



Julius Centrum

# Valkuilen methodologie

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*HGOG, Utrecht, Oktober 2016*

## 3 vragen

- Welke innovatieve designs zijn er voor de langdurige zorg?
- Complexe onderwijskundige interventies; hoe zorg je ervoor dat het onderzoek relevante, wetenschappelijk verantwoorde uitkomsten oplevert (spanningsveld tussen de weerbarstige praktijk en wetenschappelijke rigor)
- Hoe blijf je bij een kwalitatieve studie voldoende dicht (qua operationalisatie) bij het fenomeen dat je wil onderzoeken in de uitwerking van de methodologie en keuze van analysetechnieken?





# Relevant research

- Real subjects, patients, students
- Relevant outcomes (for subjects, patients, students)



# Clinical epidemiologic research

- diagnostic research
- etiologic research
- prognostic research
- therapeutic research

**Study design critically depends on clinical problem / challenge**



# Two main types clinical epidemiologic research: causal and descriptive research

## 1. causal research

- aim is to *explain* occurrence of outcome
- aim is causality assessment
- causality implies adjustment for confounders
  
- does the determinant cause the disease?
- does this intervention cause improvement in outcome?
  
- etiologic research
- therapeutic (intervention) research



# Causality: you are in court!

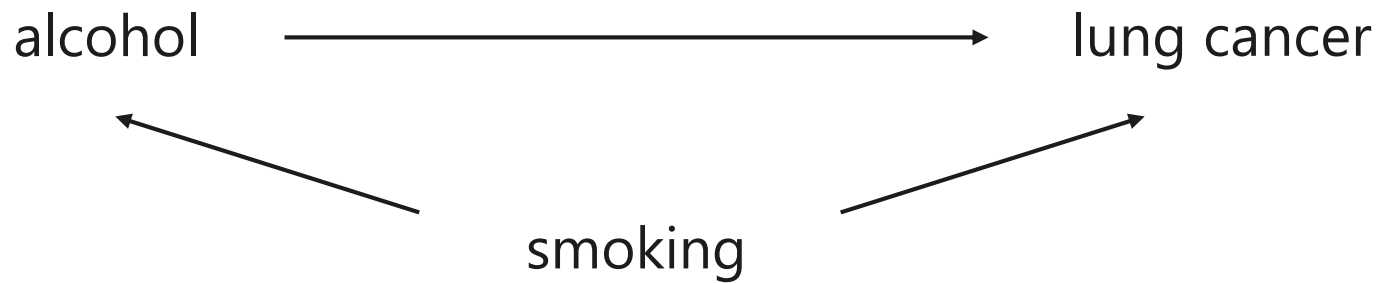


- is the determinant guilty?
- or is the "crime" explained by other factors ?
- convince the reader that the determinant is to "blame"
- exclude extraneous determinants = confounders



# Confounding in causal research

Does alcohol cause lung cancer ?





# Two main types clinical epidemiologic research: causal and descriptive research

## 2. Descriptive research

- aim is to describe occurrence of outcome
- aim it not to explain occurrence outcome
- aim to predict *presence* of disease (diagnosis)
- aim to predict *course* of disease (prognosis)
- causality is no issue (neither is confounding)
- diagnostic research
- prognostic research



If keeping goldfish or male gender predict:

- diagnosis bacterial sinusitis
- prognosis in acute bronchitis



**..why not use these items in daily practice?**



# Experimental study: randomized trial

- paradigm of causal research
- measure effect of intervention
- challenge: measured effect = true effect



# 1948: first published randomised trial

## BRITISH MEDICAL JOURNAL

LONDON SATURDAY OCTOBER 30 1948

### STREPTOMYCIN TREATMENT OF PULMONARY TUBERCULOSIS A MEDICAL RESEARCH COUNCIL INVESTIGATION

The following gives the short-term results of a controlled investigation into the effects of streptomycin on one type of pulmonary tuberculosis. The inquiry was planned and directed by the Streptomycin in Tuberculosis Trials Committee, composed of the following members: Dr. Geoffrey Marshall (chairman), Professor J.W.S. Blacklock, Professor C. Cameron, Professor N.B. Capon, Dr. R. Cruickshank, Professor J.H. Gaddum, Dr. F.R.G. Heaf, Professor A. Bradford Hill, Dr. L.E. Houghton, Dr. J. Clifford Hoyle, Professor H. Raistrick, Dr. J.G. Scadding, Professor W.H. Tytler, Professor G.S. Wislon, and Dr. P. D'Arcy Hart (secretary). The centres at which the work was carried out and the specialists in charge of patients and pathological work were follows:

*Brompton Hospital, London* - Clinician : Dr. J. W. Crofton, Streptomycin Registrar (working under the direction of the honorary staff of Brompton Hospital) ; Pathologists : Dr. J. W. Clegg, Dr. D. A. Mitchison.  
*Colindale Hospital (I.C.C.), London* - Clinicians : Dr. J. V. Hurford, Dr. B. J. Douglas Smith, Dr. W. E. Snell; Pathologists (Central Public Health Laboratory) : Dr. G. E. Forbes, Dr. H. D. Holt.  
*Harefield Hospital (M.C.C.), Harefield, Middlesex* - Clinicians : Dr. R. H. Brent, Dr. L. E. Houghton ; Pathologist : Dr. E. Nassau.

*Bangour Hospital, Bangour, West Lothian* - Clinician : Dr. F. D. Ross; Pathologist: Dr. Isabella Purdie  
*Killingbeck Hospital and Sanatorium, Leeds* - Clinicians : Dr. W. Santon Gilmour, Dr. A. M. Reeve ; Pathologist : Professor J. W. McLeod.  
*Northern Hospital (I.C.C.), Winchmore Hill, London* - Clinicians : Dr. F. A. Nash, Dr. R. Shoulman; Pathologists: Dr. J. M. Alston, Dr. A. Mohun.  
*Sully Hospital, Sully, Glain* - Clinicians : Dr. D.M.E. Thomas, Dr. L. R. West ; Pathologists: Professor W. H. Tytler.

The clinicians of the centres met periodically as a working subcommittee under the chairmanship of Dr. Geoffrey Marshall : so also did the pathologists under the chairmanship of Dr. R. Cruickshank. Dr. Marc Daniels, of the Council's scientific staff, was responsible for the clinical co-ordination of the trials, and he also prepared the report for the Committee, with assistance from Dr. D. A. Mitchison on the analysis of laboratory results. For the purpose of final analysis the radiological findings were assessed by a panel composed of Dr. L. G. Blair, Dr. Peter Kerley, and Dr. Geoffrey S. Todd.



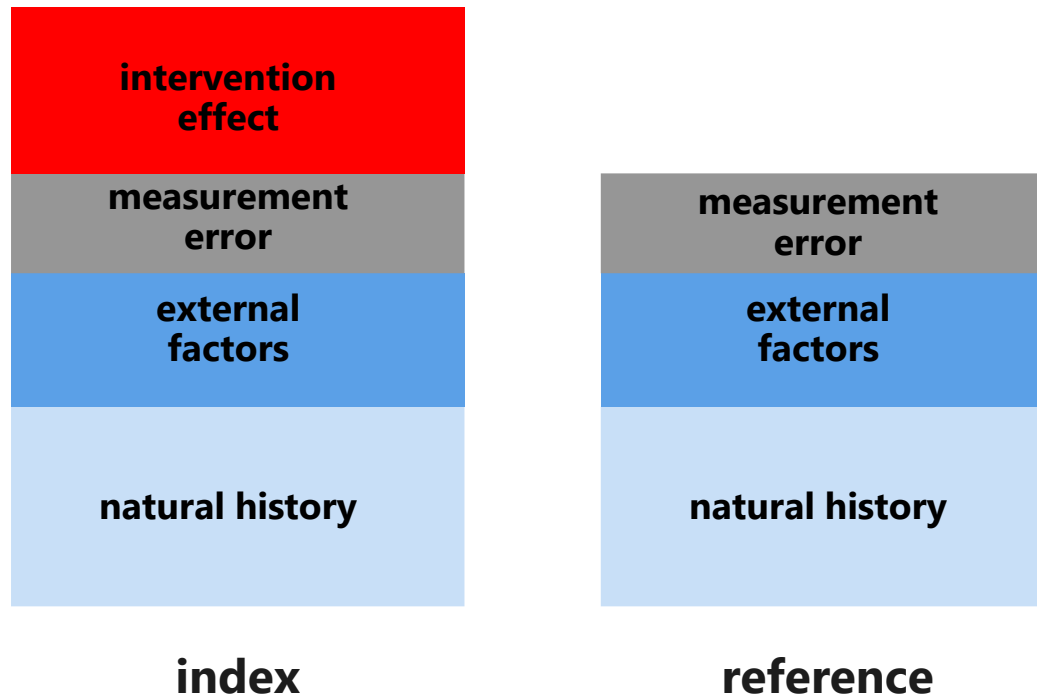
# Tools

1. to control (comparison group)
2. random allocation
3. placebo or sham treatment
4. blinding



# Measuring the true effect of an intervention

observed effect = effect intervention



ensure 3 comparabilities:

(1) natural history, (2) external factors, (3) measurement



# Double-blind placebo-controlled randomized trials

Alternative trials:

- cluster randomized trials
  - often in general practice, teaching
  - stepped-wedge cluster randomized trials
- pragmatic trials
- adaptive trials
  - change in intervention, inclusion criteria, etc?



# Pragmatic trials (vs explanatory trials)

- effect in daily practice
- placebo-effect part intervention (“whole package”)
- comparison 2 strategies
- eg antibiotic (and painkillers) vs only painkillers
  
- no placebo
- usually no blinding
- randomization: yes !!!!!





# Example pragmatic trial

## Aspirin versus anticoagulation

- explanatory:  
double blind, with double dummies; patients on aspirin need also to go to anticoagulation clinic
- pragmatic:  
open (not blind), in accordance with future practice



# Limitations randomized trials

1. many determinants cannot be randomly allocated
  - e.g. smoking, harmful interventions
  - complex interventions (that can change, black box, etc)
2. outcome may be too rare
3. duration exposure may be too short
4. participants not from relevant domain
5. costs

## BRITISH MEDICAL JOURNAL

LONDON SATURDAY SEPTEMBER 30 1950

### SMOKING AND CARCINOMA OF THE LUNG PRELIMINARY REPORT

BY  
RICHARD DOHLE, M.D., M.R.C.P.

Member of the Statistical Research Unit of the Medical Research Council

AND

A. BRADFORD HILL, Ph.D., D.Sc.

Professor of Medical Statistics, London School of Hygiene and Tropical Medicine; Honorary Director of the Statistical Research Unit of the Medical Research Council

In England and Wales the phenomenal increase in the number of deaths attributed to cancer of the lung provides one of the most striking changes in the pattern of mortality recorded by the Registrar-General. For example, in the quarter of a century between 1922 and 1947 the annual number of deaths recorded increased from 612 to 9,287, or roughly fifteenfold. This remarkable increase is, of course, not of all proportions to the increase of population—both in total and, particularly, in its older age groups. Stocks (1947), using standardized death rates to allow for these population changes, shows the following trend: rate

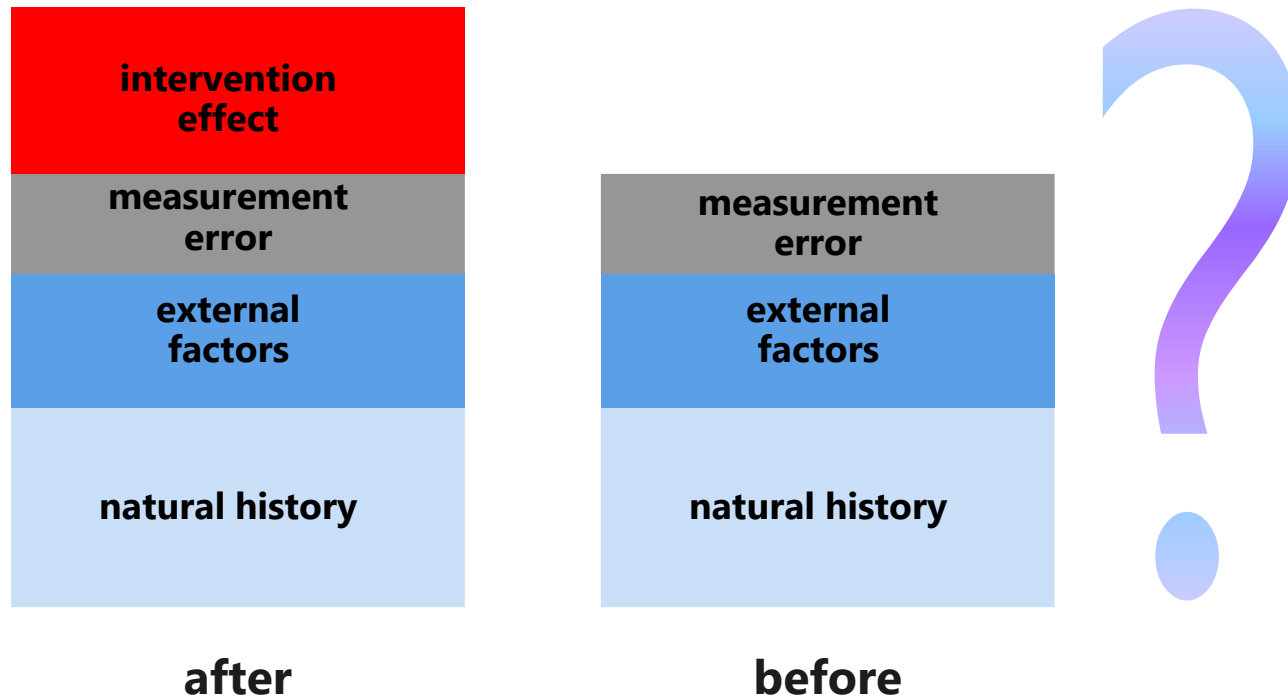
whole explanation, although no one would deny that it may well have been contributory. As a corollary, it is right and proper to look for other causes.

**Possible Causes of the Increase**

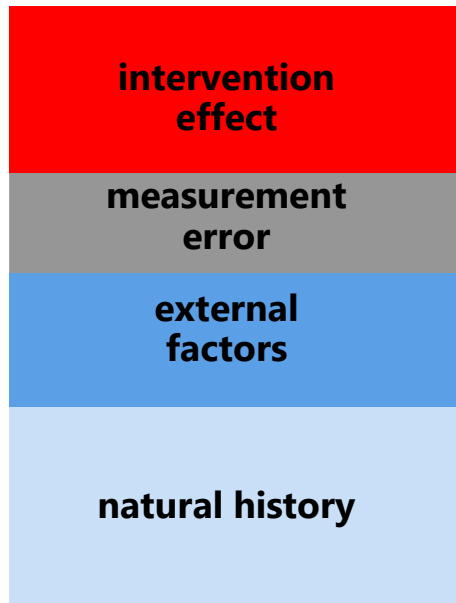
Two main causes have from time to time been put forward: (1) a general atmospheric pollution from the exhaust fumes of cars, from the surface dust of tarred roads, and from gas-works, industrial plants, and coal fires; and (2) the smoking of tobacco. Some characteristics of the former have certainly become more prevalent in the last



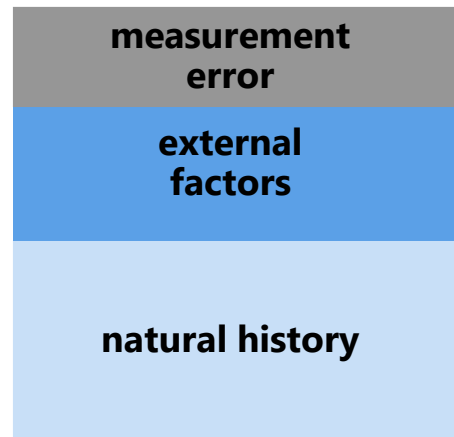
# Alternative experiments: before-after trials



# Alternative experiments: external comparison group



**index**



**comparison**



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