ERJ open research
THE BEST IN OPEN ACCESS BASIC, TRANSLATIONAL & CLINICAL RESPIRATORY RESEARCH

Early View

Research letter

An inverse relationship between asthma prevalence and medication dispensation trend: a 12-year spatial analysis of Electronic Health Records data in Alberta, Canada

Subhabrata Moitra, Andrew Fong, Mohit Bhutani

Please cite this article as: Moitra S, Fong A, Bhutani M. An inverse relationship between asthma prevalence and medication dispensation trend: a 12-year spatial analysis of Electronic Health Records data in Alberta, Canada. *ERJ Open Res* 2022; in press (https://doi.org/10.1183/23120541.00489-2022).

An inverse relationship between asthma prevalence and medication dispensation trend: a 12-year spatial analysis of Electronic Health Records data in Alberta, Canada

Subhabrata Moitra, PhD[1], Andrew Fong, MSc[2], Mohit Bhutani, MD[1,2]

[1]Division of Pulmonary Medicine, Department of Medicine, University of Alberta, Edmonton, AB, Canada (SM: moitra@ualberta.ca; MB: mohit.bhutani@ualberta.ca)

[2]Alberta Health Services, Calgary, AB, Canada (AF: Andrew.Fong@albertahealthservices.ca)

Correspondence to: Mohit Bhutani, Division of Pulmonary Medicine, Department of Medicine, University of Alberta, 3-133 Clinical Sciences Building, 11304-83 Avenue NW, Edmonton, AB, Canada T6G 2G3. Tel: 780.492.3739. Email: mohit.bhutani@ualberta.ca

Funding and acknowledgment: No funding reported.

Take home message: Despite guidelines-based asthma management in Alberta, an inverse trend between asthma prevalence and dispensation of asthma medications in the past 12 years possibly underscores the reason for a large number of emergency department visits.

Word count: 1,512

Tables/Figures: 1 Figure

Asthma is a chronic inflammatory disease of the airways that affects over 300 million people worldwide [1]. As of 2019, 2.95 million Canadians were diagnosed with asthma [2]. While there are standard recommendations and guidelines for the diagnosis and treatment of asthma, patients living with this disease often experience poor health-related quality of life [3] and continue to experience exacerbations [4]. Apart from the increasing air pollution, rapid urbanization, and a growing trend in marijuana and vaping, particularly among the adolescents [5-8], poor patient adherence to asthma medications is a major contributing factor to these outcomes [9-12]. Despite efforts to change this narrative through patient and physician education [13-15], it is well reported that adherence to treatment in asthma is varied, with rates of <50% in children [16] and 30-70% in adults [1, 17].

In Canada, Alberta Health Services (AHS) data shows an average of 21,000 emergency department (ED) admissions for asthma exacerbations each year between 2014 and 2018 [18]. Despite the availability of optimal care facilities in the province, such a high number of ED visits due to asthma exacerbations led us to understand the current use of asthma medication. In this study, we investigated the yearly prevalence of asthma and the average dispensation rate of 10 common classes of asthma medications in Alberta, Canada from 2008-2009 to 2019-2020.

In this retrospective study, we obtained medication dispensation data between 2008-2009 and 2019-2020 fiscal years from the Pharmaceutical Information Network (PIN), a platform within the provincial Electronic Health Record (EHR) of Alberta that provides information about active and previous medications of patients of all ages [18]. To identify patients with physician-diagnosed asthma in a health administrative database, we used a previously validated definition of asthma [19]. Briefly, asthma was defined based on the International Classification of Diseases-10th edition (ICD-10) codes for asthma (J45) if there was at least one hospitalization discharge record within the Discharge Abstract Database (DAD) in a fiscal year or two physician billing records within the past two years with a diagnosis of asthma-like symptoms (ICD-9-CM; code 493). Asthma incidence was identified using the same case definition above, but with the additional criteria of being an Alberta resident for 5 years before the diagnosis of asthma. We obtained the total number of dispensations for the following drug categories for patients with asthma: inhaled corticosteroids (ICS), long-acting β_2-adrenergic receptor agonists (LABA), ICS/LABA, short-acting

β_2-adrenergic receptor agonists (SABA), antibiotics, long and short-acting muscarinic receptor antagonist (LAMA and SAMA), oral corticosteroids (OCS), leukotriene receptor antagonists (LTRA), and biologics.

Descriptive statistics were presented as frequency (%). We used Spearman's rank-order correlation to analyse the association between asthma prevalence and prescription dispensation for each of the drug categories, for all patients and separately for adults and paediatric patients. The coefficients were plotted as heatmaps and a p-value < 0.05 was considered statistically significant. For representation, we denoted each fiscal year as a single year, for example, the fiscal year 2008-2009 was denoted as 2009. The study was approved by the ethics committee of the University of Alberta (Id: Pro00097627_AME1). As we used anonymized summary data from the provincial health records, signed informed consent was not required.

Between 2009 and 2020, the prevalence of asthma in Alberta increased from 231,949 to 464,040. This is an approximately 1.5 times rise in population-adjusted asthma prevalence (from 6.46% in 2009 to 9.70% in 2020). In contrast, between 2009 and 2020, the prevalence-adjusted average rate of the prescription dispensation of ICS-LABA (0.67% vs. 0.73%), ICS (0.37% vs. 0.34%), SABA (0.98% vs. 0.99%), antibiotics (0.44% vs. 0.46%), LAMA (0.12% vs. 0.15%), and LTRA (0.23% vs. 0.21%) remained low and the signal was relatively stable. There was a marginal increase in the dispensation of OCS during the period (0.14% vs. 0.20%). The dispensation of biologic medications for asthma increased by 5 times (0.006% vs. 0.03%). Upon stratification based on age, we observed that there was a decline in ICS-LABA dispensation in the paediatric patient population (0.21% vs. 0.17%) versus the adult population (0.89% vs. 0.88%). While in adults, there was a decline of ICS (0.36% vs. 30%), and SABA (1.18% vs. 1.12%), we observed an increase of dispensation of ICS (0.39% vs. 0.51%) and SABA (0.55% vs. 0.73%) in the paediatric population. The trend of dispensation between 2009 and 2020 for antibiotics, LAMA, LTRA, OCS, and biologics remained consistent in these two populations (**Figure 1**).

In the correlation analysis between asthma prevalence and medication dispensation, we observed that with increasing asthma prevalence, the average dispensation of ICS ($\rho = -0.63$, $p = 0.03$), LABA ($\rho = -0.76$, $p = 0.006$) and SAMA ($\rho = -0.78$, $p = 0.004$) reduced, while LAMA ($\rho = 0.73$, $p = 0.01$),

OCS (ρ = 0.97, p <0.001), and biologics (ρ = 0.99, p <0.001) increased significantly. Upon age stratification, we found that in addition to ICS, LABA, and SAMA, the dispensation of SABA and LTRA also reduced significantly with increasing asthma prevalence (ρ = -0.80 and -0.86, respectively, p values for both < 0.01) in adult patient population, while OCS and biologics increased. In the paediatric patient population, only ICS-LABA reduced significantly (ρ = -0.92, p < 0.001) with increasing asthma prevalence while the dispensation of LAMA (ρ = 0.69, p = 0.02), OCS (ρ = 0.89, p < 0.001) and biologics (ρ = 0.74, p = 0.008) increased significantly (**Figure 1**).

Our study reports for the first time the trend of asthma prevalence and dispensation of asthma medication over 12 years (2008-2009 to 2019-2020) using the largest public administrative database for health information in Canada with the medical records of nearly 4.5 million Albertans over the past 20 years. Our observation of an increasing prevalence of asthma in the province of Alberta was similar to the trend in other provinces and across Canada [7, 19, 20]. Our findings are also similar to a recent US-based study on the trend of asthma prevalence in US population that showed a closely similar trend in asthma prevalence 10 years apart (7.7% in 2009-10 and 9.3% in 2018-19) [21]. We observed that despite the increasing asthma prevalence, dispensation for the majority of the 10 common classes of asthma medications was either inversely correlated with asthma prevalence (ICS, LABA, and SAMA) or remained unchanged (ICS-LABA, SABA, antibiotics, SAMA, and LTRA). There was also a clear distinction in medication dispensation trends between the adult and paediatric patient populations.

While current guidelines recommend ICS or ICS-LABA as the controller medications for effective asthma management [1, 8], our observation of declining dispensation of ICS and ICS-LABA (in the paediatric population) in the past decade is a strong indicator of poor alignment of guideline-based recommendations. Although LAMA showed a positive correlation with ICS-LABA dispensation, it is not clear from our data why LAMA dispensation showed a positive correlation with asthma (in the adult population), particularly when the guidelines do not recommend LAMA as a monotherapy, and should only be used as add-on therapy with ICS-LABA [1] and has no indication in the paediatric population as per Health Canada recommendations. We also observed a significant negative association between

asthma prevalence and the dispensation of ICS and SABA. Globally, the use of SABA is recommended as rescue/reliever therapy if taken with ICS [1]. However, our results of average SABA dispensation do not reciprocate with the results of the recently published *SABa use IN Asthma* (SABINA) study where the investigators reported a mean (SD) of 3.9 (4.4) canisters/year in Alberta [22]. This difference could be due to the cross-sectional nature of the study and a different patient population that was part of the inclusion criteria of that study. We also observed the inappropriate use of other medications (ex. LAMA use in children). The increasing trend of the use of biologics in asthma could be driven by the newly marketed and approved drugs for the management of severe asthma. This trend is quite similar to the US scenario [23], and several factors such as higher income, private insurance, and access to a specialist are likely to contribute to the higher use of biologics.

Although our data demonstrate an overwhelming low rate of asthma medication dispensation over a prolonged period, the reasons for this cannot be concluded from our study. However, we believe that these findings could be driven by both physician and patient-related factors. One plausible physician-related factor for the low dispensation rates is inappropriate billing for asthma. For example, in 2019-2020, 42% of patients who met our inclusion criteria for asthma had 0 prescriptions filled for asthma-related medications [22]. Also, we cannot comment on the administrative data as to what the physician prescribed to the patients. Another possible explanation for the low dispensation rates is that the physician prescribed the appropriate medications, but the patient did not have the medication dispensed at the pharmacy. Nevertheless, this is also a limitation of using administrative data. On the other hand, patient-related factors that are likely to affect compliance include but are not limited to, affordability, lack of asthma education, understanding of the roles of the medications, and poor perception of disease severity [17, 24]. The striking nature of our data warrants further understanding as to what factors could have led to such poor dispensation rates.

Our study has some limitations to consider. Firstly, in administrative databases, the diagnosis of asthma could be over or under-represented due to a lack of information regarding confirmation of the diagnosis with the use of spirometry. Secondly, the database receives information from different sources, such as clinics, pharmacies, and diagnostic centres located all over the province, and the possibility of

errors cannot be ruled out. Thirdly, heterogeneity among the databases is common due to different algorithms, sources, or management of the records, and extraction of appropriate data can be tedious due to different data sources and algorithms used for the purpose.

In summary, using 12-year administrative data, we observed that despite higher asthma prevalence, there was a low dispensation of asthma medications in Alberta, Canada. Our findings have significant clinical and public health implications. Further work is needed to understand the drivers of this low dispensation and its clinical impact.

AUTHOR CONTRIBUTIONS

AF curated the data. SM analysed the data and wrote the manuscript. MB interpreted the data and revised the manuscript. All authors reviewed the content and finalized the manuscript.

CONFLICT OF INTEREST

SM reports personal fees from Synergy Respiratory & Cardiac Care (Canada), Permanyer Inc. (Spain), Elsevier Inc. (USA), Apollo Gleneagles Hospital (India), and Institute of Allergy-Kolkata (India), outside the submitted work. AF does not have any conflict of interest to declare. MB received grants from Canadian Institute of Health research, Sanofi Genzyme, Astra Zeneca, and GSK; and received payments from Astra Zeneca, GSK, Sanofi Genzyme, Valeo, Covis Pharmaceuticals, and Canadian Thoracic Society, outside the submitted work.

REFERENCES

1. GINA. Global Initiative for Asthma. Global strategy for asthma management and prevention 2021 2021 [cited 2022 April 04]. Available from: http://ginasthma.org/.

2. Statistics Canada. Table 13-10-0096-08 Asthma, by age group 2020 [cited 2022 April 04]. Available from: https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1310009608.

3. Lee LK, Obi E, Paknis B, Kavati A, Chipps B. Asthma control and disease burden in patients with asthma and allergic comorbidities. J Asthma 2018;55(2):208-19.

4. Bloom CI, Nissen F, Douglas IJ, Smeeth L, Cullinan P, Quint JK. Exacerbation risk and characterisation of the UK's asthma population from infants to old age. Thorax 2018;73(4):313-20.

5. Achakulwisut P, Brauer M, Hystad P, Anenberg SC. Global, national, and urban burdens of paediatric asthma incidence attributable to ambient NO(2) pollution: estimates from global datasets. Lancet Planet Health 2019;3(4):e166-e78.

6. Bosonea AM, Sharpe H, Wang T, Bakal JA, Befus AD, Svenson LW, et al. Developments in asthma incidence and prevalence in Alberta between 1995 and 2015. Allergy Asthma Clin Immunol 2020;16(1):87.

7. Radhakrishnan D, Bota SE, Price A, Ouédraogo A, Husein M, Clemens KK, et al. Comparison of childhood asthma incidence in 3 neighbouring cities in southwestern Ontario: a 25-year longitudinal cohort study. CMAJ Open 2021;9(2):E433-E42.

8. Yang CL, Hicks EA, Mitchell P, Reisman J, Podgers D, Hayward KM, et al. Canadian Thoracic Society 2021 Guideline update: Diagnosis and management of asthma in preschoolers, children and adults. Canadian Journal of Respiratory, Critical Care, and Sleep Medicine 2021;5(6):348-61.

9. Choi TN, Westermann H, Sayles W, Mancuso CA, Charlson ME. Beliefs about asthma medications: patients perceive both benefits and drawbacks. J Asthma 2008;45(5):409-14.

10. Cote I, Farris K, Feeny D. Is adherence to drug treatment correlated with health-related quality of life? Qual Life Res 2003;12(6):621-33.

11. Harrison B, Stephenson P, Mohan G, Nasser S. An ongoing Confidential Enquiry into asthma deaths in the Eastern Region of the UK, 2001-2003. Prim Care Respir J 2005;14(6):303-13.

12. Horne R. Compliance, adherence, and concordance: implications for asthma treatment. Chest 2006;130(1 Suppl):65S-72S.

13. Brown R. Asthma Patient Education: Partnership in Care. Int Forum Allergy Rhinol 2015;5 Suppl 1(S1):S68-70.

14. Cabana MD, Slish KK, Evans D, Mellins RB, Brown RW, Lin X, et al. Impact of physician asthma care education on patient outcomes. Pediatrics 2006;117(6):2149-57.

15. Cabana MD, Slish KK, Evans D, Mellins RB, Brown RW, Lin X, et al. Impact of Physician Asthma Care Education on patient outcomes. Health Educ Behav 2014;41(5):509-17.

16. Milgrom H, Bender B, Ackerson L, Bowry P, Smith B, Rand C. Noncompliance and treatment failure in children with asthma. J Allergy Clin Immunol 1996;98(6 Pt 1):1051-7.

17. Bender BG, Bender SE. Patient-identified barriers to asthma treatment adherence: responses to interviews, focus groups, and questionnaires. Immunol Allergy Clin North Am 2005;25(1):107-30.

18. Health A. Pharmaceutical Information Network (PIN) 2021 [Available from: http://www.albertanetcare.ca/learningcentre/Pharmaceutical-Information-Network.htm.

19. Gershon AS, Wang C, Guan J, Vasilevska-Ristovska J, Cicutto L, To T. Identifying patients with physician-diagnosed asthma in health administrative databases. Can Respir J 2009;16(6):183-8.

20. Canada PHAo. Report from the Canadian Chronic Disease Surveillance System: Asthma and Chronic Obstructive Pulmonary Disease (COPD) in Canada, 2018 [Available from: https://www.canada.ca/content/dam/phac-aspc/documents/services/publications/diseases-conditions/asthma-chronic-obstructive-pulmonary-disease-canada-2018/pub-eng.pdf.

21. Zhou Y, Liu Y. Recent trends in current asthma prevalence among US adults, 2009-2018. J Allergy Clin Immunol Pract 2020;8(8):2814-6.

22. Quint JK, Arnetorp S, Kocks JWH, Kupczyk M, Nuevo J, Plaza V, et al. Short-Acting Beta-2-Agonist Exposure and Severe Asthma Exacerbations: SABINA Findings From Europe and North America. J Allergy Clin Immunol Pract 2022;10(9):2297-309 e10.

23. Inselman JW, Jeffery MM, Maddux JT, Shah ND, Rank MA. Trends and Disparities in Asthma Biologic Use in the United States. J Allergy Clin Immunol Pract 2020;8(2):549-54 e1.

24. Williams LK, Joseph CL, Peterson EL, Wells K, Wang M, Chowdhry VK, et al. Patients with asthma who do not fill their inhaled corticosteroids: a study of primary nonadherence. J Allergy Clin Immunol 2007;120(5):1153-9.

FIGURE 1:

Asthma and asthma medication in Alberta. (A) The trend of asthma and dispensation of asthma medications in adult and paediatric patients between 2009 and 2020, (B) Correlation heatmap demonstrating asthma incidence and medication dispensation in all asthmatics, and separately for adults and paediatrics patients between 2009 and 2020. Numbers indicate the correlation coefficient values (Spearman's ρ).