

Primary Non-adherence to Prescribed Medications

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To the Editors:—Fisher et al.'s paper¹ highlights the largely ignored problem of primary non-adherence (i.e., failure to ever fill a new prescription). While we applaud the authors for leveraging electronic-prescribing (e-prescriptions) records to evaluate this component of adherence, we are concerned that the prevalence of primary non-adherence is substantially overestimated. This type of research is particularly vulnerable to differential misclassification bias, because every new fill not captured is misclassified as non-adherence. The authors listed inability to crosslink e-prescriptions with claims when paid in cash or fills made at out-of-plan pharmacies (e.g., the Veterans Administration) as possible limitations. Claims may also be absent if benefit medication caps are exceeded. Stripping individual identifiers to protect confidentiality precludes verification that matching algorithms function correctly. Cross-walking databases between non-integrated systems is complicated by differing database architectures, and no standard approaches exist for performing database cross-walks. The authors suggested the need for comparisons of findings from other settings.

In 2009, we published rates of primary medication non-adherence among 27,329 patients with diabetes.² Observed primary non-adherence rates were several-fold lower than those reported by Fisher et al. (e.g., 4% vs. 33.5% for diabetes medications). Among the primary adherent patients in our study, 18% of patients failed to ever refill, thus presenting a much larger adherence issue than the 4% primary non-adherence.

There are some noteworthy study differences. Our population included only patients with diabetes, while Fisher et al. included a general population. Kaiser operates a "closed pharmacy" system, where pharmacy benefits are only honored at Kaiser pharmacies, minimizing under-ascertainment of

pharmacy utilization among benefited patients. Paper prescriptions have been largely retired at Kaiser and replaced by electronic prescriptions that are transmitted directly to the Kaiser pharmacy, within an integrated database system. This facilitates unique matching on an individual level.

In summary, we recommend caution if using the primary non-adherence estimates presented by these authors in a quantitative way. From an operations perspective, too many false-positive alerts to physicians regarding their patients not taking medications may cause such reporting to be ignored because it loses meaning. Nonetheless, the public health message of the Fisher et al. paper and our paper are completely aligned: early stage non-adherence needs clinical attention. Providers should not assume that every medication they prescribe is filled (or refilled). This is critical, for just as medication cannot work if it is not taken, it cannot be taken if it is not obtained.

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