

## Publication

### Operationalization and validation of a novel method to calculate adherence to polypharmacy with refill data from the Australian pharmaceutical benefits scheme (PBS) database

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Electronic health care data contain rich information on medicine use from which adherence can be estimated. Various measures developed with medication claims data called for transparency of the equations used, predominantly because they may overestimate adherence, and even more when used with multiple medications. We aimed to operationalize a novel calculation of adherence with polypharmacy, the daily polypharmacy possession ratio (DPPR), and validate it against the common measure of adherence, the medication possession ratio (MPR) and a modified version (MPR; m; ). We used linked health data from the Australian Pharmaceutical Benefits Scheme and Western Australian hospital morbidity dataset and mortality register. We identified a strict study cohort from 16,185 patients aged  $\geq 65$  years hospitalized for myocardial infarction in 2003-2008 in Western Australia as an illustrative example. We applied iterative exclusion criteria to standardize the dispensing histories according to previous literature. A SAS program was developed to calculate the adherence measures accounting for various drug parameters. The study cohort was 348 incident patients (mean age 74.6 $\pm$ 6.8 years; 69% male) with an admission for myocardial infarction who had cardiovascular medications over a median of 727 days (range 74 to 3,798 days) prior to readmission. There were statins (96.8%), angiotensin converting enzyme inhibitors (88.8%), beta-blockers (85.6%), and angiotensin receptor blockers (13.2%) dispensed. As expected, observed adherence values were higher with mean MPR (median 89.2%; Q; 1; : 73.3%; Q; 3; : 104.6%) than mean MPR; m; (median 82.8%; Q; 1; : 68.5%; Q; 3; : 95.9%). DPPR values were the most narrow (median 83.8%; Q; 1; : 70.9%; Q; 3; : 96.4%). Mean MPR and DPPR yielded very close possession values for 37.9% of the patients. Values were similar in patients with longer observation windows. When the traditional threshold of 80% was applied to mean MPR and DPPR values to signify the threshold for good adherence, 11.6% of patients were classified as good adherers with the mean MPR relative to the DPPR. In the absence of transparent and standardized equations to calculate adherence to polypharmacy from refill databases, the novel DPPR algorithm represents a valid and robust method to estimate medication possession for multi-medication regimens.

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