The Missing Puff: Results of Multiple Imputation of Percent Predicted FEV1 in CPRD

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DISCLOSURES

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BACKGROUND

- Severity of chronic pulmonary obstructive disease (COPD), with the key component of percent predicted forced expiratory volume in 1 second (ppFEV1), is an important predictor of COPD outcomes and mortality.

OBJECTIVE

- To evaluate the effect of *missingness* in ppFEV1 for the assessment of COPD severity using spirometry and symptoms data from the Clinical Practice Research Datalink.
- To estimate mortality rates and rate ratios (RRs) adjusting by COPD severity when complete case analysis (CCA) and multiple imputation (MI) are used.

METHODS

- Cohort study of new users of aclidinium and long-acting beta$_2$-agonist (LABA) medications between 2012 and 2015, aged ≥ 40 years, with COPD.
- Severity of COPD was classified using the GOLD 2016 COPD severity categories (Figure 1) at the time of starting a study drug (start date).

Figure 1. Model of Symptoms/Risk of Evaluation for Severity of COPD[1]

GOLD classification of airflow limitation[a]	COPD Severity Categories		Exacerbation history
GOLD 3 or 4 (% predicted FEV1 < 50%)	C	D	≥ 2 or ≥ 1 leading to hospitalization
GOLD 1 or 2 (% predicted FEV1 ≥ 50%)	A	B	≤ 1 and not leading to hospitalization
	mMRC 0-1 or CAT < 10 or Breathlessness absent	mMRC ≥ 2 or CAT ≥ 10 or Breathlessness present	

CAT = COPD Assessment Test; mMRC = modified Medical Research Council.

COPD severity categories: A = Low risk, fewer symptoms; B = Low risk, more symptoms; C = High risk, fewer symptoms; D = High risk, more symptoms.

In some patients, the three ways of assessing risk of exacerbations (ppFEV1, exacerbations, hospitalizations) will not lead to the same level of risk; in this case, the risk should be determined by the method indicating the highest risk.

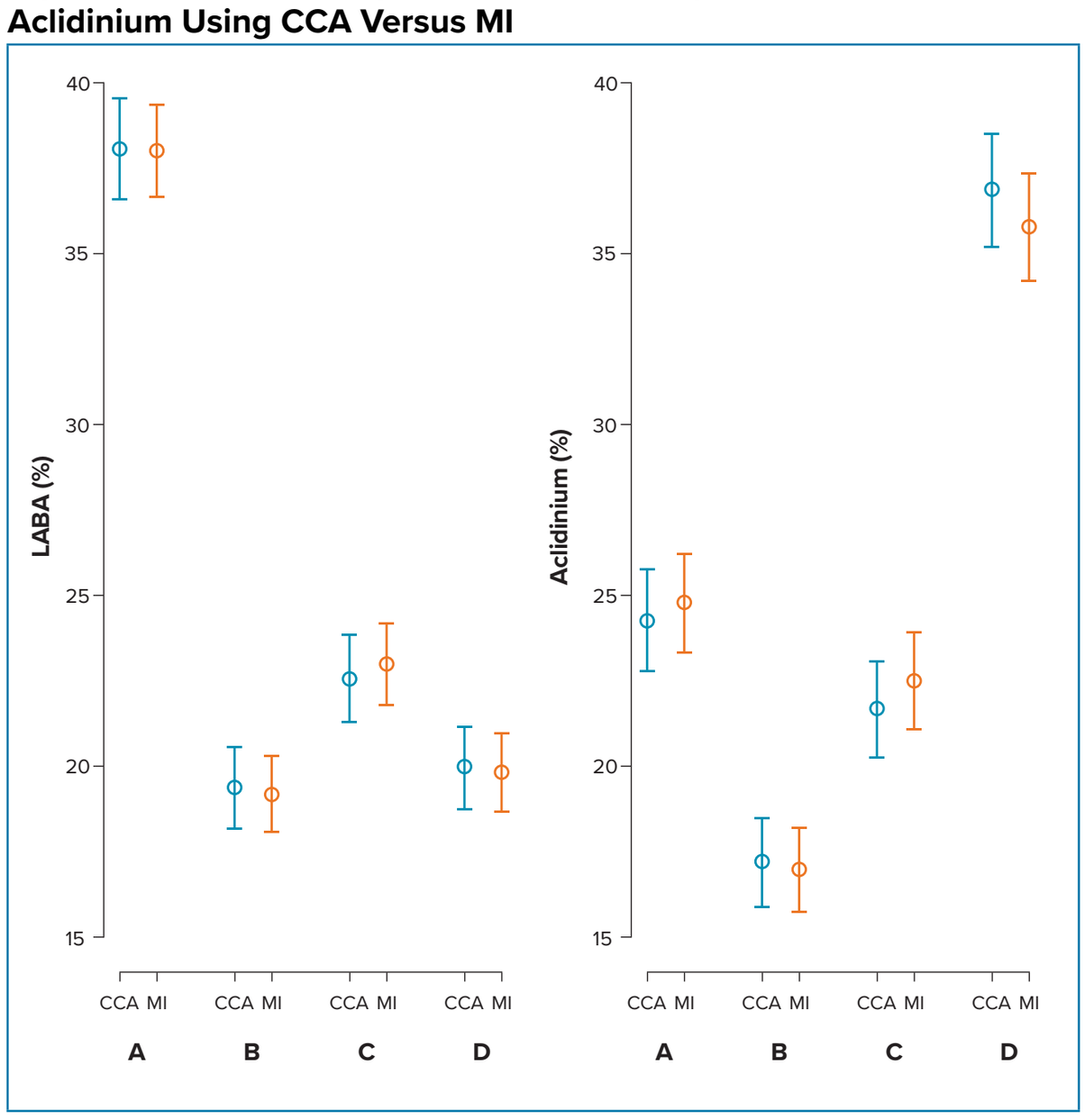
[a] The ppFEV1 was defined based on the most recent spirometry data on ppFEV1, expected FEV1, and actual FEV1 within 5 years prior to the start date. When data on ppFEV1 were not available, the ppFEV1 was calculated as follows: ppFEV1 = (FEV1 measurement/expected FEV1) × 100, using expected and measured FEV1 recorded closest to the start date within 5 years prior. When no data on expected FEV1 were recorded, the ppFEV1 was calculated by applying the Global Lungs Initiative European Respiratory Society Task Force (TF 2009-03) formulas based on the measured FEV1, age, sex, height, and ethnicity.[2]

- The mortality rates and RRs (aclidinium vs. LABA) were obtained using a negative binomial regression model adjusting for COPD severity, sex, age, smoking status, and body mass index (BMI). CCA and MI were employed to account for missing data on ppFEV1. MI was performed using the fully conditional specification method with 10 imputations. The imputation model included the outcome, exposure, available FEV1 and ppFEV1, and the following a priori relevant variables at start date:
  - Demographic and lifestyle variables: age, gender, body mass index, smoking status and race/ethnicity
  - Medical history (ever before the start date): emphysema, asthma, pneumonia, ischemic heart disease, heart failure, cerebrovascular disease, and Charlson Comorbidity Index score
  - Medications (up to 3 months prior to start date): cardiovascular medications, nebulizers, antibiotics, long-acting muscarinic antagonists (LAMAs), LABAs + inhaled glucocorticosteroids (ICSs), LABAs, ICSs, and oral glucocorticoids
  - Number of prescriptions for respiratory medications (up to 1 year prior to start date)

RESULTS

- The study included 3,555 new users of aclidinium and 4,797 new users of LABAs. Spirometry results on ppFEV1 (recorded or estimated) were missing for 12.4% of the patients. Approximately 72% of the patients with available data had a ppFEV1 > 50%.
- Figure 2 shows minor differences in the distribution of COPD severity among users of aclidinium and LABAs using CCA versus MI.

Figure 2. COPD Severity Distribution Among Users of LABAs and Aclidinium Using CCA Versus MI



- The adjusted mortality rates per 1,000 person-years for aclidinium and LABA users were somewhat higher when using MI versus CCA (Table 1).

Table 1. Adjusted Mortality Rates (95% CI) per 1,000 Person-Years

	CCA	MI
Aclidinium	23.1 (16.7-31.9)	25.6 (17.8-33.4)
LABA	29.8 (22.1-40.0)	33.9 (24.5-43.3)

CI = confidence interval.

The adjusted mortality RRs for aclidinium vs. LABA were 0.78 (95% CI, 0.58-1.03) with CCA and 0.76 (95% CI, 0.57-1.00) with MI.

CONCLUSIONS

- Minor differences were observed in the distribution of COPD severity between CCA and MI.
- No differences were seen in the mortality RRs despite minor differences in the mortality rates between both methods.
- The use of MI allowed the inclusion of all the study population in the analyses, resulting in an increased precision in the estimates.

REFERENCES

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