A Roadmap for Optimizing Asthma Care Management via Computational Approaches

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Abstract
Asthma affects 9% of Americans and incurs $56 billion in cost, 439 thousand hospitalizations, and 1.8 million emergency room visits annually. A small fraction of asthma patients with high vulnerabilities, severe disease, or great barriers to care consume most healthcare costs and resources. An effective approach is urgently needed to identify high-risk patients and intervene to improve outcomes and to reduce costs and resource use. Care management is widely used to implement tailored care plans for this, but is expensive and has limited service capacity. To maximize benefit, we should enroll only patients anticipated to have the highest costs or worst prognosis. Effective care management requires correctly identifying high-risk patients, but current patient identification approaches have major limitations. This article pinpoints these limitations and outlines multiple machine learning techniques to address them, providing a roadmap for future research.

Keywords: patient care management; clinical decision support; machine learning

1. Introduction
Asthma affects 9% of Americans [1-3] and incurs $56 billion in cost [4], 3,630 deaths, 439 thousand hospitalizations, and 1.8 million emergency room visits annually [1]. As is true for many chronic diseases, a small fraction of asthma patients with severe disease, high vulnerabilities, or great barriers to care consume most healthcare costs and resources [5, 6]. The top 20% of patients consume 80% of costs, the top 1% consume 25% [6, 7]. An effective approach is needed to find high-risk patients and implement appropriate interventions to improve outcomes and to reduce costs and resource use.

Almost all private health plans provide and most major employers purchase care management services, which implement tailored care plans with early interventions for high-risk patients to avoid high costs and health status degradation [8-10]. Care management is a cooperative process to assess, plan, coordinate, implement, evaluate, and monitor services and options to fulfill a patient’s health and service needs [11]. It includes a care manager who regularly calls the patient, arranges for health and related services, and helps make medical appointments. Asthma exacerbations account for 63% of annual total asthma cost [12, 13]. Using care management properly can reduce asthma exacerbations, cut hospital (re)admissions and emergency room visits by up to 40% [9, 14-18], trim cost by up to 15% [15-19], and enhance patient treatment adherence, quality of life, and satisfaction by 30-60% [14].

Although widely used, care management has costs of its own and can require >$5,000 per patient per year [15]. Owing to resource constraints, usually only 1-3% of asthma patients are enrolled in care management [7]. Ideally, the ones enrolled should be those at the highest risk. Predictive modeling is the best method to find high-risk patients [20]. It uses a model for predicting individual patient cost or health outcome to automatically find high-risk patients [14, 21-26]. Cost reflects use and efficiency of care, and indirectly reflects outcomes like hospitalization and emergency room visit. For patients predicted to have the highest costs or worst outcomes, care managers examine patient records, consider various factors such as social ones, and make the ultimate allocation and intervention decisions. Correct identification of high-risk patients is key to effective care management, but current identification methods have limitations. This paper makes two contributions. First, we pinpoint these limitations. Second, we outline several machine learning techniques to address them, offering a roadmap for future research. Clinical machine learning is a promising technology for finding high-risk patients [27]. Our discussion focuses on the machine learning predictive modeling aspect of care management for identifying high-risk patients. Besides this, several other factors, such as patient behavior pattern, patient motivation, trigger for patient engagement [28-30], and patient and caregiver education...
Although several dozen risk factors for adverse outcomes in asthma are known [6, 18, 36, 39, 40, 42-46], an existing model with the patient’s medical history when they need to make enrollment decisions. They need to understand why a patient is managers to spend extra time and miss suitable interventions.

Limitation 1: Low prediction accuracy causes misclassification, unnecessary costs, and suboptimal care

Current predictive models for individual patient costs and health outcomes exhibit poor accuracy causing misclassification and need improvement. When projecting individual patient cost, the \( R^2 \) accuracy measure of models reported in the literature is \(<20\%\) [32] and the average error is typically comparable to the average cost [33]. When projecting individual patient health outcome, the area under the receiver operating characteristic curve accuracy measure is usually \(<0.8\) [6, 34, page 281, 35-40]. Those large errors make enrollment miss more than half of patients a care management program can help most [14, 26]. Weir et al. [26] showed that the top 10% risk group identified by a predictive model missed \(>60\%\) of the top 10% and about 50% of the top 1% of patients who had the largest costs. If we could find 10% more of the top 1% patients who had the largest costs and enroll them, we could save up to $210 million in asthma care each year and also improve health outcomes [6, 36, 37]. In general, due to the large patient base, a small improvement in accuracy will benefit many patients, having a large positive impact. A 5% absolute improvement in accuracy already makes a healthcare system willing to deploy a new model [41].

Existing predictive models have low accuracy for multiple reasons:

1. Although several dozen risk factors for adverse outcomes in asthma are known [6, 18, 36, 39, 40, 42-46], an existing model typically uses only a few of them (e.g., \(<10\) [6, 36-39]. Existing models were often constructed using data obtained from clinical trials or old-fashioned electronic medical records that collected only a limited set of variables [47]. No published model explores all known risk factors available in modern electronic medical records, which collect an extensive set of variables [47].

2. As with many diseases, many features (a.k.a. independent variables that include both raw and transformed variables) predictive of adverse outcomes in asthma have likely not been identified. For instance, using a data-driven approach to find new predictive features from many variables in electronic medical records, Sun et al. improved prediction accuracy of heart failure onset by \(>20\%\) [48]. Existing predictive models for health outcomes of individual asthma patients were developed mainly using a small number of patients (e.g., \(<1,000\) or variables (e.g., \(<10\) [6, 36-39], creating difficulty in finding many predictive features and their interactions.

3. Existing models mainly use patient features only, presuming that each patient’s cost and health outcomes relate only to the patient’s characteristics and are unassociated with characteristics of the healthcare system (e.g., the treating physician and facility). However, system features are known to be influential, have larger impacts on patients with the worst outcomes, and can account for up to half of the variance in their outcomes in certain cases [49-52]. The use of physician characteristics has been examined in predictive modeling only minimally [35], creating a knowledge gap for system features in general.

4. Applying care management to a patient tends to improve his/her health outcomes and reduce his/her cost excluding the cost of care management. Yet, existing models omit the factor of care management enrollment.

5. A healthcare system often has limited training data, whereas a model’s accuracy generally increases with more training data. Different systems have differing data distributions [53] and collected attributes, impacting the performance and applicability of a model trained using one system’s data for another system [54-57]. To address these two issues, one can perform transfer learning and use other source systems’ information to improve model accuracy for the target system [54, 58, 59]. Transfer learning typically requires using other source systems’ raw data [60, 61]. But, systems are rarely willing to share their raw data because of confidentiality concerns with regard to patient data. Research networks [62-64] mitigate, but do not solve, the problem. Many systems are outside a network, whereas systems in it share raw data of limited attributes. Alternatively, one can conduct model updating or model/ensemble averaging that requires only the trained models, but not the raw data, from other source systems. Model updating applies to only one source system and cannot combine information from multiple source systems, limiting the improvement in model accuracy. Many model updating methods work for only certain kinds of models [65]. Model averaging usually uses the same averaging approach like weights in all regions of the feature space [66]. Yet, to boost model accuracy, different averaging approaches are often needed in differing regions [67]. Also, if the target system does not have enough data to train a reasonably accurate model as a starting point, further averaging with the trained models from other source systems may not improve the final model’s accuracy to a satisfactory level.

Limitation 2: No explanation of the reasons for a prediction causes poor adoption of the prediction and busy care managers to spend extra time and miss suitable interventions

Unlike physicians who see patients regularly, care managers often have no prior interaction with a patient and are unfamiliar with the patient’s medical history when they need to make enrollment decisions. They need to understand why a patient is forecasted to be at high risk before allocation to care management and creating a tailored care plan, but have limited time to
A care manager may develop a tailored care plan for a patient using variable and subjective clinical judgment, but may miss certain suitable interventions because: (1) Many features exist. As true for any human, a typical care manager can process ≤9 information items at once [69], making it hard to find all reasons from many possible feature combinations. (2) Considerable practice variation like by 1.6-5.6 times appears across differing care managers, facilities, and regions [5, 34, 70-78]. (3) Care accessible than patients. An intervention at the system level can affect many patients, whereas an intervention for a patient can be more efficient and effective than those for patients [50, 79]. Some system levels like treating physicians are more interventions like extending physician office hours are not identified as possible interventions. Interventions at the system level usually include in the care plan interventions addressing patient factors only. For the healthcare system, some useful at low risk, but often does not tell which of the two cases the patient falls into and does not give clear guidance on whether the Moving them off the program can lead to undesirable outcomes. An existing model can predict a patient in the program to be status and ready to safely leave the program. For some others, using the program is essential for keeping them at low risk. Limitation 3: For patients on care management, a lack of causal inference capability causes the predictive model to give no clear guidance on which patients could be moved off care management

An asthma patient’s risk changes over time, whereas a care management program can enroll only limited patients. To best use the program, all patients remaining in the health plan are re-evaluated for their risk periodically, e.g., on an annual basis. The patients who are in the program and now predicted to be at low risk are moved off the program to make room for those previously at low risk, but now at high risk. Doing this properly requires answering intervention queries via causal inference [80, 81], which is beyond most existing predictive models’ capability. Some patients in the program are in a stable status and ready to safely leave the program. For some others, using the program is essential for keeping them at low risk. Moving them off the program can lead to undesirable outcomes. An existing model can predict a patient in the program to be at low risk, but often does not tell which of the two cases the patient falls into and does not give clear guidance on whether the patient should be moved off the program. This is particularly the case if we expect care management to have greatly varying impact across different subgroups of patients and would like to consider their differences in impact explicitly.

3. Machine learning techniques for optimizing asthma care management

New techniques are needed to identify more high-risk asthma patients and provide appropriate care. Besides those proposed in our paper [27], we can use the following machine learning techniques to optimize asthma care management.

3.1 Techniques for improving prediction accuracy of individual patient costs and health outcomes

Use all known risk factors for adverse asthma outcomes available in modern electronic medical records

Many risk factors for adverse asthma outcomes are known [6, 13, 36, 39, 40, 42-46] and available in modern electronic medical records. To fully use their predictive power, we consider all of these risk factors when building models for predicting individual patient costs and health outcomes. We perform feature selection to remove known risk factors that are not predictive for reasons such as data quality and variable redundancy. Clinical experts can suggest for consideration additional features that have clear medical meaning, but have not previously been used for predicting asthma outcomes or costs. Two examples of such features are: (1) exercise vital signs and (2) whether the patient has seen an asthma specialist (allergist or pulmonologist) recently. Patients who have seen asthma specialists tend to have more severe asthma, worse health outcomes, and higher costs than those who have seen primary care physicians only. Another way to consider this factor is to build separate models for patients who have seen asthma specialists and patients who have seen primary care physicians only.

Use many asthma patients and patient features

Many features predictive of adverse outcomes in asthma have not yet been identified. To find new predictive features, we use many asthma patients and a data-driven approach to explore many standard patient features listed in the clinical predictive modeling literature [5, 34, 65]. Some patient features cover social, economic, and community factors. An example of such features is the average income level of the area that the patient lives in. To combine known risk factors and predictive features...
derived from data, during feature selection we give a higher weight to known risk factors (e.g., by multiplying their scores by a factor >1) so that they are more likely to be selected than the other features. This new approach can handle both categorical and numerical variables, discover new predictive features, and remove known risk factors that are not predictive for reasons such as data quality and variable redundancy. In contrast, the existing method for combining known risk factors and predictive features derived from data [48, 82] can neither directly handle categorical variables nor remove known, non-predictive risk factors.

Use healthcare system features
To consider their impact, we include healthcare system features in building models for predicting individual patient costs and health outcomes. For each healthcare system level like physician or facility, we construct a profile containing its own information (e.g., facility hours) and aggregated historical data of its patients (omitting the index patient) extracted from the provider’s administrative and electronic medical record systems. The count of the physician’s asthma patients [83] is an example of profile variables.

Some system features are computed using only system profile variables. Our paper [27] listed several physician-level features like the average outcome of a physician’s asthma patients. Examples of facility-level features are: (1) whether a facility is open at night or on weekends, (2) the number of staffed beds in a hospital, (3) facility type, and (4) availability of enhanced services such as asthma hotline, foreign language translation, special primary care team for asthma, and special home care. The other system features are computed by combining system profile and patient variables, reflecting the match of physician/facility and patient. An example of such features is the distance between the patient’s home and closest urgent care facility.

Use all patients
The standard approach for predicting individual patient costs or health outcomes in asthma is to build a model using only asthma patient data. In the presence of many features, we may not have enough asthma patients to train the model and to obtain high prediction accuracy. To address this issue, we add a binary indicator feature for asthma and train the model on all patients, not just asthma patients. Asthma patients and other patients share many features in common. We can better tune these features’ coefficients in the model by using all patients.

Consider the factor of care management enrollment
To consider care management’s impact on costs and health outcomes, we add a binary indicator feature for care management enrollment when building models for predicting individual patient costs and health outcomes [84].

Perform transfer learning using trained models from other source healthcare systems
To address limited training data and improve model accuracy for the target healthcare system, we perform transfer learning using trained models from other source systems. Organizations are usually more willing to share their trained models than their raw data. Publications often describe trained models in detail. A model trained using a source system’s data includes much information useful for the prediction task on the target system, particularly if the source system has lots of training data. Our transfer learning approach can handle all kinds of features, prediction targets, and models used in the source and target systems. Our approach can potentially improve model accuracy regardless of the amount of training data available at the target system. Even if the target system has enough training data in general, it may not have enough training data for a particular pattern. A trained model from a source system can help make this up if the source system contains enough training data for the pattern.

Different healthcare systems use differing schemas, medical coding systems, and medical terminologies. To enable the application of a model trained using a source system’s data to the target system’s data, we convert every source system’s and the target system’s data sets into the same common data model (e.g., OMOP [85]) format and its linked standardized terminologies [86]. For each available source system, we use the method described in our paper [27] to form a table listing various combinations of attributes. For each combination of attributes, the table includes the model trained using it and the source system’s data. For the combination of attributes collected by both the source and target systems, we find the corresponding model trained for the source system. For every data instance of the target system, we apply the model to the data instance, obtain the prediction result, and append it as a new feature to the data instance. In this way, the expanded data instance includes two types of features: (1) the new features obtained using the models trained for the source systems, with one feature per source system, and (2) the patient and system features in the target system. For the target system, we use both types of features and its data to build the final model (Figure 1). Since correlation exists among features of the first type constructed for the same prediction target, regularization is likely needed to make the final model stable. Features of the second type can either serve as inputs to the final model directly, or be used to build a model whose output serves as an input to the final model. If the target system has limited training data, we perform aggressive feature selection on the second type of features to let the number of remaining features match the amount of training data. This does not impact the first type of features. When a source system has enough data to train a model, the model can include many patient and system features as its inputs. The corresponding
Techniques for creating a new function to automatically explain prediction results for identified high-risk patients

To improve prediction accuracy, it is desirable to use machine learning to construct models for predicting individual patient costs and health outcomes [27]. For patients with projected risk above a fixed threshold like the 95th percentile, we can use our previously developed method [27, 87] to automatically explain machine learning prediction results with no accuracy loss. The explanations can help clinicians make care management enrollment decisions, identify interventions at various levels, create tailored care plans based on objective data, and inspect structured attributes in patient records more efficiently. An example of patient interventions that can be put into tailored care plans is to offer transportation for a patient living far from his/her primary care physician. An example of interventions at the system level is to launch a new primary care clinic in a region with no such clinic close by.

Each patient has the same set of patient and healthcare system features and is marked as high or not high risk. Our method mines from historical data class-based association rules related to high risk. Each rule’s left hand side is the conjunction of one or more feature-value pairs. An example rule is: the patient had ≥2 urgent care visits for asthma last year AND lives ≥15 miles away from his/her physician → high risk. Through discussion and consensus, the clinicians in the automatic explanation function’s design team check mined rules and drop those making no or little clinical sense. For every rule kept, the clinicians enumerate zero or more interventions targeting the reason the rule shows. At prediction time, for each patient the predictive model identifies as high risk, we find and display all rules of which the patient fulfills the left hand side conditions. Every rule shows a reason why the patient is projected to be at high risk.

Conditional risk factors

Our method can find a new type of risk factor termed conditional risk factors, which increase a patient’s risk only when some other variables are also present and can be used to design tailored interventions. This broadens risk factors’ scope, as ordinary risk factors are independent of other variables. Our method can automatically find appropriate cut-off thresholds for numerical variables and inform new interventions based on objective data. For instance, for the aforementioned association rule, our method would automatically find the cut-off thresholds of 2 in the number of urgent care visits and 15 miles in distance. Then we map all patients who satisfy the rule’s left hand side conditions and have adverse outcomes in the next year. For the intervention of opening new primary care clinics, this informs the new clinics’ locations by maximizing the number of these patients living <15 miles away. A cost-benefit analysis can determine whether adopting this intervention is worthwhile.

Use association rules to help understand the subtleties in the data and improve model accuracy

For each association rule related to high risk, the proportion of patients who are at high risk and satisfy the rule’s left hand side is called the rule’s support showing the rule’s coverage. Among all patients fulfilling the rule’s left hand side, the proportion of patients at high risk is called the rule’s confidence showing the rule’s accuracy. Our method discretizes each numerical feature into a categorical one, and mines rules exceeding some pre-defined minimum support $s_i$ and minimum confidence $c_i$ and containing only features that the predictive model uses to make predictions, no more than a pre-selected...
number \( n_1 \) of feature-value pairs on the left hand side, and no feature-value pairs that the automatic explanation function’s designers specify as unrelated to high risk.

Consider all of the association rules related to high risk and satisfying all conditions above except for the last one. If a feature-value pair is specified by the automatic explanation function’s designers as unrelated to high risk, but appears in many of these rules, the designers can examine the pair in detail and determine if [84]:

1. The pair is associated with a surrogate condition related to high risk. This helps us understand the subtleties in the data and how they affect machine learning. Sometimes, we can use the information to design new interventions targeting the surrogate condition. For instance, suppose the pair is that the patient had two outpatient visits for asthma last year and the associated surrogate condition is non-compliance coupled with high vulnerability, e.g., due to genetics or working environment. For each rule related to high risk and whose left hand side contains the pair and indicates the surrogate condition (e.g., by mentioning that the patient had \( \geq 2 \) hospitalizations for asthma last year), we keep the rule, inspect the patients satisfying the rule’s left hand side, and arrange regular phone checks for some of them.

2. The feature is uninformative. Retraining the predictive model after dropping the feature can possibly serve as a new way to improve model accuracy, and/or make the model generalize better to other healthcare systems beyond the one in which it was developed. Ribeiro et al. [88] showed that on non-clinical data, users of an automatic explanation function could use sparse linear model-based explanations to find uninformative features. Retraining the model after dropping these features improved model accuracy. We are unaware of any published work using rule-based explanations to do this, particularly on clinical data. As Ribeiro et al. [89] mentioned, rule-based explanations are preferred over sparse linear model-based ones. Ribeiro et al.’s approach [88] works for binary features only. In comparison, our approach can handle all kinds of features.

A healthcare system often has limited training data impacting model accuracy. To improve model accuracy, we can enlarge the training set by generating synthetic data instances:

1. Using historical data from the target and/or other source systems, we mine another set \( R_2 \) of association rules related to high risk. The clinicians in the automatic explanation function’s design team check the rules in \( R_2 \) and keep only those making much clinical sense (e.g., tending to generalize across different systems). If desired, we can remove additional rules from \( R_2 \) so that the remaining ones are not too similar to each other. For each remaining rule \( r \in R_2 \), we generate multiple synthetic data instances. Each synthetic data instance \( I_s \) satisfies \( r \)'s left hand side and is labeled high risk. For each feature not on \( r \)'s left hand side, \( I_s \)'s feature value is chosen randomly. For each numerical feature that our automatic explanation method discretizes into a categorical one, \( I_s \)'s numerical feature value is chosen randomly within the bounds of the category corresponding to \( r \)'s categorical feature value. Compared with those used for giving explanations, the rules in \( R_2 \) are required to exceed some pre-defined minimum confidence \( c_2 \) that is both \( \geq c_1 \) and close to 1 (e.g., 90%), so that the synthetic data instances are likely to be correctly labeled. To help ensure \( R_2 \) contains enough rules, each rule in \( R_2 \) needs to exceed a lower, pre-defined minimum support \( s_2 \leq s_1 \) and contains no more than a larger, pre-selected number \( n_2 > n_1 \) of feature-value pairs on the left hand side.

2. The clinicians specify some rules related to high risk based on medical knowledge. Each rule is used to generate multiple synthetic data instances in a way similar to above. Alternatively, we can use these rules and the predictive model together at prediction time. We use these rules to identify a subset of high-risk patients, and apply the predictive model to the other patients not satisfying the left hand side of any of these rules.

Using synthetic data instances to improve model accuracy has been done before, e.g., for images [90] or via making interpolations among actual data instances [91]. We are unaware of any published work using association rules for this purpose. In contrast to interpolating all feature values of each synthetic data instance, our association rule-based method retains key feature values to increase the chance that the data instance is correctly labeled.

Expand automatic explanation’s coverage of patients

The mined association rules \( R_1 \) used for giving explanations represent frequent patterns linked to high risk. Yet, certain patients are at high risk for uncommon reasons and not covered by any of these rules. To expand automatic explanation’s coverage of patients, we improve our prior method [27, 87] by generating synthetic data instances, adopting the predictive model to label them, and using them to mine additional rules to cover more patients [88]. The improved method generalizes to many clinical applications.

More specifically, during association rule mining, some rules are found and then removed because they fall below the pre-defined minimum support \( s_1 \) or minimum confidence \( c_1 \). Instead of removing them, we keep as backup all such rules \( R_1 \) that exceed both the minimum confidence \( c_1 \) and another pre-defined minimum support \( s_2 \leq s_1 \) and sort them in descending order of support. We can use techniques similar to those used in our prior method [27, 87] to prune redundant rules in \( R_1 \). At prediction time, for each patient the predictive model identifies as high risk and not covered by any rule in the set \( R_1 \), we check the rules in the backup set \( R_2 \) sequentially. For each rule \( r \in R_2 \), we generate one or more synthetic data instances in a way similar to above to make the total number of data instances satisfying \( r \)'s left hand side reach the minimum support \( s_1 \). We use the
Technique for making causal inference for periodically re-identifying high-risk patients

To provide causal inference capability, we need to estimate the impact of care management on a patient’s cost or health outcome. We use this estimate to adjust the cost or health outcome threshold for deciding whether a patient on care management should be moved off care management. Propensity score matching is one technique for doing this on observational data [80, 81, 92]. Using the same features adopted for predicting individual patient cost or health outcome, we build a model to predict whether a patient will be enrolled in care management. The propensity score is the predicted probability of enrollment. We match each patient on care management to a patient not on care management on propensity score. The impact of care management is estimated as the average cost or health outcome difference between the group of patients on care management and the matched group of patients not on care management. We can apply the propensity score matching technique to the entire group of patients. Alternatively, if we expect care management to have greatly varying impact across different subgroups of patients, we can apply the propensity score matching technique to each subgroup of patients separately.

4. Conclusions

Care management is broadly used for improving asthma outcomes and cutting costs, but current high-risk patient identification methods have major limitations degrading its effectiveness. This paper pinpoints these limitations and outlines multiple machine learning techniques to address them, offering a roadmap for future research. Besides being used for asthma, care management is also broadly adopted in managing patients with diabetes, heart diseases, or chronic obstructive pulmonary disease [5], where similar limitations in patient identification exist and techniques similar to those outlined in this paper can be used to optimize care management. The principles of many of our proposed techniques generalize to other predictive modeling tasks beyond those for care management.

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Authors’ contributions

GL was mainly responsible for the paper. He performed the literature review, conceptualized the presentation approach, and drafted the manuscript. KAS gave feedback on various medical issues and revised the manuscript. Both authors read and approved the final manuscript.

Conflicts of interest

None declared.

Ethics, consent, and permissions

This paper does not include any individual person’s data.

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