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Can't WaSH without water

Jacob Bor

Improved water and sanitation are among the oldest and most effective public health interventions. Investments in water infrastructure in U.S. cities in the early 20th century reduced child mortality by half (Cutler & Miller 2005). Today, about 800,000 children die from diarrheal illness each year, the vast majority in sub-Saharan Africa and South Asia (CDC Fact Sheet). Frequent diarrheal illness keeps children out of school (Miguel & Kremer 2004) and can lead to long run deficits in physical and cognitive development. Surely, there are few more glaring injustices in public health than the persistence of disease easily prevented by technologies scaled up in rich countries a century ago.

In this issue of *Epidemiology*, Freeman et al. assess the impact of a randomized school-based water, sanitation, and hygiene (WaSH) intervention on prevalence of diarrhea among pupils. The intervention, implemented in western Kenya in 2007–2009, was multifaceted: water supplies were treated with chlorine, students were educated about hand-washing and soap provided, latrines were built where existing facilities were sub-standard, and water was delivered to a subset of schools where water was not previously available. Intention-to-treat (ITT) analysis of these data showed that the intervention reduced diarrhea prevalence among students at water-scarce schools but not in water-available schools (Freeman et al. 2014).

As is common in effectiveness trials, not all schools participating in the study implemented their assigned intervention. As a result, the ITT effect – the effect of being assigned the WaSH intervention – under-estimates the true effect of the intervention itself. In this paper, Freeman et al. use an instrumental variables (IV) framework to recover this effect. The authors find that among water-scarce schools, implementation of two or three WaSH components reduced diarrhea prevalence by 72% (95% CI: 25%, 90%) relative to levels that would have been observed had those same schools implemented zero or one WaSH components. The schools that implemented more intervention components were more likely than other schools to have had high diarrhea prevalence in the absence of the intervention, an indication of self-targeting. Finally, adherence to the intervention was relatively high and there was no evidence that low adherence explained the null results of WaSH in the water-available schools.

Using IV to unpack trial results

When an intervention is randomly (or quasi-randomly (Bor et al. 2014)) assigned but uptake is incomplete, IV can be used to identify the intervention effect among the units induced to take up the intervention because of their treatment assignment i.e., among so-called compliers). This parameter – known as a local average treatment effect (LATE) (Imbens & Angrist 1994) or complier average causal effect (CACE) – preserves randomization and has a causal interpretation under well-defined assumptions. Despite the long availability of

instrumental variables approaches (Imbens & Angrist 1994; Robins 1994), trials still rarely report CACE, more frequently reporting “as treated” or “per protocol” analyses that lack a causal interpretation (Steele et al. 2015).

There has been a proliferation of methodological research on instrumental variables in the past decade, with new IV methods proposed for different types of data, different causal estimands, and identified under different assumptions (Hernán & Robins 2006; Clarke PS & Windmeijer 2012). Yet these methods have been slow to penetrate the clinical trials literature (Steele et al. 2015). Reasons for slow uptake may include the lack of agreement on a single “best” approach, different assumptions invoked, and different approaches to estimation. Freeman et al. use a Weighted Generalized Structural Nested Mean Model, which builds on past approaches (Robins 1994) and was developed for this specific application (Brumback et al. 2014).

Perhaps one of the overlooked strengths of IV is its value in helping to interpret the ITT. Imagine two types of patients (or schools as in Freeman et al.): patients whose actual treatment status was induced by randomization (so-called compliers) and patients whose treatment status was not influenced by randomization. IV conceptualizes the ITT as a weighted sum: the effect of the treatment in compliers and a null effect for all other units.

$$ITT = P(\text{Complier}) * E[Y(1) - Y(0) | \text{Complier}] + (1 - P(\text{complier})) * 0$$

This statement is true under two untestable assumptions – (i) that randomized treatment assignment only affects outcomes through treatment uptake (exclusion restriction) and (ii) that treatment assignment only affects treatment uptake in one direction (monotonicity). Rearranging yields the formula for CACE:

$$CACE = E[Y(1) - Y(0) | \text{Complier}] = \frac{ITT}{P(\text{Complier})} = \frac{E[Y | Z=1] - E[Y | Z=0]}{E[T | Z=1] - E[T | Z=0]}$$

where $Y(1)$ and $Y(0)$ are potential outcomes if treated/not treated, T is the treatment indicator, and Z is the instrument, e.g. randomized assignment. In other words, IV is just the ratio of the ITT effect to the effect of randomization on treatment uptake. CACE is interpretable as a risk difference, but simple formulas are also available to compute the Causal Relative Risk, $CRR = E[Y(1) | \text{Complier}] / E[Y(0) | \text{Complier}]$ using information on $E[Y | Z=1, T=1]$ and $E[Y | Z=0, T=1]$ (Hernán & Robins 2006).

I review the CACE derivation (Imbens & Angrist 1994) to make three points. First, IV can be estimated with no assumptions about the distribution of the outcome variable, the functional forms of the relationships between instrument, treatment and outcome, and no assumptions about the absence of effect modification. CACE is broadly applicable to trial settings regardless of whether the outcome is binary, count, or continuous. CACE is also generalizable to the scenario where the exposure is a count variable or measure of treatment intensity, as in Freeman et al. The same ratio estimator can be used, albeit with a slightly different interpretation: it is a weighted average of causal responses to a one-unit change in

the treatment, evaluated across the change in the exposure distribution induced by randomization (Angrist & Imbens 1995).

Second, the formula emphasizes the simplicity of IV. CACE is just a ratio and can be calculated by hand. To improve communication of study findings, trials conducting IV analyses might consider presenting unadjusted CACE results with estimates of all quantities in the numerator and denominator of the CACE formula, alongside any alternative IV models that make additional assumptions and/or include adjustment for covariates. This would be analogous to the standard practice of showing crude ITT estimates whenever an adjusted ITT is also reported.

For example, in Freeman et al., the intervention increased the average number of WaSH components implemented from 0.36 to 1.7 at water-scarce schools. Dividing the intent to treat risk difference by this change in exposure yields a CACE estimate of a $(3.4\% - 8.9\%) / (1.7 - 0.36) = -4.1$ percentage point decline in diarrhea prevalence per WaSH component implemented due to the intervention. The median school shifted from having zero WaSH components to two components, and this two-unit change would translate into a -8.2 percentage point change in the probability of diarrhea. These results are comparable to the -10 percentage point risk difference implied by the authors IV results in Table 3.

Third, the formula provides a clear model for how to think about the ITT. The promise of IV is that if you can identify a scenario in which you are willing to make exclusion restriction and monotonicity assumptions, then you can decompose the ITT into the effect of randomization on treatment uptake times the causal effect of the treatment for those induced to take up. IV therefore focuses attention on the actual implementation of the intervention (Table) and can illuminate whether the ITT is the result of a very large effect in a few units that implemented the assigned intervention or a smaller effect among many. Further, the IV framework can provide insight into the extent to which heterogeneous ITT effects can be explained by differences in intervention uptake or whether the intervention itself had different effects in different subgroups. This is the question posed by Freeman et al.

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With these reflections, I turn to a closer look at the study results. In schools with pre-existing water supplies, water treatment and hygiene education had no ITT effect on diarrhea, PR = 1.1 (0.67–1.7); building latrines had little effect, PR = 0.88 (CI not reported); and doing all three had no effect, PR = 0.94 (0.61–1.5). The authors hypothesize that low adherence may explain these null findings. And yet the intervention increased availability of safe water from 2% to 82% of schools, the availability of soap from 0% to 47% of schools, and the presence of acceptable latrines from 45% to 71% of schools relative to the control schools (Table). The WaSH intervention was implemented; it just didn't work. These results are puzzling given the strong theoretical basis for the intervention components. Yet they must be reckoned with.

In contrast, the combination of the same WaSH interventions *plus de novo clean water provision* in water-scarce schools reduced diarrhea prevalence by 62% (95% CI: 27%, 80%).

These schools had similar adherence to the intervention as the water-available schools (Table). Differences in the ITT were not due to differences in adherence as originally hypothesized. Under IV assumptions and as shown in the CACE formula, any differences in the ITT across groups not explained by adherence must be explained by differences in CACE. The intervention reduced diarrhea in water-scarce schools where it was implemented but not in water-available schools where it was implemented.

There are a number of possible explanations for these seemingly contradictory findings, but certainly, one of the simplest is that access to water – not latrines, soap, and water treatment – was the critical intervention in the water-scarce schools. Without access to clean water, hands cannot be washed and drinking water may be obtained from contaminated sources. Evidence on outbreaks of diarrheal illness during droughts is certainly consistent with such a relationship (Stanke et al. 2013). Interestingly, the intervention had no effect on availability of acceptable latrines and therefore latrines can be ruled out as a mechanism for this effect (Table).

This interpretation has important caveats. Baseline water-scarcity was not randomized and therefore school characteristics other than scarcity may modify the effect of the other WaSH components. Differential exposure to pathogens that cause diarrheal illness would be an obvious candidate. In addition, it is unclear whether the provision of clean water would have had the same impact in the water-scarce schools had the other WaSH components not been implemented. Future research could test this hypothesis directly by randomizing water-scarce schools to water delivery alone, to the package of other WaSH components, or to water delivery plus WaSH. It also bears mentioning that the efficacy of centralized water provision depends critically on the safety of the water provided; let the Broad Street Pump enter the evidence as Exhibit A. Finally, it is possible that although WaSH did not reduce diarrhea prevalence in water-available schools at the time of follow-up, these interventions may limit the epidemic of diarrheal illness and that a longer follow-up observation period would have revealed impact.

When there is a large burden of disease preventable with cheap interventions, it may seem crass to ask which components are most effective. And yet, in real-life (non-trial) implementation, it is rare that all components of WaSH are delivered together. The fact that hand-washing, latrines, and chlorine tablets can be provided by the market in a way that centralized water infrastructure and resource management policy cannot illustrates the challenge of implementing truly comprehensive WaSH interventions and offers an additional economic (and political) rationale to prioritize public investments in water availability. The potential link between water-scarcity and diarrheal illness is particularly ominous given desertification associated with climate change and rapid population growth in arid areas. The authors have identified a critical avenue for further research. If access to water has a strong causal effect on diarrheal illness, then long run planning for population health amidst a changing ecology must consider these impacts.

Biography

JACOB BOR is Assistant Professor of Global Health and Epidemiology at Boston University School of Public Health. His research uses quasi-experimental methods to evaluate global health interventions, with a focus on HIV treatment and prevention.

References

- Angrist JD, Imbens GW. Two-stage least squares estimation of average causal effects in models with variable treatment intensity. *Journal of the American statistical Association*. 1995; 90(430):431–442.
- Bor J, Moscoe E, Mutevedzi P, Newell ML, Bärnighausen T. Regression discontinuity designs in epidemiology: causal inference without randomized trials. *Epidemiology*. 2014; 25(5):729–737. [PubMed: 25061922]
- Brumback BA, He Z, Prasad M, Freeman MC, Rheingans R. Using structural-nested models to estimate the effect of cluster-level adherence on individual-level outcomes with a three-armed cluster-randomized trial. *Stat Med*. 2014; 33(9):1490–1502. [PubMed: 24288357]
- CDC. [Accessed 19 May 2016] Diarrhea: Common Illness, Global Killer. Centers of Disease Control and Prevention. US Department of Health and Human Services. <http://www.cdc.gov/healthywater/pdf/global/programs/globaldiarrhea508c.pdf>
- Clarke PS, Windmeijer F. Instrumental Variable Estimators for Binary Outcomes. *Journal of the American Statistical Association*. 2012; 107(500):1638–1652.
- Cutler D, Miller G. The role of public health improvements in health advances: the twentieth-century United States. *Demography*. 2005; 42(1):1–22. [PubMed: 15782893]
- Freeman MC, Clasen T, Dreifelbis R, Saboori S, Greene LE, Brumback B, Muga R, Rheingans R. The impact of a school-based water supply and treatment, hygiene, and sanitation programme on pupil diarrhoea: a cluster-randomized trial. *Epidemiol Infect*. 2014; 142(2):340–351. [PubMed: 23702047]
- Hernán MA, Robins JM. Instruments for causal inference: an epidemiologist's dream? *Epidemiology*. 2006; 17(4):360–372. [PubMed: 16755261]
- Imbens GW, Angrist JD. Identification and Estimation of Local Average Treatment Effects. *Econometrica*. 1994; 62(2):467–475.
- Miguel E, Kremer M. Worms: identifying impacts on education and health in the presence of treatment externalities. *Econometrica*. 2004 Jan 1; 72(1):159–217.
- Robins JM. Correcting for Noncompliance in Randomized Trials Using Structural Nested Mean Models. *Communications in Statistics-Theory and Methods*. 1994; 23(8):2379–2412.
- Stanke C, Kerac M, Prudhomme C, Medlock J, Murray V. Health Effects of Drought: a Systematic Review of the Evidence. *PLOS Currents Disasters*. 2013 Jun 5. Edition 1.
- Steele RJ, Shrier I, Kaufman JS, Platt RW. Simple Estimation of Patient-Oriented Effects From Randomized Trials: An Open and Shut CACE. *American Journal of Epidemiology*. 2015; 182(6): 557–566. [PubMed: 26283090]

Table

Changes in the Exposure Distribution Across Randomization Arms

	Water-scarce schools		Water-available schools		
	A. Control (n=25)	B. HP&WT+San +Wat (n=25)	C. Control (n=44)	D. HP&WT (n=44)	E. HP&WT +San (n=45)
None	16 (64%)	1 (4%)	23 (53%)	3 (7%)	4 (9%)
Latrine	9 (36%)	9 (36%)	20 (45%)	24 (55%)	32 (71%)
Soap	0 (0%)	14 (56%)	0 (0%)	15 (34%)	21 (47%)
Safe Water	0 (0%)	10 (40%)	1 (2%)	34 (77%)	37 (82%)
Average number of components	0.36	1.7	0.48	1.7	2.0