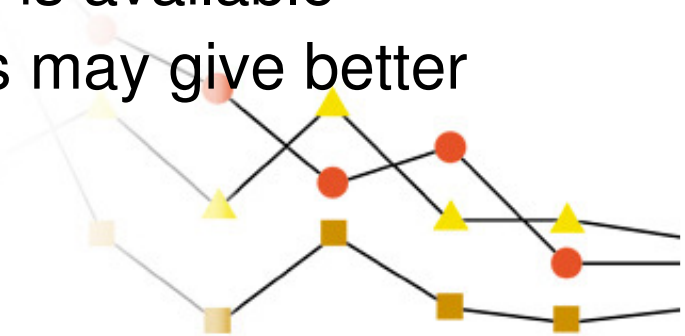
Public health implications

- Technology defines the “problem”
- Regulation is (or should be) based on environmental exposure levels
- Dangers of interventions based in individual susceptibility



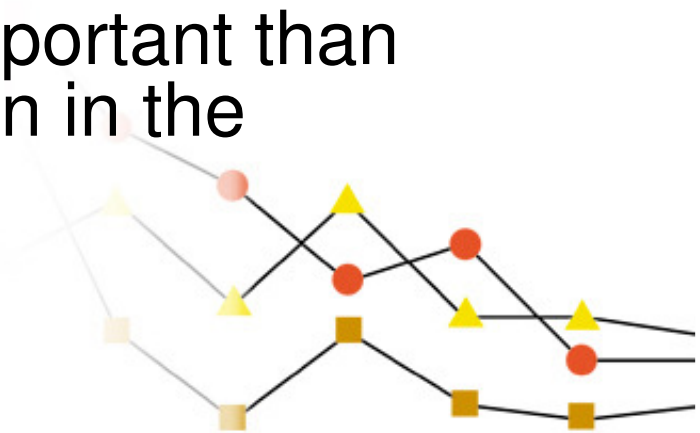
Biomarkers of exposure

- Such micro-level research can help to establish the etiologic mechanisms
- The methods (e.g. if a specific lab test becomes available) often determine the question
- Studies often have small sample sizes
- It is usually impossible to isolate the effects of a single chemical
- A particular chemical (e.g. cotinine) may be measured in a mixture simply because a biological marker is available
- Traditional methods such as questionnaires may give better estimates of long-term exposures

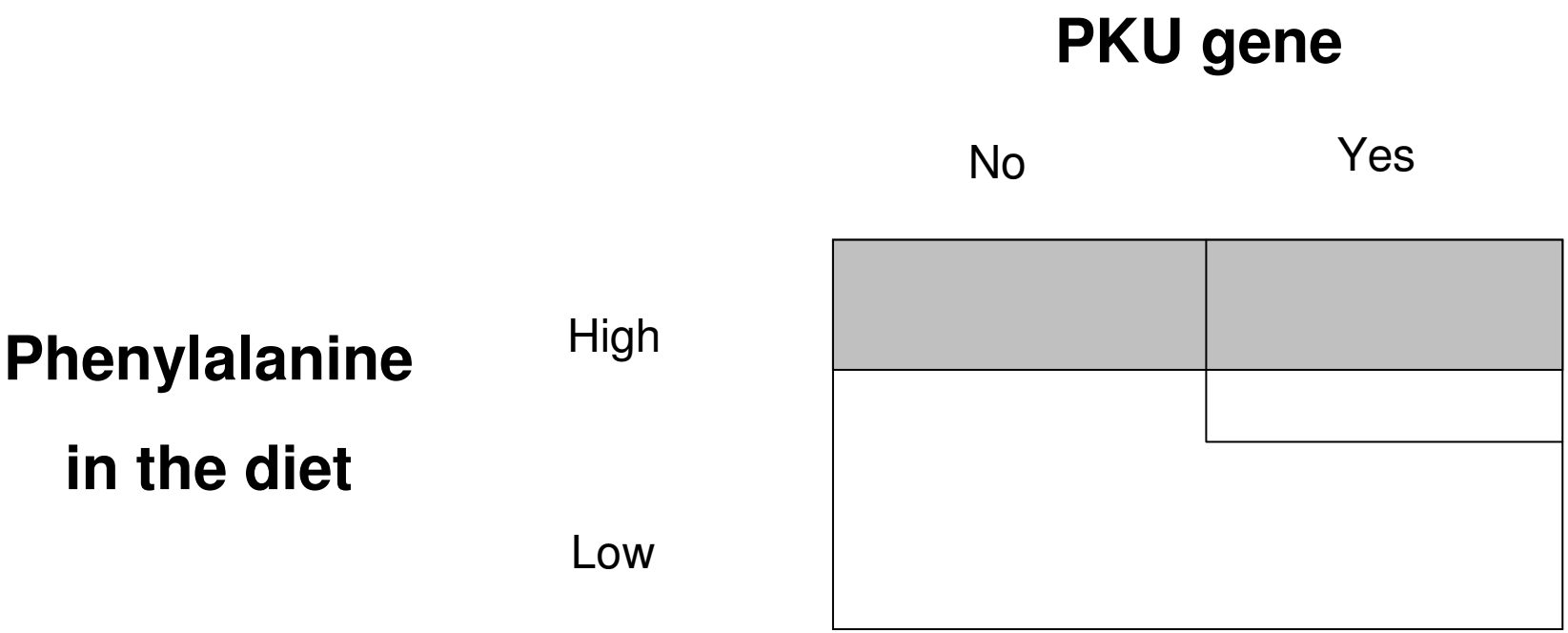


Genetic factors

- High number of false positives when many genetic polymorphisms are tested
- Lack of reproducibility
- Lack of power for testing gene-environment interactions
- Just because a disease is heritable does not mean that it is genetic
- Genetic factors may appear more important than they really are if there is little variation in the environment



Genetic factors



	% cases caused	% variance explained
High phenylalanine in the diet	100%	0%
PKU Gene	100%	100%

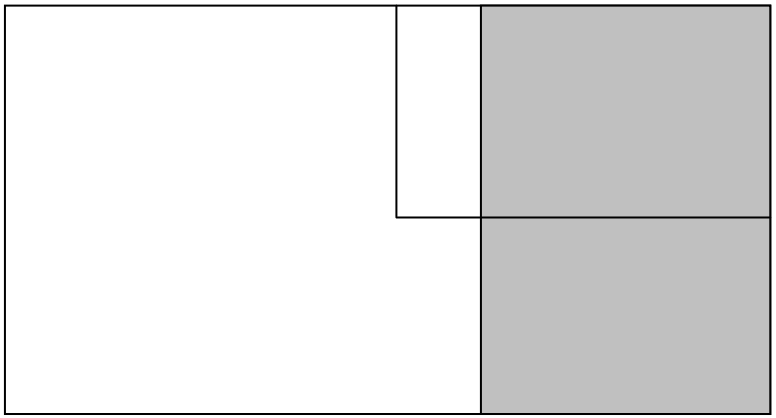
PKU gene

No | Yes

Phenylalanine in the diet

High

Low



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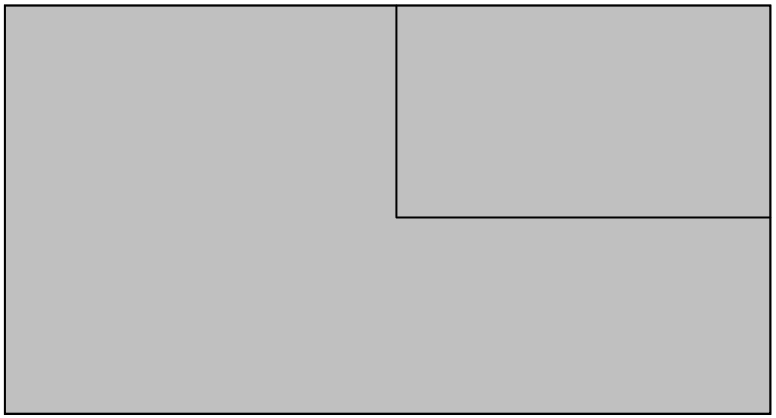
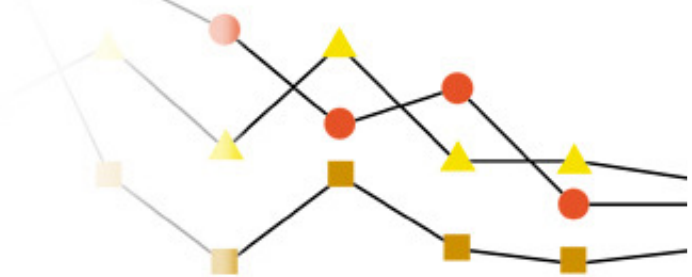


	% cases caused	% variance explained
High phenylalanine in the diet	100%	50%
PKU Gene	100%	50%

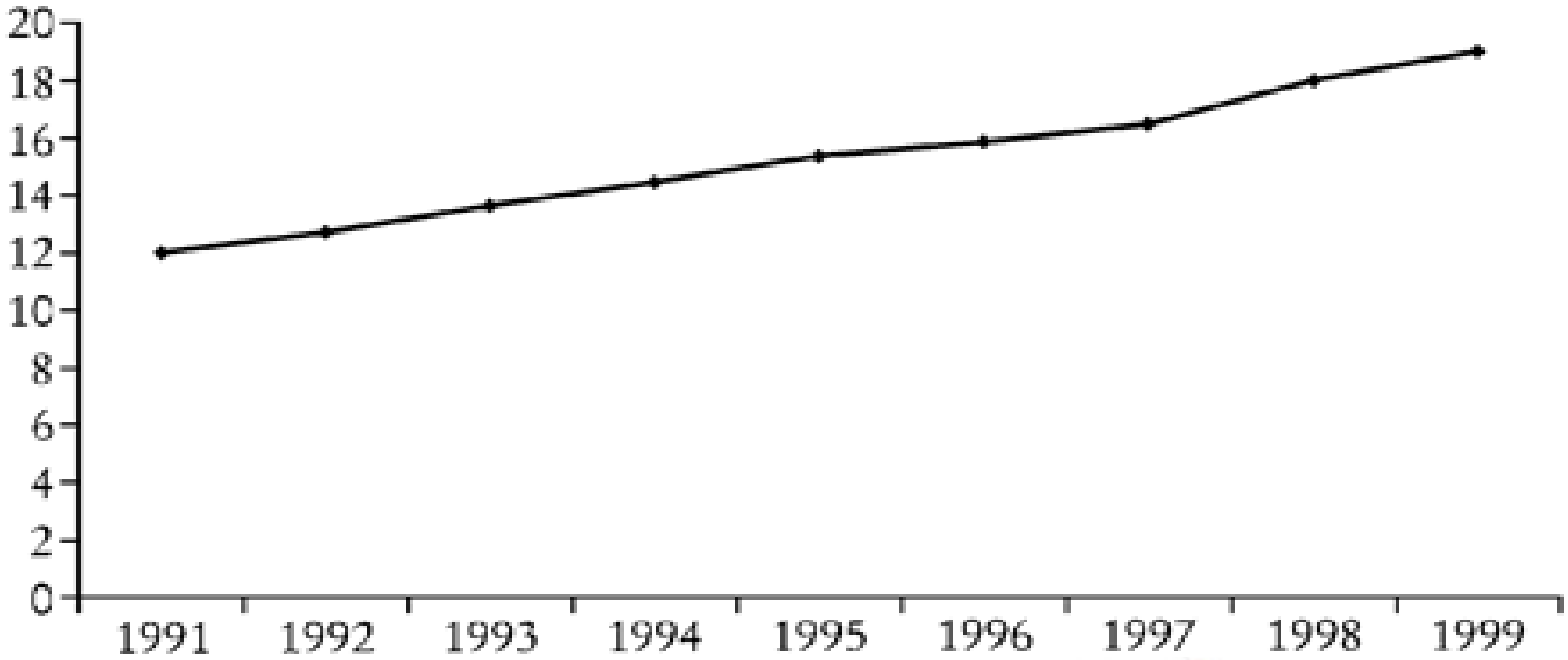
Genetics, heritability and the environment

- “Except for some cases of trauma, it is fair to say that virtually every human illness has a hereditary component.” Collins F. N Engl J Med 1999, 341: 28-37.
- Virtually every human illness also has an environmental component.
- Thus, virtually every human illness is 100% genetic and 100% environmental (e.g. PKU)
- What is the heritability of lung cancer? What would be the heritability in a population where everyone smoked?



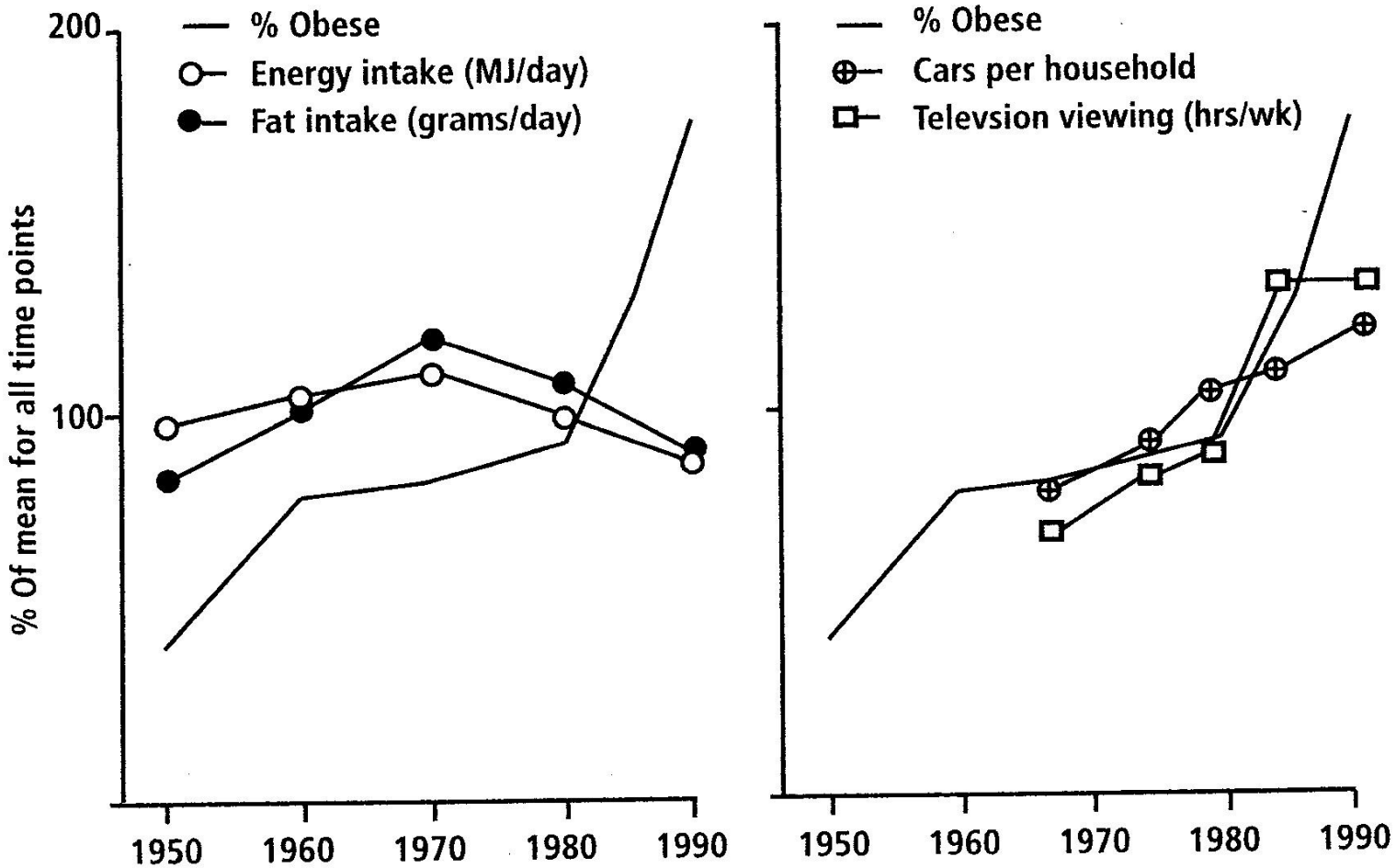
Genetic diseases

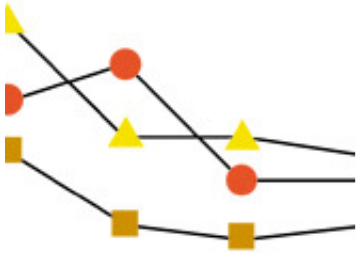
- When the environmental component is universal but the genetic component varies, then we say that the condition is entirely genetic
- When the genetic component is universal but the environmental component varies then we say that the disease is entirely environmental
- In most instances, presumably, both the genetic factors and the environmental factors vary, and whether we label the disease as “genetic” or “environmental” depends on our current knowledge



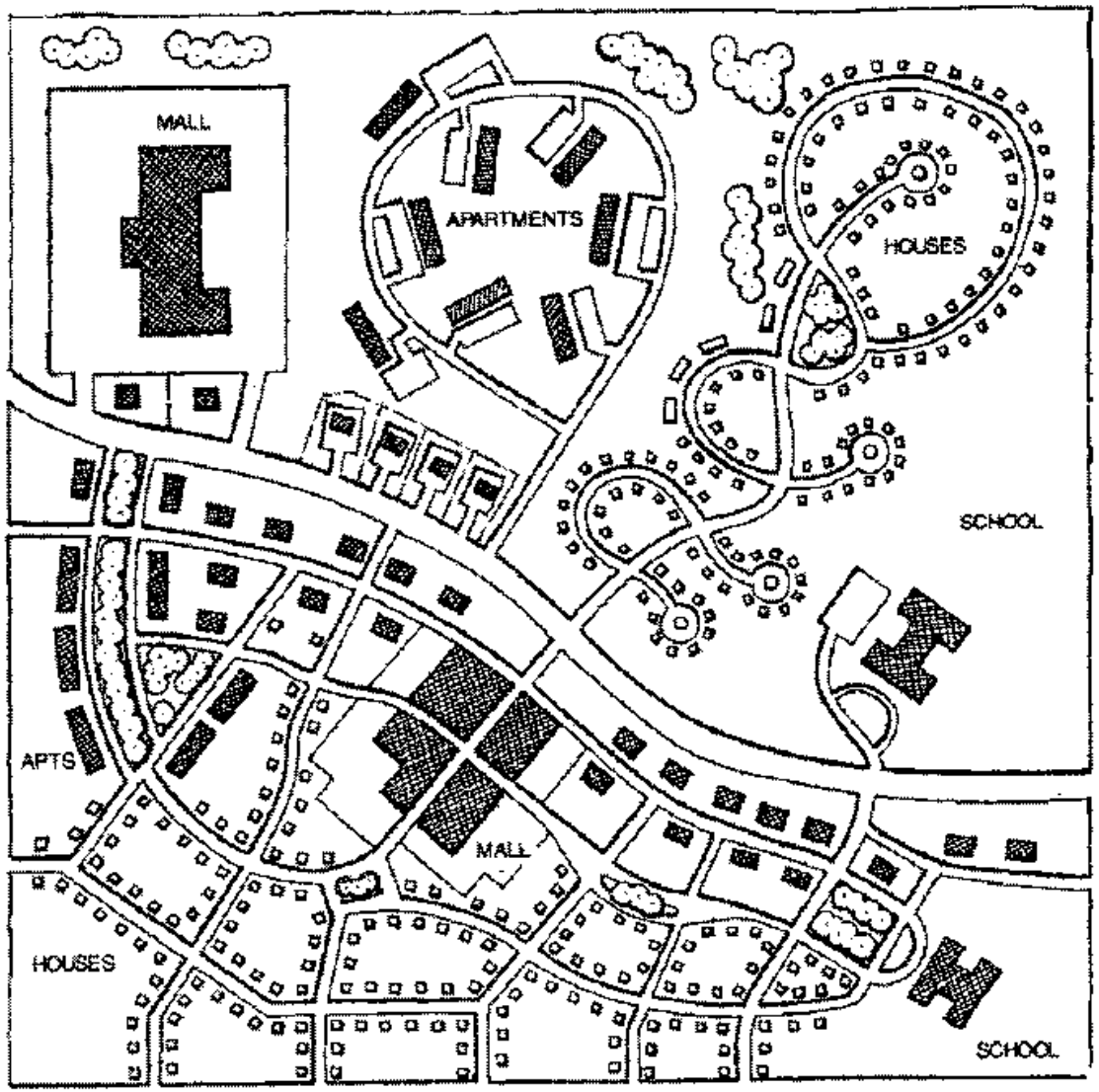
Prevalence of obesity in US adults from 1991-1999

FIGURE 5-1 Obesity trends compared to "gluttony" on the left (measured as energy intake and fat intake) and to "sloth" on the right (measured by car ownership and television viewing)





Suburban Sprawl



Traditional Neighborhood

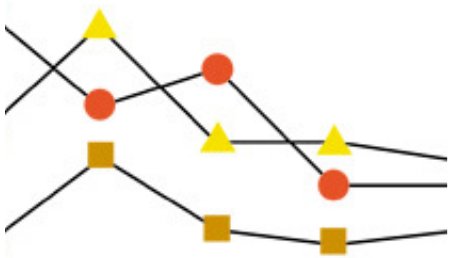
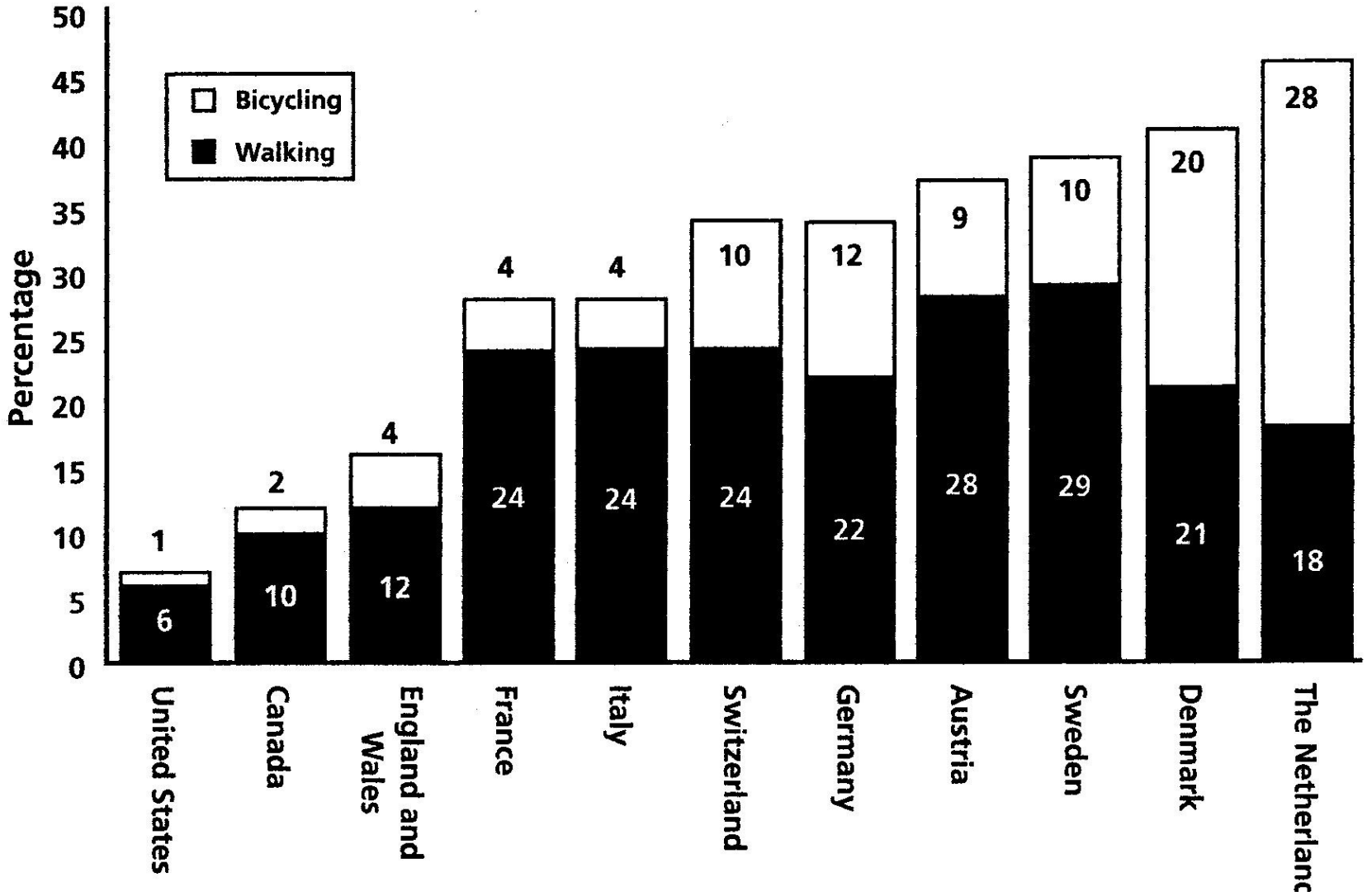


FIGURE 5-4 Proportion of trips in urban areas made by walking and bicycling in North America and Europe, 1995



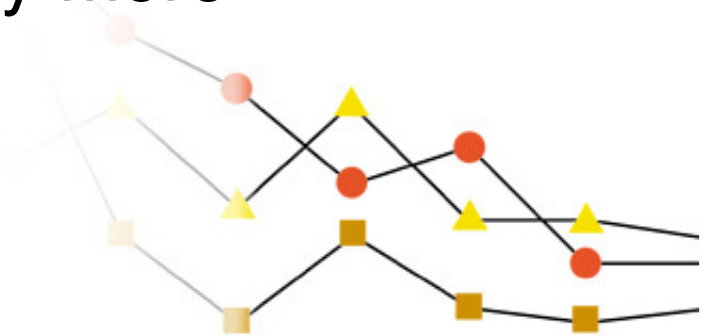

24 HOUR
FITNESS

	% cases caused	% variance explained
Obesity genes	100%	50%
Lack of exercise	100%	50%

	% cases caused	% variance explained
Obesity genes	100%	100%
Lack of exercise	100%	0%

What causes obesity?

- Twin studies show high heritability
- Time trends show that environmental factors are of overwhelming importance
- Twin studies are perfectly matched on birth cohort – and thus on factors relating to secular trends
- When there is no variation in the environment, then genetic factors appear to be relatively more important



Epidemiology in a changing world:

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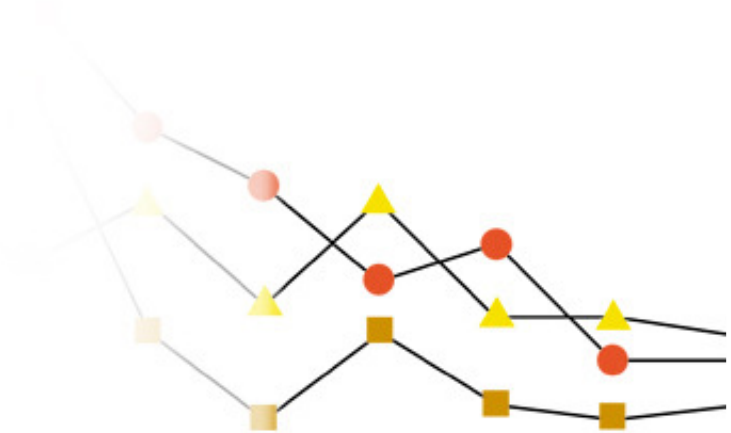
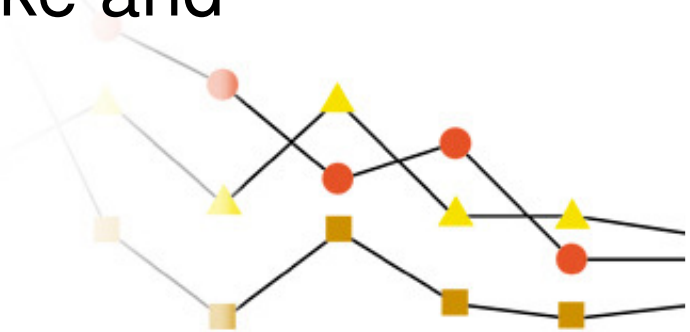
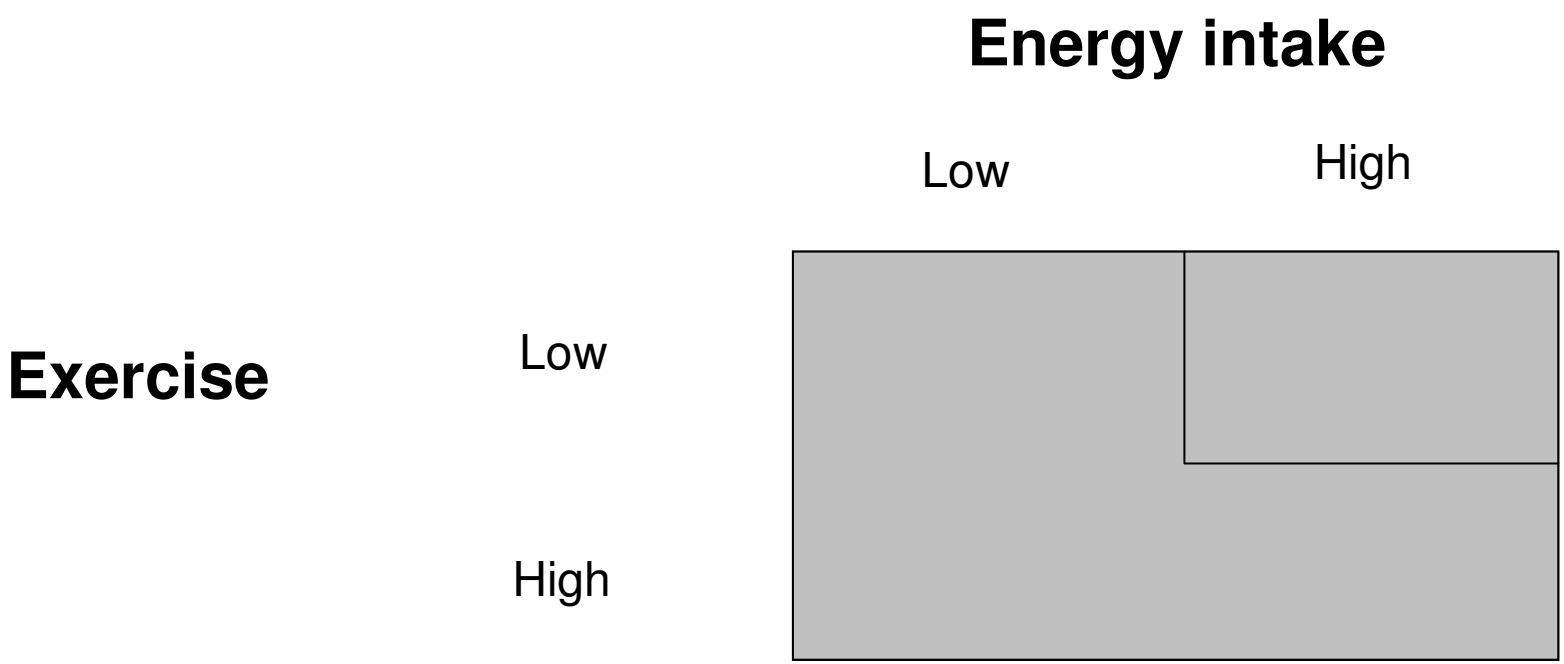
- The individual level
- The population level
- The ecosystem level
- The way forward



Epidemiology in a changing world: individual level

- Typified by “risk factor epidemiology”
- E.g. studies of health effects (e.g. lung cancer) of individual exposure to air pollution
- This approach has had many successes
- Often assumes that personal “lifestyle” and susceptibility are most important, whereas population-level and ecosystem-level exposures are “fixed” (e.g. exercise, energy intake and obesity)





	% cases caused	% variance explained
High energy intake	100%	50%
Lack of exercise	100%	50%

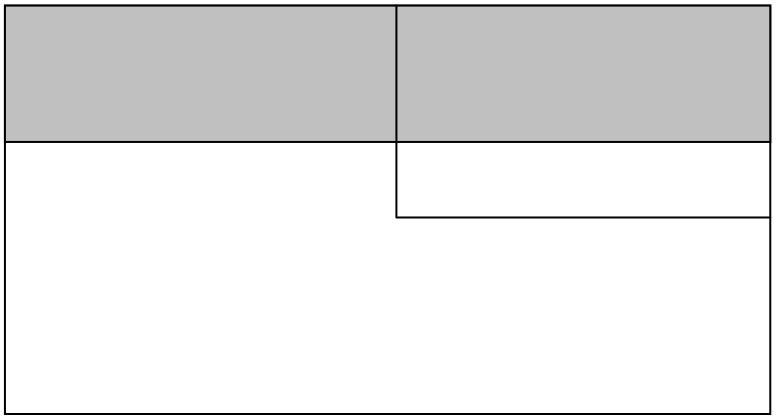
Energy intake

Low High

Exercise

Low

High



	% cases caused	% variance explained
High energy intake	100%	100%
Lack of exercise	100%	0%

Variance of exercise and variance of energy intake

Suppose that we conduct a survey of all students aged 13 years and attempt to ascertain what proportion of the variation in obesity is ‘explained’ by variation in exercise and how much is ‘explained’ by variation in energy intake

We will get completely different answers depending on which population we study:

- All students in Wellington in 2007
- All students in Wellington 1950-2007
- All students in OECD countries in 2007
- All students in the world in 2007

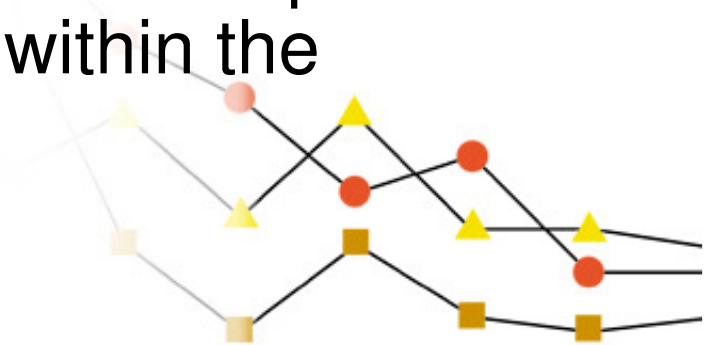
Variance of exercise and variance of energy intake

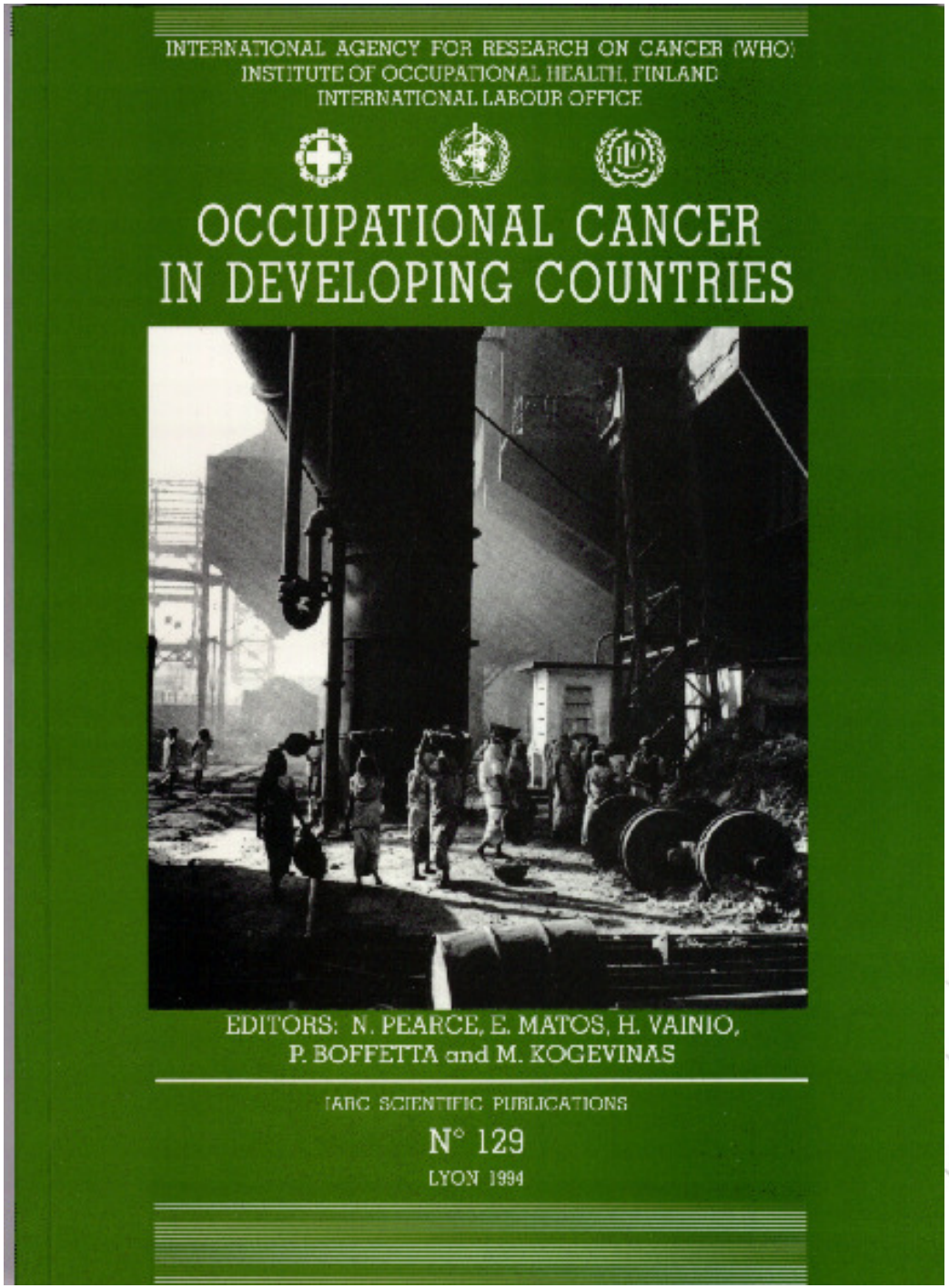
- The “percentage of variation explained” by a risk factor (e.g. exercise, energy intake) is not a generalisable (scientific) concept
- It does not make sense to say that “obesity is 40% due to (lack of) exercise and 60% due to high energy intake”
- It is scientifically invalid to estimate the proportion of variance explained under current environmental conditions – because there is little variation in the urban environment we find that the main source of variation is individual differences in lifestyle (we end up “blaming the victim”)

Problems of the Risk Factor Approach: Tobacco

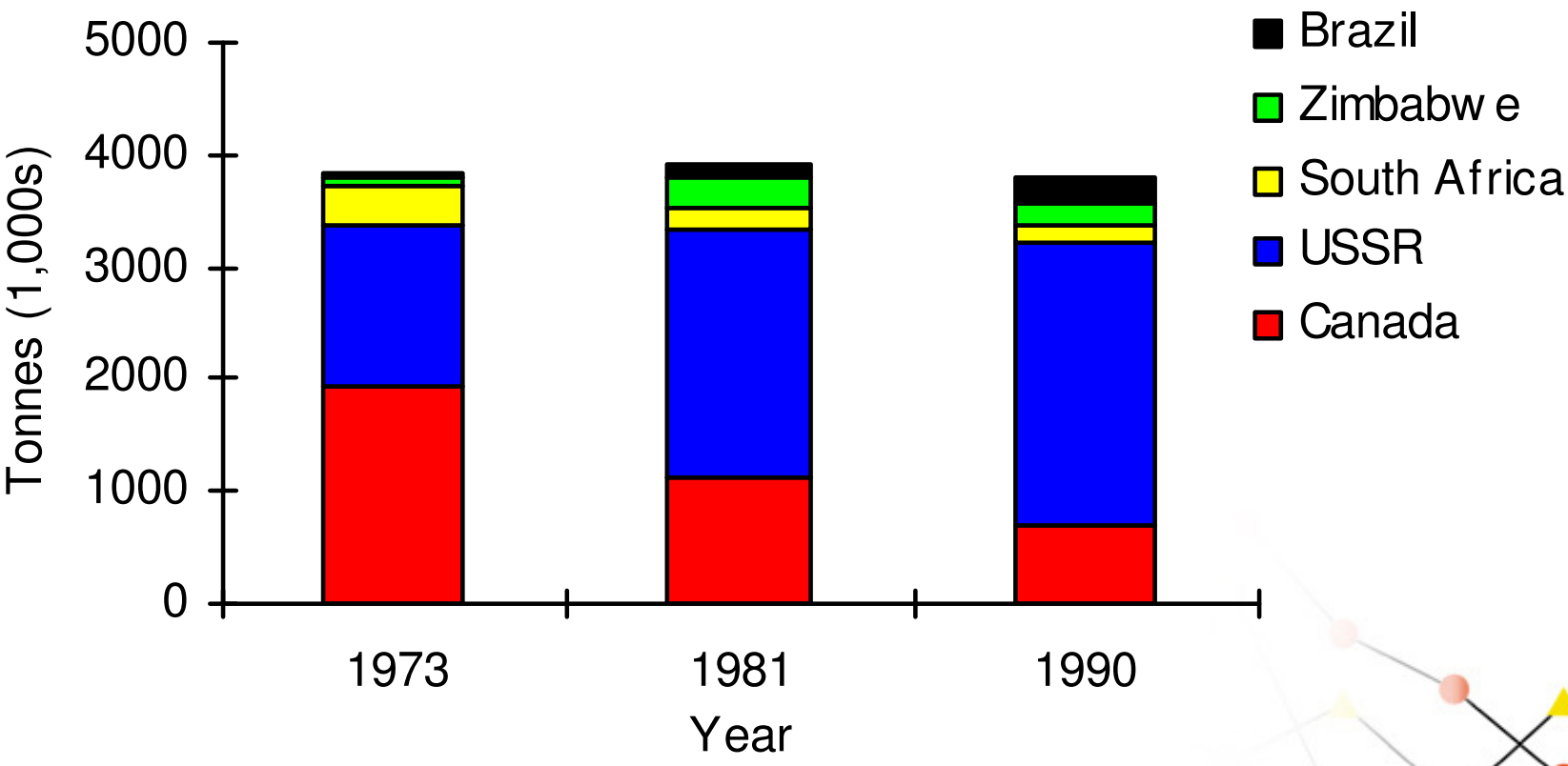
The limited success of legislative measures in industrialised countries has led the tobacco industry to shift its promotional activities to developing countries so that more people are exposed to tobacco smoke than ever before.

Thus, on a global basis the “achievement” of the public health movement has often been to move public health problems from rich countries to poor countries, and from rich populations within the industrialised countries.




INTERNATIONAL AGENCY FOR RESEARCH ON CANCER (WHO)
INSTITUTE OF OCCUPATIONAL HEALTH, FINLAND
INTERNATIONAL LABOUR OFFICE
OCCUPATIONAL CANCER
IN DEVELOPING COUNTRIES
EDITORS: N. PEARCE, E. MATOS, H. VAINIO,
P. BOFFETTA and M. KOGEVINAS
IARC SCIENTIFIC PUBLICATIONS
N° 129
LYON 1994

Problems of the Risk Factor Approach: Asbestos



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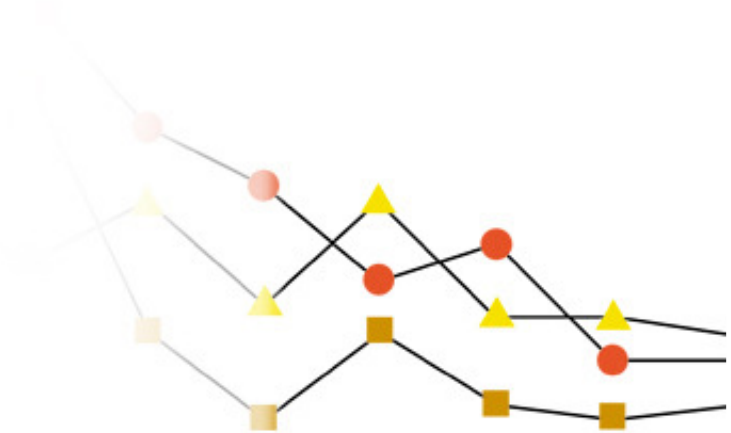
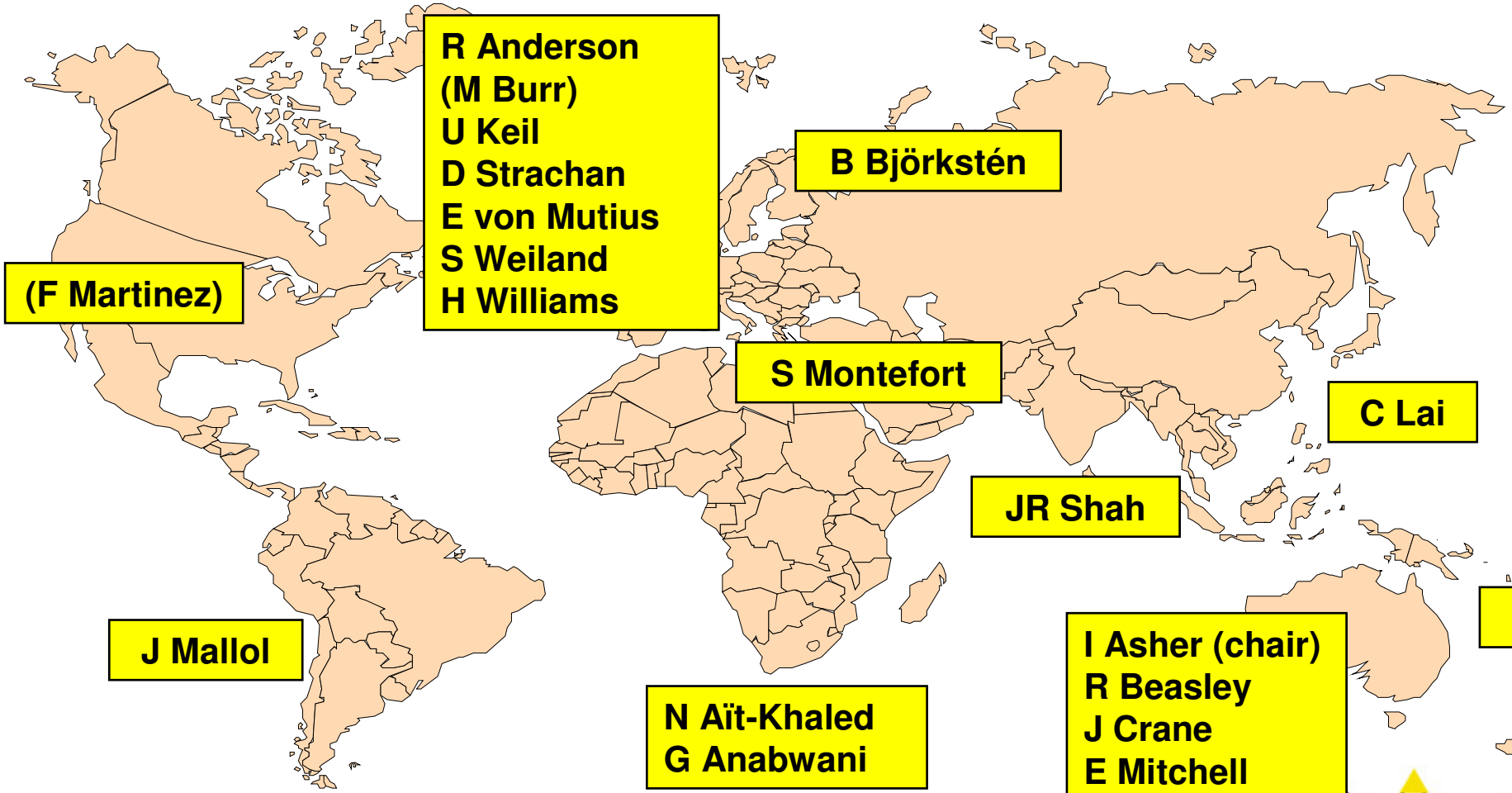


Epidemiology in a changing world: population level

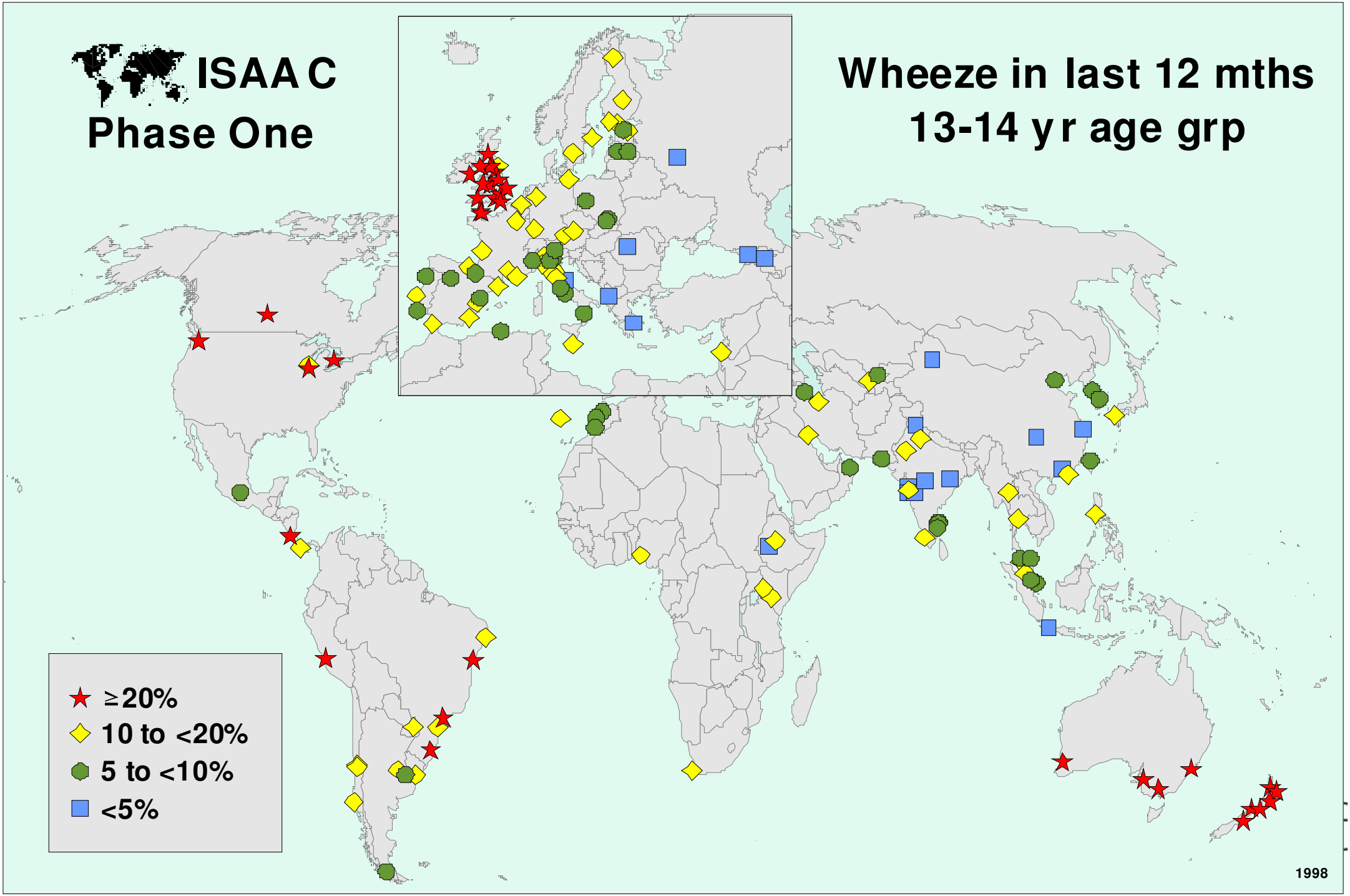
- Many of the major discoveries in cancer epidemiology followed the publication of “Cancer Incidence in Five Continents” in the 1950s and 1960s which generated new hypotheses about possible (population and individual) causes of cancer
- Of the 30-40 known occupational carcinogens, all were discovered in epidemiological studies and it often took many years of laboratory work to subsequently establish the etiologic mechanisms
- Global comparisons of asthma prevalence
  - The European Community Respiratory Health Study (ECRHS)
  - The International Study of Asthma and Allergies in Childhood (ISAAC)

ISAAC Steering Committee

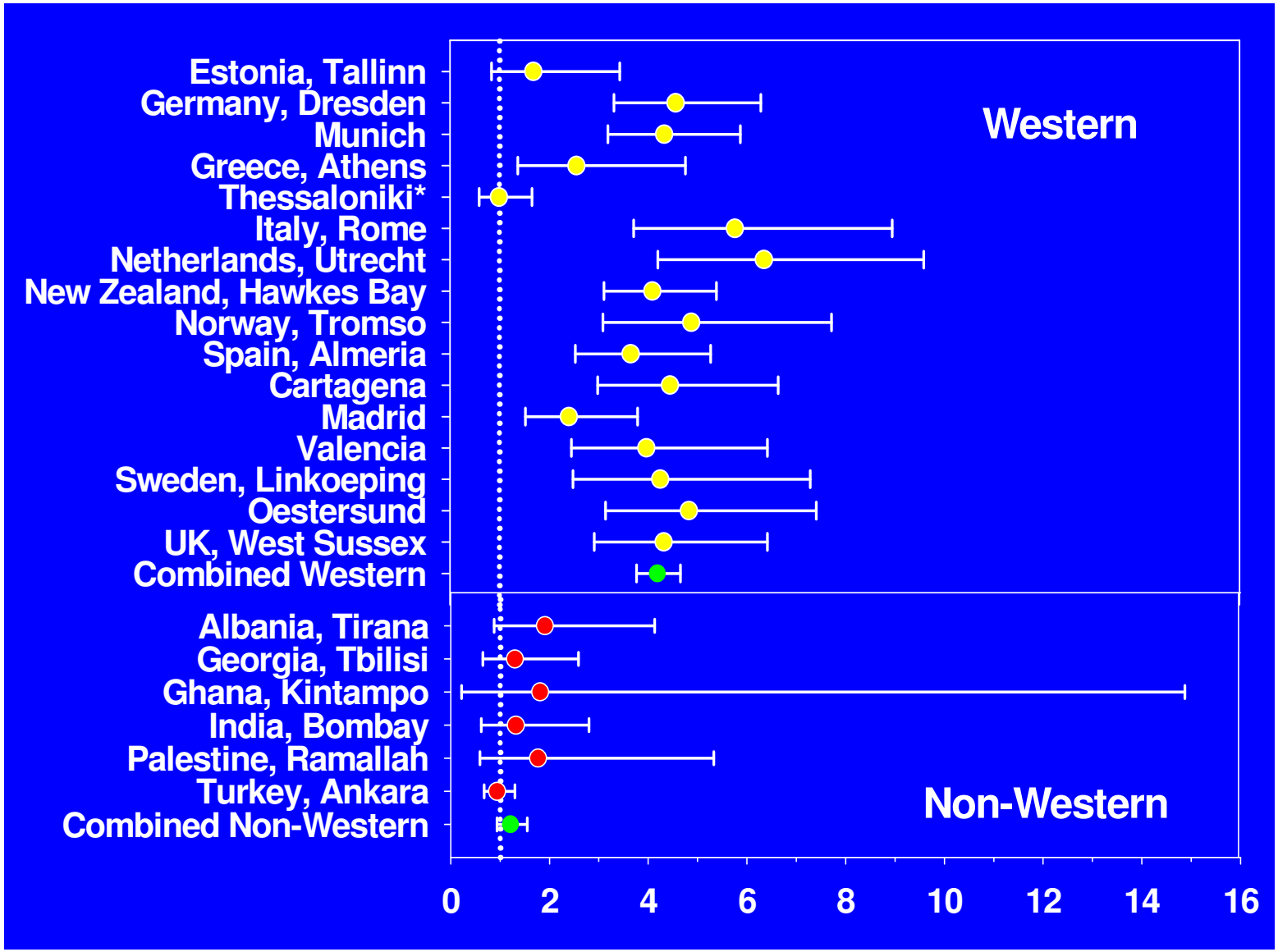


Study Centres and Participants: Phase I
13-14 Year Age Group

Region	Centre n	Participants n	Participation %
Africa	7	21,648	91%
Asia-Pacific	20	83,826	94%
Eastern Mediterranean	10	28,468	93%
Latin America	17	52,549	93%
North America	5	12,460	79%
Northern and Eastern Europe	20	60,819	93%
Oceania	10	31,301	93%
Southeast Asia	14	37,171	95%
Western Europe	52	135,559	90%
Global Total:	**155**	**463,801**	**92%**

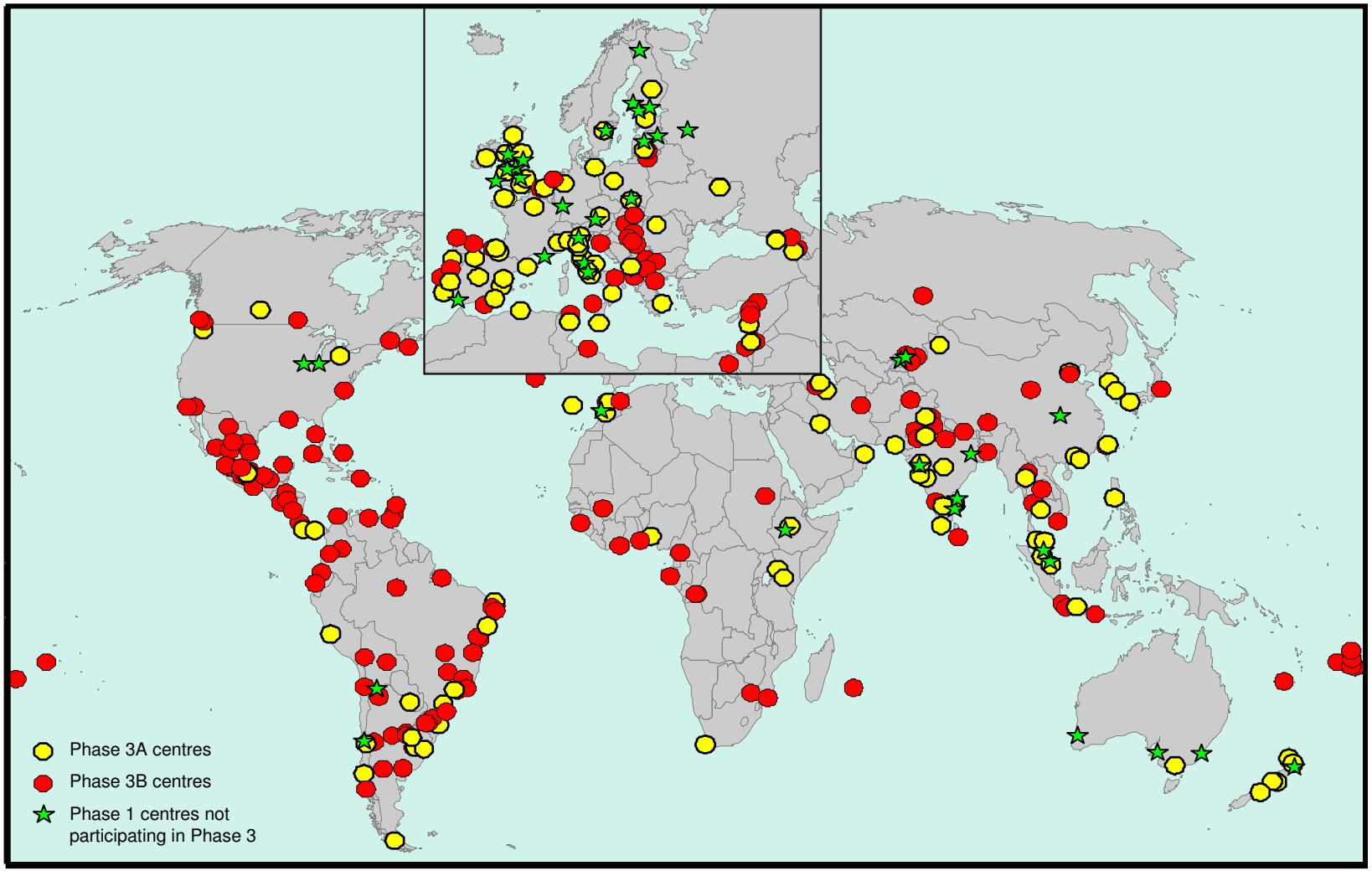

ISAAC
Phase One
Wheeze in last 12 mths
13-14 yr age grp
≥20%
10 to <20%
5 to <10%
<5%
1998

Current wheeze v skin prick test for atopy



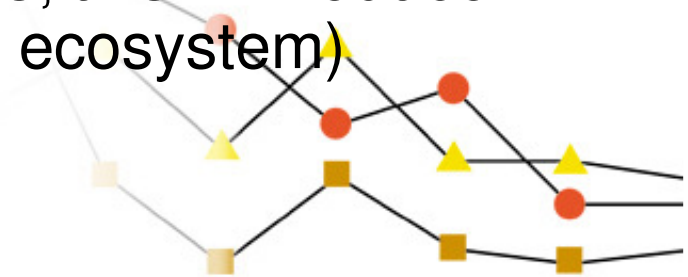
Odds ratio with 95% confidence interval

CENTRES REGISTERED FOR ISAAC PHASE THREE



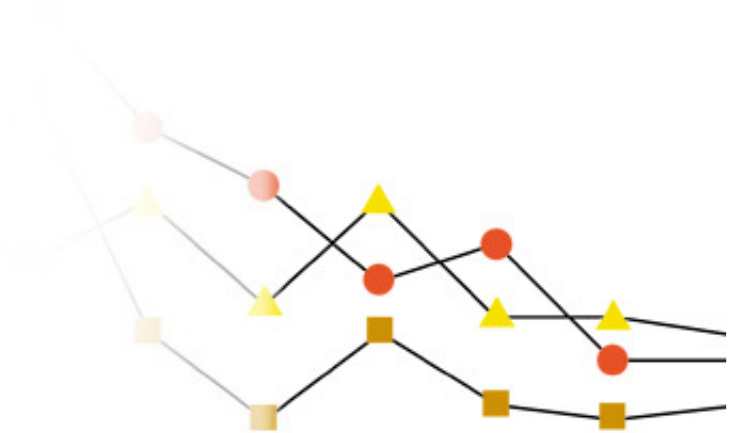
Epidemiology in a changing world: population level

- Multi-level studies that involve exposures both at the individual-level (e.g. smoking, diet) and population-level (e.g. air pollution, level of “Westernization”)
- Recognizes importance of population context (e.g. some populations may be more susceptible, and dose-response relationships may not be universal)
- Starts from the public health problem (e.g. why is asthma increasing?)
- May ignore long-term indirect effects (e.g. factories may fit “long stacks” rather than reducing emissions; this will reduce individual exposures but may endanger the ecosystem)



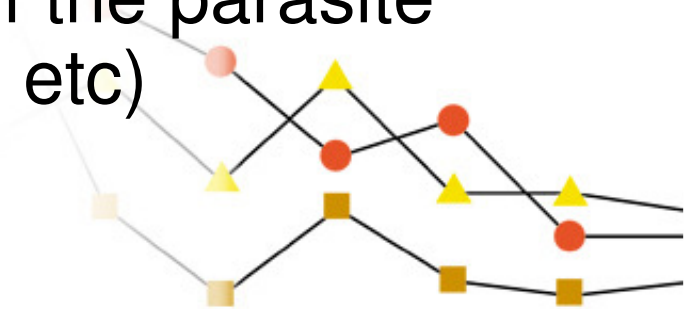
Epidemiology in a changing world:

- The molecular level
- The individual level
- The population level
- The ecosystem level
- The way forward



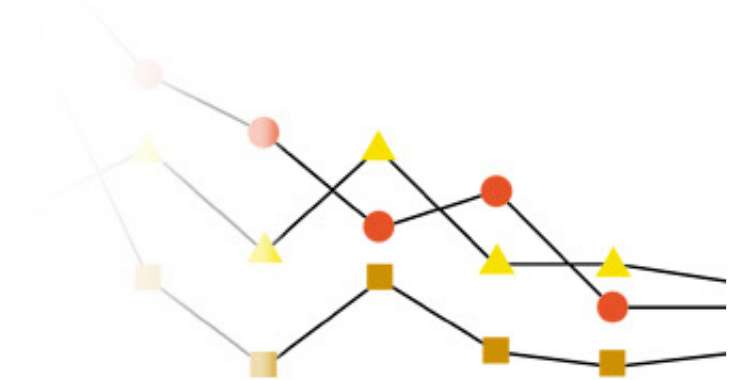
Epidemiology in a changing world: ecosystem level

- Typified by studies of the health effects of climate change
- E.g. studies of the effects of climate change on the spread of malaria
  - Models based on human-biting rate of mosquitoes, human susceptibility, mosquito susceptibility, daily survival probably of the mosquito, and incubation period of the parasite (depends on temperature, rainfall, etc)



Epidemiology in a changing world: ecosystem level

- Involves quite different methods from the usual epidemiologic techniques
- Requires a “systems based” (complexity) approach
- Integrates information from several fields of research



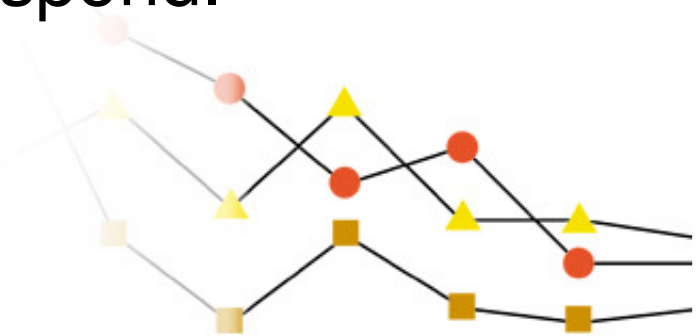
The Way Forward

- The importance of context
- Problem-based epidemiology
- Living with complexity
- Appropriate technology

The Importance of Context

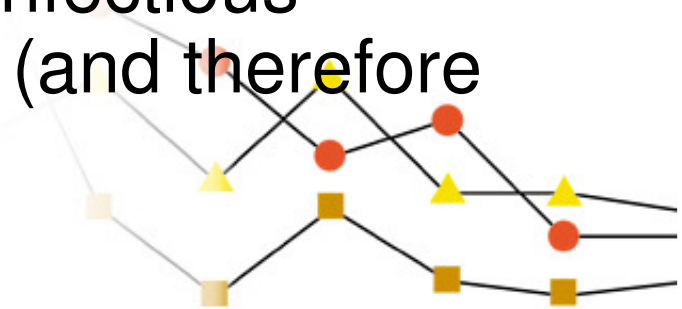
The “populations” which epidemiologists study are not just collections of individuals which are conveniently grouped for the purposes of study, but are instead historical entities.

Every population has its own history, culture, organisation, and economic and social divisions which influences how and why people are exposed to particular factors, and how they respond.



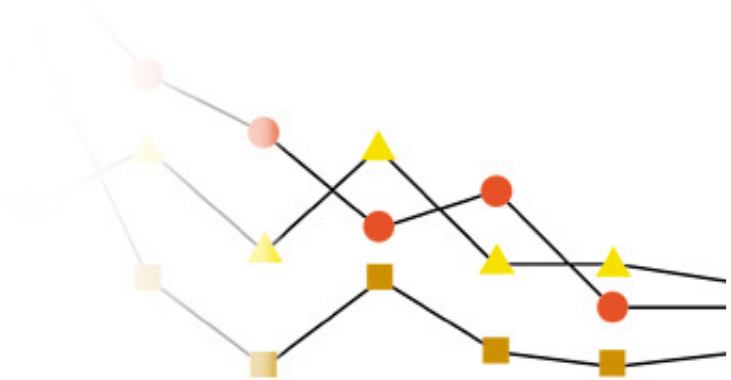
The Importance of Context

- There were large numbers of deaths amongst the indigenous people when New Zealand (Aotearoa) and other areas of the Pacific were colonised in the 19th century
- It is commonly assumed that these deaths were due to infectious diseases, and affected all populations
- In fact, many populations experienced very few deaths
- The main determinant of death from infectious disease was whether land was taken (and therefore the social systems disrupted)



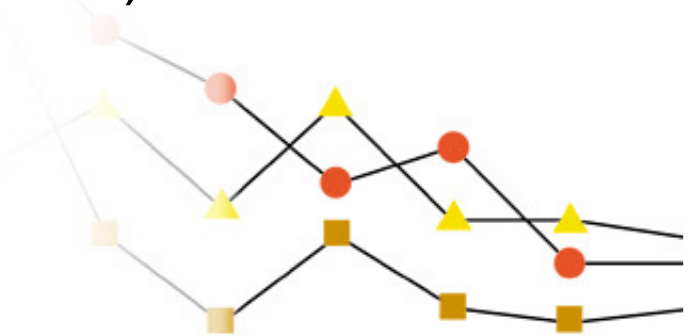
Problem-based Epidemiology

- The approach of “problem-based” medicine can be used in the teaching and practice of epidemiology
- The appropriate methods should be chosen to fit the problem rather than letting the methods define the problem



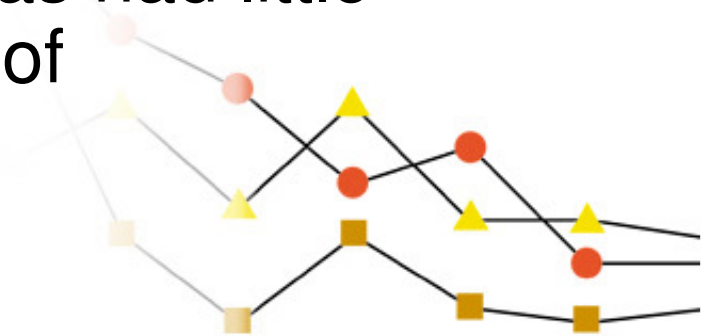
Living with complexity

- E.g. studies of the effects of climate change on the spread of malaria
  - Models based on human-biting rate of mosquitoes, human susceptibility, mosquito susceptibility, daily survival probably of the mosquito, and incubation period of the parasite (depends on temperature, rainfall, etc)



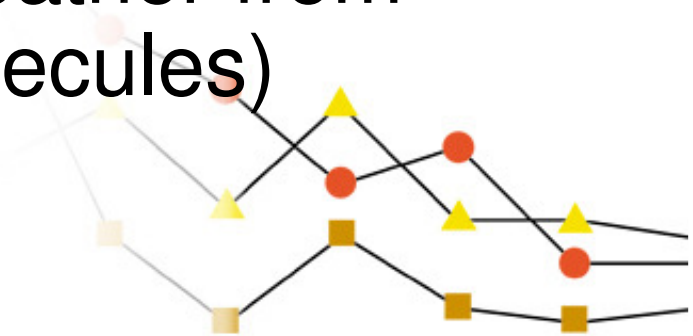
Living with complexity

- Involves quite different methods from the usual epidemiologic techniques (you can't do a cohort study of climate change unless you have two planets)
- Requires a "systems based" (complexity) approach
- Complexity theory is influencing many fields of science (physics, chemistry, geography, biology, neuroscience, economics, etc) but has had little influence on the theory and practice of epidemiology to date



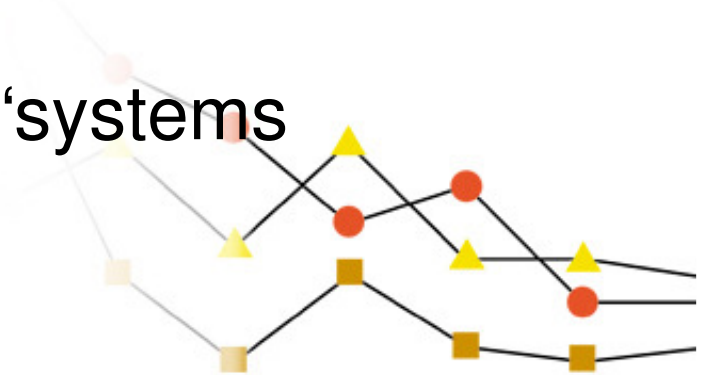
Living with complexity

- Integrates information from several fields of research
- Involves non-linearity and “feedback loops”
- What is “chaotic” at one level may be “simple” at another (we can’t predict population health from molecular biology any more than we can predict the weather from the movements of individual molecules)



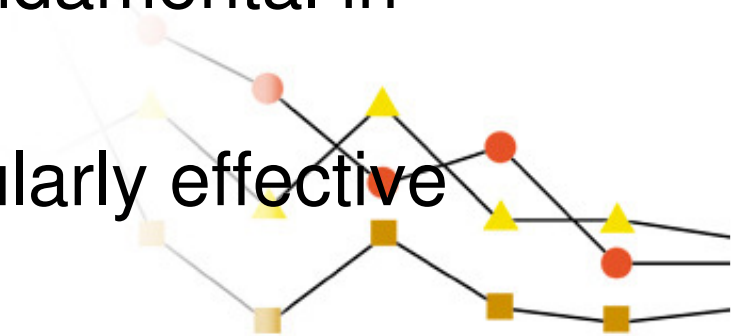
Appropriate technology

- The appropriate methods should be chosen to fit the public health problem
- It cannot be simply assumed that high-tech methods such as “molecular epidemiology” will be the most valid
- Just as case-control studies were developed for “risk factor” epidemiology, new methods need to be developed for “ecoepidemiology”
- In many instances a “complexity” or “systems approach” is required



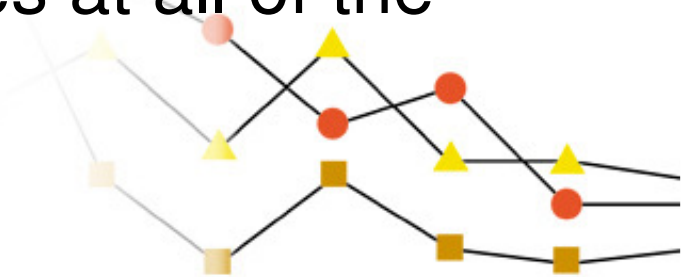
All of the different levels of analysis are important

- Population level studies are complementary to studies at the individual and micro-levels
- Individual and micro-level studies have had some real successes
- The population level is fundamental in epidemiology, just as weather systems (rather than molecular phenomena) are fundamental in climatology and macro-evolutionary processes are fundamental in evolutionary biology
- A multi-level approach may be particularly effective



Epidemiology in a changing world

- We need to restore the population perspective and develop the ecosystem perspective
- This requires not just multi-level analysis but rather "multi-level thinking"
- This multi-level thinking can be encouraged and fostered by a **problem-based** and **evidence-based** approach which uses **appropriate technology** to address the major public health issues at all of the relevant levels



Epidemiology in a changing world

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