Assessing algorithms to identify asthma patients using multiple inhaler triple therapy (comprising ICS, LABA, LAMA) in a real-world database

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Background

- The Global Initiative for Asthma (GINA) recommends a stepwise approach for asthma treatment in adults and adolescents.[1]
- At GINA Step 3 and above, daily maintenance therapy is recommended, comprising an inhaled corticosteroid (ICS) and a long-acting β_2-agonist (LABA), with the option of adding a long-acting muscarinic antagonist (LAMA) from Step 4 for patients whose asthma remains uncontrolled on ICS/LABA.[1]
- Until recently, patients with asthma in the USA using ICS, LABA, and LAMA had to use two or three separate inhalers (multiple-inhaler triple therapy [MITT]).
- Algorithms to identify the prevalence of MITT use in real-world databases were previously developed by GSK for patients with chronic obstructive pulmonary disease (COPD). However, key assumptions underlying their development have not yet been tested in asthma populations.

Aims

- To explore key algorithm assumptions by modifying existing algorithms developed for COPD and observing the consequent impact on estimates of prevalence and ability to discriminate between periods of MITT use and non-use in an asthma population.

Methods

Study design

- Exploratory analysis of a retrospective cohort study of the Truven MarketScan administrative claims database (GSK 207017/PRJ2752) conducted between 1 January 2016 and 31 December 2019 (the study period).
- Primary and secondary objectives of the retrospective cohort study have been reported elsewhere.[2]

Study cohort

- All patients with asthma from the study population who contributed data for the full period (including observation period and follow-up) from 1 July 2018 to 30 September 2019.

Methods (cont.)

Eligibility criteria

- Inclusion criteria
  - Asthma diagnosis during the study period, defined as ≥2 medical claims with an asthma code (ICD-10-CM: J45.x) in the primary or secondary position ≥30 days apart.
  - Asthma treatment, defined as ≥1 pharmacy claim for an asthma maintenance therapy during the study period.
  - ≥18 years of age at first medical/pharmacy claim.
- Exclusion criteria
  - Diagnosis of active respiratory tuberculosis, COPD, cystic fibrosis, or lung cancer (≥1 relevant medical claim with a code in any position) during the study period.

Algorithms

- Three algorithms were previously developed by GSK to measure MITT use in real-world databases in a COPD population. All three were adapted slightly and have previously been used to assess MITT use in patients with asthma in published or upcoming GSK studies.[3,4]
- Changes in assumptions in each of the three original algorithms used in asthma studies (A, B and C) to assess MITT use in an asthma population are shown in **Table 1**.

Outcomes

- Prevalence of MITT use and ability to discriminate between periods of MITT use and non-use were compared using a single modification in the assumptions in each algorithm.
  - Prevalence was measured using two definitions: the proportion of patients with ≥1 day MITT use and proportion of patients with ≥90 days continuous MITT use during the year.
  - Ability to discriminate between periods of MITT use and non-use was also measured with two definitions: as the proportion of patients with proportion of days covered (PDC) ≥50% (adherence) and number of episodes of MITT use during the year.

Table 1. Existing algorithms and modifications

	Algorithm A family				Algorithm B family			Algorithm C family		
	A	**A2**	**A3**	**A4**	**B**	**B2**	**B3**	**C**	**C2**	**C3**
Components of MITT	ICS/LABA+ LAMA	ICS/LABA+LAMA			ICS/LABA+ tiotropium	ICS/LABA+tiotropium		ICS+LABA+ LAMA (any formulation)	ICS+LABA+LAMA (any combination)	
Overlap requirements	≥1 day (dispensed on same or different days)	*≥14 days (dispensed on same or different days)*	*≥1 day (dispensed on the same day)*	≥1 day (dispensed on same or different days)	≥1 day (dispensed on same day)	≥1 day (dispensed on the same day)		≥1 day (dispensed on same or different days)	*≥7 days (dispensed on same or different days)*	≥1 day (dispensed on same or different days)
Prescription length	Assumed 30 days	Assumed 30 days	*Recorded days supply*		Recorded days supply	Recorded days supply		Recorded days supply	Recorded days supply	
Stretch periods	30 days	30 days	*None*		None	None	*Yes, 14 days*	None	None	*Yes, 30 days*
Stockpiling	None	None			Yes	Yes	*No*	None	None	
Discontinuation gap	>30 days	>30 days	*>45 days*		>90 days	*>45 days*		>45 days	>45 days	*>30 days*

Blue italicized text indicates modifications to the original algorithms (A, B and C).

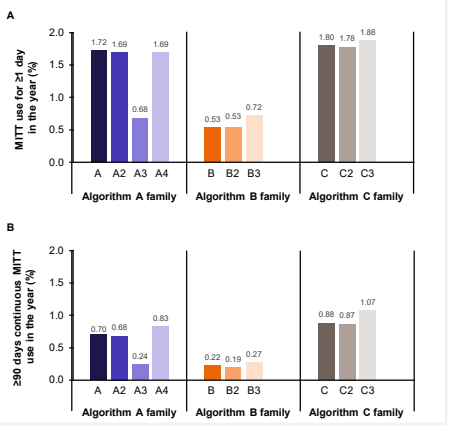
Results

- The algorithms produced different estimates of MITT use in the cohort (N=258,373) depending on the algorithm and specific modifications used and the definition of prevalence and periods of MITT use applied (prevalence range: 0.19–1.88%; adherence range 12.9–35.9% and 1.10–1.46 episodes on average; **Figures 1** and **2**).

Prevalence of MITT use

- The key algorithm modifications and associated differences observed in prevalence (measured by the proportion of patients with ≥1 day of MITT use in the year) were as follows (**Figure 1A**):
  - Requiring dispensing of MITT components on the same day (A3) significantly decreased MITT prevalence (0.68% vs 1.69% for A4; comparison shown in **Figure 3A**).
  - Increasing the required days' overlap of MITT components from ≥1 day (A) to ≥14 days (A2) had a negligible impact on prevalence (1.72% and 1.69%, respectively).
  - Halving the discontinuation gap from >90 days (B) to >45 days (B2) also did not impact prevalence (0.53% for both).
  - Allowing all combinations and any formulation of ICS+LABA+LAMA (C3) versus only ICS-LABA combination + LAMA (A) slightly increased prevalence (1.88% and 1.72%, respectively).
- The key algorithm modifications and associated differences when using an alternate measure of prevalence (proportion of patients with ≥90 days continuous MITT use in the year) are shown in **Figures 1B** and **3B.**

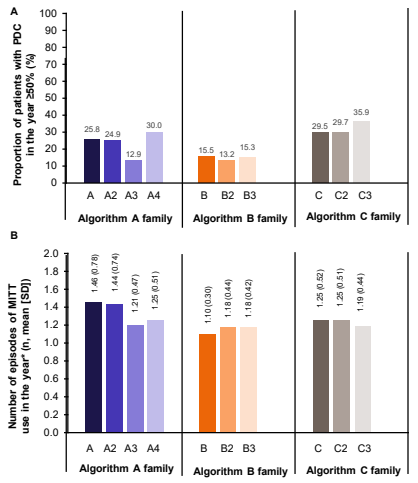
Figure 1. Ability of algorithms to estimate prevalence of MITT use measured by (A) the proportion of patients with ≥1 day of MITT use and (B) the proportion of patients with ≥90 days continuous MITT use in the year



Discrimination between periods of MITT use and non-use

- The key algorithm modifications and associated differences observed when discriminating between periods of MITT use and non-use (using the proportion of patients with PDC in the year ≥50% [adherence]) were as follows (**Figure 2A**):
  - Requiring dispensing of MITT components on the same day (A3) significantly decreased adherence to MITT (12.9% vs 30.0% for A4).
  - Increasing the required days' overlap of MITT components from ≥1 day (A) to ≥14 days (A2) had a negligible impact on adherence (25.8% and 24.9%, respectively).
  - Halving the discontinuation gap from >90 days (B) to >45 days (B2) slightly decreased adherence (15.5% and 13.2%, respectively).
  - Allowing all combinations and any formulation of ICS+LABA+LAMA (C3) versus only ICS-LABA combination + LAMA (A) considerably increased adherence (35.9% and 25.8%, respectively).
- The key algorithm modifications and associated differences when using an alternate measure to discriminate between periods of MITT use and non-use (number of episodes of MITT use in the year) are shown in **Figure 2B**.

Figure 2. Ability of algorithms to discriminate between periods of MITT use and non-use measured by (A) the proportion of patients with PDC (≥50%) and (B) the number of episodes of MITT use in the year

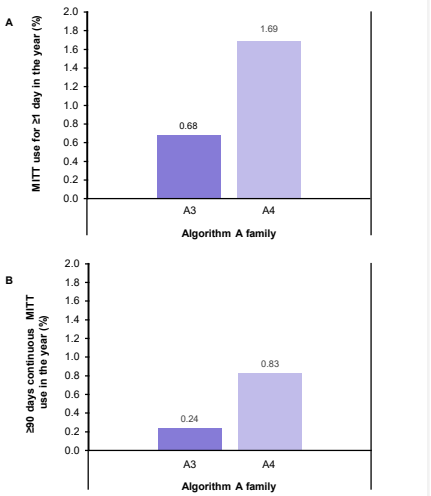


*Calculated among patients with ≥1 day MITT in the year. SD, standard deviation

Conclusions

- Algorithms on MITT use among patients with asthma produced differences in estimates of prevalence and discrimination between periods of MITT use and non-use; therefore, the algorithms developed for COPD may not be applicable to asthma.
- Sensitivity analyses should always be conducted in studies of MITT in asthma to explore the uncertainty on key assumptions.

Figure 3. Prevalence of MITT use measured by (A) the proportion of patients with ≥1 day of MITT use and (B) the proportion of patients with ≥90 days continuous MITT use in the year, estimated by algorithms A3 and A4



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- **AC** and **SZ** are employees of GSK and hold GSK stocks/shares.
- **WM** and **YL** were employees of GSK at the time of the study and hold stocks and shares.
- **BN** is an employee of CY Partners Recruitment Ltd and on assignment at GSK as a Complementary Worker.
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