

Replication of the D58 Asthma Trial in Healthcare Claims Data

DUPLICATE-D58

May 12, 2021

NCT0144430

1. RCT Details

This section provides a high-level overview of a **published** RCT that the described real-world evidence study is trying to replicate as closely as possible given the remaining limitations inherent in the healthcare databases.

1.1 Title

A 26 Week, Randomized, Double-blind, Parallel-group, Active Controlled, Multicenter, Multinational Safety Study Evaluating the Risk of Serious Asthma-related Events During Treatment With Symbicort®, a Fixed Combination of Inhaled Corticosteroid (ICS) (Budesonide) and a Long Acting β 2-agonist (LABA) (Formoterol) as Compared to Treatment With ICS (Budesonide) Alone in Adult and Adolescent (≥ 12 Years of Age) Patients With Asthma ([D5896C00027 Study NCT0144430](#))

1.2 Intended aim(s)

To assess the effects of 26 weeks treatment with budesonide-formoterol compared with formoterol alone on the incidence of first serious asthma-related event (a composite of adjudicated death, intubation, and hospitalization) in patients who had persistent asthma.

1.3 Primary endpoint for replication

First serious asthma-related event (a composite of adjudicated death, intubation, and hospitalization).

1.4 Required power for primary endpoint and noninferiority margin (if applicable)

To meet the prespecified noninferiority margin, the upper limit of the two-sided 95% confidence interval of the hazard ratio for the first serious asthma-related event with budesonide-formoterol versus budesonide had to be less than 2.0. The incidence rate of serious asthma-related events in the budesonide-only treatment group was predicted to be 0.0075 over a 26-week period. It was calculated that 87 events would have to occur for the study to have 90% power to rule out an event rate with budesonide-formoterol that was twice as high as the rate with budesonide alone.

1.5 Secondary endpoint for replication (assay sensitivity) and RCT finding

Individual components of the primary outcome

- 1) Asthma-related hospitalization
- 2) Asthma-related intubation
- 3) Asthma-related death

1.6 Trial estimate

Hazard Ratio, HR = 1.07 (95% CI, 0.70 to 1.65) comparing budesonide-formoterol versus budesonide during a 26-week

period (Peters et al., 2016).

2. Person responsible for implementation of replication in Action

Hemin Lee, MD, MPH, implemented the study design in the Aetion Evidence Platform. She is not responsible for the validity of the design and analytic choices. All implementation steps are recorded, and the implementation history is archived in the platform.

3. Data Source(s)

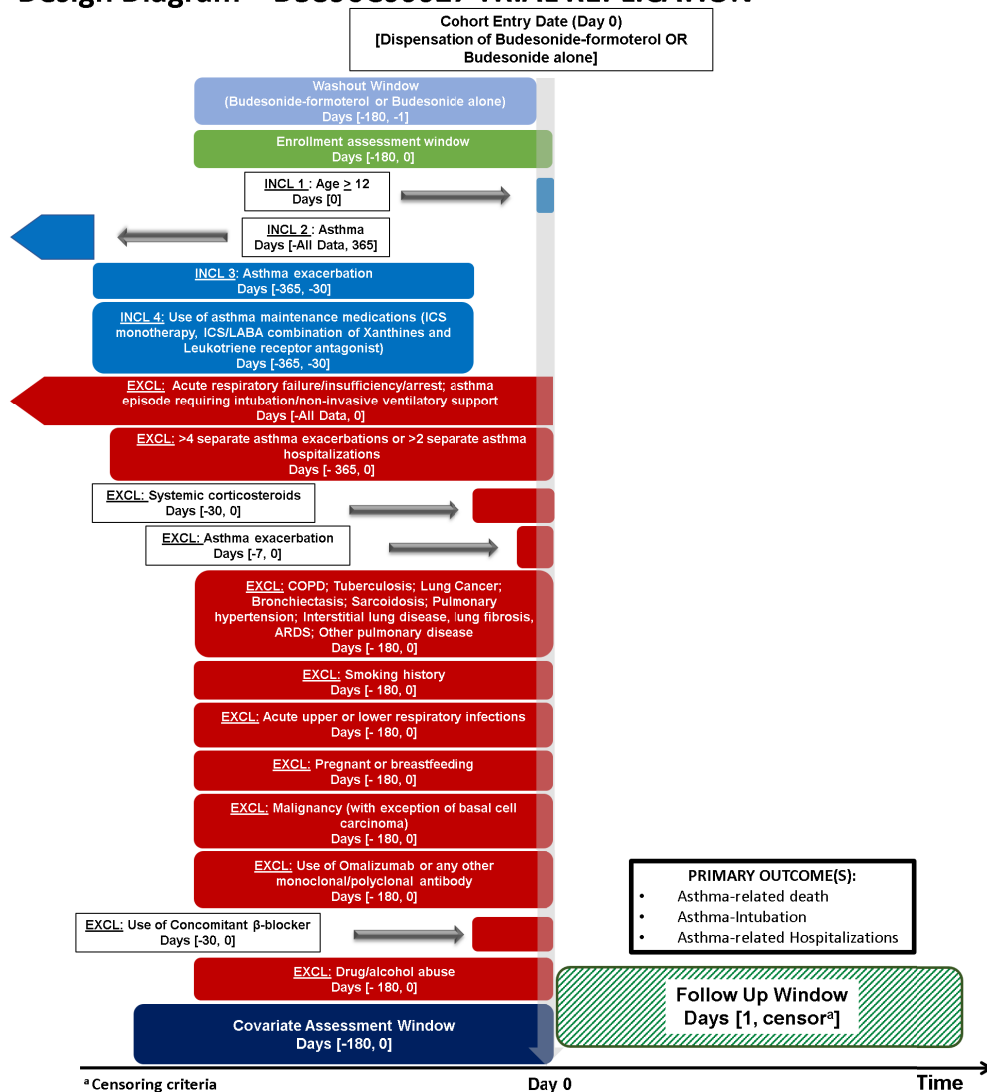
Optum CDM, IBM® MarketScan®

4. Study Design Diagram

The study design diagram visualizes key aspects of the longitudinal study design for expedited review.

Figure 1. Design Diagram – D5896C00027 (NCT 0144430) TRIAL REPLICATION

Design Diagram – D5896C00027 TRIAL REPLICATION



- ^aCensoring criteria
- Occurrence of outcome
 - Death
 - Start of additional Exposure
 - End of index exposure
 - Disenrollment
 - Specified Date reached
 - Switch (within comparison grp)
 - Nursing home admission

5. Cohort Identification

5.1 Cohort Summary

This study will involve a new user, parallel group, propensity score-matched, retrospective cohort design comparing budesonide-formoterol versus budesonide alone. The patients will be required to have continuous enrollment during a baseline period of 180 days before initiation of budesonide-formoterol or budesonide.

5.2 Important steps for cohort formation

New use of budesonide-formoterol (exposure) is defined as no use of the exposure drug within the 180 days prior to index date. This will emulate the trial requirement for which treatment with budesonide-formoterol was not allowed any time before randomization. New use of formoterol (comparator) is defined as no use of the comparator drug within the 180 days prior to index date. New users of formoterol are not allowed to receive of budesonide-formoterol within the 180 days prior to index date, and new users of budesonide-formoterol are not allowed to receive formoterol within the 180 days prior to index date.

5.2.1 Eligible cohort entry dates

Budesonide-formoterol was approved by FDA on July 21, 2006 for management of asthma. The initial eligible cohort entry date was the first date after July 21, 2006 for both the databases investigated (IBM® MarketScan®, Optum CDM). The last date eligible as cohort entry date was the end of available data for IBM® MarketScan® and Optum CDM. The following eligible cohort entry dates were included:

- IBM® MarketScan®: July 21, 2006 – December 31, 2018 (end of available data)
- Optum CDM: July 21, 2006 – June 30, 2020 (end of available data)

5.2.2 Specify inclusion/exclusion criteria for cohort entry and define the index date

Inclusion and exclusion criteria were adapted from the trial as closely as possible. Definitions for all inclusion/exclusion are provided in **Appendix A** and are summarized in the flowcharts below.

5.3 Flowchart of the study cohort assembly
For Budesonide-formoterol vs. formoterol

Less Excluded Patients	Optum CDM		IBM® MarketScan®	
	Remaining Patients	Remaining Patients	Less Excluded Patients	Remaining Patients
All patients		78,202,636		200,203,908
Did not meet cohort entry criteria	-	737,990	-	1,207,847
Excluded due to insufficient enrollment	77,464,646	623,305	198,996,061	1,050,363
Excluded due to prior use of referent	-114,685	596,213	-80,459	969,904
Excluded due to prior use of exposure	-27,092	303,264	-398,899	571,005
Excluded because patient qualified in >1 exposure category	-292,949	303,224	-139	570,866
Excluded based on Age : exclude missing	-40	303,221	0	570,866
Excluded based on Gender : exclude missing	-3	303,221	0	570,866
Excluded based on INCLUSION: Age >=12	0	303,221	0	570,866
Excluded based on Inclusion 2 - Asthma >=1 year prior to CED	-14,027	289,194	-38,285	532,581
Excluded based on Inclusion 3 - Asthma exacerbation (combination) [-365,-30]	-167,426	121,768	-316,772	215,809
Excluded based on Inclusion 4 - Asthma Therapy [-365,-30]	-59,930	61,838	-150,606	65,203
Excluded based on Inclusion 4 - Asthma Therapy [-365,-30]	-10,146	51,692	-8,560	56,643
Excluded based on Exclusion 1 - Acute respiratory failure - intubation/nivs (combination)	-4,103	47,589	-3,423	53,220
Excluded based on Exclusion 2b - Asthma exacerbation (combination) >4 in 365 days	-5,195	42,394	-3,857	49,363
Excluded based on Exclusion 2C - Asthma exacerbation (inpatient primary) >2 times in 365 days	-4,020	38,374	-109	49,254
Excluded based on Exclusion 3 - Use of oral corticosteroids (-30, 0]	-3,222	35,152	-6,184	43,070
Excluded based on Exclusion 4 - Asthma exacerbation (combination) [-7,0]	-196	34,956	-483	42,587
Excluded based on Exclusion 7 - Respiratory disease (combination)	-540	34,416	-609	41,978
Excluded based on Exclusion 8 - Smoking	-931	33,485	-657	41,321
Excluded based on Exclusion 9 - Acute upper or lower respiratory infections	-2,527	30,958	-4,278	37,043
Excluded based on Exclusion 10 - Pregnancy	-66	30,892	-85	36,958
Excluded based on Exclusion 11 - Malignancy	-308	30,584	-367	36,591
Excluded based on Exclusion 14 - Use of omalizumab	-1	30,583	-103	36,488

Excluded based on Exclusion 15 - Use of Beta-blocker	-150	30,433	-161	36,327
Excluded based on Exclusion 19 - Drug/alcohol abuse	-49	30,384	-31	36,296
Final cohort		30,384		36,296

6. Variables

6.1 Exposure-related variables:

Study drug:

New initiation of Budesonide-formoterol (80/4.5 ug or 160/4.5 ug twice daily). New initiation is defined as no use of Budesonide-formoterol in the prior **180** days before treatment initiation (washout period). New users of Budesonide-formoterol are not allowed to receive formoterol within the 180 days prior to treatment initiation.

Comparator agent:

New initiation of Formoterol (80 ug or 160ug twice daily). New initiation is defined as no use of formoterol in the prior 180 days before treatment initiation (washout period). New users of formoterol are not allowed to receive Budesonide-formoterol within the 180 days prior to treatment initiation.

6.2 Preliminary Covariates:

- Age
- Gender
- Combined Comorbidity Index (CCI), measured over the baseline covariate assessment period, defined as 180 days prior to and including index date.

Covariates listed above represent only a small subset of covariates that will ultimately be controlled for in the design and analysis. We use the covariates above only for initial feasibility analyses to judge whether there is likely to be sufficient overlap between treatment groups to proceed with the study. Remaining covariates are defined only after the study has passed the initial feasibility analysis and the initial power assessment and are listed in Table 1 (**Appendix B**).

6.3 Outcome variables and study follow-up:

6.3.1 Outcome variables

Effectiveness outcome variables of interest (definitions provided in **Appendix A**):

- **Primary outcome:** First serious asthma-related event (a composite of adjudicated death, intubation, and hospitalization)
- **Secondary outcome:** Individual components of the primary outcome
 - 1) Asthma-related hospitalization
 - 2) Asthma-related intubation
 - 3) Asthma-related death

6.3.2 Study follow-up

Both as-treated (AT) and intention-to-treat (ITT) analyses will be conducted with treatment defined as the index drug on the day of cohort entry. Because adherence in the real-world databases is expected to be much worse than in the trial, the AT analysis is the **primary analysis**, as it targets the relative hazard of outcomes on treatment.

For the AT analyses, the follow-up will start the day after initiation of Budesonide-formoterol and Budesonide and will continue until the earliest date of the following events:

- The first occurrence of the outcome of interest,
- The date of end of continuous registration in the database,
- Discontinuation of the index drugs,
- End of the study period,
- Measured death event occurs,
- Nursing home admission
 - Nursing home admissions are considered a censoring event because the data sources utilized typically provide little to no data on a patient, particularly on drug utilization, after admission. We will utilize this as an exclusion reason for cohorts for the same reason.
- The date of drug discontinuation, defined as the date of the last continuous treatment episode of the index drug (Budesonide-formoterol or a comparator) plus a defined grace period (i.e., 60 days after the end of the last prescription's days' supply in main analyses).
- The date of augmentation or switching from exposure to comparator or vice versa or augmentation
 - A dosage change on the index treatment does not fulfill this criterion

7. Initial Feasibility Analysis

Action report name:

For Budesonide-formoterol vs. formoterol

Optum CDM - <https://bwh-dope.aetion.com/projects/details/1657/results/67114/result/0>

IBM® MarketScan®- <https://bwh-dope.aetion.com/projects/details/1656/results/67113/result/0>

Date conducted: 03/16/2021

Complete Aetion feasibility analysis using age and CCI as the only covariates and the primary endpoint (Section 6.3.1) as the outcome. No measures of association will be computed nor will incidence rates stratified by treatment group.

8. Initial Power Assessment

Action report name:

- For Budesonide-formoterol vs. formoterol

Optum CDM - <https://bwh-dope.aetion.com/projects/details/1657/rwrs/67089>

IBM® MarketScan®- <https://bwh-dope.aetion.com/projects/details/1656/rwrs/67108>

Date conducted: 03/17/2021

In order to complete the initial power analysis, the dummy outcome of a 90-day gap in database enrollment will be used. This outcome is used to ensure that no information on the comparative risks of the outcomes of interest are available at this stage. Complete a 1:1 PS-matched comparative analysis using this outcome. PS should include only 3 covariates: age, gender, and combined comorbidity index. Power calculations are based on the formulas from Chow et al. (2008).

- Stop analyses until feasibility and power are reviewed by primary investigators and FDA. Reviewers evaluate the results of the analyses described above in Sections 7 and 8, including numbers of patients, patient characteristics, follow-up time, and reasons for censoring by treatment group, as well as overall rates of outcomes and study power. These parameters are re-evaluated and reported in the subsequent sections, after incorporating feedback and refining the protocol.

- Stop analyses until feasibility and power are reviewed by primary investigators, FDA, and assigned members of advisory board.

Reviewed by PI:	Shirley Wang	Date reviewed:	3/19/2021
Reviewed by FDA:	Ken Quinto	Date reviewed:	4/2/2021
Reasons for stopping analysis (if required):			

9. Balance Assessment

For Budesonide-formoterol vs. formoterol

Optum CDM: <https://bwh-dope.action.com/projects/details/1657/rwrs/68456>

IBM® MarketScan®: <https://bwh-dope.action.com/projects/details/1656/rwrs/68455>

Date conducted: 4/14/2021

After review of initial feasibility and power analyses, complete creation of the remaining covariates from Section 6.2. Again, using the dummy outcome of a 90-day gap in database enrollment, complete a 1:1 PS-matched analysis. The PS should include the complete list of covariates.

- Provide plot of PS distributions stratified by treatment group.

Note- Please refer to **Appendix B**.

- Report covariate balance after matching.

Note- For Table 1, please refer to **Appendix B**.

- Report reasons for censoring by treatment group.

	Overall	Referent	Exposure
Dummy outcome	0 (0.00%)	0 (0.00%)	0 (0.00%)
Death	14 (0.06%)	5 (0.02%)	9 (0.04%)
Start of an additional exposure	291 (1.20%)	242 (1.00%)	49 (0.20%)
End of index exposure	20257 (83.31%)	10172 (41.84%)	10085 (41.48%)
Specified date reached	486 (2.00%)	227 (0.93%)	259 (1.07%)
End of patient data	0 (0.00%)	0 (0.00%)	0 (0.00%)
End of patient enrollment	3159 (12.99%)	1463 (6.02%)	1696 (6.98%)
Nursing home admission, pharmacy disenrollment	107 (0.44%)	48 (0.20%)	59 (0.24%)

- Report follow-up time by treatment group.

Median Follow-Up Time (Days) [IQR]		
Patient Group	Optum	Marketscan
Overall Patient Population	88 [88,148]	107 [88,163]
Referent –	88 [88,148]	93 [88, 148]
Exposure	88 [88, 158]	116 [88, 177]

- Report overall risk of the primary outcome.

	Optum CDM	IBM® MarketScan®	Pooled
Risk per 1,000 patients	3.7	4.7	4.2

10. Final Power Assessment

Date conducted: 4/15/2021

- Re-calculate power in the appropriate excel table, using the revised number of matched patients from the PS-match in Section 9. All other parameters in the table should be the same as in Section 8.
 - Pooled

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Non-inferiority Analysis	
Number of patients matched	24,314
Reference	12,157
Exposed	12,157
Risk per 1,000 patients	4.2
Assumed HR from RCT	1.07
Alpha (2-sided)	0.05
Non-inferiority margin	2
Number of events expected	102.1188
Power	0.885015194

○ Optum CDM

Non-inferiority Analysis	
Number of patients matched	10,396
Reference	5,198
Exposed	5,198
Risk per 1,000 patients	3.7
Assumed HR from RCT	1.07
Alpha (2-sided)	0.05
Non-inferiority margin	2
Number of events expected	38.4652
Power	0.491896419

○ IBM® MarketScan®

Non-inferiority Analysis	
Number of patients matched	13,918
Reference	6,959
Exposed	6,959
Risk per 1,000 patients	4.7
Assumed HR from RCT	1.07
Alpha (2-sided)	0.05
Non-inferiority margin	2
Number of events expected	65.4146
Power	0.71548801

- Stop analyses until balance and final power assessment are reviewed by primary investigators, FDA, and assigned members of advisory board.

Reviewed by PI:	Shirley Wang	Date reviewed:	4/16/2021
Reviewed by FDA:	Ken Quinto	Date reviewed:	4/30/2021
Reasons for stopping analysis (if required):			

11. Study Confidence and Concerns

Deadline for voting on study confidence and listing concerns:

Date votes and concerns are summarized:

- If final feasibility and power analyses are reviewed and approved, proceed to the remaining protocol steps.
- All study team and advisory board members that review this protocol should at this stage provide their level of confidence for the success of the RWD study in the [Google Form](#). This form also provides space for reviewers to list any concerns that they feel may contribute to a failure to replicate the findings of the RCT, including differences in study populations, poor measurement of study variables, or residual confounding. All responses will be kept confidential and individual-level results will only be shared with the

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individual respondent.

- After the deadline for voting has passed, provide the distribution of responses and summarize all concerns here.

12. Register study protocol on [clinicalTrials.gov](https://clinicaltrials.gov)

Date conducted: 05/12/2021

- Register the study on [clinicalTrials.gov](https://clinicaltrials.gov) and upload this document.

13. Comparative Analyses

Action report name:

Date conducted:

13.1 For primary analysis:

13.2 For sensitivity analyses:

14. Requested Results

14.1 Table 1: Baseline characteristics before and after adjustment

Variable	Before adjustment			After adjustment		
	Referent	Exposure	Std. diff.	Referent	Exposure	Std. diff.
Number of patients			-			-
Age categories						
...						

14.2 Table 2: Follow-up time

Patient Group	Median Follow-Up Time (Days) [IQR]
Overall Patient Population	
Referent	
Exposure	

14.3 Table 3: Censoring events

	Overall	Referent	Exposure
Outcome			
Death			
Start of an additional exposure			
End of index exposure			
Specified date reached			
End of patient data			
End of patient enrollment			
...			

14.4 Table 4: Results from primary analyses:

Analysis	No. exposed events	No. referent events	Exposed rate	Referent rate	HR (95% CI)
Crude					
Analysis 1					
Analysis 2					
...					

HR, Hazard Ratio; CI, Confidence Interval.

14.5 Table 5: Results from secondary analyses.

15. References

Chow S, Shao J, Wang H. 2008. *Sample Size Calculations in Clinical Research*. 2nd Ed. Chapman & Hall/CRC Biostatistics Series. page 177.

Appendix A

#	NCT01444430 trial definitions	Implementation in routine care	Color Coding Criteria
	<p style="text-align: center;">Trial details- clincaltrial.gov NCT01444430</p> <p style="text-align: center;">EXPOSURE vs. COMPARISON</p>	<p>Please see the following Google Drive for further details or any missing information: https://drive.google.com/drive/folders/1WD6i8wrywYjEaXzftTeuK-VCen66-qV?usp=sharing</p> <p>ICD-10 codes are not listed in this document because of excel cell size limitations and excessive number of ICD-10 codes. Full ICD-10 code lists will be available in the above Google Drive Folder (link above). ICD-9 to ICD-10 code conversions were completed using a SAS macro that implements forward/ backward mapping based on the CMS ICD-9 to ICD-10 mapping: https://www.nber.org/data/icd9-icd10-cms-and-pxs-crosswalk-general-equivalence-mappings.html</p>	<p>Can be replicated in claims</p> <p>Using dummy definitions for measuring in claims</p> <p>Can't be measured in claims</p> <p>Can't be measured in claims but not important for the analysis</p>
	<p>Exposure) Budesonide-formoterol Referent) Budesonide</p> <p>Exposure: Budesonide- formoterol Two actuations of 80 ug of budesonide plus 4.5 ug of formoterol or 160 ug of budesonide plus 4.5 ug of formoterol) NDC code: 00186037020 - budesonide/formoterol fumarate 00186037028 - budesonide/formoterol fumarate 00186037228 - budesonide/formoterol fumarate 00186037228 - budesonide/formoterol fumarate 54569646600 - budesonide/formoterol fumarate 54868593600 - budesonide/formoterol fumarate 54868593700 - budesonide/formoterol fumarate</p> <p>Referent: Budesonide alone Two actuations of 80 ug or 160 ug in trial 90 ug or 180 ug will be used in replication (market available doses)</p> <p>NDC code: 00186091612 (180 ug) 00186091706 (90 ug)</p>	<p style="text-align: center;">Reference/Rationale</p>	
	<p style="text-align: center;">PRIMARY OUTCOME</p> <p>First Serious asthma-related events (Composite of asthma-related deaths, intubations, and hospitalizations)</p>	<p>Measured 1 day after drug initiation in inpatient setting</p> <p>Asthma-related death: Inpatient death with primary discharge code of asthma (Optum, Marketscan) + Patient attribute for death (Optum)</p> <p>Asthma related -Intubations: Diagnosis code for asthma in primary position plus CPT procedure code, 31500: Endotracheal intubation, emergency in inpatient or Emergency room setting</p> <p>Asthma-related Hospitalizations: Inpatient discharge diagnosis for asthma in primary position</p>	
	INCLUSION CRITERIA		
1	≥12 years of age	<p>Measured on the day of drug initiation</p> <p>Age ≥12</p>	
2	Documented clinical diagnosis of asthma for ≥1 year prior to randomization	<p>Measured between [-∞, 365] days prior to drug initiation in any position /any setting</p> <p>Asthma: ICD-9: 493.x ICD-10 : J45.*</p>	<p>Larsson K, Ståhlberg B, Lisspers K, Telg G, Johansson G, Thuresson M, Janson C. Prevalence and management of severe asthma in primary care: an observational cohort study in Sweden (PACEHR). Respir Res. 2018 Jan 18;19(1):12. doi: 10.1186/s12931-018-0719-x. PMID: 29347939; PMCID: PMC5774144.</p>
3	History of at least one asthma exacerbation in the previous year (but none in the 4 weeks prior to randomization. An asthma exacerbation was defined as an event requiring treatment with systemic corticosteroids or requiring hospitalization (i.e. an inpatient stay or >24-hour stay in the observation area of an emergency room or local equivalent)	<p>Measured between 30 to 365 days prior to drug initiation in defined position and setting</p> <p>1) Asthma diagnosis code in inpatient primary diagnosis position 2) Asthma diagnosis code in inpatient any position or outpatient setting PLUS a prescription claim for systemic steroids 14 days before and after the diagnosis code</p> <p>Asthma: ICD-9: 493.x ICD-10 : J45.*</p>	
4	Receiving:	<p>Measured between 30 to 365 days prior to drug initiation in defined position and setting</p>	
4a	A stable dose of ICS alone or in combination with a LABA, leukotriene receptor antagonist or other maintenance therapy/therapies for ≥4 weeks prior to randomization (any patient maintained on a stable high-dose ICS with or without a LABA or LTRA or other maintenance therapy/therapies was required to have an ACOG total score of <1.5 at screening) or	<p>A prescription claim for one of the following asthma maintenance medications: ICS monotherapy ICS/LABA combination Xanthines Leukotriene receptor antagonist</p> <p>Note) Did not incorporate SABA as it is difficult to capture daily use</p>	
4b	A stable dose of LTRA or xanthine monotherapy (for ≥4 weeks prior to randomization) or daily SABA (in the 4 weeks before randomization but ≥8 puffs a day on two consecutive days, or ≥25 puffs in one day, in the 7 days prior to screening). Patients on LTRAs, xanthines, or daily SABA, were eligible only if they recorded an ACOG total score of ≥1.5, and in the investigator's clinical judgment, the patient's asthma severity could have justified treatment with ICS or ICS/LABA combination	N/A	
5	Provided signed informed consent/pediatric assent prior to the study	N/A	
	EXCLUSION CRITERIA		

Appendix A

1	A history of life-threatening asthma (defined as an asthma episode that required intubation and/or was associated with hypercapnia requiring non-invasive ventilatory support)	<p>Measured any time prior to and including drug initiation date in any setting Acute respiratory failure/insufficiency/arrest ICD-9: "517.3", "518.5", "518.81", "518.82", "518.83", "518.84", "799.1", "V46.1", "V46.11", "V46.12", "V46.13", "V46.14", "V46.2" ICD-10: "J80", "J96.00", "J96.01", "J96.02", "J96.10", "J96.11", "J96.12", "J96.20", "J96.21", "J96.22", "J96.90", "J96.91", "J96.92", "R09.01", "R09.2", "Z99.11", "Z99.12", "Z99.81")</p> <p>Intubation/Non-invasive ventilatory support: ICD-9 Procedure code: "93.90", "93.92", "96.01", "96.02", "96.03", "96.04", "96.05", "96.70", "96.71", "96.72" ICD-10 procedure codes: "09HN78Z", "09HN88Z", "0BH13EZ", "0BH17EZ", "0BH18EZ", "0CHV78Z", "0CHY88Z", "0DHS78Z", "0DHS88Z", "0WHQ73Z", "5A09357", "5A09457", "5A09557", "5A1935Z", "5A1945Z", "5A1955Z")</p>	Walkey AJ, Wiener RS. Use of noninvasive ventilation in patients with acute respiratory failure, 2000-2009: a population-based study. Ann Am Thorac Soc. 2013 Feb;10(1):10-7. doi: 10.1513/AnnalsATS.201206-0340C. PMID: 23509327; PMCID: PMC3780971.
2	2a) Any asthma exacerbation requiring systemic corticosteroids within 4 weeks prior to randomization or 2b) >4 separate exacerbations or 2c) >2 hospitalizations (an inpatient stay or >24-hour stay in the observation area of an emergency room or local equivalent) due to asthma in the previous year	<p>Note: 2a) Exclusion due to systemic corticosteroid use is applied for exclusion 3</p> <p>2b) Asthma exacerbation, measured >4 times, 365 days prior to drug initiation Defined as a) Asthma diagnosis code in inpatient primary diagnosis position b) Asthma diagnosis code in inpatient any position or outpatient setting PLUS a prescription claim for systemic steroids 14 days before and after the diagnosis code 2c) Asthma hospitalization, measured >2 times, 365 days prior to drug initiation</p> <p>Asthma: ICD-9: 493x ICD-10: J45.*</p>	http://mchp-appserv.cpe.umanitoba.ca/concept/asthma_table1.html
3	Received systemic corticosteroids for any reason in the 4 weeks prior to randomization	<p>Measured 30 days prior to and including the day of drug initiation</p> <p>Cortisone, hydrocortisone, prednisone, prednisolone, methylprednisolone, triamcinolone, dexamethasone, betamethasone</p>	
4	Had an ongoing asthma exacerbation requiring systemic corticosteroids	<p>Measured 7 days prior to and including the day of drug initiation</p> <p>Asthma exacerbation Defined as a) Asthma diagnosis code in inpatient primary diagnosis position b) Asthma diagnosis code in inpatient any position or outpatient setting PLUS a prescription claim for systemic steroids 14 days before and after the diagnosis code</p> <p>Asthma: ICD-9: 493x ICD-10: J45.*</p>	
5	Unstable asthma within 7 days prior to randomization (defined as asthma symptoms that persisted throughout the day on two consecutive days, night-time awakening due to asthma during 23 nights, rescue medication use for the acute worsening of asthma symptoms of ≥8 inhalations a day over two consecutive days or ≥25 inhalations in one day, and asthma symptoms so severe that the patient was limited in their ability to perform normal daily activity)	N/A	
6	Peak expiratory flow (pre- or post-bronchodilatory) <50% of predicted normal	N/A	
7	Concurrent respiratory disease (chronic obstructive pulmonary disease, chronic bronchitis, emphysema, idiopathic pulmonary fibrosis, bronchiectasis, and/or any pulmonary disease)	<p>Measured 180 days prior to drug initiation in any care setting and position</p> <p>COPD: "491.0", "491.1", "491.2", "491.21", "491.22", "491.8", "491.9", "492.0", "J41.8", "J43.1", "J43.8", "J47.0", "491.20", "492.8", "494.0", "494.1", "506.4", "J41.0", "J41.1", "J43.0", "J43.2", "J43.9", "J44.0", "J44.1", "J47.1", "J47.9"</p> <p>Tuberculosis: ICD-9: 010.x - 018.x ICD-10: A15.x - A19.x</p> <p>Lung cancer ICD-9: 162.2x, 162.3x, 162.4x, 162.5x, 162.8x, 162.9x ICD-10: C34.0x, C34.1x, C34.2x, C34.3x, C34.8x, C34.9x</p> <p>Bronchiectasis: ICD-9: 494.x ICD-10: J47.x</p>	
8	A smoking history of >10 pack-years	<p>Measured 180 days prior at least 1 inpatient or outpatient code for: V15.82, 305.1x, 649.0x, 989.84</p> <p>OR</p> <p>CPT code 99406, 99407, G0436, G0437, G9016, S9075, S9453, S4995, G9276, G9458, 1034F, 4004F, 4001F</p> <p>OR</p> <p>use of varenicline tartrate or nicotine replacement therapy ("Nicotine", "Nicotine Bitartrate", "Nicotine Polacrilline")</p>	
9	Respiratory infection or other viral/bacterial illness	<p>Measured 180 days prior to drug initiation in any position/any setting</p> <p>Acute upper /lower respiratory infections ICD-10: J00.x, J01.x, J02.x, J03.x, J04.x, J05.x, J06.x J20.x, J21.x, J22.x ICD-9: 460.x, 461.x, 462.x, 463.x, 464.x, 461</p>	
10	Pregnancy (current/planned) and lactation	<p>Measured 180 days prior to drug initiation in any position/any setting</p> <p>See tab [Pregnancy]</p>	

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11	Malignancy (with the exception of basal cell carcinoma) within the 5 years prior to study commencement	Measured 180 days prior to drug initiation in any position /any setting See tab [Malignancy]
12	Known or suspected hypersensitivity to study medications or their excipients	N/A
13	Participation in a concurrent LABA safety study or other interventional or investigational drug study	N/A
14	Omalizumab or any other monoclonal/polyclonal antibody use in the 6 months prior to randomization	Measured 180 days prior to drug initiation Drug generic name: omalizumab
15	Concomitant β -blocker use	Measured 30 days prior to drug initiation Drug generic name: Propranolol, bisindololol, carteolol, carvedilol, labetalol, nadolol, Oxprenolol, penbutolol, pindolol, sotalol, timolol, Acetololol, Atenolol, Betaxolol, bisoprolol, Celiprolol, metoprolol, nebivolol, esmolol, butaxamine, nebivolol
16	Any other significant disease/disorder that, in the opinion of the investigator, could have either put the patient at risk, or influence the results of the study or the patient's ability to participate in the study	N/A
17	Clinically relevant abnormal findings in physical examination/vital signs at randomization	N/A
18	Risk of non-compliance	N/A
19	Drug/alcohol abuse	Measured 180 days prior to drug initiation in any diagnosis position and inpatient or outpatient care setting: Alcohol abuse or dependence: 291.xx, 303.xx, 305.0x, 571.0x, 571.1x, 571.2x, 571.3x, 357.5x, 425.5x, E860.0x, V11.3x Drug abuse or dependence: 292.xx, 304.xx, 305.2x-305.9x, 648.3x
20	Planned blood donation during the study	N/A
21	Affiliation with study sponsor and/or investigator	N/A

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Pregnancy

Diagnosis codes

650 NORMAL DELIVERY
660 OBSTRUCTED LABOR
661 ABNORMALITY OF FORCES OF LABOR
662 LONG LABOR
663 UMBILICAL CORD COMPLICATIONS DURING LABOR AND DELIVERY
664 TRAUMA TO PERINEUM AND VULVA DURING DELIVERY
665 OTHER OBSTETRICAL TRAUMA
667 RETAINED PLACENTA OR MEMBRANES WITHOUT HEMORRHAGE
668 COMPLICATIONS OF THE ADMINISTRATION OF ANESTHETIC OR OTHER SEDATION IN LABOR AND DELIVERY
669.94 UNSPECIFIED COMPLICATION OF LABOR AND DELIVERY POSTPARTUM CONDITION OR COMPLICATION
V24 POSTPARTUM CARE AND EXAMINATION
V24.0 POSTPARTUM CARE AND EXAMINATION IMMEDIATELY AFTER DELIVERY
V24.1 POSTPARTUM CARE AND EXAMINATION OF LACTATING MOTHER
V24.2 ROUTINE POSTPARTUM FOLLOW
V27 OUTCOME OF DELIVERY
V27.0 MOTHER WITH SINGLE LIVEBORN
V27.1 MOTHER WITH SINGLE STILLBORN+A2:J81
V27.2 MOTHER WITH TWINS BOTH LIVEBORN
V27.3 MOTHER WITH TWINS ONE LIVEBORN AND ONE STILLBORN
V27.4 MOTHER WITH TWINS BOTH STILLBORN
V27.5 MOTHER WITH OTHER MULTIPLE BIRTH ALL LIVEBORN
V27.6 MOTHER WITH OTHER MULTIPLE BIRTH SOME LIVEBORN
V27.7 MOTHER WITH OTHER MULTIPLE BIRTH ALL STILLBORN
V27.9 MOTHER WITH UNSPECIFIED OUTCOME OF DELIVERY

Procedure codes

72.0 LOW FORCEPS OPERATION
72.1 LOW FORCEPS OPERATION WITH EPISIOTOMY
72.2 MID FORCEPS OPERATION
72.21 MID FORCEPS OPERATION WITH EPISIOTOMY
72.29 OTHER MID FORCEPS OPERATION
72.3 HIGH FORCEPS OPERATION
72.31 HIGH FORCEPS OPERATION WITH EPISIOTOMY
72.39 OTHER HIGH FORCEPS OPERATION
72.4 FORCEPS ROTATION OF FETAL HEAD
72.5 BREECH EXTRACTION
72.51 PARTIAL BREECH EXTRACTION WITH FORCEPS TO AFTERCOMING HEAD
72.52 OTHER PARTIAL BREECH EXTRACTION

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72.53 TOTAL BREECH EXTRACTION WITH FORCEPS TO AFTERCOMING HEAD
72.54 OTHER TOTAL BREECH EXTRACTION
72.6 FORCEPS APPLICATION TO AFTERCOMING HEAD
72.7 VACUUM EXTRACTION
72.71 VACUUM EXTRACTION WITH EPISIOTOMY
72.79 OTHER VACUUM EXTRACTION
72.8 OTHER SPECIFIED INSTRUMENTAL DELIVERY
72.9 UNSPECIFIED INSTRUMENTAL DELIVERY
73.0 ARTIFICIAL RUPTURE OF MEMBRANES
73.01 INDUCTION OF LABOR BY ARTIFICIAL RUPTURE OF MEMBRANES
73.09 OTHER ARTIFICIAL RUPTURE OF MEMBRANES
73.1 OTHER SURGICAL INDUCTION OF LABOR
73.2 INTERNAL AND COMBINED VERSION AND EXTRACTION
73.21 INTERNAL AND COMBINED VERSION WITHOUT EXTRACTION
73.22 INTERNAL AND COMBINED VERSION WITH EXTRACTION
73.3 FAILED FORCEPS
73.4 MEDICAL INDUCTION OF LABOR
73.5 MANUALLY ASSISTED DELIVERY
73.51 MANUAL ROTATION OF FETAL HEAD
73.59 OTHER MANUALLY ASSISTED DELIVERY
73.6 EPISIOTOMY
73.8 OPERATIONS ON FETUS TO FACILITATE DELIVERY
73.9 OTHER OPERATIONS ASSISTING DELIVERY
73.91 EXTERNAL VERSION ASSISTING DELIVERY
73.92 REPLACEMENT OF PROLAPSED UMBILICAL CORD
73.93 INCISION OF CERVIX TO ASSIST DELIVERY
73.94 PUBIOTOMY TO ASSIST DELIVERY
73.99 OTHER OPERATIONS ASSISTING DELIVERY
74.0 CLASSICAL CESAREAN SECTION
74.1 LOW CERVICAL CESAREAN SECTION
74.2 EXTRAPERITONEAL CESAREAN SECTION
74.3 REMOVAL OF EXTRATUBAL ECTOPIC PREGNANCY
74.4 CESAREAN SECTION OF OTHER SPECIFIED TYPE
74.9 CESAREAN SECTION OF UNSPECIFIED TYPE
74.91 HYSTEROTOMY TO TERMINATE PREGNANCY
74.99 OTHER CESAREAN SECTION OF UNSPECIFIED TYPE
75.4 MANUAL REMOVAL OF RETAINED PLACENTA
75.5 REPAIR OF CURRENT OBSTETRIC LACERATION OF UTERUS
75.6 REPAIR OF OTHER CURRENT OBSTETRIC LACERATION
75.7 MANUAL EXPLORATION OF UTERINE CAVITY, POSTPARTUM
75.9 OTHER OBSTETRIC OPERATIONS

Appendix A

Malignancy

140 - MALIGNANT NEOPLASM OF LIP
140.0 - MALIGNANT NEOPLASM OF UPPER LIP VERMILION BORDER
140.1 - MALIGNANT NEOPLASM OF LOWER LIP VERMILION BORDER
140.3 - MALIGNANT NEOPLASM OF UPPER LIP INNER ASPECT
140.4 - MALIGNANT NEOPLASM OF LOWER LIP INNER ASPECT
140.5 - MALIGNANT NEOPLASM OF LIP UNSPECIFIED INNER ASPECT
140.6 - MALIGNANT NEOPLASM OF COMMISSURE OF LIP
140.8 - MALIGNANT NEOPLASM OF OTHER SITES OF LIP
140.9 - MALIGNANT NEOPLASM OF LIP UNSPECIFIED VERMILION BORDER
141 - MALIGNANT NEOPLASM OF TONGUE
141.0 - MALIGNANT NEOPLASM OF BASE OF TONGUE
141.1 - MALIGNANT NEOPLASM OF DORSAL SURFACE OF TONGUE
141.2 - MALIGNANT NEOPLASM OF TIP AND LATERAL BORDER OF TONGUE
141.3 - MALIGNANT NEOPLASM OF VENTRAL SURFACE OF TONGUE
141.4 - MALIGNANT NEOPLASM OF ANTERIOR TWO-THIRDS OF TONGUE PART UNSPECIFIED
141.5 - MALIGNANT NEOPLASM OF JUNCTIONAL ZONE OF TONGUE
141.6 - MALIGNANT NEOPLASM OF LINGUAL TONSIL
141.8 - MALIGNANT NEOPLASM OF OTHER SITES OF TONGUE
141.9 - MALIGNANT NEOPLASM OF TONGUE UNSPECIFIED
142 - MALIGNANT NEOPLASM OF MAJOR SALIVARY GLANDS
142.0 - MALIGNANT NEOPLASM OF PAROTID GLAND
142.1 - MALIGNANT NEOPLASM OF SUBMANDIBULAR GLAND
142.2 - MALIGNANT NEOPLASM OF SUBLINGUAL GLAND
142.8 - MALIGNANT NEOPLASM OF OTHER MAJOR SALIVARY GLANDS
142.9 - MALIGNANT NEOPLASM OF SALIVARY GLAND UNSPECIFIED
143 - MALIGNANT NEOPLASM OF GUM
143.0 - MALIGNANT NEOPLASM OF UPPER GUM
143.1 - MALIGNANT NEOPLASM OF LOWER GUM
143.8 - MALIGNANT NEOPLASM OF OTHER SITES OF GUM
143.9 - MALIGNANT NEOPLASM OF GUM UNSPECIFIED
144 - MALIGNANT NEOPLASM OF FLOOR OF MOUTH
144.0 - MALIGNANT NEOPLASM OF ANTERIOR PORTION OF FLOOR OF MOUTH
144.1 - MALIGNANT NEOPLASM OF LATERAL PORTION OF FLOOR OF MOUTH
144.8 - MALIGNANT NEOPLASM OF OTHER SITES OF FLOOR OF MOUTH
144.9 - MALIGNANT NEOPLASM OF FLOOR OF MOUTH PART UNSPECIFIED
145 - MALIGNANT NEOPLASM OF OTHER AND UNSPECIFIED PARTS OF MOUTH
145.0 - MALIGNANT NEOPLASM OF CHEEK MUCOSA
145.1 - MALIGNANT NEOPLASM OF VESTIBULE OF MOUTH
145.2 - MALIGNANT NEOPLASM OF HARD PALATE
145.3 - MALIGNANT NEOPLASM OF SOFT PALATE
145.4 - MALIGNANT NEOPLASM OF UVULA
145.5 - MALIGNANT NEOPLASM OF PALATE UNSPECIFIED
145.6 - MALIGNANT NEOPLASM OF RETROMOLAR AREA
145.8 - MALIGNANT NEOPLASM OF OTHER SPECIFIED PARTS OF MOUTH
145.9 - MALIGNANT NEOPLASM OF MOUTH UNSPECIFIED

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146 - MALIGNANT NEOPLASM OF OROPHARYNX
146.0 - MALIGNANT NEOPLASM OF TONSIL
146.1 - MALIGNANT NEOPLASM OF TONSILLAR FOSSA
146.2 - MALIGNANT NEOPLASM OF TONSILLAR PILLARS (ANTERIOR) (POSTERIOR)
146.3 - MALIGNANT NEOPLASM OF VALLECULA EPIGLOTTICA
146.4 - MALIGNANT NEOPLASM OF ANTERIOR ASPECT OF EPIGLOTTIS
146.5 - MALIGNANT NEOPLASM OF JUNCTIONAL REGION OF OROPHARYNX
146.6 - MALIGNANT NEOPLASM OF LATERAL WALL OF OROPHARYNX
146.7 - MALIGNANT NEOPLASM OF POSTERIOR WALL OF OROPHARYNX
146.8 - MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES OF OROPHARYNX
146.9 - MALIGNANT NEOPLASM OF OROPHARYNX UNSPECIFIED SITE
147 - MALIGNANT NEOPLASM OF NASOPHARYNX
147.0 - MALIGNANT NEOPLASM OF SUPERIOR WALL OF NASOPHARYNX
147.1 - MALIGNANT NEOPLASM OF POSTERIOR WALL OF NASOPHARYNX
147.2 - MALIGNANT NEOPLASM OF LATERAL WALL OF NASOPHARYNX
147.3 - MALIGNANT NEOPLASM OF ANTERIOR WALL OF NASOPHARYNX
147.8 - MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES OF NASOPHARYNX
147.9 - MALIGNANT NEOPLASM OF NASOPHARYNX UNSPECIFIED SITE
148 - MALIGNANT NEOPLASM OF HYPOPHARYNX
148.0 - MALIGNANT NEOPLASM OF POSTCRICOID REGION OF HYPOPHARYNX
148.1 - MALIGNANT NEOPLASM OF PYRIFORM SINUS
148.2 - MALIGNANT NEOPLASM OF ARYEPIGLOTTIC FOLD HYPOPHARYNGEAL ASPECT
148.3 - MALIGNANT NEOPLASM OF POSTERIOR HYPOPHARYNGEAL WALL
148.8 - MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES OF HYPOPHARYNX
148.9 - MALIGNANT NEOPLASM OF HYPOPHARYNX UNSPECIFIED SITE
149 - MALIGNANT NEOPLASM OF OTHER AND ILL-DEFINED SITES WITHIN THE LIP ORAL CAVITY AND PHARYNX
149.0 - MALIGNANT NEOPLASM OF PHARYNX UNSPECIFIED
149.1 - MALIGNANT NEOPLASM OF WALDEYER'S RING
149.8 - MALIGNANT NEOPLASM OF OTHER SITES WITHIN THE LIP AND ORAL CAVITY
149.9 - MALIGNANT NEOPLASM OF ILL-DEFINED SITES WITHIN THE LIP AND ORAL CAVITY
150 - MALIGNANT NEOPLASM OF ESOPHAGUS
150.0 - MALIGNANT NEOPLASM OF CERVICAL ESOPHAGUS
150.1 - MALIGNANT NEOPLASM OF THORACIC ESOPHAGUS
150.2 - MALIGNANT NEOPLASM OF ABDOMINAL ESOPHAGUS
150.3 - MALIGNANT NEOPLASM OF UPPER THIRD OF ESOPHAGUS
150.4 - MALIGNANT NEOPLASM OF MIDDLE THIRD OF ESOPHAGUS
150.5 - MALIGNANT NEOPLASM OF LOWER THIRD OF ESOPHAGUS
150.8 - MALIGNANT NEOPLASM OF OTHER SPECIFIED PART OF ESOPHAGUS
150.9 - MALIGNANT NEOPLASM OF ESOPHAGUS UNSPECIFIED SITE
151 - MALIGNANT NEOPLASM OF STOMACH
151.0 - MALIGNANT NEOPLASM OF CARDIA
151.1 - MALIGNANT NEOPLASM OF PYLORUS
151.2 - MALIGNANT NEOPLASM OF PYLORIC ANTRUM
151.3 - MALIGNANT NEOPLASM OF FUNDUS OF STOMACH
151.4 - MALIGNANT NEOPLASM OF BODY OF STOMACH
151.5 - MALIGNANT NEOPLASM OF LESSER CURVATURE OF STOMACH UNSPECIFIED

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151.6 - MALIGNANT NEOPLASM OF GREATER CURVATURE OF STOMACH UNSPECIFIED
151.8 - MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES OF STOMACH
151.9 - MALIGNANT NEOPLASM OF STOMACH UNSPECIFIED SITE
152 - MALIGNANT NEOPLASM OF SMALL INTESTINE INCLUDING DUODENUM
152.0 - MALIGNANT NEOPLASM OF DUODENUM
152.1 - MALIGNANT NEOPLASM OF JEJUNUM
152.2 - MALIGNANT NEOPLASM OF ILEUM
152.3 - MALIGNANT NEOPLASM OF MECKEL'S DIVERTICULUM
152.8 - MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES OF SMALL INTESTINE
152.9 - MALIGNANT NEOPLASM OF SMALL INTESTINE UNSPECIFIED SITE
153 - MALIGNANT NEOPLASM OF COLON
153.0 - MALIGNANT NEOPLASM OF HEPATIC FLEXURE
153.1 - MALIGNANT NEOPLASM OF TRANSVERSE COLON
153.2 - MALIGNANT NEOPLASM OF DESCENDING COLON
153.3 - MALIGNANT NEOPLASM OF SIGMOID COLON
153.4 - MALIGNANT NEOPLASM OF CECUM
153.5 - MALIGNANT NEOPLASM OF APPENDIX VERMIFORMIS
153.6 - MALIGNANT NEOPLASM OF ASCENDING COLON
153.7 - MALIGNANT NEOPLASM OF SPLENIC FLEXURE
153.8 - MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES OF LARGE INTESTINE
153.9 - MALIGNANT NEOPLASM OF COLON UNSPECIFIED SITE
154 - MALIGNANT NEOPLASM OF RECTUM RECTOSIGMOID JUNCTION AND ANUS
154.0 - MALIGNANT NEOPLASM OF RECTOSIGMOID JUNCTION
154.1 - MALIGNANT NEOPLASM OF RECTUM
154.2 - MALIGNANT NEOPLASM OF ANAL CANAL
154.3 - MALIGNANT NEOPLASM OF ANUS UNSPECIFIED SITE
154.8 - MALIGNANT NEOPLASM OF OTHER SITES OF RECTUM RECTOSIGMOID JUNCTION AND ANUS
155 - MALIGNANT NEOPLASM OF LIVER AND INTRAHEPATIC BILE DUCTS
155.0 - MALIGNANT NEOPLASM OF LIVER PRIMARY
155.1 - MALIGNANT NEOPLASM OF INTRAHEPATIC BILE DUCTS
155.2 - MALIGNANT NEOPLASM OF LIVER NOT SPECIFIED AS PRIMARY OR SECONDARY
156 - MALIGNANT NEOPLASM OF GALLBLADDER AND EXTRAHEPATIC BILE DUCTS
156.0 - MALIGNANT NEOPLASM OF GALLBLADDER
156.1 - MALIGNANT NEOPLASM OF EXTRAHEPATIC BILE DUCTS
156.2 - MALIGNANT NEOPLASM OF AMPULLA OF VATER
156.8 - MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES OF GALLBLADDER AND EXTRAHEPATIC BILE DUCTS
156.9 - MALIGNANT NEOPLASM OF BILIARY TRACT PART UNSPECIFIED SITE
157 - MALIGNANT NEOPLASM OF PANCREAS
157.0 - MALIGNANT NEOPLASM OF HEAD OF PANCREAS
157.1 - MALIGNANT NEOPLASM OF BODY OF PANCREAS
157.2 - MALIGNANT NEOPLASM OF TAIL OF PANCREAS
157.3 - MALIGNANT NEOPLASM OF PANCREATIC DUCT
157.4 - MALIGNANT NEOPLASM OF ISLETS OF LANGERHANS
157.8 - MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES OF PANCREAS
157.9 - MALIGNANT NEOPLASM OF PANCREAS PART UNSPECIFIED
158 - MALIGNANT NEOPLASM OF RETROPERITONEUM AND PERITONEUM

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158.0 - MALIGNANT NEOPLASM OF RETROPERITONEUM
158.8 - MALIGNANT NEOPLASM OF SPECIFIED PARTS OF PERITONEUM
158.9 - MALIGNANT NEOPLASM OF PERITONEUM UNSPECIFIED
159 - MALIGNANT NEOPLASM OF OTHER AND ILL-DEFINED SITES WITHIN THE DIGESTIVE ORGANS AND PERITONEUM
159.0 - MALIGNANT NEOPLASM OF INTESTINAL TRACT PART UNSPECIFIED
159.1 - MALIGNANT NEOPLASM OF SPLEEN NOT ELSEWHERE CLASSIFIED
159.8 - MALIGNANT NEOPLASM OF OTHER SITES OF DIGESTIVE SYSTEM AND INTRA-ABDOMINAL ORGANS
159.9 - MALIGNANT NEOPLASM OF ILL-DEFINED SITES WITHIN THE DIGESTIVE ORGANS AND PERITONEUM
160 - MALIGNANT NEOPLASM OF NASAL CAVITIES MIDDLE EAR AND ACCESSORY SINUSES
160.0 - MALIGNANT NEOPLASM OF NASAL CAVITIES
160.1 - MALIGNANT NEOPLASM OF AUDITORY TUBE MIDDLE EAR AND MASTOID AIR CELLS
160.2 - MALIGNANT NEOPLASM OF MAXILLARY SINUS
160.3 - MALIGNANT NEOPLASM OF ETHMOIDAL SINUS
160.4 - MALIGNANT NEOPLASM OF FRONTAL SINUS
160.5 - MALIGNANT NEOPLASM OF SPHENOIDAL SINUS
160.8 - MALIGNANT NEOPLASM OF OTHER ACCESSORY SINUSES
160.9 - MALIGNANT NEOPLASM OF ACCESSORY SINUS UNSPECIFIED
161 - MALIGNANT NEOPLASM OF LARYNX
161.0 - MALIGNANT NEOPLASM OF GLOTTIS
161.1 - MALIGNANT NEOPLASM OF SUPRAGLOTTIS
161.2 - MALIGNANT NEOPLASM OF SUBGLOTTIS
161.3 - MALIGNANT NEOPLASM OF LARYNGEAL CARTILAGES
161.8 - MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES OF LARYNX
161.9 - MALIGNANT NEOPLASM OF LARYNX UNSPECIFIED
162 - MALIGNANT NEOPLASM OF TRACHEA BRONCHUS AND LUNG
162.0 - MALIGNANT NEOPLASM OF TRACHEA
162.2 - MALIGNANT NEOPLASM OF MAIN BRONCHUS
162.3 - MALIGNANT NEOPLASM OF UPPER LOBE BRONCHUS OR LUNG
162.4 - MALIGNANT NEOPLASM OF MIDDLE LOBE BRONCHUS OR LUNG
162.5 - MALIGNANT NEOPLASM OF LOWER LOBE BRONCHUS OR LUNG
162.8 - MALIGNANT NEOPLASM OF OTHER PARTS OF BRONCHUS OR LUNG
162.9 - MALIGNANT NEOPLASM OF BRONCHUS AND LUNG UNSPECIFIED
163 - MALIGNANT NEOPLASM OF PLEURA
163.0 - MALIGNANT NEOPLASM OF PARIETAL PLEURA
163.1 - MALIGNANT NEOPLASM OF VISCERAL PLEURA
163.8 - MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES OF PLEURA
163.9 - MALIGNANT NEOPLASM OF PLEURA UNSPECIFIED
164 - MALIGNANT NEOPLASM OF THYMUS HEART AND MEDIASTINUM
164.0 - MALIGNANT NEOPLASM OF THYMUS
164.1 - MALIGNANT NEOPLASM OF HEART
164.2 - MALIGNANT NEOPLASM OF ANTERIOR MEDIASTINUM
164.3 - MALIGNANT NEOPLASM OF POSTERIOR MEDIASTINUM
164.8 - MALIGNANT NEOPLASM OF OTHER PARTS OF MEDIASTINUM
164.9 - MALIGNANT NEOPLASM OF MEDIASTINUM PART UNSPECIFIED
165 - MALIGNANT NEOPLASM OF OTHER AND ILL-DEFINED SITES WITHIN THE RESPIRATORY SYSTEM AND INTRATHORACIC ORGANS
165.0 - MALIGNANT NEOPLASM OF UPPER RESPIRATORY TRACT PART UNSPECIFIED

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165.8 - MALIGNANT NEOPLASM OF OTHER SITES WITHIN THE RESPIRATORY SYSTEM AND INTRATHORACIC ORGANS
165.9 - MALIGNANT NEOPLASM OF ILL-DEFINED SITES WITHIN THE RESPIRATORY SYSTEM
170 - MALIGNANT NEOPLASM OF BONE AND ARTICULAR CARTILAGE
170.0 - MALIGNANT NEOPLASM OF BONES OF SKULL AND FACE EXCEPT MANDIBLE
170.1 - MALIGNANT NEOPLASM OF MANDIBLE
170.2 - MALIGNANT NEOPLASM OF VERTEBRAL COLUMN EXCLUDING SACRUM AND COCCYX
170.3 - MALIGNANT NEOPLASM OF RIBS STERNUM AND CLAVICLE
170.4 - MALIGNANT NEOPLASM OF SCAPULA AND LONG BONES OF UPPER LIMB
170.5 - MALIGNANT NEOPLASM OF SHORT BONES OF UPPER LIMB
170.6 - MALIGNANT NEOPLASM OF PELVIC BONES SACRUM AND COCCYX
170.7 - MALIGNANT NEOPLASM OF LONG BONES OF LOWER LIMB
170.8 - MALIGNANT NEOPLASM OF SHORT BONES OF LOWER LIMB
170.9 - MALIGNANT NEOPLASM OF BONE AND ARTICULAR CARTILAGE SITE UNSPECIFIED
171 - MALIGNANT NEOPLASM OF CONNECTIVE AND OTHER SOFT TISSUE
171.0 - MALIGNANT NEOPLASM OF CONNECTIVE AND OTHER SOFT TISSUE OF HEAD FACE AND NECK
171.2 - MALIGNANT NEOPLASM OF CONNECTIVE AND OTHER SOFT TISSUE OF UPPER LIMB INCLUDING SHOULDER
171.3 - MALIGNANT NEOPLASM OF CONNECTIVE AND OTHER SOFT TISSUE OF LOWER LIMB INCLUDING HIP
171.4 - MALIGNANT NEOPLASM OF CONNECTIVE AND OTHER SOFT TISSUE OF THORAX
171.5 - MALIGNANT NEOPLASM OF CONNECTIVE AND OTHER SOFT TISSUE OF ABDOMEN
171.6 - MALIGNANT NEOPLASM OF CONNECTIVE AND OTHER SOFT TISSUE OF PELVIS
171.7 - MALIGNANT NEOPLASM OF CONNECTIVE AND OTHER SOFT TISSUE OF TRUNK UNSPECIFIED
171.8 - MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES OF CONNECTIVE AND OTHER SOFT TISSUE
171.9 - MALIGNANT NEOPLASM OF CONNECTIVE AND OTHER SOFT TISSUE SITE UNSPECIFIED
172 - MALIGNANT MELANOMA OF SKIN
172.0 - MALIGNANT MELANOMA OF SKIN OF LIP
172.1 - MALIGNANT MELANOMA OF SKIN OF EYELID INCLUDING CANTHUS
172.2 - MALIGNANT MELANOMA OF SKIN OF EAR AND EXTERNAL AUDITORY CANAL
172.3 - MALIGNANT MELANOMA OF SKIN OF OTHER AND UNSPECIFIED PARTS OF FACE
172.4 - MALIGNANT MELANOMA OF SKIN OF SCALP AND NECK
172.5 - MALIGNANT MELANOMA OF SKIN OF TRUNK EXCEPT SCROTUM
172.6 - MALIGNANT MELANOMA OF SKIN OF UPPER LIMB INCLUDING SHOULDER
172.7 - MALIGNANT MELANOMA OF SKIN OF LOWER LIMB INCLUDING HIP
172.8 - MALIGNANT MELANOMA OF OTHER SPECIFIED SITES OF SKIN
172.9 - MELANOMA OF SKIN SITE UNSPECIFIED
174 - MALIGNANT NEOPLASM OF FEMALE BREAST
174.0 - MALIGNANT NEOPLASM OF NIPPLE AND AREOLA OF FEMALE BREAST
174.1 - MALIGNANT NEOPLASM OF CENTRAL PORTION OF FEMALE BREAST
174.2 - MALIGNANT NEOPLASM OF UPPER-INNER QUADRANT OF FEMALE BREAST
174.3 - MALIGNANT NEOPLASM OF LOWER-INNER QUADRANT OF FEMALE BREAST
174.4 - MALIGNANT NEOPLASM OF UPPER-OUTER QUADRANT OF FEMALE BREAST
174.5 - MALIGNANT NEOPLASM OF LOWER-OUTER QUADRANT OF FEMALE BREAST
174.6 - MALIGNANT NEOPLASM OF AXILLARY TAIL OF FEMALE BREAST
174.8 - MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES OF FEMALE BREAST
174.9 - MALIGNANT NEOPLASM OF BREAST (FEMALE) UNSPECIFIED SITE
175 - MALIGNANT NEOPLASM OF MALE BREAST
175.0 - MALIGNANT NEOPLASM OF NIPPLE AND AREOLA OF MALE BREAST

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175.9 - MALIGNANT NEOPLASM OF OTHER AND UNSPECIFIED SITES OF MALE BREAST
176 - KAPOSII'S SARCOMA
176.0 - KAPOSII'S SARCOMA SKIN
176.1 - KAPOSII'S SARCOMA SOFT TISSUE
176.2 - KAPOSII'S SARCOMA PALATE
176.3 - KAPOSII'S SARCOMA GASTROINTESTINAL SITES
176.4 - KAPOSII'S SARCOMA LUNG
176.5 - KAPOSII'S SARCOMA LYMPH NODES
176.8 - KAPOSII'S SARCOMA OTHER SPECIFIED SITES
176.9 - KAPOSII'S SARCOMA UNSPECIFIED SITE
179 - MALIGNANT NEOPLASM OF UTERUS-PART UNS
180 - MALIGNANT NEOPLASM OF CERVIX UTERI
180.0 - MALIGNANT NEOPLASM OF ENDOCERVIX
180.1 - MALIGNANT NEOPLASM OF EXOCERVIX
180.8 - MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES OF CERVIX
180.9 - MALIGNANT NEOPLASM OF CERVIX UTERI UNSPECIFIED SITE
181 - MALIGNANT NEOPLASM OF PLACENTA
182 - MALIGNANT NEOPLASM OF BODY OF UTERUS
182.0 - MALIGNANT NEOPLASM OF CORPUS UTERI EXCEPT ISTHMUS
182.1 - MALIGNANT NEOPLASM OF ISTHMUS
182.8 - MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES OF BODY OF UTERUS
183 - MALIGNANT NEOPLASM OF OVARY AND OTHER UTERINE ADNEXA
183.0 - MALIGNANT NEOPLASM OF OVARY
183.2 - MALIGNANT NEOPLASM OF FALLOPIAN TUBE
183.3 - MALIGNANT NEOPLASM OF BROAD LIGAMENT OF UTERUS
183.4 - MALIGNANT NEOPLASM OF PARAMETRIUM
183.5 - MALIGNANT NEOPLASM OF ROUND LIGAMENT OF UTERUS
183.8 - MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES OF UTERINE ADNEXA
183.9 - MALIGNANT NEOPLASM OF UTERINE ADNEXA UNSPECIFIED SITE
184 - MALIGNANT NEOPLASM OF OTHER AND UNSPECIFIED FEMALE GENITAL ORGANS
184.0 - MALIGNANT NEOPLASM OF VAGINA
184.1 - MALIGNANT NEOPLASM OF LABIA MAJORA
184.2 - MALIGNANT NEOPLASM OF LABIA MINORA
184.3 - MALIGNANT NEOPLASM OF CLITORIS
184.4 - MALIGNANT NEOPLASM OF VULVA UNSPECIFIED SITE
184.8 - MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES OF FEMALE GENITAL ORGANS
184.9 - MALIGNANT NEOPLASM OF FEMALE GENITAL ORGAN SITE UNSPECIFIED
185 - MALIGNANT NEOPLASM OF PROSTATE
186 - MALIGNANT NEOPLASM OF TESTIS
186.0 - MALIGNANT NEOPLASM OF UNDESCENDED TESTIS
186.9 - MALIGNANT NEOPLASM OF OTHER AND UNSPECIFIED TESTIS
187 - MALIGNANT NEOPLASM OF PENIS AND OTHER MALE GENITAL ORGANS
187.1 - MALIGNANT NEOPLASM OF PREPUCE
187.2 - MALIGNANT NEOPLASM OF GLANS PENIS
187.3 - MALIGNANT NEOPLASM OF BODY OF PENIS
187.4 - MALIGNANT NEOPLASM OF PENIS PART UNSPECIFIED

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187.5 - MALIGNANT NEOPLASM OF EPIDIDYMIS
187.6 - MALIGNANT NEOPLASM OF SPERMATIC CORD
187.7 - MALIGNANT NEOPLASM OF SCROTUM
187.8 - MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES OF MALE GENITAL ORGANS
187.9 - MALIGNANT NEOPLASM OF MALE GENITAL ORGAN SITE UNSPECIFIED
188 - MALIGNANT NEOPLASM OF BLADDER
188.0 - MALIGNANT NEOPLASM OF TRIGONE OF URINARY BLADDER
188.1 - MALIGNANT NEOPLASM OF DOME OF URINARY BLADDER
188.2 - MALIGNANT NEOPLASM OF LATERAL WALL OF URINARY BLADDER
188.3 - MALIGNANT NEOPLASM OF ANTERIOR WALL OF URINARY BLADDER
188.4 - MALIGNANT NEOPLASM OF POSTERIOR WALL OF URINARY BLADDER
188.5 - MALIGNANT NEOPLASM OF BLADDER NECK
188.6 - MALIGNANT NEOPLASM OF URETERIC ORIFICE
188.7 - MALIGNANT NEOPLASM OF URACHUS
188.8 - MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES OF BLADDER
188.9 - MALIGNANT NEOPLASM OF BLADDER PART UNSPECIFIED
189 - MALIGNANT NEOPLASM OF KIDNEY AND OTHER AND UNSPECIFIED URINARY ORGANS
189.0 - MALIGNANT NEOPLASM OF KIDNEY EXCEPT PELVIS
189.1 - MALIGNANT NEOPLASM OF RENAL PELVIS
189.2 - MALIGNANT NEOPLASM OF URETER
189.3 - MALIGNANT NEOPLASM OF URETHRA
189.4 - MALIGNANT NEOPLASM OF PARAURETHRAL GLANDS
189.8 - MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES OF URINARY ORGANS
189.9 - MALIGNANT NEOPLASM OF URINARY ORGAN SITE UNSPECIFIED
190 - MALIGNANT NEOPLASM OF EYE
190.0 - MALIGNANT NEOPLASM OF EYEBALL EXCEPT CONJUNCTIVA CORNEA RETINA AND CHOROID
190.1 - MALIGNANT NEOPLASM OF ORBIT
190.2 - MALIGNANT NEOPLASM OF LACRIMAL GLAND
190.3 - MALIGNANT NEOPLASM OF CONJUNCTIVA
190.4 - MALIGNANT NEOPLASM OF CORNEA
190.5 - MALIGNANT NEOPLASM OF RETINA
190.6 - MALIGNANT NEOPLASM OF CHOROID
190.7 - MALIGNANT NEOPLASM OF LACRIMAL DUCT
190.8 - MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES OF EYE
190.9 - MALIGNANT NEOPLASM OF EYE PART UNSPECIFIED
191 - MALIGNANT NEOPLASM OF BRAIN
191.0 - MALIGNANT NEOPLASM OF CEREBRUM EXCEPT LOBES AND VENTRICLES
191.1 - MALIGNANT NEOPLASM OF FRONTAL LOBE
191.2 - MALIGNANT NEOPLASM OF TEMPORAL LOBE
191.3 - MALIGNANT NEOPLASM OF PARIETAL LOBE
191.4 - MALIGNANT NEOPLASM OF OCCIPITAL LOBE
191.5 - MALIGNANT NEOPLASM OF VENTRICLES
191.6 - MALIGNANT NEOPLASM OF CEREBELLUM NOT OTHERWISE SPECIFIED
191.7 - MALIGNANT NEOPLASM OF BRAIN STEM
191.8 - MALIGNANT NEOPLASM OF OTHER PARTS OF BRAIN
191.9 - MALIGNANT NEOPLASM OF BRAIN UNSPECIFIED SITE

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192 - MALIGNANT NEOPLASM OF OTHER AND UNSPECIFIED PARTS OF NERVOUS SYSTEM
192.0 - MALIGNANT NEOPLASM OF CRANIAL NERVES
192.1 - MALIGNANT NEOPLASM OF CEREBRAL MENINGES
192.2 - MALIGNANT NEOPLASM OF SPINAL CORD
192.3 - MALIGNANT NEOPLASM OF SPINAL MENINGES
192.8 - MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES OF NERVOUS SYSTEM
192.9 - MALIGNANT NEOPLASM OF NERVOUS SYSTEM PART UNSPECIFIED
193 - MALIGNANT NEOPLASM OF THYROID GLAND
194 - MALIGNANT NEOPLASM OF OTHER ENDOCRINE GLANDS AND RELATED STRUCTURES
194.0 - MALIGNANT NEOPLASM OF ADRENAL GLAND
194.1 - MALIGNANT NEOPLASM OF PARATHYROID GLAND
194.3 - MALIGNANT NEOPLASM OF PITUITARY GLAND AND CRANIOPHARYNGEAL DUCT
194.4 - MALIGNANT NEOPLASM OF PINEAL GLAND
194.5 - MALIGNANT NEOPLASM OF CAROTID BODY
194.6 - MALIGNANT NEOPLASM OF AORTIC BODY AND OTHER PARAGANGLIA
194.8 - MALIGNANT NEOPLASM OF OTHER ENDOCRINE GLANDS AND RELATED STRUCTURES
194.9 - MALIGNANT NEOPLASM OF ENDOCRINE GLAND SITE UNSPECIFIED
195 - MALIGNANT NEOPLASM OF OTHER AND ILL-DEFINED SITES
195.0 - MALIGNANT NEOPLASM OF HEAD FACE AND NECK
195.1 - MALIGNANT NEOPLASM OF THORAX
195.2 - MALIGNANT NEOPLASM OF ABDOMEN
195.3 - MALIGNANT NEOPLASM OF PELVIS
195.4 - MALIGNANT NEOPLASM OF UPPER LIMB
195.5 - MALIGNANT NEOPLASM OF LOWER LIMB
195.8 - MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES
196 - SECONDARY AND UNSPECIFIED MALIGNANT NEOPLASM OF LYMPH NODES
196.0 - SECONDARY AND UNSPECIFIED MALIGNANT NEOPLASM OF LYMPH NODES OF HEAD FACE AND NECK
196.1 - SECONDARY AND UNSPECIFIED MALIGNANT NEOPLASM OF INTRATHORACIC LYMPH NODES
196.2 - SECONDARY AND UNSPECIFIED MALIGNANT NEOPLASM OF INTRA-ABDOMINAL LYMPH NODES
196.3 - SECONDARY AND UNSPECIFIED MALIGNANT NEOPLASM OF LYMPH NODES OF AXILLA AND UPPER LIMB
196.5 - SECONDARY AND UNSPECIFIED MALIGNANT NEOPLASM OF LYMPH NODES OF INGUINAL REGION AND LOWER LIMB
196.6 - SECONDARY AND UNSPECIFIED MALIGNANT NEOPLASM OF INTRAPELVIC LYMPH NODES
196.8 - SECONDARY AND UNSPECIFIED MALIGNANT NEOPLASM OF LYMPH NODES OF MULTIPLE SITES
196.9 - SECONDARY AND UNSPECIFIED MALIGNANT NEOPLASM OF LYMPH NODES SITE UNSPECIFIED
197 - SECONDARY MALIGNANT NEOPLASM OF RESPIRATORY AND DIGESTIVE SYSTEMS
197.0 - SECONDARY MALIGNANT NEOPLASM OF LUNG
197.1 - SECONDARY MALIGNANT NEOPLASM OF MEDIASTINUM
197.2 - SECONDARY MALIGNANT NEOPLASM OF PLEURA
197.3 - SECONDARY MALIGNANT NEOPLASM OF OTHER RESPIRATORY ORGANS
197.4 - SECONDARY MALIGNANT NEOPLASM OF SMALL INTESTINE INCLUDING DUODENUM
197.5 - SECONDARY MALIGNANT NEOPLASM OF LARGE INTESTINE AND RECTUM
197.6 - SECONDARY MALIGNANT NEOPLASM OF RETROPERITONEUM AND PERITONEUM
197.7 - MALIGNANT NEOPLASM OF LIVER SECONDARY
197.8 - SECONDARY MALIGNANT NEOPLASM OF OTHER DIGESTIVE ORGANS AND SPLEEN
198 - SECONDARY MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES
198.0 - SECONDARY MALIGNANT NEOPLASM OF KIDNEY

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198.1 - SECONDARY MALIGNANT NEOPLASM OF OTHER URINARY ORGANS
198.2 - SECONDARY MALIGNANT NEOPLASM OF SKIN
198.3 - SECONDARY MALIGNANT NEOPLASM OF BRAIN AND SPINAL CORD
198.4 - SECONDARY MALIGNANT NEOPLASM OF OTHER PARTS OF NERVOUS SYSTEM
198.5 - SECONDARY MALIGNANT NEOPLASM OF BONE AND BONE MARROW
198.6 - SECONDARY MALIGNANT NEOPLASM OF OVARY
198.7 - SECONDARY MALIGNANT NEOPLASM OF ADRENAL GLAND
198.8 - SECONDARY MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES
198.81 - SECONDARY MALIGNANT NEOPLASM OF BREAST
198.82 - SECONDARY MALIGNANT NEOPLASM OF GENITAL ORGANS
198.89 - SECONDARY MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES
199 - MALIGNANT NEOPLASM WITHOUT SPECIFICATION OF SITE
199.0 - DISSEMINATED MALIGNANT NEOPLASM
199.1 - OTHER MALIGNANT NEOPLASM OF UNSPECIFIED SITE
199.2 - MALIGNANT NEOPLASM ASSOCIATED WITH TRANSPLANTED ORGAN
200 - LYMPHOSARCOMA AND RETICULOSARCOMA AND OTHER SPECIFIED MALIGNANT TUMORS OF LYMPHATIC TISSUE
200.0 - RETICULOSARCOMA
200.00 - RETICULOSARCOMA UNSPECIFIED SITE
200.01 - RETICULOSARCOMA INVOLVING LYMPH NODES OF HEAD FACE AND NECK
200.02 - RETICULOSARCOMA INVOLVING INTRATHORACIC LYMPH NODES
200.03 - RETICULOSARCOMA INVOLVING INTRA-ABDOMINAL LYMPH NODES
200.04 - RETICULOSARCOMA INVOLVING LYMPH NODES OF AXILLA AND UPPER LIMB
200.05 - RETICULOSARCOMA INVOLVING LYMPH NODES OF INGUINAL REGION AND LOWER LIMB
200.06 - RETICULOSARCOMA INVOLVING INTRAPELVIC LYMPH NODES
200.07 - RETICULOSARCOMA INVOLVING SPLEEN
200.08 - RETICULOSARCOMA INVOLVING LYMPH NODES OF MULTIPLE SITES
200.1 - LYMPHOSARCOMA
200.10 - LYMPHOSARCOMA UNSPECIFIED SITE
200.11 - LYMPHOSARCOMA INVOLVING LYMPH NODES OF HEAD FACE AND NECK
200.12 - LYMPHOSARCOMA INVOLVING INTRATHORACIC LYMPH NODES
200.13 - LYMPHOSARCOMA INVOLVING INTRA-ABDOMINAL LYMPH NODES
200.14 - LYMPHOSARCOMA INVOLVING LYMPH NODES OF AXILLA AND UPPER LIMB
200.15 - LYMPHOSARCOMA INVOLVING LYMPH NODES OF INGUINAL REGION AND LOWER LIMB
200.16 - LYMPHOSARCOMA INVOLVING INTRAPELVIC LYMPH NODES
200.17 - LYMPHOSARCOMA INVOLVING SPLEEN
200.18 - LYMPHOSARCOMA INVOLVING LYMPH NODES OF MULTIPLE SITES
200.2 - BURKITT'S TUMOR OR LYMPHOMA
200.20 - BURKITT'S TUMOR OR LYMPHOMA UNSPECIFIED SITE
200.21 - BURKITT'S TUMOR OR LYMPHOMA INVOLVING LYMPH NODES OF HEAD FACE AND NECK
200.22 - BURKITT'S TUMOR OR LYMPHOMA INVOLVING INTRATHORACIC LYMPH NODES
200.23 - BURKITT'S TUMOR OR LYMPHOMA INVOLVING INTRA-ABDOMINAL LYMPH NODES
200.24 - BURKITT'S TUMOR OR LYMPHOMA INVOLVING LYMPH NODES OF AXILLA AND UPPER LIMB
200.25 - BURKITT'S TUMOR OR LYMPHOMA INVOLVING LYMPH NODES OF INGUINAL REGION AND LOWER LIMB
200.26 - BURKITT'S TUMOR OR LYMPHOMA INVOLVING INTRAPELVIC LYMPH NODES
200.27 - BURKITT'S TUMOR OR LYMPHOMA INVOLVING SPLEEN
200.28 - BURKITT'S TUMOR OR LYMPHOMA INVOLVING LYMPH NODES OF MULTIPLE SITES

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200.3 - MARGINAL ZONE LYMPHOMA
200.30 - MARGINAL ZONE LYMPHOMA UNSPECIFIED SITE
200.31 - MARGINAL ZONE LYMPHOMA INVOLVING LYMPH NODES OF HEAD FACE AND NECK
200.32 - MARGINAL ZONE LYMPHOMA INVOLVING INTRATHORACIC LYMPH NODES
200.33 - MARGINAL ZONE LYMPHOMA INVOLVING INTRA-ABDOMINAL LYMPH NODES
200.34 - MARGINAL ZONE LYMPHOMA INVOLVING LYMPH NODES OF AXILLA AND UPPER LIMB
200.35 - MARGINAL ZONE LYMPHOMA INVOLVING LYMPH NODES OF INGUINAL REGION AND LOWER LIMB
200.36 - MARGINAL ZONE LYMPHOMA INVOLVING INTRAPELVIC LYMPH NODES
200.37 - MARGINAL ZONE LYMPHOMA INVOLVING SPLEEN
200.38 - MARGINAL ZONE LYMPHOMA INVOLVING LYMPH NODES OF MULTIPLE SITES
200.4 - MANTLE CELL LYMPHOMA
200.40 - MANTLE CELL LYMPHOMA UNSPECIFIED SITE
200.41 - MANTLE CELL LYMPHOMA INVOLVING LYMPH NODES OF HEAD FACE AND NECK
200.42 - MANTLE CELL LYMPHOMA INVOLVING INTRATHORACIC LYMPH NODES
200.43 - MANTLE CELL LYMPHOMA INVOLVING INTRA-ABDOMINAL LYMPH NODES
200.44 - MANTLE CELL LYMPHOMA INVOLVING LYMPH NODES OF AXILLA AND UPPER LIMB
200.45 - MANTLE CELL LYMPHOMA INVOLVING LYMPH NODES OF INGUINAL REGION AND LOWER LIMB
200.46 - MANTLE CELL LYMPHOMA INVOLVING INTRAPELVIC LYMPH NODES
200.47 - MANTLE CELL LYMPHOMA INVOLVING SPLEEN
200.48 - MANTLE CELL LYMPHOMA INVOLVING LYMPH NODES OF MULTIPLE SITES
200.5 - PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA
200.50 - PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA UNSPECIFIED SITE
200.51 - PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA INVOLVING LYMPH NODES OF HEAD FACE AND NECK
200.52 - PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA INVOLVING INTRATHORACIC LYMPH NODES
200.53 - PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA INVOLVING INTRA-ABDOMINAL LYMPH NODES
200.54 - PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA INVOLVING LYMPH NODES OF AXILLA AND UPPER LIMB
200.55 - PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA INVOLVING LYMPH NODES OF INGUINAL REGION AND LOWER LIMB
200.56 - PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA INVOLVING INTRAPELVIC LYMPH NODES
200.57 - PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA INVOLVING SPLEEN
200.58 - PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA INVOLVING LYMPH NODES OF MULTIPLE SITES
200.6 - ANAPLASTIC LARGE CELL LYMPHOMA
200.60 - ANAPLASTIC LARGE CELL LYMPHOMA UNSPECIFIED SITE
200.61 - ANAPLASTIC LARGE CELL LYMPHOMA INVOLVING LYMPH NODES OF HEAD FACE AND NECK
200.62 - ANAPLASTIC LARGE CELL LYMPHOMA INVOLVING INTRATHORACIC LYMPH NODES
200.63 - ANAPLASTIC LARGE CELL LYMPHOMA INVOLVING INTRA-ABDOMINAL LYMPH NODES
200.64 - ANAPLASTIC LARGE CELL LYMPHOMA INVOLVING LYMPH NODES OF AXILLA AND UPPER LIMB
200.65 - ANAPLASTIC LARGE CELL LYMPHOMA INVOLVING LYMPH NODES OF INGUINAL REGION AND LOWER LIMB
200.66 - ANAPLASTIC LARGE CELL LYMPHOMA INVOLVING INTRAPELVIC LYMPH NODES
200.67 - ANAPLASTIC LARGE CELL LYMPHOMA INVOLVING SPLEEN
200.68 - ANAPLASTIC LARGE CELL LYMPHOMA INVOLVING LYMPH NODES OF MULTIPLE SITES
200.7 - LARGE CELL LYMPHOMA
200.70 - LARGE CELL LYMPHOMA UNSPECIFIED SITE
200.71 - LARGE CELL LYMPHOMA INVOLVING LYMPH NODES OF HEAD FACE AND NECK
200.72 - LARGE CELL LYMPHOMA INVOLVING INTRATHORACIC LYMPH NODES
200.73 - LARGE CELL LYMPHOMA INVOLVING INTRA-ABDOMINAL LYMPH NODES
200.74 - LARGE CELL LYMPHOMA INVOLVING LYMPH NODES OF AXILLA AND UPPER LIMB

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200.75 - LARGE CELL LYMPHOMA INVOLVING LYMPH NODES OF INGUINAL REGION AND LOWER LIMB
200.76 - LARGE CELL LYMPHOMA INVOLVING INTRAPELVIC LYMPH NODES
200.77 - LARGE CELL LYMPHOMA INVOLVING SPLEEN
200.78 - LARGE CELL LYMPHOMA INVOLVING LYMPH NODES OF MULTIPLE SITES
200.8 - OTHER NAMED VARIANTS OF LYMPHOSARCOMA AND RETICULOSARCOMA
200.80 - OTHER NAMED VARIANTS OF LYMPHOSARCOMA AND RETICULOSARCOMA UNSPECIFIED SITE
200.81 - OTHER NAMED VARIANTS OF LYMPHOSARCOMA AND RETICULOSARCOMA INVOLVING LYMPH NODES OF HEAD FACE AND NECK
200.82 - OTHER NAMED VARIANTS OF LYMPHOSARCOMA AND RETICULOSARCOMA INVOLVING INTRATHORACIC LYMPH NODES
200.83 - OTHER NAMED VARIANTS OF LYMPHOSARCOMA AND RETICULOSARCOMA INVOLVING INTRA-ABDOMINAL LYMPH NODES
200.84 - OTHER NAMED VARIANTS OF LYMPHOSARCOMA AND RETICULOSARCOMA INVOLVING LYMPH NODES OF AXILLA AND UPPER LIMB
200.85 - OTHER NAMED VARIANTS OF LYMPHOSARCOMA AND RETICULOSARCOMA INVOLVING LYMPH NODES OF INGUINAL REGION AND LOWER LIMB
200.86 - OTHER NAMED VARIANTS OF LYMPHOSARCOMA AND RETICULOSARCOMA INVOLVING INTRAPELVIC LYMPH NODES
200.87 - OTHER NAMED VARIANTS OF LYMPHOSARCOMA AND RETICULOSARCOMA INVOLVING SPLEEN
200.88 - OTHER NAMED VARIANTS OF LYMPHOSARCOMA AND RETICULOSARCOMA INVOLVING LYMPH NODES OF MULTIPLE SITES
201 - HODGKIN'S DISEASE
201.0 - HODGKIN'S PARAGRANULOMA
201.00 - HODGKIN'S PARAGRANULOMA UNSPECIFIED SITE
201.01 - HODGKIN'S PARAGRANULOMA INVOLVING LYMPH NODES OF HEAD FACE AND NECK
201.02 - HODGKIN'S PARAGRANULOMA INVOLVING INTRATHORACIC LYMPH NODES
201.03 - HODGKIN'S PARAGRANULOMA INVOLVING INTRA-ABDOMINAL LYMPH NODES
201.04 - HODGKIN'S PARAGRANULOMA INVOLVING LYMPH NODES OF AXILLA AND UPPER LIMB
201.05 - HODGKIN'S PARAGRANULOMA INVOLVING LYMPH NODES OF INGUINAL REGION AND LOWER LIMB
201.06 - HODGKIN'S PARAGRANULOMA INVOLVING INTRAPELVIC LYMPH NODES
201.07 - HODGKIN'S PARAGRANULOMA INVOLVING SPLEEN
201.08 - HODGKIN'S PARAGRANULOMA INVOLVING LYMPH NODES OF MULTIPLE SITES
201.1 - HODGKIN'S GRANULOMA
201.10 - HODGKIN'S GRANULOMA UNSPECIFIED SITE
201.11 - HODGKIN'S GRANULOMA INVOLVING LYMPH NODES OF HEAD FACE AND NECK
201.12 - HODGKIN'S GRANULOMA INVOLVING INTRATHORACIC LYMPH NODES
201.13 - HODGKIN'S GRANULOMA INVOLVING INTRA-ABDOMINAL LYMPH NODES
201.14 - HODGKIN'S GRANULOMA INVOLVING LYMPH NODES OF AXILLA AND UPPER LIMB
201.15 - HODGKIN'S GRANULOMA INVOLVING LYMPH NODES OF INGUINAL REGION AND LOWER LIMB
201.16 - HODGKIN'S GRANULOMA INVOLVING INTRAPELVIC LYMPH NODES
201.17 - HODGKIN'S GRANULOMA INVOLVING SPLEEN
201.18 - HODGKIN'S GRANULOMA INVOLVING LYMPH NODES OF MULTIPLE SITES
201.2 - HODGKIN'S SARCOMA
201.20 - HODGKIN'S SARCOMA UNSPECIFIED SITE
201.21 - HODGKIN'S SARCOMA INVOLVING LYMPH NODES OF HEAD FACE AND NECK
201.22 - HODGKIN'S SARCOMA INVOLVING INTRATHORACIC LYMPH NODES
201.23 - HODGKIN'S SARCOMA INVOLVING INTRA-ABDOMINAL LYMPH NODES
201.24 - HODGKIN'S SARCOMA INVOLVING LYMPH NODES OF AXILLA AND UPPER LIMB
201.25 - HODGKIN'S SARCOMA INVOLVING LYMPH NODES OF INGUINAL REGION AND LOWER LIMB
201.26 - HODGKIN'S SARCOMA INVOLVING INTRAPELVIC LYMPH NODES
201.27 - HODGKIN'S SARCOMA INVOLVING SPLEEN
201.28 - HODGKIN'S SARCOMA INVOLVING LYMPH NODES OF MULTIPLE SITES
201.4 - HODGKIN'S DISEASE LYMPHOCYTIC-HISTIOCYTIC PREDOMINANCE

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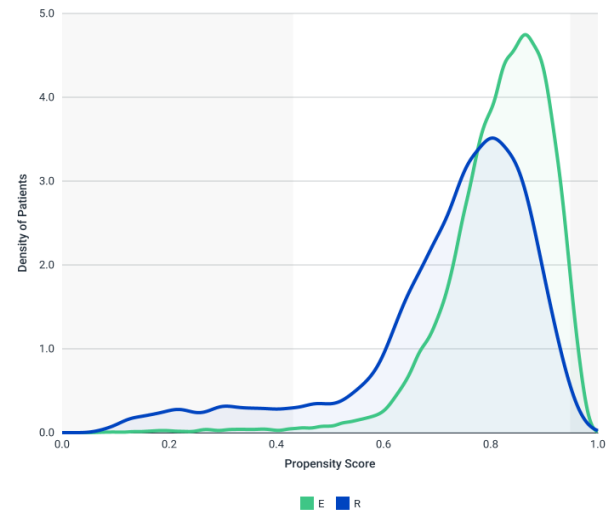
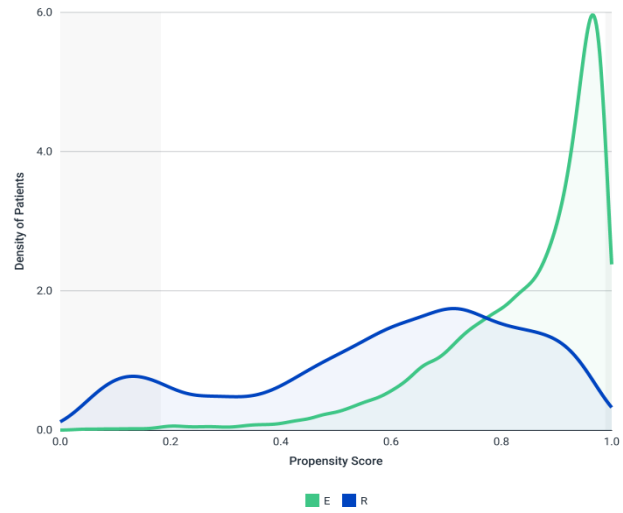
201.40 - HODGKIN'S DISEASE LYMPHOCYTIC-HISTIOCYTIC PREDOMINANCE UNSPECIFIED SITE
201.41 - HODGKIN'S DISEASE LYMPHOCYTIC-HISTIOCYTIC PREDOMINANCE INVOLVING LYMPH NODES OF HEAD FACE AND NECK
201.42 - HODGKIN'S DISEASE LYMPHOCYTIC-HISTIOCYTIC PREDOMINANCE INVOLVING INTRATHORACIC LYMPH NODES
201.43 - HODGKIN'S DISEASE LYMPHOCYTIC-HISTIOCYTIC PREDOMINANCE INVOLVING INTRA-ABDOMINAL LYMPH NODES
201.44 - HODGKIN'S DISEASE LYMPHOCYTIC-HISTIOCYTIC PREDOMINANCE INVOLVING LYMPH NODES OF AXILLA AND UPPER LIMB
201.45 - HODGKIN'S DISEASE LYMPHOCYTIC-HISTIOCYTIC PREDOMINANCE INVOLVING LYMPH NODES OF INGUINAL REGION AND LOWER LIMB
201.46 - HODGKIN'S DISEASE LYMPHOCYTIC-HISTIOCYTIC PREDOMINANCE INVOLVING INTRAPELVIC LYMPH NODES
201.47 - HODGKIN'S DISEASE LYMPHOCYTIC-HISTIOCYTIC PREDOMINANCE INVOLVING SPLEEN
201.48 - HODGKIN'S DISEASE LYMPHOCYTIC-HISTIOCYTIC PREDOMINANCE INVOLVING LYMPH NODES OF MULTIPLE SITES
201.5 - HODGKIN'S DISEASE NODULAR SCLEROSIS
201.50 - HODGKIN'S DISEASE NODULAR SCLEROSIS UNSPECIFIED SITE
201.51 - HODGKIN'S DISEASE NODULAR SCLEROSIS INVOLVING LYMPH NODES OF HEAD FACE AND NECK
201.52 - HODGKIN'S DISEASE NODULAR SCLEROSIS INVOLVING INTRATHORACIC LYMPH NODES
201.53 - HODGKIN'S DISEASE NODULAR SCLEROSIS INVOLVING INTRA-ABDOMINAL LYMPH NODES
201.54 - HODGKIN'S DISEASE NODULAR SCLEROSIS INVOLVING LYMPH NODES OF AXILLA AND UPPER LIMB
201.55 - HODGKIN'S DISEASE NODULAR SCLEROSIS INVOLVING LYMPH NODES OF INGUINAL REGION AND LOWER LIMB
201.56 - HODGKIN'S DISEASE NODULAR SCLEROSIS INVOLVING INTRAPELVIC LYMPH NODES
201.57 - HODGKIN'S DISEASE NODULAR SCLEROSIS INVOLVING SPLEEN
201.58 - HODGKIN'S DISEASE NODULAR SCLEROSIS INVOLVING LYMPH NODES OF MULTIPLE SITES
201.6 - HODGKIN'S DISEASE MIXED CELLULARITY
201.60 - HODGKIN'S DISEASE MIXED CELLULARITY UNSPECIFIED SITE
201.61 - HODGKIN'S DISEASE MIXED CELLULARITY INVOLVING LYMPH NODES OF HEAD FACE AND NECK
201.62 - HODGKIN'S DISEASE MIXED CELLULARITY INVOLVING INTRATHORACIC LYMPH NODES
201.63 - HODGKIN'S DISEASE MIXED CELLULARITY INVOLVING INTRA-ABDOMINAL LYMPH NODES
201.64 - HODGKIN'S DISEASE MIXED CELLULARITY INVOLVING LYMPH NODES OF AXILLA AND UPPER LIMB
201.65 - HODGKIN'S DISEASE MIXED CELLULARITY INVOLVING LYMPH NODES OF INGUINAL REGION AND LOWER LIMB
201.66 - HODGKIN'S DISEASE MIXED CELLULARITY INVOLVING INTRAPELVIC LYMPH NODES
201.67 - HODGKIN'S DISEASE MIXED CELLULARITY INVOLVING SPLEEN
201.68 - HODGKIN'S DISEASE MIXED CELLULARITY INVOLVING LYMPH NODES OF MULTIPLE SITES
201.7 - HODGKIN'S DISEASE LYMPHOCYTIC DEPLETION
201.70 - HODGKIN'S DISEASE LYMPHOCYTIC DEPLETION UNSPECIFIED SITE
201.71 - HODGKIN'S DISEASE LYMPHOCYTIC DEPLETION INVOLVING LYMPH NODES OF HEAD FACE AND NECK
201.72 - HODGKIN'S DISEASE LYMPHOCYTIC DEPLETION INVOLVING INTRATHORACIC LYMPH NODES
201.73 - HODGKIN'S DISEASE LYMPHOCYTIC DEPLETION INVOLVING INTRA-ABDOMINAL LYMPH NODES
201.74 - HODGKIN'S DISEASE LYMPHOCYTIC DEPLETION INVOLVING LYMPH NODES OF AXILLA AND UPPER LIMB
201.75 - HODGKIN'S DISEASE LYMPHOCYTIC DEPLETION INVOLVING LYMPH NODES OF INGUINAL REGION AND LOWER LIMB
201.76 - HODGKIN'S DISEASE LYMPHOCYTIC DEPLETION INVOLVING INTRAPELVIC LYMPH NODES
201.77 - HODGKIN'S DISEASE LYMPHOCYTIC DEPLETION INVOLVING SPLEEN
201.78 - HODGKIN'S DISEASE LYMPHOCYTIC DEPLETION INVOLVING LYMPH NODES OF MULTIPLE SITES
201.9 - HODGKIN'S DISEASE UNSPECIFIED TYPE
201.90 - HODGKIN'S DISEASE UNSPECIFIED TYPE UNSPECIFIED SITE
201.91 - HODGKIN'S DISEASE, UNSPECIFIED TYPE, LYMPH NODES OF HEAD, FACE, AND NECK

Appendix B

Optum

MarketScan

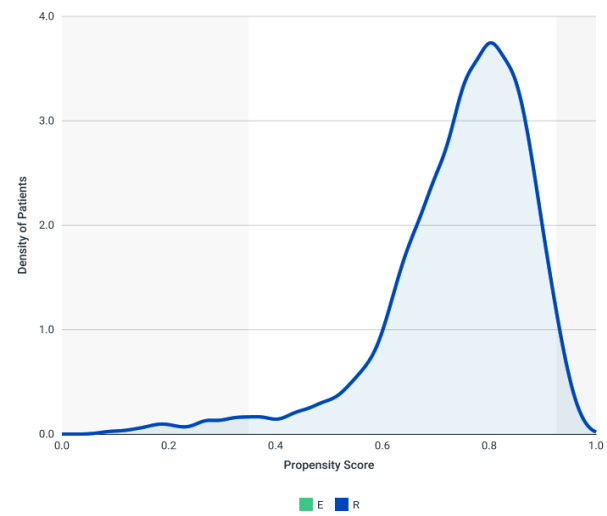
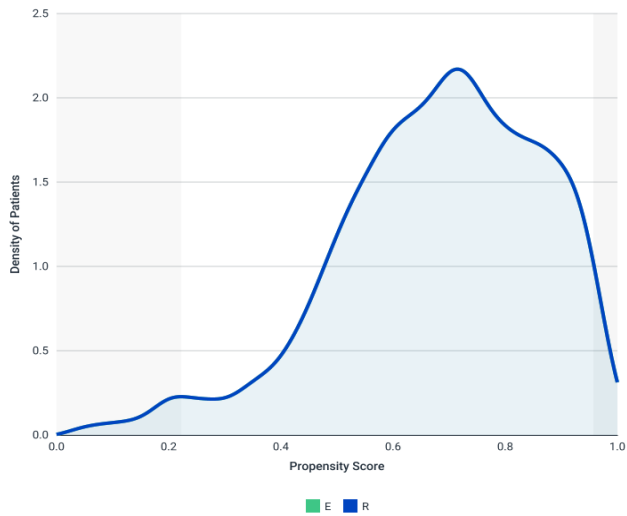
BEFORE PS MATCHING



The c-statistics for the propensity score model, pre-matching was 0.815.
The postmatching c-statistic was 0.533.

The c-statistics for the propensity score model, pre-matching was 0.695.
The postmatching c-statistic was 0.526.

AFTER PS MATCHING



Appendix B

Variable	Unmatched								
	Optum			Marketscan			POOLED		
	Budesonide alone	Budesonide-formoterol	St. Diff.	Budesonide alone	Budesonide-formoterol	St. Diff.	Budesonide alone	Budesonide-formoterol	St. Diff.
Number of patients	6,337	24,000		7,380	28,864		13,717	52,864	
Year of Cohort Entry Date									
...2007; n (%)	1,064 (16.8%)	255 (1.1%)	0.053	690 (9.3%)	366 (1.3%)	0.035	1,754 (12.8%)	621 (1.2%)	0.467
...2008; n (%)	841 (13.3%)	968 (4.0%)	0.032	559 (7.6%)	1,296 (4.5%)	0.013	1,400 (10.2%)	2,264 (4.3%)	0.229
...2009; n (%)	699 (11.0%)	1,427 (5.9%)	0.018	663 (9.0%)	2,025 (7.0%)	0.007	1,362 (9.9%)	3,452 (6.5%)	0.124
...2010; n (%)	651 (10.3%)	1,868 (7.8%)	0.008	686 (9.3%)	2,777 (9.6%)	-0.001	1,337 (9.7%)	4,645 (8.8%)	0.031
...2011; n (%)	568 (9.0%)	1,747 (7.3%)	0.006	688 (9.3%)	2,691 (9.3%)	0.000	1,256 (9.2%)	4,438 (8.4%)	0.028
...2012; n (%)	497 (7.8%)	1,832 (7.6%)	0.001	763 (10.3%)	3,144 (10.9%)	-0.002	1,260 (9.2%)	4,976 (9.4%)	-0.007
...2013; n (%)	497 (7.8%)	2,017 (8.4%)	-0.002	723 (9.8%)	3,125 (10.8%)	-0.003	1,220 (8.9%)	5,142 (9.7%)	-0.028
...2014; n (%)	439 (6.9%)	1,485 (6.2%)	0.003	784 (10.6%)	4,332 (15.0%)	-0.012	1,223 (8.9%)	5,817 (11.0%)	-0.070
...2015; n (%)	393 (6.2%)	1,076 (4.5%)	0.007	642 (8.7%)	2,723 (9.4%)	-0.002	1,035 (7.5%)	3,799 (7.2%)	0.011
...2016; n (%)	250 (3.9%)	2,197 (9.2%)	-0.021	493 (6.7%)	2,082 (7.2%)	-0.002	743 (5.4%)	4,279 (8.1%)	-0.108
...2017; n (%)	143 (2.3%)	2,112 (8.8%)	-0.028	379 (5.1%)	1,780 (6.2%)	-0.005	522 (3.8%)	3,892 (7.4%)	-0.157
...2018; n (%)	130 (2.1%)	2,606 (10.9%)	-0.035	310 (4.2%)	2,523 (8.7%)	-0.018	440 (3.2%)	5,129 (9.7%)	-0.267
...2019; n (%)	121 (1.9%)	2,779 (11.6%)	-0.037	NA	NA	NA	NA	NA	NA
...2020; n (%)	44 (0.7%)	1,631 (6.8%)	-0.032	NA	NA	NA	NA	NA	NA
Age									
...mean (sd)	42.71 (20.00)	51.86 (19.19)	-0.467	43.92 (20.01)	48.36 (17.11)	-0.238	43.36 (20.01)	49.95 (18.08)	-0.346
...median [IQR]	43.00 [27.00, 58.00]	54.00 [39.00, 67.00]	-0.561	47.00 [27.00, 59.00]	51.00 [39.00, 60.00]	-0.215	45.15 (20.01)	52.36 (18.08)	-0.378
Age categories									
...12-17; n (%)	1,167 (18.4%)	1,752 (7.3%)	0.031	1,275 (17.3%)	2,255 (7.8%)	0.027	2,442 (17.8%)	4,007 (7.6%)	0.310
...18-39; n (%)	1,616 (25.5%)	4,397 (18.3%)	0.015	1,641 (22.2%)	5,370 (18.6%)	0.008	3,257 (23.7%)	9,767 (18.5%)	0.128
...40 - 64; n (%)	2,590 (40.9%)	10,603 (44.2%)	-0.005	3,478 (47.1%)	17,391 (60.3%)	-0.018	6,068 (44.2%)	27,994 (53.0%)	-0.177
...>= 65; n (%)	964 (15.2%)	7,248 (30.2%)	-0.032	986 (13.4%)	3,848 (13.3%)	0.000	1,950 (14.2%)	11,096 (21.0%)	-0.179
Geographic Region									
...Northeast; n (%)	916 (14.5%)	2,632 (11.0%)	0.010	1,649 (22.3%)	5,792 (20.1%)	0.005	2,565 (18.7%)	8,424 (15.9%)	0.074
...South; n (%)	2,191 (34.6%)	10,968 (45.7%)	-0.018	2,151 (29.1%)	11,533 (40.0%)	-0.019	4,342 (31.7%)	22,501 (42.6%)	-0.227
...Midwest; n (%)	1,960 (30.9%)	5,075 (21.1%)	0.019	2,404 (32.6%)	7,125 (24.7%)	0.015	4,364 (31.8%)	12,200 (23.1%)	0.196
...West; n (%)	1,270 (20.0%)	5,325 (22.2%)	-0.005	1,118 (15.1%)	4,153 (14.4%)	0.002	2,388 (17.4%)	9,478 (17.9%)	-0.013
...Unknown/Missing; n (%)	NA	NA	NA	58 (0.8%)	261 (0.9%)	-0.001	NA	NA	NA
Metropolitan Statistical Area									
...Urban; n (%)	NA	NA	NA	6,069 (82.2%)	22,803 (79.0%)	0.004	NA	NA	NA
...Rural; n (%)	NA	NA	NA	108 (1.5%)	705 (2.4%)	-0.006	NA	NA	NA
...Unknown/Missing; n (%)	NA	NA	NA	1,203 (16.3%)	5,356 (18.6%)	-0.006	NA	NA	NA
General Health Related Measures									
Alcohol/Drug abuse or dependence; n (%)	12 (0.2%)	216 (0.9%)	-0.009	30 (0.4%)	127 (0.4%)	0.000	042 (0.3%)	343 (0.6%)	-0.045
Obesity or Overweight; n (%)	333 (5.3%)	3,464 (14.4%)	-0.029	440 (6.0%)	2,772 (9.6%)	-0.013	773 (5.6%)	6,236 (11.8%)	-0.221
Obesity; n (%)	269 (4.2%)	2,786 (11.6%)	-0.026	376 (5.1%)	2,344 (8.1%)	-0.012	645 (4.7%)	5,130 (9.7%)	-0.194
Overweight; n (%)	66 (1.0%)	798 (3.3%)	-0.016	74 (1.0%)	511 (1.8%)	-0.007	140 (1.0%)	1,309 (2.5%)	-0.115
Cardiovascular Measures									
Hypertension; n (%)	1,467 (23.1%)	9,667 (40.3%)	-0.031	1,708 (23.1%)	9,051 (31.4%)	-0.016	3,175 (23.1%)	18,718 (35.4%)	-0.273
Hyperlipidemia; n (%)	1,280 (20.2%)	7,113 (29.6%)	-0.019	1,309 (17.7%)	6,483 (22.5%)	-0.011	2,589 (18.9%)	13,596 (25.7%)	-0.164
MI, angina, Coronary atherosclerosis and other forms of chronic ischemic heart disease; n (%)	199 (3.1%)	1,404 (5.9%)	-0.013	243 (3.3%)	1,231 (4.3%)	-0.005	442 (3.2%)	2,635 (5.0%)	-0.091
Old MI; n (%)	22 (0.3%)	140 (0.6%)	-0.004	20 (0.3%)	78 (0.3%)	0.000	042 (0.3%)	218 (0.4%)	-0.017
Acute MI; n (%)	8 (0.1%)	51 (0.2%)	-0.003	11 (0.1%)	48 (0.2%)	-0.003	019 (0.1%)	099 (0.2%)	-0.026
Stable angina; n (%)	27 (0.4%)	277 (1.2%)	-0.009	29 (0.4%)	207 (0.7%)	-0.004	056 (0.4%)	484 (0.9%)	-0.062
Coronary atherosclerosis and other forms of chronic ischemic heart disease; n (%)	179 (2.8%)	1,219 (5.1%)	-0.012	204 (2.8%)	1,045 (3.6%)	-0.004	383 (2.8%)	2,264 (4.3%)	-0.081
History of CABG or PTCA; n (%)	32 (0.5%)	250 (1.0%)	-0.006	20 (0.3%)	124 (0.4%)	-0.002	052 (0.4%)	374 (0.7%)	-0.041

Appendix B

Cerebrovascular disease (Stroke, TIA, Late effects); n (%)	38 (0.6%)	321 (1.3%)	-0.007	62 (0.8%)	270 (0.9%)	-0.001	100 (0.7%)	591 (1.1%)	-0.042
Stroke (Ischemic or hemorrhagic); n (%)	19 (0.3%)	157 (0.7%)	-0.006	26 (0.4%)	148 (0.5%)	-0.001	045 (0.3%)	305 (0.6%)	-0.045
TIA; n (%)	14 (0.2%)	127 (0.5%)	-0.005	33 (0.4%)	113 (0.4%)	0.000	047 (0.3%)	240 (0.5%)	-0.032
Late effects of cerebrovascular disease; n (%)	10 (0.2%)	102 (0.4%)	-0.004	12 (0.2%)	62 (0.2%)	0.000	022 (0.2%)	164 (0.3%)	-0.020
Atrial fibrillation and Other cardiac dysrhythmia; n (%)	229 (3.6%)	1,188 (5.0%)	-0.007	337 (4.6%)	1,045 (3.6%)	0.005	566 (4.1%)	2,233 (4.2%)	-0.005
Atrial fibrillation; n (%)	108 (1.7%)	639 (2.7%)	-0.007	169 (2.3%)	460 (1.6%)	0.005	277 (2.0%)	1,099 (2.1%)	-0.007
Other cardiac dysrhythmia; n (%)	155 (2.4%)	978 (4.1%)	-0.009	223 (3.0%)	776 (2.7%)	0.002	378 (2.8%)	1,754 (3.3%)	-0.029
Diabetes Related Measures									
Diabetes with or w/o complications; n (%)	447 (7.1%)	3,349 (14.0%)	-0.021	520 (7.0%)	3,147 (10.9%)	-0.013	967 (7.0%)	6,496 (12.3%)	-0.180
Diabetes mellitus without mention of complications; n (%)	430 (6.8%)	3,099 (12.9%)	-0.019	485 (6.6%)	2,986 (10.3%)	-0.013	915 (6.7%)	6,085 (11.5%)	-0.167
Diabetes with specified complications; n (%)	75 (1.2%)	814 (3.4%)	-0.015	87 (1.2%)	489 (1.7%)	-0.004	162 (1.2%)	1,303 (2.5%)	-0.097
Diabetes with unspecified complications; n (%)	17 (0.3%)	151 (0.6%)	-0.004	17 (0.2%)	126 (0.4%)	-0.004	034 (0.2%)	277 (0.5%)	-0.051
GI Conditions									
GERD; n (%)	559 (8.8%)	3,512 (14.6%)	-0.017	606 (8.2%)	3,258 (11.3%)	-0.010	1,165 (8.5%)	6,770 (12.8%)	-0.140
Upper GI (Diseases of esophagus, stomach and duodenum including GERD); n (%)	698 (11.0%)	4,098 (17.1%)	-0.016	788 (10.7%)	4,062 (14.1%)	-0.010	1,486 (10.8%)	8,160 (15.4%)	-0.137
GI bleeding; n (%)	78 (1.2%)	339 (1.4%)	-0.002	84 (1.1%)	392 (1.4%)	-0.003	162 (1.2%)	731 (1.4%)	-0.018
Non-infective enteritis and colitis; n (%)	189 (3.0%)	757 (3.2%)	-0.001	238 (3.2%)	952 (3.3%)	-0.001	427 (3.1%)	1,709 (3.2%)	-0.006
Intraoperative and postprocedural complications and disorders of digestive system; n (%)	86 (1.4%)	297 (1.2%)	0.002	80 (1.1%)	361 (1.3%)	-0.002	166 (1.2%)	658 (1.2%)	0.000
Disorders of gallbladder, biliary tract and pancreas; n (%)	50 (0.8%)	264 (1.1%)	-0.003	61 (0.8%)	283 (1.0%)	-0.002	111 (0.8%)	547 (1.0%)	-0.021
Rheumatic Conditions									
Rheumatoid arthritis and other inflammatory polyarthropathies; n (%)	68 (1.1%)	405 (1.7%)	-0.005	108 (1.5%)	414 (1.4%)	0.001	176 (1.3%)	819 (1.5%)	-0.017
Osteoarthritis; n (%)	405 (6.4%)	2,814 (11.7%)	-0.018	562 (7.6%)	2,559 (8.9%)	-0.005	967 (7.0%)	5,373 (10.2%)	-0.114
Other rheumatic disorders (including gout); n (%)	1,177 (18.6%)	6,074 (25.3%)	-0.014	1,481 (20.1%)	6,665 (23.1%)	-0.006	2,658 (19.4%)	12,739 (24.1%)	-0.114
Gout and other crystal arthropathies; n (%)	37 (0.6%)	359 (1.5%)	-0.009	40 (0.5%)	294 (1.0%)	-0.006	077 (0.6%)	653 (1.2%)	-0.064
Other rheumatic disorders; n (%)	1,156 (18.2%)	5,834 (24.3%)	-0.013	1,455 (19.7%)	6,470 (22.4%)	-0.006	2,611 (19.0%)	12,304 (23.3%)	-0.105
Neuro Conditions									
Alzheimer and other Dementia Disease; n (%)	37 (0.6%)	276 (1.1%)	-0.005	34 (0.5%)	141 (0.5%)	0.000	071 (0.5%)	417 (0.8%)	-0.037
Seizure disorders (epilepsy); n (%)	30 (0.5%)	158 (0.7%)	-0.003	40 (0.5%)	164 (0.6%)	-0.001	070 (0.5%)	322 (0.6%)	-0.014
Delirium/Psychosis; n (%)	50 (0.8%)	228 (0.9%)	-0.001	46 (0.6%)	175 (0.6%)	0.000	096 (0.7%)	403 (0.8%)	-0.012
Other Conditions									
Hypothyroidism; n (%)	550 (8.7%)	2,811 (11.7%)	-0.009	552 (7.5%)	2,594 (9.0%)	-0.005	1,102 (8.0%)	5,405 (10.2%)	-0.077
Chronic kidney disease stages I-III; n (%)	100 (1.6%)	1,021 (4.3%)	-0.016	61 (0.8%)	422 (1.5%)	-0.007	161 (1.2%)	1,443 (2.7%)	-0.109
Chronic kidney disease stages IV-V, ESRD; n (%)	31 (0.5%)	229 (1.0%)	-0.006	20 (0.3%)	121 (0.4%)	-0.002	051 (0.4%)	350 (0.7%)	-0.041
COPD; n (%)	283 (4.5%)	2,954 (12.3%)	-0.027	381 (5.2%)	2,608 (9.0%)	-0.014	664 (4.8%)	5,562 (10.5%)	-0.216
Obstructive sleep apnea; n (%)	302 (4.8%)	2,390 (10.0%)	-0.019	378 (5.1%)	2,438 (8.4%)	-0.013	680 (5.0%)	4,828 (9.1%)	-0.161
Syncope; n (%)	67 (1.1%)	319 (1.3%)	-0.002	75 (1.0%)	315 (1.1%)	-0.001	142 (1.0%)	634 (1.2%)	-0.019
Falls; n (%)	67 (1.1%)	422 (1.8%)	-0.006	39 (0.5%)	174 (0.6%)	-0.001	106 (0.8%)	596 (1.1%)	-0.031
VTE; n (%)	35 (0.6%)	200 (0.8%)	-0.002	61 (0.8%)	266 (0.9%)	-0.001	096 (0.7%)	466 (0.9%)	-0.022
Combined comorbidity score, 365 days									
...mean (sd)	1.14 (0.91)	1.38 (1.37)	-0.206	1.15 (0.89)	1.14 (0.97)	0.011	1.15 (0.90)	1.25 (1.17)	-0.096
...median [IQR]	1.00 [1.00, 1.00]	1.00 [1.00, 2.00]	0.000	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	0.000	1.00 (0.90)	1.00 (1.17)	0.000
Frailty Score: Empirical Version 365 days as Categories									
...<0.1 non frail; n (%)	4,334 (68.4%)	16,797 (70.0%)	-0.002	4,405 (59.7%)	15,841 (54.9%)	0.006	8,739 (63.7%)	32,638 (61.7%)	0.041
...0.1 - <0.2 prefrail; n (%)	1,342 (21.2%)	4,099 (17.1%)	0.009	1,854 (25.1%)	7,413 (25.7%)	-0.001	3,196 (23.3%)	11,512 (21.8%)	0.036
... >0.2 frail; n (%)	661 (10.4%)	3,104 (12.9%)	-0.007	1,121 (15.2%)	5,610 (19.4%)	-0.010	1,782 (13.0%)	8,714 (16.5%)	-0.099
Medication Use									
Use of oral corticosteroids; n (%)	2,830 (44.7%)	13,878 (57.8%)	-0.018	7,014 (95.0%)	27,411 (95.0%)	0.000	9,844 (71.8%)	41,289 (78.1%)	-0.146
Use of antidepressants; n (%)	1,161 (18.3%)	6,021 (25.1%)	-0.015	1,607 (21.8%)	7,480 (25.9%)	-0.008	2,768 (20.2%)	13,501 (25.5%)	-0.126
Use of anticonvulsants; n (%)	339 (5.3%)	2,529 (10.5%)	-0.019	536 (7.3%)	2,666 (9.2%)	-0.007	875 (6.4%)	5,195 (9.8%)	-0.125
Use of beta blocker OR calcium channel blocker; n (%)	579 (9.1%)	3,575 (14.9%)	-0.017	803 (10.9%)	3,549 (12.3%)	-0.004	1,382 (10.1%)	7,124 (13.5%)	-0.106
Use of PPIs; n (%)	870 (13.7%)	5,203 (21.7%)	-0.019	1,526 (20.7%)	7,048 (24.4%)	-0.008	2,396 (17.5%)	12,251 (23.2%)	-0.142
Use of opioids; n (%)	937 (14.8%)	4,912 (20.5%)	-0.014	1,378 (18.7%)	7,123 (24.7%)	-0.013	2,315 (16.9%)	12,035 (22.8%)	-0.148

Appendix B

Use of antipsychotics; n (%)	83 (1.3%)	527 (2.2%)	-0.007	107 (1.4%)	534 (1.9%)	-0.004	190 (1.4%)	1,061 (2.0%)	-0.046
Use of anxiolytics/hypnotics; n (%)	329 (5.2%)	1,814 (7.6%)	-0.009	486 (6.6%)	2,517 (8.7%)	-0.008	815 (5.9%)	4,331 (8.2%)	-0.090
Use of dementia meds; n (%)	23 (0.4%)	220 (0.9%)	-0.006	26 (0.4%)	122 (0.4%)	0.000	049 (0.4%)	342 (0.6%)	-0.028
Use of antiparkinsonian meds; n (%)	58 (0.9%)	448 (1.9%)	-0.008	104 (1.4%)	519 (1.8%)	-0.003	162 (1.2%)	967 (1.8%)	-0.049
Use of Benzodiazepine; n (%)	541 (8.5%)	2,733 (11.4%)	-0.009	880 (11.9%)	3,889 (13.5%)	-0.004	1,421 (10.4%)	6,622 (12.5%)	-0.066
All antidiabetic medications; n (%)	351 (5.5%)	2,778 (11.6%)	-0.021	499 (6.8%)	2,817 (9.8%)	-0.010	850 (6.2%)	5,595 (10.6%)	-0.159
ACEI/ARB; n (%)	996 (15.7%)	6,682 (27.8%)	-0.026	1,410 (19.1%)	7,124 (24.7%)	-0.012	2,406 (17.5%)	13,806 (26.1%)	-0.209
Use of Anticoagulants; n (%)	116 (1.8%)	674 (2.8%)	-0.007	165 (2.2%)	608 (2.1%)	0.001	281 (2.0%)	1,282 (2.4%)	-0.027
Use of Amiodarone; n (%)	11 (0.2%)	55 (0.2%)	0.000	17 (0.2%)	44 (0.2%)	0.000	028 (0.2%)	099 (0.2%)	0.000
Digoxin; n (%)	26 (0.4%)	100 (0.4%)	0.000	45 (0.6%)	114 (0.4%)	0.003	071 (0.5%)	214 (0.4%)	0.015
Use of Diuretics; n (%)	813 (12.8%)	5,229 (21.8%)	-0.022	1,183 (16.0%)	5,938 (20.6%)	-0.011	1,996 (14.6%)	11,167 (21.1%)	-0.170
Use of Aspirin; n (%)	21 (0.3%)	110 (0.5%)	-0.003	26 (0.4%)	144 (0.5%)	-0.001	047 (0.3%)	254 (0.5%)	-0.032
NSAIDs (NOT including aspirin); n (%)	533 (8.4%)	3,311 (13.8%)	-0.016	861 (11.7%)	4,372 (15.1%)	-0.009	1,394 (10.2%)	7,683 (14.5%)	-0.131
HRT (Use of estrogens, progestins, androgens); n (%)	889 (14.0%)	2,782 (11.6%)	0.007	1,178 (16.0%)	4,006 (13.9%)	0.005	2,067 (15.1%)	6,788 (12.8%)	0.066
Use of Statins ; n (%)	1,037 (16.4%)	6,365 (26.5%)	-0.022	1,290 (17.5%)	6,323 (21.9%)	-0.010	2,327 (17.0%)	12,688 (24.0%)	-0.174
Healthcare Utilization Measures									
Use of any drugs claims									
...mean (sd)	22.04 (17.13)	26.38 (19.37)	-0.237	24.69 (17.07)	27.04 (18.47)	-0.132	23.47 (17.10)	26.74 (18.88)	-0.182
...median [IQR]	18.00 [10.00, 29.00]	22.00 [12.00, 35.00]	-0.219	21.00 [12.00, 33.00]	23.00 [14.00, 36.00]	-0.112	19.61 (17.10)	22.55 (18.88)	-0.163
Number of office visits									
...mean (sd)	9.78 (7.99)	11.67 (9.61)	-0.214	11.12 (8.19)	11.44 (7.91)	-0.040	10.50 (8.10)	11.54 (8.72)	-0.124
...median [IQR]	8.00 [5.00, 12.00]	9.00 [5.00, 15.00]	-0.113	9.00 [6.00, 14.00]	10.00 [6.00, 15.00]	-0.124	8.54 (8.10)	9.55 (8.72)	-0.120
Number of ED visits									
...mean (sd)	0.31 (0.75)	0.45 (1.08)	-0.151	0.52 (1.14)	0.56 (1.20)	-0.034	0.42 (0.98)	0.51 (1.15)	-0.084
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 1.00]	0.000	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.000	0.00 (0.98)	0.00 (1.15)	0.000
Number of hospitalizations									
...mean (sd)	0.02 (0.19)	0.04 (0.27)	-0.086	0.16 (1.28)	0.17 (1.23)	-0.008	0.10 (0.95)	0.11 (0.93)	-0.011
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.000	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.000	0.00 (0.95)	0.00 (0.93)	0.000
Recent hospitalization (-30 days to Index Rx date); n (%)	14 (0.2%)	152 (0.6%)	-0.006	40 (0.5%)	186 (0.6%)	-0.001	054 (0.4%)	338 (0.6%)	-0.028
Old hospitalizations (-365 to -31 days); n (%)	354 (5.6%)	1,508 (6.3%)	-0.003	503 (6.8%)	1,972 (6.8%)	0.000	857 (6.2%)	3,480 (6.6%)	-0.016
Number of Pulmonologist/Allergist visits									
...mean (sd)	0.02 (0.23)	0.04 (0.43)	-0.058	1.37 (3.61)	1.35 (3.58)	0.006	0.75 (2.65)	0.76 (2.66)	-0.004
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.000	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.000	0.00 (2.65)	0.00 (2.66)	0.000
Pulmonologist /allergist on CED; n (%)	3 (0.0%)	61 (0.3%)	-0.008	465 (6.3%)	2,178 (7.5%)	-0.005	468 (3.4%)	2,239 (4.2%)	-0.042
Number of hospital days									
...mean (sd)	0.18 (2.69)	0.28 (2.91)	-0.036	0.16 (1.28)	0.17 (1.23)	-0.008	0.17 (2.06)	0.22 (2.16)	-0.024
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.000	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.000	0.00 (2.06)	0.00 (2.16)	0.000
Occurrence of basic or comprehensive metabolic blood chemistry test; n (%)									
1,597 (25.2%)	9,025 (37.6%)	-0.022	1,762 (23.9%)	8,401 (29.1%)	-0.010	3,359 (24.5%)	17,426 (33.0%)	-0.189	
Number of HbA1C test ordered									
...mean (sd)	0.29 (0.82)	0.62 (1.17)	-0.327	0.28 (0.77)	0.40 (0.94)	-0.140	0.28 (0.79)	0.50 (1.05)	-0.237
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 1.00]	0.000	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.000	0.00 (0.79)	0.00 (1.05)	0.000
Flexible Sigmoidoscopy or colonoscopy or CT virtual colonoscopy; n (%)									
194 (3.1%)	890 (3.7%)	-0.003	250 (3.4%)	1,119 (3.9%)	-0.003	444 (3.2%)	2,009 (3.8%)	-0.033	
Number of Mammograms (Breast cancer screening); n (%)									
849 (13.4%)	3,434 (14.3%)	-0.002	993 (13.5%)	3,999 (13.9%)	-0.001	1,842 (13.4%)	7,433 (14.1%)	-0.020	
Number of Pap smear (Cervical cancer screening); n (%)									
898 (14.2%)	2,170 (9.0%)	0.015	1,035 (14.0%)	3,178 (11.0%)	0.008	1,933 (14.1%)	5,348 (10.1%)	0.123	
Flu vaccine; n (%)									
1,130 (17.8%)	4,320 (18.0%)	0.000	1,247 (16.9%)	4,546 (15.7%)	0.003	2,377 (17.3%)	8,866 (16.8%)	0.013	
Pneumococcal vaccine; n (%)									
325 (5.1%)	3,234 (13.5%)	-0.028	449 (6.1%)	2,077 (7.2%)	-0.004	774 (5.6%)	5,311 (10.0%)	-0.165	
Copay for pharmacy cost (charges in U.S. \$)									
...mean (sd)	35.24 (31.61)	35.92 (35.15)	-0.020	25.32 (23.84)	25.69 (25.62)	-0.015	29.90 (27.70)	30.33 (30.32)	-0.015
...median [IQR]	29.02 [16.72, 45.16]	29.15 [15.10, 46.93]	-0.004	21.25 [9.74, 34.71]	20.90 [10.28, 34.52]	0.014	24.84 (27.70)	24.65 (30.32)	0.007
Business Type									
...Commercial; n (%)	5,566 (87.8%)	16,395 (68.3%)	0.022	NA	NA	NA	NA	NA	NA
...Medicare; n (%)	771 (12.2%)	7,605 (31.7%)	-0.042	NA	NA	NA	NA	NA	NA
Insurance Plan Type									

Appendix B

...Comprehensive; n (%)	NA	NA	NA	601 (8.1%)	2,299 (8.0%)	0.000	NA	NA	NA
...HMO; n (%)	NA	NA	NA	978 (13.3%)	3,421 (11.9%)	0.004	NA	NA	NA
...PPO; n (%)	NA	NA	NA	4,270 (57.9%)	16,728 (58.0%)	0.000	NA	NA	NA
...Others; n (%)	NA	NA	NA	1,531 (20.7%)	6,416 (22.2%)	-0.003	NA	NA	NA
SABA; n (%)	3,308 (52.2%)	12,697 (52.9%)	-0.001	4,699 (63.7%)	18,511 (64.1%)	-0.001	8,007 (58.4%)	31,208 (59.0%)	-0.012
SAMA; n (%)	95 (1.5%)	450 (1.9%)	-0.003	204 (2.8%)	744 (2.6%)	0.001	299 (2.2%)	1,194 (2.3%)	-0.007
SABA/SAMA; n (%)	116 (1.8%)	835 (3.5%)	-0.010	269 (3.6%)	1,517 (5.3%)	-0.008	385 (2.8%)	2,352 (4.4%)	-0.086
ICS without budesonide; n (%)	1,922 (30.3%)	6,879 (28.7%)	0.003	2,746 (37.2%)	10,504 (36.4%)	0.001	4,668 (34.0%)	17,383 (32.9%)	0.023
LABA; n (%)	493 (7.8%)	240 (1.0%)	0.032	502 (6.8%)	447 (1.5%)	0.026	995 (7.3%)	687 (1.3%)	0.299
LAMA; n (%)	126 (2.0%)	1,049 (4.4%)	-0.013	248 (3.4%)	1,685 (5.8%)	-0.011	374 (2.7%)	2,734 (5.2%)	-0.129
ICS/LABA (without budesonide-formoterol); n (%)	635 (10.0%)	3,591 (15.0%)	-0.014	825 (11.2%)	5,565 (19.3%)	-0.021	1,460 (10.6%)	9,156 (17.3%)	-0.194
Blood eosinophilia test ; n (%)	26 (0.4%)	53 (0.2%)	0.004	14 (0.2%)	88 (0.3%)	-0.002	040 (0.3%)	141 (0.3%)	0.000
Serum immunoglobulin E (IgE) level test; n (%)	72 (1.1%)	346 (1.4%)	-0.003	121 (1.6%)	659 (2.3%)	-0.005	193 (1.4%)	1,005 (1.9%)	-0.039
H2 blocker; n (%)	59 (0.9%)	649 (2.7%)	-0.013	233 (3.2%)	982 (3.4%)	-0.001	292 (2.1%)	1,631 (3.1%)	-0.063
Oxygen codes; n (%)	15 (0.2%)	156 (0.7%)	-0.007	37 (0.5%)	226 (0.8%)	-0.004	052 (0.4%)	382 (0.7%)	-0.041
Respiratory arrest/dependence on oxygen; n (%)	1 (0.0%)	6 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	001 (0.0%)	006 (0.0%)	#DIV/0!

Action link to Optum results: <https://bwh-dope.aetion.com/projects/details/1657/rwrs/68456>

Action link to MarketScan results: <https://bwh-dope.aetion.com/projects/details/1656/rwrs/68455>

Appendix B

PS-matched									
Variable	Optum			Marketscan			POOLED		
	Budesonide alone	Budesonide-formoterol	St. Diff.	Budesonide alone	Budesonide-formoterol	St. Diff.	Budesonide alone	Budesonide-formoterol	St. Diff.
Number of patients	5,198	5,198		6,959	6,959		12,157	12,157	
Year of Cohort Entry Date									
...2007; n (%)	250 (4.8%)	245 (4.7%)	0.0005	336 (4.8%)	330 (4.7%)	0.0005	586 (4.8%)	575 (4.7%)	0.0005
...2008; n (%)	627 (12.1%)	656 (12.6%)	-0.0014	521 (7.5%)	529 (7.6%)	-0.0004	1,148 (9.4%)	1,185 (9.7%)	-0.010
...2009; n (%)	647 (12.4%)	658 (12.7%)	-0.0008	648 (9.3%)	668 (9.6%)	-0.0010	1,295 (10.7%)	1,326 (10.9%)	-0.006
...2010; n (%)	636 (12.2%)	625 (12.0%)	0.0006	680 (9.8%)	692 (9.9%)	-0.0003	1,316 (10.8%)	1,317 (10.8%)	0.000
...2011; n (%)	552 (10.6%)	538 (10.4%)	0.0006	687 (9.9%)	711 (10.2%)	-0.0009	1,239 (10.2%)	1,249 (10.3%)	-0.003
...2012; n (%)	494 (9.5%)	518 (10.0%)	-0.0016	761 (10.9%)	756 (10.9%)	0.0000	1,255 (10.3%)	1,274 (10.5%)	-0.007
...2013; n (%)	496 (9.5%)	463 (8.9%)	0.0020	723 (10.4%)	685 (9.8%)	0.0019	1,219 (10.0%)	1,148 (9.4%)	0.020
...2014; n (%)	435 (8.4%)	444 (8.5%)	-0.0003	783 (11.3%)	793 (11.4%)	-0.0003	1,218 (10.0%)	1,237 (10.2%)	-0.007
...2015; n (%)	373 (7.2%)	356 (6.8%)	0.0015	641 (9.2%)	644 (9.3%)	-0.0003	1,014 (8.3%)	1,000 (8.2%)	0.004
...2016; n (%)	250 (4.8%)	242 (4.7%)	0.0005	491 (7.1%)	469 (6.7%)	0.0015	741 (6.1%)	711 (5.8%)	0.013
...2017; n (%)	143 (2.8%)	151 (2.9%)	-0.0006	378 (5.4%)	397 (5.7%)	-0.0013	521 (4.3%)	548 (4.5%)	-0.010
...2018; n (%)	130 (2.5%)	146 (2.8%)	-0.0018	310 (4.5%)	285 (4.1%)	0.0019	440 (3.6%)	431 (3.5%)	0.005
...2019; n (%)	121 (2.3%)	117 (2.3%)	0.0000	NA	NA	NA	NA	NA	NA
...2020; n (%)	44 (0.8%)	39 (0.8%)	0.0000	NA	NA	NA	NA	NA	NA
Age*									
...mean (sd)	43.68 (20.21)	43.29 (19.29)	0.0197	43.76 (19.95)	43.63 (18.37)	0.0068	43.73 (20.06)	43.48 (18.77)	0.013
...median [IQR]	44.00 [28.00, 59.00]	44.00 [28.00, 58.00]	0.0000	47.00 [27.00, 59.00]	46.00 [29.00, 58.00]	0.0521	45.72 (20.06)	45.14 (18.77)	0.030
Age categories									
...12-17; n (%)	901 (17.3%)	757 (14.6%)	0.0068	1,206 (17.3%)	938 (13.5%)	0.0097	2,107 (17.3%)	1,695 (13.9%)	0.094
...18-39; n (%)	1,308 (25.2%)	1,394 (26.8%)	-0.0031	1,566 (22.5%)	1,677 (24.1%)	-0.0033	2,874 (23.6%)	3,071 (25.3%)	-0.040
...40 - 64; n (%)	2,107 (40.5%)	2,267 (43.6%)	-0.0048	3,281 (47.1%)	3,660 (52.6%)	-0.0078	5,388 (44.3%)	5,927 (48.8%)	-0.090
...>= 65; n (%)	882 (17.0%)	780 (15.0%)	0.0050	906 (13.0%)	684 (9.8%)	0.0095	1,788 (14.7%)	1,464 (12.0%)	0.079
Geographic Region*									
...Northeast; n (%)	715 (13.8%)	748 (14.4%)	-0.0016	1,576 (22.6%)	1,560 (22.4%)	0.0004	2,291 (18.8%)	2,308 (19.0%)	-0.005
...South; n (%)	1,950 (37.5%)	1,928 (37.1%)	0.0007	2,066 (29.7%)	2,040 (29.3%)	0.0007	4,016 (33.0%)	3,968 (32.6%)	0.009
...Midwest; n (%)	1,445 (27.8%)	1,455 (28.0%)	-0.0004	2,220 (31.9%)	2,261 (32.5%)	-0.0011	3,665 (30.1%)	3,716 (30.6%)	-0.011
...West; n (%)	1,088 (20.9%)	1,067 (20.5%)	0.0009	1,042 (15.0%)	1,031 (14.8%)	0.0005	2,130 (17.5%)	2,098 (17.3%)	0.005
...Unknown/Missing; n (%)	NA	NA	NA	55 (0.8%)	67 (1.0%)	-0.0021	NA	NA	NA
Metropolitan Statistical Area*									
...Urban; n (%)	NA	NA	NA	5,712 (82.1%)	5,672 (81.5%)	0.0007	NA	NA	NA
...Rural; n (%)	NA	NA	NA	108 (1.6%)	104 (1.5%)	0.0008	NA	NA	NA
...Unknown/Missing; n (%)	NA	NA	NA	1,139 (16.4%)	1,183 (17.0%)	-0.0015	NA	NA	NA
General Health Related Measures									
Alcohol/Drug abuse or dependence; n (%)	12 (0.2%)	26 (0.5%)	-0.0051	29 (0.4%)	20 (0.3%)	0.0017	041 (0.3%)	046 (0.4%)	-0.017
Obesity or Overweight; n (%)*	319 (6.1%)	293 (5.6%)	0.0021	436 (6.3%)	427 (6.1%)	0.0008	755 (6.2%)	720 (5.9%)	0.013
Obesity; n (%)	258 (5.0%)	251 (4.8%)	0.0009	372 (5.3%)	353 (5.1%)	0.0009	630 (5.2%)	604 (5.0%)	0.009
Overweight; n (%)	63 (1.2%)	50 (1.0%)	0.0019	73 (1.0%)	83 (1.2%)	-0.0019	136 (1.1%)	133 (1.1%)	0.000
Cardiovascular Measures									
Hypertension; n (%)*	1,300 (25.0%)	1,268 (24.4%)	0.0012	1,630 (23.4%)	1,621 (23.3%)	0.0002	2,930 (24.1%)	2,889 (23.8%)	0.007
Hyperlipidemia; n (%)*	1,109 (21.3%)	1,050 (20.2%)	0.0024	1,252 (18.0%)	1,235 (17.7%)	0.0007	2,361 (19.4%)	2,285 (18.8%)	0.015
MI, angina, Coronary atherosclerosis and other forms of chronic ischemic heart disease; n (%)*	176 (3.4%)	159 (3.1%)	0.0017	224 (3.2%)	215 (3.1%)	0.0006	400 (3.3%)	374 (3.1%)	0.011
Old MI; n (%)	17 (0.3%)	15 (0.3%)	0.0000	19 (0.3%)	14 (0.2%)	0.0020	036 (0.3%)	029 (0.2%)	0.020
Acute MI; n (%)	7 (0.1%)	6 (0.1%)	0.0000	11 (0.2%)	4 (0.1%)	0.0026	018 (0.1%)	010 (0.1%)	0.000
Stable angina; n (%)	25 (0.5%)	31 (0.6%)	-0.0013	28 (0.4%)	25 (0.4%)	0.0000	053 (0.4%)	056 (0.5%)	-0.015
Coronary atherosclerosis and other forms of chronic ischemic heart disease; n (%)	159 (3.1%)	134 (2.6%)	0.0030	186 (2.7%)	192 (2.8%)	-0.0006	345 (2.8%)	326 (2.7%)	0.006
History of CABG or PTCA; n (%)	29 (0.6%)	26 (0.5%)	0.0013	20 (0.3%)	24 (0.3%)	0.0000	049 (0.4%)	050 (0.4%)	0.000

Appendix B

Cerebrovascular disease (Stroke, TIA, Late effects); n (%)*	31 (0.6%)	37 (0.7%)	-0.0012	58 (0.8%)	58 (0.8%)	0.0000	089 (0.7%)	095 (0.8%)	-0.012
Stroke (Ischemic or hemorrhagic); n (%)	17 (0.3%)	20 (0.4%)	-0.0017	23 (0.3%)	35 (0.5%)	-0.0032	040 (0.3%)	055 (0.5%)	-0.032
TIA; n (%)	11 (0.2%)	14 (0.3%)	-0.0020	32 (0.5%)	26 (0.4%)	0.0015	043 (0.4%)	040 (0.3%)	0.017
Late effects of cerebrovascular disease; n (%)	8 (0.2%)	9 (0.2%)	0.0000	12 (0.2%)	13 (0.2%)	0.0000	020 (0.2%)	022 (0.2%)	0.000
Atrial fibrillation and Other cardiac dysrhythmia; n (%)*	200 (3.8%)	191 (3.7%)	0.0005	312 (4.5%)	312 (4.5%)	0.0000	512 (4.2%)	503 (4.1%)	0.005
Atrial fibrillation; n (%)	96 (1.8%)	89 (1.7%)	0.0008	158 (2.3%)	123 (1.8%)	0.0035	254 (2.1%)	212 (1.7%)	0.029
Other cardiac dysrhythmia; n (%)	136 (2.6%)	138 (2.7%)	-0.0006	209 (3.0%)	242 (3.5%)	-0.0028	345 (2.8%)	380 (3.1%)	-0.018
Diabetes Related Measures									
Diabetes with or w/o complications; n (%)*	411 (7.9%)	354 (6.8%)	0.0041	496 (7.1%)	503 (7.2%)	-0.0004	907 (7.5%)	857 (7.0%)	0.019
Diabetes mellitus without mention of complications; n (%)	395 (7.6%)	329 (6.3%)	0.0049	463 (6.7%)	481 (6.9%)	-0.0008	858 (7.1%)	810 (6.7%)	0.016
Diabetes with specified complications; n (%)	73 (1.4%)	57 (1.1%)	0.0027	83 (1.2%)	66 (0.9%)	0.0029	156 (1.3%)	123 (1.0%)	0.028
Diabetes with unspecified complications; n (%)	16 (0.3%)	13 (0.3%)	0.0000	17 (0.2%)	14 (0.2%)	0.0000	033 (0.3%)	027 (0.2%)	0.020
GI Conditions									
GERD; n (%)*	492 (9.5%)	467 (9.0%)	0.0016	591 (8.5%)	611 (8.8%)	-0.0010	1,083 (8.9%)	1,078 (8.9%)	0.000
Upper GI (Diseases of esophagus, stomach and duodenum including GERD) ; n (%)	611 (11.8%)	597 (11.5%)	0.0009	763 (11.0%)	783 (11.3%)	-0.0009	1,374 (11.3%)	1,380 (11.4%)	-0.003
GI bleeding; n (%)*	71 (1.4%)	63 (1.2%)	0.0018	77 (1.1%)	94 (1.4%)	-0.0027	148 (1.2%)	157 (1.3%)	-0.009
Non-infective enteritis and colitis; n (%)	153 (2.9%)	164 (3.2%)	-0.0017	229 (3.3%)	215 (3.1%)	0.0011	382 (3.1%)	379 (3.1%)	0.000
Intraoperative and postprocedural complications and disorders of digestive system; n (%)	75 (1.4%)	55 (1.1%)	0.0027	71 (1.0%)	70 (1.0%)	0.0000	146 (1.2%)	125 (1.0%)	0.019
Disorders of gallbladder, biliary tract and pancreas; n (%)*	42 (0.8%)	40 (0.8%)	0.0000	56 (0.8%)	57 (0.8%)	0.0000	098 (0.8%)	097 (0.8%)	0.000
Rheumatic Conditions									
Rheumatoid arthritis and other inflammatory polyarthropathies; n (%)*	59 (1.1%)	52 (1.0%)	0.0010	100 (1.4%)	108 (1.6%)	-0.0016	159 (1.3%)	160 (1.3%)	0.000
Osteoarthritis; n (%)*	366 (7.0%)	347 (6.7%)	0.0011	525 (7.5%)	498 (7.2%)	0.0011	891 (7.3%)	845 (7.0%)	0.012
Other rheumatic disorders (including gout); n (%)*	1,007 (19.4%)	989 (19.0%)	0.0009	1,405 (20.2%)	1,420 (20.4%)	-0.0004	2,412 (19.8%)	2,409 (19.8%)	0.000
Gout and other crystal arthropathies; n (%)	35 (0.7%)	41 (0.8%)	-0.0012	35 (0.5%)	55 (0.8%)	-0.0037	070 (0.6%)	096 (0.8%)	-0.024
Other rheumatic disorders; n (%)	988 (19.0%)	960 (18.5%)	0.0012	1,382 (19.9%)	1,381 (19.8%)	0.0002	2,370 (19.5%)	2,341 (19.3%)	0.005
Neuro Conditions*									
Alzheimer and other Dementia Disease ; n (%)	35 (0.7%)	31 (0.6%)	0.0012	30 (0.4%)	37 (0.5%)	-0.0015	065 (0.5%)	068 (0.6%)	-0.014
Seizure disorders (epilepsy); n (%)	26 (0.5%)	28 (0.5%)	0.0000	40 (0.6%)	41 (0.6%)	0.0000	066 (0.5%)	069 (0.6%)	-0.014
Delirium/Psychosis; n (%)	44 (0.8%)	43 (0.8%)	0.0000	43 (0.6%)	46 (0.7%)	-0.0012	087 (0.7%)	089 (0.7%)	0.000
Other Conditions									
Hypothyroidism; n (%)*	484 (9.3%)	484 (9.3%)	0.0000	531 (7.6%)	512 (7.4%)	0.0007	1,015 (8.3%)	996 (8.2%)	0.004
Chronic kidney disease stages I-III; n (%)*	100 (1.9%)	101 (1.9%)	0.0000	59 (0.8%)	60 (0.9%)	-0.0011	159 (1.3%)	161 (1.3%)	0.000
Chronic kidney disease stages IV-V, ESRD; n (%)	31 (0.6%)	25 (0.5%)	0.0013	17 (0.2%)	16 (0.2%)	0.0000	048 (0.4%)	041 (0.3%)	0.017
COPD; n (%)*	261 (5.0%)	258 (5.0%)	0.0000	352 (5.1%)	347 (5.0%)	0.0004	613 (5.0%)	605 (5.0%)	0.000
Obstructive sleep apnea; n (%)*	274 (5.3%)	263 (5.1%)	0.0009	372 (5.3%)	378 (5.4%)	-0.0004	646 (5.3%)	641 (5.3%)	0.000
Syncope; n (%)	62 (1.2%)	50 (1.0%)	0.0019	72 (1.0%)	86 (1.2%)	-0.0019	134 (1.1%)	136 (1.1%)	0.000
Falls; n (%)	58 (1.1%)	42 (0.8%)	0.0031	39 (0.6%)	30 (0.4%)	0.0028	097 (0.8%)	072 (0.6%)	0.024
VTE; n (%)*	32 (0.6%)	36 (0.7%)	-0.0012	57 (0.8%)	59 (0.8%)	0.0000	089 (0.7%)	095 (0.8%)	-0.012
Combined comorbidity score, 365 days*									
...mean (sd)	1.17 (0.96)	1.15 (0.97)	0.0207	1.15 (0.89)	1.13 (0.86)	0.0229	1.16 (0.92)	1.14 (0.91)	0.022
...median [IQR]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	0.0000	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	0.0000	1.00 (0.92)	1.00 (0.91)	0.000
Frailty Score: Empirical Version 365 days as Categories*									
... < 0.1 non frail; n (%)	3,483 (67.0%)	3,450 (66.4%)	0.0007	4,163 (59.8%)	4,169 (59.9%)	-0.0001	7,646 (62.9%)	7,619 (62.7%)	0.004
... 0.1 - < 0.2 prefrail; n (%)	1,118 (21.5%)	1,168 (22.5%)	-0.0021	1,741 (25.0%)	1,748 (25.1%)	-0.0002	2,859 (23.5%)	2,916 (24.0%)	-0.012
... > 0.2 frail; n (%)	597 (11.5%)	580 (11.2%)	0.0009	1,055 (15.2%)	1,042 (15.0%)	0.0005	1,652 (13.6%)	1,622 (13.3%)	0.009
Medication Use									
Use of oral corticosteroids; n (%)*	2,474 (47.6%)	2,528 (48.6%)	-0.0014	6,612 (95.0%)	6,635 (95.3%)	-0.0003	9,086 (74.7%)	9,163 (75.4%)	-0.016
Use of antidepressants; n (%)*	981 (18.9%)	984 (18.9%)	0.0000	1,520 (21.8%)	1,525 (21.9%)	-0.0002	2,501 (20.6%)	2,509 (20.6%)	0.000
Use of anticonvulsants; n (%)*	297 (5.7%)	284 (5.5%)	0.0008	509 (7.3%)	487 (7.0%)	0.0011	806 (6.6%)	771 (6.3%)	0.012
Use of beta blocker OR calcium channel blocker; n (%)*	505 (9.7%)	474 (9.1%)	0.0020	751 (10.8%)	732 (10.5%)	0.0009	1,256 (10.3%)	1,206 (9.9%)	0.013
Use of PPIs; n (%)*	744 (14.3%)	734 (14.1%)	0.0005	1,413 (20.3%)	1,430 (20.5%)	-0.0004	2,157 (17.7%)	2,164 (17.8%)	-0.003

Appendix B

Use of opioids; n (%)*	808 (15.5%)	781 (15.0%)	0.0013	1,307 (18.8%)	1,308 (18.8%)	0.0000	2,115 (17.4%)	2,089 (17.2%)	0.005
Use of antipsychotics; n (%)*	73 (1.4%)	73 (1.4%)	0.0000	101 (1.5%)	99 (1.4%)	0.0008	174 (1.4%)	172 (1.4%)	0.000
Use of anxiolytics/hypnotics; n (%)*	289 (5.6%)	285 (5.5%)	0.0004	457 (6.6%)	489 (7.0%)	-0.0015	746 (6.1%)	774 (6.4%)	-0.012
Use of dementia meds; n (%)*	23 (0.4%)	23 (0.4%)	0.0000	21 (0.3%)	23 (0.3%)	0.0000	044 (0.4%)	046 (0.4%)	0.000
Use of antiparkinsonian meds; n (%)*	53 (1.0%)	51 (1.0%)	0.0000	98 (1.4%)	103 (1.5%)	-0.0008	151 (1.2%)	154 (1.3%)	-0.009
Use of Benzodiazepine; n (%)*	467 (9.0%)	454 (8.7%)	0.0010	822 (11.8%)	839 (12.1%)	-0.0009	1,289 (10.6%)	1,293 (10.6%)	0.000
All antidiabetic medications; n (%)*	328 (6.3%)	286 (5.5%)	0.0033	474 (6.8%)	491 (7.1%)	-0.0011	802 (6.6%)	777 (6.4%)	0.008
ACEI/ARB; n (%)	875 (16.8%)	865 (16.6%)	0.0005	1,316 (18.9%)	1,334 (19.2%)	-0.0007	2,191 (18.0%)	2,199 (18.1%)	-0.003
Use of Anticoagulants; n (%)*	104 (2.0%)	91 (1.8%)	0.0015	154 (2.2%)	150 (2.2%)	0.0000	258 (2.1%)	241 (2.0%)	0.007
Use of Amiodarone; n (%)	9 (0.2%)	10 (0.2%)	0.0000	16 (0.2%)	9 (0.1%)	0.0026	025 (0.2%)	019 (0.2%)	0.000
Digoxin; n (%)	22 (0.4%)	17 (0.3%)	0.0017	41 (0.6%)	30 (0.4%)	0.0028	063 (0.5%)	047 (0.4%)	0.015
Use of Diuretics; n (%)*	705 (13.6%)	689 (13.3%)	0.0008	1,104 (15.9%)	1,108 (15.9%)	0.0000	1,809 (14.9%)	1,797 (14.8%)	0.003
Use of Aspirin; n (%)	16 (0.3%)	17 (0.3%)	0.0000	25 (0.4%)	27 (0.4%)	0.0000	041 (0.3%)	044 (0.4%)	-0.017
NSAIDs (NOT including aspirin); n (%)	463 (8.9%)	523 (10.1%)	-0.0039	811 (11.7%)	929 (13.3%)	-0.0045	1,274 (10.5%)	1,452 (11.9%)	-0.044
HRT (Use of estrogens, progestins, androgens); n (%)*	716 (13.8%)	735 (14.1%)	-0.0008	1,088 (15.6%)	1,111 (16.0%)	-0.0010	1,804 (14.8%)	1,846 (15.2%)	-0.011
Use of Statins ; n (%)*	909 (17.5%)	870 (16.7%)	0.0019	1,203 (17.3%)	1,188 (17.1%)	0.0005	2,112 (17.4%)	2,058 (16.9%)	0.013
Healthcare Utilization Measures									
Use of any drugs claims*									
...mean (sd)	22.17 (17.48)	22.00 (16.75)	0.0099	24.51 (16.99)	24.60 (17.10)	-0.0053	23.51 (17.20)	23.49 (16.95)	0.001
...median [IQR]	18.00 [10.00, 29.00]	18.00 [10.00, 29.00]	0.0000	20.00 [12.00, 32.00]	21.00 [12.00, 32.00]	-0.0587	19.14 (17.20)	19.72 (16.95)	-0.034
Number of office visits*									
...mean (sd)	10.07 (8.28)	10.04 (8.68)	0.0035	11.05 (8.13)	11.08 (7.78)	-0.0038	10.63 (8.19)	10.64 (8.18)	-0.001
...median [IQR]	8.00 [5.00, 13.00]	8.00 [5.00, 12.25]	0.0000	9.00 [6.00, 14.00]	9.00 [6.00, 14.00]	0.0000	8.57 (8.19)	8.57 (8.18)	0.000
Number of ED visits*									
...mean (sd)	0.33 (0.77)	0.32 (0.76)	0.0131	0.52 (1.15)	0.52 (1.07)	0.0000	0.44 (1.01)	0.43 (0.95)	0.010
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.0000	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.0000	0.00 (1.01)	0.00 (0.95)	0.000
Number of hospitalizations*									
...mean (sd)	0.03 (0.20)	0.03 (0.25)	0.0000	0.16 (1.29)	0.14 (1.09)	0.0167	0.10 (0.98)	0.09 (0.84)	0.011
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.0000	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.0000	0.00 (0.98)	0.00 (0.84)	0.000
Recent hospitalization (-30 days to Index Rx date); n (%)*	14 (0.3%)	8 (0.2%)	0.0020	38 (0.5%)	40 (0.6%)	-0.0013	052 (0.4%)	048 (0.4%)	0.000
Old hospitalizations (-365 to -31 days); n (%)*	295 (5.7%)	303 (5.8%)	-0.0004	468 (6.7%)	482 (6.9%)	-0.0008	763 (6.3%)	785 (6.5%)	-0.008
Number of Pulmonologist/Allergist visits*									
...mean (sd)	0.02 (0.26)	0.02 (0.27)	0.0000	1.38 (3.64)	1.39 (3.52)	-0.0028	0.80 (2.76)	0.80 (2.67)	0.000
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.0000	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.0000	0.00 (2.76)	0.00 (2.67)	0.000
Pulmonologist /allergist on CED; n (%)*	3 (0.1%)	2 (0.0%)	0.0045	456 (6.6%)	466 (6.7%)	-0.0004	459 (3.8%)	468 (3.8%)	0.000
Number of hospital days*									
...mean (sd)	0.21 (2.95)	0.19 (2.73)	0.0070	0.16 (1.29)	0.14 (1.09)	0.0167	0.18 (2.16)	0.16 (1.97)	0.010
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.0000	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.0000	0.00 (2.16)	0.00 (1.97)	0.000
Occurrence of basic or comprehensive metabolic blood chemistry test; n (%)*	1,406 (27.0%)	1,348 (25.9%)	0.0021	1,693 (24.3%)	1,679 (24.1%)	0.0004	3,099 (25.5%)	3,027 (24.9%)	0.014
Number of HbA1C test ordered*									
...mean (sd)	0.33 (0.88)	0.29 (0.80)	0.0476	0.29 (0.78)	0.29 (0.78)	0.0000	0.31 (0.82)	0.29 (0.79)	0.025
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.0000	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.0000	0.00 (0.82)	0.00 (0.79)	0.000
Flexible Sigmoidoscopy or colonoscopy or CT virtual colonoscopy; n (%)*	162 (3.1%)	159 (3.1%)	0.0000	236 (3.4%)	244 (3.5%)	-0.0005	398 (3.3%)	403 (3.3%)	0.000
Number of Mammograms (Breast cancer screening); n (%)*	687 (13.2%)	669 (12.9%)	0.0008	918 (13.2%)	918 (13.2%)	0.0000	1,605 (13.2%)	1,587 (13.1%)	0.003
Number of Pap smear (Cervical cancer screening); n (%)*	690 (13.3%)	707 (13.6%)	-0.0008	961 (13.8%)	954 (13.7%)	0.0003	1,651 (13.6%)	1,661 (13.7%)	-0.003
Flu vaccine; n (%)*	973 (18.7%)	982 (18.9%)	-0.0005	1,201 (17.3%)	1,155 (16.6%)	0.0017	2,174 (17.9%)	2,137 (17.6%)	0.008
Pneumococcal vaccine; n (%)*	307 (5.9%)	306 (5.9%)	0.0000	443 (6.4%)	448 (6.4%)	0.0000	750 (6.2%)	754 (6.2%)	0.000
Copay for pharmacy cost (charges in U.S. \$)*									
...mean (sd)	35.89 (33.14)	36.20 (29.55)	-0.0099	25.00 (23.64)	24.90 (23.97)	0.0042	29.66 (28.10)	29.73 (26.50)	-0.003
...median [IQR]	29.37 [16.66, 46.02]	31.05 [18.46, 47.50]	-0.0535	21.00 [9.54, 34.19]	20.80 [10.00, 34.36]	0.0084	24.58 (28.10)	25.18 (26.50)	-0.022
Business Type*									
...Commercial; n (%)	4,456 (85.7%)	4,494 (86.5%)	-0.0009	NA	NA	NA	NA	NA	NA

Appendix B

...Medicare; n (%)	742 (14.3%)	704 (13.5%)	0.0021	NA	NA	NA	NA	NA	NA
Insurance Plan Type*									
...Comprehensive; n (%)	NA	NA	NA	547 (7.9%)	554 (8.0%)	-0.0004	NA	NA	NA
...HMO; n (%)	NA	NA	NA	902 (13.0%)	896 (12.9%)	0.0003	NA	NA	NA
...PPO; n (%)	NA	NA	NA	4,037 (58.0%)	4,052 (58.2%)	-0.0003	NA	NA	NA
...Others; n (%)	NA	NA	NA	1,473 (21.2%)	1,457 (20.9%)	0.0007	NA	NA	NA
SABA; n (%)*	2,756 (53.0%)	2,770 (53.3%)	-0.0004	4,454 (64.0%)	4,477 (64.3%)	-0.0004	7,210 (59.3%)	7,247 (59.6%)	-0.006
SAMA; n (%)*	79 (1.5%)	66 (1.3%)	0.0017	182 (2.6%)	187 (2.7%)	-0.0006	261 (2.1%)	253 (2.1%)	0.000
SABA/SAMA; n (%)*	101 (1.9%)	100 (1.9%)	0.0000	255 (3.7%)	265 (3.8%)	-0.0005	356 (2.9%)	365 (3.0%)	-0.006
ICS without budesonide; n (%)*	1,600 (30.8%)	1,649 (31.7%)	-0.0016	2,596 (37.3%)	2,705 (38.9%)	-0.0026	4,196 (34.5%)	4,354 (35.8%)	-0.027
LABA; n (%)*	209 (4.0%)	191 (3.7%)	0.0015	340 (4.9%)	349 (5.0%)	-0.0004	549 (4.5%)	540 (4.4%)	0.005
LAMA; n (%)*	111 (2.1%)	115 (2.2%)	-0.0007	228 (3.3%)	243 (3.5%)	-0.0011	339 (2.8%)	358 (2.9%)	-0.006
ICS/LABA (without budesonide-formoterol); n (%)*	546 (10.5%)	568 (10.9%)	-0.0012	813 (11.7%)	857 (12.3%)	-0.0017	1,359 (11.2%)	1,425 (11.7%)	-0.016
Blood eosinophilia test ; n (%)*	15 (0.3%)	16 (0.3%)	0.0000	13 (0.2%)	15 (0.2%)	0.0000	028 (0.2%)	031 (0.3%)	-0.020
Serum immunoglobulin E (IgE) level test; n (%)*	62 (1.2%)	72 (1.4%)	-0.0018	119 (1.7%)	119 (1.7%)	0.0000	181 (1.5%)	191 (1.6%)	-0.008
H2 blocker; n (%)*	56 (1.1%)	60 (1.2%)	-0.0009	213 (3.1%)	193 (2.8%)	0.0017	269 (2.2%)	253 (2.1%)	0.007
Oxygen codes; n (%)*	14 (0.3%)	7 (0.1%)	0.0045	32 (0.5%)	29 (0.4%)	0.0015	046 (0.4%)	036 (0.3%)	0.017
Respiratory arrest/dependence on oxygen; n (%)*	1 (0.0%)	0 (0.0%)	#DIV/0!	0 (0.0%)	0 (0.0%)	#DIV/0!	001 (0.0%)	000 (0.0%)	#DIV/0!

*Included in the 1:1 PS matching model