We performed a systematic literature review of all studies that used IV methods in observational studies of relatively well-defined medical interventions. We searched for references published on PubMed, Embase, PsycInfo, Web of Science, and Econlit through 15 October 2012. The key search term in all search engines was ‘instrumental variable\*’; for PsycInfo, Web of Science, and Econlit, we refined this search by further requiring at least one of the following keywords: drug\*, medicat\*, medicine\*, treatment (and variants), therapy (and variants), pharmacol\*, pharmaceut\*, vaccin\*, innocul\*, and prescrib\*. This resulted in 3,638 hits or 2,269 unique publications. Titles and abstracts were reviewed, and 2,084 of these articles were excluded for not meeting our inclusion criteria. Of the 185 remaining, 106 more were excluded, either because the exposure was not a well-defined medical intervention (N=33), there was no implementation of standard IV methods (N=38), the study design was a randomized trial (N=11), or we had found a recently published abstract with no related publication (N=24). After reviewing references in the included articles, one study was added to our review; we further added the Davies et al study published in the same issue of this journal. Thus, our literature review included 81 studies.1-81

This issue of EPIDEMIOLOGY includes another review of IV applications by Davies et al. 82 The eligibility criteria of the reviews differed, as they asked different questions. We required a relatively well-defined single medical intervention as an exposure, while Davies et al included any clinical exposure. We excluded studies that did not use standard IV methods, while some papers in Davies et al included ‘adaptations’ of IV methods. Davies et al restricted to studies with clinical outcomes, while we had no limits set on outcome type (e.g., some outcomes in our review are economic). Davies et al excluded theoretical papers and reviews; we included any such paper that presented an IV application using observational data. The two reviews share 54 studies. We include 27 studies not included by Davies et al. and they include 36 not included in our review.

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Supplementary Figure. Summary of Literature Review

N=3,638 references retrieved

N=743 PubMed

N=847 Embase

N=504 PsycInfo

N=1,110 Web of Science

N=434 Econlit

N=2,269 unique titles and abstracts reviewed

N=185 full articles reviewed further

N=79 articles met inclusion and exclusion criteria

N=81 articles included in the literature review

N=1,369 duplicates removed

N=2,084 articles excluded

N=106 articles excluded

N=33 not well-defined exposure

N=38 not an IV application

N=11 RCTs

N=24 recently published abstracts

with no related publication

N=1 added article after reviewing bibliographies

N=1 added article in this issue of Epidemiology