

## **Generalizability of an Automatic Explanation Method for Machine Learning Prediction Results on Asthma-Related Hospital Visits in Patients with Asthma: Quantitative Analysis**

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## Abstract

**Background:** Asthma brings a huge burden to patients and healthcare systems. To facilitate preventive care for asthma management and improve patient outcomes, we recently developed two machine learning models, one on Intermountain Healthcare data and the other on Kaiser Permanente Southern California (KPSC) data, to forecast asthma-related hospital visits including emergency department visits and hospitalizations in the succeeding 12 months in patients with asthma. As is typical for machine learning approaches, these two models give no explanation of their forecasting results. To address black-box models' interpretability issue, we designed an automatic method to supply rule-format explanations for any machine learning model's forecasting results on imbalanced tabular data and to suggest customized interventions with no accuracy loss. Our method worked well for explaining our Intermountain Healthcare model's forecasting results, but its generalizability to other healthcare systems stays unknown.

**Objective:** This study aims to evaluate our automatic explanation method's generalizability to KPSC for forecasting asthma-related hospital visits.

**Methods:** Through secondary analysis of 987,506 data instances from 2012 to 2017 at KPSC, we employed our method to explain our KPSC model's forecasting results and to suggest customized interventions. The patient cohort covered a random sample of 70% of patients with asthma who had a KPSC health plan for any period between 2015 and 2018.

**Results:** Our method explained the forecasting results for 97.57% (2,204/2,259) of the patients with asthma our KPSC model correctly forecasted to undergo asthma-related hospital visits in the succeeding 12 months.

**Conclusions:** For forecasting asthma-related hospital visits, our automatic explanation method exhibited decent generalizability to KPSC.

**Keywords:** Asthma; forecasting; patient care management; machine learning

## Introduction

### Background

Asthma affects 8.4% of the U.S. population [1], resulting in over 3,000 deaths, almost 500,000 hospitalizations, and over 2,000,000 emergency department (ED) visits every year [1,2]. The state-of-the-art method for cutting asthma-related hospital visits including ED visits and hospitalizations is to use a model to forecast which patients with asthma are prone to future poor outcomes. We then enroll these patients in care management, letting care managers call them periodically and help them schedule health and related services. As used by healthcare systems like University of Washington Medicine, Intermountain Healthcare, and Kaiser Permanente Northern California [3] and by health plans in nine of 12 metropolitan communities [4], this method, if implemented properly, can cut up to 40% of patients' future hospital visits [5-8].

Having a limited capacity, a care management program can enroll only a small portion of patients [9], with its effectiveness upper bounded by the predictive model's accuracy. Due to missing certain important features, the existing models for forecasting asthma-related hospital visits in patients with asthma [3,10-22] are inaccurate, each missing over half of those who will undergo future asthma-related hospital visits and mislabeling many other to make such visits. As a result, care management programs continue to be used inefficiently by being unable to focus on the highest-risk patients. Also, patient outcomes deteriorate while healthcare costs rise. To address this problem, we recently considered many candidate features and developed two extreme gradient boosting (XGBoost) [23] machine learning models, one on Intermountain Healthcare data [24] and the other on Kaiser Permanente Southern California (KPSC) data [25], to forecast asthma-related hospital visits in the succeeding 12 months in patients with asthma with higher accuracy. As is typical for machine learning approaches, these two models give no explanation of their forecasting results. Clinicians would know that a patient is considered high risk by the model, but the model offers no reason why this is the case. This creates difficulty for clinicians to understand and trust the model's prediction result, determine whether the patient should be put into care management, and pinpoint interventions suitable for the patient. To address black-box models' interpretability issue, we designed an automatic method to supply rule-format explanations for any machine learning model's forecasting results on imbalanced tabular data and to suggest customized interventions with no accuracy loss [26]. Our method worked well for explaining our Intermountain Healthcare model's forecasting results [26], but its generalizability to other healthcare systems stays unknown.

### Objectives

This study aims to evaluate our automatic explanation method's generalizability to KPSC regarding forecasting asthma-related hospital visits. In the following, we describe our evaluation approach and results.

## Methods

### Ethics approval and study design

Approved by KPSC’s and University of Washington Medicine’s institutional review boards, this study conducted secondary analysis on retrospective data.

### Patient population

We adopted the same patient cohort from our prior KPSC predictive model paper [25]: a random sample of 70% of patients with asthma who had a KPSC health plan for any period between 2015 and 2018. This sample size is the largest one permitted by KPSC for sharing its data with another non-Kaiser Permanente institution for research. KPSC owns 227 clinics and 15 hospitals. It is the largest integrated healthcare system in Southern California, supplying care to ~19% of residents there [27]. A patient was deemed asthmatic in a specific year if during that year, at least one asthma diagnosis code (International Classification of Diseases, Tenth Revision [ICD-10]: J45.x; International Classification of Diseases, Ninth Revision [ICD-9]: 493.0x, 493.1x, 493.8x, 493.9x) was recorded on the patient in the encounter billing database [11,28,29]. Patient death during that year serves as the exclusion criterion.

### Prediction target (also known as the dependent variable)

We adopted the same prediction target from our prior KPSC predictive model paper [25]. For every patient deemed to have asthma in a specific year, the indicator of any asthma-related hospital visit in the succeeding year is the outcome. An asthma-related hospital visit is a hospitalization or ED visit with asthma as its principal diagnosis (ICD-10: J45.x; ICD-9: 493.0x, 493.1x, 493.8x, 493.9x). When training and testing our automatic explanation method and our KPSC XGBoost model, for each patient with asthma, we employed the patient’s data through each year’s last day to forecast the patient’s outcome in the succeeding year, if the patient had a KPSC health plan on the former year’s last day and was also deemed asthmatic in the former year.

### Data set

We adopted the same administrative and clinical data set from our prior KPSC predictive model paper [25]. Obtained from KPSC’s research data warehouse, this structured data set covered our patient cohort’s visits at KPSC between 2010 and 2018.

### Features (also known as independent variables), predictive model, and data pre-processing

Our KPSC model [25] uses the XGBoost classification algorithm [23] and 221 features to forecast asthma-related hospital visits in the succeeding year in patients with asthma. These features are listed in Table 2 in our prior KPSC predictive model paper’s [25] Appendix, were computed on the structured attributes in our data set, and cover various characteristics like patient demographics, medications, visits, diagnoses, vital signs, procedures, and laboratory tests. An example feature is the total number of asthma relievers that the patient filled in the prior 12 months. Every input data instance to our KPSC model aims at a (patient, index year) pair, includes these 221 features, and is used to forecast the succeeding year’s outcome of the patient. As in our prior KPSC predictive model paper [25], the top 10% of patients with asthma projected at the highest risk were used as the cutoff point for making binary classification. We used the same data pre-processing approach adopted in our prior KPSC predictive model paper [25] to clean, normalize, and prepare the data.

### Review of our automatic explanation method

Previously, we designed an automatic method to supply rule-format explanations for any machine learning model’s forecasting results on tabular data and to suggest customized interventions with no accuracy loss. Our original method [30] was designed for relatively balanced data. Recently, we extended the method to handle imbalanced data [26], where one value of the outcome variable has a much lower prevalence rate than another. This fits the case of forecasting asthma-related hospital visits in patients with asthma. At KPSC, the prevalence rate of undergoing asthma-related hospital visits in the succeeding year is ~2%. In the rest of the paper, we focus on the extended automatic explanation method.

### Main idea

The central idea of our automatic explanation method is to use two models side by side to separate forecasting and offering explanations. Each model serves a differing purpose. The first model is employed for forecasting. Typically chosen to be the most accurate one, this model can be any built on continuous and categorical features. The second model contains class-based association rules [31,32] mined from past data. It is used not to forecast, but to explain the first model’s forecasting results. After employing an automatic discretization method [31,33] to convert continuous features to categorical ones, we use a standard approach like Apriori to mine the association rules [32]. Each rule presents a feature pattern linking to a value  $u$  of the outcome variable and has the form

$$r_1 \text{ AND } r_2 \text{ AND } \dots \text{ AND } r_s \rightarrow u.$$

$s'$  and  $u$ 's values can differ across rules. For binary classification on poor vs. good outcomes,  $u$  is typically the poor outcome value. Each item  $r_i$  ( $1 \leq i \leq s$ ) is a feature-value pair ( $g, v$ ). When  $v$  is a value,  $r_i$  shows feature  $g$  has value  $v$ . When  $v$  is a range,  $r_i$  shows  $g$ 's value is within  $v$ . The rule signifies that a patient's outcome is apt to be  $u$  if  $r_1, r_2, \dots$ , and  $r_s$  are all satisfied on the patient. An exemplar rule is:

The patient had 8 or 9 primary or principal asthma diagnoses in the prior 12 months  
AND the patient had  $\geq 6$  no shows in the prior 12 months  
→ the patient will undergo  $\geq 1$  asthma-related hospital visit in the succeeding 12 months.

The rule mining and pruning process

Our automatic explanation method uses five parameters: the minimum commonality threshold, the minimum confidence threshold, the largest number of items permitted on an association rule's left hand side, the confidence difference threshold, and the number of top features used to construct rules. For a given rule

$r_1$  AND  $r_2$  AND ... AND  $r_s \rightarrow u$ ,

its commonality reflects its coverage in the context of  $u$  and refers to the fraction of data instances fulfilling  $r_1, r_2, \dots$ , and  $r_s$  among all of the data instances connecting to  $u$ . Its confidence reflects its precision and refers to the fraction of data instances connecting to  $u$  among all of the data instances fulfilling  $r_1, r_2, \dots$ , and  $r_s$ . Our method uses those rules whose commonality is  $\geq$  the minimum commonality threshold, whose confidence is  $\geq$  the minimum confidence threshold, and each containing no more than the maximum permitted number of items on its left hand side.

We use three techniques to reduce the number of association rules and prevent it from being excessively large. First, we remove every more specific rule  $q_1$  in the presence of a more general rule  $q_2$  satisfying  $q_2$ 's confidence  $\geq q_1$ 's confidence - the confidence difference threshold. Second, certain machine learning algorithms like XGBoost [23] can automatically compute every feature's importance value. When handling a large data set with many features, only the top few features having the largest importance values and used in the first model are adopted to construct rules. Third, a clinician in the design team of the automatic explanation function examines all of the possible values and value ranges of the features adopted to construct rules, and labels those values and value ranges that could have a positive correlation with the poor outcome value. Only those labeled feature values and value ranges are adopted to form rules.

For each feature-value pair item that is adopted to construct association rules, a clinician in the design team of the automatic explanation function compiles zero or more interventions. We tag an item actionable if it links to at least one intervention. Each rule passing the rule pruning process is automatically linked to the interventions related to the actionable items on the rule's left hand side. We tag a rule actionable if it contains at least one actionable item on its left hand side, i.e., it links to at least one intervention.

The explanation approach

For every patient the first model forecasts to take a poor outcome value, we explain the forecasting result by showing the association rules in the second model having this value on their right hand sides and whose left hand sides are satisfied by the patient. Each rule provides a reason why the patient is forecasted to take this value. For each actionable rule shown, the interventions connecting to it are listed next to it. The automatic explanation function's user can find from them customized interventions fitting the patient. Usually, the rules in the second model present common reasons for incurring poor outcomes. Some patients will incur poor outcomes for other reasons. Thus, the second model can explain most, but not all, of the poor outcomes correctly forecasted by the first model.

Parameter setting

When doing our experiments, we used the same parameter setting approach employed in our previous automatic explanation paper [26]. Each association rule had on its left hand side no more than five items. Our KPSC XGBoost model [25] used 221 features to forecast asthma-related hospital visits. We used the top 50 features that our KPSC model ranked with the largest importance values to construct association rules. Our KPSC model gained an area under the receiver operating characteristic curve (AUC) of 0.820 using all of the 221 features, and an AUC of 0.815 using the top 50 features.

For forecasting asthma-related hospital visits, our KPSC model [25] obtained a lower AUC on KPSC data than our Intermountain Healthcare model on Intermountain Healthcare data [24]. As mentioned in our previous automatic explanation paper [26], the harder it is to forecast the outcome, the smaller the minimum commonality and confidence thresholds need to be to ensure our automatic explanation method can supply explanations for a large percentage of the patients whom the first model correctly forecasts to take a poor outcome value. Following this guideline, on KPSC data, we set the minimum commonality threshold to 0.08%, which is lower than the corresponding value of 0.2% we used on Intermountain Healthcare data [26]. We set the minimum confidence threshold to 25%, which is lower than the corresponding value of 50% we used on Intermountain Healthcare data [26]. Despite not looking large, 25% is much greater than 2%, the percentage of KPSC data

instances associated with asthma-related hospital visits in the succeeding year, as well as our KPSC model’s positive predictive value of 11.03% [25].

To set the value of the confidence difference threshold  $\tau$ , we charted the number of association rules passing the rule pruning process vs.  $\tau$ . Our previous paper [26] shows that this number of rules first drops quickly as  $\tau$  rises, and then drops slowly when  $\tau$  becomes large enough.  $\tau$ ’s value is set at the transition point.

## Data analysis

### Partitioning of the training and test sets

We used the same method adopted in our prior KPSC predictive model paper [25] to partition the entire data set into the training and test sets. As several features were computed on the data from up to two years prior to the index year and the outcomes came from the succeeding year, our data set included six years of effective data (2012-2017) over the nine-year period of 2010-2018. To match our KPSC model’s and our automatic explanation method’s use in clinical practice, we used the 2012-2016 data as the training set to train our KPSC model and mine the association rules adopted by our automatic explanation method. We used the 2017 data as the test set to gauge the performance of our KPSC model and automatic explanation method.

### Performance metrics

We used the same performance metrics from our previous automatic explanation paper [26] to assess our automatic explanation method’s performance. A performance metric on our method’s explanation power is: the fraction of patients with asthma our method could offer explanations for among those our KPSC model correctly forecasted to undergo asthma-related hospital visits in the succeeding year. We computed the average number of rules as well as the average number of actionable rules suiting such a patient. A rule suits a patient if all of the items on its left hand side are satisfied on the patient.

As our previous automatic explanation paper [26] showed, several rules suiting a patient often differ by a single item on their left hand sides. When multiple rules suit a patient, the amount of non-redundant information included in them is usually much less than the number of rules in them. To plot a full picture of the amount of information included in the automatic explanations given on the patients, we computed three distributions of the patients with asthma whom our KPSC model correctly forecasted to undergo asthma-related hospital visits in the succeeding year: 1) by the number of actionable rules suiting a patient, 2) by the number of different actionable items included in all of the rules suiting a patient, and 3) by the number of rules suiting a patient.

## Results

### Demographic and clinical characteristics of our patient cohort

Remember that each data instance aims at a different (patient, index year) pair. Tables 1 and 2 present the demographic and clinical characteristics of our KPSC patient cohort during 2012-2016 and 2017 separately. The two sets of characteristics are sufficiently similar to each other. During 2012-2016, 2.42% (18,925/782,762) of data instances linked to asthma-related hospital visits in the succeeding year. During 2017, this fraction was 2.13% (4,353/204,744). Our prior KPSC predictive model paper [25] gave a detailed comparison of the two sets of characteristics.

**Table 1.** Demographic and clinical characteristics of our KPSC patient cohort during 2012-2016.

Characteristic	Data instances associated with no asthma-related hospital visit in the succeeding year ( $N=763,837$ ), $n$ (%)	Data instances associated with asthma-related hospital visits in the succeeding year ( $N=18,925$ ), $n$ (%)	Data instances ( $N=782,762$ ), $n$ (%)
<b>Age</b>			
65+	108,662 (14.23)	2,288 (12.09)	110,950 (14.17)
18 to 65	415,889 (54.45)	8,557 (45.22)	424,446 (54.22)
6 to <18	188,583 (24.69)	5,039 (26.63)	193,622 (24.74)
<6	50,703 (6.64)	3,041 (16.07)	53,744 (6.87)
<b>Gender</b>			
Female	443,410 (58.05)	10,590 (55.96)	454,000 (58.00)
Male	320,427 (41.95)	8,335 (44.04)	328,762 (42.00)
<b>Race</b>			
White	477,542 (62.52)	10,040 (53.05)	487,582 (62.29)
Native Hawaiian or other Pacific islander	7,692 (1.01)	230 (1.22)	7,922 (1.01)
Black or African American	110,869 (14.51)	4,982 (26.33)	115,851 (14.80)

Asian	68,781 (9.00)	1,282 (6.77)	70,063 (8.95)
American Indian or Alaska native	3,745 (0.49)	86 (0.45)	3,831 (0.49)
Unknown or unreported	95,208 (12.46)	2,305 (12.18)	97,513 (12.46)
<b>Ethnicity</b>			
Non-Hispanic	449,795 (58.89)	10,577 (55.89)	460,372 (58.81)
Hispanic	299,240 (39.18)	8,131 (42.96)	307,371 (39.27)
Unknown or unreported	14,802 (1.94)	217 (1.15)	15,019 (1.92)
<b>Insurance</b>			
Self-paid plan	104,479 (13.68)	2,224 (11.75)	106,703 (13.63)
Public	216,320 (28.32)	7,469 (39.47)	223,789 (28.59)
High deductible plan	80,393 (10.52)	1,426 (7.54)	81,819 (10.45)
Exchange (a.k.a. marketplace)	39,050 (5.11)	735 (3.88)	39,785 (5.08)
Commercial (employer-paid)	521,101 (68.22)	11,311 (59.77)	532,412 (68.02)
Other	265,264 (34.73)	6,064 (32.04)	271,328 (34.66)
<b># of years from the first visit related to asthma in the data set</b>			
>3	439,930 (57.59)	10,919 (57.70)	450,849 (57.60)
≤3	323,907 (42.41)	8,006 (42.30)	331,913 (42.40)
<b>Asthma medication fill</b>			
Systemic corticosteroid	236,246 (30.93)	10,837 (57.26)	247,083 (31.57)
Short-acting, inhaled beta-2 agonist	537,442 (70.36)	16,242 (85.82)	553,684 (70.73)
Mast cell stabilizer	20 (0.00)	0 (0.00)	20 (0.00)
Long-acting beta-2 agonist	33,576 (4.40)	1,694 (8.95)	35,270 (4.51)
Leukotriene modifier	85,299 (11.17)	4,125 (21.80)	89,424 (11.42)
Combination of long-acting beta-2 agonist and inhaled corticosteroid	88,847 (11.63)	3,975 (21.00)	92,822 (11.86)
Inhaled corticosteroid	325,156 (42.57)	11,841 (62.57)	336,997 (43.05)
<b>Comorbidity</b>			
Sleep apnea	20,465 (2.68)	575 (3.04)	21,040 (2.69)
Sinusitis	112,341 (14.71)	2,832 (14.96)	115,173 (14.71)
Premature birth	16,607 (2.17)	690 (3.65)	17,297 (2.21)
Obesity	171,666 (22.47)	4,776 (25.24)	176,442 (22.54)
Gastroesophageal reflux	101,180 (13.25)	2,778 (14.68)	103,958 (13.28)
Eczema	82,425 (10.79)	2,944 (15.56)	85,369 (10.91)
Cystic fibrosis	135 (0.02)	3 (0.02)	138 (0.02)
Chronic obstructive pulmonary disease	27,388 (3.59)	999 (5.28)	28,387 (3.63)
Bronchopulmonary dysplasia	241 (0.03)	22 (0.12)	263 (0.03)
Anxiety or depression	160,719 (21.04)	4,231 (22.36)	164,950 (21.07)
Allergic rhinitis	164,036 (21.48)	4,673 (24.69)	168,709 (21.55)
<b>Smoking status</b>			
Never smoker or unknown	477,263 (62.48)	11,885 (62.80)	489,148 (62.49)
Former smoker	133,456 (17.47)	2,870 (15.17)	136,326 (17.42)
Current smoker	153,118 (20.05)	4,170 (22.03)	157,288 (20.09)

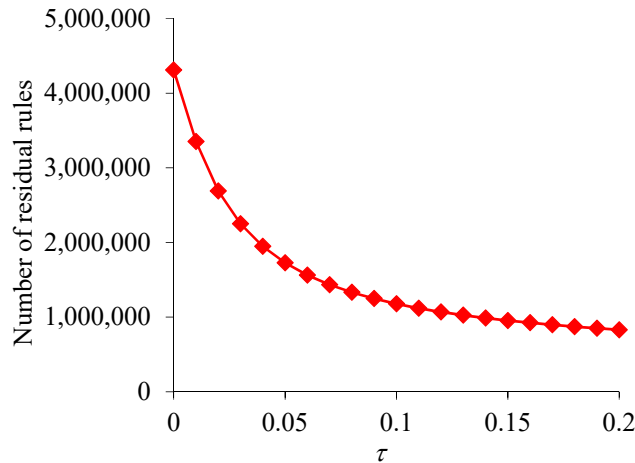
**Table 2.** Demographic and clinical characteristics of our KPSC patient cohort in 2017.

Characteristic	Data instances associated with no asthma-related hospital visit in the succeeding year (N=200,391), n (%)	Data instances associated with asthma-related hospital visits in the succeeding year (N=4,353), n (%)	Data instances (N=204,744), n (%)
<b>Age</b>			
65+	35,342 (17.64)	679 (15.60)	36,021 (17.59)
18 to 65	109,969 (54.88)	2,052 (47.14)	112,021 (54.71)
6 to <18	43,856 (21.89)	1,012 (23.25)	44,868 (21.91)
<6	11,224 (5.60)	610 (14.01)	11,834 (5.78)
<b>Gender</b>			

Female	118,013 (58.89)	2,482 (57.02)	120,495 (58.85)
Male	82,378 (41.11)	1,871 (42.98)	84,249 (41.15)
<b>Race</b>			
White	124,514 (62.14)	2,302 (52.88)	126,816 (61.94)
Native Hawaiian or other Pacific islander	1,910 (0.95)	42 (0.96)	1,952 (0.95)
Black or African American	26,864 (13.41)	1,075 (24.70)	27,939 (13.65)
Asian	18,555 (9.26)	319 (7.33)	18,874 (9.22)
American Indian or Alaska native	987 (0.49)	31 (0.71)	1,018 (0.50)
Unknown or unreported	27,561 (13.75)	584 (13.42)	28,145 (13.75)
<b>Ethnicity</b>			
Non-Hispanic	116,801 (58.29)	2,410 (55.36)	119,211 (58.22)
Hispanic	78,153 (39.00)	1,868 (42.91)	80,021 (39.08)
Unknown or unreported	5,437 (2.71)	75 (1.72)	5,512 (2.69)
<b>Insurance</b>			
Self-paid plan	33,758 (16.85)	647 (14.86)	34,405 (16.80)
Public	64,727 (32.30)	1,904 (43.74)	66,631 (32.54)
High deductible plan	24,647 (12.30)	356 (8.18)	25,003 (12.21)
Exchange (a.k.a. marketplace)	17,677 (8.82)	269 (6.18)	17,946 (8.77)
Commercial (employer-paid)	127,724 (63.74)	2,420 (55.59)	130,144 (63.56)
Other	83,108 (41.47)	1,675 (38.48)	84,783 (41.41)
<b># of years from the first visit related to asthma in the data set</b>			
>3	116,285 (58.03)	2,616 (60.10)	118,901 (58.07)
≤3	84,106 (41.97)	1,737 (39.90)	85,843 (41.93)
<b>Asthma medication fill</b>			
Systemic corticosteroid	64,878 (32.38)	2,597 (59.66)	67,475 (32.96)
Short-acting, inhaled beta-2 agonist	137,077 (68.40)	3,742 (85.96)	140,819 (68.78)
Mast cell stabilizer	0 (0.00)	0 (0.00)	0 (0.00)
Long-acting beta-2 agonist	11,343 (5.66)	467 (10.73)	11,810 (5.77)
Leukotriene modifier	26,996 (13.47)	1,099 (25.25)	28,095 (13.72)
Combination of long-acting beta-2 agonist and inhaled corticosteroid	28,580 (14.26)	1,151 (26.44)	29,731 (14.52)
Inhaled corticosteroid	78,220 (39.03)	2,586 (59.41)	80,806 (39.47)
<b>Comorbidity</b>			
Sleep apnea	12,811 (6.39)	333 (7.65)	13,144 (6.42)
Sinusitis	29,202 (14.57)	680 (15.62)	29,882 (14.59)
Premature birth	4,381 (2.19)	132 (3.03)	4,513 (2.20)
Obesity	48,548 (24.23)	1,190 (27.34)	49,738 (24.29)
Gastroesophageal reflux	32,462 (16.20)	797 (18.31)	33,259 (16.24)
Eczema	20,521 (10.24)	638 (14.66)	21,159 (10.33)
Cystic fibrosis	40 (0.02)	2 (0.05)	42 (0.02)
Chronic obstructive pulmonary disease	7,306 (3.65)	285 (6.55)	7,591 (3.71)
Bronchopulmonary dysplasia	29 (0.01)	1 (0.02)	30 (0.01)
Anxiety or depression	46,176 (23.04)	1,124 (25.82)	47,300 (23.10)
Allergic rhinitis	39,849 (19.89)	1,084 (24.90)	40,933 (19.99)
<b>Smoking status</b>			
Never smoker or unknown	125,245 (62.50)	2,663 (61.18)	127,908 (62.47)
Former smoker	36,026 (17.98)	717 (16.47)	36,743 (17.95)
Current smoker	39,120 (19.52)	973 (22.35)	40,093 (19.58)

#### The number of residual association rules

Taking the top 50 features our KPSC model ranked with the largest importance values, we mined 11,628,850 association rules from the training set. Figure 1 displays the number of residual rules vs. the confidence difference threshold  $\tau$ . This number first drops quickly as  $\tau$  rises, and then drops slowly when  $\tau$  becomes  $\geq 0.15$ . Accordingly,  $\tau$ 's value was set to 0.15, ending up with 954,493 residual rules.



**Figure 1.** The number of residual rules vs. the confidence difference threshold  $\tau$ .

An asthma clinical expert in our team labeled the top 50 features' values and value ranges that could have a positive correlation with asthma-related hospital visits in the succeeding year. After we removed those rules involving any other value or value range, 725,632 association rules remained. Each rule provides a reason why a patient is forecasted to undergo future asthma-related hospital visits. Almost all (725,623) of these rules were actionable. Thus, our automatic explanation method's performance numbers are almost the same regardless of whether all of these rules or only the actionable rules were used. In the rest of this section, we present solely the performance numbers when only the actionable rules were used.

#### Example association rules the second model adopted

To let the reader gain a sense of the association rules the second model adopted, we present five example rules.

- 1) Rule 1: The patient filled  $\geq 89$  asthma relievers in total in the prior 12 months  
 → the patient will undergo  $\geq 1$  asthma-related hospital visit in the succeeding 12 months.  
 Using a lot of asthma relievers indicates poor asthma control. An intervention tied to the item “the patient filled  $\geq 89$  asthma relievers in total in the prior 12 months” is to tailor prescribed medications and to suggest the patient to maximize adherence to asthma control medications or to improve avoidance of asthma triggers.
- 2) Rule 2: The patient had  $\geq 25$  nebulizer medication orders in the prior 12 months  
 AND the patient incurred  $\geq 16$  major visits for asthma in the prior 12 months  
 → the patient will undergo  $\geq 1$  asthma-related hospital visit in the succeeding 12 months.  
 Using a lot of nebulizer medications indicates poor asthma control. An intervention tied to the item “the patient had  $\geq 25$  nebulizer medication orders in the prior 12 months” is to tailor prescribed medications and to suggest the patient to maximize adherence to asthma control medications or to improve avoidance of asthma triggers.  
 As defined in our previous paper [24], major visits for asthma cover outpatient visits linked to a primary diagnosis of asthma, as well as ED visits and hospitalizations linked to an asthma diagnosis code. Outpatient visits linked to a secondary, but not a primary diagnosis of asthma are deemed minor visits for asthma. Having many major visits for asthma indicates poor asthma control. An intervention tied to the item “the patient incurred  $\geq 16$  major visits for asthma in the prior 12 months” is to adopt control strategies for the patient to avoid needing emergency care.
- 3) Rule 3: The patient had 8 or 9 primary or principal asthma diagnoses in the prior 12 months  
 AND the patient had  $\geq 6$  no shows in the prior 12 months  
 → the patient will undergo  $\geq 1$  asthma-related hospital visit in the succeeding 12 months.  
 Having many primary or principal asthma diagnoses indicates poor asthma control. An intervention tied to the item “the patient had 8 or 9 primary or principal asthma diagnoses in the prior 12 months” is to offer the patient suggestions on how to improve asthma control.  
 Having many no shows is correlated with poor outcomes. An intervention tied to the item “the patient had  $\geq 6$  no shows in the prior 12 months” is to give the patient social resources to handle socioeconomic challenges to keep appointments.
- 4) Rule 4: The patient incurred  $\geq 8$  ED visits in the prior 12 months  
 AND the patient was ordered  $\geq 28$  short-acting beta-2 agonist medications in total in the prior 12 months  
 AND the patient is black or African American  
 → the patient will undergo  $\geq 1$  asthma-related hospital visit in the succeeding 12 months.



In the US, black and African American people tend to have poorer asthma outcomes than others. Having frequent ED visits indicates poor asthma control. An intervention tied to the item “the patient incurred  $\geq 8$  ED visits in the prior 12 months” is to adopt control strategies for the patient to avoid needing emergency care.

Short-acting beta-2 agonists are rescue medications for quick relief of asthma symptoms. Using a lot of short-acting beta-2 agonists indicates poor asthma control. An intervention tied to the item “the patient was ordered  $\geq 28$  short-acting beta-2 agonist medications in total in the prior 12 months” is to tailor prescribed medications and to suggest the patient to maximize adherence to asthma control medications or to improve avoidance of asthma triggers.

5) Rule 5: The highest exacerbation severity of all of the asthma diagnoses recorded on the patient in the prior 12 months is status asthmaticus

AND the patient incurred  $\geq 11$  and  $\leq 17$  visits with same day appointments in the prior 12 months

AND the admission type of the patient’s last visit in the prior 12 months is non-elective

→ the patient will undergo  $\geq 1$  asthma-related hospital visit in the succeeding 12 months.

Status asthmaticus is the most severe form of asthma exacerbation. An intervention tied to the item “the highest exacerbation severity of all of the asthma diagnoses recorded on the patient in the prior 12 months is status asthmaticus” is to offer the patient suggestions on how to improve asthma control.

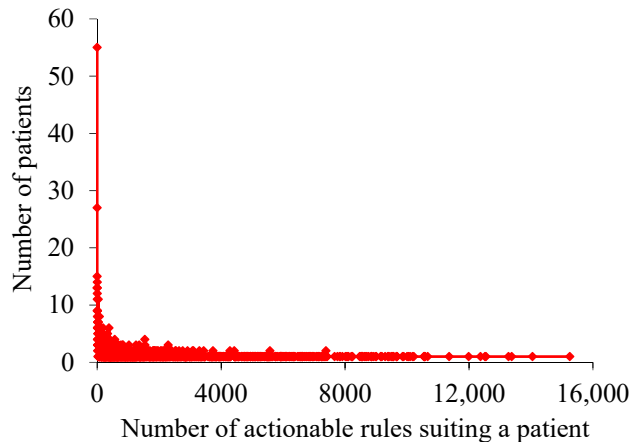
Having many visits with same day appointments indicates poor asthma control. An intervention tied to the item “the patient incurred  $\geq 11$  and  $\leq 17$  visits with same day appointments in the prior 12 months” is to improve support given to the patient between visits to enhance medication adherence, address asthma triggers, and maximize the value of each visit.

A patient incurs a non-elective visit when the patient’s condition requires immediate medical attention, e.g., when the patient experiences a severe asthma exacerbation. An intervention tied to the item “the admission type of the patient’s last visit in the prior 12 months is non-elective” is to adopt control strategies for the patient to avoid needing emergency care.

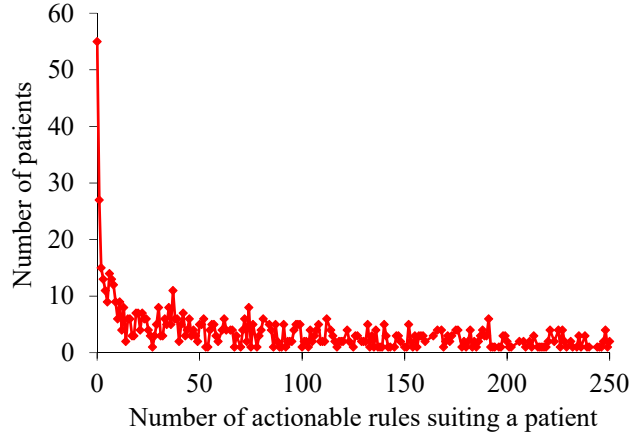
#### Our automatic explanation method’s performance

We evaluated our automatic explanation method on the test set. Our method explained the forecasting results for 97.88% (599/612) of the children (age  $< 18$ ) with asthma and 97.45% (1,605/1,647) of the adults (age  $\geq 18$ ) with asthma our KPSC model correctly forecasted to undergo asthma-related hospital visits in the succeeding year. Put together, our method explained the forecasting results for 97.57% (2,204/2,259) of the patients with asthma our KPSC model correctly forecasted to undergo asthma-related hospital visits in the succeeding year. For every such patient, on average our method provided 1,516.25 (SD 2161.30) explanations, each from one rule, and found 24.04 (SD 8.68) actionable items.

For the patients with asthma whom our KPSC model correctly forecasted to undergo asthma-related hospital visits in the succeeding year, Figures 2 and 3 display the patient distribution by the number of actionable rules suiting a patient. Having a long tail, this distribution is greatly skewed towards the left. As the number of rules suiting a patient rises, the number of patients each covered by so many rules tends to decline non-monotonically. The biggest number of rules suiting a patient is fairly large: 15,252. Yet, only one patient matches so many rules.

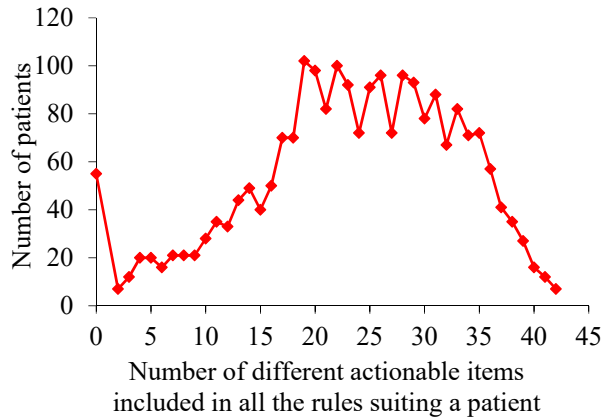


**Figure 2.** For the patients with asthma whom our KPSC model correctly forecasted to undergo asthma-related hospital visits in the succeeding year, the patient distribution by the number of actionable rules suiting a patient.



**Figure 3.** For the patients with asthma whom our KPSC model correctly forecasted to undergo asthma-related hospital visits in the succeeding year, the patient distribution by the number of actionable rules suiting a patient when this number is  $\leq 250$ .

For the patients with asthma whom our KPSC model correctly forecasted to undergo asthma-related hospital visits in the succeeding year, Figure 4 displays the patient distribution by the number of different actionable items included in all of the rules suiting a patient. The biggest number of different actionable items included in all of the rules suiting a patient is 42, much less than the biggest number of actionable rules suiting a patient. As noticed in our previous automatic explanation paper [26], two or more actionable items included in the rules suiting a patient often connect to the same intervention.



**Figure 4.** For the patients with asthma whom our KPSC model correctly forecasted to undergo asthma-related hospital visits in the succeeding year, the patient distribution by the number of different actionable items included in all the rules suiting a patient.

Our automatic explanation method provided explanations for 67.61% (2,943/4,353) of the patients with asthma who would undergo asthma-related hospital visits in the succeeding year.

## Discussion

### Principal results

The results presented in this paper are similar to those given in our previous automatic explanation paper [26]. For forecasting asthma-related hospital visits, our automatic explanation method exhibited decent generalizability to KPSC. In particular, our method explained the forecasting results for 97.57% (2,204/2,259) of the patients with asthma our KPSC model correctly forecasted to undergo asthma-related hospital visits in the succeeding year. This fraction is comparable to that (89.68%) on Intermountain Healthcare data in our previous automatic explanation paper [26], and is large enough for putting our automatic explanation method into daily clinical use. After further development to boost its accuracy, our KPSC model combined with our automatic explanation method could be employed to guide asthma care management’s use to help enhance patient outcomes and drop healthcare costs.

Our automatic explanation method provided explanations for 67.61% (2,943/4,353) of the patients with asthma who would undergo asthma-related hospital visits in the succeeding year. This fraction is less than the 97.57% (2,204/2,259) success rate,

at which our method explained the forecasting results for the patients with asthma our KPSC model correctly forecasted to undergo asthma-related hospital visits in the succeeding year. This is possibly due to correlation among the association rules' and our KPSC model's forecasting results. Among the patients with asthma whom our KPSC model correctly forecasted to undergo asthma-related hospital visits in the succeeding year, many are easy cases for us to explain their outcomes using association rules. Among the patients with asthma who would undergo asthma-related hospital visits in the succeeding year and whose outcomes were incorrectly forecasted by our KPSC model, many are hard cases for any model to correctly explain or forecast their outcomes.

### Displaying the automatic explanations

Many rules could suit a patient. In this case, it is undesirable to list all of them all at once and overwhelm the automatic explanation function's user. Instead, we should rank these rules and display the top few (e.g., three) of them by default. If desired, the user can ask the automatic explanation function to show more rules. In ranking the rules suiting a patient and the items on the left hand side of a rule, we consider the following factors and strike a balance among them:

- 1) All else being equal, rules with fewer items on their left hand sides are easier to understand and should be ranked higher.
- 2) All else being equal, rules with higher confidence are more precise and should be ranked higher.
- 3) All else being equal, rules with higher commonality cover more patients with the poor outcome and should be ranked higher.
- 4) The automatic explanation function's user tends to read the rules one by one in the display order. All else being equal, the more items on the left hand side of a rule appear in higher-ranked rules, the less new information that the user has not seen so far is contained in the rule and the lower the rule should be ranked.
- 5) Consider the items on the left hand side of a rule. The automatic explanation function's user tends to read the items one by one in the display order. All else being equal, the items that have appeared in higher-ranked rules contain repeated information and should be put after the other items that have not appeared in any of the higher-ranked rules.
- 6) The automatic explanation function's user cares about finding suitable interventions for the patient. Consider the items on the left hand side of a rule. All else being equal, the actionable items should be put before the non-actionable items.
- 7) Actionable rules should be ranked higher than non-actionable rules.

We are in the process of preparing a paper describing our rule ranking method in detail.

### Related work

As described in the book [34] and the survey paper [35], many other researchers have proposed miscellaneous methods for automatically offering explanations for machine learning models' forecasting results. Such explanations are typically not in rule format. Many such methods sacrifice part of the forecasting accuracy, and/or are designed for a particular machine learning algorithm. Also, none of those methods can automatically suggest customized interventions. In comparison, our automatic explanation method supplies rule-format explanations for any machine learning model's forecasting results on tabular data, as well as suggests customized interventions with no accuracy loss. Rule-format explanations are easier to apprehend and can suggest customized interventions more directly than other forms of explanations.

To the best of our knowledge, we were the first to use association rules to automatically supply rule-format explanations for any machine learning model's forecasting results on tabular data and to suggest customized interventions with no accuracy loss [30]. Our original method [30] was designed for relatively balanced data and initially tested on the case of forecasting type 2 diabetes diagnoses. Subsequently, Alaa *et al.* [36,37] applied our original method to multiple medical prediction tasks. So far, no researcher outside of our group has applied our extended automatic explanation method [26], which can handle imbalanced data, to any prediction task. Rudin *et al.* [38,39] used rules to automatically supply explanations for any machine learning model's forecasting results. Those rules are not association rules, are unknown before the prediction time, and hence cannot be used to automatically suggest customized interventions at the prediction time. In comparison, the association rules used in our automatic explanation method are mined before the prediction time and used to automatically suggest customized interventions at the prediction time.

### Limitations

This study has three limitations, all of which can be fine areas for future work:

- (1) For forecasting asthma-related hospital visits, our study evaluated our automatic explanation method's generalizability to a single healthcare system. It would be nice to assess our automatic explanation method's generalizability to other healthcare systems like academic ones, which have differing properties from Intermountain Healthcare and KPSC. In comparison to non-academic ones, academic healthcare systems tend to handle more complex and sicker patients [40]. To prepare for such an evaluation, we are currently retrieving a data set of patients with asthma from the enterprise data warehouse of University of Washington Medicine [41].

- (2) Our study evaluated our automatic explanation method's generalizability only for forecasting asthma-related hospital visits. It would be nice to assess our automatic explanation method's generalizability for other diseases and outcomes [41].
- (3) Our current automatic explanation method is designed for structured data and traditional machine learning algorithms that are not deep learning ones. It would be nice to extend our method so it can also handle deep learning models built directly on longitudinal data. [41,42].

## Conclusions

In its first generalizability assessment, our automatic explanation method for imbalanced tabular data exhibited decent generalizability to KPSC for forecasting asthma-related hospital visits. After further development to boost its accuracy, our KPSC model combined with our automatic explanation method could be employed to guide asthma care management's use to help enhance patient outcomes and drop healthcare costs.

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## Authors' contributions

GL was mainly responsible for the paper. He conceptualized and designed the study, performed literature review and data analysis, and wrote the paper. CK, CLN, WWC, MS, and RSZ provided feedback on various medical issues, contributed to conceptualizing the presentation, and revised the paper. CK and CLN took part in retrieving the KPSC data set and interpreting its detected peculiarities.

## Conflicts of interest

None declared.

## Abbreviations:

AUC: Area Under the receiver operating characteristic Curve  
ED: emergency department  
ICD-9: International Classification of Diseases, Ninth Revision  
ICD-10: International Classification of Diseases, Tenth Revision  
KPSC: Kaiser Permanente Southern California  
XGBoost: extreme gradient boosting

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