

# Customized adherence estimation for polypharmacy: Validation of new algorithms to combine dispensing, prescription, and hospitalization data

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**Background** Tailored adherence management requires accurate measurement of medication use, accounting for polypharmacy, dose adjustments, and treatment interruptions. Administrative healthcare data are increasingly used to estimate adherence and identify patients for targeted interventions, but methodological heterogeneity and proprietary algorithms lead to inconsistent and unreliable results.

**Purpose** We aimed to implement new functions to improve accuracy and transparency for estimating adherence to polypharmacy in AdhereR, an open-source package for the statistical software R. The functions were validated with a set of patients with cystic fibrosis (CF).

**Method** We implemented functions to combine dispensing, prescription, and hospitalization data and estimate adherence to polypharmacy. We estimated adherence as continuous medication availability (CMA), using the simple CMA7 function in AdhereR. We considered 4 aggregation methods for polypharmacy: a) any treatment available, b) all treatments available, c) unweighted mean of CMA for individual treatments, d) mean of CMA for individual treatments, weighted by treatment episode. Treatments were grouped by ATC codes on the 4th level (chemical subgroup). For validation, we used prospective data from medical records from four CF centers in the Rhône-Alpes region (France) linked to regional health insurance claims data.

**Findings** We analyzed data from 228 patients (135 children and 93 adults, median age = 15.5 years [range 0.1-65.8 years]), available for the years 2014-2016. We calculated adherence during the year 2015 for medications dispensed at least once during the 3-year follow-up window. Median number of CF chronic medications prescribed was 10 (range 1-21) for adults and 7 (range 1-16) for children. Patients experiencing dosage changes, treatment interruptions, and hospitalizations were 59.0%, 14.4%, and 25.4% of the sample, respectively. When accounting for these events, mean adherence estimations were 93.5% (any treatment available), 18.6% (all treatments available), 62.0% (unweighted mean), and 63.5% (weighted mean), respectively. For patients experiencing dosage changes, treatment interruptions, or hospitalizations, weighted means of CMAs were up to 24% higher when not considering such events.

**Conclusion** Dosage changes, treatment interruptions, and hospitalizations may have a substantial impact on adherence estimates. Different methods to calculate adherence for polypharmacy may affect adherence rates considerably. The novel functions in AdhereR can account for these variations in a reproducible and transparent way, and thus improve targeted and tailored adherence management.