IEA
International Epidemiological Association

Webinar

INSIDE THE SEVENTH EDITION OF THE DICTIONARY OF EPIDEMIOLOGY: THE FUTURE OF EPIDEMIOLOGY

THURSDAY 9 APRIL, 2026 | 3:00 PM CET

The language of epidemiology in science and society.

Introducing the 7th edition
of 'A dictionary of epidemiology'.

Miquel Porta, MD, MPH, PhD
https://linktr.ee/mporta

Hospital del Mar Research Institute
Barcelona

Previous Editions

1. **Last JM (ed.), Abramson JH, Greenland S, Thuriaux MC (assoc. eds.), 1983.**
2. **Last JM (ed.), 1988.**
3. **Last JM (ed.), Abramson JH, Friedman GD, Porta M, Spasoff RA, Thuriaux MC (assoc. eds.), 1995.**
4. **Last JM (ed.), Spasoff RA, Harris SS, Thuriaux MC (assoc. eds.), 2001.**
5. **Porta M (ed.), Greenland S, Last M (assoc. eds.), 2008.**
6. **Porta M (ed.), Greenland S, Hernán M, dos Santos Silva I, Last JM (assoc. eds.), 2014.**

43 years ago

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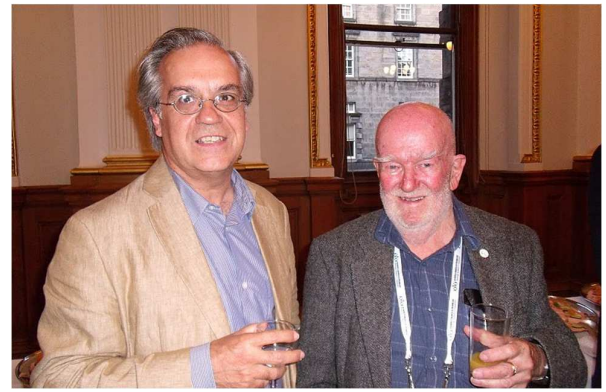
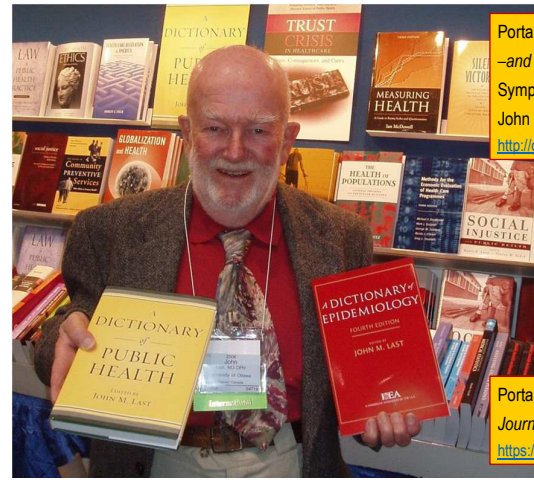
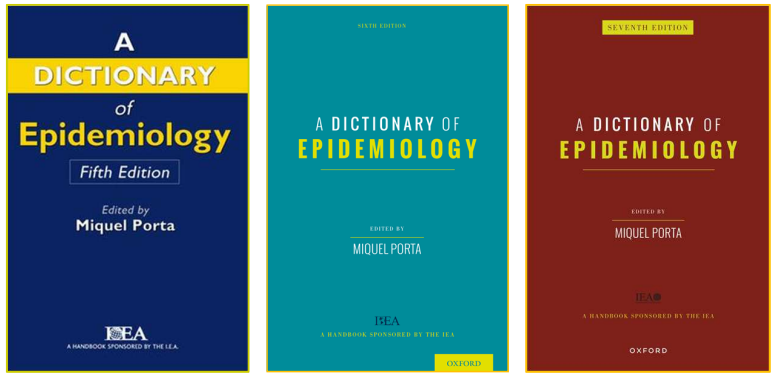


IEA World Congress of Epidemiology, Edinburgh, August 2011



Porta M. *To celebrate the influence of John Last –and the system.* In: Festschrift for John Last. Symposium to celebrate the life and career of Prof. John Last. University of Ottawa, May 19, 2016. http://goo.gl/ujtvaY.

Porta M. Obituary: John Murray Last. *International Journal of Epidemiology* 2020. https://academic.oup.com/ije/article/49/2/703/5802545.



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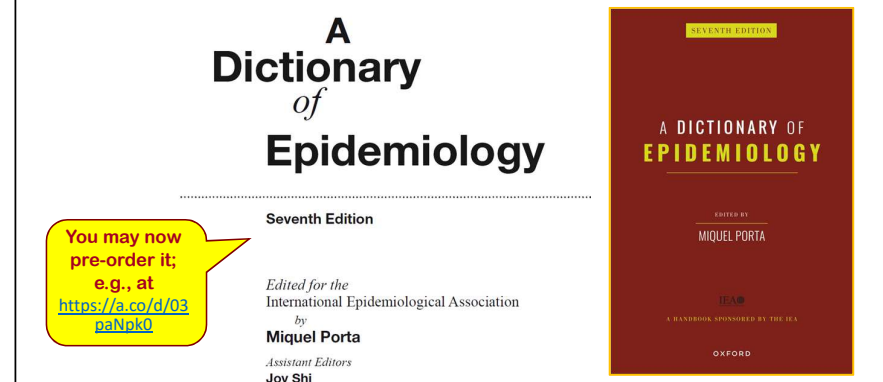

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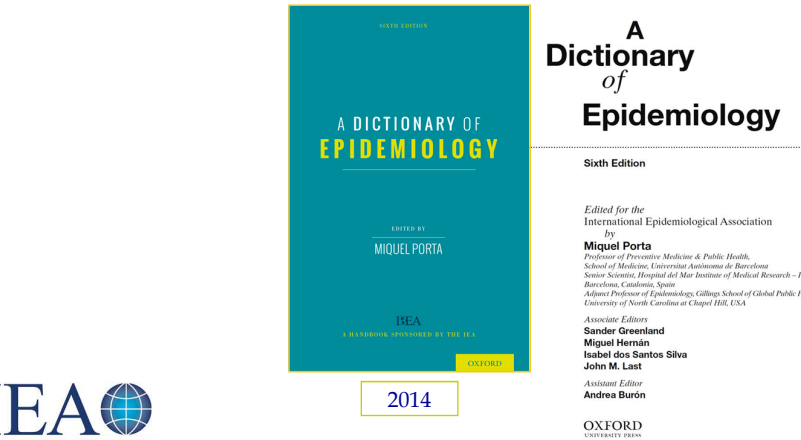

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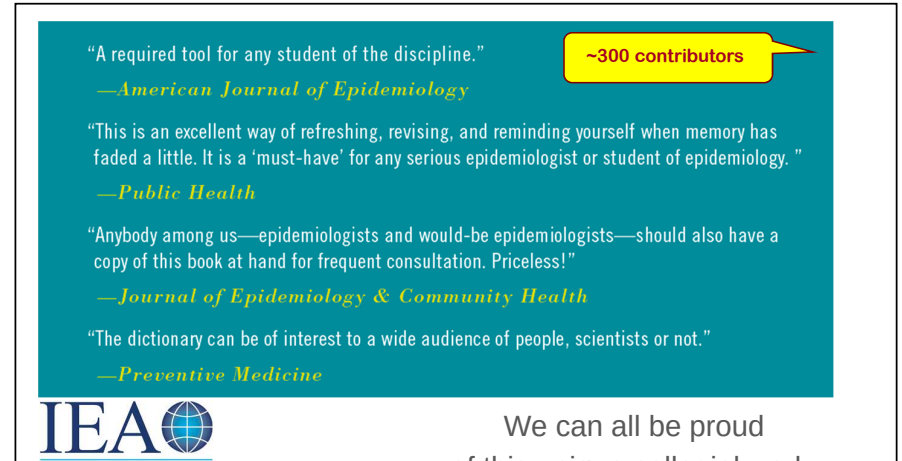

Miquel Porta - IEA Webinar - 9 April 2026
The language of epidemiology in science and society.
Introducing the 7th edition of 'A dictionary of epidemiology'.

Available in print and digital media...

Digital editions have been available since the 5th. edition (2008), and will remain available for the new 7th. (2026): the dictionary also exists as an Ebook, Kindle, Nook book, etc.

The entire 6th & 7th editions will remain available in *Oxford Reference*, which is not only useful for epidemiologists and other health professionals: it also enables thousands of other users of Oxford Reference to access the definitions of the dictionary when searching for terms that our dictionary includes.

Thus, Oxford Reference contributes significantly to **disseminate epidemiological concepts beyond epidemiological networks.**

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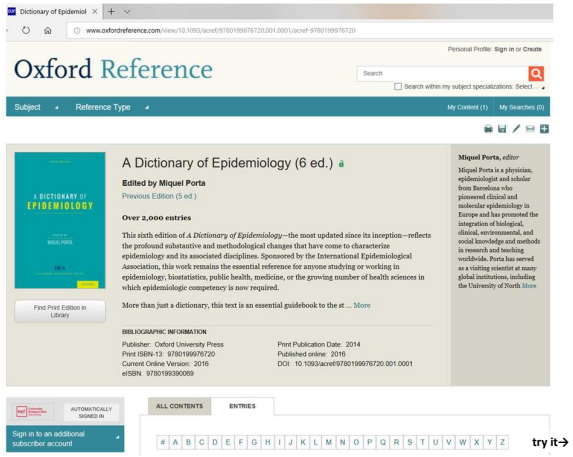

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The vision for the Dictionary

We favor comprehensive, inclusive, and **integrative practices of the science of epidemiology**.

Focused on research and public health policies & services.

Relevant as well for any other activities that influence citizens' health.

> In short, if you live in a "foreign" land and have come to visit this book from "outside" epidemiology, be welcome. If you are an epidemiologist on the eve of a "trip" to a foreign discipline, please take this book with you. And, again, if you mostly work "inside" epidemiology, please keep it at hand: This is your territory—yet I hope you will here discover new landscapes of unsuspected beauty.
>
> Preface (5th., 6th., and 7th. editions).

The present of the IEA Dictionary

- The Dictionary is among the **most valid** and, thus, **trustworthy sources of knowledge on epidemiology, public health**, and related disciplines, worldwide.
- **For epidemiologists and other users of epidemiology in all fields**: academia (research & teaching), public health services, medicine and the other health professions, policy-makers, citizens, institutions, the social networks & media.
- **For students** in most health, social, and biological sciences.

This is also the future.

Miquel Porta - IEA Webinar - 9 April 2026
The language of epidemiology in science and society.
Introducing the 7th edition of 'A dictionary of epidemiology'.

I will not hold back: a dictionary is absolutely necessary and it is a pleasure to hold the new edition and browse through it. Miquel Porta, editor of the fifth and sixth editions, discusses precisely this issue in the preface (very entertaining: recommended reading!) and suggests that '[the dictionary] can be more relevant and useful than ever before because nowadays we suffer from an unprecedented level of air pollution, noise and potential confusion'.

Lorenzo Richiardi

International Journal of Epidemiology, 2015

EPIDEMIOLOGY The study of the occurrence and distribution of health-related events, states, and processes in specified populations, including the study of the DETERMINANTS influencing such processes, and the application of this knowledge to control relevant health problems.

The primary "knowledge object" of epidemiology as a scientific discipline are causes of health-related events, states, and processes in groups and populations. In the past 90 years, the definition has broadened from concern with communicable disease epidemics to include all phenomena related to health in populations.

Therefore, epidemiology is much more than a branch of medicine treating of epidemics.

try it → http://www.oxfordreference.com/view/10.1093/acref/9780199976720.001.0001/acref-9780199976720

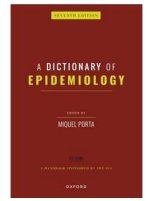
EPIDEMIOLOGY The study of the occurrence and distribution of health-related events, states, and processes in specified populations, including the study of the DETERMINANTS influencing such processes, and the application of this knowledge to control relevant health problems.

Study includes surveillance, observation, screening, hypothesis testing, analytic research, experiments, and prediction. *Distribution* refers to analysis by time, place (or space), and population (i.e., classes or subgroups of persons affected in an organization, population, or society, or at regional and global scales). *Determinants* are the geophysical, biological, behavioral, social, cultural, economic, and political factors that influence health. *Health-related events, states, and processes* include outbreaks, diseases, disorders, causes of death, behaviors, environmental and socioeconomic processes, effects of preventive programs, and use of health and social services. *Specified populations* are those with common contexts and identifiable characteristics. *Application to control*… makes explicit the aim of epidemiology—to promote, protect, and restore health, and to advance scientific knowledge.

APPLIED EPIDEMIOLOGY The application and evaluation of epidemiological knowledge and methods (e.g., in public health or in health care). It includes applications of etiological research, priority setting, and evaluation of health programs, policies, technologies, and services. It is epidemiological practice aimed at protecting and/or improving the health of a defined population. It usually involves identifying and investigating health problems, MONITORING changes in health status, and/or evaluating the outcomes of interventions. It is generally conducted in a time frame determined by the need to protect the health of an exposed population and an administrative context that results in PUBLIC HEALTH action.[28,72]

FIELD EPIDEMIOLOGY The practice of epidemiology in the field—in the community—commonly in a public health service (i.e., a unit of government or a closely allied institution). Field epidemiology is how epidemics and outbreaks are investigated, and it is a tool for implementing measures to protect and improve the health of the public. Field epidemiologists must deal with unexpected, sometimes urgent problems that demand immediate solution. Its methods are designed to answer specific epidemiological questions in order to plan, implement, and/or evaluate public health interventions. These studies must consider the needs of those who will use the results. The task of a field epidemiologist is not complete until results of a study have been clearly communicated in a timely manner to those who need to know and an intervention has been made to improve the health of the people.[28,191] See also APPLIED EPIDEMIOLOGY.

PANDEMICS (OUTBREAKS) END, SENTINEL SURVEILLANCE, PANDEMIC PREPAREDNESS, EXHALED PUFF, LOCKDOWN, WOMEN'S HEALTH, GENDER, GENDER GAP, GENDER BIAS HEALTH CO-BENEFIT, SOCIAL EXPOSOME PLANETARY BOUNDARIES, TRIPLE PLANETARY CRISIS, SYNDEMIC, VIRULENCE, EPIDEMIOLOGIC INTELLIGENCE, 'IN SILICO' STUDY, SYNTHETIC DATA, TRANSMISSION OF INFECTION, AIRBORNE INFECTION, BASIC REPRODUCTIVE NUMBER, SUPERSPREADER, QUANTA EMISSION RATE, DROPLET NUCLEI...



A dictionary of epidemiology. 7th. edition (2026).

I cannot believe that I'm actually enjoying reading formulas, examining charts and graphics, and perusing exact definitions. The clarity and depth of them all are truly striking. Do not miss the definition of the epidemiologist, which includes the observation that "epidemiologists show a rich plurality of scientific cultures and practices" (p. 95). Perhaps my favorite, though, is the insight into public health today: "Like most sculptures, symphonies, and other works of art, certain important things in life have several dimensions. The definition of public health has four dimensions."

Not all symphonies are created equal. But this particular one brings magnificent music for any rainy day.

by Hugh H. Tilson

2014 American Journal of Preventive Medicine

PUBLIC HEALTH Like most sculptures, symphonies, and other works of art, certain important things in life have several dimensions. The definition of public health has four dimensions. Public health is:

1. The health of a whole society. It can be measured and assessed through quantitative and qualitative indicators and analytic processes.
2. The specific policies, services, programs and other essential efforts agreed (ideally, and often, democratically), organized, structured, financed, monitored, and evaluated by society to collectively protect, promote, and restore the people's health and its determinants.
3. The institutions, public and private organizations—including private and public companies—, and other citizens organizations, that plan, develop, fund, and implement such efforts, and which are thus an integral part of local, national, regional, and global public health systems.
4. The scientific disciplines and professions, knowledge, methods, art, and craft essential to positively influence HEALTH DETERMINANTS, and thus prevent disease and disability, prolong life, and promote HEALTH through the organized and collective efforts of society.

A dictionary of epidemiology. 6th. edition (2014).

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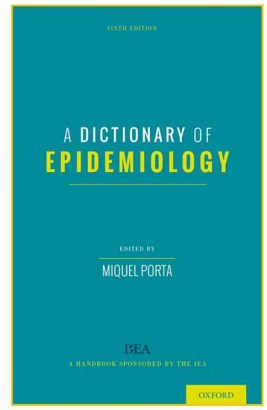
actions of public health + and ⬬
during the COVID-19 pandemic made it clear, massively.

Public health takes care daily of what we breathe, drink, and eat, how we work, move, and live together. Economic, environmental, social, educational, occupational, medical, and other policies intertwined with public health change with changing social values and networks, policies and technologies; yet, the goals—diverse as they are in democratic societies—remain the same: to reduce the amount of health-related suffering, disease, disability, and premature death in the population. Public health is a SYSTEM of professions and scientific disciplines, social organizations and institutions, values, and actions.

epidemiology & public health are
existing realities,
partly (in)visible;
and a diverse set of proposals
(scientific, ethical, cultural,
political, civic).

RISK FACTOR (Syn: determinant) A factor that is causally related with a change in the RISK of a relevant health process, outcome or condition. The causal nature of the relationship is established on the basis of scientific evidence (including, naturally, evidence from EPIDEMIOLOGICAL RESEARCH) and CAUSAL INFERENCE. The causal relationship is inherently probabilistic, as it happens in many other spheres of nature and human life.[101] Examples of types of risk factors are offered throughout this book; they may be a socioeconomic characteristic, personal behavior or lifestyle, environmental exposure, inherited characteristic or another TRAIT. Risk factors for human health often have individual and social components; even when individual and social risk factors can be separated, they often interact.

To prevent MEDICALIZATION of life and IATROGENESIS, the RELEVANCE and SIGNIFICANCE of the factor-outcome risk relationship must be cautiously assessed; so must uncertainties and ambiguities in risk-related concepts, as well as different legitimate meanings of risk across and within cultures.[1,2,3,5,6,9,13,29,33,38,42,56,58,91,106-108,113,158,215,248,270,279,292,303,304,332-336,350,361,426,539,600,603,712-718]



OBSERVATIONAL STUDY (Syn: nonexperimental study) A study that does not involve any intervention (experimental or otherwise) on the part of the investigator.[1-3,6,9,25,26,39-42,197,239,269,270,272,795] A study with RANDOM ALLOCATION of treatments or other exposures is inherently experimental or nonobservational. Observations are not just a haphazard collection of facts; in their own way, observational studies must apply the same rigor as experiments, and vice versa.[201,276] Many important preclinical, clinical, and epidemiological studies (and studies in other branches of science) are completely observational or have strong observational components.[101] Dismissive attitudes toward observational research have a weak scientific basis. In the health, life, and social sciences—and in other sciences as well—there has long been a fruitful dialectic tension between observation and experiment; facts and reasons; actions, explanations, mechanisms.[1,3,6,9,26,38-42,64,83,101,201-203,639-641,798,800] Often, observational and experimental studies on the apparently same issue actually answer *different questions*; for example, a randomized clinical trial will compare women allocated to hormone replacement therapy (HRT) and women allocated to another therapy or a placebo, and perform an INTENTION-TO-TREAT ANALYSIS, whereas an observational study will compare rather different women (than those included in a RCT) who were actually exposed to HRT and women exposed to other therapies or none; characteristics of subjects, context, exposures, timing, confounders, and interactions are just six of the many reasons that usually make different designs answer different questions. Also, different designs have different strengths and weaknesses to help make decisions and CAUSAL INFERENCES. Some observational studies may be analyzed as experiments; and some experiments, as observational studies.[2,641,800] See also CASE REPORTS; CLINICAL STUDY.

Observational Studies Analysed Like Randomised Experiments

The ongoing methodological revolution?

Randomised Experiments Analysed Like Observational Studies

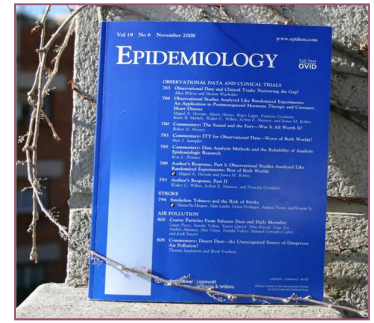
Sessions d'Epidemiologia
& Salut Pública

IMIM, 27 January 2009

Miquel Porta

IMIM hospitaldelmar

UAB Universitat Autònoma de Barcelona



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EXPERIMENTAL STUDY A study in which the investigator intentionally alters one or more factors and controls the other study conditions in order to analyze the effects of so doing. A study in which conditions are under the direct control of the investigator.[7,101]

INTENTION-TO-TREAT ANALYSIS (ITT) A fundamental way to analyze a RANDOMIZED CONTROLLED TRIAL in which all subjects allocated to each arm of the trial are analyzed "as intended" upon randomization, whether or not they actually received the exposure allocated or completed treatment.[1,2,24,272,443-445,641,800] Failure to follow this approach defeats the main purpose and advantage of RANDOM ALLOCATION and can cause serious CONFOUNDING BIAS. This approach is virtually always required as part of the primary analysis of studies aiming to influence clinical or public-health decisions and policy formulation. It may be complemented by an explanatory analysis, in which subjects are analyzed according to the exposure they actually experienced (with adjustment for possible confounders, i.e., with an analytic approach similar to an observational cohort study), or in which some participants (e.g., subjects who complied poorly with the protocol) are excluded from analyses.[1,6,9,26,58,101,270,272,641,800] An intention-to-treat analysis does not determine whether and how to impute missing data on the outcome measure. Because of its pragmatic nature, ITT can underestimate treatment efficacy or have a low explanatory capacity

A dictionary of epidemiology. 6th. edition (2014).
→ http://www.oxfordreference.com/view/10.1093/acref/9780199976720.001.0001/acref-9780199976720

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KEY CONCEPTS IN CLINICAL EPIDEMIOLOGY

Intention to treat and per protocol analyses: differences and similarities

Javier Molero-Calafell[a,b,c], Andrea Burón[a,b,d,e,*], Xavier Castells[a,b,e,f], Miquel Porta[b,f,g,h,i,**]

Adherence is unlikely to occur completely at random: participants who adhere and do not adhere to the protocol often have different prognostic factors. This presents a challenge for PP analysis because once nonadherents are excluded, the groups being compared are often no longer similar as they were just after randomization: the precious value of randomization is thus lost, and the crude, unadjusted comparison of treatment effects across groups may be highly biased. In other words, when prerandomization factors are no longer balanced between groups, confounding is likely and must be controlled [14]. Moreover, adherence to the protocol during follow-up is often influenced by clinical and social factors that operate after randomization.

With low internal validity, the results cannot be of practical use. As for observational studies, the validity of many PP analyses depends on how much we can control confounding with the available data, as suggested by knowledge on the study matter. To avoid residual confounding, data must be of high quality and comprehensive (eg, valid and relevant data on lifestyle and life conditions are required). In summary, a PP analysis of a randomized trial is an analysis of what actually has become an observational study, because we are comparing groups that differ from the groups that resulted from randomization.

- Both randomized studies and observational studies often contribute to knowledge.
- Properly designed observational studies may allow to make valid causal inferences.

Journal of Clinical Epidemiology 173 (2024)

PREVENTION Actions that prevent disease occurrence. Actions aimed at eradicating, eliminating, or minimizing the impact of disease and disability, or if none of these is feasible, retarding the progress of disease and disability.
The concept is best defined in the context of *levels* of prevention, traditionally called primary, secondary, and tertiary prevention.[24] Other levels (primordial prevention, quaternary prevention) are also used. There is significant conceptual and practical overlapping among levels—largely, depending on the type of disease (e.g., on the NATURAL HISTORY OF THE DISEASE). Effective prevention STRATEGIES often interact and operate across levels.

PRIMARY PREVENTION aims to reduce the incidence of disease by personal and communal efforts, such as decreasing environmental risks, enhancing nutritional status, immunizing against communicable diseases, or improving water supplies.[3,5,13,24,28,67,84,121,211,214,366,426] It is a core task of PUBLIC HEALTH, including HEALTH PROMOTION. See also COSTS OF INACTION.

A DICTIONARY OF EPIDEMIOLOGY

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SECONDARY PREVENTION aims to reduce the prevalence of disease by shortening its duration. If the disease has no cure, it may increase survival and QUALITY OF LIFE; it will also increase the prevalence of the disease. It seldom prevents disease occurrence; it does so only when EARLY DETECTION of a precursor lesion leads to complete removal of all such lesions. It is a set of measures available to individuals and communities for the early detection and prompt intervention to control disease and minimize disability; e.g., by the use of SCREENING programs. It is a core task of PREVENTIVE MEDICINE. Both EARLY CLINICAL DETECTION and population-based SCREENING usually aim at achieving secondary prevention. in certain diseases, these activities may also contribute to tertiary prevention.[5]

TERTIARY PREVENTION: measures aimed at softening the impact of long-term disease and disability by eliminating or reducing impairment, disability, and handicap; minimizing suffering; and maximizing potential years or useful life. It is mainly a task of rehabilitation.

A DICTIONARY OF EPIDEMIOLOGY

QUATERNARY PREVENTION: procedures and policies that identify individuals and groups at risk of overdiagnosis or overmedication, and that decrease excessive medical and sanitary intervention.[679] Actions that prevent IATROGENESIS and "DISEASE MONGERING."

MEDICALIZATION The process by which conditions, processes, or emotional states traditionally considered nonmedical are redefined and treated as medical issues. The process of identification and labeling of a personal or social condition as a medical issue subject to medical intervention. The expansion of the influence and authority of the health professions and industries into the domains of everyday existence.[248,292,323,337,338,363,364,470,482,600] See also GENETIZATION; INTEGRATION; REDUCTIONISM.

A DICTIONARY OF EPIDEMIOLOGY

The current deconstruction of paradoxes: one sign of the ongoing methodological "revolution"

Eur J Epidemiol (2015)

Miquel Porta[1,2,3] · Paolo Vineis[4,5] · Francisco Bolúmar[3,6,7]

Collider, immortal time, time zero, backdoor biasing path, collapsibility, target trial, treatment-confounder feedback, M-bias, censoring, causal structure, residual confounding...

https://pubmed.ncbi.nlm.nih.gov/26164615/

http://blog.oup.com/2014/10/deconstruction-paradoxes-sociology-epidemiology/

https://www.oxfordreference.com/page/medicineandhealth/medicine-and-health#Featured-author

→ **plus:** sustained & dynamic treatment strategies, time-varying and time-fixed treatments & confounders; lagged effects, survival outcome, identification assumptions, competing risk...

Collider, immortal time, time zero, backdoor biasing path, collapsibility, target trial, treatment-confounder feedback, M-bias, censoring, causal structure, residual confounding...

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Collider, immortal time, time zero, backdoor biasing path, collapsibility, target trial, treatment-confounder feedback, M-bias, censoring, causal structure, residual confounding...

When we really aim at making causal inferences valid and relevant for human health; e.g., to assess clinical effectiveness or population impact.

when data, technology or methods in themselves are just means, not ends.

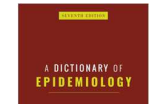
→ **plus:** sustained & dynamic treatment strategies, time-varying and time-fixed treatments & confounders; lagged effects, survival outcome, identification assumptions, competing risk...

Collider, immortal time, time zero, backdoor biasing path, collapsibility, target trial, treatment-confounder feedback, M-bias, censoring, causal structure, residual confounding...

→ **plus old terms** ~~with new definitions~~ **redefined:**
intention-to-treat (ITT) ↔ per-protocol (PP) analyses...
generalizability ↔ transportability ↔ external validity ↔
↔ representativeness... observational ↔ experimental

+ data, data science, real world, 'in silico' study, synthetic data...

When we aim at making causal inferences valid and relevant for human health.



DATA A set of items of information amenable to analysis. A data set or a DATABASE containing valid (unbiased) data is an essential part of a clinical or epidemiological study, but does not constitute in itself a STUDY, and it does not automatically, nor easily yield knowledge. In medicine, epidemiology and the other health sciences, data from a research study do not speak by themselves: data may lead to reasonably unbiased information, and to knowledge of RELEVANCE for human health, if study design, data collection and analysis have been carefully conceived, performed, and interpreted. Thinking.[1-4,9,20,39,40,56,102-106,121,124]

In medicine, epidemiology, public health... economy... (...) data do not speak by themselves. Data do not tell us what is a valid and relevant human effect.

Principles that have not changed, and upon which so much is being built.

A valid and relevant study in humans requires:

→ In-depth knowledge on the pathophysiology of the disease, and on its "natural" history in the specific society & health system.

→ An appropriate design, quantitative analysis (e.g., to prevent selection bias, info bias, confounding) (to properly test the relevant question), and interpretation.

→ Valid data (e.g., to minimize residual confounding and other biases).

REAL WORLD The actual social and clinical contexts where the EFFECTIVENESS of policies, interventions and other types of exposures, and diagnostic or therapeutic procedures is assessed, outside the often highly unusual laboratory and hospital facilities where individuals are treated or exposed in ways that otherwise they will rarely or never encounter in their lives. Much knowledge on the causes of diseases and other health states stems as well from studies conducted under real conditions of health care, in non-institutionalized groups, and in the GENERAL POPULATION. Medicine and epidemiology, in particular, have long studied what happens to individuals and populations in the real world.[274] Today the fundamental differences and relationships between EFFECTIVENESS and EFFICACY remain of deep RELEVANCE to science, to millions of individuals, and to virtually all populations, daily, worldwide.[269,271-273,309]

See also CLINICAL STUDY; EPIDEMIOLOGICAL RESEARCH; VALIDITY; and the many terms that in this dictionary include the noun STUDY; in addition, a dozen definitions include the expression REAL WORLD.

REAL WORLD DATA Data collected from real individuals and populations living in the REAL WORLD, under usual conditions of life and health care, by contrast with conditions habitual in laboratory, research-intensive or academic settings where, for instance, the EFFICACY of procedures is initially assessed, or where other fundamental issues concerning pathophysiology, mechanisms, CAUSALITY and other issues are first tested. Real-world DATA can be collected specifically for a newly conceived STUDY (observational or experimental), or originate from data collected routinely from a large variety of administrative or other registries and DATABASES. There are no scientific reasons why the VALIDITY of analyses of real world data should be lower than that of other studies, including other types of PRAGMATIC STUDIES.[271-274,309]

Estimating the Effect of Preventive Services With Databases of Administrative Claims: Reasons to Be Concerned

Am J Epidemiol. 2019

Xabier García-Albéniz*, John Hsu, Michael Bretthauer, and Miguel A. Hernán

A key concern in claims-based emulation of trials of preventive interventions is unmeasured confounding.

Observational estimates from the randomized trials also found intractable confounding when comparing adherers to screening sigmoidoscopy with nonadherers—adherers had an implausibly lower mortality risk (15)—because data on potentially crucial confounders (e.g., behaviors related to health-consciousness, like exercise, weight control, smoking) were not available and therefore those confounders could not be adjusted for.

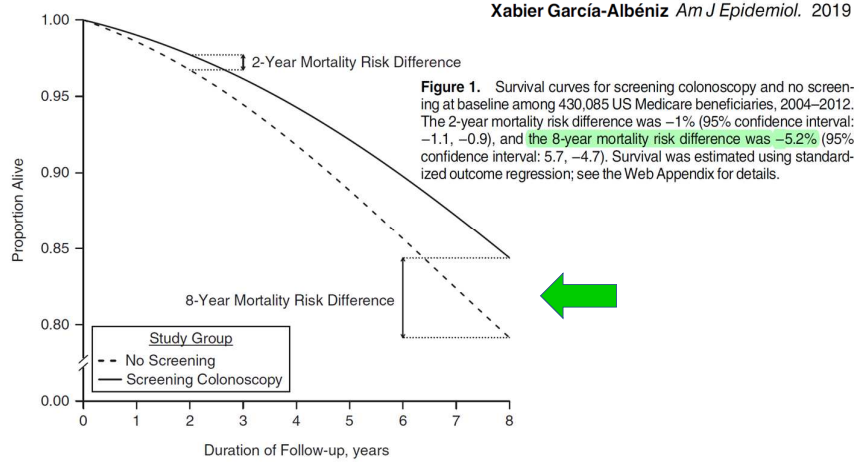


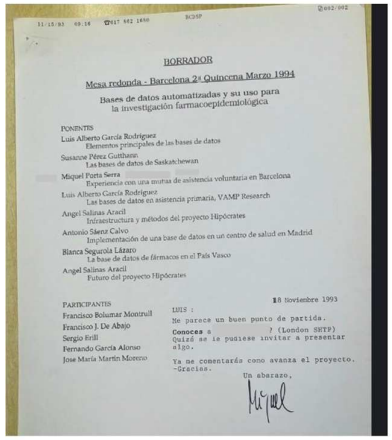
Figure 1. Survival curves for screening colonoscopy and no screening at baseline among 430,085 US Medicare beneficiaries, 2004–2012. The 2-year mortality risk difference was −1% (95% confidence interval: −1.1, −0.9), and the 8-year mortality risk difference was −5.2% (95% confidence interval: 5.7, −4.7). Survival was estimated using standardized outcome regression; see the Web Appendix for details.

https://ieaweb.org/ - 9 April 2026

a reduction of 5 percentage points in the 8-year mortality risk, reflects an implausibly large benefit because of the low proportion of deaths due to colorectal cancer. A more likely interpretation is that the estimates are severely confounded. The validity of this interpretation is strengthened by the substantially lower risk in the screening group after only 2 years of follow-up, which again represents an implausibly large benefit.

Observational estimates from the randomized trials also found intractable confounding when comparing adherers to screening sigmoidoscopy with nonadherers—adherers had an implausibly lower mortality risk (15)—because data on potentially crucial confounders (e.g., behaviors related to health-consciousness, like exercise, weight control, smoking) were not available and therefore those confounders could not be adjusted for.

In summary, no matter what approach we used to select and adjust for confounders, we could not successfully estimate the effect of a preventive service on mortality using administrative data. The expectation that currently available automated, data-driven procedures may significantly improve upon expert knowledge may not be realized for many health-care databases. Previously, a study on nonsteroidal antiinflammatory drugs versus cyclooxygenase 2 inhibitors and upper gastrointestinal bleeding had also shown that methods like the high-dimensional propensity score could not improve upon expert selection of confounders (16).



BORRADOR

Mesa redonda - Barcelona 2ª Quincena Marzo 1994

Bases de datos automatizadas y su uso para la investigación farmacoepidemiológica

PONENTES

Luis Alberto García Rodríguez
Elementos principales de las bases de datos

Susanne Pérez Gutthann
Las bases de datos de Saskatchewan

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Experiencia con una mutua de asistencia voluntaria en Barcelona

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Las bases de datos en asistencia primaria, VAMP Research

Angel Salinas Aracil
Infraestructura y métodos del proyecto Hipócrates

Antonio Sáenz Calvo
Implementación de una base de datos en un centro de salud en Madrid

Bianca Segarola Lázaro
La base de datos de fármacos en el País Vasco

Angel Salinas Aracil
Futuro del proyecto Hipócrates

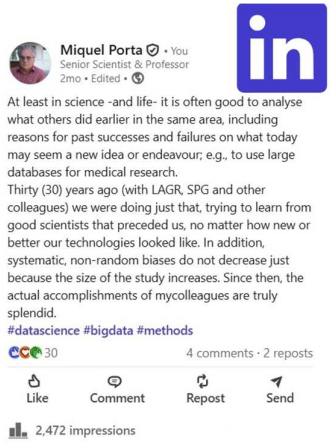
PARTICIPANTES

Francisco Bolumar Montrull
Francisco J. De Abajo
Sergio Brill
Fernando García Alonso
José María Martín Moreno

LUIS :
Me parece un buen punto de partida.
Conoces a ? (London SHTP)
Quizá se le pudiese invitar a presentar algo.
Ya me comentarás como avanza el proyecto.
~Gracias.

Un abrazo,

18 noviembre 1993



Miquel Porta • You
Senior Scientist & Professor
2mo • Edited •

At least in science -and life- it is often good to analyse what others did earlier in the same area, including reasons for past successes and failures on what today may seem a new idea or endeavour; e.g., to use large databases for medical research.
Thirty (30) years ago (with LAGR, SPG and other colleagues) we were doing just that, trying to learn from good scientists that preceded us, no matter how new or better our technologies looked like. In addition, systematic, non-random biases do not decrease just because the size of the study increases. Since then, the actual accomplishments of mycolleagues are truly splendid.
#datascience #bigdata #methods

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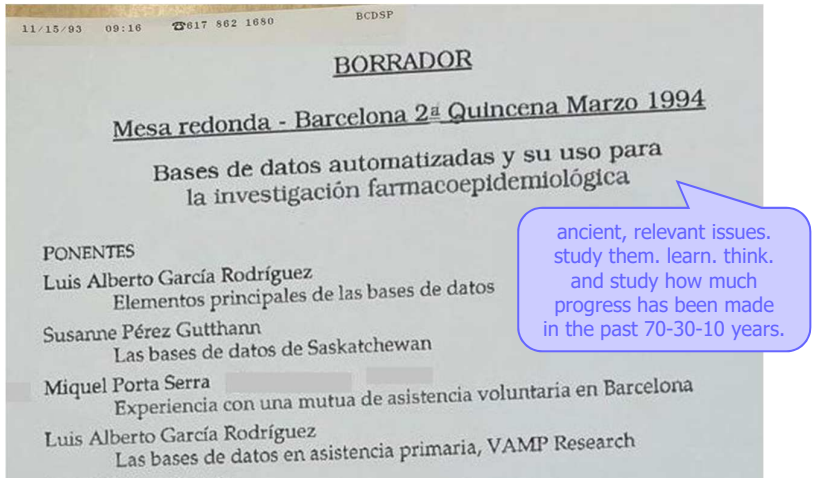

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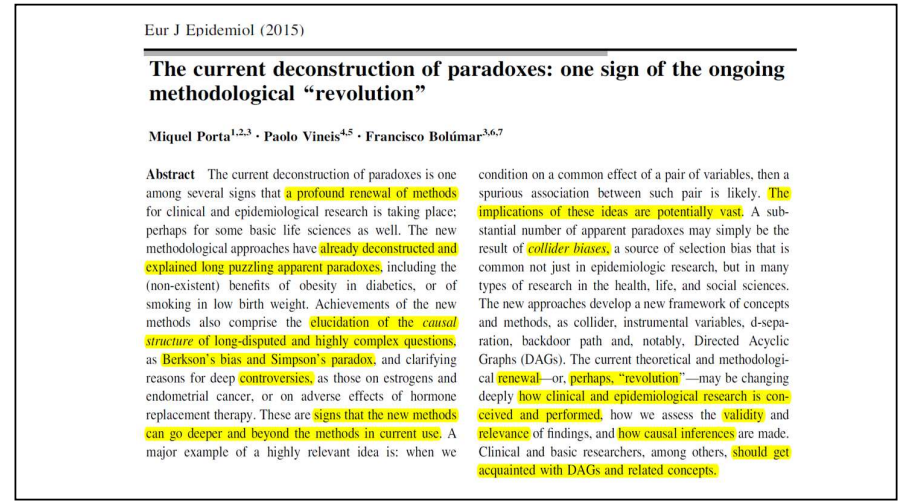
ancient, relevant issues. study them. learn. think. and study how much progress has been made in the past 70-30-10 years.

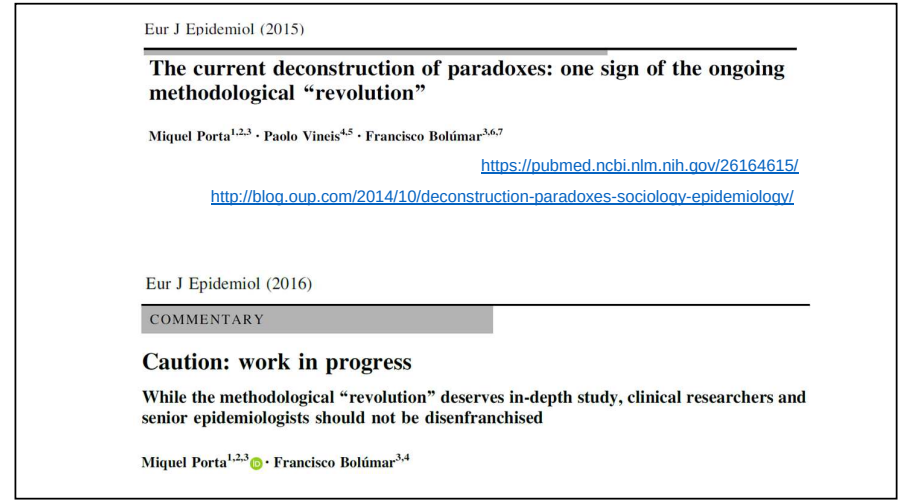


Eur J Epidemiol (2015)

The current deconstruction of paradoxes: one sign of the ongoing methodological "revolution"

Miquel Porta[1,2,3] · Paolo Vineis[4,5] · Francisco Bolúmar[3,6,7]

Abstract The current deconstruction of paradoxes is one among several signs that a profound renewal of methods for clinical and epidemiological research is taking place; perhaps for some basic life sciences as well. The new methodological approaches have already deconstructed and explained long puzzling apparent paradoxes, including the (non-existent) benefits of obesity in diabetics, or of smoking in low birth weight. Achievements of the new methods also comprise the elucidation of the *causal structure* of long-disputed and highly complex questions, as Berkson's bias and Simpson's paradox, and clarifying reasons for deep controversies, as those on estrogens and endometrial cancer, or on adverse effects of hormone replacement therapy. These are signs that the new methods can go deeper and beyond the methods in current use. A major example of a highly relevant idea is: when we condition on a common effect of a pair of variables, then a spurious association between such pair is likely. The implications of these ideas are potentially vast. A substantial number of apparent paradoxes may simply be the result of *collider biases*, a source of selection bias that is common not just in epidemiologic research, but in many types of research in the health, life, and social sciences. The new approaches develop a new framework of concepts and methods, as collider, instrumental variables, d-separation, backdoor path and, notably, Directed Acyclic Graphs (DAGs). The current theoretical and methodological renewal—or, perhaps, "revolution"—may be changing deeply how clinical and epidemiological research is conceived and performed, how we assess the validity and relevance of findings, and how causal inferences are made. Clinical and basic researchers, among others, should get acquainted with DAGs and related concepts.



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https://pubmed.ncbi.nlm.nih.gov/26164615/

http://blog.oup.com/2014/10/deconstruction-paradoxes-sociology-epidemiology/

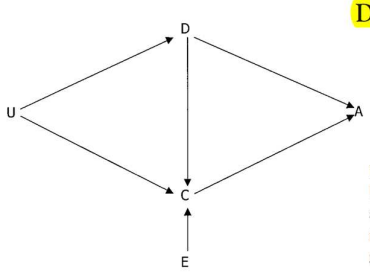
Eur J Epidemiol (2016)

COMMENTARY

Caution: work in progress

While the methodological "revolution" deserves in-depth study, clinical researchers and senior epidemiologists should not be disenfranchised

Miquel Porta[1,2,3] · Francisco Bolúmar[3,4]



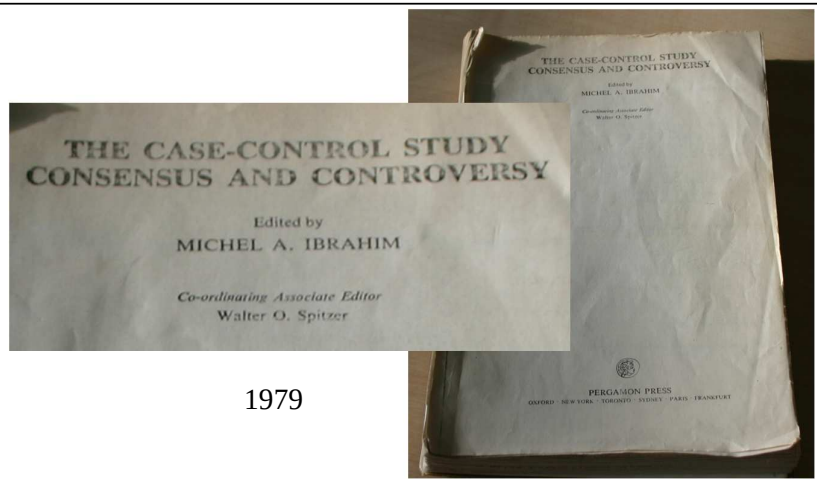
Data, Design, and Background Knowledge in Etiologic Inference

James M. Robins

I use two examples to demonstrate that an appropriate etiologic analysis of an epidemiologic study depends as much on study design and background subject-matter knowledge as on the data. The demonstration is facilitated by the use of causal graphs. (Epidemiology 2001;11:313–320)

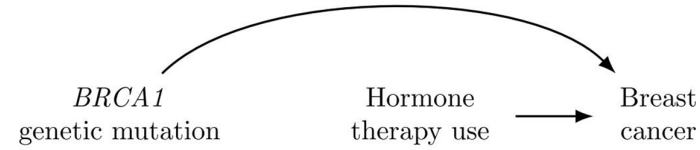
DAG for Thought Experiment 2. D = endometrial cancer; A = ascertained endometrial cancer; C = vaginal bleeding; E = exogenous estrogens; U = an unmeasured common cause of D and C.

- Several such controversies (among highly intelligent scientists) have been clarified and overcome by the new methods (Robins, Hernán, VanderWeele, Dahabreh, Dickerman...).



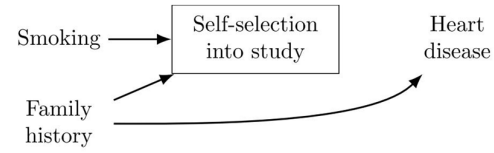
1979

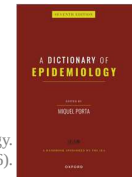
Causal diagram representing breast cancer as a common effect of *BRCA1* genetic mutation and hormone therapy use. An analysis restricted to individuals with breast cancer will induce a noncausal inverse association between a *BRCA1* genetic mutation and hormone therapy use, because individuals with breast cancer who lack a *BRCA1* genetic mutation are more likely to have another cause of breast cancer (such as hormone therapy use) present.



A dictionary of epidemiology. 7th. edition (2026).

Causal diagram representing selection bias arising from self-selection into a study. The relationship between smoking and heart disease will be biased if study participation is affected by an exposure (smoking) and a cause of the outcome (family history of heart disease).





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when we aim at making causal inferences valid & relevant for human health

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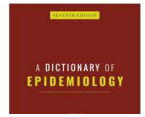
In medicine and public health data do not speak by themselves.
Data do not tell us what is a valid and relevant human effect.
A valid and relevant study in humans requires:

principles that have not changed.

→ In-depth knowledge on the pathophysiology of the disease, and on its course in the specific society & health system.
→ An appropriate design, quantitative analysis (e.g., to prevent selection bias, info bias, confounding) (to properly test the relevant question), and interpretation.
→ Valid data (e.g., to minimize residual confounding).

when we aim at making causal inferences valid & relevant for human health



DATA A set of items of information amenable to analysis. A data set or a DATABASE containing valid (unbiased) data is an essential part of a clinical or epidemiological study, but does not constitute in itself a STUDY, and it does not automatically, nor easily yield knowledge. In medicine, epidemiology and the other health sciences, data from a research study do not speak by themselves: data may lead to reasonably unbiased information, and to knowledge of RELEVANCE for human health, if study design, data collection and analysis have been carefully conceived, performed, and interpreted. Thinking.[1-4,9,20,39,40,56,102-106,121,124]

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the design, conduct, analysis, and interpretation of studies must be based on the following[90]:

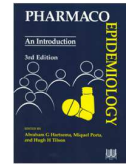
1. a *causal model hypothesis*, which includes knowledge of the basic and clinical pharmacology of the drug and of the molecular biology, pathophysiology, and clinical course of the disease; and
2. a *healthcare pathway hypothesis*, which in turn includes knowledge of patient behavior, referral patterns, actual diagnostic and therapeutic strategies, as well as other aspects of the functioning of the health system relevant to the assessment of potential selection and information biases.

most important: integrate subject-matter knowledge and methodological knowledge.

when we aim at making causal inferences valid & relevant for human health

Med Clin (Barc) 1990; 94: 107-115

1 **The Contribution of Epidemiology to the Study of Drug Uses and Effects**
Miquel Porta
Abraham G Hartzema
Hugh H Tilson



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it is always necessary to integrate subject-matter knowledge and methodological knowledge.

valid & relevant methodological decisions cannot + must not be taken in a vacuum (without) of expert knowledge.

when we aim at making causal inferences valid & relevant for human health

- In public health and medicine, there is no high-quality research (valid and relevant) without valid methods, valid data, and expert knowledge on the subject matter.
- Data do not speak for themselves.
- Studies that are well-designed, executed, analyzed, and interpreted (meaning those reasonably free from selection, information, and confounding biases) do reflect modest fragments of knowledge.
- Systematic errors or biases do not decrease by increasing the number of participants.
- The internal validity of a study does not improve simply by increasing the sample size.

it is always necessary to integrate subject-matter knowledge and methodological knowledge.

when we aim at making causal inferences valid & relevant for human health

valid & relevant methodological decisions cannot + must not be taken in a vacuum (without) of expert knowledge.

when we really aim at making causal inferences valid & relevant for human health; e.g., to assess clinical effectiveness or population impact.

when data, technology or methods in themselves are just means, not ends.

when we really care about human health these are concepts / frameworks that we must know and apply.

how much do I know?

how much do I care?

... somehow, I must care.

one of the top 10+
contemporary terms / concepts...

COLLIDER A variable directly affected by two or more other variables ("parents" of the variable) in the CAUSAL DIAGRAM;[1,2,34,100,101,209,242,243] e.g., a variable that is the common effect of an exposure and an outcome. In the following "inverted fork" X → C ← Y the arrow represents a direct effect of the tail variable on the head variable; C is then a collider on the X-C-Y pathway in the graph. Conditioning on a collider (i.e., controlling for the collider through stratification, restriction, or adjustment) will tend to induce a noncausal association (often referred to as *collider bias*) between the parent variables (i.e., the shared direct causes) of the collider.

COLLIDER BIAS See COLLIDER.

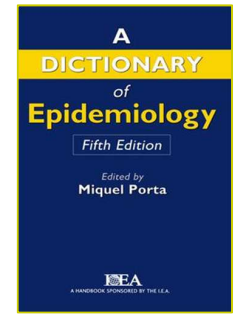
Source: A dictionary of epidemiology. 6th. edition (2014). The definition was already present in the edition of 2008, 17 years ago.

DAG (DIRECTED ACYCLIC GRAPH) See CAUSAL DIAGRAM.

These are truly basic (and not new) methodological terms:

COLLIDER
M-BIAS
BACK-DOOR PATH
CAUSAL DIAGRAM
COLLAPSIBILITY
OVERADJUSTMENT
Simpson's paradox***
Berkson's bias* . . .**

***For some terms, definitions have changed.
Even for RATE, for RISK FACTOR...

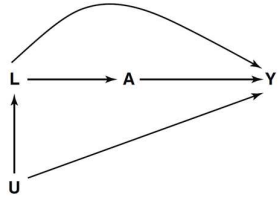


2008

try it → http://www.oxfordreference.com/view/10.1093/acref/9780199976720.001.0001/acref-9780199976720

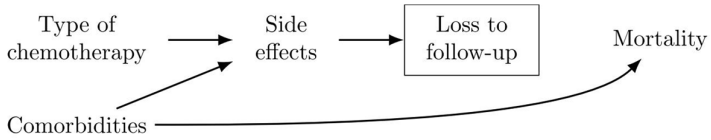
CAUSAL DIAGRAM (Syn: causal graph, path diagram) A graphical display of causal relations among variables, in which each variable is assigned a fixed location on the graph (called a *node*), and in which each direct causal effect of one variable on another is represented by an arrow with its tail at the cause and its head at the effect.[100] Direct noncausal associations are usually represented by lines without arrowheads. Graphs with only directed arrows (in which all direct associations are causal) are called *directed graphs*. Graphs in which no variable can affect itself (no feedback loop) are called *acyclic*. Methods have been developed to determine from causal diagrams which sets of variables are sufficient to control CONFOUNDING and for when control of variables leads to BIAS.[1,2,34,84,101,209,210]

A dictionary of epidemiology. 6th. edition (2014).



Causal diagram representing outcome Y, exposure A, their unmeasured common cause U, and risk factor L. Graph theory can be used to show that data on L are sufficient to eliminate the confounding, caused by the presence of U, for the effect of A on Y.

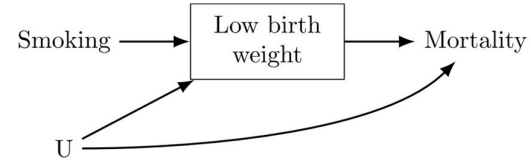
Causal diagram representing selection bias arising from loss to follow-up. The relationship between type of chemotherapy and mortality will be biased if loss to follow-up is differential with respect to treatment (e.g., one type of chemotherapy has increased risk of side effects, which affects loss to follow-up) and a cause of the outcome (e.g., existing comorbidities increase the risk of mortality and also increase the risk of side effects, which in turn affects loss to follow-up). Here, selection bias arises from conditioning not on a collider itself but rather on a variable that is downstream of a COLLIDER.



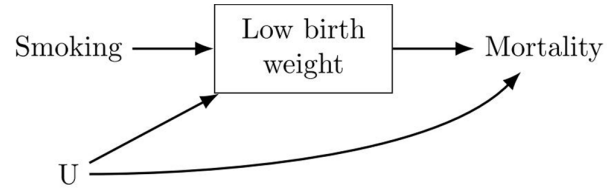
A dictionary of epidemiology 7th. edition (2026)

LOW BIRTH WEIGHT PARADOX The observation that low birth weight infants born to smokers have a lower risk of infant mortality than low birth weight infants born to nonsmokers. The observation can be explained by COLLIDER-stratification bias, which is introduced by restricting the analysis to infants with low birth weight. Among low birth weight infants, if they were not exposed to tobacco, then they are more likely to be exposed to other causes of low birth weight, such as birth defects. If these other causes of low birth weight are associated with an increased risk in infant mortality, then the risk of infant mortality would appear high among low birth weight infants born to nonsmokers compared to those born to smokers. The low birth weight paradox may involve exposures other than maternal smoking, such as race or multiple versus single pregnancies; they all share a similar underlying CAUSAL STRUCTURE.

This type of PARADOX arises when adjusting for any variable affected by the exposure of interest.
A similar structure may explain the "obesity paradox", the observation that among individuals with heart conditions, patients with excess weight have better mortality outcomes than patients of normal weight.



Causal diagram representing the low birth weight paradox. Collider-stratification bias is introduced when evaluating the relationship between maternal smoking and infant mortality among low birth weight infants due to restrictrion to low birth weight, a collider. This introduces the biasing path: maternal smoking to low birth weight to U (a common cause between low birth weight and infant mortality, e.g., birth defects) to infant mortality.

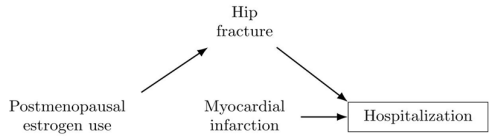


A dictionary of epidemiology. 7th. edition (2026).

BERKSON'S BIAS A form of SELECTION BIAS that arises when the variables whose association is under study affect the selection of subjects into the study. It is a particular concern in hospital-based studies, especially when prevalent or previously diagnosed cases are not excluded. (...) In Berkson's original example, hospitalization is a COLLIDER for two or more diseases whose prevalences are independent in the population, but for which different fractions of the population are hospitalized. The selection process into the hospital is such that a hospital-based case-control study inevitably yields an association between prevalent diseases. The CAUSAL STRUCTURE of Berkson's bias is the same of all biases due to conditioning on a collider.

Among hospitalized patients, hip fracture and myocardial infarction may be associated because both conditions affect the probability of hospitalization. There is a disease-disease association because hospitalized patients without a hip fracture are more likely to be hospitalized for other conditions, such as a myocardial infarction. This bias can be extended to an exposure-disease association: consider a case-control study of postmenopausal estrogen use and myocardial infarction; if hospitalized patients with hip fractures are oversampled as controls, then there will be a non-causal association between postmenopausal estrogen use and myocardial infarction due to stratification on a collider.

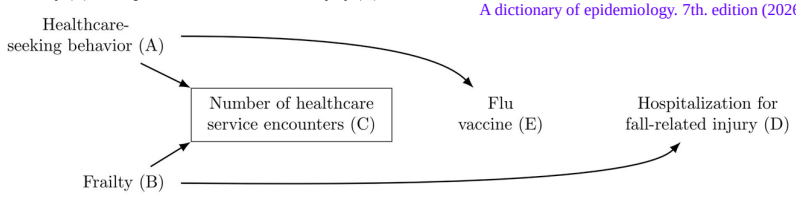
Source: A dictionary of epidemiology. 7th. edition (2026). Author: Joy Shi. and Int J Epidemiol 2014.



M-BIAS BIAS in the association between exposure (E) and disease (D) arising from stratifying or restricting on a COLLIDER (C) in an "M pattern" within the underlying CAUSAL STRUCTURE (in which there is a common cause (A) between C and E, and a common cause (B) between C and D). It is called "M" because of the M shape of the corresponding CAUSAL DIAGRAM when the events are temporally arranged from top (earliest) to bottom (latest), where C is a collider on the BACKDOOR path from E to D passing through A, C and B. Like other collider-stratification biases and SELECTION BIASES, M-bias arises from adjustment for a variable C that numerically behaves like a classical CONFOUNDER (in that the effect estimate changes upon adjustment for C). (...)

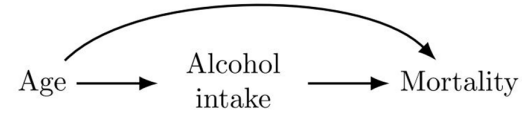
An analysis which stratifies on the number of healthcare service encounters (C), a collider, would introduce bias due to the open path: flu vaccine (E) to healthcare-seeking behavior (A) to number of healthcare service encounters (C) to frailty (B) to hospitalization for fall-related injury (D).

A dictionary of epidemiology. 7th. edition (2026).



BACKDOOR (BIASING PATH) A path on a CAUSAL DIAGRAM from the exposure to the outcome that begins with an arrow pointing into the exposure. If control is not made for a variable on the path CONFOUNDING will be introduced.

Causal diagram representing a backdoor path between the exposure (alcohol intake) and the outcome (mortality).
The **backdoor path, from alcohol intake to age to mortality,** induces a non-causal association between alcohol intake and mortality due to confounding by age.

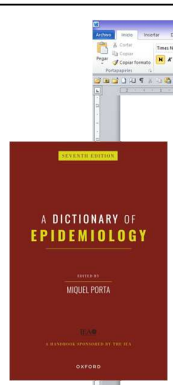


Source: A dictionary of epidemiology. 7th. edition (2026). Author: Joy Shi.

TREATMENT-CONFOUNDER FEEDBACK A situation in which a time-varying confounder is affected by (or shares common causes with) previous TREATMENT. For example, when evaluating the effect of antiretroviral therapy on mortality, CD4 cell count is a time-varying confounder affected by previous use of antiretroviral therapy. **G-METHODS** are required to validly estimate causal effects in the presence of treatment-confounder feedback. See also TIME-VARYING TREATMENT.

TREATMENT In contemporary methodology, a synonymous for EXPOSURE and INTERVENTION. See also IATROGENESIS; SUSTAINED TREATMENT STRATEGIES; TIME-FIXED TREATMENT.

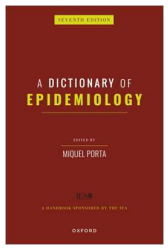
A dictionary of epidemiology. 7th. edition (2026).



The upper age limit for this fate is 44 –sometimes 49– years in most jurisdictions.

GENERALIZABILITY The degree to which results of a study may apply, be relevant, or be extended to populations or groups that include individuals who were eligible for but did not participate in the study. Contrast with TRANSPORTABILITY, which assesses the extension of findings to individuals who may not have been eligible for the original study. In etiological research, assessing generalizability is not a mere statistical process, in nature; rather, it must integrate theory, judgment, and evidence external to the study (e.g., available knowledge on biological, clinical, or social mechanisms linking an exposure to an outcome). Inferences may partly be subjective, but not arbitrary. REPRESENTATIVENESS of the study sample may enhance generalizability in studies with strong descriptive components; yet, knowledge of subject matter, context and study conditions enables generalization in studies of etiologic nature that are not based on a representative sample. Scientific and statistical inferences build on different types of logic.[1,3,8,28-30,522-524] See also VALIDITY.

Source: A dictionary of epidemiology. 7th. edition (New York: OUP, 2026).



TRANSPORTABILITY The degree to which the results of a study may be extended to a target population that includes individuals who may not have been eligible for the original study.[523,524] Contrast with GENERALIZABILITY, which expresses the degree to which findings may be applicable to individuals who were eligible for but did not participate in the original study.

2. EXTERNAL VALIDITY The degree to which results of a study may apply, be generalized or transported to populations or groups that did not participate in the study. A study is externally valid if it allows unbiased inferences regarding some other specific target population beyond the subjects in the study. May refer to GENERALIZABILITY of results to populations or groups who are eligible for but did not participate in the original study, or TRANSPORTABILITY of results to populations or groups which include individuals who are not eligible for the original study.

Valid conclusions about the internal and external validity of a study require wisdom and rigor to apply expert judgment based on knowledge of the subject-matter and of methodology.[1-4,8,11,65,107,120,289,457,524] See also BIAS; GENERALIZABILITY; REPRESENTATIVENESS; TRANSPORTABILITY.

IMMORTAL TIME A period during which, by study design, a person cannot develop an outcome of interest. The generation of "immortal time" is the result of an incorrect STUDY DESIGN.

TIME ZERO In a RANDOMIZED TRIAL, the time at which evaluation of the ELIGIBILITY CRITERIA, RANDOMIZATION, and start of FOLLOW-UP occur. In TARGET TRIAL emulation, misalignment of these three components of time zero can result in immortal time or selection bias.

A dictionary of epidemiology. 7th. edition (2026).

A Structural Description of Biases That Generate Immortal Time

Epidemiology 2025

Miguel A. Hernán,[a,b] *Jonathan A. C. Sterne,*[c,d,e] *Julian P. T. Higgins,*[c] *Ian Shrier,*[f] *Sonia Hernández-Díaz*[a]

Abstract: Immortal time may arise in survival analyses when individuals are assigned to treatment strategies based on post-eligibility information or selected based on post-assignment eligibility criteria. Selection based on eligibility criteria applied after treatment assignment results in immortal time when the analysis starts the follow-up at assignment. Misclassification of assignment to treatment strategies based on treatment received after eligibility results in immortal time when the treatment strategies are not distinguishable at the start of follow-up. Target trial emulation prevents the introduction of immortal time by explicitly specifying eligibility and assignment to the treatment strategies, and by synchronizing them at the start of follow-up. We summarize analytic approaches that prevent immortal time when longitudinal data are available to emulate the target trial from the time of treatment assignment. The term "immortal time bias" suggests that the source of the bias is the immortal time, but it is selection or misclassification that generates the immortal time, leading to bias.

"... what is fascinating is that "immortal time" doesn't exist in the data. Rather, we generate immortal time when analyzing the data incorrectly. "

Talk :"How to make people immortal and why it's not a good idea: improving causal analyses of healthcare databases". "
Tue., October 14 at 4pm.
To register:
https://survey.ki.se/Survey/44292

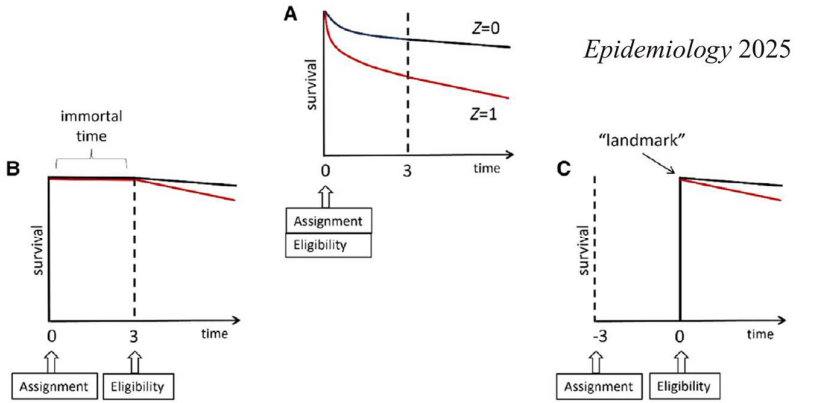


FIGURE 1. Survival curves from a follow-up study based on all data (A), on data restricted to those who survive at least 3 months with follow-up starting at assignment (B), and on data restricted to those who survive at least 3 months with follow-up starting at 3 months (C).

Per-Protocol Analyses of Pragmatic Trials

Miguel A. Hernán, M.D., Dr.P.H., and James M. Robins, M.D.

N ENGL J MED 2017

The validity of both intention-to-treat and per-protocol effect estimates requires correct adjustment for selection bias due to differential loss to follow-up.[6] Moreover, the validity of per-protocol effect estimates also requires correct adjustment for confounding due to incomplete adherence to the assigned treatments or use of off-protocol concomitant therapies. Because both adherence and loss to follow-up may be influenced by social and clinical factors that occur after randomization,

First, data from participants should not be censored when they stop treatment for clinical reasons.

Second, data from participants should be censored when it is no longer certain that they are receiving treatment.

Third, adjustment should be made for confounding due to incomplete adherence. A naive per-protocol analysis, that is, one with no adjustment for confounding, will be valid only if adherence occurred completely at random.[4] However, because participants who adhere to the protocol and those who do not adhere generally differ with respect to prognostic factors, a per-protocol analysis that censors patient data at the time of nonadherence must adjust for prerandomization and postrandomization prognostic factors that predict adherence.

Per-Protocol Analyses of Pragmatic Trials

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N ENGL J MED 2017

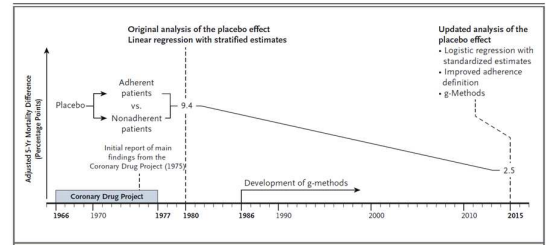


Figure 1. Adjusted Difference in 5-Year Mortality between Patients Who Adhered to Placebo and Those Who Did Not in the Coronary Drug Project Randomized Trial.

An intention-to-treat analysis of the Coronary Drug Project randomized trial (performed between 1966 and 1975) showed no difference in 5-year mortality between patients who received the active treatment (clofibrate) and those who received placebo. In 1980, a post hoc analysis showed that, in the placebo group, mortality among participants who adhered to placebo throughout the study was lower than mortality among those who did not adhere, even after adjustment for multiple baseline factors. Because placebo cannot affect mortality, the difference in mortality in the placebo group was interpreted as evidence that comparisons between patients who adhere to a regimen and those who do not are inherently biased. An updated analysis performed in 2015 used logistic regression, decoupled the definitions of adherence and loss to follow-up, used standardization to adjust for prerandomization covariates, and used g-methods to adjust for postrandomization covariates.[10] In the updated analysis, the difference in 5-year mortality between the patients who adhered to placebo and those who did not was estimated to decrease from 9.4 percentage points in the 1980 analysis to 2.5 percentage points in the 2015 analysis.

the analysis was designed to be analogous to the original analysis except that it used logistic regression (rather than linear regression) for the binary mortality outcome, decoupled the definition of adherence and loss to follow-up, used standardization to adjust for prerandomization covariates, and used inverse-probability weighting to adjust for postrandomization covariates.

huge progress has been made in the past 45 years.

J. chron. Dis. 1967, Vol. 20, pp. 637–648. Pergamon Press Ltd. Printed in Great Britain

EXPLANATORY AND PRAGMATIC ATTITUDES IN THERAPEUTICAL TRIALS

DANIEL SCHWARTZ and JOSEPH LELLOUCH
Unité de Recherches Statistiques, Institut National de la Santé et de la Recherche Medicale, 94 Villejuif, France

(*Received* 6 *January* 1967; *in revised form* 24 *March* 1967)

Schwartz D, Flamant L, Lellouch J. *L'essai therapéutique chez l'homme*. Paris: Flammarion, 1970, 1981.
English translation of the 1st French edition: *Clinical trials*. London: Academic Press, 1980.

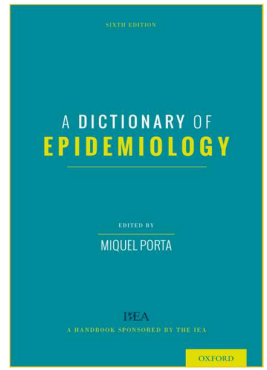
ancient, relevant issues. study them. learn. think. and study how much progress has been made in the past 70-30-10 years.

TABLA 1. **La formulación del problema en un ensayo clínico: actitudes explicativa y pragmática o asistencial**[41]

	Actitud explicativa	Actitud pragmática
Objetivo y pregunta principal	Mejorar los *conocimientos*, comprensión; eficacia. ¿Es eficaz, por qué, cómo?	Mejorar las *decisiones*, aplicación; efectividad ¿Es más efectivo que lo habitual, es más aceptable para los pacientes, vale la pena cambiar?
Condiciones de realización	Experimentales «de laboratorio» (p. e., dosis fijas, médicos, exploraciones sofisticadas); énfasis en *igualar* los tratamientos, para conocer los efectos específicos.	Parecidas a las reales, «de consulta» (p. e., dosis ajustables, seguimiento habitual); énfasis en *optimizar* los tratamientos, para escoger el más interesante.
Criterios de inclusión	Estrictos	Amplios
Sujetos	*Homogéneos*, cumplidores; los más adecuados para detectar un efecto biológico.	*heterogéneos*, aquellos a los que se extrapolarán los resultados.
Tratamiento del grupo control	Fármaco o placebo.	El habitual: fármaco, placebo o abstención.
Criterios de valoración	Enfasis en los de *significación biológica* (p. e., regresión del tumor, hipocolesterolemia); pocos, objetivos y analizados por separado.	*Duración y calidad de la vida* (p. e., supervivencia, efectos indeseables, capacidad laboral); numerosos, objetivos y subjetivos, analizados en conjunto.
Modo de comparación	Pruebas estadísticas convencionales.	Pruebas de análisis de decisiones.
Repercusiones	Extrapolación a la práctica habitual no asegurada (más probable si la respuesta a la pregunta principal es negativa).	Repercusión sobre los conocimientos fisiopatológicos no asegurada (más probable si la respuesta a la pregunta principal es positiva).

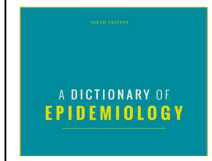
M. Porta Serra. — ATENCION PRIMARIA - Vol. 2, Núm. 2, 1985

EXPLANATORY ↔ PRAGMATIC STUDIES
OBSERVATIONAL ↔ EXPERIMENTAL STUDIES
INTENTION-TO-TREAT (ITT) ↔ PER PROTOCOL
RATE, RISK RATIO, BIAS, SELECTION BIAS,
RESIDUAL CONFOUNDING,
CUMULATIVE & DENSITY SAMPLING,
OPEN POPULATION, CAUSAL NULL,
CAUSAL INFERENCE, STANDARDIZATION,
OVERADJUSTMENT, COLLIDER, M-BIAS,
CAUSAL DIAGRAM, INSTRUMENTAL VARIABLE,
NEGATIVE CONTROLS, G-ESTIMATION,
INVERSE PROBABILITY WEIGHTING,
IDENTIFIABILITY, POSITIVITY, IGNORABILITY,
COLLAPSIBILITY, EXCHANGEABLE,
MARGINAL STRUCTURAL MODELS, RISK SET,
MENDELIAN RANDOMIZATION,
COUNTERFACTUAL OUTCOME, POTENTIAL OUTCOME,
SAMPLE SPACE, FALSE DISCOVERY RATE,
DYSREGULATION.



Oxford University Press, **2014**

try it → http://www.oxfordreference.com/view/10.1093/acref/9780199976720.001.0001/acref-9780199976720



OBSERVATIONAL STUDY (Syn: nonexperimental study) A study that does not involve any intervention (experimental or otherwise) on the part of the investigator.[1-3,6,9,25,26,39-42,197239,269,270,272,795] A study with RANDOM ALLOCATION of treatments or other exposures is inherently experimental or nonobservational. Observations are not just a haphazard collection of facts; in their own way, observational studies must apply the same rigor as experiments, and vice versa.[201,276] Many important preclinical, clinical, and epidemiological studies (and studies in other branches of science) are completely observational or have strong observational components.[101] Dismissive attitudes toward observational research have a weak scientific basis. In the health, life, and social sciences—and in other sciences as well—there has long been a fruitful dialectic tension between observation and experiment; facts and reasons; actions, explanations, mechanisms.[1,3,6,9,26,38-42,64,83,101,201-203,639-641,798,800] Often, observational and experimental studies on the apparently same issue actually answer *different questions*; for example, a randomized clinical trial will compare women allocated to hormone replacement therapy (HRT) and women allocated to another therapy or a placebo, and perform an INTENTION-TO-TREAT ANALYSIS, whereas an observational study will compare rather different women (than those included in a RCT) who were actually exposed to HRT and women exposed to other therapies or none; characteristics of subjects, context, exposures, timing, confounders, and interactions are just six of the many reasons that usually make different designs answer different questions. Also, different designs have different strengths and weaknesses to help make decisions and CAUSAL INFERENCES. Some observational studies may be analyzed as experiments; and some experiments, as observational studies.[2,641,800] See also CASE REPORTS; CLINICAL STUDY.

The NEW ENGLAND JOURNAL of MEDICINE

Oct. 30, 1980 Vol. 303

INFLUENCE OF ADHERENCE TO TREATMENT AND RESPONSE OF CHOLESTEROL ON MORTALITY IN THE CORONARY DRUG PROJECT

THE CORONARY DRUG PROJECT RESEARCH GROUP

Abstract The Coronary Drug Project was carried out to evaluate the efficacy and safety of several lipid-influencing drugs in the long-term treatment of coronary heart disease. The five-year mortality in 1103 men treated with clofibrate was 20.0 per cent, as compared with 20.9 per cent in 2789 men given placebo (P = 0.55). Good adherers to clofibrate, i.e., patients who took 80 per cent or more of the protocol prescription during the five-year follow-up period, had a substantially lower five-year mortality than did poor adherers to clofibrate (15.0 vs. 24.6 per cent; P = 0.00011). However, similar findings were noted in the placebo group, i.e., 15.1 per cent mortality for good adherers and 28.3 per cent for poor adherers ($P = 4.7 \times 10^{-16}$). These findings and various other analyses of mortality in the clofibrate and placebo groups of the project show the serious difficulty, if not impossibility, of evaluating treatment efficacy in subgroups determined by patient responses (e.g., adherence or cholesterol change) to the treatment protocol after randomization. (N Engl J Med. 1980; 303:1038-41.)

Good adherers to clofibrate had a substantially lower five-year mortality than did poor adherers to clofibrate (15.0 vs. 24.6 per cent; P = 0.00011). However, similar findings were noted in the placebo group, i.e., 15.1 per cent mortality for good adherers and 28.3 per cent for poor adherers ($P = 4.7 \times 10^{-16}$).

ancient, relevant issues. study them. learn. think. and study how much progress has been made in the past 70-30-10 years.

Oct. 30, 1980 Vol. 303

5-year Mortality (%)	Clofibrate (n=1.065)	Placebo (n=2.695)
TOTAL	18,2	19,4
C <80%	24,6	28,2
C ≥80%	15,0	15,1

??!!

5-year Mortality (%) Figures adjusted for 40 baseline characteristics	Clofibrate	Placebo
TOTAL	18,0	19,5
C <80%	22,5	25,8
C ≥80%	15,7	16,4

(«Poor adherers» had slightly more risk factors at baseline)

* Adjusting for baseline characteristics «explains little».
* It is difficult to identify predictors of response, of adherence.
* **It is NOT CORRECT to evaluate treatment efficacy in subgroups determined** by patient responses to the treatment protocol (e.g., adherence or cholesterol change) **AFTER randomisation.**
* Only comparisons between groups defined BEFORE randomisation are VALID.
* Make sure that patients who will be randomized will accept any of the possible treatments; when signing informed consent, always before randomization.

we used to say

± wrong

5-year Mortality (%) Figures adjusted for 40 baseline characteristics	Clofibrate	Placebo
TOTAL	18,0	19,5
C <80%	22,5	25,8
C ≥80%	15,7	16,4

(«Poor adherers» had slightly more risk factors at baseline)

Murray and Hernán *Trials* (2018)

Improved adherence adjustment in the Coronary Drug Project

Background: The survival difference between adherers and non-adherers to placebo in the Coronary Drug Project has been used to support the thesis that adherence adjustment in randomized trials is not generally possible and, therefore, that only intention-to-treat analyses should be trusted. We previously demonstrated that adherence adjustment can be validly conducted in the Coronary Drug Project using a simplistic approach. Here, we re-analyze the data using an approach that takes full advantage of recent methodological developments.

Methods: We used inverse-probability weighted hazards models to estimate the 5-year survival and mortality risk when individuals in the placebo arm of the Coronary Drug Project adhere to at least 80% of the drug continuously or never during the 5-year follow-up period.

Results: Adjustment for post-randomization covariates resulted in 5-year mortality risk difference estimates ranging from −0.7 (95% confidence intervals (CI), −12.2, 10.7) to 4.5 (95% CI, −6.3, 15.3) percentage points.

Conclusions: Our analysis confirms that appropriate adjustment for post-randomization predictors of adherence largely removes the association between adherence to placebo and mortality originally described in this trial.

huge progress has been made in the past 20-10 years.

JAMA | Special Communication

JAMA. 2025;334(12):1084-1093.

Transparent Reporting of Observational Studies Emulating a Target Trial—The TARGET Statement

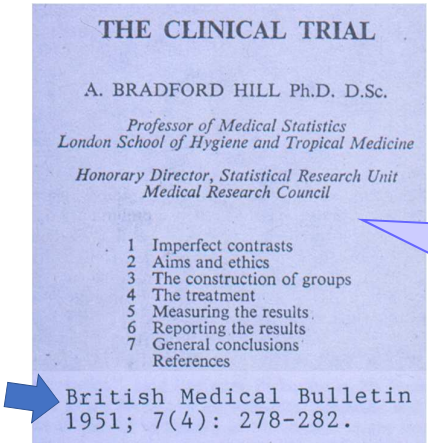
Aidan G. Cashin, PhD; Harrison J. Hansford, BSc (Hons); Miguel A. Hernán, MD; Sonja A. Swanson, ScD;

FINDINGS The 21-item TARGET checklist is organized into 6 sections (abstract, introduction, methods, results, discussion, other information). TARGET provides guidance for reporting observational studies of interventions explicitly emulating a parallel group, individually randomized target trial, with adjustment for baseline confounders. Key recommendations are to (1) identify the study as an observational emulation of a target trial; (2) summarize the causal question and reason for emulating a target trial, (3) clearly specify the target trial protocol (ie, the causal estimand, identifying assumptions, data analysis plan) and how it was mapped to the observational data, and (4) report the estimate obtained for each causal estimand, its precision, and findings from additional analyses to assess the sensitivity of the estimates to assumptions, and design and analysis choices.

JAMA. 2025;334(12):1084-1093.

Table 1. Glossary of Terms Commonly Used in Studies Emulating a Target Trial[a]

Target trial framework	A methodological framework for causal inference from observational data, which applies the design principles of randomized trials. This involves designing observational analyses to explicitly emulate a hypothetical pragmatic randomized trial that would answer the question at hand: the target trial. The framework has 2 components: specification of the target trial and mapping that target trial to the data (emulation).
Confounding	Confounding occurs when groups receiving different treatment strategies differ in their distribution of prognostic factors at time zero.[17] When there is confounding, differences in the outcome distribution between treatment groups may be explained by differences in prognostic factors rather than differences in treatment. A key concern for target trial emulation is whether some confounding bias remains after adjustment for measured confounders.



THE CLINICAL TRIAL

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

Professor of Medical Statistics
London School of Hygiene and Tropical Medicine

Honorary Director, Statistical Research Unit
Medical Research Council

1 Imperfect contrasts
2 Aims and ethics
3 The construction of groups
4 The treatment
5 Measuring the results
6 Reporting the results
7 General conclusions
References

British Medical Bulletin
1951; 7(4): 278-282.

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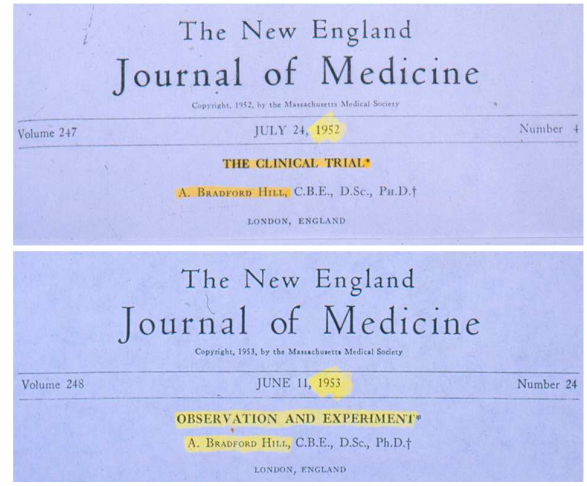
https://ieaweb.org/ - 9 April 2026



The New England
Journal of Medicine

Volume 247 JULY 24, 1952 Number 4

THE CLINICAL TRIAL*

A. BRADFORD HILL, C.B.E., D.Sc., PH.D.†

LONDON, ENGLAND

The New England
Journal of Medicine

Volume 248 JUNE 11, 1953 Number 24

OBSERVATION AND EXPERIMENT*

A. BRADFORD HILL, C.B.E., D.Sc., Ph.D.†

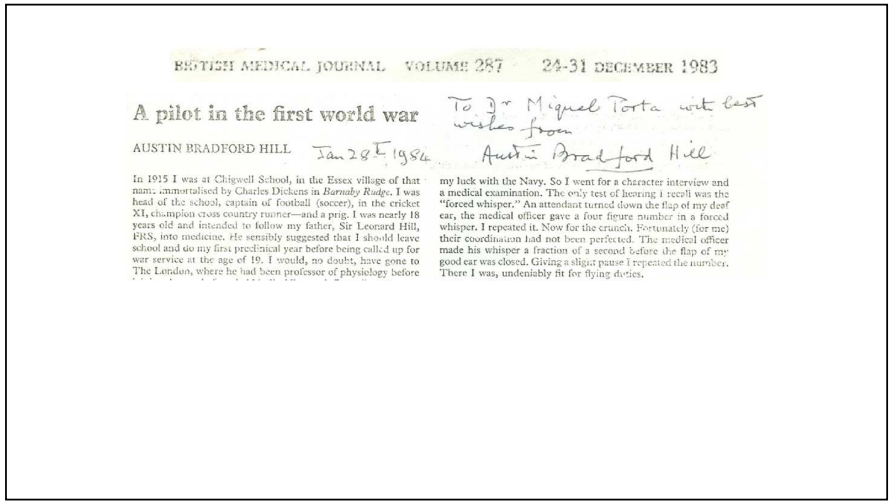
LONDON, ENGLAND

We must, I believe, invariably

return to man

for the final proof or proofs.

Sir Austin Bradford Hill
Observation and experiment
N Engl J Med 1953



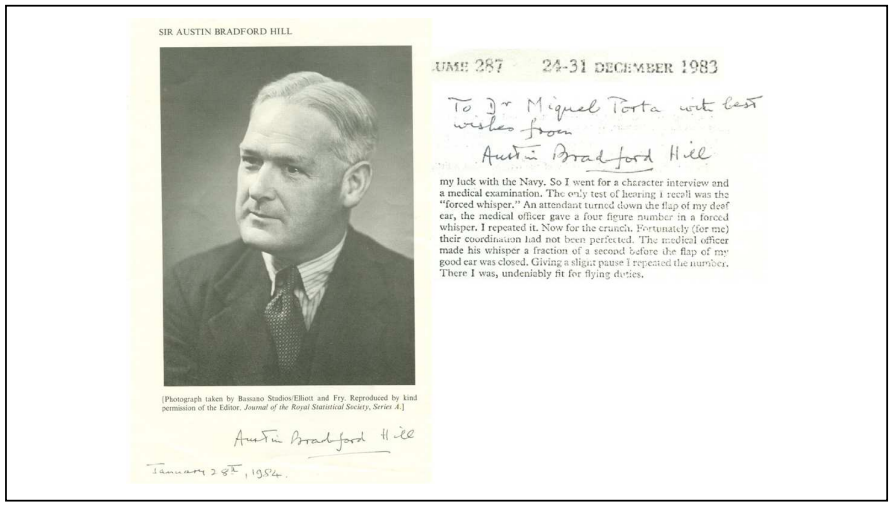
BRITISH MEDICAL JOURNAL VOLUME 287 24-31 DECEMBER 1983

A pilot in the first world war

To Dr Miguel Porta with best wishes from Austin Bradford Hill

AUSTIN BRADFORD HILL Jan 28th 1984

In 1915 I was at Chigwell School, in the Essex village of that name, immortalised by Charles Dickens in *Barnaby Rudge*. I was head of the school, captain of football (soccer), in the cricket XI, champion cross country runner—and a prig. I was nearly 18 years old and intended to follow my father, Sir Leonard Hill, FRS, into medicine. He sensibly suggested that I should leave school and do my first preclinical year before being called up for war service at the age of 19. I would, no doubt, have gone to The London, where he had been professor of physiology before my luck with the Navy. So I went for a character interview and a medical examination. The only test of hearing I recall was the "forced whisper." An attendant turned down the flap of my deaf ear, the medical officer gave a four figure number in a forced whisper, I repeated it. Now for the crunch. Fortunately (for me) their coordination had not been perfected. The medical officer made his whisper a fraction of a second before the flap of my good ear was closed. Giving a slight pause I repeated the number. There I was, undeniably fit for flying duties.



SIR AUSTIN BRADFORD HILL

[Photograph taken by Bassano Studios/Elliott and Fry. Reproduced by kind permission of the Editor. *Journal of the Royal Statistical Society, Series A.*]

Austin Bradford Hill

January 28th, 1984.

BRITISH MEDICAL JOURNAL VOLUME 287 24-31 DECEMBER 1983

To Dr Miguel Porta with best wishes from Austin Bradford Hill

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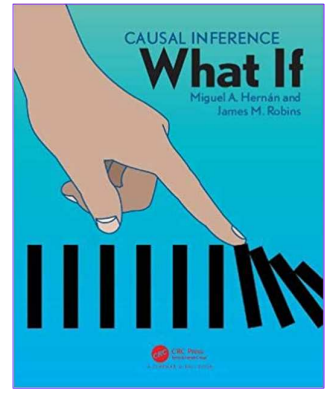

https://hsph.harvard.edu/research/causalab/
https://miguelhernan.org/
https://miguelhernan.org/whatifbook

CAUSALab
A Center to Learn What Works

a great course: **90,032** learners enrolled

CAUSAL DIAGRAMS

DRAW *your assumptions* **BEFORE** *your conclusions*

The C-Word: Scientific Euphemisms Do Not Improve Causal Inference From Observational Data *Am J Public Health.* 2018 *Miguel A. Hernán*

A Second Chance to Get Causal Inference Right: A Classification of Data Science Tasks

Miguel A. Hernán, John Hsu, and Brian Healy **CHANCE VOL. 32.1, 2019**

The C-Word: Scientific Euphemisms Do Not Improve Causal Inference From Observational Data

Am J Public Health. 2018 — *Miguel A. Hernán*

causation. The analysis of the observational study is necessarily associational, even though the goal of the observational study is causal.

Interestingly, the same is true of randomized trials. All we can estimate from randomized trials data are associations; we just feel more confident giving a causal interpretation to the association between treatment assignment and outcome because of the expected lack of confounding that physical randomization entails.

However, the association measures from randomized trials cannot be given a free pass. Although randomization eliminates systematic confounding, even a perfect randomized trial only provides probabilistic bounds on "random confounding"—as reflected in the confidence interval of the association measure—and many randomized trials are far from perfect.

IEA International Epidemiological Association

INSIDE THE SEVENTH EDITION OF THE DICTIONARY OF EPIDEMIOLOGY: THE FUTURE OF EPIDEMIOLOGY

Thank you very much
for your kind attention.

The language of epidemiology in science and society.
Introducing the 7th edition
of 'A dictionary of epidemiology'.

https://a.co/d/03paNpk0

Miquel Porta, MD, MPH, PhD
https://linktr.ee/mporta

Hospital del Mar Research Institute
Barcelona

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EXCHANGEABILITY (Syn: exogeneity) Independence between the observed treatment and POTENTIAL OUTCOMES (outcomes under alternative treatment levels).

Two groups are exchangeable with respect to certain variables if group membership labels can be interchanged (exchanged) without altering any probability statement involving the variables.

Suppose two groups A and B are exchangeable with respect to their POTENTIAL OUTCOMES. Then the probability that group A has a better outcome than group B when A is exposed and B is not is equal to the probability that group B has a better outcome than group A when B is exposed and A is not. Here, exchanging A and B does not change the probability of the statement, or the probability of any other statement involving A, B, their exposures, and their outcomes.

Exchangeability implies that no CONFOUNDING is present. Groups can also be conditionally exchangeable if there is no RESIDUAL CONFOUNDING; in this case, their exchangeability is conditional on adjusting for the set of measured confounders. When the treated and the untreated are exchangeable, we may say that treatment is *exogenous*, and thus exogeneity is used as a synonym for exchangeability.

A dictionary of epidemiology. 7th. edition (2026).

COLLAPSIBILITY Equality of stratum-specific effect measures with the unstratified (if no confounding) or standardized effect measure. In early papers, lack of collapsibility was sometimes incorrectly equated with CONFOUNDING, but non-collapsibility is not a bias, just the expected result of using a non-collapsible effect measure (such as an ODDS RATIO or a hazard ratio).

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Causal diagram representing instrumental variable Z, exposure A, outcome Y and unmeasured common cause U. Instrumental variable analysis can estimate the effect of exposure A on outcome Y even in the presence of unmeasured variables U.

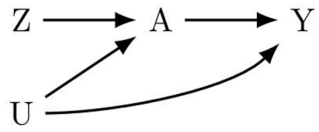
The 3 instrumental conditions can be evaluated in the causal diagram:

1.- Z is associated with A through the direct arrow from Z to A,

2.- Z affects Y only through A, and

3.- There are no common causes between Z and Y.

(...)



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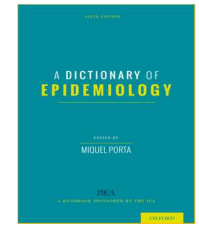
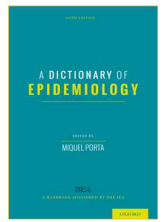
SIGNIFICANCE, CLINICAL Importance, RELEVANCE, or meaning for the care of individuals, who often are—in clinical research—patients. A difference in effect size considered to be important (e.g., by a patient or a professional) in medical decisions regardless of the degree of statistical significance. statistical significance can never be taken to equal clinical significance. For example, when large numbers of subjects are studied, some differences will be statistically significant even if their magnitude or size is small; hence they will be of little importance for patient care. Conversely, when small numbers of subjects are studied, some differences will not be statistically significant even if their magnitude is large; hence they may be of importance for patient care.[1,3,6,9,25,26,38,58,91,202,203,225] See also MINIMALLY IMPORTANT DIFFERENCE.



IEA. *A dictionary of epidemiology*. 6th. edition (2014).

RELEVANCE

1. The importance for existing ideas or practices. The degree to which a study, program, policy, or organization should theoretically change or can actually influence knowledge, beliefs, ideas, attitudes, decisions, actions, policies, structures, procedures, techniques, or processes of all sorts (social, cultural, political, organizational, individual, medical, biological, etc.).
2. In epidemiology, a relevant study or program may be one that makes a practical or a theoretical contribution to the identification, characterization, understanding, or solution of a public health, environmental, social, clinical, biological, or technological problem. EPIDEMIOLOGICAL RESEARCH usually aims at having social, environmental, or public health relevance; epidemiological studies often also have clinical, biological, methodological, or technological relevance.
3. In clinical and epidemiological research, *relevance* is commonly used as a synonym of importance and of SIGNIFICANCE. Statistical significance must be distinguished from clinical and public health significance. A statistically significant effect may be found in a study with a large number of participants and yet lack clinical or public health significance (because the magnitude of the effect is small, for instance). Hence, statistical significance should never be assumed to equal *significance*, and *significance* encompasses more than statistical significance. Clinical studies usually aim at being clinically significant, important, or relevant for the care of patients. Sometimes, epidemiological and clinical studies are also mechanistically relevant; e.g., they produce knowledge on mechanisms of disease.[1-3,5-9,25,26,28,91,101,202,222] See also



SIGNIFICANCE, PUBLIC HEALTH Importance, RELEVANCE, or meaning from a public health perspective; e.g., if exposure to an environmental factor that causes a small increase in the individual risk of a disease is common in a population, the factor may have public health significance or importance because of its impact on the BURDEN OF DISEASE in the population.[12,28,83,101,366,426] See also STRATEGY.

SIGNIFICANCE, STATISTICAL

1. The probability of the observed or a larger value of a test statistic under the NULL HYPOTHESIS. Often equivalent to the probability of the observed or larger degree of association under the null hypothesis. This usage is synonymous with *P* VALUE.[1,7,101,270]
2. The event of the *P* value falling below a prespecified cutoff or ALPHA LEVEL for declaring a result "statistically significant"; typically 0.05. This event should not be confused with clinical, public health, or scientific SIGNIFICANCE. See also CHI-SQUARE

A dictionary of epidemiology. 6th. edition (2014).

CREATIVITY

1. The ability to produce ideas, knowledge, policies, and objects (including scientific knowledge and "knowledge objects") that are both novel or original and worthwhile or appropriate (i.e., useful, attractive, meaningful, relevant, and valid).[237]

2. In EPIDEMIOLOGICAL RESEARCH, the capacity of a set of studies to harmonize relevance, validity, meaning, innovation, feasibility, and precision—ideally, beauty and simplicity as well. An epidemiological study reflects creativity to the extent that it generates knowledge that is relevant, new, valid, practical, and precise. Complexity may be a plus; it need not clash with simplicity and elegance. Relevance may be social, environmental, sanitary, clinical, biological, methodological, ethical, technological, intellectual.... Studies may blend, weave, knit, or weld such qualities in extraordinarily different ways.

3. A public health policy or program shows creativity when it is relevant, meaningful, useful, and attractive for populations, persons, companies, and institutions... when it is innovative, imaginative, simple... if effective and efficient in abating harmful determinants of health and significantly improving important health indicators. It may be morally and socially relevant if it increases freedom, justice, education, equity, or social cohesion. It needs to be culturally, environmentally, and economically sustainable. Creativity is an important value for epidemiology and the other health, life, and social sciences.[26,38,58,202,290,482]

EPIDEMIOLOGICAL RESEARCH Scientific research among human populations and defined groups of individuals into the frequency of occurrence, distribution and causes of phenomena of public health, clinical, social, or biological RELEVANCE, with valid selection of subjects and measurements, and formal CAUSAL INFERENCES on the DETERMINANTS of such phenomena.[1-3,5-9,24-26,39-42,58,85,128,202,270,279] See also CREATIVITY; INTEGRATIVE RESEARCH.

RESEARCH A class of activities designed to develop or contribute to knowledge. In applied science, the goal is generalizable knowledge, where the latter consists of theories, principles, relationships, products, or the accumulation of information on which these are based that can be corroborated by acceptable scientific methods of observation, inference, or experiment. When humans are the subjects of EPIDEMIOLOGICAL RESEARCH, ethical review is mandatory; however, there is a blurry boundary between research, which must undergo review, and common clinical or public health practice (e.g., SURVEILLANCE and epidemic control), to which the same rules may not apply, but that still must comply with ethical requirements.[1,3,5-9,26,202,270] See also INTEGRATIVE RESEARCH.

Source: Porta M, ed. A dictionary of epidemiology. 6th. edition (2014).

EPIDEMIOLOGICAL RESEARCH Scientific research among human populations and defined groups of individuals into the frequency of occurrence, distribution and causes of phenomena of public health, clinical, social, or biological RELEVANCE, with valid selection of subjects and measurements, and formal CAUSAL INFERENCES on the DETERMINANTS of such phenomena.[1-3,5-9,24-26,39-42,58,85,128,202,270,279] See also CREATIVITY; INTEGRATIVE RESEARCH.

INTEGRATIVE RESEARCH Research that integrates knowledge, data, methods, techniques, reasoning, and other scientific and cultural referents from multiple disciplines, approaches, and levels of analysis to generate knowledge that no discipline alone could achieve. For instance, research that integrates cultural, economic, and other "macro-level" or contextual factors with individual factors, as in MUTILEVEL ANALYSIS; analyses of the relationships among gene structure, expression, and function; research on the relationships among molecular pathways, PATHOPHYSIOLOGY, and clinical phenotypes, as in clinical pharmacology and clinical genetics; research that integrates interactions among environmental, genetic, and epigenetic processes.[1,13,26,33,80,146,202,323,339,411,548,799] Epidemiology is an inherently integrative discipline, and so are many of its subspecialities, and approaches, like CLINICAL and MOLECULAR EPIDEMIOLOGY, SOCIAL EPIDEMIOLOGY or ENVIRONMENTAL EPIDEMIOLOGY; DEVELOPMENTAL AND LIFE COURSE EPIDEMIOLOGY, for instance, attempts to integrate biological and social risk processes.[23,25] See also CLINICAL STUDY; HEALTH IMPACT ASSESSMENT; TRANSDISCIPLINARITY; REDUCTIONISM.

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INTEGRATION

1. The action or process of integrating. To integrate: to make a new whole; to combine parts into a new system and get them to interact so that the system expresses functions unavailable to the parts. The organizing of elements to form a coherent whole or system. Integration of knowledge from different scientific disciplines yields knowledge that no discipline alone may achieve.
2. In HEALTH PROMOTION and disease PREVENTION, strategies that target several risk factors, use multiple STRATEGIES at various levels of influence, and require INTERSECTORAL ACTION.[121] Integration entails multiplicity (more than one RISK FACTOR, level, sector, agent), and synergy resulting from multiplicity.[17]

Integration is no less crucial to science than to the functioning of postmodern societies. Examples: quality public transportation favors integration of disabled individuals and disadvantaged groups into society; integration of racial and ethnic minorities into the educational system; integration of preventive services into clinical care.[25,33,426,548] Synonyms, analogies, and METAPHORS are here useful as well: *integration* involves and refers to interaction, dialogue, complicity, performance, symbiosis, sharing, pooling, porousness, amalgamation, merging, coalescing, fusing, welding, blending, weaving.

A dictionary of epidemiology. 6th. edition (2014).