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Contrasting causal effects of workplace interventions

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Abstract

Occupational exposure guidelines are ideally based on estimated effects of static interventions that assign constant exposure over a working lifetime. Static effects are difficult to estimate when follow-up extends beyond employment because their identifiability requires additional assumptions. Effects of dynamic interventions that assign exposure while at work, allowing subjects to leave and become unexposed thereafter, are more easily identifiable but result in different estimates. Given the practical implications of exposure limits, we explored the drivers of the differences between static and dynamic interventions in a simulation study where workers could terminate employment due to an intermediate adverse health event that functions as a time-varying confounder. The two effect estimates became more similar with increasing strength of the health event and outcome relationship, and with increasing time between health event and employment termination. Estimates were most dissimilar when the intermediate health event occurred early in employment, providing an effective screening mechanism.

Keywords

Healthy-worker survivor effect; workplace interventions; dynamic interventions; static interventions

INTRODUCTION

Assessments of workplace risk are generally based on observational studies of occupational cohorts. Estimates from these studies are often subject to bias due to the healthy worker survivor effect (HWSE), a ubiquitous process that results in the healthiest workers accruing the most exposure over their lifetimes.^{1–4} The potential outcomes framework defines causal effects as contrasts between the distributions of counterfactual outcomes under hypothetical interventions.⁵ Counterfactuals may be defined under static regimens that assign exposure independently of a worker's characteristics, or under dynamic regimens that assign exposure according to a worker's observed past.

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Data and Code Availability: The code for simulating datasets and conducting analyses is provided in the eAppendix.

A static workplace intervention corresponds to a target trial^{6,7} in which workers hired into an industry at the start of their working lives are assigned a fixed exposure level until retirement age. The effects of static interventions reflect the biologic effect of exposure that would have been observed if workers did not select out of the workforce. Since workers that experience exposure-related adverse health outcomes tend to leave work, such strategies do not correspond to anything commonly observed in the real world. Given the paucity of observed data to estimate such effects, most estimates necessarily rely on the assumption of no unmeasured confounding between leaving work and the outcome.⁸

A dynamic intervention also corresponds to a target trial in which workers hired at the start of their working lives are assigned a fixed exposure level while at work; however, workers may leave and become unexposed for the remainder of follow-up. These strategies more closely resemble the real-world observed data, and their effects are more straightforward to estimate.

The US Occupational Safety and Health Administration (OSHA) is mandated to establish standards for occupational hazards that assure, “on the basis of the best available evidence that no employee will suffer material impairment of health or functional capacity, even if such employee has a regular exposure to the hazard dealt with by such standard for the period of his working life.”⁹ This directive is typically interpreted as requiring that OSHA risk assessments be based on static effects of 45 years of exposure.¹⁰ Since static effects are difficult to estimate¹¹, we conducted a simulation study to investigate the factors that drive differences between the static and dynamic measures in workplace studies.

METHODS

Motivated by typical aspects of occupational studies, we simulated 500 cohorts of 50,000 workers, under four scenarios, for a maximum follow-up of 20 years. For each worker and year t of follow-up, we simulated the indicators: $W(t)$, for active employment; $E(t)$ for workplace exposure; $Y(t)$, for the outcome; and $H(t)$, for the intermediate adverse health event, one of the mechanisms through which exposure affects the outcome. Exposure had a direct effect on the outcome in addition to that mediated by $H(t)$. We additionally simulated S , an indicator of a worker’s susceptibility to $H(t)$ and $Y(t)$. Only susceptible workers were at risk of experiencing $H(t)$ and $Y(t)$ and, once they experienced $H(t)$, workers maintained that status. Workers could only terminate employment if in poor health.

Defining the Interventions

We generated outcomes by setting the nodes $E(t)$ and $W(t)$ in the data generating system sequentially for each worker and year of follow-up. Our static interventions $\{d_{s,1}, d_{s,0}\}$ set exposure $E(t)$ to 1 or 0 respectively, and $W(t)$ to 1 for all years. The counterfactual outcomes $Y_{i,d_{s,1}}(t)$ and $Y_{i,d_{s,0}}(t)$ denote the outcomes that worker i would experience in year t if they were always at work, and respectively always exposed or unexposed.

Our dynamic interventions assigned exposure according to employment status. Intervention $d_{d,1}$ set exposure to 1 while a worker was actively employed and to 0 once the worker terminated employment. Intervention $d_{d,0}$ assigned workers to no exposure before and after

termination. The counterfactual outcomes $Y_{i,d_{d,1}}(t)$ and $Y_{i,d_{d,0}}(t)$ correspond to worker i 's outcome in year t if they were always exposed and unexposed while at work, respectively.

The causal relationships between the variables under the two interventions are presented in the directed acyclic graph (DAG) in Figure 1.

Simulation Scenarios

The eAppendix includes the data-generating equations, the *R* code used to create the datasets and results, and the distribution of covariates under intervention $d_{d,1}$ (eTable 1), for each scenario. In Scenario 1, $H(t)$ was predicted by cumulative exposure, and workers who experienced $H(t)$ terminated employment in the following year. $H(t)$ had a moderate effect on the probability of developing the outcome, as might be the case with asthma [$H(t)$] and chronic obstructive pulmonary disease [COPD, $Y(t)$]. Scenarios 2, 3, and 4 were compared to Scenario 1.

In Scenario 2, $H(t)$ was a stronger predictor of the outcome than in Scenario 1, as might be the case with abnormal lung function and COPD.

In Scenario 3 we altered Scenario 1 by increasing the time between $H(t)$ and leaving work. For example, years may pass before an asthmatic worker terminates employment due to worsening of symptoms. To reflect this temporal relationship, employment status was predicted by adverse health events occurring 10 years prior.

Finally, in Scenario 4 we altered the temporal relationship between the exposure and $H(t)$. Here $H(t)$ is an acute response that occurs in the first year of exposure, as may be the case if workers exposed to an irritant immediately experience severe asthma.

Comparing static and dynamic interventions

For each scenario, dataset, and worker, we generated four counterfactual outcomes: exposed and unexposed for both the static and dynamic interventions. The reported scenario-specific survival (Figures 2–4) and cumulative incidence (Table) estimates under each exposure level and intervention were averages across the 500 datasets. Static and dynamic exposure effects were measured by the risk differences (*RD*) contrasting the cumulative incidence of disease between exposed and unexposed workers. The ratio (*R*) of static and dynamic *RD*s represents the factor by which the risk among the exposed was reduced by early employment termination.

All datasets were simulated using the *simcausalR* package.¹² All analyses were performed in the *R* programming language, version 3.3.2.¹³

RESULTS

In the Table we report static and dynamic exposure effects for each scenario, and their ratios over time. In Scenario 1, a static effect of 0.42 indicates that the 20-year risk of disease if always exposed would be 42% greater than if unexposed. A dynamic effect of 0.07 indicates that, when workers terminated employment for health-related reasons, the 20-year risk was

only 7% greater if exposed while at work versus unexposed. The corresponding static-to-dynamic effect ratio of 6.00 in year 20 [$R_1(20) = 6.00$] indicates that the effect of exposure under a static intervention was six times stronger than under a dynamic intervention.

Figures 2 – 4 present comparisons of Scenarios 2, 3, and 4 with Scenario 1. For each scenario, we present survival curves for exposed and unexposed workers according to static and dynamic interventions. Survival probabilities were identical for the “never expose” regimen under both static and dynamic interventions; survival probabilities were smaller under the static “always expose” versus the dynamic “expose while at work” interventions (Figures 2–4).

The first comparison assesses how the static-to-dynamic effect ratio changes as a function of the strength of the intermediate health events and outcome relationship (Figure 2). Static and dynamic effects were more alike when intermediate health had a stronger effect on the outcome (Scenario 2), reflected by smaller ratios in Scenario 2 than in 1 (Table, $R_1(20) = 6.00$, $R_2(20) = 2.00$).

In Figure 3 we contrast Scenarios 1 and 3. Leaving work was determined by health status in the previous year in Scenario 1, but 10 years prior in Scenario 3. Static effects were the same in both scenarios (0.42). However, because exposed workers remained at work longer in Scenario 3, the dynamic effect was larger (0.07 vs. 0.32) and the ratio was smaller ($R_1(20) = 6.00$, $R_3(20) = 1.31$).

In Figure 4 we contrast Scenarios 3 and 4, where workers only experienced the adverse health event during their very first year of exposure. While static effects were similar in both scenarios (0.42 vs. 0.43), dynamic effects were smaller in Scenario 4 (0.07 vs. 0.05) and the ratio increased [$R_1(20) = 6.00$, $R_4(20) = 8.60$].

DISCUSSION

Static and dynamic interventions are expected to result in different exposure effect estimates.¹¹ We aimed to examine key features of the data generating distribution likely to drive the differences between static and dynamic intervention effects, since both can answer causal questions. This matter has practical implications in the context of the OSHA mandate: It is important to note that not all causal effects of the same exposure level, on the same disease, in the same population, over the same follow-up period, are necessarily equivalent.

Dynamic parameters better approximate static estimates if the consequences of exposure that cause leaving work are strongly related to the outcome, or if symptomatic workers remain at work despite declining health. In both cases, the amount of exposure accrued while actively employed already places workers at high risk for the outcome. Dynamic parameters generally provide conservative estimates of the disease risk associated with long-term exposure when the consequences of exposure that lead to leaving work occur early in employment. In this case, leaving work provides a screening mechanism for susceptible workers, while a larger proportion of unsusceptible survivors remain at work (eTable 1).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Abbreviations

HWSE	Healthy-worker survivor effect
RD	risk difference

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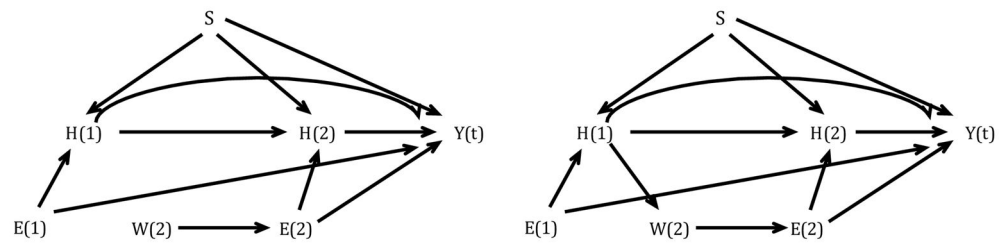


Figure 1. Directed acyclic graphs (DAGs) representing the relationships between variables in scenarios 1 under the static (a) and dynamic (b) regimens of interest

$E(t)$, $H(t)$, $W(t)$, $Y(t)$ denote workplace exposure, intermediate adverse health event, active employment status, and the outcome in year t . S is a baseline indicator of a worker's susceptibility to $H(t)$ and $Y(t)$ that modifies the effect of the exposure. The active employment ($W(2)$) and exposure ($E(1)$, $E(2)$) nodes are set rather than predicted by the past under the static regimen. Under the dynamic intervention, $H(1)$ predicts subsequent employment status ($W(2)$), which determines future exposure ($E(2)$).

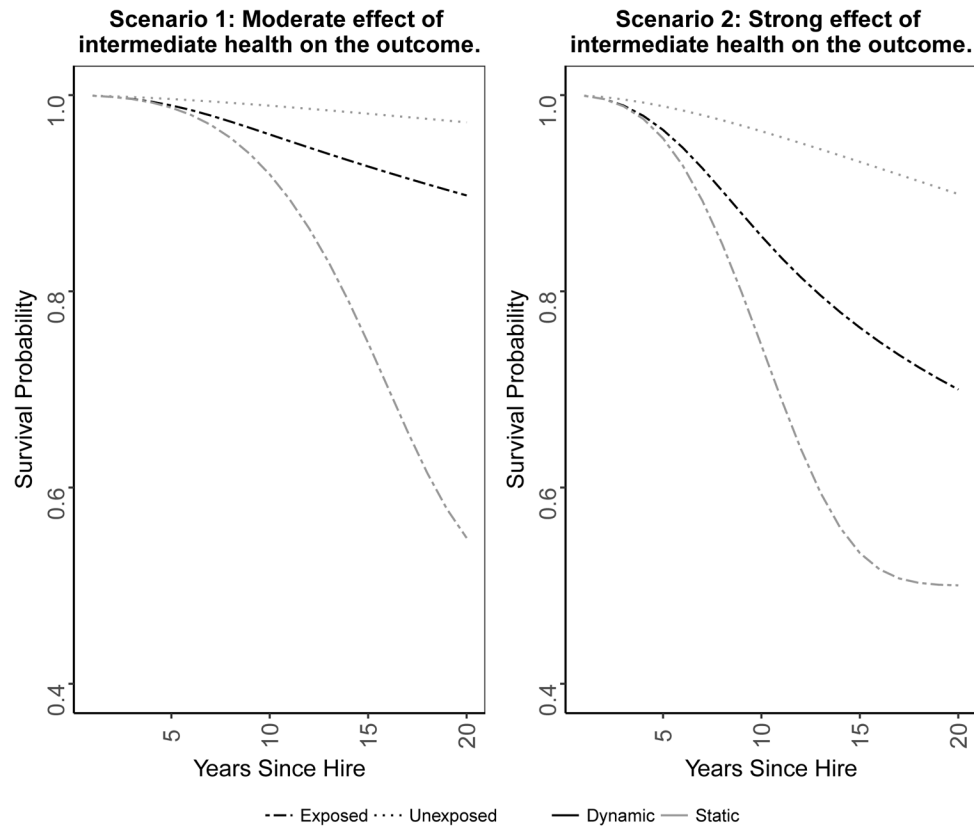


Figure 2. Evaluating the role of the intermediate health event - outcome relationship
Counterfactual survival curves among cohorts of exposed (dashed line) and unexposed (dotted line) workers following static (grey line) and dynamic (black line) interventions under Scenarios 1 and 2.

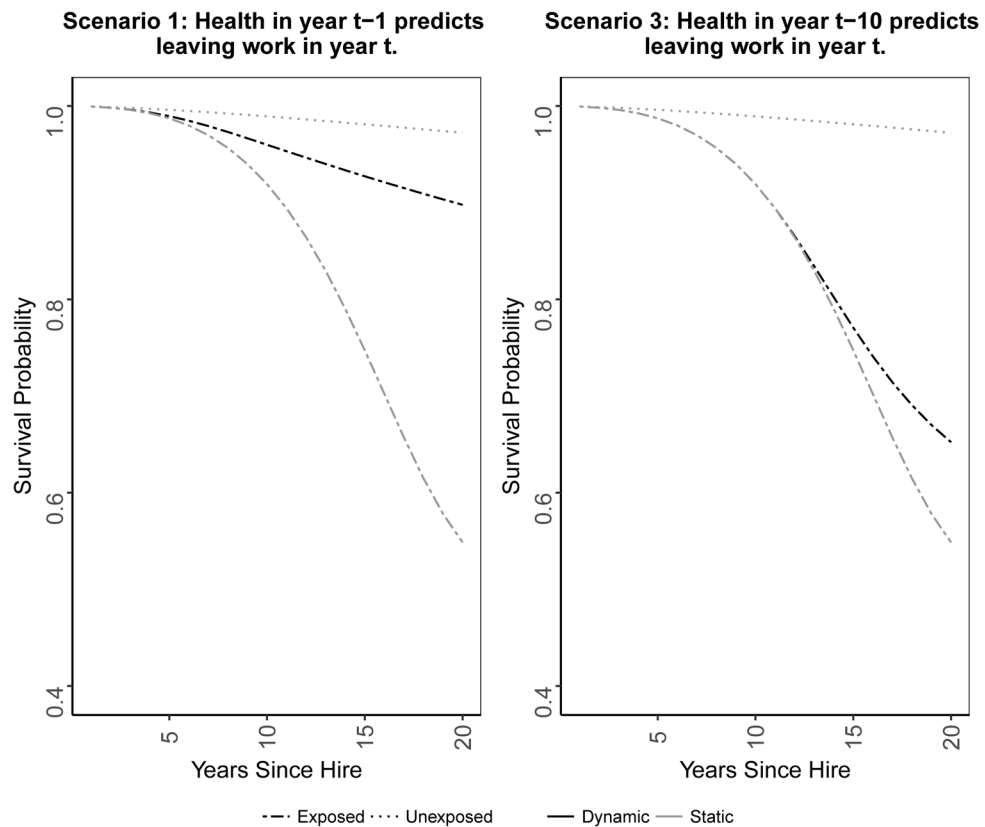


Figure 3. Evaluating the role of the temporal relationship between the intermediate health event and leaving work

Counterfactual survival curves among cohorts of exposed (dashed line) and unexposed (dotted line) workers following static (grey line) and dynamic (black line) interventions under Scenarios 1 and 3.

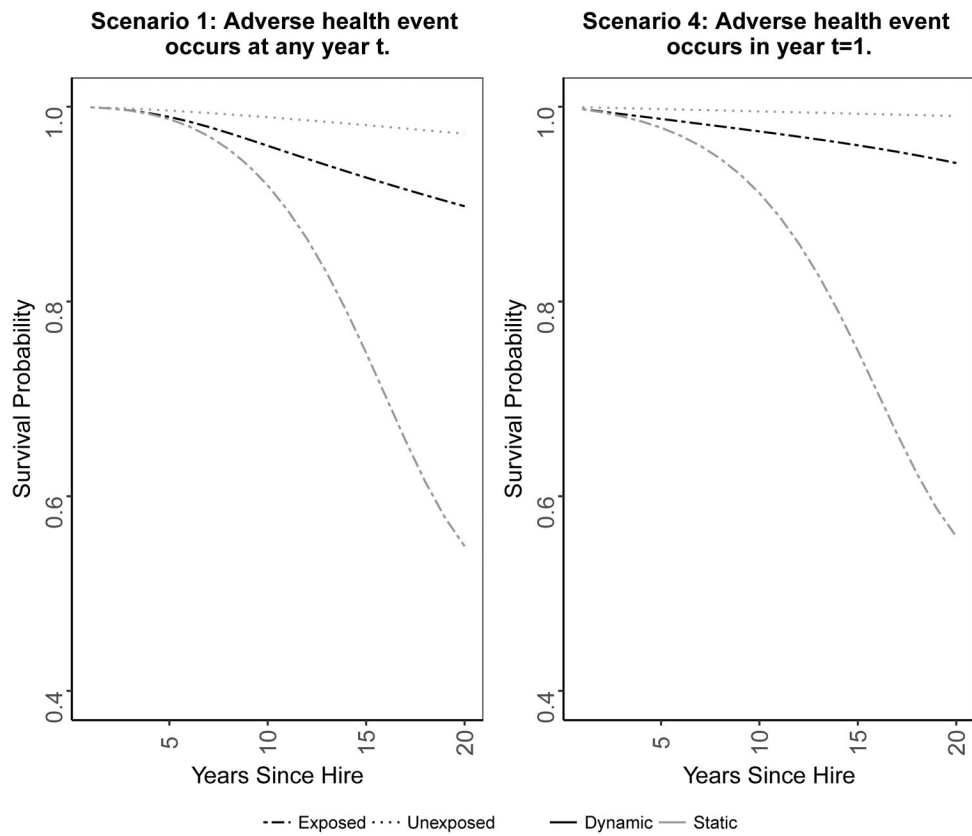


Figure 4. Evaluating the role of the temporal relationship between exposure and the intermediate health event

Counterfactual survival curves among cohorts of exposed (dashed line) and unexposed (dotted line) following static (grey line) and dynamic (black line) interventions under Scenarios 1 and 4.

Table

Risk difference (RD) estimates for static and dynamic interventions, as well as the ratios (R) of static and dynamic risk differences, over time (t).

	Year of follow-up									
	t = 2	t = 4	t = 6	t = 8	t = 10	t = 12	t = 14	t = 16	t = 18	t = 20
Scenario 1^a										
Static RD	0.00	0.00	0.01	0.04	0.07	0.12	0.19	0.28	0.36	0.42
Dynamic RD	0.00	0.00	0.01	0.02	0.03	0.04	0.05	0.06	0.07	0.07
$R_1(t)$	--	--	1.00	2.00	2.33	3.00	3.80	4.67	5.14	6.00
Scenario 2^b										
Static RD	0.00	0.02	0.06	0.13	0.22	0.31	0.38	0.41	0.41	0.40
Dynamic RD	0.00	0.01	0.04	0.07	0.11	0.14	0.16	0.18	0.19	0.20
$R_2(t)$	--	2.00	1.50	1.86	2.00	2.21	2.38	2.28	2.16	2.00
Scenario 3^c										
Static RD	0.00	0.00	0.01	0.04	0.07	0.12	0.19	0.28	0.36	0.42
Dynamic RD	0.00	0.00	0.01	0.04	0.07	0.12	0.18	0.24	0.29	0.32
$R_3(t)$	--	--	1.00	1.00	1.00	1.00	1.06	1.17	1.24	1.31
Scenario 4^d										
Static RD	0.00	0.01	0.03	0.05	0.08	0.13	0.20	0.29	0.37	0.43
Dynamic RD	0.00	0.01	0.01	0.02	0.02	0.03	0.03	0.04	0.04	0.05
$R_4(t)$	--	1.00	3.00	2.50	4.00	4.33	6.67	7.25	9.25	8.60

^aScenario 1: The intermediate health had a moderate effect on the outcome, it could occur in any year t , and the intermediate health event in year $t-1$ predicted leaving work in year t .

^bScenario 2: The intermediate health event had a stronger effect on the outcome than in Scenario 1. All other relationships between variables were as in Scenario 1.

^cScenario 3: The intermediate health event in year $t-10$ predicted leaving work in year t . All other relationships between variables were as in Scenario 1.

^dScenario 4: The intermediate health event could only occur during the first year, $t=1$. All other relationships between variables were as in Scenario 1.