Causal Inference in Public Health

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The determination that an association is causal can have **profound public health consequences**, signaling the need or at least the possibility to **take an action** to reduce exposure to a hazardous agent or to increase exposure to a beneficial one.

Consequently, **causal inference** is implicitly and sometimes explicitly embedded in public health **practice and policy formulation**.

Practitioners **decide on interventions** on the basis of consequences produced by a presumed causal relationship.
Public health evidence may be prominent in legal proceedings in which judgment about the existence of a causal relationship is pivotal in determining guilt and liability for damages.

Decisions about harms or benefits of therapeutic agents are based, in part, on rules for how to measure the strength of evidence for causal connections between interventions and health outcomes.
Philosophy of causation

Two distinct classes of causation theory:

- On one side are the descendants of Locke and John Stuart Mill, who argued that causation can be verified through the careful implementation of the scientific method and the power of experimentation.

- On the other side is a parallel line of discourse that extends from David Hume, who argued that even though nature may contain real causal “connexions” between phenomena, causation cannot be empirically verified.
  
  "Reason is, and ought only to be the slave of the passions".
Bertrand Russell

“The law of causality, I believe, like much that passes muster among philosophers, is a relic of a bygone age, surviving, like the monarchy, only because it is erroneously supposed to do no harm”
The legacy of Hume and Russell urges us to be cautious because assigning causal significance to some phenomena also provides an easy target for skeptics and, potentially, affected stakeholders to derail reasonable interventions on the basis of an absence of proof.
Over that history, a variety of “frameworks” for thinking about causation have risen to coincide with the dominant problems of the day and the scientific understanding of their etiology.

- John snow ------------> chain of inference
- Koch ------------------> germ-disease
- Bradford Hill ----------> causal criteria
Smoking and cancer

Even as the epidemiological evidence mounted, the tobacco industry implemented a wide-ranging strategy to question the credibility of epidemiological evidence generally and of the most pivotal studies specifically.

This tactic of creating doubt about the evidence heightened tension around then challenge of interpreting the findings of epidemiological research, and its use attests to the societal importance of causal determinations.

The manufacture and dissemination of doubt remain strategies today, widely used by stakeholders whose interests are potentially threatened by a causal finding.
This framework, described below, was effective for smoking and lung cancer, one of its first applications and has proven useful and has driven decision making in public health for decades.
Smoking is a potent cause:
- increasing the risk of lung cancer about 20-fold
- leading to most cases of lung cancer; consequently,
- the evidence from observational studies was consistent and strong,
- temporality was clear.

These criteria (or what Hill calls “viewpoints”) are not absolute nor does inference of a causal relationship require that all criteria be met. In fact, only temporality is requisite.
Figure 3
The International Agency for Research on Cancer (IARC) classifications based on evidence from human and experimental evaluations. From IARC. For further information, see the Preamble to the IARC monograph on the evaluation of carcinogenic risk to humans, 2006 (40). ESLC, evidence suggesting lack of carcinogenicity.
Limitations

- Lack of a formal basis for evaluating causal hypotheses.
  - Investigators explored more formally the foundational mathematical and conceptual issues required for rigorous estimation of causal effects, particularly in circumstances where randomization of treatment assignment that insures exchangeable comparison groups is unfeasible.

- This approach is vulnerable to subjectivity in the evaluation of evidence and to manipulation of the evidence, and stakeholders potentially affected by the finding that an association is or is not causal may take opposing positions on evidence interpretation.

- As constructed and applied, the framework assumes a simplistic direct relationship between cause and putative effect without explicit consideration of the structure of the underlying causal processes.

- The causal conclusions were not couched in the consequences of specific actions:
  - Causal determinations were made by epidemiologists and others in public health about various risk factors without considering the effect of a specific way of changing them.
At the highest level, what would be the disease burden, absent the upstream factor (e.g., the tobacco industry), and at the lowest level, what would be the disease risk for genetically susceptible individuals, absent the environmental factor (e.g., smoking)?
potential outcomes framework

- Compares what is observed to what might have been observed, all other things being equal, under a counterfactual scenario.

- The potential outcomes framework is a powerful tool that has implications for how we see the world and to determine what types of questions can be answered in a useful way for public health purposes and what kinds of questions are beyond our capacity to answer.
potential outcomes framework

- It is an analytic effort to approximate the experimental paradigm that balances treated (exposed) and untreated (unexposed) groups on other factors.

- Counterfactual approach to the broad and multilevel nature of causal questions, and consider causal inference in the context of such questions and their implications for public health actions.
Causal inference in public health is the comparison of the distribution of health outcomes after different interventions.

In an ideal world these comparisons would be conducted via randomized experiments, and all public health decisions would be based on the findings of those experiments.

Experiments are often unethical, impractical, or simply too lengthy for timely decision making.
One way to address this concern and bridge the gap between the observational data and public health decision making is to design observational analyses in such a way that the observational data emulate those from hypothetical randomized experiments with relatively well-defined interventions.

This approach is built into the counterfactual or potential outcomes framework.
Confounding

- Even well-defined intervention groups will not usually be directly comparable because the key characteristics of individuals in each group are likely to differ.

- The most common approach to mitigate confounding is to measure as many variables as possible that are responsible for the noncomparability and to adjust for them in the statistical analysis.

- The available methods to adjust for measured confounders are stratification, matching, standardization, inverse probability weighting, and g-estimation.
Confounding: propensity score

- When the measured confounders are used to estimate each study participant’s probability of receiving the exposure of interest. For binary exposures (e.g., yes/no), this probability is referred to as the propensity score.

- Inverse probability weighting and g-estimation are methods based on propensity scores.

- Propensity scores can also be used to adjust for confounding via matching, and standardization.
Confounding: instrumental variable

- Instrument is roughly defined as a variable that has an effect on the exposure and that is unassociated with the outcome except through its effect on the exposure.

**Good:**
- One alternative method to eliminate confounding effect
- It does not require investigators to measure any confounders. Rather, it requires them to identify and appropriately measure an instrument.

**Bad:**
- It is impossible to verify empirically that a particular variable is an appropriate instrument.
- Valid instruments can provide only lower and upper bounds for the magnitude of the causal effect of interest.
Confounding: instrumental variable

- Valid adjustment for measured confounding in complex Settings:
  - parametric g-formula (a generalization of standardization)
  - inverse probability of marginal structural models
  - g-estimation of nested structural models

- These methods, are often referred to as causal methods because they can be applied to obtain valid causal inferences, in complex situation; e.g with time-varying confounders.
Confounding: DAG

- Causal diagrams are not a data-analysis method themselves, but they are used to represent the structure of the causal networks linking exposure, outcome, confounders, and other variables, requiring an explicit formulation of the relationships among these factors.

- Causal diagrams are a helpful tool to detect, graphically, possible sources of bias and to guide investigators in the design of their data analysis.
Challenges to Implementing the Potential Outcomes Framework

- Inherent features of the individual (such as sex, race/ethnicity, or age) that cannot be reasonably translated into hypothetical interventions

- Investigations into the association between nonmanipulable factors and health outcomes can be seen as a prelude to other studies on hypothetical interventions.
Challenges to Implementing the Potential Outcomes Framework

- In a multilevel situation, even when hypothetical interventions on national or regional policies can be imagined (though often impossible to implement), many of these contextual exposures are uniform within a society, which makes it difficult to gather the data needed to conduct an evaluation.

- As a result, in practice, epidemiologists and public health practitioners can be induced to prioritize the study of proximal, downstream interventions at the individual level.
Complex systems approaches have begun to offer new frameworks for causal processes across multiple geographic and time scales.

They call for a mapping of the agents and processes involved in producing outcomes and, consequently, are useful for framing many of the most pressing public health challenges that result from processes at levels ranging from local to global.

They point to the data that should be collected, how the data should be organized, and how the data should be analyzed in the potential outcomes framework.
Current causal inference methods are relevant and useful because they are directed not at identifying causes, but at identifying effects of interventions.

Even if we understood a causal chain perfectly, i.e., knew every factor that could be considered a cause, we still might not know how best to change the outcome.

Newer causal inference methods move us away from the philosophical exercise of identifying causes and force us to consider more profoundly how to improve health through specific interventions.
The effect of smoking cessation is amenable to randomized evaluation, but characterizing the consequences of raising taxes and other forms of social intervention may not be.

In such situations, we must use observational data to emulate the experiment that cannot be conducted.

If we succumb to focusing on interventions that are easy to evaluate, we may ignore upstream interventions for which the randomized experiment cannot be conducted or emulated but which may have the greatest potential to effect change.
We have touched on new analytical tools developed to sharpen analyses of observational data within this framework, recognizing that true randomized trials are not possible for many issues.

As public health data are collected, they need to have enough richness for interventional purposes.

Public health professionals need not shy from causal inference using these newer approaches because of perceived complexities.