Asthma in Scotland: prescribing trends since the National Review of Asthma Deaths (NRAD)

Quentin Kenner
*University of Kentucky*, kenner.quentin@gmail.com

Follow this and additional works at: [https://uknowledge.uky.edu/cph_etds](https://uknowledge.uky.edu/cph_etds)

Part of the Public Health Commons

Right click to open a feedback form in a new tab to let us know how this document benefits you.

**Recommended Citation**


[https://uknowledge.uky.edu/cph_etds/275](https://uknowledge.uky.edu/cph_etds/275)

This Graduate Capstone Project is brought to you for free and open access by the College of Public Health at UKnowledge. It has been accepted for inclusion in Theses and Dissertations–Public Health (M.P.H. & Dr.P.H.) by an authorized administrator of UKnowledge. For more information, please contact UKnowledge@lsv.uky.edu.
STUDENT AGREEMENT:

I represent that my capstone and abstract are my original work. Proper attribution has been given to all outside sources. I understand that I am solely responsible for obtaining any needed copyright permissions. I have obtained needed written permission statement(s) from the owner(s) of each third-party copyrighted matter to be included in my work, allowing electronic distribution (if such use is not permitted by the fair use doctrine) which will be submitted to UKnowledge as Additional File.

I hereby grant to The University of Kentucky and its agents the irrevocable, non-exclusive, and royalty-free license to archive and make accessible my work in whole or in part in all forms of media, now or hereafter known. I agree that the document mentioned above may be made available immediately for worldwide access unless an embargo applies.

I retain all other ownership rights to the copyright of my work. I also retain the right to use in future works (such as articles or books) all or part of my work. I understand that I am free to register the copyright to my work.

REVIEW, APPROVAL AND ACCEPTANCE

The document mentioned above has been reviewed and accepted by the student’s advisor, on behalf of the advisory committee, and by the Director of Graduate Studies (DGS), on behalf of the program; we verify that this is the final, approved version of the student’s capstone including all changes required by the advisory committee. The undersigned agree to abide by the statements above.

Quentin Kenner, Student

Dr. Richard Ingram, Committee Chair

Dr. Sarah Wackerbarth, Director of Graduate Studies
Asthma in Scotland: prescribing trends since the National Review of Asthma Deaths (NRAD)

CAPSTONE PROJECT PAPER

A paper submitted in partial fulfillment of the Requirements for the degree of Master of Public Health in the University of Kentucky College of Public Health

By
Quentin Kenner
Frankfort, Kentucky

Final Examination:
Via zoom on 04/17/2020

Capstone Committee:
Richard Ingram, DrPH (Chair)
Martha Riddell, DrPH
Clark Kebodeaux, PharmD
Acknowledgments

I would like to thank my friends and family for support during my education. I would like to express gratitude to my capstone committee Dr. Ingram, Dr. Riddell, and Dr. Kebodeaux, for the support and guidance they gave me on this project. Their knowledge and expertise allowed me to reflect and grow. I also want to thank Stuart McTaggart, Barry Media, and the IDS department at NHS Scotland. Their work and guidance were pivotal in the development of this project. Lastly, I want to thank the College of Public Health and the College of Pharmacy for allowing such opportunities to grow knowledge and desire to improve healthcare in the United States.
Abstract

Asthma in Scotland: prescribing trends since the National Review of Asthma Deaths (NRAD)

Purpose: Asthma remains prevalent worldwide with implications for morbidity and mortality. In Scotland, 1 in 14 people are currently being treated for asthma. Asthma burden prompted the creation of the National Review of Asthma Deaths (NRAD), which identified contributing factors. Since the NRAD, guidelines have changed and therapeutic indicators have been developed with an increased emphasis on controller medications. Few publications describe how the NRAD study affected prescribing and if inequalities among the asthmatic population exist. This study aimed to determine whether patients were receiving appropriate treatment according to therapeutic guidelines and how prescribing has changed over time.

Methods: Scotland’s Prescribing Information System (PIS) was used to gain access to population-based outpatient prescription drug claims for Short-Acting Beta-Agonists (SABAs), Long-Acting Beta-Agonists (LABAs), and Inhaled Corticosteroids (ICSs), to create a cohort of asthma patients aged 0-39. All ethical approvals necessary were obtained according to the National Health System (NHS) of Scotland’s specified guidelines for de-identified patient data. Patients were stratified by age, gender, socioeconomic status (SES), and medication type to compare rates of prescribing for different populations. Using NRAD and the national therapeutic indicators as metrics, the data was analyzed to assess changes over time. The primary outcomes included whether there was a difference in asthma prescribing from 2014 to 2018; if there were any significant demographics differences among those with uncontrolled asthma; and whether drug claims were consistent with asthma guidelines.

Results: A total of 222,637 patients were analyzed from 2014 and 205,758 from 2018. In 2018, 7.42% of those received more than 12 SABAs per year, 20.77% received more than 6, and 42.39% received more than 3, only slightly lower than in 2014 (8.85%, 21.83%, 43.73% respectively). For the most recent year that data was available (2018) further analyses were completed. Prevalence of receiving more than 12 SABAs was found to be higher among patients who were male, as well as patients aged 30-39, or those with lower SES. Use of greater than 12 SABAs varied almost two-fold between the populations with the highest and lowest SES (lowest SES – 9.0%; highest SES – 4.6%). When looking at measures related to the therapeutic guidelines, only 89% of patients receiving more than 12 SABAs had received an ICS; of those, only 41% received an adequate amount of ICS medications over the year.

Conclusion: Prescribing practices have changed slowly since the NRAD study was published. When looking at the therapeutic guidelines, prescription drug claims show a disconnect with the recommendations. There appears to remain an over-reliance on reliever medications with a deficit in controller medications. This study shows that a large Scottish asthmatic population remains at increased risk of poor outcomes. More studies are needed to further research hospitalization, morbidity, and mortality rates as well as cost analyses, to further characterize change over time and whether new measures are needed to improve outcomes.
Keywords:
Scotland, asthma, short-acting beta-agonist, prescribing trends, NRAD, socioeconomic status

List of Abbreviations:

WHO – World Health Organization
UK – United Kingdom
NRAD – National Review of Asthma Deaths
NHS – National Health System
SABA – short-acting beta-agonist
LABA – long-acting beta-agonist
ICS – inhaled corticosteroid
NTI – National Therapeutic Indictors
SIGN – Scottish Intercollegiate Guideline Network
BTS – British Thoracic Society
NICE – National Institute for Health and Care Excellence
GINA – Global Initiative for Asthma
PIS – Prescribing Information System
ISD – Information Services Division
NSS – National Services Scotland
UPI – Unique Patient Identifier
BNF – British National Formulary
SIMD – Scottish Index of Multiple Deprivation
Table of Contents

**Introduction** ................................................................. 6

**Methods** ........................................................................ 10
  - Trial Design ................................................................. 12

**Results** ........................................................................ 15

**Discussion** ...................................................................... 23
  - Limitations ................................................................. 30
  - Implications ............................................................... 31

**Conclusion** ................................................................. 32

**References** ..................................................................... 34

**Appendices** ............................................................... 38
Introduction

Asthma is a chronic inflammatory disease of the respiratory system that can result in dyspnea, wheezing, cough, and chest tightness due to airway obstruction [1]. The underlying pathophysiology and resulting airway obstruction can lead to potentially severe respiratory symptoms, limitations of activity, and asthma attacks (exacerbations) that can require urgent healthcare attention and can even be fatal [2]. Poorly controlled asthma has been linked to increases in the risk of poor quality of life, increased asthma attacks, increased healthcare expenditures, and even premature death [3,4].

Asthma remains a prevalent issue worldwide, with approximately 300 million people estimated to have asthma and an estimated 100 million more to be affected by the year 2025 [5,6]. While asthma-related hospitalizations and deaths have been shown to decrease in most countries [7], the global burden for patients with exacerbations and day-to-day symptoms has increased by almost 30% in the past 20 years [8]. In addition, the World Health Organization (WHO) has estimated that 15 million disability-adjusted life years are lost, and 250,000 asthma deaths are reported annually worldwide [9]. In the United Kingdom (UK), 5.4 million people are currently receiving treatment for asthma [10]. More concerning is that the UK had a 20% increase in the rate of asthma attack deaths over the five-year period from 2010 to 2015, culminating in 1434 people dying of an asthma attack in 2015 [11]. This spike prompted the National Review of Asthma Deaths (NRAD) in which the asthma deaths were reviewed to see if any common preventable mistakes might have precipitated the deaths.

The factors the NRAD looked at included: the use of National Health System (NHS) services, medical & professional care, prescribing & medicines use, patient factors,
and perception of risk or poor control [12]. The findings of the prescribing and medicines use component represents the basis for this study. Common asthma medications classes include short-acting beta-agonists (SABAs), long-acting beta-agonists (LABAs), and inhaled corticosteroids (ICSs). These medication classes can be categorized into reliever (SABAs and LABAs) or preventer medications (ICSs). Reliever medications only relieve the symptoms through dilating the airways allowing more air to pass through. In contrast, preventer medications help prevent the underlying cause of inflammation, allowing reversal of the pathophysiological changes that occur due to asthma [13]. Among the findings of NRAD in prescribing and medicines use was that there was evidence of excessive prescribing of reliever medications (SABAs), under-prescribing of preventer medications (ICSs), and evidence of inappropriate prescribing of LABA inhalers [12]. In addition to this, the NRAD found that 65% of the asthma deaths reviewed had a preventable factor [12]. These results showed that asthma treatment can be vastly improved in the UK and that there remains a population at-risk for fatal consequences despite advances in asthma treatment over the years.

In response to the NRAD, NHS Scotland issued National Therapeutic Indicators (NTI) aimed at medication findings of the study. NTIs are used to alert healthcare practitioners of a potential marker for poor disease state management that can be tracked over time. These NTIs represent a way to use prescription data to inform and monitor markers for potential poor economic outcomes, reduced healthcare outcomes, including impacts of morbidity and mortality, as well to track prescribing patterns in various regions of Scotland [14]. An example of an asthma NTI issued after the NRAD relevant to this study is, “More than 12 SABAs per annum as a percentage of all people prescribed SABAs
In addition to NTIs, disease-specific guidelines exist for numerous healthcare topics. For asthma, the main guidelines of reference in Scotland are the Scottish Intercollegiate Guideline Network/ British Thoracic Society (SIGN/BTS), but there also exists the National Institute for Health and Care Excellence (NICE), and the Global Initiative for Asthma (GINA). There is one specific change in the SIGN/BTS guidelines that is of interest to this study. This change is the add on of ICS medications as first-line options in the treatment of asthma. When the NRAD was published in 2014, the guidelines stated to start SABA medication as first-line then if the asthma is not controlled add on ICS [Figure 1, appendix]. In 2016 an update was released, and the main treatment change was considering add-on of ICS as soon as someone is diagnosed with asthma [Figure 2, appendix]. This change could result in ICS medications being started earlier in the treatment of asthma and could have implications on asthma outcomes.

When looking at the history of medication usage for asthma, there are many instances of changes to prescribing guidelines as more information and new medications are introduced. Medications have played a direct role in the decrease in mortality in the last 50 years but can also be linked to spikes in mortality during specific time frames [12,16,17]. These publications help to show the changes over time of asthma prescribing and give a snapshot of the implications that asthma medications have on outcomes. The interplay of evidence-based medicine and uptake into practice is a relevant interest for the data-driven and connected world. It is suggested that it sometimes takes more than a decade to implement research results in clinical practice and that it is often challenging to sustain innovations over time [18]. With all of the available resources and guidelines specific to asthma, it is understandably a daunting task for healthcare providers to remain up to date.
with this complex disease that represents just one of the numerous chronic diseases. It is of interest to understand and have methods to influence prescribing habits to coincide with the most recent information.

Based upon the NRAD, Scotland’s NTIs, and changes in asthma guidelines, there is a lot of evidence for how asthma should be treated and the implications on health for asthma that is not managed adequately. While research forms the basis for these guidelines, there are a multitude of other factors that can influence whether or not the health outcomes reflect treatment under ideal situations. Some of these factors that affect asthma outcomes include adherence, proper inhaler technique, prescribing that matches the latest guidelines, and socioeconomic factors [19,20,21,22]. Few publications describe how the NRAD study affected prescribing in Scotland and if inequalities exist in their asthmatic populations. This study aimed to determine whether patients were receiving appropriate treatment according to therapeutic guidelines and how asthma medication prescribing has changed over time. NHS Scotland data was used to see the effects over time, utilizing the Prescribing Information System (PIS) dataset. The objectives of this study include: determine if there has been a change in asthma prescribing since the NRAD study was published using NRAD and NTI measures; determine if there is a difference for asthma medication prescribing among age, gender, and socioeconomic status; determine if the SIGN/BTS guidelines are being followed in those receiving medications used to treat asthma.
Methods

Scotland’s Prescribing Information System (PIS) was used as the data source for this study. PIS is the definitive data source for prescribing information of all items dispensed in the outpatient setting in Scotland. The data is maintained and used by the Information Services Division (ISD) of the NHS National Services Scotland (NSS). The data includes unique patient identifier (UPI), patient demographics, prescriber and dispenser details, geographical and deprivation details, as well as costs and drug information. The data have been collected since 1993 and gets updated monthly. The UPI has been attached to the prescribing data since 2009 and allows for linking of prescription events to an individual as well as linking of prescription events for a population based on patient-specific information and demographics. The main limitation of PIS is that there are no diagnosis codes attached to the dispensing information. As a result, assumptions were made regarding indication, the severity of asthma, and adherence. The study population is only those in Scotland that have gotten a SABA medication. Because SABAs can be used for other ailments besides asthma, a quantity filter was added to help differentiate between short-term SABA use for ailments like pneumonia and long-term SABA use for asthma. The quantity filter stratified patients into those receiving greater than 3, 6, and 12 SABAs. These quantity filters are not mutually exclusive; a patient receiving 13 SABAs in the year would be included in patient counts of each SABA quantity category (>3, >6, and >12 SABAs). These quantity filters were selected because they have been used in previous studies, including the NRAD [12]. There is also overlap with asthma and COPD. To account for this age boundaries and age strata were also used to lessen the amount of COPD.
patients among the study population and to be able to see how SABA use changed with age. COPD is a chronic disease that becomes apparent after 40 or 50 years of age [23]. Limiting the study population of asthma to patients aged 39 or younger allows less overlap between asthma and COPD.

Another assumption that was made was the definition of uncontrolled asthma. For this, it is assumed that patients in higher SABA quantity strata had asthma that was less well-controlled than patients in the lower SABA quantity strata. In the context of outside literature definition of asthma control, the SIGN/BTS guidelines have a practical definition. It defines uncontrolled asthma in need of additional therapy as the use of 3 doses or more of a SABA per week [24]. To put this into context, in 2018, the most dispensed SABA is one that contains 200 doses per canister. This medication accounted for approximately 78% of SABA dispensing. By the SIGN/BTS definition for uncontrolled asthma, this would mean that if they had controlled asthma, then they would only be using a max of 2 doses per week. With the most commonly dispensed inhaler, it would last them 100 weeks, meaning they would only need one inhaler per year. While some circumstances can result in an asthmatic needing inhalers on-hand in different locations that are not actively being used, the quantity filters can help to gauge the control of a patient’s asthma. The last assumption is that adherence is not a confounder for potential differences in the 2014 and 2018 data. It is assumed that adherence is constant between the years so that inferences can be made about prescribing trends. This is further discussed in the discussion section and represents an area to investigate in follow-up studies. The result of these assumptions can over-estimate the asthmatic population, but the filters allow a more accurate representation of those with asthma and allow a reference point to try and gauge poorly controlled asthma.
When factoring in a comparison between two years, this can also allow for a good overview of how asthma prescribing has changed.

Trial Design

The study was conducted as a cross-sectional study using PIS data in the years 2014 and 2018. The two years were used to assess changes over time in prescribing trends to see the effect of guideline changes, NTI, and the NRAD. Then the year 2018 data was expanded to look more in-depth at the demographics of the Scotland asthma population to assess risk-factors for poorly controlled asthma in the most recent complete years data. The program SAP BusinessObjects Business Intelligence 4.1 was used to retrieve data. This program was used to query the data and pull data specific to set parameters. While the year 2018 was used because it was the most recent available, the year 2014 was used because this was the year that the NRAD was published and the baseline/reference population data for the study. The data was retrieved on June and July 2019.

The queries were designed to make a study population that included all of those that received a SABA medication as defined by the British National Formulary (BNF) in 2014 and 2018 that were aged 0-39. This population was then filtered using age strata (0-9, 10-19, 20-29, 30-39), approved drug name, drug formulation, paid calendar year, BNF item description, medications by paid quantity (SABA, LABA, ICS, and combo inhalers), Scottish Index of Multiple Deprivation (SIMD), and gender description in various combinations to test the objectives. These filters were selected and used as categorical data as opposed to continuous data to allow more insight into which part of the Scotland population is most at-risk for poor outcomes. This choice was assumed to give more
information that can be used for follow-up studies or interventions, than if continuous variables were utilized.

For objective 1, the two years were compared to see how asthma prescribing has changed over time. This compared the prescribing of SABA, LABA, and ICS between the two years. Patient counts were conducted for the total number of patients that received a SABA, patient count receiving >3, >6, and >12 SABAs; patient count of any ICS, ≥12 ICS, and >14 ICS; patient count receiving any LABA, and LABA monotherapy. The patient counts were then changed into percent, and rates, utilizing rate per 1000 patients. Relative risk was then calculated between 2014 and 2018, with the year 2014 being used as a baseline to see if there were changes over time. For objective 2, the data from 2018 was filtered by age, gender, and socioeconomic status to look to see if there were any demographic differences for those utilizing SABA inhalers or if there was a difference in demographics for those with poorly controlled asthma. Rates were compared in the >3, >6, and >12 SABA groups between age, gender, and SIMD. Relative risk was used to calculate differences in the groups, with the entire population being used as the reference population, with figures and tables being made to show the results. For gender, the relative risk calculation utilized the comparison between males and females, with females being the baseline. For age, the relative risk was compared between age strata with the entire population as the reference population to assess which age groups had increased risk of uncontrolled asthma. For socioeconomic status, the SIMD category was used to find the relative risk between each category with the entire population as the reference population to see if there were any differences in socioeconomic status contributing to asthma burden. SIMD is a numerical ranking of socioeconomic status. It separates the population into equal
categories from 1 to 5, with 1 being the most deprived and 5 being the least deprived. This means that 1 represents the lowest socioeconomic status, while 5 represents the highest socioeconomic status. Objective 3 looked at asthma prescribing in 2014 and 2018 and compared the claims to the SIGN/BTS guidelines to assess changes over time. This looked at the co-prescribing of SABA and ICS prescriptions and broke it down to percent of $>3$, $>6$, $>12$ SABAs, Any ICS, and ICS $\geq 12$. SABA and ICS are the main medications used to treat asthma, and when looking at the SIGN/BTS guidelines, they now represent first-line treatment (Figure 2, appendix). The treatment guidelines become more complicated after the first two steps and become more complicated to test. Relative risks were then calculated to see if there were changes over time in ICS prescribing, utilizing 2014 as the baseline data. Those receiving SABA and ICS inhalers were further broken down into the percent receiving $\geq 12$ ICS to assess if there were an adequate number of ICS inhalers prescribed. This again utilized 2014 as the baseline data for the relative risk calculations. The data extraction and figures were made with BusinessObjects. The raw data was also exported into Microsoft Excel where the calculations, including relative risk, were made.
Results

A total of 222,637 patients received a SABA medication in 2014 and 205,758 patients in 2018. These numbers represent the total study population utilized. Table 1 shows the patient counts for those receiving SABAs, LABAs, and ICSs.

Table 1 – Patient counts

<table>
<thead>
<tr>
<th></th>
<th>2014</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Population aged 0-39</td>
<td>2,545,486</td>
<td>2,592,524</td>
</tr>
<tr>
<td>Any SABA (study population)</td>
<td>222,637</td>
<td>205,758</td>
</tr>
<tr>
<td>&gt;3 SABA</td>
<td>97,363</td>
<td>87,227</td>
</tr>
<tr>
<td>&gt;6 SABA</td>
<td>48,602</td>
<td>42,732</td>
</tr>
<tr>
<td>&gt;12 SABA</td>
<td>19,705</td>
<td>15,263</td>
</tr>
<tr>
<td>Any ICS</td>
<td>126,136</td>
<td>122,763</td>
</tr>
<tr>
<td>ICS &gt;/= 12</td>
<td>12,579</td>
<td>11,340</td>
</tr>
<tr>
<td>ICS &gt;14</td>
<td>5,443</td>
<td>4,541</td>
</tr>
<tr>
<td>Any LABA</td>
<td>42,518</td>
<td>44,920</td>
</tr>
<tr>
<td>Single-component LABA</td>
<td>3,375</td>
<td>1,345</td>
</tr>
<tr>
<td>Any LABA and no ICS</td>
<td>231</td>
<td>171</td>
</tr>
</tbody>
</table>

When looking at the total population aged 0-39 in Scotland for the two years (2,592,524 in 2018 and 2,545,486 in 2014), 7.9% of the population in 2018 and 8.7% of the population in 2014 received a SABA. Of those receiving a SABA in 2018, 7.42% received >12 SABAs per year, 20.77% received >6 SABAs per year, and 42.39% received >3 SABAs per year. In 2014, those numbers were 8.85%, 21.83%, and 43.73% respectively. To show the differences, the relative risk was calculated and put into a table listing the relative change
along with the absolute change. The relative risk calculations used 2014 as a baseline, and therefore it is the reference population. The results of objective 1 are shown in Table 2.

Table 2 – Relative and absolute change between years

<table>
<thead>
<tr>
<th></th>
<th>2014</th>
<th>2018</th>
<th>Relative Risk (CI)</th>
<th>Relative change</th>
<th>Absolute change</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;3 SABAs</td>
<td>43.73%</td>
<td>42.39%</td>
<td>0.97 (0.96 – 0.98 P &lt;0.001)</td>
<td>3.06% decrease</td>
<td>1.43% decrease</td>
</tr>
<tr>
<td>&gt;6 SABAs</td>
<td>21.83%</td>
<td>20.77%</td>
<td>0.95 (0.94 – 0.96 P &lt;0.001)</td>
<td>4.87% decrease</td>
<td>1.06% decrease</td>
</tr>
<tr>
<td>&gt;12 SABAs</td>
<td>8.85%</td>
<td>7.42%</td>
<td>0.84 (0.82 – 0.86 P &lt;0.001)</td>
<td>16.19% decrease</td>
<td>1.34% decrease</td>
</tr>
<tr>
<td>Any ICS</td>
<td>56.66%</td>
<td>59.66%</td>
<td>1.05 (1.04 – 1.06 P &lt;0.001)</td>
<td>5.31% increase</td>
<td>3% increase</td>
</tr>
<tr>
<td>ICS &gt;/= 12</td>
<td>5.65%</td>
<td>5.51%</td>
<td>0.97 (0.95 – 0.99 P =0.048)</td>
<td>2.5% decrease</td>
<td>0.14% decrease</td>
</tr>
<tr>
<td>&gt;14 ICS</td>
<td>2.44%</td>
<td>2.21%</td>
<td>0.90 (0.87 – 0.94 P &lt;0.001)</td>
<td>9.73% decrease</td>
<td>0.23% decrease</td>
</tr>
<tr>
<td>Any LABA</td>
<td>19.09%</td>
<td>21.83%</td>
<td>1.14 (1.13 – 1.16 P &lt;0.001)</td>
<td>14% increase</td>
<td>2.74% increase</td>
</tr>
<tr>
<td>Single component LABA</td>
<td>1.52%</td>
<td>0.65%</td>
<td>0.43 (0.40 – 0.46 P &lt;0.001)</td>
<td>57% decrease</td>
<td>0.87% decrease</td>
</tr>
<tr>
<td>Any LABA, no ICS</td>
<td>0.10%</td>
<td>0.08%</td>
<td>0.80 (0.66 – 0.98 P =0.028)</td>
<td>19% decrease</td>
<td>0.02% decrease</td>
</tr>
</tbody>
</table>

For objective 2, only the year 2018 was examined. Utilizing the amount of SABA inhalers prescribed to gauge asthma control, SABAs received per year were analyzed in >12, >6, and >3 inhaler groups and compared between demographics. The rates of these various SABA quantities were graphed with gender, age strata, and SIMD. On the y-axis
of the histograms is the rate of those receiving >3, >6, or >12 SABA inhalers out of all those receiving at least one SABA inhaler per 1000. On the x-axis, it is broken down into the age bands, gender, and SIMD. The blue bars represent the females, and the green bars represent the males. The numbers 1-5 represent the SIMD or socioeconomic status, with 1 representing the lowest socioeconomic status and 5 representing the highest socioeconomic status. The age bands are ordered from left to right of the 0-9, 10-19, 20-29, and 30-39 age bands. This gives a broad snapshot of every demographic component that was measured in objective 2. These are shown in figures 3, 4, and 5.

Figure 3 – Rate of >3 SABA per 1000 stratified by age, SIMD, and gender
Figure 4 – Rate of >6 SABA per 1000 stratified by age, SIMD, and gender

Figure 5 – Rate of >12 SABA per 1000 stratified by age, SIMD, and gender
Age

When looking at the figures, figure 3 shows the rate of >3 SABAs is highest in the age band 0-9, followed by 30-39. When looking at figure 4, the rate of >6 SABAs the figure levels off between age strata, but more differences can be seen between gender and SIMD. Lastly, figure 5, the >12 SABAs figure, shows that the relative risk becomes greater for the age band 30-39. To illustrate these figures numerically, the relative risk was calculated in >3, >6, and >12 SABA groups between the age strata. These age results are tabulated and shown in table 3.

Table 3 – Age relative risk stratified by SABA quantity

<table>
<thead>
<tr>
<th></th>
<th>0-9</th>
<th>10-19</th>
<th>20-29</th>
<th>30-39</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;3 SABAs</td>
<td>1.45 (1.43 – 1.46 P&lt;0.001)</td>
<td>0.78 (0.77 – 0.79 P&lt;0.001)</td>
<td>0.84 (0.83 – 0.85 P&lt;0.0001)</td>
<td>1.01 (0.99 – 1.02 P=0.075)</td>
</tr>
<tr>
<td>&gt;6 SABAs</td>
<td>1.14 (1.12 – 1.16 P&lt;0.0001)</td>
<td>0.70 (0.70 – 0.71 P&lt;0.0001)</td>
<td>0.96 (0.94 – 0.98 P&lt;0.001)</td>
<td>1.21 (1.19 – 1.24 P&lt;0.0001)</td>
</tr>
<tr>
<td>&gt;12 SABAs</td>
<td>0.99 (0.95 – 1.02 P=0.49)</td>
<td>0.62 (0.60 – 0.65 P&lt;0.0001)</td>
<td>1.05 (1.02 – 1.09 P=0.0034)</td>
<td>1.34 (1.30 – 1.39 P&lt;0.0001)</td>
</tr>
</tbody>
</table>

Gender

When looking at gender, there is an increased relative risk for males when compared to females. There is a 30% increased risk of receiving >12 SABAs, 25% increased risk for >6 SABAs, and 21% increased risk for >3 SABAs. The results are shown in table 4.

Table 4 – Gender relative risk stratified by SABA quantity

<table>
<thead>
<tr>
<th></th>
<th>Relative Risk (CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;12 SABAs</td>
<td>1.30 (1.26, 1.34)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt;6 SABAs</td>
<td>1.25 (1.22, 1.27)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt;3 SABAs</td>
<td>1.21 (1.20, 1.22)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
When looking at SIMD, there is an apparent higher relative risk attributed to the lowest socioeconomic status groups, and as the socioeconomic status category decreases, the relative risk increases. This is shown in figures 6, 7, 8.

Figures 6 – SIMD relative risk in >3 SABA group

Figure 7 – SIMD relative risk in >6 SABA inhaler group
For objective 3, the SIGN/BTS guidelines were used. The co-prescribing of SABA and ICS represents the optimum treatment, with both a reliever and preventer medication. The year 2014 and 2018 were compared to see the changes over time. In 2018, 89% of those receiving >12 SABAs had received an ICS. When looking at the number of ICS inhalers received in those receiving >12 SABAs and at least 1 ICS, 41% received the recommended 12 ICS inhalers. Table 5 shows the comparison between years in the co-prescribing of SABA and ICS.

Table 5 – Co-prescribing of SABA and ICS

<table>
<thead>
<tr>
<th>&gt;3 SABA</th>
<th>2014 %</th>
<th>2018 %</th>
<th>Relative Risk (CI)</th>
<th>Relative Change</th>
<th>Absolute Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any ICS</td>
<td>77.02</td>
<td>78.62</td>
<td>1.02 (1.01 – 1.03) P&lt;0.0001</td>
<td>2.07% increase</td>
<td>1.6% increase</td>
</tr>
<tr>
<td>Percent ICS ≥12 of those with Any ICS</td>
<td>15.88</td>
<td>15.48</td>
<td>0.98 (0.95 – 0.99) P=0.0395</td>
<td>2.49% decrease</td>
<td>0.4% decrease</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>&gt;6 SABA</th>
<th>2014 %</th>
<th>2018 %</th>
<th>Relative Risk (CI)</th>
<th>Relative Change</th>
<th>Absolute Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any ICS</td>
<td>84.88</td>
<td>86.09 &amp;</td>
<td>1.01 (1.01 – 1.02) P&lt;0.0001</td>
<td>1.43% increase</td>
<td>1.21% increase</td>
</tr>
<tr>
<td>SABA</td>
<td>Percent ICS ≥12 of those with Any ICS</td>
<td>25.64%</td>
<td>24.86%</td>
<td>0.97 (0.95 – 0.99 P=0.0123)</td>
<td>3.05% decrease</td>
</tr>
<tr>
<td>---------------</td>
<td>--------------------------------------</td>
<td>--------</td>
<td>--------</td>
<td>----------------------------</td>
<td>-----------------</td>
</tr>
<tr>
<td>&gt;12 SABA</td>
<td>Any ICS</td>
<td>87.96%</td>
<td>89.08%</td>
<td>1.01 (1.01 – 1.02 P=0.0011)</td>
<td>1.27% increase</td>
</tr>
<tr>
<td></td>
<td>Percent ICS ≥12 of those with Any ICS</td>
<td>41.13%</td>
<td>41.39%</td>
<td>1.01 (0.98 – 1.03 P=0.6415)</td>
<td>0.64% increase</td>
</tr>
</tbody>
</table>
Discussion

When looking at asthma medication prescribing, one can see that there are a good number of patients in Scotland that received a SABA medication. While this undoubtedly over-estimates the number of asthmatics in Scotland, when looking at reported incidences, comparisons can be made to see how much it overestimates. The incidence of asthma in Scotland is said to be 1 in 14 that are currently receiving treatment [10]. Utilizing population counts in the determined age strata showed the study population had an incidence of 1 in 11 receiving SABA claims in 2014 and 1 in 13 in 2018. This shows that while it may overestimate the number of asthmatics, it represents a study population that should encompass the asthma population in the age strata, with additional patients that utilize SABAs for other ailments.

When comparing the 2014 and 2018 data, it shows the total 0-39 population increases between the years while the number of patients receiving a SABA medication decreases. This result is consistent throughout the filter quantity of SABA inhalers. When looking at relative risk, there is a relative decrease of patients receiving drug claims for SABAs, and this becomes greater as the filter for the number of SABA inhaler increases. The most substantial reduction in patient SABA claims occurs in the >12 SABA group. This reduction shows that there is a relative decrease of 16.19% compared to 2014. When thinking about the NTI and guideline changes, this is in line with them because there was an emphasis on patients receiving >12 SABAs after the NRAD data was published. It appears prescription drug claims for the asthmatics with the least controlled asthma, that are receiving the most SABAs, have had a greater reduction. This could be due to any one
of the changes mentioned previously, but the change is significant enough to show positive changes that have occurred after the NRAD. Although, when looking at the absolute change, there has been a small change of 1.34% between the years. This small absolute change likely indicates there is more room for improvement. When looking at the other measures, there is not as large of a decrease in both relative risk change and absolute risk change. This may show that the patients receiving the most inhalers are getting the most attention when it comes to the over-reliance of reliever medications. At the same time, it appears that there remains room for improvement in the other categories. The amount of room for improvement in the other categories needs additional review so that more definitive information with diagnosis codes can help dictate measures. Additionally, this data shows that there remain 15,263 patients that receive >12 SABAs, a risk for poor outcomes.

The changes in ICS drug claims between the years shows a decrease in the number of patients with ICS claims in all three categories. When looking at relative risk, there is a 9.73% decrease in patients receiving >14 ICS. This represents a cost-saving initiative for the NHS and does not relate to clinical outcomes. When looking at the clinical measures, there was an increase in the percentage of patients receiving any ICS inhaler. This equated to a 3% absolute increase (the largest absolute change in objective 1) and a 5.31% relative increase between the years. ICS inhalers have become more common due to the preventative nature of their mechanism. In the guidelines, they have become an option for first-line therapy. These relative and absolute increases coincide with the guideline changes and could show that more patients are being started on ICS inhalers. If the patient has asthma, then they have an indication for an ICS inhaler. When considering the amount of
ICS inhalers, a patient needs, you have to consider the mechanism of action. ICSs are a medication that a patient needs to take every day. Given that the NHS/BTS formulary has only ICS inhalers that contain 30-day supplies, one would expect asthmatics to need 12 ICS inhalers per year if they are prescribed them. When looking at the data, there is a 2.5% relative decrease between years of patients receiving ≥ 12 ICS inhalers compared to 2014. This statistic alone is hard to analyze, but in objective 3, it looks more into this and assesses if those with uncontrolled asthma are adequately getting treated with goal-directed therapy.

The big take-away from the ICS component of objective 1 is that those receiving SABA inhalers in 2018 are receiving ICS inhalers at a higher frequency than in 2014. While the frequency of those receiving ≥12 has decreased.

LABA inhalers’ place in therapy is more convoluted than SABAs and ICSs. While SABA and ICS represent first-line therapy options, LABA inhalers represent therapy later in the sequential stepwise nature of the SIGN/BTS guidelines. Given previous studies’ results on the use of LABA as monotherapy [25], assessing if prescribing has changed is pertinent to ensuring optimum therapy. While the percentage of patients receiving any LABA has increased between the years, when breaking it down to single-component and monotherapy, LABA prescribing has decreased. The single-component LABA statistic represents something that could have a clinical difference. The NRAD showed that single-component LABA was a risk factor for poorly controlled asthma. If a patient receives a prescription for a single-component LABA, they may only be using that inhaler regardless of other inhalers that have been prescribed to them. This increases the chance that an asthmatic is using LABA as monotherapy. Instead, NRAD and guidelines have moved towards prescribing LABAs that are included in combo inhalers [12]. That is LABA and
ICS in one inhaler. Combo inhalers can increase compliance to goal-directed medical therapy and decrease the chances that a patient uses LABA as monotherapy. Looking at the changes in monotherapy or single-component LABAs shows the greatest relative decrease in all medication categories. There was a 57% relative decrease in patients prescribed single-component LABAs between the years, a 19% relative decrease in any LABA without an ICS, and a 47% relative decrease in single-component LABA without an ICS. This represents a decrease in the prescribing of LABAs and a potential decrease in those at-risk for poor outcomes that coincide with LABA monotherapy.

For objective 2, the year 2018 was used to assess demographic and socioeconomic status differences. SABA inhaler claims were the only medication examined and again under the assumption that the more inhaler claims, the less the asthma is controlled. When looking at the figures of the number of SABA inhalers with age strata, gender, and socioeconomic status, it gives a good insight into how prescribing differs between these various groups. The y-axis of figures 3, 4, and 5 show the rate of SABA inhalers per 1000 patients. While the scale changes in each of the three figures, making it harder to compare, the rate in the various groups in the individual figures can be compared. In figure 3, the age band 0-9 has the highest rate of >3 SABAs, and there is not an easily visible difference between socioeconomic status among this age band. Then when looking at figure 4 (>6 SABAs), the rate between age strata starts to level off. The differences between gender and socioeconomic status become more pronounced in this figure, as well. Figure 5 has the most noticeable differences between socioeconomic status and gender. Also worth noting is that the age band 30-39 now has the highest rate of those receiving >12 SABAs when compared to the other age strata.
As discussed previously, the 0-9 age band has the highest rate in >3 SABAs with 45% increased relative risk of getting >3 SABAs compared to the other age strata. As the number of inhalers increases to the >6 SABAs and >12 SABAs groups, the relative risk decreases for the 0-9 age band. While in the age band 30-39, the relative risk increases as the number of SABA inhalers increases. In the >12 SABAs group, there is a 34% increased relative risk in the 30-39 group compared to the other age strata. These increases in rate in the oldest population group as the number of SABA inhalers increase may be due to behavioral health factors. This observation would coincide with previous data on smoking and asthma, showing that smoking increases the risk of asthma and asthma that is more difficult to control [26]. The takeaway from this portion of the data is that younger age individuals may be at greater risk of needing a SABA, but as age increases, so does the apparent rates of uncontrolled asthma and the need for large quantities of SABA inhalers. When trying to understand and treat asthma for those in adulthood, these results should be taken into consideration, and behavioral health factors must be assessed. Being able to identify behavioral health factors like smoking or environmental exposures can help to aid in the treatment of asthma.

When looking at gender, there is a clear and definitive takeaway. Males are at an increased risk of needing SABA inhalers, and that risk increases as the number of SABA inhaler increases. The difference between the two genders is significant, with a 21% relative increase in >3 SABAs, a 25% relative increase in >6 SABAs, and a 30% relative increase in >12 SABAs. Males appear to be at an increased risk of asthma in this population, and the data shows they are also at an increased risk of needing SABA inhalers.

The last component of objective 2 is the socioeconomic status. As discussed
previously, SIMD is the NHS breakdown of socioeconomic status. SIMD 1 represents the most deprived or the lowest socioeconomic status, and SIMD 5 represents the least deprived of the highest socioeconomic status. To make the results more evident, the relative risks and 95% confidence intervals were graphed as a forest plot. One can see that there is a linear difference in relative risk; going from the highest SES to the lowest SES, the relative risk for SABA inhalers increases. When comparing the three figures, one can see that as the number of inhalers increase, so does the spread between the groups. In the >12 SABA figure, the most significant spread between relative risk in the SIMD groups. Those in the lower SIMD groups were assumed to have the least controlled asthma, and the graphs/data support this assumption. This represents some information that can help identify those at the highest risk, so that catered, and individually focused plans can be initiated by providers to try and lessen the burden that coincides with SES. When thinking about reasons for these discrepancies, environmental exposures, and behavioral health factors such as smoking emerge as potential culprits. Understanding likely socioeconomic differences can help healthcare and public health workers to more easily identify those at risk so that campaigns can be developed to limit the differences in exposure while also allowing tighter monitoring with medical therapy. Practitioners in Scotland should be alert to risk factors that their patients may have in relation to their SES.

For objective 3, changes in the SIGN/BTS guidelines were investigated, and data was analyzed to ascertain how they may have changed prescribing habits. The two first-line therapy medications of SABA and ICS were investigated. The significant changes in the guidelines have been the increasing priority of adding on ICSs and adding them to first-line therapy options. Previously ICS were down the stepwise guidelines path, reserved for
those not controlled by SABAs. It is assumed that as the number of SABA inhaler claims increases, so too will the need for ICS. If patients do not have controlled asthma, then they should be on an ICS. When thinking about how ICS medications work, if a patient is on an ICS medication, they should receive one inhaler every month. This means that in a calendar year, they should have 12 claims for ICS medications. As the number of SABA medications increase, it is hypothesized that asthma is less controlled. So those receiving >12 SABAs should have ICS claims, and they should have ≥12 ICS claims. The ICS and SABA co-prescribing data were compared between the years to see how the guidelines might have influenced prescribing. When looking at the data, prescribing of ICSs has changed little. In the >3 SABA group, the prescribing of any ICS occurred in 77% in 2014 and increased to 79% in 2018, a relative risk increase of 2.07%. In this group, there was a decrease in those receiving ≥12 ICS inhalers from 15.88% to 15.48%. In the >6 SABA group, there was an increase in those having any ICS claims from 84.88% to 86.09%. There was also a decrease in those receiving ≥12 ICS medications, moving from 25.64% to 24.86%. In the last group, those receiving >12 SABAs, there was an increase in those receiving any ICS from 87.96% to 89.08%. This change resulted in only a 1.27% relative risk increase between the years. This group was the only group that had an increase in those receiving ≥12 ICS inhalers. But this was only a 0.64% relative increase between the years.

It is more difficult to take away much information from the >3 or >6 SABAs groups due to the uncertainty of determining asthma control and uncertainty of the timing of the paid claims in the year. But when looking at the >12 SABA group, it is a bit easier to make assumptions about asthma control. In those receiving >12 SABAs, it is a clear indication for an ICS medication. One would expect that if they need that many reliever medications
that they would get at least one preventer medication. While this number has increased, it still is not at 100%. There remains 11% of the population that receives >12 SABAs that do not have adequate therapy based upon the SIGN/BTS guidelines. This equates to 1,667 patients that are not receiving adequate goal-directed medical therapy and are therefore at-risk for poor outcomes. For those receiving >12 SABAs and having claims for an ICS, the rates of those receiving ≥12 ICSs are lower than anticipated. Only 41.39% had received ≥12 ICSs in 2018; a number only slightly increased from 2014 at 41.13%. This results in 7,968 patients that are not receiving an adequate number of ICS inhalers per year. This number could represent poor compliance with ICS medications for those receiving >12 SABAs. It is clear that ICS medications have numerous side effects [27]; this represents a potential reason for patients to stop taking them. If this does accurately represent a picture of poor compliance for ICS medications, then this is a clear area where healthcare providers and public health workers can make a difference. Poor adherence presents an opportunity to develop campaigns aimed at either the patients with asthma or the providers to address concerns of ICSs directly. These campaigns could ultimately allow higher compliance and better outcomes. If this is an issue with prescribing, then awareness campaigns can be created to target prescribers and the areas with poor co-prescribing.

Limitations

Limitations of this study include the lack of diagnosis codes. Without the diagnosis codes, the population had to be assumed to have asthma. This assumption overestimated those with asthma. It also forced the creation of age strata in which populations at-risk may have been suppressed. The age groups 40 and greater could represent additional data that could help show how guideline changes, studies, and NTI influenced prescribing. Data
analysis was limited to relative risk. Other statistical tests could be used with this data, and alternative study design could be made to give more definitive results and show new results. This data does not consider adherence. Without adherence, assumptions must be made about prescribing. If it turns out adherence is an issue, then the focus could shift to addressing poor adherence as opposed to influencing prescribing. The last perceived limitation is the lack of outcome measures, including hospitalization records or cost-saving measures. Hospitalizations represent a clinical and cost measure. Seeing the demographics of those needing hospitalization for asthma could either bolster data from this study, or it could bring additional information about who is at-risk for poor outcomes.

Implications

This study shows how asthma prescribing has changed over the years. It highlights areas where good progress has been made and shows areas where there remains room for improvement. Since the NRAD, there have been changes to try and influence outcomes. Seeing the data change and looking in-depth in the most recent full year of data gives an understanding of how these changes have influenced outcomes. It appears that more considerable attention has been focused on those with a higher risk of poor outcomes. More studies will be needed to investigate those below the far extreme category of this study. Still, there remain 15,263 patients at risk for poor outcomes due to excessive SABA use, 1,667 patients not on goal-directed medical therapy with ICS medications, and 7,968 patients were not receiving adequate amounts of ICS inhalers. This highlights areas that are still in need of improvement. When looking at the demographical analysis, this represents excellent insight to those at-risk for poor outcomes. The demographical analysis can be used to initiate more studies in these demographics to confirm the results and
investigate reasons for the differences. It can also be used as a marker for patients that may be at higher risk so that public health officials and practitioners can implement strategies to curtail any burden associated with these demographics.

The resources NHS Scotland have at their disposal and ability to analyze their full population allow better monitoring and implementation of public health measures. Data replicated on patients in the United States may not be able to encompass the entire demographics, environmental differences, and regional differences that coincide with the United States. But this study can highlight how the implementation of guidelines and public health measures like the NTI, can change prescribing habits. NTIs could ultimately be replicated in the United States to more easily compare data throughout the country. Another advantage of the publicly funded healthcare system is that there is no cost for prescriptions to the patients. This likely eliminates an area for medical access issues and removes a potential confounder for outcomes that can be apparent in the United States. This likely means more patients are on the medications that were prescribed to them. While this does not guarantee a patient takes the medications as prescribed to them, it likely means fewer hurdles for the patients and more compliance. Thus, more can be concluded about the changes in prescribing habits and how guidelines, public health initiatives, and research can influence prescribing habits.

Conclusion

There appears to be an over-reliance on reliever medications, with a deficit in preventer medication use. This finding has improved from previous years’ data but highlights areas with room for improvement. Certain groups of the Scotland population are
at increased risk for large numbers of SABA inhalers – males, low socioeconomic status, and the age band 30-39. Lastly, based on NRAD findings, there seems to remain a large population at risk for poor outcomes.
References


[16] Nelson HS, Weiss ST, Bleecker ER, Yancey SW, Dorinsky, PM. SMART Study Group. The salmeterol multicenter asthma research trial: a comparison of usual
pharmacotherapy for asthma or usual pharmacotherapy plus salmeterol. Chest
2006;129(1):15-26

[17] Dissanayake S.B. Safety of beta2-agonists in asthma: Linking mechanisms, meta-
analyses and regulatory practice. AAPS J. 2015;17:754–757. doi: 10.1208/s12248-015-
9734-8.

[18] Kristensen N, Nymann C, Konradsen H. Implementing research results in clinical

asthma control and asthma-specific health-related quality of life among children. Respir

adherence and the risk of severe asthma exacerbations: a systematic review. European

[21] Murphy Anna. How to help patients optimize their inhaler technique. The
Pharmaceutical Journal. 2016 JUL 27. https://www.pharmaceutical-
journal.com/learning/learning-article/how-to-help-patients-optimise-their-inhaler-
technique/20201442.article

[22] Erick Forno, M.D., M.P.H. and Juan C. Celedón, M.D., Dr.P.H. Health Disparities in
Care Med. 2012 May 15; 185(10): 1033–1035. Published online 2012 May 15. doi:
10.1164/rcrm.201202-0350ED


Appendix

Figure 1 – 2014 SIGN/BTS asthma guidelines

Source: [28]
Figure 2 – 2016 SIGN/BTS asthma guidelines

<table>
<thead>
<tr>
<th>Asthma - suspected</th>
<th>Adult asthma - diagnosed</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diagnosis and Assessment</strong></td>
<td><strong>Evaluation:</strong> • assess symptoms, measure lung function, check inhaler technique and adherence • adjust dose • update self-management plan • move up and down as appropriate</td>
</tr>
</tbody>
</table>

Source: [29]