

From Patients to Policy

Population Intervention Effects in Epidemiology

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Abstract: Interest in implementation science and recent calls for consequentialist epidemiology urge epidemiologists to produce work more immediately applicable to public health practice. A clear vocabulary for such approaches is lacking. Here, we present a potential taxonomy of causal effects, distinguishing between “exposure effects” more relevant to patients and individuals; and “population intervention effects” more relevant to public health policy. We discuss this range of effects using figures and a simple numerical example. (*Epidemiology* 2017;28: 525–528)

Recent years have seen a marked increase in interest around the translation of research findings into public health policy and practice, often discussed under the heading of “implementation” or “program” science.^{1–5} Although most discussions of translating research into practice regard epidemiology as critical to that process, to date the role of epidemiology has been left largely implicit, with some exceptions.^{6–10} In this age of calls for more consequentialist epidemiology,^{11,12} it is vital to have common vocabulary with which to discuss different types of effect estimates, and their relevance to clinical practice on one hand and intervention planning on

another. Here, we synthesize work by numerous authors^{6,13–16} to describe a range of contrasts that can be produced by epidemiologic analysis. For conceptual clarity, here we consider causal effects in a closed population with a binary, time-fixed, harmful exposure (equivalently, treatment); a dichotomous, time-fixed outcome which can be summarized as a risk¹⁷; and no competing risks.^{15,17} Further, we largely concentrate on issues of internal validity, ignoring issues of generalizability and transportability.^{15,18} Finally, the main text is conceptual; formal definitions of effects are proposed in the Technical eAppendix (<http://links.lww.com/EDE/B181>).

SELECTED EPIDEMIOLOGIC EFFECTS

The Figure shows several possible contrasts in a single population under real and hypothetical exposure distributions; this Figure owes a debt of influence to Figures 1.1 and 4.1 in Hernán and Robins.¹³

Figure part A shows an observed population as a circle in which a minority of individuals are exposed (shaded) and the remainder are unexposed (unshaded); the risk of the outcome is not indicated in the Figure.

In Figure part B, we show what is sometimes called a population average causal effect¹⁹ (alternately, average causal effect,¹³ average treatment effect,^{20–22} and other names^{20,23}). The two contrasting exposure distributions in Figure B (all-exposed; none-exposed) are both counterfactual in the literal sense of not corresponding to the factual exposure distribution in the observed sample (Figure A). In part because neither exposure distribution in Figure B coincides with a population in the real world, all/none comparisons may not be directly applicable in setting policy.^{14,24}

In Figure part C, we show a population attributable average causal effect (hereafter population attributable effect), which compares disease risk in the observed population (with the observed level of an exposure) with the risk that would be observed in the same population under a counterfactual exposure distribution in which 100% of the exposure was removed.^{25–29} The best known population attributable effect is the population attributable fraction^{15,30}; closely related quantities have been referred to by other names elsewhere.^{15,23,31} In passing we note that Greenland and Robins³⁰ distinguished between the excess and etiologic fractions; here we are interested in their “excess” usage.^{30,32}

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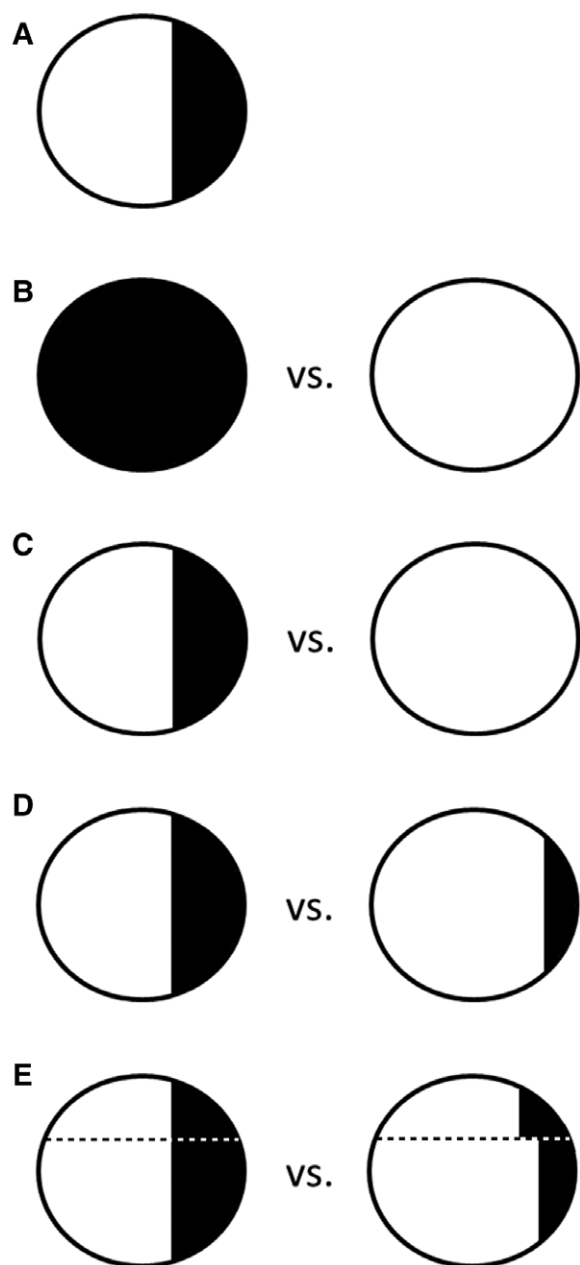


FIGURE. Several possible contrasts in real and hypothetical populations. A, An observed population, showing two levels of an exposure as shaded/unshaded. B, Population average causal effect, comparing “entirely exposed” and “entirely unexposed.” C, Population attributable effect, comparing those observed to be exposed to a population in which no one was exposed. D, Generalized intervention effect, comparing those observed to be exposed to a population in which fewer individuals were exposed. E, Dynamic intervention effect, comparing those observed to be exposed to a population in which fewer individuals were exposed at different levels with heterogeneity by the value of an additional variable (above and below the dotted line). Broadly we refer to B as an “exposure effect,” and C, D, and E as “population intervention effects.”

In contrast to population average causal effects (Figure B), population attributable effects require only a single counterfactual exposure distribution, as one of the two groups being compared is the observed population (Figure part A). Population attributable effects may therefore be more readily applicable to questions of population interventions, which seek to alter the (observed, factual) exposure distribution of the world to improve population health.¹⁴ Unlike the population average causal effect, however, population attributable effects depend on the population prevalence of the exposure,¹⁴ which may be a particular consideration in transporting a population attributable effect to an external target population.^{14,15}

The Figure (D) shows a generalized intervention average causal effect (hereafter, generalized intervention effect) which compares observed exposure distribution (again identical to the observed exposure in Figure part A) to a counterfactual in which there is less exposure. Because “no exposure” is a special case of “less exposure,” the population attributable effect (Figure part C) is a special case of the generalized intervention effect (Figure part D). Generalized impact (or attributable) fractions were described by several authors^{33–35} in the 1980s; the estimation of the quantity in complex data was explored by Greenland and Drescher,³⁶ and can proceed either stochastically^{10,37} or deterministically.³³

A generalized intervention effect assumes that the intervention removes exposure with an equal probability among all participants (homogeneously with respect to participant characteristics). This is frequently not true: an intervention may incidentally succeed at removing a harmful exposure at a higher rate in one group (e.g., younger people) than another (older people), or may be deliberately targeted at a higher-risk group. In such a situation, the dynamic intervention average causal effect (hereafter, dynamic intervention effect) may be useful: the dynamic intervention effect compares the observed exposure distribution (Figure part A) to a counterfactual in which there are fewer exposed participants, allowing for heterogeneity in amount of exposure removed by the intervention within covariate-defined subpopulations.¹⁰ Figure part E shows a dynamic intervention effect: heterogeneity in the study sample is shown with the dotted line, and different amounts of exposure are removed on each side of the line. In general, for a fixed percentage of exposure removed (e.g., 20%) and a fixed intervention the generalized and dynamic intervention effects can be expected to differ if (i) there is heterogeneity of the causal effect of the exposure on the outcome by some set of covariates *Z*, and (ii) the effectiveness of the intervention at removing the harmful exposure differs by *Z*, either by design or happenstance (see Numerical eAppendix; <http://links.lww.com/EDE/B182> for an example.) The generalized intervention effect can thus be thought of as a special case of the dynamic intervention effect, under at least one homogeneity assumption (or in which the set of covariates *Z* is empty). Similar methods and concepts under varying names have been described and

applied elsewhere^{6–8,16,38,39} (see Technical eAppendix; <http://links.lww.com/EDE/B181> for discussion).

REMARKS

We remind the reader that for didactic purposes we are focusing on a binary, time-fixed, harmful exposure. With such an exposure, the population average causal effect (contrasting an entire population under all-exposed, all-unexposed conditions) is the default target of estimation in the bulk of the population health literature. Such a contrast was of primary interest to Neyman,⁴⁰ and is estimated by the vast majority of randomized trials.^{41,42} In particular, an intention-to-treat analysis of a randomized trial with a dichotomous exposure frequently estimates this contrast for treatment assignment, while compliance-corrected (or as-treated) analysis estimates this contrast for treatment received. Such “all/none” effects are typically what are estimated in observational analysis as well, using the default tools: standard regression approaches estimate covariate-conditional population average causal effects, while inverse probability weighting generally estimates marginal population average causal effects in a manner equivalent to total population standardization.^{43,44}

The fact that population average causal effects are the result of a contrast in two counterfactual exposure distributions may mean that they have less immediate and direct applicability to questions of setting policy at the population level,^{14,22} differing from measures which compare the factual exposure distribution with a counterfactual one. In broad terms, we therefore **consider the population attributable, and generalized and dynamic intervention effects to be population intervention effects^{6,14}** (in that they are tied to potential interventions on real-world exposure distributions), while we might think of the population average causal effect as an exposure effect (in that it contrasts all-exposed to none-exposed). These designations have fuzzy boundaries, and may coincide in certain settings: a smoking cessation intervention (which naturally targets only smokers) is an intervention in a population with 100% exposure prevalence (and thus the population average causal effect might coincide with the population attributable effect). Such measures may also coincide in community randomized trials of realistic interventions that may be immediately deployed on a large scale. This fuzziness aside, population intervention effects, especially when explicitly tied to real-world interventions,¹⁵ may better reflect real-world impacts than exposure effects; thus, population intervention effects may be of relatively higher utility to cost-effectiveness modelers and policy planners trying to understand how a particular intervention may affect total population health.

All contrasts discussed here will be interpretable as causal effects only under the usual causal identifiability assumptions or equivalents. A sufficient set includes exchangeability or conditional exchangeability⁴⁴ with positivity,⁴⁵ no versions of treatment or treatment variation irrelevance⁴⁶ or an alternative,⁴⁷ and correct model specification including attention to dependent

happenings.⁴⁸ The interpretation of population intervention effects as causal may require additional assumptions (or refinements in thinking about those assumptions). One key issue is the correct modeling of all consequences of an intervention, including (critically) assumptions about size of the population at risk (15 and 49 (p. 297)). Careful articulation of identifiability conditions for population intervention effects is a subject for future work, as are discussions of methods for estimation of such effects (although interested readers should see 10,25,29).

Here we have reviewed two broad categories (and several subtypes) of epidemiologic effect estimates: exposure effects and population intervention effects. While there is room for refinement, improvement, and expansion of this categorization, we believe that this vocabulary will help clarify discussions of causal effect estimation in epidemiology. This work may also help answer recent calls to focus on more “consequentialist” epidemiology,⁵⁰ which looks beyond individual causes of disease to interventions which improve population health, building bridges from exposures to population interventions, and thereby from patients to policy.

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