



# Advantages and pitfalls of different types of studies for investigations of the impact of food on health

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## Why study the effect of food on health?

- The importance of food quality for human health has been recognised since prehistoric times.
- We all want to know which diet is best for our health, but even the best experts often disagree.
- Each study method has its strengths and limitations, and any data can be misinterpreted if assessed in an inappropriate context.
- Reliable conclusions require that we understand what each type of study can provide, and how data from different types of studies can and must support each other.



## Different types of studies

1. Epidemiological (observational) studies of humans.
2. Intervention studies with animals or humans.
3. In vitro studies using cell cultures, isolated organs or on enzyme activities.
4. Combining different types of studies.



# 1. Epidemiological (observational) studies

- Prospective studies
  - Information is collected about the diet etc. of a large number of generally healthy people.
  - The subsequent or concurrent occurrence of ill health is recorded.
  - The information about diet is compared with the information about health.



# 1. Epidemiological (observational) studies

- Retrospective studies
  - Patients (or their relatives) with a particular disease are identified.
  - Control persons are selected among healthy people to match each patient for gender, age, and other relevant factors.
  - Patients and control persons are interviewed about diet and lifestyle.
  - Data are processed to identify systematic differences in diet/lifestyle.



# 1. Epidemiological (observational) studies

## Advantages

- When significant differences are found, they will be directly applicable to real populations and diets, both qualitatively and quantitatively.
- Relatively low cost, since there is no need for monitoring or controlling participants between assessments.
- Allows quantification of the maximal impact of a food component on health.



# 1. Epidemiological (observational) studies

## Disadvantages

- Requires that the disease is common and that there is substantial variation in the relevant dietary factor in the population.
- Effects of factors that are correlated cannot be distinguished, such as components that occur in the same food.



# Example of epidemiological study: Prevalence of allergic diseases in children in Steiner schools (the PARSIFAL study)

|   | Steiner school children | Reference children | Odds ratio | 95% confidence interval |
|---|-------------------------|--------------------|------------|-------------------------|
| Current rhinoconjunctivitis (common cold) (%) | 8.0                     | 10.6               | 0.69       | 0.56-0.86               |
| Current atopic eczema symptoms (%)            | 11.6                    | 14.6               | 0.68       | 0.57-0.81               |
| Dr's diagnosis of atopic eczema (%)           | 11.5                    | 12.3               | 0.88       | 0.73-1.06               |
| Height (cm)                                   | 139.2                   | 137.7              |            |                         |
| Weight (kg)                                   | 32.2                    | 32.5               |            |                         |





## 2. Intervention studies

- With humans
  - Volunteers are given certain foods or supplements and asked to avoid certain foods.
  - Health aspects are recorded before and after the intervention.
  - As far as possible the participants should not know which treatment they receive.
  - Cross-over design (different consecutive treatments to each person) can be used to improve the control of random variation among persons for short-term effects.



## 2. Intervention studies

- With animals
  - Groups of animals are fed with diets designed to show a difference in effect.
  - Health aspects are recorded before, during and after the intervention.
  - Duration can be from a few hours to several years.
  - Animal models for disease can allow direct test on the disease progression, although only if it has been shown in advance that the animal model responds in the same way as humans to dietary factors that are known to affect the human disease.



## 2. Intervention studies

### Advantages (humans)

- Allows, in principle, control or avoidance of most types of confounding factors (that are anticipated)
- The only type of study that can provide evidence for a causal relationship.
- Results are directly applicable to human populations regarding the same type of diet and population as was used in the study.



## 2. Intervention studies

### Disadvantages (humans)

- Practical and economic aspects severely restricts the number of participants, the proportion of the diet being controlled and the duration of the study.
- Humans are very variable, and difficult to control.
- Assessing long-term effects of diet on health requires biomarkers that measure the first steps of a disease progression or increased susceptibility, but few such good biomarkers are known.



## 2. Intervention studies

### Advantages (animals)

- Some animal populations are very uniform, allowing more sensitive tests than with humans.
- Easy to control the full diet for long periods.
- Less ethical issues than for humans.
- Organs, tissues and cells can be examined directly when the animals are killed after the study.
- Animal studies are very useful to assess which aspects of health are affected by diet, since these same aspect are likely also to be affected in humans.



## 2. Intervention studies

### Disadvantages (animals)

- Most animal species are different from humans in the way they digest and metabolise food components - and the most similar (primates) are rarely available or suitable for such studies.
- So even clear-cut results can only be taken as indications that a similar effect is likely in humans.
- In the standard design it will not easily be revealed if the experimental diets makes the food unattractive to eat, since the animals can't complain.



### 3. In vitro studies

- Cell cultures
  - Cells can be grown in a nutrient solution and exposed to components derived from food.
  - The impact on molecular mechanisms in the cells can be studied in great detail.



## 3. In vitro studies

### Advantages

- Few ethical issues.
- Very easy to test many compounds and concentrations, to indicate which ones are most worthwhile to test in other systems.
- Very important tool to discover and confirm mechanisms of those effects that have been shown (definitively or tentatively) in “whole-body” experiments.





### 3. In vitro studies

#### Disadvantages

- Difficult to ensure that the cell is in a natural state where it will react as when it is in a body.
- Risk that some of the concentrations tested are not relevant for the actual levels encountered inside human tissues.
- Due to this, in vitro results cannot be used on their own to determine effects on health.



## 4. Combining different types of studies

- A cause and effect statement requires independent results in all 3 types of studies, which must all indicate the same general trends for the same food component.
- If the results from different types of studies are contradictory, then each design should be carefully examined for confounding factors.
- Normally it is best to start with epidemiological and in vitro studies, to determine the likely type and magnitude of effect, and then design an intervention study based on this data.



## Summary/conclusions

- The 3 types of studies, epidemiological, intervention and in vitro, are all important to investigate effects of food on health.
- Each method is prone to misinterpretation of the results.
- Only human intervention can provide a definitive proof, but it is so expensive that it is unrealistic for all but the simplest dietary constituents.
- The best strategy is to start with methods that allow estimation of many aspects at moderate cost, and then proceed to more definitive specific tests of a few effects.