**Supplemental Appendix to *Safety of hydroxychloroquine, alone or in combination with azithromycin, in light of rapid wide-spread use for COVID-19: a multinational, network cohort and self-controlled case series study***

All artefacts generated as part of this study are publicly available in an interactive, web-based application at: <https://data.ohdsi.org/Covid19EstimationHydroxychloroquine/>

**Contents**

[**S1. Data sources** 4](#_Toc37020183)

[**S2. Cohort definitions** 6](#_Toc37020184)

[**S2.1. Exposures** 6](#_Toc37020185)

[**S5.1.1. New users of Hydroxychloroquine with prior rheumatoid arthritis** 6](#_Toc37020186)

[**S5.1.2. New users of sulfasazine with prior rheumatoid arthritis** 6](#_Toc37020187)

[**S5.1.3. Users of Hydroxychloroquine + Azithromycin** 7](#_Toc37020188)

[**S5.1.4. Users of Hydroxychloroquine + Amoxicillin** 7](#_Toc37020189)

[**S2.2. Outcomes** 8](#_Toc37020190)

[**S3. Negative control outcomes** 8](#_Toc37020191)

[**S4. Covariate construction** 9](#_Toc37020192)

[**S5. Exposure cohort counts** 9](#_Toc37020193)

[**S6. Covariate balance before and after PS stratification** 10](#_Toc37020194)

[**S6.1. HCQ vs SSZ** 10](#_Toc37020195)

[**S6.1.1. AmbEMR** 10](#_Toc37020196)

[**S6.1.2. CCAE** 12](#_Toc37020197)

[**S6.1.3. CPRD** 13](#_Toc37020198)

[**S6.1.4. DAGermany** 14](#_Toc37020199)

[**S6.1.5. IMRD** 16](#_Toc37020200)

[**S6.1.6. IPCI** 18](#_Toc37020201)

[**S6.1.7. JMDC** 18](#_Toc37020202)

[**S6.1.8. MDCD** 20](#_Toc37020203)

[**S6.1.9. MDCR** 22](#_Toc37020204)

[**S6.1.10. OpenClaims** 23](#_Toc37020205)

[**S6.1.11. Optum** 24](#_Toc37020206)

[**S6.1.12. PanTher** 26](#_Toc37020207)

[**S6.1.13. SIDIAP** 28](#_Toc37020208)

[**S6.1.14. VA** 29](#_Toc37020209)

[**S6.2. AZM vs AMX** 31](#_Toc37020210)

[**S6.2.1. AmbEMR** 31](#_Toc37020211)

[**S6.2.2. CCAE** 33](#_Toc37020212)

[**S6.2.3. CPRD** 34](#_Toc37020213)

[**S6.2.4. DAGermany** 35](#_Toc37020214)

[**S6.2.5. IMRD** 36](#_Toc37020215)

[**S6.2.6 IPCI** 37](#_Toc37020216)

[**S6.2.7. MDCD** 38](#_Toc37020217)

[**S6.2.8. MDCR** 40](#_Toc37020218)

[**S6.2.9. OpenClaims** 41](#_Toc37020219)

[**S6.2.10. Optum** 41](#_Toc37020220)

[**S6.2.11. PanTher** 43](#_Toc37020221)

[**S6.2.12. SIDIAP** 45](#_Toc37020222)

[**S6.2.13. VA** 46](#_Toc37020223)

[**S7. Patient counts, events, incident rates** 48](#_Toc37020224)

[**S8. Calibrated hazard ratio forest plots** 53](#_Toc37020225)

[**S9. Evidence evaluation diagnostics** 54](#_Toc37020226)

[**S9.1. AmbEMR** 54](#_Toc37020227)

[**S9.2. CCAE** 55](#_Toc37020228)

[**S9.3. CPRD** 56](#_Toc37020229)

[**S9.4. DAGermany** 57](#_Toc37020230)

[**S9.5. IMRD** 58](#_Toc37020231)

[**S9.6. IPCI** 59](#_Toc37020232)

[**S9.7. JMDC** 60](#_Toc37020233)

[**S9.8. MDCD** 61](#_Toc37020234)

[**S9.9. MDCR** 62](#_Toc37020235)

[**S9.10. OpenClaims** 63](#_Toc37020236)

[**S9.11. Optum** 64](#_Toc37020237)

[**S9.12. PanTher** 65](#_Toc37020238)

[**S9.13. SIDIAP** 66](#_Toc37020239)

[**S9.14. VA** 67](#_Toc37020240)

[**S10. Self Controlled Case Series (SCCS) results: Hydroxychloroquine** 68](#_Toc37020241)

[**S10.1 CPRD** 68](#_Toc37020242)

[**S10.2 JMDC** 69](#_Toc37020243)

[**S10.3 CCAE** 70](#_Toc37020244)

[**S10.4 MDCD** 71](#_Toc37020245)

[**S10.5 MDCR** 72](#_Toc37020246)

[**S10.6 Optum** 73](#_Toc37020247)

[**S11. Literature review search** 74](#_Toc37020248)

[**S11.1 Pubmed search strategy** 74](#_Toc37020249)

[**S11.2 Embase (1974 to present) search strategy** 74](#_Toc37020250)

[**S11.3 Clinicaltrials search strategy** 78](#_Toc37020251)

[**S11.2 ICTRP search strategy** 78](#_Toc37020252)

# **S1. Data sources**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Database name** | **Population** | **Patient Count (millions)** | **Data History** | **Data capture process and short database description** |
| VA OMOP | USA (Veteran population) | ~12M | 2000 – | VA OMOP data reflects the national Department of Veterans Affairs health care system, which is the largest integrated provider of medical and mental health services in the United States. Care is provided at 170 VA Medical Centers and 1,063 outpatient sites serving more than 9 million enrolled Veterans each year. |
| IQVIA Disease Analyzer Germany | Germany (General population) | 37M | 1992 – | Anonymized patient records collected from Patient Management software used by general practitioners and selected specialists to document patients’ medical records within their office-based practice during a visit . |
| IQVIA UK Integrated Medical Record Data (IMRD) | UK (General population) | 15M | 1989 – | Pseudonymized Electronic Medical Records collected from patient management software used within UK Primary Care |
| IQVIA US Ambulatory EMR | USA (General population) | 49M | 2006 – | General practice EHR, Outpatient specialist EHR - Dataset consists of longitudinal, de-identified ambulatory electronic health records data |
| IQVIA US LRxDx Open Claims | USA (General population) | 654M | 2010 – | Pre-adjudicated claims at the anonymized patient level collected from office-based physicians and specialists via office management software and clearinghouse switch sources for the purpose of reimbursement. |
| Clinical Practice Research Datalink (CPRD) | UK (General population) | 13M | 1995 – | De-identified patient data from a network of general practiotioners practices across the UK. Primary care data are linked to a range of other health related data to provide a longitudinal, representative UK population health dataset. |
| IBM MarketScan Commercial Claims (CCAE) | USA (Patients with commercial insurance aged <65 years) | 142M | 2000 – | Data from individuals enrolled in US employer-sponsored insurance health plans. The data includes adjudicated health insurance claims (e.g. inpatient, outpatient, and outpatient pharmacy) as well as enrollment data from large employers and health plans who provide private healthcare coverage to employees, their spouses,and dependents. Additionally, it captures laboratory tests for a subset of the covered lives. |
| IBM MarketScan Multi-State Medicaid Database (MDCD) | USA | 26M | 2006 – | Adjudicated US health insurance claims for Medicaid enrollees from multiple states and includes hospital discharge diagnoses, outpatient diagnoses and procedures, and outpatient pharmacy claims as well as ethnicity and Medicare eligibility. |
| IBM MarketScan Medicare Supplemental Database (MDCR) | USA (Patients with commercial insurance aged 65+ years) | 10M | 2000 – | Represents health services of retirees (aged 65 or older) in the United States with primary or Medicare supplemental coverage through privately insured fee-for-service, point-of-service, or capitated health plans. These data include adjudicated health insurance claims (e.g. inpatient, outpatient, and outpatient pharmacy). Additionally, it captures laboratory tests for a subset of the covered lives. |
| Integrated Primary Care Information (IPCI) | Netherlands (General Population) | 2.5M | 1996- | Complete medical records collected from 450 general practitioners with geographical representation of the country. |
| Japan Medical Data Center (JMDC) | Japan (insured general population) | 5.5M | 2005 – | Data from 60 Society-Managed Health Insurance plans covering workers aged 18 to 65 and their dependents (children younger than 18 years old and elderly peopleolder than 65 years old). JMDC data includes membership status of the insured people and claims data provided byinsurers under contract (e.g. patient-level demographic information, inpatient and outpatient data inclusive of diagnosis and procedures, and prescriptions as dispensed claims information) |
| Optum De-Identified Clinformatics Data Mart Database - SES & DOD | USA (Patients with commercial insurance or commercial Medicare insurance) | 85M | 2000 - | Inpatient and outpatient healthcare insurance claims |
| Optum De-identified Electronic Health Record Dataset (PANTHER) | USA (General population) | 93M | 2006 – | Optum’s de-identified electronic health record data medical records database. The medical record data includes clinical information, inclusive of prescriptions as prescribed and administered, lab results, vital signs, body measurements, diagnoses, procedures, and information derived from clinical notes using Natural Language Processing (NLP). |
| The Information System for Research in Primary Care (SIDIAP) | Spain-Catalonia (80% of general population) | 7.7M | 2006 – | Electronic health records from primary care partially linked to inpatient data. SIDIAP is also linked to a pharmacy dispensations and primary care laboratories. Healthcare is universal and tax-payer funded in the region, and primary care physicians are gatekeepers for all care and responsible for repeat prescriptions. |

# **S2. Cohort definitions**

## **S2.1. Exposures**

The four exposure cohorts were constructed using the logic below. The complete specification, including complete code sets and computer readable JSON and SQL representations are publicly available at the URLs below:

### **S5.1.1. New users of Hydroxychloroquine with prior rheumatoid arthritis**

<https://atlas.ohdsi.org/#/cohortdefinition/173>

Initial Event Cohort

People having any of the following:

* a drug exposure of [OHDSI Cov19] Hydroxychloroquine1
  + for the first time in the person's history
  + with age >= 18

with continuous observation of at least 365 days prior and 0 days after event index date, and limit initial events to: **earliest event per person.**

Inclusion Rules

Inclusion Criteria #1: has rheumatoid arthritis recorded any time on or prior to treatment

Having any of the following criteria:

* at least 1 occurrences of a condition occurrence of [OHDSI Cov19] Rheumatoid arthritis2

where event starts between all days Before and 0 days After index start date

* or at least 1 occurrences of an observation of [OHDSI Cov19] Rheumatoid arthritis2

where event starts between all days Before and 0 days After index start date

Limit qualifying cohort to: **earliest event per person.**

End Date Strategy

Custom Drug Era Exit Criteria

This strategy creates a drug era from the codes found in the specified concept set. If the index event is found within an era, the cohort end date will use the era's end date. Otherwise, it will use the observation period end date that contains the index event.

Use the era end date of [OHDSI Cov19] Hydroxychloroquine1

* allowing 90 days between exposures
* adding 0 days after exposure end

Cohort Collapse Strategy:

Collapse cohort by era with a gap size of 0 days.

### **S5.1.2. New users of sulfasazine with prior rheumatoid arthritis**

<https://atlas.ohdsi.org/#/cohortdefinition/45>

Initial Event Cohort

People having any of the following:

* a drug exposure of [OHDSI Cov19] sulfasalazine2
  + for the first time in the person's history

with continuous observation of at least 365 days prior and 0 days after event index date, and limit initial events to: **earliest event per person.**

Inclusion Rules

Inclusion Criteria #1: has rheumatoid arthritis recorded any time on or prior to treatment

Having all of the following criteria:

* at least 1 occurrences of a condition occurrence of [OHDSI Cov19] Rheumatoid arthritis1

where event starts between all days Before and 0 days After index start date

Limit qualifying cohort to: **earliest event per person.**

End Date Strategy

Custom Drug Era Exit Criteria

This strategy creates a drug era from the codes found in the specified concept set. If the index event is found within an era, the cohort end date will use the era's end date. Otherwise, it will use the observation period end date that contains the index event.

Use the era end date of [OHDSI Cov19] sulfasalazine2

* allowing 90 days between exposures
* adding 0 days after exposure end

Cohort Collapse Strategy:

Collapse cohort by era with a gap size of 0 days.

### **S5.1.3. Users of Hydroxychloroquine + Azithromycin**

<https://atlas.ohdsi.org/#/cohortdefinition/170>

Initial Event Cohort

People having any of the following:

* a drug exposure of Hydroxychloroquine1
  + with age >= 18
* a drug exposure of [OHDSI Covid19] Azithromycin3
  + with age >= 18

with continuous observation of at least 365 days prior and 0 days after event index date, and limit initial events to: **all events per person.**

Inclusion Rules

Inclusion Criteria #1: has both drugs on index

Having all of the following criteria:

* at least 1 occurrences of a drug exposure of Hydroxychloroquine1

where event starts between 30 days Before and 0 days After index start date

* and at least 1 occurrences of a drug exposure of [OHDSI Covid19] Azithromycin3

where event starts between 30 days Before and 0 days After index start date

Inclusion Criteria #2: prior diagnosis of RA

Having any of the following criteria:

* at least 1 occurrences of a condition occurrence of [OHDSI Cov19] Rheumatoid arthritis2

where event starts between all days Before and 0 days After index start date

* or at least 1 occurrences of an observation of [OHDSI Cov19] Rheumatoid arthritis2

where event starts between all days Before and 0 days After index start date

Limit qualifying cohort to: **earliest event per person.**

End Date Strategy

Custom Drug Era Exit Criteria

This strategy creates a drug era from the codes found in the specified concept set. If the index event is found within an era, the cohort end date will use the era's end date. Otherwise, it will use the observation period end date that contains the index event.

Use the era end date of [OHDSI Covid19] Azithromycin3

* allowing 30 days between exposures
* adding 0 days after exposure end

Cohort Collapse Strategy:

Collapse cohort by era with a gap size of 0 days.

### **S5.1.4. Users of Hydroxychloroquine + Amoxicillin**

<https://atlas.ohdsi.org/#/cohortdefinition/171>

Initial Event Cohort

People having any of the following:

* a drug exposure of Hydroxychloroquine1
  + with age >= 18
* a drug exposure of [OHDSI Covid19] Amoxicillin3
  + with age >= 18

with continuous observation of at least 365 days prior and 0 days after event index date, and limit initial events to: **all events per person.**

Inclusion Rules

Inclusion Criteria #1: has both drugs on index

Having all of the following criteria:

* at least 1 occurrences of a drug exposure of Hydroxychloroquine1

where event starts between 30 days Before and 0 days After index start date

* and at least 1 occurrences of a drug exposure of [OHDSI Covid19] Amoxicillin3

where event starts between 30 days Before and 0 days After index start date

Inclusion Criteria #2: Prior diagnosis of RA

Having any of the following criteria:

* at least 1 occurrences of a condition occurrence of [OHDSI Cov19] Rheumatoid arthritis2

where event starts between all days Before and 0 days After index start date

* or at least 1 occurrences of an observation of [OHDSI Cov19] Rheumatoid arthritis2

where event starts between all days Before and 0 days After index start date

Limit qualifying cohort to: **earliest event per person.**

End Date Strategy

Custom Drug Era Exit Criteria

This strategy creates a drug era from the codes found in the specified concept set. If the index event is found within an era, the cohort end date will use the era's end date. Otherwise, it will use the observation period end date that contains the index event.

Use the era end date of [OHDSI Covid19] Amoxicillin3

* allowing 30 days between exposures
* adding 0 days after exposure end

Cohort Collapse Strategy:

Collapse cohort by era with a gap size of 0 days.

## **S2.2. Outcomes**

All safety outcomes for this study were defined as described in the supplementary appendix to Suchard et al (2019): <https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(19)32317-7/fulltext>

# **S3. Negative control outcomes**

|  |  |
| --- | --- |
| **Concept ID** | **Concept Name** |
| 378256 | Abnormal reflex |
| 4092879 | Absent kidney |
| 433753 | Alcohol abuse |
| 321689 | Apnea |
| 78200 | Benign mammary dysplasia |
| 4195873 | Breath smells unpleasant |
| 443792 | Calculus of bile duct |
| 434327 | Cannabis abuse |
| 197318 | Cholesterolosis of gallbladder |
| 432303 | Cocaine abuse |
| 439125 | Complete trisomy 21 syndrome |
| 433270 | Cord entanglement without compression |
| 4311591 | Cramp in limb |
| 441267 | Cystic fibrosis |
| 436233 | Delayed milestone |
| 40486120 | Delay in physiological development |
| 439791 | Emotional upset |
| 374801 | Foreign body in ear |
| 259995 | Foreign body in orifice |
| 196456 | Gallstone |
| 4166231 | Genetic predisposition |
| 434164 | Glycosuria |
| 4163735 | Hemochromatosis |
| 439871 | Hemospermia |
| 4058388 | Hypertrophic scar |
| 435522 | Hypervitaminosis D |
| 443236 | Hypnotic or anxiolytic dependence |
| 4098604 | Hypomagnesemia |
| 435371 | Hypothermia |
| 443447 | Iatrogenic hypotension |
| 374375 | Impacted cerumen |
| 4344500 | Impingement syndrome of shoulder region |
| 440382 | Learning difficulties |
| 435516 | Lipoprotein deficiency disorder |
| 438808 | Mammary duct ectasia |
| 441553 | Myoclonus |
| 4119307 | Neurogenic claudication |
| 4209423 | Nicotine dependence |
| 438130 | Opioid abuse |
| 313601 | Oxygen supply absent |
| 44782778 | Pain disorder with psychological factor |
| 4091513 | Passing flatus |
| 4022076 | Patient dependence on care provider |
| 439971 | Poisoning by anticoagulant |
| 46286594 | Problem related to lifestyle |
| 199876 | Prolapse of female genital organs |
| 4049367 | Psychologic conversion disorder |
| 440068 | Psychosexual dysfunction |
| 436246 | Reduced libido |
| 73754 | Restless legs |
| 4168212 | Restlessness and agitation |
| 138821 | Seborrhea |
| 4198492 | Shoulder joint unstable |
| 25518 | Sickle cell trait |
| 4176908 | Snapping thumb syndrome |
| 4248728 | Snoring |
| 138278 | Sprains and strains of joints and adjacent muscles |
| 4008710 | Stenosis due to any device, implant AND/OR graft |
| 40479573 | Stimulant abuse |
| 40483172 | Stimulant dependence |
| 440233 | Strain of supraspinatus muscle AND/OR tendon |
| 4194160 | Thyroid function tests abnormal |
| 4216708 | Urgent desire for stool |
| 4275889 | Visual hallucinations |
| 4193634 | Worried |

# **S4. Covariate construction**

The following consistently extracted set of baseline patient characteristics will be constructed for input in the PS model. From this large set of typically tens of thousands of covariates, key predictors of exposure classification will be selected for inclusion in the PS model. Note that not all data sources necessarily include data for all covariates. Covariates to be included:

* Demographics (age in 5-year bands, sex, race, ethnicity, index year, index month)
* All conditions occurrence records aggregated to SNOMED clinical finding level during the following lookback windows:
  + in 365 days prior to and including index date
  + in 30 days prior to and including index date
* All drug exposure records aggregated to RxNorm ingredient level and ATC classes during the following lookback windows:
  + in 365 days prior to and including index date
  + in 30 days prior to and including index date
  + persistent exposure that overlaps index date
* All procedure occurrence records during the following lookback windows:
  + in 365 days prior to and including index date
  + in 30 days prior to and including index date
* Measurements (including laboratories) within, above, and below normal range during the following lookback window:
  + in 365 days prior to and including index date
* Device exposure records during the following lookback windows:
  + in 365 days prior to and including index date
  + in 30 days prior to and including index date
* Comorbidity or risk scores including:
  + Charlson
  + DCSI
  + CHADS2
  + CHADS2VASc

# **S5. Exposure cohort counts**

Table here

# **S6. Covariate balance before and after PS stratification**

## **S6.1. HCQ vs SSZ**

### **S6.1.1. AmbEMR**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Before stratification |  |  | After stratification |  |  |
|  | HCQ | SSZ |  | HCQ | SSZ |  |
| Characteristic | % | % | Std. diff | % | % | Std. diff |
| Age group |  |  |  |  |  |  |
| 15-19 | 0.1 | 0.1 | 0.00 | 0.1 | 0.1 | 0.00 |
| 20-24 | 0.7 | 0.6 | 0.01 | 0.7 | 0.6 | 0.01 |
| 25-29 | 1.3 | 1.4 | -0.01 | 1.3 | 1.4 | 0.00 |
| 30-34 | 2.4 | 2.2 | 0.02 | 2.3 | 2.3 | 0.00 |
| 35-39 | 3.5 | 3.7 | -0.01 | 3.5 | 3.4 | 0.01 |
| 40-44 | 5.4 | 5.0 | 0.02 | 5.3 | 5.1 | 0.01 |
| 45-49 | 7.4 | 7.0 | 0.02 | 7.4 | 7.5 | 0.00 |
| 50-54 | 10.4 | 11.0 | -0.02 | 10.5 | 10.5 | 0.00 |
| 55-59 | 13.1 | 13.4 | -0.01 | 13.2 | 12.9 | 0.01 |
| 60-64 | 13.8 | 14.4 | -0.02 | 13.9 | 14.1 | 0.00 |
| 65-69 | 13.7 | 14.2 | -0.01 | 13.8 | 13.7 | 0.00 |
| 70-74 | 13.1 | 13.3 | -0.01 | 13.1 | 13.9 | -0.02 |
| 75-79 | 11.2 | 9.8 | 0.05 | 10.9 | 11.0 | 0.00 |
| 80-84 | 3.9 | 3.9 | 0.00 | 3.9 | 3.7 | 0.01 |
| Gender: female | 79.7 | 74.1 | 0.13 | 78.3 | 78.4 | 0.00 |
| Race |  |  |  |  |  |  |
| race = Asian | 1.4 | 1.5 | -0.02 | 1.4 | 1.3 | 0.00 |
| race = White | 70.9 | 71.7 | -0.02 | 71.1 | 71.3 | 0.00 |
| race = African American | 8.0 | 7.8 | 0.01 | 8.0 | 7.7 | 0.01 |
| Ethnicity |  |  |  |  |  |  |
| ethnicity = Hispanic or Latino | 1.3 | 1.8 | -0.04 | 1.4 | 1.5 | -0.01 |
| ethnicity = Not Hispanic or Latino | 80.3 | 81.0 | -0.02 | 80.5 | 80.3 | 0.00 |
| Medical history: General |  |  |  |  |  |  |
| Acute respiratory disease | 13.5 | 14.2 | -0.02 | 13.7 | 13.8 | 0.00 |
| Attention deficit hyperactivity disorder | 0.6 | 0.4 | 0.02 | 0.6 | 0.5 | 0.01 |
| Chronic liver disease | 1.5 | 1.5 | 0.00 | 1.5 | 1.4 | 0.01 |
| Chronic obstructive lung disease | 7.0 | 7.2 | -0.01 | 7.1 | 6.9 | 0.01 |
| Crohn's disease | 0.4 | 1.1 | -0.08 | 0.5 | 0.6 | -0.02 |
| Dementia | 0.6 | 0.5 | 0.02 | 0.6 | 0.6 | 0.00 |
| Diabetes mellitus | 13.2 | 13.2 | 0.00 | 13.2 | 13.7 | -0.02 |
| Gastroesophageal reflux disease | 15.9 | 14.6 | 0.04 | 15.6 | 15.7 | 0.00 |
| Gastrointestinal hemorrhage | 1.2 | 1.2 | 0.00 | 1.2 | 1.2 | 0.00 |
| Human immunodeficiency virus infection | 0.1 | 0.1 | 0.00 | 0.1 | 0.1 | 0.00 |
| Hyperlipidemia | 29.0 | 28.1 | 0.02 | 28.8 | 29.1 | -0.01 |
| Hypertensive disorder | 38.0 | 37.1 | 0.02 | 37.8 | 38.2 | -0.01 |
| Lesion of liver | 0.9 | 0.8 | 0.01 | 0.9 | 0.8 | 0.01 |
| Obesity | 8.9 | 8.9 | 0.00 | 8.9 | 9.0 | 0.00 |
| Osteoarthritis | 25.5 | 27.1 | -0.04 | 25.8 | 25.2 | 0.01 |
| Pneumonia | 3.1 | 3.4 | -0.01 | 3.2 | 3.1 | 0.01 |
| Psoriasis | 1.5 | 3.2 | -0.11 | 1.7 | 2.0 | -0.02 |
| Renal impairment | 5.3 | 4.8 | 0.02 | 5.2 | 5.3 | -0.01 |
| Rheumatoid arthritis | 84.0 | 82.2 | 0.05 | 83.6 | 84.4 | -0.02 |
| Ulcerative colitis | 0.3 | 1.2 | -0.10 | 0.4 | 0.6 | -0.03 |
| Urinary tract infectious disease | 6.0 | 5.2 | 0.04 | 5.8 | 5.5 | 0.01 |
| Viral hepatitis C | 1.0 | 1.0 | 0.00 | 1.0 | 0.9 | 0.01 |
| Visual system disorder | 8.6 | 8.8 | 0.00 | 8.6 | 8.5 | 0.00 |
| Medical history: Cardiovascular disease |  |  |  |  |  |  |
| Atrial fibrillation | 3.3 | 3.1 | 0.01 | 3.2 | 3.2 | 0.00 |
| Cerebrovascular disease | 3.1 | 2.8 | 0.02 | 3.1 | 3.1 | 0.00 |
| Coronary arteriosclerosis | 5.7 | 5.6 | 0.00 | 5.7 | 5.6 | 0.00 |
| Heart disease | 15.9 | 14.6 | 0.04 | 15.6 | 15.6 | 0.00 |
| Heart failure | 2.6 | 2.3 | 0.02 | 2.6 | 2.4 | 0.01 |
| Ischemic heart disease | 1.7 | 1.6 | 0.01 | 1.7 | 1.5 | 0.02 |
| Pulmonary embolism | 0.8 | 0.7 | 0.01 | 0.8 | 0.7 | 0.01 |
| Venous thrombosis | 1.3 | 1.2 | 0.01 | 1.3 | 1.4 | -0.01 |
| Medical history: Neoplasms |  |  |  |  |  |  |
| Hematologic neoplasm | 0.4 | 0.3 | 0.02 | 0.4 | 0.4 | 0.01 |
| Malignant lymphoma | 0.4 | 0.5 | -0.01 | 0.4 | 0.6 | -0.03 |
| Malignant neoplasm of anorectum | 0.1 | 0.1 | -0.01 | 0.1 | 0.1 | 0.00 |
| Malignant neoplastic disease | 6.9 | 6.6 | 0.01 | 6.8 | 7.0 | -0.01 |
| Malignant tumor of breast | 1.5 | 1.4 | 0.01 | 1.4 | 1.6 | -0.01 |
| Malignant tumor of colon | 0.3 | 0.3 | 0.00 | 0.3 | 0.3 | -0.01 |
| Malignant tumor of lung | 0.3 | 0.4 | -0.02 | 0.3 | 0.3 | -0.01 |
| Malignant tumor of urinary bladder | 0.2 | 0.3 | -0.01 | 0.2 | 0.2 | 0.00 |
| Primary malignant neoplasm of prostate | 0.4 | 0.3 | 0.00 | 0.4 | 0.3 | 0.01 |
| Medication use |  |  |  |  |  |  |
| Agents acting on the renin-angiotensin system | 33.2 | 33.6 | -0.01 | 33.3 | 33.6 | -0.01 |
| Antibacterials for systemic use | 24.7 | 25.3 | -0.01 | 24.9 | 24.5 | 0.01 |
| Antidepressants | 36.1 | 34.9 | 0.02 | 35.7 | 35.7 | 0.00 |
| Antiepileptics | 24.0 | 24.1 | 0.00 | 24.0 | 24.0 | 0.00 |
| Antiinflammatory and antirheumatic products | 42.8 | 44.4 | -0.03 | 43.1 | 43.4 | 0.00 |
| Antineoplastic agents | 35.9 | 41.4 | -0.11 | 37.3 | 37.8 | -0.01 |
| Antipsoriatics | 0.6 | 0.7 | 0.00 | 0.6 | 0.7 | 0.00 |
| Antithrombotic agents | 25.2 | 23.5 | 0.04 | 24.9 | 25.2 | -0.01 |
| Beta blocking agents | 25.2 | 25.1 | 0.00 | 25.2 | 25.8 | -0.02 |
| Calcium channel blockers | 17.5 | 17.7 | 0.00 | 17.5 | 17.7 | 0.00 |
| Diuretics | 30.6 | 30.0 | 0.01 | 30.5 | 31.2 | -0.01 |
| Drugs for obstructive airway diseases | 30.9 | 30.0 | 0.02 | 30.8 | 31.0 | 0.00 |
| Drugs used in diabetes | 14.2 | 14.3 | 0.00 | 14.3 | 14.8 | -0.01 |
| Immunosuppressants | 49.4 | 61.2 | -0.24 | 52.2 | 52.1 | 0.00 |
| Lipid modifying agents | 33.2 | 33.7 | -0.01 | 33.3 | 33.5 | 0.00 |
| Opioids | 28.4 | 30.7 | -0.05 | 28.9 | 28.8 | 0.00 |
| Psycholeptics | 26.3 | 25.6 | 0.02 | 26.1 | 26.1 | 0.00 |
| Psychostimulants, agents used for adhd and nootropics | 4.0 | 3.8 | 0.01 | 4.0 | 4.0 | 0.00 |

### **S6.1.2. CCAE**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Before stratification |  |  | After stratification |  |  |
|  | HCQ | SSZ |  | HCQ | SSZ |  |
| Characteristic | % | % | Std. diff | % | % | Std. diff |
| Age group |  |  |  |  |  |  |
| 20-24 | 1.9 | 1.9 | 0.00 | 1.8 | 2.0 | -0.01 |
| 25-29 | 2.6 | 2.6 | 0.00 | 2.5 | 2.7 | -0.01 |
| 30-34 | 4.5 | 4.6 | 0.00 | 4.5 | 4.4 | 0.00 |
| 40-44 | 9.8 | 9.5 | 0.01 | 9.7 | 9.5 | 0.01 |
| 45-49 | 13.7 | 12.9 | 0.02 | 13.6 | 13.4 | 0.00 |
| 50-54 | 18.2 | 18.1 | 0.00 | 18.2 | 18.0 | 0.01 |
| 55-59 | 20.6 | 21.0 | -0.01 | 20.8 | 20.8 | 0.00 |
| 60-64 | 19.0 | 19.8 | -0.02 | 19.4 | 19.8 | -0.01 |
| 65-69 | 1.8 | 1.7 | 0.00 | 1.8 | 1.6 | 0.01 |
| Gender: female | 82.0 | 74.3 | 0.19 | 80.1 | 79.7 | 0.01 |
| Medical history: General |  |  |  |  |  |  |
| Acute respiratory disease | 35.5 | 34.4 | 0.02 | 35.1 | 34.8 | 0.01 |
| Chronic liver disease | 3.2 | 3.2 | 0.00 | 3.2 | 3.3 | 0.00 |
| Chronic obstructive lung disease | 4.2 | 4.5 | -0.01 | 4.3 | 4.5 | -0.01 |
| Crohn's disease | 0.6 | 1.8 | -0.12 | 0.7 | 1.1 | -0.04 |
| Dementia | 0.2 | 0.2 | 0.01 | 0.2 | 0.2 | 0.00 |
| Depressive disorder | 13.4 | 13.5 | 0.00 | 13.3 | 13.5 | 0.00 |
| Diabetes mellitus | 13.5 | 13.4 | 0.00 | 13.6 | 13.8 | -0.01 |
| Gastroesophageal reflux disease | 13.7 | 13.5 | 0.01 | 13.6 | 13.5 | 0.00 |
| Gastrointestinal hemorrhage | 2.9 | 3.4 | -0.03 | 3.0 | 3.2 | -0.01 |
| Human immunodeficiency virus infection | 0.1 | 0.2 | -0.01 | 0.1 | 0.1 | 0.00 |
| Hyperlipidemia | 31.5 | 30.5 | 0.02 | 31.2 | 31.4 | 0.00 |
| Hypertensive disorder | 34.7 | 34.9 | 0.00 | 34.8 | 35.0 | 0.00 |
| Lesion of liver | 0.9 | 0.8 | 0.01 | 0.9 | 0.8 | 0.00 |
| Obesity | 9.3 | 9.1 | 0.00 | 9.2 | 9.5 | -0.01 |
| Osteoarthritis | 43.4 | 44.4 | -0.02 | 43.5 | 44.2 | -0.01 |
| Pneumonia | 4.0 | 3.9 | 0.00 | 4.0 | 4.0 | 0.00 |
| Psoriasis | 3.0 | 8.9 | -0.25 | 3.8 | 5.2 | -0.07 |
| Renal impairment | 3.1 | 2.8 | 0.02 | 3.0 | 2.8 | 0.01 |
| Rheumatoid arthritis | 84.2 | 85.7 | -0.04 | 84.9 | 85.3 | -0.01 |
| Schizophrenia | 0.1 | 0.1 | -0.01 | 0.1 | 0.1 | -0.01 |
| Ulcerative colitis | 0.6 | 1.9 | -0.12 | 0.7 | 1.0 | -0.04 |
| Urinary tract infectious disease | 11.9 | 10.8 | 0.03 | 11.6 | 11.5 | 0.00 |
| Viral hepatitis C | 1.1 | 1.0 | 0.01 | 1.1 | 1.0 | 0.01 |
| Visual system disorder | 25.7 | 26.2 | -0.01 | 25.7 | 25.9 | 0.00 |
| Medical history: Cardiovascular disease |  |  |  |  |  |  |
| Atrial fibrillation | 1.4 | 1.3 | 0.02 | 1.4 | 1.3 | 0.01 |
| Cerebrovascular disease | 2.8 | 2.6 | 0.01 | 2.8 | 2.9 | -0.01 |
| Heart disease | 15.7 | 15.0 | 0.02 | 15.5 | 15.4 | 0.00 |
| Heart failure | 1.9 | 2.0 | 0.00 | 1.9 | 2.0 | 0.00 |
| Ischemic heart disease | 2.9 | 3.1 | -0.01 | 3.0 | 3.1 | -0.01 |
| Peripheral vascular disease | 1.6 | 1.5 | 0.01 | 1.5 | 1.6 | -0.01 |
| Pulmonary embolism | 0.8 | 0.5 | 0.03 | 0.8 | 0.6 | 0.02 |
| Medical history: Neoplasms |  |  |  |  |  |  |
| Hematologic neoplasm | 1.0 | 1.0 | 0.00 | 1.0 | 1.0 | 0.00 |
| Malignant lymphoma | 0.5 | 0.5 | 0.00 | 0.5 | 0.4 | 0.02 |
| Malignant neoplasm of anorectum | 0.1 | 0.1 | 0.00 | 0.1 | 0.1 | 0.00 |
| Malignant tumor of breast | 1.8 | 1.6 | 0.02 | 1.7 | 1.7 | 0.00 |
| Malignant tumor of colon | 0.2 | 0.2 | 0.00 | 0.2 | 0.2 | 0.00 |
| Malignant tumor of lung | 0.1 | 0.2 | -0.01 | 0.2 | 0.1 | 0.00 |
| Primary malignant neoplasm of prostate | 0.4 | 0.4 | -0.01 | 0.4 | 0.4 | 0.00 |
| Medication use |  |  |  |  |  |  |
| Agents acting on the renin-angiotensin system | 24.3 | 24.9 | -0.01 | 24.5 | 24.6 | 0.00 |
| Antibacterials for systemic use | 43.8 | 44.3 | -0.01 | 43.8 | 44.0 | 0.00 |
| Antidepressants | 36.4 | 36.5 | 0.00 | 36.3 | 36.5 | 0.00 |
| Antiepileptics | 20.3 | 21.0 | -0.02 | 20.4 | 20.2 | 0.00 |
| Antiinflammatory and antirheumatic products | 55.3 | 57.4 | -0.04 | 55.8 | 56.7 | -0.02 |
| Antineoplastic agents | 30.7 | 37.8 | -0.15 | 33.0 | 33.1 | 0.00 |
| Antipsoriatics | 0.7 | 1.2 | -0.06 | 0.7 | 1.0 | -0.03 |
| Antithrombotic agents | 7.4 | 7.3 | 0.01 | 7.4 | 7.3 | 0.00 |
| Beta blocking agents | 15.8 | 16.2 | -0.01 | 15.9 | 16.2 | -0.01 |
| Calcium channel blockers | 11.7 | 11.5 | 0.01 | 11.7 | 11.8 | 0.00 |
| Drugs for acid related disorders | 32.3 | 33.6 | -0.03 | 32.6 | 32.6 | 0.00 |
| Drugs for obstructive airway diseases | 29.7 | 29.3 | 0.01 | 29.5 | 29.5 | 0.00 |
| Drugs used in diabetes | 10.4 | 10.5 | 0.00 | 10.5 | 10.8 | -0.01 |
| Immunosuppressants | 39.6 | 53.0 | -0.27 | 43.4 | 43.6 | 0.00 |
| Lipid modifying agents | 22.6 | 23.5 | -0.02 | 22.8 | 23.2 | -0.01 |
| Opioids | 38.5 | 40.7 | -0.05 | 39.0 | 39.3 | -0.01 |
| Psycholeptics | 33.6 | 33.7 | 0.00 | 33.4 | 33.3 | 0.00 |
| Psychostimulants, agents used for adhd and nootropics | 5.9 | 5.6 | 0.01 | 5.8 | 5.7 | 0.01 |

### **S6.1.3. CPRD**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Before stratification |  |  | After stratification |  |  |
|  | HCQ | SSZ |  | HCQ | SSZ |  |
| Characteristic | % | % | Std. diff | % | % | Std. diff |
| Age group |  |  |  |  |  |  |
| 15-19 | 0.3 | 0.2 | 0.01 | 0.3 | 0.2 | 0.00 |
| 20-24 | 0.8 | 1.0 | -0.02 | 0.9 | 0.9 | -0.01 |
| 25-29 | 1.2 | 1.7 | -0.04 | 1.4 | 1.6 | -0.02 |
| 30-34 | 2.7 | 3.1 | -0.02 | 3.0 | 3.0 | 0.00 |
| 35-39 | 4.6 | 4.6 | 0.00 | 4.7 | 4.6 | 0.01 |
| 40-44 | 5.6 | 6.6 | -0.04 | 6.2 | 6.4 | 0.00 |
| 45-49 | 8.9 | 8.1 | 0.03 | 8.6 | 8.5 | 0.00 |
| 50-54 | 11.4 | 10.8 | 0.02 | 11.2 | 10.9 | 0.01 |
| 55-59 | 13.2 | 12.6 | 0.02 | 13.4 | 12.8 | 0.02 |
| 60-64 | 13.1 | 13.2 | 0.00 | 12.8 | 13.0 | -0.01 |
| 65-69 | 12.6 | 12.7 | 0.00 | 12.6 | 12.7 | 0.00 |
| 70-74 | 10.8 | 11.6 | -0.02 | 11.2 | 11.2 | 0.00 |
| 80-84 | 4.5 | 4.3 | 0.01 | 4.2 | 4.4 | -0.01 |
| 85-89 | 1.6 | 1.3 | 0.03 | 1.3 | 1.4 | -0.01 |
| 90-94 | 0.3 | 0.2 | 0.03 | 0.3 | 0.2 | 0.03 |
| Medical history: General |  |  |  |  |  |  |
| Acute respiratory disease | 9.2 | 9.1 | 0.00 | 9.4 | 9.3 | 0.01 |
| Chronic obstructive lung disease | 2.3 | 2.0 | 0.02 | 2.2 | 2.0 | 0.01 |
| Crohn's disease | <0.1 | 0.1 | -0.03 | 0.1 | 0.1 | -0.01 |
| Depressive disorder | 2.7 | 3.2 | -0.03 | 3.0 | 3.1 | 0.00 |
| Diabetes mellitus | 2.2 | 2.1 | 0.01 | 2.1 | 2.2 | -0.01 |
| Gastroesophageal reflux disease | 0.5 | 0.4 | 0.02 | 0.4 | 0.4 | 0.00 |
| Gastrointestinal hemorrhage | 1.0 | 1.4 | -0.04 | 1.2 | 1.4 | -0.02 |
| Hyperlipidemia | 1.2 | 1.0 | 0.02 | 1.2 | 1.0 | 0.01 |
| Hypertensive disorder | 3.0 | 3.9 | -0.05 | 3.2 | 3.6 | -0.02 |
| Lesion of liver | 0.1 | 0.1 | 0.01 | 0.1 | 0.1 | 0.01 |
| Obesity | 0.4 | 0.5 | -0.01 | 0.4 | 0.5 | -0.01 |
| Osteoarthritis | 7.6 | 10.4 | -0.10 | 8.6 | 8.9 | -0.01 |
| Pneumonia | 0.8 | 0.6 | 0.03 | 0.9 | 0.6 | 0.03 |
| Psoriasis | 0.7 | 1.9 | -0.10 | 1.2 | 1.5 | -0.03 |
| Renal impairment | 2.3 | 1.8 | 0.03 | 1.9 | 2.2 | -0.02 |
| Rheumatoid arthritis | 61.3 | 72.3 | -0.24 | 67.4 | 66.3 | 0.02 |
| Visual system disorder | 7.0 | 6.9 | 0.00 | 6.7 | 6.9 | -0.01 |
| Medical history: Cardiovascular disease |  |  |  |  |  |  |
| Atrial fibrillation | 0.7 | 0.7 | 0.00 | 0.8 | 0.7 | 0.02 |
| Cerebrovascular disease | 0.4 | 0.8 | -0.05 | 0.5 | 0.7 | -0.03 |
| Coronary arteriosclerosis | 0.1 | 0.1 | 0.00 | 0.1 | 0.1 | 0.00 |
| Heart disease | 3.0 | 3.4 | -0.02 | 3.4 | 3.1 | 0.01 |
| Heart failure | 0.5 | 0.7 | -0.02 | 0.7 | 0.6 | 0.01 |
| Ischemic heart disease | 1.0 | 1.5 | -0.04 | 1.2 | 1.3 | -0.01 |
| Peripheral vascular disease | 0.2 | 0.2 | 0.01 | 0.3 | 0.2 | 0.02 |
| Pulmonary embolism | 0.2 | 0.2 | -0.01 | 0.2 | 0.2 | -0.02 |
| Venous thrombosis | 0.8 | 1.0 | -0.01 | 0.9 | 1.0 | 0.00 |
| Medical history: Neoplasms |  |  |  |  |  |  |
| Malignant neoplastic disease | 1.3 | 1.0 | 0.02 | 1.1 | 1.0 | 0.01 |
| Malignant tumor of breast | 0.1 | 0.1 | 0.00 | 0.1 | 0.1 | -0.01 |
| Medication use |  |  |  |  |  |  |
| Agents acting on the renin-angiotensin system | 22.0 | 16.8 | 0.13 | 19.4 | 19.4 | 0.00 |
| Antibacterials for systemic use | 37.3 | 35.0 | 0.05 | 35.7 | 36.2 | -0.01 |
| Antidepressants | 26.6 | 22.6 | 0.09 | 25.0 | 24.9 | 0.00 |
| Antiepileptics | 6.5 | 4.3 | 0.10 | 5.4 | 5.2 | 0.01 |
| Antiinflammatory and antirheumatic products | 60.5 | 67.7 | -0.15 | 64.3 | 63.8 | 0.01 |
| Antineoplastic agents | 51.4 | 28.6 | 0.48 | 39.3 | 40.8 | -0.03 |
| Antipsoriatics | 0.7 | 1.3 | -0.06 | 0.9 | 1.2 | -0.02 |
| Antithrombotic agents | 17.9 | 16.7 | 0.03 | 17.3 | 17.2 | 0.00 |
| Beta blocking agents | 14.4 | 13.5 | 0.03 | 14.4 | 13.9 | 0.02 |
| Calcium channel blockers | 15.5 | 12.1 | 0.10 | 13.4 | 13.6 | 0.00 |
| Diuretics | 19.0 | 20.9 | -0.05 | 20.0 | 20.1 | 0.00 |
| Drugs for acid related disorders | 58.3 | 51.0 | 0.15 | 54.1 | 54.6 | -0.01 |
| Drugs used in diabetes | 7.1 | 5.8 | 0.05 | 6.2 | 6.6 | -0.02 |
| Immunosuppressants | 55.2 | 30.0 | 0.53 | 42.2 | 43.0 | -0.02 |
| Lipid modifying agents | 23.0 | 17.1 | 0.15 | 19.5 | 19.8 | -0.01 |
| Opioids | 36.3 | 41.1 | -0.10 | 39.0 | 38.9 | 0.00 |
| Psycholeptics | 16.5 | 16.4 | 0.00 | 16.7 | 16.5 | 0.00 |
| Psychostimulants, agents used for adhd and nootropics | 0.1 | 0.1 | 0.01 | 0.1 | 0.1 | 0.01 |

### **S6.1.4. DAGermany**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Before stratification |  |  | After stratification |  |  |
|  | HCQ | SSZ |  | HCQ | SSZ |  |
| Characteristic | % | % | Std. diff | % | % | Std. diff |
| Age group |  |  |  |  |  |  |
| 15-19 | 0.3 | 0.5 | -0.03 | 0.3 | 0.5 | -0.03 |
| 20-24 | 1.1 | 1.3 | -0.02 | 1.1 | 1.2 | -0.01 |
| 25-29 | 1.9 | 2.4 | -0.04 | 2.0 | 2.4 | -0.03 |
| 30-34 | 2.4 | 3.5 | -0.07 | 2.9 | 3.0 | -0.01 |
| 35-39 | 4.0 | 4.1 | -0.01 | 3.9 | 4.1 | -0.01 |
| 40-44 | 5.8 | 6.6 | -0.03 | 6.1 | 6.3 | -0.01 |
| 50-54 | 12.0 | 12.7 | -0.02 | 12.7 | 12.5 | 0.01 |
| 55-59 | 14.2 | 14.8 | -0.02 | 14.8 | 14.9 | 0.00 |
| 60-64 | 13.2 | 12.1 | 0.03 | 12.3 | 12.4 | 0.00 |
| 65-69 | 11.4 | 10.6 | 0.03 | 11.2 | 10.6 | 0.02 |
| 70-74 | 10.2 | 9.5 | 0.02 | 9.8 | 9.7 | 0.00 |
| 75-79 | 9.1 | 7.5 | 0.06 | 8.2 | 8.1 | 0.01 |
| 80-84 | 4.4 | 3.9 | 0.02 | 4.2 | 4.0 | 0.01 |
| 85-89 | 1.4 | 1.0 | 0.04 | 1.2 | 1.0 | 0.02 |
| 90-94 | 0.2 | 0.2 | 0.00 | 0.2 | 0.2 | 0.00 |
| Gender: female | 81.4 | 72.5 | 0.21 | 76.0 | 77.2 | -0.03 |
| Medical history: General |  |  |  |  |  |  |
| Acute respiratory disease | 11.9 | 12.6 | -0.02 | 12.2 | 12.0 | 0.01 |
| Attention deficit hyperactivity disorder | <0.1 | 0.1 | -0.01 | <0.1 | <0.1 | 0.02 |
| Chronic liver disease | 0.6 | 0.3 | 0.05 | 0.6 | 0.3 | 0.05 |
| Chronic obstructive lung disease | 3.4 | 4.0 | -0.03 | 3.4 | 3.7 | -0.02 |
| Crohn's disease | 0.2 | 1.5 | -0.14 | 0.5 | 1.0 | -0.06 |
| Dementia | 0.6 | 0.5 | 0.01 | 0.6 | 0.5 | 0.01 |
| Depressive disorder | 8.3 | 8.3 | 0.00 | 8.2 | 8.0 | 0.01 |
| Diabetes mellitus | 6.9 | 7.6 | -0.03 | 7.3 | 7.1 | 0.01 |
| Gastroesophageal reflux disease | 1.9 | 2.0 | -0.01 | 1.9 | 2.0 | 0.00 |
| Gastrointestinal hemorrhage | 0.4 | 0.6 | -0.03 | 0.5 | 0.6 | -0.02 |
| Hyperlipidemia | 7.1 | 8.4 | -0.05 | 8.0 | 7.7 | 0.01 |
| Hypertensive disorder | 18.5 | 19.2 | -0.02 | 19.0 | 18.3 | 0.02 |
| Lesion of liver | 0.5 | 0.3 | 0.03 | 0.4 | 0.3 | 0.02 |
| Obesity | 2.2 | 2.4 | -0.01 | 2.2 | 2.2 | 0.00 |
| Osteoarthritis | 11.4 | 13.2 | -0.06 | 12.4 | 12.1 | 0.01 |
| Pneumonia | 1.9 | 1.5 | 0.03 | 2.0 | 1.6 | 0.04 |
| Psoriasis | 2.3 | 4.4 | -0.12 | 3.7 | 3.5 | 0.01 |
| Renal impairment | 2.6 | 2.3 | 0.02 | 2.4 | 2.4 | 0.00 |
| Rheumatoid arthritis | 46.4 | 54.7 | -0.17 | 52.4 | 50.1 | 0.04 |
| Schizophrenia | <0.1 | 0.1 | -0.03 | <0.1 | 0.1 | -0.01 |
| Ulcerative colitis | 0.2 | 1.6 | -0.16 | 0.4 | 1.1 | -0.08 |
| Urinary tract infectious disease | 4.0 | 4.1 | -0.01 | 4.0 | 3.9 | 0.00 |
| Viral hepatitis C | 0.3 | 0.1 | 0.04 | 0.3 | 0.1 | 0.04 |
| Visual system disorder | 5.8 | 5.6 | 0.01 | 5.6 | 5.5 | 0.01 |
| Medical history: Cardiovascular disease |  |  |  |  |  |  |
| Atrial fibrillation | 0.8 | 0.8 | 0.00 | 0.8 | 0.7 | 0.00 |
| Cerebrovascular disease | 1.4 | 1.8 | -0.03 | 1.4 | 1.6 | -0.02 |
| Coronary arteriosclerosis | 1.0 | 1.1 | -0.01 | 1.1 | 1.1 | 0.00 |
| Heart disease | 10.5 | 11.4 | -0.03 | 10.6 | 10.6 | 0.00 |
| Heart failure | 2.1 | 2.6 | -0.04 | 2.0 | 2.4 | -0.03 |
| Ischemic heart disease | 4.3 | 5.2 | -0.04 | 4.7 | 4.6 | 0.00 |
| Peripheral vascular disease | 1.0 | 1.0 | 0.00 | 0.9 | 0.9 | 0.00 |
| Pulmonary embolism | 0.6 | 0.3 | 0.04 | 0.6 | 0.4 | 0.03 |
| Venous thrombosis | 1.3 | 1.4 | -0.02 | 1.5 | 1.5 | 0.00 |
| Medical history: Neoplasms |  |  |  |  |  |  |
| Hematologic neoplasm | 0.3 | 0.2 | 0.03 | 0.3 | 0.2 | 0.02 |
| Malignant lymphoma | 0.2 | 0.2 | 0.01 | 0.2 | 0.1 | 0.01 |
| Malignant neoplasm of anorectum | 0.2 | 0.2 | 0.01 | 0.1 | 0.1 | 0.00 |
| Malignant neoplastic disease | 3.4 | 3.2 | 0.01 | 3.2 | 3.2 | 0.00 |
| Malignant tumor of breast | 0.7 | 0.6 | 0.01 | 0.6 | 0.6 | 0.00 |
| Malignant tumor of colon | 0.3 | 0.1 | 0.03 | 0.3 | 0.1 | 0.04 |
| Malignant tumor of lung | <0.1 | <0.1 | 0.02 | <0.1 | <0.1 | 0.00 |
| Malignant tumor of urinary bladder | <0.1 | 0.2 | -0.05 | <0.1 | 0.2 | -0.05 |
| Primary malignant neoplasm of prostate | 0.2 | 0.3 | -0.03 | 0.2 | 0.2 | -0.02 |
| Medication use |  |  |  |  |  |  |
| Agents acting on the renin-angiotensin system | 16.7 | 17.1 | -0.01 | 16.8 | 16.5 | 0.01 |
| Antibacterials for systemic use | 12.7 | 14.7 | -0.06 | 13.5 | 13.7 | 0.00 |
| Antiepileptics | 3.0 | 2.3 | 0.04 | 2.6 | 2.2 | 0.02 |
| Antiinflammatory and antirheumatic products | 33.3 | 36.1 | -0.06 | 35.4 | 34.7 | 0.01 |
| Antineoplastic agents | 31.8 | 26.8 | 0.11 | 29.4 | 30.4 | -0.02 |
| Antipsoriatics | 0.2 | 0.3 | -0.01 | 0.2 | 0.2 | 0.00 |
| Antithrombotic agents | 10.1 | 9.9 | 0.01 | 9.6 | 9.4 | 0.01 |
| Beta blocking agents | 13.7 | 13.3 | 0.01 | 13.0 | 13.1 | 0.00 |
| Calcium channel blockers | 7.6 | 7.7 | 0.00 | 7.6 | 7.3 | 0.01 |
| Diuretics | 13.9 | 14.6 | -0.02 | 14.5 | 13.7 | 0.02 |
| Drugs for acid related disorders | 32.1 | 32.7 | -0.01 | 32.3 | 32.5 | 0.00 |
| Drugs for obstructive airway diseases | 7.0 | 7.7 | -0.03 | 7.4 | 7.2 | 0.01 |
| Drugs used in diabetes | 4.4 | 4.8 | -0.02 | 4.7 | 4.5 | 0.01 |
| Immunosuppressants | 40.7 | 35.0 | 0.12 | 38.9 | 38.5 | 0.01 |
| Lipid modifying agents | 7.3 | 9.2 | -0.07 | 8.2 | 8.2 | 0.00 |
| Opioids | 12.5 | 12.9 | -0.01 | 12.2 | 12.3 | 0.00 |
| Psycholeptics | 4.8 | 6.0 | -0.05 | 4.8 | 5.3 | -0.02 |
| Psychostimulants, agents used for adhd and nootropics | 0.2 | 0.4 | -0.03 | 0.2 | 0.3 | -0.03 |

### **S6.1.5. IMRD**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Before stratification |  |  | After stratification |  |  |
|  | HCQ | SSZ |  | HCQ | SSZ |  |
| Characteristic | % | % | Std. diff | % | % | Std. diff |
| Age group |  |  |  |  |  |  |
| 15-19 | 0.2 | 0.2 | 0.02 | 0.2 | 0.2 | 0.01 |
| 20-24 | 0.8 | 1.0 | -0.03 | 0.8 | 1.0 | -0.02 |
| 25-29 | 1.2 | 1.6 | -0.03 | 1.4 | 1.6 | -0.01 |
| 30-34 | 2.8 | 3.2 | -0.02 | 2.9 | 3.1 | -0.01 |
| 35-39 | 4.8 | 5.0 | -0.01 | 5.0 | 4.8 | 0.01 |
| 40-44 | 6.0 | 6.1 | 0.00 | 6.3 | 6.0 | 0.01 |
| 45-49 | 8.7 | 7.8 | 0.03 | 8.4 | 8.5 | 0.00 |
| 50-54 | 11.3 | 10.8 | 0.02 | 11.2 | 11.0 | 0.01 |
| 55-59 | 13.0 | 12.4 | 0.02 | 12.7 | 12.4 | 0.01 |
| 60-64 | 13.2 | 13.8 | -0.02 | 13.5 | 13.5 | 0.00 |
| 65-69 | 13.0 | 12.8 | 0.01 | 12.9 | 13.0 | 0.00 |
| 70-74 | 11.0 | 11.4 | -0.01 | 11.2 | 11.2 | 0.00 |
| 75-79 | 7.7 | 8.3 | -0.02 | 7.8 | 8.0 | 0.00 |
| 80-84 | 4.4 | 4.1 | 0.02 | 4.1 | 4.2 | 0.00 |
| 85-89 | 1.5 | 1.3 | 0.02 | 1.3 | 1.4 | -0.01 |
| 90-94 | 0.3 | 0.2 | 0.02 | 0.2 | 0.2 | 0.00 |
| Gender: female | 73.2 | 68.0 | 0.11 | 70.7 | 71.0 | 0.00 |
| Race |  |  |  |  |  |  |
| race = Asian | 0.1 | 0.1 | 0.02 | 0.1 | 0.1 | 0.00 |
| race = White | 29.8 | 25.8 | 0.09 | 27.4 | 27.6 | 0.00 |
| race = Asian Indian | 0.7 | 0.4 | 0.04 | 0.6 | 0.5 | 0.02 |
| race = Bangladeshi | 0.1 | <0.1 | 0.02 | <0.1 | <0.1 | 0.02 |
| race = Chinese | 0.1 | <0.1 | 0.03 | 0.1 | <0.1 | 0.03 |
| race = Pakistani | 0.3 | 0.2 | 0.03 | 0.3 | 0.2 | 0.03 |
| race = Black | 0.4 | 0.2 | 0.03 | 0.3 | 0.2 | 0.02 |
| race = African | 0.2 | <0.1 | 0.05 | 0.2 | <0.1 | 0.04 |
| race = European | 0.1 | <0.1 | 0.02 | 0.1 | <0.1 | 0.02 |
| Medical history: General |  |  |  |  |  |  |
| Acute respiratory disease | 9.2 | 9.3 | 0.00 | 9.2 | 9.1 | 0.00 |
| Chronic liver disease | 0.1 | 0.1 | 0.00 | <0.1 | <0.1 | 0.00 |
| Chronic obstructive lung disease | 2.1 | 2.5 | -0.02 | 2.2 | 2.3 | -0.01 |
| Crohn's disease | <0.1 | 0.2 | -0.05 | <0.1 | 0.1 | -0.04 |
| Dementia | 0.2 | 0.1 | 0.03 | 0.1 | 0.1 | 0.02 |
| Depressive disorder | 2.6 | 2.9 | -0.02 | 2.9 | 2.7 | 0.01 |
| Diabetes mellitus | 2.3 | 2.2 | 0.01 | 2.2 | 2.1 | 0.01 |
| Gastroesophageal reflux disease | 0.3 | 0.6 | -0.03 | 0.4 | 0.6 | -0.03 |
| Gastrointestinal hemorrhage | 0.9 | 1.3 | -0.04 | 1.0 | 1.1 | -0.01 |
| Hyperlipidemia | 1.1 | 1.3 | -0.02 | 1.1 | 1.2 | 0.00 |
| Hypertensive disorder | 3.1 | 3.7 | -0.03 | 3.2 | 3.3 | 0.00 |
| Lesion of liver | 0.1 | 0.1 | 0.01 | 0.1 | <0.1 | 0.01 |
| Obesity | 0.3 | 0.5 | -0.03 | 0.4 | 0.6 | -0.03 |
| Osteoarthritis | 7.5 | 9.4 | -0.07 | 8.1 | 8.2 | 0.00 |
| Pneumonia | 0.7 | 0.6 | 0.00 | 0.7 | 0.7 | 0.00 |
| Psoriasis | 0.8 | 2.2 | -0.12 | 1.3 | 1.6 | -0.02 |
| Rheumatoid arthritis | 61.4 | 69.3 | -0.17 | 65.6 | 63.7 | 0.04 |
| Schizophrenia | <0.1 | <0.1 | 0.01 | <0.1 | <0.1 | 0.02 |
| Ulcerative colitis | <0.1 | <0.1 | -0.01 | <0.1 | <0.1 | -0.01 |
| Urinary tract infectious disease | 3.1 | 2.9 | 0.01 | 3.1 | 3.0 | 0.01 |
| Visual system disorder | 6.6 | 7.0 | -0.02 | 6.6 | 6.8 | 0.00 |
| Medical history: Cardiovascular disease |  |  |  |  |  |  |
| Atrial fibrillation | 0.7 | 0.7 | 0.00 | 0.7 | 0.6 | 0.01 |
| Cerebrovascular disease | 0.5 | 0.7 | -0.03 | 0.5 | 0.7 | -0.02 |
| Coronary arteriosclerosis | 0.1 | 0.1 | 0.01 | 0.1 | 0.1 | 0.02 |
| Heart disease | 2.7 | 2.9 | -0.01 | 2.8 | 2.6 | 0.01 |
| Heart failure | 0.4 | 0.4 | -0.01 | 0.4 | 0.4 | 0.01 |
| Ischemic heart disease | 0.8 | 1.2 | -0.04 | 1.0 | 1.0 | 0.00 |
| Peripheral vascular disease | 0.2 | 0.2 | 0.01 | 0.3 | 0.2 | 0.02 |
| Pulmonary embolism | 0.2 | 0.2 | -0.01 | 0.2 | 0.3 | -0.02 |
| Venous thrombosis | 0.8 | 1.1 | -0.03 | 0.8 | 1.1 | -0.02 |
| Medical history: Neoplasms |  |  |  |  |  |  |
| Hematologic neoplasm | 0.1 | 0.1 | 0.01 | 0.1 | <0.1 | 0.02 |
| Malignant neoplasm of anorectum | <0.1 | <0.1 | 0.02 | <0.1 | <0.1 | 0.02 |
| Malignant neoplastic disease | 1.3 | 1.1 | 0.02 | 1.2 | 1.0 | 0.02 |
| Malignant tumor of breast | 0.2 | 0.2 | 0.02 | 0.2 | 0.2 | 0.01 |
| Malignant tumor of colon | <0.1 | <0.1 | -0.01 | <0.1 | <0.1 | 0.00 |
| Malignant tumor of lung | 0.1 | 0.1 | 0.01 | 0.1 | 0.1 | 0.02 |
| Medication use |  |  |  |  |  |  |
| Agents acting on the renin-angiotensin system | 0.6 | 0.6 | 0.00 | 0.6 | 0.8 | -0.02 |
| Antibacterials for systemic use | 3.8 | 3.4 | 0.02 | 3.6 | 3.5 | 0.01 |
| Antidepressants | 1.1 | 1.1 | -0.01 | 1.0 | 1.2 | -0.02 |
| Antiepileptics | 0.1 | 0.2 | -0.03 | 0.1 | 0.2 | -0.03 |
| Antiinflammatory and antirheumatic products | 1.6 | 1.9 | -0.03 | 1.6 | 1.8 | -0.01 |
| Antineoplastic agents | 1.5 | 0.6 | 0.08 | 1.2 | 0.9 | 0.02 |
| Antithrombotic agents | 1.1 | 1.1 | 0.00 | 1.2 | 1.2 | 0.00 |
| Beta blocking agents | 0.4 | 0.6 | -0.02 | 0.5 | 0.6 | -0.01 |
| Calcium channel blockers | 0.6 | 0.5 | 0.00 | 0.6 | 0.5 | 0.02 |
| Diuretics | 0.8 | 1.0 | -0.02 | 1.0 | 0.9 | 0.01 |
| Drugs for acid related disorders | 1.6 | 1.7 | 0.00 | 1.7 | 1.7 | 0.01 |
| Drugs for obstructive airway diseases | 0.4 | 0.4 | 0.00 | 0.5 | 0.4 | 0.00 |
| Drugs used in diabetes | 0.2 | 0.2 | 0.01 | 0.2 | 0.2 | 0.00 |
| Immunosuppressants | 1.6 | 0.7 | 0.08 | 1.3 | 1.0 | 0.02 |
| Lipid modifying agents | 0.9 | 0.9 | 0.00 | 0.9 | 1.0 | -0.01 |
| Opioids | 0.6 | 0.6 | -0.01 | 0.6 | 0.6 | -0.01 |
| Psycholeptics | 0.4 | 0.5 | -0.01 | 0.4 | 0.4 | -0.01 |

### **S6.1.6. IPCI**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Before stratification |  |  | After stratification |  |  |
|  | HCQ | SSZ |  | HCQ | SSZ |  |
| Characteristic | % | % | Std. diff | % | % | Std. diff |
| Age group |  |  |  |  |  |  |
| 15-19 | 0.4 | <0.9 | 0.00 | 0.4 | <0.9 | 0.02 |
| 20-24 | 0.6 | 1.3 | -0.07 | 0.6 | 1.0 | -0.04 |
| 25-29 | 1.4 | 3.0 | -0.11 | 1.5 | 2.7 | -0.08 |
| 30-34 | 1.6 | 4.4 | -0.16 | 1.8 | 3.7 | -0.12 |
| 35-39 | 3.2 | 4.0 | -0.04 | 3.4 | 4.0 | -0.03 |
| 40-44 | 6.0 | 4.4 | 0.08 | 6.4 | 3.4 | 0.14 |
| 45-49 | 8.5 | 10.4 | -0.06 | 9.0 | 10.1 | -0.04 |
| 50-54 | 10.5 | 9.7 | 0.03 | 11.0 | 9.1 | 0.06 |
| 55-59 | 11.2 | 14.6 | -0.10 | 11.5 | 14.4 | -0.09 |
| 60-64 | 12.2 | 12.3 | 0.00 | 11.7 | 12.7 | -0.03 |
| 65-69 | 11.8 | 12.9 | -0.03 | 11.9 | 12.4 | -0.02 |
| 70-74 | 12.3 | 9.8 | 0.08 | 12.0 | 10.6 | 0.04 |
| 75-79 | 9.0 | 8.5 | 0.02 | 8.8 | 9.8 | -0.04 |
| 80-84 | 7.4 | 3.2 | 0.19 | 6.7 | 4.3 | 0.11 |
| 85-89 | 2.8 | 0.9 | 0.14 | 2.7 | 1.4 | 0.09 |
| 90-94 | 0.8 | <0.9 | 0.09 | 0.8 | <0.9 | 0.08 |
| Gender: female | 68.4 | 68.0 | 0.01 | 68.6 | 67.2 | 0.03 |
| Medical history: General |  |  |  |  |  |  |
| Acute respiratory disease | 14.1 | 16.1 | -0.06 | 14.3 | 16.2 | -0.05 |
| Attention deficit hyperactivity disorder | <0.3 | <0.9 | -0.03 | <0.3 | <0.9 | -0.01 |
| Depressive disorder | 4.7 | 4.2 | 0.02 | 4.8 | 4.5 | 0.02 |
| Diabetes mellitus | 8.6 | 8.9 | -0.01 | 8.2 | 9.9 | -0.06 |
| Gastroesophageal reflux disease | 0.7 | <0.9 | 0.02 | 0.7 | <0.9 | 0.04 |
| Gastrointestinal hemorrhage | 1.1 | 1.9 | -0.07 | 1.0 | 1.8 | -0.07 |
| Hyperlipidemia | 3.4 | 4.0 | -0.03 | 3.4 | 4.3 | -0.05 |
| Hypertensive disorder | 16.3 | 17.6 | -0.04 | 15.6 | 17.6 | -0.06 |
| Obesity | 1.1 | 1.1 | 0.00 | 1.2 | 1.1 | 0.01 |
| Osteoarthritis | 9.7 | 6.4 | 0.12 | 9.4 | 6.7 | 0.10 |
| Pneumonia | 4.1 | 4.5 | -0.02 | 3.9 | 4.4 | -0.02 |
| Psoriasis | 1.1 | 2.8 | -0.12 | 1.2 | 2.5 | -0.09 |
| Renal impairment | 2.1 | 1.5 | 0.04 | 2.0 | 1.4 | 0.05 |
| Ulcerative colitis | <0.3 | 0.9 | -0.10 | <0.3 | 1.1 | -0.12 |
| Urinary tract infectious disease | 9.1 | 7.4 | 0.06 | 9.0 | 7.0 | 0.08 |
| Visual system disorder | 13.3 | 13.4 | 0.00 | 13.4 | 12.1 | 0.04 |
| Medical history: Cardiovascular disease |  |  |  |  |  |  |
| Atrial fibrillation | 2.9 | 2.3 | 0.04 | 2.7 | 2.3 | 0.02 |
| Cerebrovascular disease | 2.6 | 3.0 | -0.03 | 2.4 | 3.4 | -0.06 |
| Coronary arteriosclerosis | 0.5 | <0.9 | 0.05 | 0.5 | <0.9 | 0.07 |
| Heart disease | 10.2 | 9.1 | 0.04 | 9.7 | 10.0 | -0.01 |
| Heart failure | 1.6 | 1.1 | 0.04 | 1.5 | 1.4 | 0.01 |
| Ischemic heart disease | 4.5 | 4.4 | 0.00 | 4.3 | 5.0 | -0.03 |
| Peripheral vascular disease | 3.6 | 4.4 | -0.04 | 3.7 | 4.6 | -0.05 |
| Pulmonary embolism | 0.4 | <0.9 | -0.02 | 0.4 | <0.9 | -0.01 |
| Venous thrombosis | 1.4 | 0.9 | 0.04 | 1.4 | <0.9 | 0.07 |
| Medical history: Neoplasms |  |  |  |  |  |  |
| Malignant lymphoma | <0.3 | <0.9 | -0.02 | <0.3 | <0.9 | 0.01 |
| Malignant neoplasm of anorectum | 0.5 | <0.9 | -0.04 | 0.4 | <0.9 | -0.04 |
| Malignant neoplastic disease | 4.5 | 4.4 | 0.01 | 4.5 | 4.3 | 0.01 |
| Malignant tumor of breast | 1.1 | <0.9 | 0.06 | 1.2 | <0.9 | 0.10 |
| Malignant tumor of lung | 0.5 | 0.9 | -0.06 | 0.5 | 1.3 | -0.09 |
| Medication use |  |  |  |  |  |  |
| Agents acting on the renin-angiotensin system | 29.6 | 23.5 | 0.14 | 28.0 | 26.6 | 0.03 |
| Antibacterials for systemic use | 30.4 | 29.5 | 0.02 | 30.4 | 29.1 | 0.03 |
| Antidepressants | 12.8 | 13.6 | -0.02 | 12.8 | 13.8 | -0.03 |
| Antiepileptics | 5.0 | 4.9 | 0.00 | 5.0 | 5.6 | -0.03 |
| Antiinflammatory and antirheumatic products | 42.7 | 45.1 | -0.05 | 42.5 | 42.9 | -0.01 |
| Antineoplastic agents | 42.5 | 41.1 | 0.03 | 41.2 | 45.5 | -0.09 |
| Antipsoriatics | 0.7 | <0.9 | 0.00 | 0.8 | 0.9 | 0.00 |
| Antithrombotic agents | 22.2 | 18.4 | 0.10 | 20.5 | 22.6 | -0.05 |
| Beta blocking agents | 24.0 | 21.4 | 0.06 | 22.7 | 24.2 | -0.04 |
| Calcium channel blockers | 16.0 | 12.5 | 0.10 | 15.2 | 14.5 | 0.02 |
| Diuretics | 25.3 | 23.1 | 0.05 | 24.0 | 24.5 | -0.01 |
| Drugs for acid related disorders | 66.9 | 67.8 | -0.02 | 66.0 | 67.6 | -0.03 |
| Drugs for obstructive airway diseases | 25.4 | 26.7 | -0.03 | 25.6 | 26.8 | -0.03 |
| Drugs used in diabetes | 11.5 | 11.4 | 0.00 | 11.0 | 13.9 | -0.09 |
| Immunosuppressants | 44.8 | 46.8 | -0.04 | 44.0 | 49.1 | -0.10 |
| Lipid modifying agents | 29.3 | 25.0 | 0.10 | 27.6 | 29.5 | -0.04 |
| Opioids | 20.8 | 21.2 | -0.01 | 20.6 | 22.7 | -0.05 |
| Psycholeptics | 19.5 | 19.3 | 0.01 | 19.4 | 19.9 | -0.01 |
| Psychostimulants, agents used for adhd and nootropics | 0.9 | 1.1 | -0.03 | 0.9 | 1.7 | -0.07 |

### **S6.1.7. JMDC**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Before stratification |  |  | After stratification |  |  |
|  | HCQ | SSZ |  | HCQ | SSZ |  |
| Characteristic | % | % | Std. diff | % | % | Std. diff |
| Age group |  |  |  |  |  |  |
| 15-19 | <2.1 | <0.2 | 0.12 | <0.8 | <0.3 | 0.04 |
| 20-24 | 4.1 | 1.1 | 0.19 | 1.4 | 1.2 | 0.02 |
| 25-29 | 5.4 | 2.2 | 0.17 | 1.8 | 2.2 | -0.03 |
| 30-34 | 9.1 | 3.8 | 0.22 | 3.1 | 3.8 | -0.04 |
| 35-39 | 9.5 | 7.4 | 0.08 | 3.2 | 7.1 | -0.17 |
| 40-44 | 15.4 | 10.3 | 0.15 | 38.4 | 10.4 | 0.65 |
| 50-54 | 16.6 | 16.5 | 0.00 | 16.6 | 16.6 | 0.00 |
| 55-59 | 13.7 | 16.0 | -0.06 | 15.6 | 16.3 | -0.02 |
| 60-64 | 4.1 | 13.4 | -0.33 | 1.4 | 13.0 | -0.46 |
| 65-69 | 3.3 | 8.4 | -0.22 | 1.1 | 8.7 | -0.35 |
| 70-74 | <2.1 | 3.4 | -0.22 | <0.8 | 3.6 | -0.26 |
| Gender: female | 89.6 | 68.2 | 0.54 | 85.5 | 69.6 | 0.38 |
| Medical history: General |  |  |  |  |  |  |
| Acute respiratory disease | 57.3 | 52.4 | 0.10 | 63.6 | 53.6 | 0.20 |
| Chronic liver disease | 10.8 | 5.5 | 0.20 | 3.7 | 5.9 | -0.10 |
| Chronic obstructive lung disease | <2.1 | 1.5 | 0.02 | <0.8 | 1.5 | -0.09 |
| Crohn's disease | <2.1 | 0.5 | -0.02 | <0.8 | 0.7 | -0.08 |
| Depressive disorder | 12.0 | 8.6 | 0.11 | 37.3 | 9.2 | 0.66 |
| Diabetes mellitus | 39.8 | 18.5 | 0.48 | 13.5 | 19.8 | -0.16 |
| Gastroesophageal reflux disease | <2.1 | 0.3 | 0.01 | <0.8 | 0.3 | -0.04 |
| Gastrointestinal hemorrhage | 5.4 | 1.3 | 0.23 | 12.8 | 1.4 | 0.42 |
| Hyperlipidemia | 46.5 | 26.4 | 0.43 | 48.9 | 27.5 | 0.43 |
| Hypertensive disorder | 49.0 | 23.6 | 0.55 | 27.6 | 24.8 | 0.06 |
| Lesion of liver | 5.8 | 1.5 | 0.23 | 2.0 | 1.5 | 0.03 |
| Obesity | <2.1 | 0.8 | -0.05 | <0.8 | 0.9 | -0.10 |
| Osteoarthritis | 20.3 | 38.7 | -0.41 | 17.9 | 38.1 | -0.45 |
| Pneumonia | 9.5 | 4.8 | 0.19 | 47.4 | 5.2 | 1.02 |
| Psoriasis | 3.3 | 5.5 | -0.10 | 1.1 | 5.6 | -0.25 |
| Renal impairment | 9.5 | 1.9 | 0.34 | 3.2 | 2.2 | 0.06 |
| Rheumatoid arthritis | 86.3 | 99.0 | -0.50 | 95.4 | 98.9 | -0.20 |
| Schizophrenia | 3.3 | 2.3 | 0.06 | 1.1 | 2.5 | -0.10 |
| Ulcerative colitis | <2.1 | 1.5 | -0.02 | <0.8 | 1.8 | -0.13 |
| Urinary tract infectious disease | 4.6 | 2.5 | 0.11 | 34.7 | 2.8 | 0.83 |
| Viral hepatitis C | 2.5 | 1.8 | 0.05 | 0.8 | 1.8 | -0.08 |
| Visual system disorder | 93.4 | 43.1 | 1.28 | 53.6 | 47.5 | 0.12 |
| Medical history: Cardiovascular disease |  |  |  |  |  |  |
| Cerebrovascular disease | 4.1 | 2.8 | 0.08 | 1.4 | 2.9 | -0.10 |
| Coronary arteriosclerosis | <2.1 | <0.2 | 0.05 | <0.8 | <0.3 | -0.02 |
| Heart disease | 40.7 | 12.7 | 0.67 | 13.8 | 13.8 | 0.00 |
| Heart failure | 20.3 | 5.8 | 0.44 | 6.9 | 6.6 | 0.01 |
| Ischemic heart disease | 22.8 | 5.1 | 0.53 | 7.7 | 5.7 | 0.08 |
| Peripheral vascular disease | 6.2 | 2.7 | 0.17 | 2.1 | 2.8 | -0.04 |
| Pulmonary embolism | <2.1 | 0.2 | 0.12 | <0.8 | 0.4 | 0.00 |
| Venous thrombosis | 9.1 | 1.6 | 0.34 | 3.1 | 2.0 | 0.07 |
| Medical history: Neoplasms |  |  |  |  |  |  |
| Hematologic neoplasm | <2.1 | 0.9 | 0.00 | <0.8 | 0.9 | -0.08 |
| Malignant lymphoma | 2.5 | 1.2 | 0.09 | 0.8 | 1.5 | -0.06 |
| Malignant neoplastic disease | 6.2 | 6.7 | -0.02 | 2.1 | 7.1 | -0.24 |
| Malignant tumor of breast | <2.1 | 1.4 | -0.06 | <0.8 | 1.5 | -0.13 |
| Malignant tumor of colon | <2.1 | 0.6 | -0.03 | <0.8 | 0.6 | -0.08 |
| Medication use |  |  |  |  |  |  |
| Agents acting on the renin-angiotensin system | 26.1 | 12.7 | 0.35 | 8.9 | 13.5 | -0.14 |
| Antibacterials for systemic use | 71.4 | 50.9 | 0.43 | 79.3 | 52.5 | 0.57 |
| Antidepressants | 10.8 | 7.2 | 0.13 | 3.7 | 7.7 | -0.17 |
| Antiepileptics | 11.6 | 10.9 | 0.02 | 3.9 | 11.6 | -0.28 |
| Antiinflammatory and antirheumatic products | 39.4 | 72.9 | -0.72 | 79.5 | 71.9 | 0.17 |
| Antineoplastic agents | 15.4 | 28.7 | -0.33 | 16.2 | 28.5 | -0.29 |
| Antipsoriatics | 2.1 | 3.2 | -0.07 | <0.8 | 3.4 | -0.19 |
| Antithrombotic agents | 44.8 | 12.1 | 0.78 | 15.2 | 13.3 | 0.05 |
| Beta blocking agents | 7.9 | 3.9 | 0.17 | 13.6 | 4.3 | 0.31 |
| Calcium channel blockers | 19.5 | 12.4 | 0.20 | 17.6 | 12.8 | 0.13 |
| Diuretics | 9.5 | 4.0 | 0.22 | 3.2 | 4.3 | -0.05 |
| Drugs for acid related disorders | 90.0 | 81.8 | 0.24 | 96.6 | 81.8 | 0.48 |
| Drugs for obstructive airway diseases | 25.7 | 23.3 | 0.06 | 52.9 | 24.3 | 0.59 |
| Drugs used in diabetes | 8.7 | 6.6 | 0.08 | 3.0 | 7.1 | -0.19 |
| Immunosuppressants | 66.8 | 32.6 | 0.73 | 33.6 | 33.8 | 0.00 |
| Lipid modifying agents | 27.4 | 14.7 | 0.32 | 9.3 | 15.6 | -0.18 |
| Opioids | 27.4 | 23.3 | 0.09 | 42.5 | 24.4 | 0.37 |
| Psycholeptics | 43.2 | 27.5 | 0.33 | 58.8 | 28.7 | 0.61 |
| Psychostimulants, agents used for adhd and nootropics | <2.1 | 0.9 | -0.06 | <0.8 | 0.9 | -0.11 |

### **S6.1.8. MDCD**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Before stratification |  |  | After stratification |  |  |
|  | HCQ | SSZ |  | HCQ | SSZ |  |
| Characteristic | % | % | Std. diff | % | % | Std. diff |
| Age group |  |  |  |  |  |  |
| 15-19 | 1.2 | 1.2 | 0.00 | 1.2 | 1.3 | -0.01 |
| 20-24 | 2.1 | 2.8 | -0.04 | 2.1 | 3.1 | -0.06 |
| 25-29 | 4.4 | 3.8 | 0.03 | 4.3 | 4.2 | 0.00 |
| 30-34 | 6.6 | 6.8 | -0.01 | 6.4 | 6.9 | -0.02 |
| 35-39 | 9.0 | 8.8 | 0.01 | 8.8 | 8.8 | 0.00 |
| 40-44 | 10.2 | 9.3 | 0.03 | 10.0 | 9.1 | 0.03 |
| 45-49 | 13.3 | 13.0 | 0.01 | 13.2 | 13.7 | -0.01 |
| 50-54 | 15.9 | 16.1 | 0.00 | 16.2 | 15.9 | 0.01 |
| 55-59 | 15.8 | 16.2 | -0.01 | 15.9 | 15.5 | 0.01 |
| 60-64 | 12.0 | 13.9 | -0.06 | 12.3 | 12.9 | -0.02 |
| 65-69 | 4.5 | 4.0 | 0.02 | 4.6 | 4.2 | 0.02 |
| 70-74 | 2.0 | 1.9 | 0.01 | 2.0 | 1.9 | 0.00 |
| 75-79 | 1.6 | 1.0 | 0.06 | 1.6 | 1.0 | 0.05 |
| 80-84 | 1.0 | 1.0 | 0.00 | 1.0 | 1.0 | 0.00 |
| 85-89 | 0.4 | <0.2 | 0.04 | 0.4 | 0.3 | 0.01 |
| Gender: female | 85.9 | 79.0 | 0.18 | 84.4 | 84.5 | 0.00 |
| Race |  |  |  |  |  |  |
| race = Black or African American | 28.8 | 24.7 | 0.09 | 27.9 | 26.2 | 0.04 |
| race = White | 54.4 | 57.4 | -0.06 | 55.1 | 54.9 | 0.00 |
| Ethnicity |  |  |  |  |  |  |
| ethnicity = Hispanic or Latino | 2.3 | 1.9 | 0.03 | 2.4 | 2.1 | 0.02 |
| Medical history: General |  |  |  |  |  |  |
| Acute respiratory disease | 41.8 | 40.5 | 0.03 | 41.5 | 41.6 | 0.00 |
| Attention deficit hyperactivity disorder | 2.6 | 2.0 | 0.04 | 2.6 | 2.1 | 0.03 |
| Chronic liver disease | 6.9 | 7.4 | -0.02 | 6.9 | 7.4 | -0.02 |
| Chronic obstructive lung disease | 21.0 | 21.6 | -0.02 | 21.2 | 21.5 | -0.01 |
| Crohn's disease | 0.8 | 3.5 | -0.19 | 1.0 | 1.9 | -0.08 |
| Dementia | 1.2 | 0.9 | 0.03 | 1.1 | 1.1 | 0.01 |
| Depressive disorder | 36.0 | 35.4 | 0.01 | 35.5 | 35.8 | -0.01 |
| Gastroesophageal reflux disease | 29.5 | 30.8 | -0.03 | 29.5 | 30.7 | -0.03 |
| Gastrointestinal hemorrhage | 4.9 | 6.4 | -0.06 | 5.0 | 5.9 | -0.04 |
| Human immunodeficiency virus infection | 0.5 | 0.7 | -0.02 | 0.5 | 0.8 | -0.03 |
| Hyperlipidemia | 36.4 | 36.7 | -0.01 | 36.4 | 38.3 | -0.04 |
| Hypertensive disorder | 55.7 | 53.0 | 0.05 | 55.2 | 54.6 | 0.01 |
| Lesion of liver | 2.0 | 1.9 | 0.01 | 2.0 | 2.2 | -0.01 |
| Obesity | 21.5 | 20.0 | 0.04 | 21.2 | 20.2 | 0.02 |
| Osteoarthritis | 57.1 | 57.0 | 0.00 | 57.4 | 57.6 | 0.00 |
| Pneumonia | 8.7 | 8.0 | 0.02 | 8.5 | 8.0 | 0.02 |
| Psoriasis | 2.0 | 6.6 | -0.23 | 2.5 | 3.4 | -0.06 |
| Renal impairment | 9.4 | 8.0 | 0.05 | 9.2 | 8.3 | 0.03 |
| Rheumatoid arthritis | 80.9 | 84.4 | -0.09 | 81.9 | 83.4 | -0.04 |
| Schizophrenia | 1.7 | 2.1 | -0.03 | 1.6 | 2.3 | -0.05 |
| Ulcerative colitis | 0.5 | 1.7 | -0.11 | 0.6 | 1.2 | -0.06 |
| Urinary tract infectious disease | 17.8 | 16.5 | 0.04 | 17.4 | 16.6 | 0.02 |
| Viral hepatitis C | 5.9 | 6.0 | 0.00 | 5.9 | 6.3 | -0.02 |
| Visual system disorder | 39.9 | 40.7 | -0.02 | 40.0 | 39.9 | 0.00 |
| Medical history: Cardiovascular disease |  |  |  |  |  |  |
| Atrial fibrillation | 3.3 | 2.3 | 0.06 | 3.2 | 3.2 | 0.00 |
| Cerebrovascular disease | 5.3 | 5.2 | 0.00 | 5.1 | 5.3 | -0.01 |
| Coronary arteriosclerosis | 9.7 | 8.7 | 0.04 | 9.6 | 10.1 | -0.02 |
| Heart disease | 29.7 | 26.8 | 0.07 | 29.0 | 28.8 | 0.00 |
| Ischemic heart disease | 7.3 | 7.0 | 0.01 | 7.1 | 8.0 | -0.03 |
| Peripheral vascular disease | 4.8 | 4.1 | 0.03 | 4.6 | 4.3 | 0.02 |
| Pulmonary embolism | 2.0 | 1.0 | 0.08 | 1.9 | 1.6 | 0.02 |
| Venous thrombosis | 3.1 | 2.5 | 0.04 | 2.9 | 3.2 | -0.02 |
| Medical history: Neoplasms |  |  |  |  |  |  |
| Hematologic neoplasm | 1.5 | 1.2 | 0.03 | 1.5 | 1.2 | 0.02 |
| Malignant lymphoma | 0.4 | 0.5 | 0.00 | 0.4 | 0.3 | 0.01 |
| Malignant neoplasm of anorectum | 0.2 | 0.2 | -0.02 | 0.2 | <0.2 | 0.00 |
| Malignant neoplastic disease | 7.2 | 7.5 | -0.01 | 7.1 | 7.4 | -0.02 |
| Malignant tumor of breast | 2.0 | 1.7 | 0.02 | 1.9 | 1.6 | 0.02 |
| Malignant tumor of colon | 0.3 | 0.3 | 0.00 | 0.4 | 0.3 | 0.01 |
| Malignant tumor of lung | 0.4 | 0.3 | 0.02 | 0.4 | 0.3 | 0.02 |
| Malignant tumor of urinary bladder | 0.2 | <0.2 | 0.02 | 0.2 | <0.2 | 0.04 |
| Primary malignant neoplasm of prostate | 0.2 | 0.2 | -0.01 | 0.2 | <0.2 | 0.01 |
| Medication use |  |  |  |  |  |  |
| Agents acting on the renin-angiotensin system | 32.6 | 32.2 | 0.01 | 32.5 | 32.9 | -0.01 |
| Antibacterials for systemic use | 50.4 | 48.5 | 0.04 | 50.1 | 47.8 | 0.04 |
| Antidepressants | 53.7 | 53.0 | 0.01 | 53.5 | 53.0 | 0.01 |
| Antiepileptics | 43.0 | 41.7 | 0.02 | 42.7 | 42.3 | 0.01 |
| Antiinflammatory and antirheumatic products | 58.2 | 60.0 | -0.04 | 58.4 | 59.8 | -0.03 |
| Antineoplastic agents | 30.7 | 41.0 | -0.22 | 33.9 | 32.0 | 0.04 |
| Antipsoriatics | 0.8 | 0.7 | 0.01 | 0.8 | 0.6 | 0.03 |
| Antithrombotic agents | 18.8 | 17.0 | 0.05 | 18.5 | 17.9 | 0.02 |
| Beta blocking agents | 24.9 | 22.9 | 0.05 | 24.4 | 23.3 | 0.03 |
| Calcium channel blockers | 20.0 | 19.2 | 0.02 | 19.7 | 20.4 | -0.02 |
| Diuretics | 33.7 | 32.1 | 0.04 | 33.3 | 32.7 | 0.02 |
| Drugs for acid related disorders | 50.0 | 51.2 | -0.02 | 50.3 | 48.0 | 0.05 |
| Drugs for obstructive airway diseases | 46.2 | 46.9 | -0.01 | 46.2 | 46.5 | -0.01 |
| Drugs used in diabetes | 18.5 | 19.6 | -0.03 | 18.4 | 19.1 | -0.02 |
| Immunosuppressants | 39.8 | 56.0 | -0.33 | 44.4 | 41.8 | 0.05 |
| Lipid modifying agents | 29.2 | 30.0 | -0.02 | 29.3 | 30.9 | -0.04 |
| Opioids | 62.1 | 62.6 | -0.01 | 62.0 | 62.7 | -0.01 |
| Psycholeptics | 49.8 | 49.5 | 0.00 | 49.3 | 50.0 | -0.01 |
| Psychostimulants, agents used for adhd and nootropics | 7.4 | 6.7 | 0.02 | 7.2 | 6.9 | 0.01 |

### **S6.1.9. MDCR**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Before stratification |  |  | After stratification |  |  |
|  | HCQ | SSZ |  | HCQ | SSZ |  |
| Characteristic | % | % | Std. diff | % | % | Std. diff |
| Age group |  |  |  |  |  |  |
| 45-49 | 0.1 | <0.1 | 0.01 | 0.1 | <0.1 | 0.01 |
| 55-59 | 0.7 | 1.0 | -0.03 | 0.8 | 0.8 | -0.01 |
| 60-64 | 1.7 | 2.1 | -0.03 | 1.8 | 2.0 | -0.02 |
| 65-69 | 23.7 | 26.3 | -0.06 | 24.4 | 24.4 | 0.00 |
| 70-74 | 28.1 | 30.9 | -0.06 | 28.6 | 28.8 | 0.00 |
| 75-79 | 22.6 | 20.6 | 0.05 | 22.2 | 21.9 | 0.01 |
| 80-84 | 14.6 | 13.2 | 0.04 | 14.3 | 14.2 | 0.00 |
| 90-94 | 1.3 | 1.2 | 0.02 | 1.3 | 1.3 | 0.00 |
| 95-99 | 0.1 | 0.1 | 0.01 | 0.1 | 0.1 | 0.01 |
| Gender: female | 72.9 | 68.6 | 0.10 | 71.8 | 71.5 | 0.00 |
| Medical history: General |  |  |  |  |  |  |
| Acute respiratory disease | 27.5 | 26.4 | 0.02 | 27.4 | 27.2 | 0.00 |
| Attention deficit hyperactivity disorder | 0.2 | 0.2 | 0.00 | 0.2 | 0.2 | 0.00 |
| Chronic liver disease | 2.1 | 1.9 | 0.02 | 2.1 | 1.8 | 0.02 |
| Chronic obstructive lung disease | 15.8 | 16.0 | -0.01 | 15.7 | 16.0 | -0.01 |
| Crohn's disease | 0.5 | 1.3 | -0.08 | 0.6 | 1.1 | -0.05 |
| Dementia | 2.0 | 1.7 | 0.03 | 2.0 | 1.8 | 0.01 |
| Depressive disorder | 9.2 | 9.2 | 0.00 | 9.2 | 9.2 | 0.00 |
| Diabetes mellitus | 23.1 | 22.6 | 0.01 | 22.9 | 22.7 | 0.00 |
| Gastroesophageal reflux disease | 16.5 | 16.6 | 0.00 | 16.2 | 16.5 | -0.01 |
| Gastrointestinal hemorrhage | 4.8 | 5.1 | -0.01 | 4.8 | 4.9 | -0.01 |
| Human immunodeficiency virus infection | 0.1 | <0.1 | 0.01 | 0.1 | <0.1 | 0.01 |
| Hyperlipidemia | 41.3 | 39.2 | 0.04 | 40.7 | 41.3 | -0.01 |
| Hypertensive disorder | 61.8 | 59.3 | 0.05 | 61.1 | 61.3 | 0.00 |
| Lesion of liver | 1.0 | 1.0 | -0.01 | 1.0 | 1.0 | -0.01 |
| Obesity | 5.6 | 5.4 | 0.01 | 5.5 | 5.4 | 0.01 |
| Osteoarthritis | 62.0 | 59.5 | 0.05 | 61.2 | 61.9 | -0.01 |
| Pneumonia | 9.2 | 9.2 | 0.00 | 9.2 | 9.1 | 0.00 |
| Psoriasis | 2.3 | 4.9 | -0.14 | 2.7 | 3.3 | -0.04 |
| Renal impairment | 11.3 | 10.5 | 0.03 | 11.1 | 11.2 | 0.00 |
| Rheumatoid arthritis | 88.4 | 89.7 | -0.04 | 88.9 | 89.3 | -0.02 |
| Schizophrenia | 0.1 | <0.1 | 0.00 | 0.1 | 0.1 | -0.01 |
| Ulcerative colitis | 0.6 | 2.0 | -0.12 | 0.7 | 1.2 | -0.05 |
| Urinary tract infectious disease | 13.6 | 12.7 | 0.03 | 13.5 | 12.7 | 0.02 |
| Viral hepatitis C | 0.5 | 0.6 | -0.01 | 0.5 | 0.5 | 0.00 |
| Visual system disorder | 55.3 | 55.4 | 0.00 | 55.3 | 55.1 | 0.00 |
| Medical history: Cardiovascular disease |  |  |  |  |  |  |
| Atrial fibrillation | 10.6 | 9.5 | 0.04 | 10.4 | 10.2 | 0.01 |
| Heart failure | 10.1 | 9.9 | 0.01 | 10.0 | 10.4 | -0.01 |
| Ischemic heart disease | 10.1 | 10.1 | 0.00 | 10.1 | 10.4 | -0.01 |
| Peripheral vascular disease | 6.4 | 5.5 | 0.04 | 6.3 | 6.0 | 0.01 |
| Pulmonary embolism | 1.5 | 1.3 | 0.02 | 1.5 | 1.3 | 0.02 |
| Venous thrombosis | 3.4 | 3.4 | 0.00 | 3.3 | 3.6 | -0.01 |
| Medical history: Neoplasms |  |  |  |  |  |  |
| Hematologic neoplasm | 2.2 | 2.3 | 0.00 | 2.2 | 2.4 | -0.01 |
| Malignant lymphoma | 1.3 | 1.5 | -0.02 | 1.3 | 1.4 | -0.01 |
| Malignant neoplasm of anorectum | 0.4 | 0.4 | 0.00 | 0.4 | 0.4 | 0.00 |
| Malignant neoplastic disease | 18.5 | 19.8 | -0.03 | 18.7 | 19.0 | -0.01 |
| Malignant tumor of breast | 3.8 | 4.0 | -0.01 | 3.8 | 3.8 | 0.00 |
| Malignant tumor of colon | 0.8 | 0.7 | 0.02 | 0.9 | 0.7 | 0.02 |
| Malignant tumor of lung | 0.7 | 0.6 | 0.00 | 0.7 | 0.5 | 0.02 |
| Malignant tumor of urinary bladder | 1.0 | 1.1 | -0.02 | 1.0 | 0.9 | 0.00 |
| Primary malignant neoplasm of prostate | 2.4 | 2.8 | -0.02 | 2.5 | 2.4 | 0.01 |
| Medication use |  |  |  |  |  |  |
| Antibacterials for systemic use | 46.3 | 49.0 | -0.05 | 47.0 | 46.3 | 0.01 |
| Antidepressants | 31.5 | 31.4 | 0.00 | 31.7 | 31.3 | 0.01 |
| Antiepileptics | 20.1 | 21.8 | -0.04 | 20.3 | 20.6 | -0.01 |
| Antiinflammatory and antirheumatic products | 44.0 | 44.4 | -0.01 | 44.1 | 44.8 | -0.02 |
| Antineoplastic agents | 32.1 | 40.3 | -0.17 | 34.8 | 33.3 | 0.03 |
| Antipsoriatics | 1.0 | 1.4 | -0.03 | 1.0 | 1.3 | -0.02 |
| Antithrombotic agents | 22.8 | 22.1 | 0.02 | 22.6 | 22.5 | 0.00 |
| Beta blocking agents | 39.4 | 39.3 | 0.00 | 39.3 | 39.2 | 0.00 |
| Calcium channel blockers | 30.0 | 28.6 | 0.03 | 29.6 | 30.3 | -0.02 |
| Diuretics | 47.1 | 45.2 | 0.04 | 46.7 | 46.2 | 0.01 |
| Drugs for acid related disorders | 44.6 | 45.6 | -0.02 | 44.7 | 45.1 | -0.01 |
| Drugs for obstructive airway diseases | 33.2 | 32.4 | 0.02 | 33.2 | 32.8 | 0.01 |
| Drugs used in diabetes | 17.4 | 16.9 | 0.01 | 17.3 | 16.9 | 0.01 |
| Immunosuppressants | 41.2 | 54.9 | -0.28 | 45.5 | 42.8 | 0.05 |
| Lipid modifying agents | 49.8 | 48.5 | 0.03 | 49.5 | 49.4 | 0.00 |
| Opioids | 43.6 | 44.0 | -0.01 | 43.8 | 43.2 | 0.01 |
| Psycholeptics | 34.6 | 34.1 | 0.01 | 34.5 | 33.6 | 0.02 |
| Psychostimulants, agents used for adhd and nootropics | 2.0 | 2.0 | 0.00 | 2.0 | 1.9 | 0.01 |

### **S6.1.10. OpenClaims**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Before stratification |  |  | After stratification |  |  |
|  | HCQ | SSZ |  | HCQ | SSZ |  |
| Characteristic | % | % | Std. diff | % | % | Std. diff |
| Age group |  |  |  |  |  |  |
| 15-19 | 0.3 | 0.3 | -0.01 | 0.3 | 0.3 | 0.00 |
| 20-24 | 1.2 | 1.2 | -0.01 | 1.2 | 1.2 | 0.00 |
| 25-29 | 1.9 | 1.9 | 0.00 | 1.9 | 1.8 | 0.00 |
| 30-34 | 3.0 | 2.9 | 0.00 | 2.9 | 2.9 | 0.00 |
| 35-39 | 4.3 | 4.4 | -0.01 | 4.3 | 4.3 | 0.00 |
| 40-44 | 5.8 | 5.9 | 0.00 | 5.8 | 5.7 | 0.00 |
| 45-49 | 8.3 | 8.3 | 0.00 | 8.2 | 8.1 | 0.00 |
| 50-54 | 11.5 | 11.9 | -0.01 | 11.5 | 11.5 | 0.00 |
| 55-59 | 13.6 | 14.2 | -0.02 | 13.7 | 13.8 | 0.00 |
| 60-64 | 13.4 | 13.8 | -0.01 | 13.6 | 13.5 | 0.00 |
| 70-74 | 9.9 | 9.6 | 0.01 | 9.9 | 10.0 | 0.00 |
| 75-79 | 10.7 | 9.0 | 0.06 | 10.3 | 10.6 | -0.01 |
| 80-84 | 3.7 | 3.5 | 0.01 | 3.6 | 3.6 | 0.00 |
| 85-89 | 0.2 | 0.2 | 0.00 | 0.2 | 0.2 | 0.00 |
| Gender: female | 81.0 | 73.5 | 0.18 | 79.3 | 79.1 | 0.00 |
| Medical history: General |  |  |  |  |  |  |
| Acute respiratory disease | 20.1 | 19.2 | 0.02 | 19.9 | 19.9 | 0.00 |
| Chronic liver disease | 2.1 | 2.0 | 0.00 | 2.0 | 2.1 | 0.00 |
| Chronic obstructive lung disease | 7.6 | 7.7 | 0.00 | 7.6 | 7.8 | 0.00 |
| Crohn's disease | 0.4 | 1.6 | -0.11 | 0.5 | 0.9 | -0.04 |
| Dementia | 0.8 | 0.7 | 0.01 | 0.8 | 0.8 | 0.00 |
| Depressive disorder | 9.7 | 9.6 | 0.00 | 9.6 | 9.8 | -0.01 |
| Diabetes mellitus | 15.6 | 16.1 | -0.01 | 15.7 | 16.0 | -0.01 |
| Gastrointestinal hemorrhage | 2.4 | 2.5 | -0.01 | 2.4 | 2.4 | 0.00 |
| Hyperlipidemia | 26.0 | 25.8 | 0.01 | 26.0 | 26.4 | -0.01 |
| Hypertensive disorder | 35.0 | 34.5 | 0.01 | 34.9 | 35.2 | -0.01 |
| Lesion of liver | 0.8 | 0.7 | 0.01 | 0.8 | 0.8 | 0.00 |
| Obesity | 6.3 | 6.6 | -0.01 | 6.4 | 6.5 | 0.00 |
| Osteoarthritis | 36.0 | 37.0 | -0.02 | 36.1 | 36.8 | -0.02 |
| Psoriasis | 1.9 | 5.4 | -0.19 | 2.2 | 3.3 | -0.06 |
| Renal impairment | 6.2 | 5.5 | 0.03 | 6.1 | 6.0 | 0.00 |
| Rheumatoid arthritis | 69.0 | 69.6 | -0.01 | 69.3 | 69.8 | -0.01 |
| Schizophrenia | 0.2 | 0.2 | 0.00 | 0.2 | 0.2 | 0.00 |
| Ulcerative colitis | 0.4 | 1.7 | -0.12 | 0.5 | 1.0 | -0.06 |
| Viral hepatitis C | 1.1 | 1.1 | 0.00 | 1.1 | 1.1 | 0.00 |
| Visual system disorder | 21.9 | 20.7 | 0.03 | 21.6 | 21.6 | 0.00 |
| Medical history: Cardiovascular disease |  |  |  |  |  |  |
| Atrial fibrillation | 3.6 | 3.4 | 0.01 | 3.6 | 3.6 | 0.00 |
| Cerebrovascular disease | 3.4 | 2.8 | 0.03 | 3.2 | 3.3 | 0.00 |
| Coronary arteriosclerosis | 6.8 | 6.8 | 0.00 | 6.8 | 6.9 | 0.00 |
| Heart disease | 18.3 | 17.3 | 0.03 | 18.1 | 18.3 | 0.00 |
| Heart failure | 4.0 | 3.7 | 0.02 | 3.9 | 4.0 | 0.00 |
| Ischemic heart disease | 3.5 | 3.4 | 0.01 | 3.5 | 3.6 | 0.00 |
| Peripheral vascular disease | 9.7 | 9.1 | 0.02 | 9.6 | 9.6 | 0.00 |
| Venous thrombosis | 1.5 | 1.4 | 0.01 | 1.5 | 1.5 | 0.00 |
| Medical history: Neoplasms |  |  |  |  |  |  |
| Hematologic neoplasm | 0.9 | 0.9 | 0.00 | 0.9 | 1.0 | 0.00 |
| Malignant neoplasm of anorectum | 0.1 | 0.1 | 0.00 | 0.1 | 0.1 | 0.00 |
| Malignant neoplastic disease | 7.2 | 7.2 | 0.00 | 7.2 | 7.3 | 0.00 |
| Malignant tumor of breast | 1.8 | 1.6 | 0.01 | 1.7 | 1.7 | 0.00 |
| Malignant tumor of lung | 0.3 | 0.3 | 0.00 | 0.3 | 0.3 | 0.00 |
| Malignant tumor of urinary bladder | 0.2 | 0.3 | -0.01 | 0.3 | 0.3 | 0.00 |
| Medication use |  |  |  |  |  |  |
| Agents acting on the renin-angiotensin system | 30.8 | 33.0 | -0.05 | 31.4 | 31.4 | 0.00 |
| Antibacterials for systemic use | 36.1 | 38.8 | -0.06 | 36.8 | 36.6 | 0.00 |
| Antidepressants | 34.5 | 35.7 | -0.03 | 34.7 | 34.8 | 0.00 |
| Antiepileptics | 24.0 | 26.4 | -0.05 | 24.5 | 24.6 | 0.00 |
| Antiinflammatory and antirheumatic products | 41.0 | 45.2 | -0.08 | 42.0 | 41.9 | 0.00 |
| Antineoplastic agents | 31.6 | 38.0 | -0.14 | 33.3 | 33.4 | 0.00 |
| Antipsoriatics | 0.7 | 1.0 | -0.03 | 0.8 | 0.9 | -0.01 |
| Beta blocking agents | 23.1 | 24.1 | -0.02 | 23.3 | 23.5 | 0.00 |
| Drugs used in diabetes | 14.0 | 15.4 | -0.04 | 14.3 | 14.6 | -0.01 |
| Immunosuppressants | 41.9 | 53.4 | -0.23 | 44.7 | 44.7 | 0.00 |
| Lipid modifying agents | 29.0 | 31.5 | -0.05 | 29.6 | 29.8 | 0.00 |
| Opioids | 34.8 | 37.8 | -0.06 | 35.4 | 35.5 | 0.00 |
| Psycholeptics | 29.5 | 30.8 | -0.03 | 29.7 | 29.9 | 0.00 |
| Psychostimulants, agents used for adhd and nootropics | 4.5 | 4.8 | -0.01 | 4.5 | 4.6 | 0.00 |

### **S6.1.11. Optum**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Before stratification |  |  | After stratification |  |  |
|  | HCQ | SSZ |  | HCQ | SSZ |  |
| Characteristic | % | % | Std. diff | % | % | Std. diff |
| Age group |  |  |  |  |  |  |
| 15-19 | 0.3 | 0.4 | -0.01 | 0.3 | 0.4 | -0.02 |
| 20-24 | 1.1 | 1.1 | -0.01 | 1.1 | 1.1 | -0.01 |
| 25-29 | 1.8 | 2.0 | -0.01 | 1.8 | 1.8 | 0.00 |
| 30-34 | 3.4 | 3.2 | 0.01 | 3.3 | 3.3 | 0.00 |
| 35-39 | 4.9 | 5.2 | -0.02 | 4.9 | 4.8 | 0.00 |
| 40-44 | 6.8 | 6.7 | 0.01 | 6.8 | 6.5 | 0.01 |
| 45-49 | 8.9 | 9.1 | 0.00 | 8.9 | 8.9 | 0.00 |
| 50-54 | 11.6 | 11.6 | 0.00 | 11.6 | 11.7 | 0.00 |
| 55-59 | 12.5 | 13.3 | -0.02 | 12.7 | 12.8 | 0.00 |
| 60-64 | 11.6 | 12.6 | -0.03 | 11.9 | 11.9 | 0.00 |
| 65-69 | 11.3 | 12.2 | -0.03 | 11.6 | 11.7 | 0.00 |
| 70-74 | 10.8 | 10.6 | 0.01 | 10.9 | 10.6 | 0.01 |
| 75-79 | 7.9 | 6.9 | 0.04 | 7.7 | 7.7 | 0.00 |
| 80-84 | 5.0 | 3.8 | 0.06 | 4.7 | 4.9 | -0.01 |
| 85-89 | 1.9 | 1.3 | 0.05 | 1.8 | 1.7 | 0.01 |
| Gender: female | 79.6 | 71.9 | 0.18 | 77.6 | 77.6 | 0.00 |
| Medical history: General |  |  |  |  |  |  |
| Acute respiratory disease | 34.7 | 33.2 | 0.03 | 34.2 | 34.2 | 0.00 |
| Attention deficit hyperactivity disorder | 1.2 | 1.1 | 0.00 | 1.2 | 1.1 | 0.00 |
| Chronic liver disease | 3.7 | 3.8 | -0.01 | 3.7 | 3.9 | -0.01 |
| Chronic obstructive lung disease | 11.2 | 10.9 | 0.01 | 11.1 | 11.2 | 0.00 |
| Crohn's disease | 0.7 | 2.4 | -0.14 | 0.9 | 1.4 | -0.05 |
| Dementia | 1.3 | 1.2 | 0.01 | 1.2 | 1.5 | -0.02 |
| Depressive disorder | 18.5 | 18.1 | 0.01 | 18.4 | 18.2 | 0.00 |
| Diabetes mellitus | 20.9 | 20.2 | 0.02 | 20.7 | 21.1 | -0.01 |
| Gastroesophageal reflux disease | 21.6 | 21.1 | 0.01 | 21.5 | 21.8 | -0.01 |
| Gastrointestinal hemorrhage | 4.0 | 4.5 | -0.02 | 4.0 | 4.1 | 0.00 |
| Human immunodeficiency virus infection | 0.2 | 0.2 | -0.01 | 0.2 | 0.2 | -0.01 |
| Hyperlipidemia | 46.8 | 45.3 | 0.03 | 46.4 | 47.1 | -0.01 |
| Hypertensive disorder | 51.4 | 51.0 | 0.01 | 51.2 | 51.9 | -0.01 |
| Lesion of liver | 1.3 | 1.2 | 0.00 | 1.3 | 1.3 | 0.00 |
| Obesity | 12.2 | 12.5 | -0.01 | 12.2 | 12.2 | 0.00 |
| Osteoarthritis | 56.4 | 55.4 | 0.02 | 56.1 | 56.7 | -0.01 |
| Pneumonia | 6.5 | 5.8 | 0.03 | 6.3 | 6.4 | 0.00 |
| Psoriasis | 3.2 | 8.0 | -0.21 | 3.9 | 4.9 | -0.05 |
| Renal impairment | 9.9 | 9.2 | 0.03 | 9.7 | 9.9 | 0.00 |
| Rheumatoid arthritis | 84.3 | 85.5 | -0.04 | 84.8 | 85.2 | -0.01 |
| Schizophrenia | 0.2 | 0.1 | 0.01 | 0.2 | 0.1 | 0.01 |
| Ulcerative colitis | 0.7 | 2.2 | -0.13 | 0.9 | 1.3 | -0.04 |
| Viral hepatitis C | 1.5 | 1.7 | -0.02 | 1.5 | 1.7 | -0.02 |
| Visual system disorder | 40.3 | 39.7 | 0.01 | 40.0 | 39.8 | 0.00 |
| Medical history: Cardiovascular disease |  |  |  |  |  |  |
| Atrial fibrillation | 5.1 | 4.1 | 0.04 | 4.8 | 4.8 | 0.00 |
| Cerebrovascular disease | 6.3 | 5.5 | 0.03 | 6.1 | 6.0 | 0.00 |
| Coronary arteriosclerosis | 10.8 | 10.5 | 0.01 | 10.7 | 11.0 | -0.01 |
| Heart disease | 27.8 | 26.1 | 0.04 | 27.3 | 27.9 | -0.01 |
| Heart failure | 6.3 | 5.8 | 0.02 | 6.1 | 6.4 | -0.01 |
| Ischemic heart disease | 6.5 | 6.4 | 0.01 | 6.5 | 6.6 | -0.01 |
| Peripheral vascular disease | 4.7 | 4.3 | 0.02 | 4.7 | 4.6 | 0.00 |
| Pulmonary embolism | 1.2 | 0.9 | 0.03 | 1.2 | 1.1 | 0.01 |
| Venous thrombosis | 2.3 | 2.1 | 0.02 | 2.2 | 2.4 | -0.01 |
| Medical history: Neoplasms |  |  |  |  |  |  |
| Hematologic neoplasm | 1.4 | 1.2 | 0.02 | 1.4 | 1.3 | 0.01 |
| Malignant lymphoma | 0.7 | 0.8 | -0.01 | 0.7 | 0.8 | -0.01 |
| Malignant neoplasm of anorectum | 0.2 | 0.3 | -0.02 | 0.2 | 0.2 | -0.02 |
| Malignant neoplastic disease | 10.4 | 10.4 | 0.00 | 10.4 | 10.6 | -0.01 |
| Malignant tumor of breast | 2.5 | 2.0 | 0.04 | 2.4 | 2.4 | 0.00 |
| Malignant tumor of colon | 0.4 | 0.5 | -0.01 | 0.4 | 0.5 | -0.01 |
| Malignant tumor of lung | 0.4 | 0.4 | 0.01 | 0.4 | 0.4 | 0.01 |
| Malignant tumor of urinary bladder | 0.3 | 0.4 | -0.01 | 0.3 | 0.3 | 0.00 |
| Primary malignant neoplasm of prostate | 1.0 | 1.2 | -0.02 | 1.0 | 1.0 | 0.00 |
| Medication use |  |  |  |  |  |  |
| Agents acting on the renin-angiotensin system | 32.3 | 32.6 | -0.01 | 32.4 | 32.7 | -0.01 |
| Antibacterials for systemic use | 41.2 | 41.9 | -0.01 | 41.3 | 41.1 | 0.00 |
| Antidepressants | 35.1 | 35.2 | 0.00 | 35.0 | 34.9 | 0.00 |
| Antiinflammatory and antirheumatic products | 47.9 | 50.1 | -0.04 | 48.5 | 49.0 | -0.01 |
| Antineoplastic agents | 29.8 | 38.5 | -0.18 | 32.6 | 32.2 | 0.01 |
| Antipsoriatics | 0.9 | 1.1 | -0.03 | 0.9 | 0.9 | 0.00 |
| Antithrombotic agents | 11.8 | 10.6 | 0.04 | 11.5 | 11.4 | 0.00 |
| Beta blocking agents | 23.2 | 22.4 | 0.02 | 23.1 | 23.2 | 0.00 |
| Calcium channel blockers | 17.8 | 16.6 | 0.03 | 17.6 | 17.8 | 0.00 |
| Diuretics | 30.3 | 29.0 | 0.03 | 30.0 | 30.7 | -0.02 |
| Drugs for acid related disorders | 33.7 | 34.4 | -0.02 | 33.8 | 34.4 | -0.01 |
| Drugs for obstructive airway diseases | 29.4 | 28.9 | 0.01 | 29.2 | 29.5 | 0.00 |
| Drugs used in diabetes | 14.1 | 14.1 | 0.00 | 14.1 | 14.5 | -0.01 |
| Immunosuppressants | 38.7 | 53.1 | -0.29 | 43.0 | 42.2 | 0.02 |
| Lipid modifying agents | 31.9 | 32.1 | 0.00 | 32.0 | 32.6 | -0.01 |
| Opioids | 38.4 | 40.2 | -0.04 | 38.8 | 38.9 | 0.00 |
| Psycholeptics | 30.4 | 29.3 | 0.02 | 30.1 | 29.9 | 0.00 |
| Psychostimulants, agents used for adhd and nootropics | 4.0 | 3.7 | 0.02 | 4.0 | 3.7 | 0.01 |

### **S6.1.12. PanTher**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Before stratification |  |  | After stratification |  |  |
|  | HCQ | SSZ |  | HCQ | SSZ |  |
| Characteristic | % | % | Std. diff | % | % | Std. diff |
| Age group |  |  |  |  |  |  |
| 15-19 | 0.2 | 0.3 | -0.02 | 0.2 | 0.3 | -0.01 |
| 20-24 | 1.0 | 1.0 | 0.00 | 1.0 | 1.0 | 0.00 |
| 25-29 | 1.8 | 1.9 | -0.01 | 1.8 | 1.9 | -0.01 |
| 30-34 | 3.1 | 3.0 | 0.00 | 3.1 | 3.0 | 0.00 |
| 35-39 | 4.2 | 4.6 | -0.02 | 4.2 | 4.2 | 0.00 |
| 40-44 | 5.9 | 5.8 | 0.01 | 5.9 | 5.6 | 0.01 |
| 45-49 | 7.9 | 8.2 | -0.01 | 7.9 | 7.9 | 0.00 |
| 50-54 | 11.5 | 11.9 | -0.01 | 11.6 | 11.5 | 0.00 |
| 55-59 | 13.8 | 14.7 | -0.03 | 14.0 | 14.3 | -0.01 |
| 60-64 | 13.3 | 13.9 | -0.02 | 13.5 | 13.4 | 0.00 |
| 65-69 | 12.1 | 12.7 | -0.02 | 12.3 | 12.6 | -0.01 |
| 70-74 | 10.1 | 9.6 | 0.02 | 10.0 | 9.9 | 0.00 |
| 75-79 | 8.1 | 6.9 | 0.04 | 7.8 | 7.9 | 0.00 |
| 80-84 | 5.5 | 4.2 | 0.06 | 5.2 | 5.3 | -0.01 |
| 85-89 | 1.6 | 1.2 | 0.03 | 1.5 | 1.4 | 0.00 |
| Gender: female | 80.1 | 72.4 | 0.18 | 78.2 | 78.6 | -0.01 |
| Race |  |  |  |  |  |  |
| race = Asian | 1.5 | 1.1 | 0.04 | 1.5 | 1.4 | 0.01 |
| race = Black or African American | 10.1 | 8.4 | 0.06 | 9.7 | 9.6 | 0.00 |
| race = White | 81.4 | 83.3 | -0.05 | 81.8 | 81.9 | 0.00 |
| Ethnicity |  |  |  |  |  |  |
| ethnicity = Hispanic or Latino | 5.3 | 6.1 | -0.04 | 5.4 | 5.4 | 0.00 |
| Medical history: General |  |  |  |  |  |  |
| Acute respiratory disease | 17.9 | 18.3 | -0.01 | 17.9 | 18.1 | 0.00 |
| Attention deficit hyperactivity disorder | 1.0 | 0.8 | 0.01 | 0.9 | 0.8 | 0.01 |
| Chronic liver disease | 2.7 | 3.0 | -0.02 | 2.8 | 2.9 | -0.01 |
| Chronic obstructive lung disease | 8.5 | 9.2 | -0.03 | 8.6 | 8.9 | -0.01 |
| Crohn's disease | 0.5 | 1.6 | -0.12 | 0.6 | 0.9 | -0.04 |
| Dementia | 1.1 | 0.9 | 0.02 | 1.0 | 1.1 | -0.01 |
| Depressive disorder | 15.7 | 15.4 | 0.01 | 15.6 | 15.7 | 0.00 |
| Diabetes mellitus | 14.9 | 15.0 | 0.00 | 15.0 | 15.3 | -0.01 |
| Gastroesophageal reflux disease | 18.4 | 18.1 | 0.01 | 18.3 | 18.1 | 0.00 |
| Gastrointestinal hemorrhage | 2.1 | 2.4 | -0.02 | 2.1 | 2.2 | 0.00 |
| Human immunodeficiency virus infection | 0.1 | 0.2 | -0.01 | 0.1 | 0.2 | -0.01 |
| Hyperlipidemia | 30.4 | 31.1 | -0.02 | 30.5 | 30.6 | 0.00 |
| Hypertensive disorder | 38.9 | 38.6 | 0.01 | 38.8 | 39.2 | -0.01 |
| Lesion of liver | 1.1 | 0.9 | 0.02 | 1.0 | 1.0 | 0.01 |
| Obesity | 11.3 | 12.1 | -0.03 | 11.4 | 11.6 | -0.01 |
| Osteoarthritis | 35.1 | 36.2 | -0.02 | 35.3 | 35.7 | -0.01 |
| Pneumonia | 5.0 | 5.1 | 0.00 | 5.0 | 5.0 | 0.00 |
| Psoriasis | 1.7 | 4.4 | -0.16 | 2.1 | 2.7 | -0.04 |
| Renal impairment | 7.7 | 6.7 | 0.04 | 7.4 | 7.7 | -0.01 |
| Rheumatoid arthritis | 84.8 | 84.7 | 0.00 | 84.9 | 85.5 | -0.02 |
| Ulcerative colitis | 0.4 | 1.5 | -0.11 | 0.5 | 0.8 | -0.04 |
| Urinary tract infectious disease | 7.6 | 6.3 | 0.05 | 7.2 | 7.1 | 0.00 |
| Viral hepatitis C | 1.2 | 1.5 | -0.02 | 1.3 | 1.4 | -0.01 |
| Visual system disorder | 13.8 | 13.6 | 0.00 | 13.7 | 13.4 | 0.01 |
| Medical history: Cardiovascular disease |  |  |  |  |  |  |
| Coronary arteriosclerosis | 8.3 | 8.5 | 0.00 | 8.3 | 8.5 | -0.01 |
| Heart disease | 20.9 | 20.2 | 0.02 | 20.7 | 21.1 | -0.01 |
| Heart failure | 4.7 | 4.4 | 0.02 | 4.7 | 4.9 | -0.01 |
| Ischemic heart disease | 4.4 | 4.5 | 0.00 | 4.4 | 4.5 | 0.00 |
| Peripheral vascular disease | 2.6 | 2.4 | 0.01 | 2.6 | 2.5 | 0.00 |
| Pulmonary embolism | 1.0 | 1.0 | 0.00 | 1.0 | 1.0 | -0.01 |
| Venous thrombosis | 1.9 | 2.0 | -0.01 | 1.9 | 2.0 | -0.01 |
| Medical history: Neoplasms |  |  |  |  |  |  |
| Hematologic neoplasm | 1.1 | 1.2 | -0.01 | 1.1 | 1.2 | -0.01 |
| Malignant lymphoma | 0.6 | 0.7 | -0.01 | 0.6 | 0.7 | 0.00 |
| Malignant neoplasm of anorectum | 0.2 | 0.2 | 0.01 | 0.2 | 0.2 | 0.01 |
| Malignant neoplastic disease | 8.5 | 8.8 | -0.01 | 8.5 | 8.8 | -0.01 |
| Malignant tumor of breast | 1.9 | 1.7 | 0.02 | 1.9 | 1.9 | 0.00 |
| Malignant tumor of colon | 0.4 | 0.3 | 0.00 | 0.4 | 0.4 | 0.00 |
| Malignant tumor of lung | 0.4 | 0.4 | -0.01 | 0.4 | 0.4 | -0.01 |
| Malignant tumor of urinary bladder | 0.2 | 0.4 | -0.03 | 0.2 | 0.3 | -0.02 |
| Primary malignant neoplasm of prostate | 0.6 | 0.8 | -0.03 | 0.7 | 0.7 | 0.00 |
| Medication use |  |  |  |  |  |  |
| Agents acting on the renin-angiotensin system | 30.6 | 31.6 | -0.02 | 30.8 | 31.3 | -0.01 |
| Antibacterials for systemic use | 28.1 | 29.8 | -0.04 | 28.3 | 28.2 | 0.00 |
| Antidepressants | 36.0 | 35.6 | 0.01 | 35.8 | 36.3 | -0.01 |
| Antiepileptics | 24.0 | 24.8 | -0.02 | 24.2 | 24.4 | -0.01 |
| Antiinflammatory and antirheumatic products | 43.7 | 47.2 | -0.07 | 44.5 | 44.6 | 0.00 |
| Antineoplastic agents | 34.4 | 38.1 | -0.08 | 35.4 | 36.4 | -0.02 |
| Antipsoriatics | 0.6 | 0.7 | -0.01 | 0.6 | 0.6 | 0.00 |
| Antithrombotic agents | 33.0 | 31.7 | 0.03 | 32.6 | 33.2 | -0.01 |
| Beta blocking agents | 26.7 | 27.0 | -0.01 | 26.8 | 27.2 | -0.01 |
| Calcium channel blockers | 17.2 | 16.7 | 0.01 | 17.1 | 17.5 | -0.01 |
| Diuretics | 29.2 | 28.3 | 0.02 | 29.1 | 29.4 | -0.01 |
| Drugs for acid related disorders | 45.1 | 45.5 | -0.01 | 45.1 | 45.4 | 0.00 |
| Drugs for obstructive airway diseases | 34.5 | 35.2 | -0.02 | 34.6 | 35.0 | -0.01 |
| Drugs used in diabetes | 15.1 | 15.7 | -0.02 | 15.3 | 15.8 | -0.01 |
| Immunosuppressants | 47.1 | 56.1 | -0.18 | 49.2 | 50.2 | -0.02 |
| Lipid modifying agents | 30.2 | 31.7 | -0.03 | 30.6 | 31.0 | -0.01 |
| Opioids | 39.3 | 41.1 | -0.04 | 39.6 | 40.3 | -0.01 |
| Psycholeptics | 35.2 | 35.0 | 0.00 | 35.1 | 35.5 | -0.01 |
| Psychostimulants, agents used for adhd and nootropics | 4.3 | 4.0 | 0.01 | 4.2 | 4.1 | 0.01 |

### **S6.1.13. SIDIAP**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Before stratification |  |  | After stratification |  |  |
|  | HCQ | SSZ |  | HCQ | SSZ |  |
| Characteristic | % | % | Std. diff | % | % | Std. diff |
| Age group |  |  |  |  |  |  |
| 20-24 | 0.6 | <1.3 | -0.02 | 0.6 | <1.0 | -0.02 |
| 25-29 | 2.2 | 2.9 | -0.05 | 2.0 | 4.6 | -0.15 |
| 30-34 | 4.4 | 4.7 | -0.02 | 4.6 | 4.3 | 0.01 |
| 35-39 | 7.1 | 9.7 | -0.09 | 7.2 | 13.3 | -0.20 |
| 40-44 | 8.0 | 6.8 | 0.05 | 8.3 | 5.6 | 0.11 |
| 45-49 | 7.5 | 9.4 | -0.07 | 7.4 | 7.3 | 0.00 |
| 50-54 | 10.1 | 12.3 | -0.07 | 10.5 | 7.7 | 0.10 |
| 55-59 | 11.5 | 9.4 | 0.07 | 11.5 | 9.5 | 0.06 |
| 60-64 | 11.2 | 10.8 | 0.02 | 10.9 | 11.1 | -0.01 |
| 65-69 | 10.8 | 10.2 | 0.02 | 11.1 | 8.7 | 0.08 |
| 70-74 | 9.9 | 6.8 | 0.11 | 9.6 | 9.6 | 0.00 |
| 75-79 | 7.5 | 9.4 | -0.07 | 7.6 | 9.1 | -0.05 |
| 80-84 | 6.2 | 5.8 | 0.02 | 6.0 | 8.0 | -0.08 |
| 85-89 | 2.0 | <1.3 | 0.13 | 2.0 | <1.0 | 0.16 |
| 90-94 | 0.6 | <1.3 | 0.06 | 0.6 | <1.0 | 0.06 |
| Gender: female | 79.2 | 66.7 | 0.29 | 75.9 | 79.8 | -0.09 |
| Medical history: General |  |  |  |  |  |  |
| Acute respiratory disease | 17.9 | 17.3 | 0.02 | 17.4 | 26.6 | -0.22 |
| Chronic liver disease | 1.0 | <1.3 | -0.01 | 1.0 | <1.0 | 0.04 |
| Chronic obstructive lung disease | 2.6 | 2.6 | 0.00 | 2.4 | 1.7 | 0.05 |
| Depressive disorder | 3.0 | 4.7 | -0.09 | 3.1 | 9.0 | -0.25 |
| Diabetes mellitus | 2.9 | 3.1 | -0.02 | 2.8 | 2.3 | 0.03 |
| Gastroesophageal reflux disease | 1.0 | 1.3 | -0.02 | 1.1 | 1.5 | -0.04 |
| Gastrointestinal hemorrhage | 2.7 | 3.7 | -0.05 | 2.9 | 3.6 | -0.04 |
| Hyperlipidemia | 4.3 | 3.4 | 0.04 | 4.0 | 7.8 | -0.16 |
| Hypertensive disorder | 5.3 | 6.6 | -0.05 | 5.7 | 7.9 | -0.09 |
| Obesity | 4.8 | 4.2 | 0.03 | 4.6 | 3.3 | 0.07 |
| Osteoarthritis | 3.0 | 3.1 | -0.01 | 3.2 | 4.9 | -0.09 |
| Pneumonia | 2.0 | 2.4 | -0.02 | 2.2 | 7.3 | -0.24 |
| Psoriasis | 0.7 | 2.1 | -0.12 | 0.6 | 2.0 | -0.12 |
| Renal impairment | 1.8 | 2.4 | -0.04 | 2.0 | 2.1 | -0.01 |
| Rheumatoid arthritis | 35.6 | 26.5 | 0.20 | 33.2 | 42.3 | -0.19 |
| Urinary tract infectious disease | 7.5 | 5.8 | 0.07 | 7.4 | 6.0 | 0.06 |
| Viral hepatitis C | 0.9 | <1.3 | 0.04 | 0.9 | <1.0 | 0.07 |
| Visual system disorder | 16.0 | 17.3 | -0.03 | 15.6 | 19.5 | -0.10 |
| Medical history: Cardiovascular disease |  |  |  |  |  |  |
| Atrial fibrillation | 0.6 | 1.3 | -0.08 | 0.5 | 4.1 | -0.24 |
| Cerebrovascular disease | 2.2 | <1.3 | 0.09 | 2.2 | <1.0 | 0.13 |
| Heart disease | 7.2 | 6.8 | 0.02 | 7.0 | 9.2 | -0.08 |
| Heart failure | 1.1 | <1.3 | 0.01 | 1.1 | 3.3 | -0.15 |
| Ischemic heart disease | 1.6 | <1.3 | 0.10 | 1.5 | <1.0 | 0.13 |
| Peripheral vascular disease | 3.6 | 2.4 | 0.07 | 3.8 | 1.7 | 0.13 |
| Pulmonary embolism | 0.4 | <1.3 | 0.02 | 0.4 | <1.0 | 0.04 |
| Medical history: Neoplasms |  |  |  |  |  |  |
| Hematologic neoplasm | <0.4 | <1.3 | -0.08 | <0.4 | <1.0 | -0.06 |
| Malignant neoplastic disease | 3.0 | 3.4 | -0.02 | 3.0 | 2.4 | 0.04 |
| Malignant tumor of breast | 0.4 | <1.3 | -0.02 | <0.4 | <1.0 | -0.02 |
| Malignant tumor of colon | <0.4 | <1.3 | 0.01 | <0.4 | <1.0 | 0.04 |
| Malignant tumor of lung | <0.4 | <1.3 | -0.04 | <0.4 | <1.0 | -0.03 |
| Malignant tumor of urinary bladder | <0.4 | <1.3 | -0.05 | <0.4 | <1.0 | -0.02 |
| Medication use |  |  |  |  |  |  |
| Agents acting on the renin-angiotensin system | 26.2 | 30.7 | -0.10 | 27.2 | 27.0 | 0.00 |
| Antibacterials for systemic use | 17.4 | 17.8 | -0.01 | 17.1 | 19.2 | -0.05 |
| Antidepressants | 21.9 | 22.8 | -0.02 | 21.9 | 27.7 | -0.13 |
| Antiepileptics | 9.9 | 11.8 | -0.06 | 9.9 | 11.9 | -0.06 |
| Antiinflammatory and antirheumatic products | 70.0 | 71.7 | -0.04 | 69.8 | 68.2 | 0.03 |
| Antineoplastic agents | 21.3 | 21.0 | 0.01 | 21.3 | 20.6 | 0.02 |
| Antipsoriatics | 1.3 | 1.6 | -0.02 | 1.4 | <1.0 | 0.04 |
| Antithrombotic agents | 17.4 | 16.3 | 0.03 | 17.3 | 15.6 | 0.05 |
| Beta blocking agents | 11.2 | 10.5 | 0.02 | 11.5 | 10.1 | 0.04 |
| Calcium channel blockers | 10.3 | 6.0 | 0.16 | 9.8 | 9.7 | 0.00 |
| Diuretics | 22.9 | 21.8 | 0.03 | 22.6 | 19.2 | 0.08 |
| Drugs for acid related disorders | 77.9 | 83.5 | -0.14 | 78.8 | 78.0 | 0.02 |
| Drugs for obstructive airway diseases | 24.7 | 25.5 | -0.02 | 24.2 | 21.1 | 0.07 |
| Drugs used in diabetes | 10.5 | 10.8 | -0.01 | 10.6 | 9.2 | 0.05 |
| Immunosuppressants | 32.6 | 36.2 | -0.08 | 33.1 | 30.3 | 0.06 |
| Lipid modifying agents | 25.3 | 21.5 | 0.09 | 24.5 | 23.3 | 0.03 |
| Opioids | 22.6 | 23.4 | -0.02 | 22.9 | 23.5 | -0.01 |
| Psycholeptics | 36.3 | 40.7 | -0.09 | 37.1 | 44.2 | -0.14 |
| Psychostimulants, agents used for adhd and nootropics | 1.3 | 3.1 | -0.13 | 1.3 | 2.0 | -0.05 |

### **S6.1.14. VA**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Before stratification |  |  | After stratification |  |  |
|  | HCQ | SSZ |  | HCQ | SSZ |  |
| Characteristic | % | % | Std. diff | % | % | Std. diff |
| Age group |  |  |  |  |  |  |
| 20-24 | 0.1 | 0.1 | 0.00 | 0.1 | 0.2 | -0.02 |
| 25-29 | 0.6 | 0.6 | 0.00 | 0.6 | 0.6 | -0.01 |
| 30-34 | 1.2 | 1.0 | 0.02 | 1.1 | 1.1 | 0.00 |
| 35-39 | 1.6 | 1.7 | 0.00 | 1.5 | 1.7 | -0.02 |
| 40-44 | 2.7 | 3.0 | -0.02 | 2.7 | 2.8 | -0.01 |
| 45-49 | 5.1 | 5.1 | 0.00 | 5.1 | 5.0 | 0.00 |
| 50-54 | 8.4 | 9.7 | -0.05 | 8.8 | 8.7 | 0.00 |
| 55-59 | 12.8 | 14.5 | -0.05 | 13.4 | 13.1 | 0.01 |
| 60-64 | 17.1 | 17.8 | -0.02 | 17.3 | 17.6 | -0.01 |
| 65-69 | 16.9 | 17.0 | 0.00 | 17.1 | 17.0 | 0.00 |
| 70-74 | 13.8 | 13.7 | 0.00 | 13.9 | 13.7 | 0.00 |
| 75-79 | 10.0 | 9.1 | 0.03 | 9.8 | 9.7 | 0.00 |
| 80-84 | 6.5 | 4.7 | 0.08 | 5.9 | 6.2 | -0.01 |
| 85-89 | 2.5 | 1.6 | 0.06 | 2.2 | 2.2 | 0.00 |
| 90-94 | 0.5 | 0.3 | 0.03 | 0.5 | 0.3 | 0.03 |
| Gender: female | 14.5 | 10.4 | 0.13 | 13.2 | 13.1 | 0.00 |
| Race |  |  |  |  |  |  |
| race = Asian | 0.5 | 0.4 | 0.00 | 0.5 | 0.4 | 0.01 |
| race = Black or African American | 14.4 | 12.9 | 0.04 | 13.9 | 13.6 | 0.01 |
| race = White | 73.6 | 74.6 | -0.02 | 73.9 | 74.1 | 0.00 |
| race = Unknown | 9.9 | 10.4 | -0.02 | 10.1 | 10.2 | 0.00 |
| race = Native Hawaiian or Other Pacific Islander | 0.7 | 0.8 | -0.01 | 0.7 | 0.8 | -0.02 |
| race = American Indian or Alaska Native | 0.9 | 0.9 | 0.00 | 0.9 | 0.8 | 0.01 |
| Ethnicity |  |  |  |  |  |  |
| ethnicity = Hispanic or Latino | 4.8 | 4.9 | 0.00 | 4.9 | 4.7 | 0.00 |
| ethnicity = Not Hispanic or Latino | 89.3 | 88.6 | 0.02 | 89.0 | 89.1 | 0.00 |
| Medical history: General |  |  |  |  |  |  |
| Acute respiratory disease | 11.4 | 12.3 | -0.03 | 11.8 | 11.3 | 0.02 |
| Attention deficit hyperactivity disorder | 0.4 | 0.4 | 0.00 | 0.4 | 0.5 | -0.01 |
| Chronic liver disease | 3.4 | 3.4 | 0.00 | 3.5 | 3.6 | 0.00 |
| Crohn's disease | 0.3 | 0.9 | -0.07 | 0.4 | 0.6 | -0.02 |
| Dementia | 1.2 | 1.0 | 0.02 | 1.1 | 1.1 | 0.00 |
| Depressive disorder | 21.9 | 21.6 | 0.01 | 21.8 | 21.6 | 0.00 |
| Diabetes mellitus | 24.5 | 23.8 | 0.02 | 24.1 | 24.1 | 0.00 |
| Gastroesophageal reflux disease | 5.8 | 5.4 | 0.01 | 5.6 | 5.5 | 0.01 |
| Gastrointestinal hemorrhage | 2.1 | 2.8 | -0.04 | 2.3 | 2.3 | 0.00 |
| Human immunodeficiency virus infection | 0.2 | 0.2 | 0.00 | 0.2 | 0.2 | 0.00 |
| Hypertensive disorder | 58.1 | 57.6 | 0.01 | 58.0 | 58.0 | 0.00 |
| Lesion of liver | 1.4 | 1.4 | 0.00 | 1.4 | 1.4 | 0.01 |
| Obesity | 14.3 | 14.3 | 0.00 | 14.2 | 14.3 | 0.00 |
| Psoriasis | 2.2 | 7.0 | -0.23 | 3.2 | 4.1 | -0.05 |
| Renal impairment | 7.2 | 6.6 | 0.02 | 7.0 | 7.1 | 0.00 |
| Rheumatoid arthritis | 90.4 | 89.6 | 0.02 | 90.5 | 90.2 | 0.01 |
| Schizophrenia | 0.6 | 0.7 | -0.01 | 0.6 | 0.6 | 0.01 |
| Ulcerative colitis | 0.4 | 1.0 | -0.06 | 0.5 | 0.7 | -0.02 |
| Urinary tract infectious disease | 3.5 | 3.1 | 0.02 | 3.4 | 3.1 | 0.02 |
| Viral hepatitis C | 3.7 | 3.7 | 0.00 | 3.7 | 3.8 | 0.00 |
| Visual system disorder | 38.5 | 41.9 | -0.07 | 39.5 | 38.7 | 0.02 |
| Medical history: Cardiovascular disease |  |  |  |  |  |  |
| Atrial fibrillation | 6.1 | 5.4 | 0.03 | 5.9 | 5.8 | 0.00 |
| Cerebrovascular disease | 4.3 | 4.0 | 0.02 | 4.3 | 4.3 | 0.00 |
| Coronary arteriosclerosis | 14.7 | 15.1 | -0.01 | 14.8 | 15.2 | -0.01 |
| Heart disease | 30.5 | 30.4 | 0.00 | 30.6 | 31.1 | -0.01 |
| Heart failure | 5.9 | 6.1 | -0.01 | 5.9 | 6.1 | -0.01 |
| Ischemic heart disease | 11.0 | 11.2 | 0.00 | 11.1 | 11.1 | 0.00 |
| Pulmonary embolism | 0.7 | 0.8 | 0.00 | 0.7 | 0.8 | -0.01 |
| Venous thrombosis | 1.4 | 1.3 | 0.01 | 1.4 | 1.3 | 0.01 |
| Medical history: Neoplasms |  |  |  |  |  |  |
| Hematologic neoplasm | 1.1 | 1.0 | 0.02 | 1.1 | 1.0 | 0.01 |
| Malignant lymphoma | 0.8 | 0.6 | 0.01 | 0.8 | 0.6 | 0.02 |
| Malignant neoplasm of anorectum | 0.1 | 0.1 | 0.00 | 0.2 | 0.1 | 0.01 |
| Malignant tumor of breast | 0.4 | 0.2 | 0.02 | 0.3 | 0.3 | 0.01 |
| Malignant tumor of colon | 0.6 | 0.6 | 0.00 | 0.6 | 0.6 | 0.00 |
| Malignant tumor of lung | 0.3 | 0.4 | -0.01 | 0.4 | 0.4 | 0.00 |
| Malignant tumor of urinary bladder | 0.8 | 0.8 | -0.01 | 0.7 | 0.9 | -0.01 |
| Medication use |  |  |  |  |  |  |
| Agents acting on the renin-angiotensin system | 38.5 | 39.2 | -0.01 | 38.8 | 39.0 | 0.00 |
| Antibacterials for systemic use | 22.8 | 25.3 | -0.06 | 23.8 | 23.2 | 0.01 |
| Antidepressants | 35.0 | 36.1 | -0.02 | 35.3 | 34.8 | 0.01 |
| Antiepileptics | 21.3 | 20.9 | 0.01 | 21.1 | 21.0 | 0.00 |
| Antiinflammatory and antirheumatic products | 47.8 | 52.1 | -0.09 | 49.2 | 47.8 | 0.03 |
| Antineoplastic agents | 36.8 | 41.7 | -0.10 | 38.8 | 38.2 | 0.01 |
| Antipsoriatics | 1.0 | 2.0 | -0.09 | 1.1 | 1.5 | -0.03 |
| Antithrombotic agents | 28.6 | 28.9 | -0.01 | 28.8 | 28.6 | 0.01 |
| Beta blocking agents | 32.0 | 32.2 | 0.00 | 32.0 | 32.1 | 0.00 |
| Calcium channel blockers | 21.8 | 21.8 | 0.00 | 21.9 | 22.3 | -0.01 |
| Diuretics | 32.8 | 33.5 | -0.02 | 33.1 | 33.2 | 0.00 |
| Drugs for acid related disorders | 52.3 | 55.9 | -0.07 | 53.5 | 52.8 | 0.01 |
| Drugs for obstructive airway diseases | 27.8 | 28.9 | -0.02 | 28.2 | 28.0 | 0.00 |
| Drugs used in diabetes | 19.7 | 19.4 | 0.01 | 19.4 | 19.6 | 0.00 |
| Immunosuppressants | 44.0 | 51.9 | -0.16 | 47.0 | 46.3 | 0.01 |
| Lipid modifying agents | 45.7 | 45.1 | 0.01 | 45.5 | 45.6 | 0.00 |
| Opioids | 31.0 | 34.1 | -0.06 | 32.0 | 31.5 | 0.01 |
| Psycholeptics | 23.7 | 24.8 | -0.03 | 24.0 | 24.0 | 0.00 |
| Psychostimulants, agents used for adhd and nootropics | 1.8 | 1.6 | 0.02 | 1.8 | 1.6 | 0.01 |

## **S6.2. AZM vs AMX**

### **S6.2.1. AmbEMR**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Before stratification |  |  | After stratification |  |  |
|  | AZM | AMX |  | AZM | AMX |  |
| Characteristic | % | % | Std. diff | % | % | Std. diff |
| Age group |  |  |  |  |  |  |
| 20-24 | 0.8 | 0.7 | 0.01 | 0.8 | 0.7 | 0.01 |
| 25-29 | 1.2 | 1.3 | -0.01 | 1.3 | 1.2 | 0.00 |
| 30-34 | 2.5 | 2.3 | 0.02 | 2.6 | 2.3 | 0.02 |
| 35-39 | 3.5 | 3.9 | -0.02 | 3.7 | 3.7 | 0.00 |
| 40-44 | 5.8 | 5.1 | 0.03 | 5.8 | 5.4 | 0.02 |
| 45-49 | 7.5 | 7.3 | 0.01 | 7.7 | 7.3 | 0.01 |
| 50-54 | 10.1 | 10.4 | -0.01 | 10.1 | 10.5 | -0.01 |
| 55-59 | 13.4 | 13.7 | -0.01 | 13.5 | 14.0 | -0.01 |
| 60-64 | 14.1 | 14.4 | -0.01 | 13.9 | 14.2 | -0.01 |
| 65-69 | 13.8 | 14.1 | -0.01 | 13.7 | 14.1 | -0.01 |
| 70-74 | 12.7 | 12.1 | 0.02 | 12.2 | 11.9 | 0.01 |
| 75-79 | 10.6 | 10.1 | 0.02 | 10.6 | 10.3 | 0.01 |
| 80-84 | 3.9 | 4.5 | -0.03 | 4.1 | 4.2 | -0.01 |
| Gender: female | 83.2 | 82.5 | 0.02 | 83.2 | 82.9 | 0.01 |
| Race |  |  |  |  |  |  |
| race = Asian | 1.5 | 1.1 | 0.03 | 1.4 | 1.1 | 0.02 |
| race = White | 75.6 | 75.3 | 0.01 | 75.7 | 75.6 | 0.00 |
| race = African American | 8.2 | 8.1 | 0.00 | 8.2 | 8.1 | 0.00 |
| Ethnicity |  |  |  |  |  |  |
| ethnicity = Hispanic or Latino | 1.5 | 1.2 | 0.03 | 1.4 | 1.2 | 0.02 |
| ethnicity = Not Hispanic or Latino | 85.2 | 84.5 | 0.02 | 85.3 | 84.8 | 0.02 |
| Medical history: General |  |  |  |  |  |  |
| Acute respiratory disease | 43.3 | 34.9 | 0.17 | 39.9 | 40.4 | -0.01 |
| Attention deficit hyperactivity disorder | 0.7 | 0.9 | -0.03 | 0.7 | 0.9 | -0.03 |
| Chronic liver disease | 1.5 | 1.7 | -0.02 | 1.5 | 1.7 | -0.02 |
| Chronic obstructive lung disease | 10.6 | 8.4 | 0.07 | 9.2 | 10.4 | -0.04 |
| Crohn's disease | 0.4 | 0.6 | -0.02 | 0.4 | 0.5 | -0.01 |
| Dementia | 0.7 | 0.9 | -0.03 | 0.7 | 0.9 | -0.02 |
| Depressive disorder | 19.4 | 19.5 | 0.00 | 19.8 | 19.7 | 0.00 |
| Diabetes mellitus | 14.0 | 15.1 | -0.03 | 14.6 | 14.9 | -0.01 |
| Gastroesophageal reflux disease | 20.6 | 21.1 | -0.01 | 20.9 | 21.3 | -0.01 |
| Gastrointestinal hemorrhage | 1.6 | 1.8 | -0.01 | 1.7 | 1.7 | 0.00 |
| Human immunodeficiency virus infection | 0.1 | 0.1 | 0.00 | 0.1 | 0.1 | 0.00 |
| Hyperlipidemia | 33.2 | 32.8 | 0.01 | 33.2 | 32.8 | 0.01 |
| Hypertensive disorder | 41.4 | 42.2 | -0.02 | 41.8 | 41.6 | 0.00 |
| Lesion of liver | 0.8 | 1.1 | -0.03 | 0.9 | 1.1 | -0.02 |
| Obesity | 11.7 | 11.6 | 0.00 | 12.0 | 11.8 | 0.00 |
| Osteoarthritis | 28.3 | 29.7 | -0.03 | 28.8 | 28.8 | 0.00 |
| Pneumonia | 6.5 | 5.0 | 0.06 | 5.7 | 6.5 | -0.03 |
| Psoriasis | 1.6 | 1.8 | -0.02 | 1.6 | 1.7 | -0.01 |
| Renal impairment | 6.5 | 7.3 | -0.03 | 6.7 | 7.2 | -0.02 |
| Rheumatoid arthritis | 80.0 | 78.7 | 0.03 | 79.5 | 79.2 | 0.01 |
| Schizophrenia | 0.1 | 0.1 | 0.01 | 0.1 | 0.1 | 0.01 |
| Ulcerative colitis | 0.5 | 0.4 | 0.02 | 0.6 | 0.4 | 0.04 |
| Urinary tract infectious disease | 9.5 | 11.9 | -0.08 | 10.4 | 10.5 | -0.01 |
| Viral hepatitis C | 0.8 | 1.1 | -0.03 | 0.8 | 1.0 | -0.02 |
| Visual system disorder | 12.0 | 12.4 | -0.01 | 12.2 | 12.2 | 0.00 |
| Medical history: Cardiovascular disease |  |  |  |  |  |  |
| Atrial fibrillation | 3.3 | 4.0 | -0.04 | 3.4 | 3.9 | -0.03 |
| Cerebrovascular disease | 3.5 | 3.7 | -0.01 | 3.6 | 3.4 | 0.01 |
| Heart disease | 17.5 | 18.4 | -0.02 | 17.7 | 18.2 | -0.01 |
| Heart failure | 3.5 | 3.6 | -0.01 | 3.4 | 3.7 | -0.02 |
| Ischemic heart disease | 1.9 | 2.0 | 0.00 | 2.0 | 1.9 | 0.01 |
| Peripheral vascular disease | 2.0 | 2.2 | -0.01 | 2.0 | 2.0 | 0.00 |
| Pulmonary embolism | 1.0 | 1.0 | 0.00 | 1.0 | 1.0 | 0.00 |
| Venous thrombosis | 1.6 | 1.9 | -0.03 | 1.7 | 1.8 | -0.01 |
| Medical history: Neoplasms |  |  |  |  |  |  |
| Hematologic neoplasm | 0.6 | 0.4 | 0.02 | 0.5 | 0.5 | 0.00 |
| Malignant neoplastic disease | 7.4 | 7.7 | -0.01 | 7.4 | 7.7 | -0.01 |
| Malignant tumor of breast | 1.6 | 1.6 | 0.00 | 1.6 | 1.6 | 0.00 |
| Malignant tumor of lung | 0.5 | 0.4 | 0.02 | 0.4 | 0.5 | -0.01 |
| Malignant tumor of urinary bladder | 0.2 | 0.3 | -0.01 | 0.2 | 0.3 | -0.01 |
| Primary malignant neoplasm of prostate | 0.3 | 0.2 | 0.03 | 0.3 | 0.2 | 0.02 |
| Medication use |  |  |  |  |  |  |
| Agents acting on the renin-angiotensin system | 35.5 | 36.7 | -0.02 | 35.8 | 36.0 | 0.00 |
| Antibacterials for systemic use | 41.3 | 44.0 | -0.05 | 42.9 | 43.4 | -0.01 |
| Antidepressants | 43.1 | 44.5 | -0.03 | 44.2 | 44.2 | 0.00 |
| Antiepileptics | 28.9 | 30.3 | -0.03 | 30.1 | 29.8 | 0.01 |
| Antiinflammatory and antirheumatic products | 46.2 | 47.0 | -0.02 | 46.7 | 46.7 | 0.00 |
| Antineoplastic agents | 39.6 | 38.0 | 0.03 | 38.4 | 39.1 | -0.02 |
| Antipsoriatics | 0.9 | 0.9 | 0.00 | 1.0 | 0.8 | 0.02 |
| Antithrombotic agents | 25.1 | 27.4 | -0.05 | 25.9 | 26.1 | 0.00 |
| Beta blocking agents | 26.4 | 28.5 | -0.05 | 27.4 | 27.6 | 0.00 |
| Calcium channel blockers | 19.5 | 20.2 | -0.02 | 19.9 | 19.9 | 0.00 |
| Diuretics | 35.3 | 35.5 | 0.00 | 35.6 | 35.4 | 0.00 |
| Drugs for acid related disorders | 49.4 | 51.4 | -0.04 | 50.5 | 50.9 | -0.01 |
| Drugs for obstructive airway diseases | 53.3 | 45.1 | 0.16 | 49.3 | 50.8 | -0.03 |
| Drugs used in diabetes | 14.6 | 15.9 | -0.04 | 15.2 | 15.4 | 0.00 |
| Immunosuppressants | 55.9 | 54.7 | 0.02 | 55.1 | 55.5 | -0.01 |
| Lipid modifying agents | 34.4 | 34.8 | -0.01 | 34.9 | 34.5 | 0.01 |
| Opioids | 34.8 | 36.9 | -0.04 | 36.1 | 35.4 | 0.02 |
| Psychostimulants, agents used for adhd and nootropics | 5.4 | 5.4 | 0.00 | 5.5 | 5.4 | 0.01 |

### **S6.2.2. CCAE**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Before stratification |  |  | After stratification |  |  |
|  | AZM | AMX |  | AZM | AMX |  |
| Characteristic | % | % | Std. diff | % | % | Std. diff |
| Age group |  |  |  |  |  |  |
| 15-19 | 0.5 | 0.4 | 0.00 | 0.5 | 0.5 | 0.00 |
| 20-24 | 1.4 | 1.3 | 0.01 | 1.4 | 1.4 | 0.00 |
| 25-29 | 2.2 | 2.1 | 0.01 | 2.2 | 2.2 | 0.00 |
| 30-34 | 4.0 | 3.7 | 0.02 | 4.0 | 3.9 | 0.01 |
| 35-39 | 6.8 | 6.5 | 0.02 | 6.8 | 6.7 | 0.00 |
| 40-44 | 9.5 | 8.9 | 0.02 | 9.3 | 9.3 | 0.00 |
| 45-49 | 13.1 | 13.2 | 0.00 | 13.2 | 13.3 | 0.00 |
| 50-54 | 18.3 | 17.9 | 0.01 | 18.1 | 18.0 | 0.00 |
| 55-59 | 21.5 | 22.0 | -0.01 | 21.5 | 21.8 | -0.01 |
| 60-64 | 20.6 | 21.8 | -0.03 | 21.1 | 21.1 | 0.00 |
| 65-69 | 2.0 | 2.1 | 0.00 | 2.0 | 2.0 | 0.00 |
| Medical history: General |  |  |  |  |  |  |
| Acute respiratory disease | 62.5 | 50.7 | 0.24 | 58.0 | 57.5 | 0.01 |
| Attention deficit hyperactivity disorder | 1.4 | 1.5 | -0.01 | 1.4 | 1.5 | 0.00 |
| Chronic liver disease | 2.7 | 2.9 | -0.01 | 2.7 | 2.8 | -0.01 |
| Chronic obstructive lung disease | 5.6 | 4.4 | 0.06 | 5.0 | 5.2 | -0.01 |
| Dementia | 0.3 | 0.2 | 0.01 | 0.3 | 0.2 | 0.01 |
| Depressive disorder | 14.7 | 14.7 | 0.00 | 14.7 | 14.8 | 0.00 |
| Diabetes mellitus | 12.7 | 13.3 | -0.02 | 13.2 | 13.1 | 0.00 |
| Gastroesophageal reflux disease | 16.5 | 16.8 | -0.01 | 16.7 | 16.8 | 0.00 |
| Human immunodeficiency virus infection | 0.1 | 0.1 | 0.01 | 0.1 | 0.1 | 0.01 |
| Hyperlipidemia | 30.4 | 30.4 | 0.00 | 30.4 | 30.3 | 0.00 |
| Lesion of liver | 0.8 | 0.8 | -0.01 | 0.8 | 0.8 | 0.00 |
| Obesity | 9.4 | 10.8 | -0.05 | 10.2 | 10.1 | 0.00 |
| Osteoarthritis | 40.1 | 42.2 | -0.04 | 41.5 | 41.0 | 0.01 |
| Pneumonia | 6.8 | 4.3 | 0.11 | 5.7 | 5.5 | 0.01 |
| Psoriasis | 3.1 | 3.0 | 0.00 | 3.0 | 3.0 | 0.00 |
| Renal impairment | 3.9 | 4.3 | -0.02 | 4.2 | 4.1 | 0.00 |
| Rheumatoid arthritis | 83.6 | 82.2 | 0.04 | 82.9 | 83.0 | 0.00 |
| Ulcerative colitis | 0.7 | 0.7 | 0.00 | 0.7 | 0.7 | 0.00 |
| Urinary tract infectious disease | 13.6 | 14.3 | -0.02 | 14.0 | 13.9 | 0.00 |
| Viral hepatitis C | 0.7 | 0.9 | -0.02 | 0.8 | 0.9 | -0.01 |
| Visual system disorder | 36.8 | 37.0 | 0.00 | 36.9 | 37.1 | 0.00 |
| Medical history: Cardiovascular disease |  |  |  |  |  |  |
| Atrial fibrillation | 1.5 | 1.9 | -0.03 | 1.7 | 1.8 | 0.00 |
| Cerebrovascular disease | 3.2 | 3.1 | 0.00 | 3.1 | 3.2 | -0.01 |
| Coronary arteriosclerosis | 4.8 | 5.0 | -0.01 | 5.0 | 4.9 | 0.00 |
| Heart disease | 17.3 | 18.2 | -0.02 | 17.8 | 17.9 | 0.00 |
| Heart failure | 2.5 | 2.3 | 0.01 | 2.5 | 2.4 | 0.01 |
| Ischemic heart disease | 3.2 | 3.2 | 0.00 | 3.3 | 3.1 | 0.01 |
| Peripheral vascular disease | 1.6 | 1.7 | -0.01 | 1.6 | 1.7 | -0.01 |
| Pulmonary embolism | 0.9 | 1.0 | -0.01 | 0.9 | 1.0 | -0.01 |
| Venous thrombosis | 1.6 | 1.8 | -0.01 | 1.7 | 1.8 | 0.00 |
| Medical history: Neoplasms |  |  |  |  |  |  |
| Hematologic neoplasm | 1.2 | 1.1 | 0.01 | 1.2 | 1.1 | 0.00 |
| Malignant lymphoma | 0.7 | 0.6 | 0.00 | 0.6 | 0.6 | 0.00 |
| Malignant neoplastic disease | 7.6 | 7.5 | 0.00 | 7.6 | 7.5 | 0.00 |
| Malignant tumor of colon | 0.2 | 0.2 | -0.01 | 0.2 | 0.2 | 0.00 |
| Malignant tumor of lung | 0.2 | 0.2 | 0.01 | 0.2 | 0.2 | 0.01 |
| Malignant tumor of urinary bladder | 0.2 | 0.1 | 0.00 | 0.1 | 0.1 | 0.00 |
| Primary malignant neoplasm of prostate | 0.2 | 0.3 | -0.02 | 0.2 | 0.3 | -0.01 |
| Medication use |  |  |  |  |  |  |
| Agents acting on the renin-angiotensin system | 26.6 | 27.2 | -0.01 | 27.1 | 26.9 | 0.00 |
| Antibacterials for systemic use | 50.6 | 50.3 | 0.00 | 51.1 | 51.0 | 0.00 |
| Antidepressants | 43.3 | 42.0 | 0.02 | 43.0 | 42.8 | 0.00 |
| Antiinflammatory and antirheumatic products | 51.0 | 53.1 | -0.04 | 51.9 | 52.0 | 0.00 |
| Antipsoriatics | 0.9 | 0.9 | -0.01 | 0.9 | 0.9 | 0.00 |
| Antithrombotic agents | 8.9 | 10.8 | -0.06 | 9.8 | 9.9 | 0.00 |
| Beta blocking agents | 18.1 | 18.6 | -0.01 | 18.7 | 18.4 | 0.01 |
| Calcium channel blockers | 13.8 | 14.0 | -0.01 | 14.1 | 13.9 | 0.00 |
| Diuretics | 28.0 | 28.0 | 0.00 | 28.3 | 28.3 | 0.00 |
| Drugs for acid related disorders | 40.7 | 40.1 | 0.01 | 40.5 | 40.8 | -0.01 |
| Drugs for obstructive airway diseases | 43.6 | 37.0 | 0.13 | 41.1 | 40.7 | 0.01 |
| Drugs used in diabetes | 9.8 | 10.4 | -0.02 | 10.3 | 10.2 | 0.00 |
| Immunosuppressants | 52.5 | 49.8 | 0.05 | 51.1 | 51.2 | 0.00 |
| Lipid modifying agents | 22.5 | 22.9 | -0.01 | 22.7 | 22.6 | 0.00 |
| Opioids | 40.1 | 42.0 | -0.04 | 41.4 | 41.2 | 0.00 |
| Psycholeptics | 38.6 | 37.4 | 0.02 | 38.2 | 38.1 | 0.00 |
| Psychostimulants, agents used for adhd and nootropics | 7.3 | 7.1 | 0.01 | 7.3 | 7.4 | 0.00 |

### **S6.2.3. CPRD**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Before stratification |  |  | After stratification |  |  |
|  | AZM | AMX |  | AZM | AMX |  |
| Characteristic | % | % | Std. diff | % | % | Std. diff |
| Age group |  |  |  |  |  |  |
| 20-24 | <4.3 | 0.3 | 0.07 | 2.8 | 0.3 | 0.20 |
| 25-29 | <4.3 | 1.0 | -0.01 | 2.8 | 1.0 | 0.13 |
| 35-39 | <4.3 | 3.4 | 0.00 | 9.4 | 3.4 | 0.24 |
| 40-44 | <4.3 | 4.8 | -0.07 | 8.9 | 4.8 | 0.16 |
| 45-49 | 7.0 | 7.2 | -0.01 | 4.4 | 7.2 | -0.12 |
| 50-54 | 5.2 | 10.1 | -0.18 | 8.1 | 10.0 | -0.07 |
| 55-59 | 13.9 | 12.9 | 0.03 | 9.4 | 12.9 | -0.11 |
| 60-64 | 20.9 | 14.2 | 0.18 | 13.3 | 14.2 | -0.03 |
| 65-69 | 13.0 | 14.3 | -0.04 | 9.2 | 14.3 | -0.16 |
| 70-74 | 14.8 | 12.2 | 0.08 | 13.3 | 12.2 | 0.03 |
| 75-79 | 8.7 | 9.6 | -0.03 | 5.3 | 9.6 | -0.17 |
| 80-84 | 6.1 | 5.6 | 0.02 | 10.3 | 5.6 | 0.17 |
| 85-89 | <4.3 | 1.9 | -0.09 | <1.9 | 1.9 | -0.16 |
| 90-94 | <4.3 | 0.6 | 0.03 | 2.5 | 0.6 | 0.15 |
| Gender: female | 78.3 | 73.4 | 0.11 | 73.9 | 73.4 | 0.01 |
| Medical history: General |  |  |  |  |  |  |
| Acute respiratory disease | 30.4 | 20.9 | 0.22 | 29.2 | 21.1 | 0.19 |
| Chronic obstructive lung disease | 13.0 | 3.7 | 0.34 | 6.7 | 3.8 | 0.13 |
| Depressive disorder | <4.3 | 2.5 | 0.06 | <1.9 | 2.5 | -0.10 |
| Diabetes mellitus | 4.3 | 2.3 | 0.11 | 3.6 | 2.3 | 0.08 |
| Gastroesophageal reflux disease | <4.3 | 0.7 | 0.02 | <1.9 | 0.7 | -0.06 |
| Gastrointestinal hemorrhage | <4.3 | 1.6 | -0.07 | <1.9 | 1.6 | -0.14 |
| Hyperlipidemia | <4.3 | 0.9 | -0.01 | <1.9 | 0.9 | -0.08 |
| Hypertensive disorder | <4.3 | 2.7 | -0.01 | <1.9 | 2.7 | -0.14 |
| Lesion of liver | <4.3 | 0.1 | 0.11 | <1.9 | <0.1 | 0.04 |
| Obesity | <4.3 | 0.3 | 0.07 | <1.9 | 0.3 | -0.01 |
| Osteoarthritis | 6.1 | 4.4 | 0.07 | 8.1 | 4.5 | 0.15 |
| Pneumonia | <4.3 | 1.4 | 0.09 | <1.9 | 1.4 | -0.05 |
| Renal impairment | <4.3 | 3.5 | -0.18 | 2.5 | 3.5 | -0.06 |
| Rheumatoid arthritis | 45.2 | 36.8 | 0.17 | 36.4 | 36.9 | -0.01 |
| Urinary tract infectious disease | <4.3 | 5.2 | -0.25 | <1.9 | 5.2 | -0.30 |
| Visual system disorder | 7.0 | 8.3 | -0.05 | 9.4 | 8.3 | 0.04 |
| Medical history: Cardiovascular disease |  |  |  |  |  |  |
| Atrial fibrillation | <4.3 | 1.1 | 0.12 | <1.9 | 1.1 | -0.03 |
| Heart disease | <4.3 | 3.8 | -0.02 | <1.9 | 3.8 | -0.18 |
| Medical history: Neoplasms |  |  |  |  |  |  |
| Hematologic neoplasm | <4.3 | <0.1 | 0.12 | <1.9 | <0.1 | 0.05 |
| Malignant lymphoma | <4.3 | <0.1 | 0.12 | <1.9 | <0.1 | 0.05 |
| Malignant neoplastic disease | <4.3 | 1.8 | 0.11 | 3.3 | 1.8 | 0.10 |
| Malignant tumor of breast | <4.3 | 0.1 | 0.10 | 2.5 | 0.1 | 0.20 |
| Medication use |  |  |  |  |  |  |
| Agents acting on the renin-angiotensin system | 28.7 | 26.5 | 0.05 | 22.2 | 26.5 | -0.10 |
| Antibacterials for systemic use | 73.9 | 44.5 | 0.63 | 49.2 | 45.0 | 0.08 |
| Antidepressants | 38.3 | 31.8 | 0.14 | 29.7 | 31.9 | -0.05 |
| Antiepileptics | 15.7 | 8.7 | 0.21 | 5.0 | 8.8 | -0.15 |
| Antiinflammatory and antirheumatic products | 53.0 | 52.1 | 0.02 | 50.3 | 52.2 | -0.04 |
| Antineoplastic agents | 37.4 | 52.7 | -0.31 | 45.3 | 52.5 | -0.14 |
| Antipsoriatics | <4.3 | 0.9 | -0.01 | 2.5 | 0.9 | 0.12 |
| Antithrombotic agents | 27.0 | 23.8 | 0.07 | 15.8 | 23.9 | -0.20 |
| Beta blocking agents | 10.4 | 16.7 | -0.18 | 7.8 | 16.7 | -0.27 |
| Calcium channel blockers | 18.3 | 18.8 | -0.02 | 11.9 | 18.8 | -0.19 |
| Diuretics | 18.3 | 23.3 | -0.12 | 15.0 | 23.3 | -0.21 |
| Drugs for acid related disorders | 74.8 | 63.9 | 0.24 | 64.7 | 64.1 | 0.01 |
| Drugs for obstructive airway diseases | 69.6 | 32.3 | 0.80 | 29.2 | 33.0 | -0.08 |
| Drugs used in diabetes | 10.4 | 8.8 | 0.06 | 10.3 | 8.8 | 0.05 |
| Immunosuppressants | 47.0 | 58.1 | -0.22 | 50.6 | 57.9 | -0.15 |
| Lipid modifying agents | 32.2 | 28.3 | 0.08 | 16.9 | 28.4 | -0.27 |
| Opioids | 46.1 | 39.2 | 0.14 | 45.3 | 39.3 | 0.12 |
| Psycholeptics | 20.9 | 19.9 | 0.02 | 15.6 | 19.9 | -0.11 |

### **S6.2.4. DAGermany**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Before stratification |  |  | After stratification |  |  |
|  | AZM | AMX |  | AZM | AMX |  |
| Characteristic | % | % | Std. diff | % | % | Std. diff |
| Age group |  |  |  |  |  |  |
| 20-24 | <5.6 | <2.5 | 0.02 | <5.6 | <2.5 | 0.02 |
| 30-34 | <5.6 | 4.0 | -0.10 | <5.6 | 4.0 | -0.10 |
| 35-39 | 6.7 | 4.5 | 0.10 | 6.7 | 4.5 | 0.10 |
| 40-44 | 12.4 | 4.0 | 0.31 | 12.4 | 4.0 | 0.31 |
| 45-49 | 7.9 | 9.4 | -0.06 | 7.9 | 9.4 | -0.06 |
| 50-54 | 13.5 | 9.4 | 0.13 | 13.5 | 9.4 | 0.13 |
| 55-59 | 16.9 | 13.4 | 0.10 | 16.9 | 13.4 | 0.10 |
| 60-64 | 12.4 | 10.9 | 0.05 | 12.4 | 10.9 | 0.05 |
| 65-69 | 10.1 | 12.4 | -0.07 | 10.1 | 12.4 | -0.07 |
| 70-74 | 7.9 | 9.4 | -0.06 | 7.9 | 9.4 | -0.06 |
| 75-79 | 5.6 | 6.9 | -0.05 | 5.6 | 6.9 | -0.05 |
| 80-84 | <5.6 | 6.9 | -0.22 | <5.6 | 6.9 | -0.22 |
| Gender: female | 89.9 | 79.2 | 0.30 | 89.9 | 79.2 | 0.30 |
| Medical history: General |  |  |  |  |  |  |
| Acute respiratory disease | 61.8 | 55.4 | 0.13 | 61.8 | 55.4 | 0.13 |
| Chronic liver disease | <5.6 | <2.5 | -0.07 | <5.6 | <2.5 | -0.07 |
| Chronic obstructive lung disease | 6.7 | 11.4 | -0.16 | 6.7 | 11.4 | -0.16 |
| Depressive disorder | 14.6 | 10.4 | 0.13 | 14.6 | 10.4 | 0.13 |
| Diabetes mellitus | 5.6 | 13.4 | -0.27 | 5.6 | 13.4 | -0.27 |
| Hyperlipidemia | 9.0 | 13.4 | -0.14 | 9.0 | 13.4 | -0.14 |
| Hypertensive disorder | 28.1 | 40.1 | -0.26 | 28.1 | 40.1 | -0.25 |
| Obesity | <5.6 | 5.0 | -0.02 | <5.6 | 5.0 | -0.02 |
| Osteoarthritis | 11.2 | 13.4 | -0.06 | 11.2 | 13.4 | -0.06 |
| Pneumonia | <5.6 | 6.9 | -0.22 | <5.6 | 6.9 | -0.22 |
| Psoriasis | <5.6 | <2.5 | 0.15 | <5.6 | <2.5 | 0.15 |
| Renal impairment | <5.6 | 4.5 | -0.06 | <5.6 | 4.5 | -0.06 |
| Rheumatoid arthritis | 56.2 | 57.9 | -0.04 | 56.2 | 57.9 | -0.04 |
| Urinary tract infectious disease | 5.6 | 9.9 | -0.16 | 5.6 | 9.9 | -0.16 |
| Visual system disorder | 11.2 | 16.8 | -0.16 | 11.2 | 16.8 | -0.16 |
| Medical history: Cardiovascular disease |  |  |  |  |  |  |
| Cerebrovascular disease | <5.6 | <2.5 | 0.14 | <5.6 | <2.5 | 0.14 |
| Coronary arteriosclerosis | <5.6 | <2.5 | 0.06 | <5.6 | <2.5 | 0.06 |
| Heart disease | 11.2 | 21.8 | -0.29 | 11.2 | 21.8 | -0.29 |
| Heart failure | <5.6 | 6.9 | -0.30 | <5.6 | 6.9 | -0.30 |
| Ischemic heart disease | <5.6 | 7.9 | -0.14 | <5.6 | 7.9 | -0.14 |
| Peripheral vascular disease | <5.6 | 2.5 | -0.10 | <5.6 | 2.5 | -0.10 |
| Venous thrombosis | <5.6 | 5.9 | -0.12 | <5.6 | 5.9 | -0.12 |
| Medical history: Neoplasms |  |  |  |  |  |  |
| Malignant neoplastic disease | <5.6 | 6.4 | -0.08 | <5.6 | 6.4 | -0.08 |
| Medication use |  |  |  |  |  |  |
| Agents acting on the renin-angiotensin system | 29.2 | 39.6 | -0.22 | 29.2 | 39.6 | -0.22 |
| Antibacterials for systemic use | 29.2 | 37.6 | -0.18 | 29.2 | 37.6 | -0.18 |
| Antidepressants | 16.9 | 18.8 | -0.05 | 16.9 | 18.8 | -0.05 |
| Antiepileptics | <5.6 | 7.9 | -0.14 | <5.6 | 7.9 | -0.14 |
| Antiinflammatory and antirheumatic products | 43.8 | 46.5 | -0.06 | 43.8 | 46.5 | -0.05 |
| Antineoplastic agents | 29.2 | 27.2 | 0.04 | 29.2 | 27.2 | 0.04 |
| Antithrombotic agents | 13.5 | 26.2 | -0.32 | 13.5 | 26.2 | -0.32 |
| Beta blocking agents | 25.8 | 35.6 | -0.21 | 25.8 | 35.6 | -0.21 |
| Calcium channel blockers | 16.9 | 18.3 | -0.04 | 16.9 | 18.3 | -0.04 |
| Diuretics | 19.1 | 39.1 | -0.45 | 19.1 | 39.1 | -0.45 |
| Drugs for acid related disorders | 65.2 | 69.8 | -0.10 | 65.2 | 69.8 | -0.10 |
| Drugs for obstructive airway diseases | 19.1 | 21.8 | -0.07 | 19.1 | 21.8 | -0.07 |
| Drugs used in diabetes | 6.7 | 12.9 | -0.21 | 6.7 | 12.9 | -0.21 |
| Immunosuppressants | 37.1 | 32.7 | 0.09 | 37.1 | 32.7 | 0.09 |
| Lipid modifying agents | 5.6 | 17.8 | -0.39 | 5.6 | 17.8 | -0.38 |
| Opioids | 20.2 | 27.2 | -0.16 | 20.2 | 27.2 | -0.16 |
| Psycholeptics | 16.9 | 10.4 | 0.19 | 16.9 | 10.4 | 0.19 |

### **S6.2.5. IMRD**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Before stratification |  |  | After stratification |  |  |
|  | AZM | AMX |  | AZM | AMX |  |
| Characteristic | % | % | Std. diff | % | % | Std. diff |
| Age group |  |  |  |  |  |  |
| 25-29 | <4.5 | 0.9 | 0.13 | 3.6 | 0.9 | 0.18 |
| 30-34 | <4.5 | 1.7 | -0.07 | 6.7 | 1.7 | 0.25 |
| 35-39 | 4.5 | 3.1 | 0.07 | 10.0 | 3.1 | 0.28 |
| 40-44 | <4.5 | 4.3 | -0.09 | 3.3 | 4.3 | -0.05 |
| 45-49 | 5.4 | 7.3 | -0.08 | 4.0 | 7.2 | -0.14 |
| 50-54 | <4.5 | 10.1 | -0.26 | 3.8 | 10.1 | -0.25 |
| 55-59 | 9.8 | 12.4 | -0.08 | 2.6 | 12.4 | -0.38 |
| 60-64 | 17.9 | 14.6 | 0.09 | 16.6 | 14.5 | 0.06 |
| 65-69 | 13.4 | 14.6 | -0.04 | 19.7 | 14.7 | 0.13 |
| 70-74 | 19.6 | 12.7 | 0.19 | 14.2 | 12.7 | 0.04 |
| 75-79 | 9.8 | 9.5 | 0.01 | 6.9 | 9.5 | -0.10 |
| 80-84 | 8.0 | 5.7 | 0.09 | 8.3 | 5.7 | 0.10 |
| 85-89 | <4.5 | 2.0 | -0.10 | <1.6 | 2.1 | -0.17 |
| 90-94 | <4.5 | 0.5 | 0.04 | <1.6 | 0.5 | -0.05 |
| Gender: female | 78.6 | 73.8 | 0.11 | 74.1 | 73.8 | 0.01 |
| Race |  |  |  |  |  |  |
| race = White | 30.4 | 30.8 | -0.01 | 48.2 | 30.7 | 0.36 |
| race = Asian Indian | <4.5 | 0.6 | 0.03 | 2.9 | 0.6 | 0.17 |
| race = Pakistani | <4.5 | 0.4 | 0.07 | 1.7 | 0.4 | 0.13 |
| Medical history: General |  |  |  |  |  |  |
| Acute respiratory disease | 29.5 | 20.8 | 0.20 | 20.6 | 20.9 | -0.01 |
| Chronic obstructive lung disease | 17.0 | 3.7 | 0.45 | 5.9 | 3.9 | 0.09 |
| Depressive disorder | 4.5 | 2.5 | 0.11 | 2.6 | 2.5 | 0.00 |
| Diabetes mellitus | 8.0 | 2.1 | 0.27 | 8.3 | 2.1 | 0.28 |
| Gastroesophageal reflux disease | <4.5 | 0.6 | 0.03 | <1.6 | 0.6 | -0.06 |
| Gastrointestinal hemorrhage | <4.5 | 1.4 | -0.05 | <1.6 | 1.4 | -0.13 |
| Hyperlipidemia | <4.5 | 1.0 | -0.01 | <1.6 | 1.0 | -0.10 |
| Hypertensive disorder | <4.5 | 2.6 | 0.00 | <1.6 | 2.6 | -0.15 |
| Obesity | <4.5 | 0.4 | 0.14 | 3.1 | 0.4 | 0.21 |
| Osteoarthritis | <4.5 | 4.6 | -0.05 | 7.4 | 4.6 | 0.12 |
| Pneumonia | <4.5 | 1.1 | 0.17 | <1.6 | 1.1 | -0.02 |
| Renal impairment | <4.5 | 3.1 | -0.03 | <1.6 | 3.2 | -0.18 |
| Rheumatoid arthritis | 33.9 | 37.3 | -0.07 | 42.0 | 37.4 | 0.09 |
| Urinary tract infectious disease | <4.5 | 4.5 | -0.16 | 5.2 | 4.6 | 0.03 |
| Visual system disorder | 9.8 | 8.3 | 0.05 | 10.2 | 8.3 | 0.06 |
| Medical history: Cardiovascular disease |  |  |  |  |  |  |
| Atrial fibrillation | <4.5 | 1.1 | -0.02 | <1.6 | 1.1 | -0.11 |
| Cerebrovascular disease | <4.5 | 0.6 | 0.11 | <1.6 | 0.6 | -0.02 |
| Heart disease | <4.5 | 3.8 | -0.12 | <1.6 | 3.8 | -0.23 |
| Venous thrombosis | <4.5 | 0.8 | 0.01 | 6.7 | 0.8 | 0.31 |
| Medical history: Neoplasms |  |  |  |  |  |  |
| Malignant lymphoma | <4.5 | 0.1 | 0.11 | <1.6 | 0.1 | 0.03 |
| Malignant neoplastic disease | <4.5 | 1.9 | 0.06 | 5.5 | 1.9 | 0.19 |
| Malignant tumor of breast | <4.5 | 0.2 | 0.09 | 5.0 | 0.2 | 0.30 |
| Medication use |  |  |  |  |  |  |
| Antibacterials for systemic use | 9.8 | 4.6 | 0.20 | 2.6 | 4.6 | -0.11 |
| Antidepressants | <4.5 | 1.1 | 0.16 | <1.6 | 1.1 | -0.02 |
| Antiinflammatory and antirheumatic products | <4.5 | 1.2 | -0.03 | <1.6 | 1.2 | -0.11 |
| Antineoplastic agents | <4.5 | 1.6 | -0.06 | <1.6 | 1.6 | -0.14 |
| Antithrombotic agents | <4.5 | 1.4 | 0.10 | 3.3 | 1.4 | 0.13 |
| Beta blocking agents | <4.5 | 0.5 | 0.05 | <1.6 | 0.5 | -0.04 |
| Diuretics | <4.5 | 1.0 | -0.01 | <1.6 | 1.0 | -0.10 |
| Drugs for acid related disorders | <4.5 | 1.8 | -0.08 | <1.6 | 1.8 | -0.16 |
| Drugs for obstructive airway diseases | <4.5 | 0.7 | 0.02 | <1.6 | 0.7 | -0.07 |
| Immunosuppressants | <4.5 | 1.8 | -0.08 | <1.6 | 1.8 | -0.16 |
| Lipid modifying agents | <4.5 | 1.3 | 0.10 | 3.3 | 1.3 | 0.13 |

### **S6.2.6 IPCI**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Before stratification |  |  | After stratification |  |  |
|  | AZM | AMX |  | AZM | AMX |  |
| Characteristic | % | % | Std. diff | % | % | Std. diff |
| Age group |  |  |  |  |  |  |
| 20-24 | <4.1 | <1.0 | 0.05 | <4.1 | <1.0 | 0.05 |
| 35-39 | <4.1 | <1.0 | 0.19 | <4.1 | <1.0 | 0.19 |
| 40-44 | 6.6 | 4.6 | 0.09 | 6.6 | 4.6 | 0.09 |
| 45-49 | 9.1 | 6.6 | 0.09 | 9.1 | 6.6 | 0.09 |
| 50-54 | 7.4 | 6.8 | 0.02 | 7.4 | 6.8 | 0.02 |
| 55-59 | 8.3 | 11.0 | -0.09 | 8.3 | 11.0 | -0.09 |
| 60-64 | 13.2 | 14.9 | -0.05 | 13.2 | 14.9 | -0.05 |
| 65-69 | 16.5 | 10.6 | 0.18 | 16.5 | 10.6 | 0.18 |
| 70-74 | 12.4 | 13.5 | -0.03 | 12.4 | 13.5 | -0.03 |
| 75-79 | 9.9 | 11.8 | -0.06 | 9.9 | 11.8 | -0.06 |
| 80-84 | 8.3 | 8.9 | -0.02 | 8.3 | 8.9 | -0.02 |
| 85-89 | <4.1 | 6.8 | -0.16 | <4.1 | 6.8 | -0.16 |
| Gender: female | 65.3 | 72.0 | -0.15 | 65.3 | 72.0 | -0.15 |
| Medical history: General |  |  |  |  |  |  |
| Acute respiratory disease | 37.2 | 31.9 | 0.11 | 37.2 | 31.9 | 0.11 |
| Depressive disorder | <4.1 | 3.7 | -0.02 | <4.1 | 3.7 | -0.02 |
| Diabetes mellitus | 6.6 | 8.3 | -0.06 | 6.6 | 8.3 | -0.06 |
| Gastrointestinal hemorrhage | <4.1 | 1.7 | 0.06 | <4.1 | 1.7 | 0.06 |
| Hyperlipidemia | <4.1 | 2.7 | -0.14 | <4.1 | 2.7 | -0.14 |
| Hypertensive disorder | 19.0 | 17.6 | 0.04 | 19.0 | 17.6 | 0.04 |
| Obesity | <4.1 | 1.4 | 0.12 | <4.1 | 1.4 | 0.12 |
| Osteoarthritis | 4.1 | 7.0 | -0.13 | 4.1 | 7.0 | -0.13 |
| Pneumonia | 14.9 | 14.9 | 0.00 | 14.9 | 14.9 | 0.00 |
| Renal impairment | <4.1 | 3.5 | -0.06 | <4.1 | 3.5 | -0.06 |
| Ulcerative colitis | <4.1 | <1.0 | 0.15 | <4.1 | <1.0 | 0.15 |
| Urinary tract infectious disease | 9.9 | 18.8 | -0.26 | 9.9 | 18.8 | -0.26 |
| Visual system disorder | 21.5 | 15.9 | 0.14 | 21.5 | 15.9 | 0.14 |
| Medical history: Cardiovascular disease |  |  |  |  |  |  |
| Atrial fibrillation | <4.1 | 4.1 | -0.04 | <4.1 | 4.1 | -0.04 |
| Cerebrovascular disease | <4.1 | 2.7 | -0.01 | <4.1 | 2.7 | -0.01 |
| Heart disease | 12.4 | 14.5 | -0.06 | 12.4 | 14.5 | -0.06 |
| Heart failure | 4.1 | 3.5 | 0.03 | 4.1 | 3.5 | 0.03 |
| Ischemic heart disease | 4.1 | 6.0 | -0.08 | 4.1 | 6.0 | -0.08 |
| Peripheral vascular disease | <4.1 | 5.0 | -0.25 | <4.1 | 5.0 | -0.25 |
| Venous thrombosis | <4.1 | 1.0 | -0.02 | <4.1 | <1.0 | -0.02 |
| Medical history: Neoplasms |  |  |  |  |  |  |
| Malignant neoplastic disease | 7.4 | 7.7 | -0.01 | 7.4 | 7.7 | -0.01 |
| Medication use |  |  |  |  |  |  |
| Agents acting on the renin-angiotensin system | 34.7 | 35.4 | -0.02 | 34.7 | 35.4 | -0.01 |
| Antibacterials for systemic use | 48.8 | 47.0 | 0.04 | 48.8 | 47.0 | 0.04 |
| Antidepressants | 18.2 | 19.9 | -0.04 | 18.2 | 19.9 | -0.04 |
| Antiepileptics | 9.1 | 8.9 | 0.01 | 9.1 | 8.9 | 0.01 |
| Antiinflammatory and antirheumatic products | 36.4 | 41.8 | -0.11 | 36.4 | 41.8 | -0.11 |
| Antineoplastic agents | 46.3 | 48.4 | -0.04 | 46.3 | 48.4 | -0.04 |
| Antipsoriatics | <4.1 | 1.9 | -0.09 | <4.1 | 1.9 | -0.09 |
| Antithrombotic agents | 30.6 | 32.5 | -0.04 | 30.6 | 32.5 | -0.04 |
| Beta blocking agents | 27.3 | 31.9 | -0.10 | 27.3 | 31.9 | -0.10 |
| Calcium channel blockers | 19.8 | 20.3 | -0.01 | 19.8 | 20.3 | -0.01 |
| Diuretics | 32.2 | 32.9 | -0.02 | 32.2 | 32.9 | -0.02 |
| Drugs for acid related disorders | 77.7 | 80.3 | -0.06 | 77.7 | 80.3 | -0.06 |
| Drugs for obstructive airway diseases | 54.5 | 42.0 | 0.25 | 54.5 | 42.0 | 0.25 |
| Drugs used in diabetes | 13.2 | 12.0 | 0.04 | 13.2 | 12.0 | 0.04 |
| Immunosuppressants | 53.7 | 52.4 | 0.03 | 53.7 | 52.4 | 0.03 |
| Lipid modifying agents | 34.7 | 38.1 | -0.07 | 34.7 | 38.1 | -0.07 |
| Opioids | 24.8 | 28.8 | -0.09 | 24.8 | 28.8 | -0.09 |
| Psycholeptics | 33.9 | 27.3 | 0.14 | 33.9 | 27.3 | 0.14 |
| Psychostimulants, agents used for adhd and nootropics | <4.1 | <1.0 | 0.15 | <4.1 | <1.0 | 0.15 |

### **S6.2.7. MDCD**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Before stratification |  |  | After stratification |  |  |
|  | AZM | AMX |  | AZM | AMX |  |
| Characteristic | % | % | Std. diff | % | % | Std. diff |
| Age group |  |  |  |  |  |  |
| 15-19 | 1.3 | 1.5 | -0.02 | 1.2 | 1.5 | -0.02 |
| 20-24 | 2.4 | 2.3 | 0.01 | 2.7 | 2.3 | 0.03 |
| 25-29 | 4.5 | 4.9 | -0.02 | 5.1 | 4.5 | 0.03 |
| 30-34 | 6.1 | 7.4 | -0.05 | 6.9 | 7.0 | -0.01 |
| 35-39 | 9.1 | 10.2 | -0.04 | 9.0 | 9.5 | -0.02 |
| 40-44 | 10.5 | 11.1 | -0.02 | 10.8 | 10.7 | 0.00 |
| 45-49 | 13.1 | 13.6 | -0.02 | 12.8 | 13.7 | -0.03 |
| 50-54 | 16.5 | 15.3 | 0.03 | 16.3 | 16.0 | 0.01 |
| 55-59 | 15.6 | 15.8 | -0.01 | 15.5 | 16.2 | -0.02 |
| 60-64 | 12.3 | 10.8 | 0.05 | 11.8 | 11.0 | 0.02 |
| 65-69 | 4.3 | 3.2 | 0.06 | 4.1 | 3.5 | 0.03 |
| 70-74 | 2.2 | 1.7 | 0.04 | 2.0 | 1.8 | 0.02 |
| 85-89 | 0.3 | 0.4 | 0.00 | 0.3 | 0.4 | -0.02 |
| Gender: female | 89.1 | 89.7 | -0.02 | 89.3 | 89.9 | -0.02 |
| Race |  |  |  |  |  |  |
| race = Black or African American | 27.4 | 29.9 | -0.06 | 27.5 | 28.0 | -0.01 |
| race = White | 57.3 | 54.2 | 0.06 | 56.9 | 56.3 | 0.01 |
| Medical history: General |  |  |  |  |  |  |
| Acute respiratory disease | 69.7 | 54.0 | 0.33 | 61.4 | 63.4 | -0.04 |
| Attention deficit hyperactivity disorder | 2.6 | 2.6 | 0.00 | 2.7 | 2.7 | 0.00 |
| Chronic liver disease | 6.5 | 6.8 | -0.01 | 6.8 | 6.8 | 0.00 |
| Chronic obstructive lung disease | 28.0 | 20.4 | 0.18 | 22.3 | 25.6 | -0.08 |
| Crohn's disease | 1.1 | 0.7 | 0.04 | 1.1 | 0.7 | 0.04 |
| Dementia | 1.2 | 1.5 | -0.03 | 1.2 | 1.6 | -0.03 |
| Depressive disorder | 39.9 | 41.4 | -0.03 | 40.9 | 41.1 | 0.00 |
| Diabetes mellitus | 26.6 | 25.6 | 0.02 | 26.3 | 26.1 | 0.00 |
| Gastroesophageal reflux disease | 35.4 | 33.9 | 0.03 | 34.5 | 34.6 | 0.00 |
| Gastrointestinal hemorrhage | 5.0 | 5.8 | -0.04 | 5.1 | 5.8 | -0.03 |
| Human immunodeficiency virus infection | 0.3 | 0.7 | -0.06 | 0.5 | 0.6 | -0.02 |
| Hyperlipidemia | 38.8 | 35.6 | 0.07 | 37.9 | 37.0 | 0.02 |
| Hypertensive disorder | 59.2 | 58.0 | 0.03 | 59.0 | 59.4 | -0.01 |
| Lesion of liver | 1.3 | 1.7 | -0.03 | 1.5 | 1.9 | -0.03 |
| Obesity | 23.3 | 24.8 | -0.04 | 23.6 | 24.0 | -0.01 |
| Osteoarthritis | 55.2 | 55.1 | 0.00 | 54.6 | 55.7 | -0.02 |
| Pneumonia | 15.9 | 9.1 | 0.21 | 12.1 | 12.4 | -0.01 |
| Psoriasis | 2.1 | 1.9 | 0.01 | 2.2 | 2.1 | 0.00 |
| Renal impairment | 11.6 | 12.0 | -0.01 | 10.8 | 12.0 | -0.04 |
| Rheumatoid arthritis | 81.8 | 83.1 | -0.03 | 82.4 | 83.2 | -0.02 |
| Schizophrenia | 1.6 | 1.7 | -0.01 | 1.7 | 1.7 | 0.00 |
| Ulcerative colitis | 0.5 | 0.6 | -0.01 | 0.7 | 0.6 | 0.01 |
| Urinary tract infectious disease | 20.6 | 22.1 | -0.04 | 21.3 | 21.2 | 0.00 |
| Viral hepatitis C | 4.8 | 5.5 | -0.03 | 5.5 | 5.6 | 0.00 |
| Visual system disorder | 50.0 | 50.4 | -0.01 | 50.1 | 51.1 | -0.02 |
| Medical history: Cardiovascular disease |  |  |  |  |  |  |
| Atrial fibrillation | 3.1 | 2.8 | 0.02 | 2.8 | 3.0 | -0.01 |
| Cerebrovascular disease | 5.9 | 5.8 | 0.00 | 6.2 | 6.1 | 0.00 |
| Coronary arteriosclerosis | 11.3 | 9.0 | 0.08 | 9.8 | 10.0 | 0.00 |
| Heart disease | 35.0 | 31.0 | 0.09 | 32.2 | 33.2 | -0.02 |
| Heart failure | 10.9 | 9.2 | 0.06 | 9.4 | 10.5 | -0.04 |
| Ischemic heart disease | 9.4 | 6.9 | 0.09 | 8.4 | 7.5 | 0.04 |
| Peripheral vascular disease | 4.6 | 5.2 | -0.03 | 4.3 | 5.2 | -0.04 |
| Pulmonary embolism | 2.6 | 2.8 | -0.01 | 2.4 | 2.9 | -0.04 |
| Venous thrombosis | 3.5 | 3.9 | -0.02 | 3.6 | 4.0 | -0.02 |
| Medical history: Neoplasms |  |  |  |  |  |  |
| Hematologic neoplasm | 1.4 | 1.5 | 0.00 | 1.5 | 1.5 | -0.01 |
| Malignant lymphoma | 0.5 | 0.5 | 0.01 | 0.6 | 0.4 | 0.03 |
| Malignant neoplasm of anorectum | <0.1 | 0.2 | -0.03 | 0.1 | 0.2 | -0.02 |
| Malignant neoplastic disease | 7.2 | 7.0 | 0.01 | 7.1 | 6.9 | 0.01 |
| Malignant tumor of lung | 0.5 | 0.6 | -0.01 | 0.4 | 0.6 | -0.03 |
| Malignant tumor of urinary bladder | <0.1 | <0.1 | 0.02 | <0.1 | <0.1 | 0.02 |
| Primary malignant neoplasm of prostate | <0.1 | 0.2 | -0.02 | <0.1 | 0.1 | -0.01 |
| Medication use |  |  |  |  |  |  |
| Agents acting on the renin-angiotensin system | 36.3 | 34.4 | 0.04 | 35.0 | 35.0 | 0.00 |
| Antibacterials for systemic use | 60.5 | 59.7 | 0.02 | 60.1 | 59.8 | 0.00 |
| Antidepressants | 62.3 | 61.3 | 0.02 | 62.3 | 62.4 | 0.00 |
| Antiepileptics | 51.0 | 49.8 | 0.02 | 51.1 | 50.2 | 0.02 |
| Antiinflammatory and antirheumatic products | 56.8 | 59.4 | -0.05 | 59.3 | 58.0 | 0.03 |
| Antineoplastic agents | 36.9 | 34.2 | 0.06 | 36.0 | 35.6 | 0.01 |
| Antipsoriatics | 0.7 | 1.0 | -0.03 | 0.6 | 1.1 | -0.05 |
| Antithrombotic agents | 22.8 | 22.6 | 0.00 | 22.1 | 22.9 | -0.02 |
| Beta blocking agents | 28.6 | 27.3 | 0.03 | 27.7 | 28.3 | -0.01 |
| Calcium channel blockers | 23.4 | 22.0 | 0.03 | 22.3 | 22.7 | -0.01 |
| Diuretics | 40.4 | 37.6 | 0.06 | 39.1 | 39.2 | 0.00 |
| Drugs for acid related disorders | 61.7 | 59.8 | 0.04 | 60.3 | 61.6 | -0.03 |
| Drugs for obstructive airway diseases | 65.5 | 53.5 | 0.25 | 59.0 | 60.3 | -0.03 |
| Drugs used in diabetes | 19.8 | 18.8 | 0.02 | 19.5 | 18.9 | 0.02 |
| Immunosuppressants | 53.1 | 49.4 | 0.07 | 51.5 | 51.8 | 0.00 |
| Lipid modifying agents | 32.0 | 30.2 | 0.04 | 31.0 | 31.3 | -0.01 |
| Opioids | 66.6 | 68.3 | -0.04 | 67.6 | 68.7 | -0.02 |
| Psycholeptics | 58.0 | 56.7 | 0.03 | 57.4 | 57.6 | 0.00 |
| Psychostimulants, agents used for adhd and nootropics | 8.3 | 7.7 | 0.02 | 8.2 | 7.7 | 0.02 |

### **S6.2.8. MDCR**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Before stratification |  |  | After stratification |  |  |
|  | AZM | AMX |  | AZM | AMX |  |
| Characteristic | % | % | Std. diff | % | % | Std. diff |
| Age group |  |  |  |  |  |  |
| 45-49 | 0.1 | 0.1 | 0.02 | 0.1 | 0.1 | 0.02 |
| 55-59 | 1.0 | 1.1 | 0.00 | 1.0 | 1.2 | -0.02 |
| 60-64 | 2.1 | 2.2 | -0.01 | 2.2 | 2.3 | -0.01 |
| 65-69 | 29.2 | 28.1 | 0.03 | 29.0 | 28.7 | 0.01 |
| 70-74 | 27.7 | 28.2 | -0.01 | 27.8 | 28.0 | 0.00 |
| 75-79 | 19.6 | 20.2 | -0.01 | 19.8 | 20.0 | 0.00 |
| 80-84 | 12.3 | 13.0 | -0.02 | 12.4 | 12.6 | -0.01 |
| 85-89 | 5.8 | 5.3 | 0.02 | 5.7 | 5.3 | 0.02 |
| 90-94 | 1.4 | 1.4 | 0.00 | 1.4 | 1.3 | 0.01 |
| 95-99 | 0.1 | 0.2 | -0.01 | 0.1 | 0.2 | -0.02 |
| Gender: female | 78.1 | 74.0 | 0.10 | 75.7 | 75.7 | 0.00 |
| Medical history: General |  |  |  |  |  |  |
| Acute respiratory disease | 53.3 | 34.2 | 0.39 | 42.5 | 44.4 | -0.04 |
| Attention deficit hyperactivity disorder | 0.1 | 0.2 | -0.01 | 0.1 | 0.2 | -0.01 |
| Chronic liver disease | 1.7 | 2.0 | -0.03 | 1.7 | 2.1 | -0.03 |
| Chronic obstructive lung disease | 20.3 | 14.7 | 0.15 | 16.7 | 18.1 | -0.04 |
| Crohn's disease | 0.6 | 0.5 | 0.02 | 0.7 | 0.5 | 0.03 |
| Dementia | 2.1 | 2.3 | -0.02 | 2.2 | 2.3 | 0.00 |
| Depressive disorder | 10.4 | 11.0 | -0.02 | 10.3 | 11.0 | -0.02 |
| Diabetes mellitus | 20.7 | 20.7 | 0.00 | 20.6 | 20.4 | 0.00 |
| Gastroesophageal reflux disease | 19.4 | 18.8 | 0.02 | 19.2 | 19.7 | -0.01 |
| Gastrointestinal hemorrhage | 4.4 | 5.1 | -0.03 | 4.6 | 5.0 | -0.02 |
| Human immunodeficiency virus infection | <0.1 | 0.1 | -0.02 | <0.1 | 0.1 | -0.02 |
| Hyperlipidemia | 39.1 | 40.0 | -0.02 | 39.8 | 39.7 | 0.00 |
| Hypertensive disorder | 62.2 | 61.6 | 0.01 | 61.9 | 61.4 | 0.01 |
| Lesion of liver | 0.9 | 1.1 | -0.02 | 0.9 | 1.1 | -0.02 |
| Obesity | 5.5 | 6.3 | -0.04 | 5.8 | 6.2 | -0.02 |
| Osteoarthritis | 53.3 | 57.7 | -0.09 | 56.1 | 55.5 | 0.01 |
| Pneumonia | 14.3 | 9.2 | 0.16 | 11.6 | 12.0 | -0.01 |
| Psoriasis | 2.0 | 2.4 | -0.03 | 2.2 | 2.4 | -0.02 |
| Renal impairment | 12.6 | 12.5 | 0.00 | 12.7 | 12.5 | 0.01 |
| Rheumatoid arthritis | 87.0 | 86.5 | 0.02 | 86.7 | 86.6 | 0.00 |
| Schizophrenia | <0.1 | 0.1 | -0.01 | <0.1 | 0.1 | -0.01 |
| Ulcerative colitis | 0.7 | 0.7 | -0.01 | 0.6 | 0.7 | -0.01 |
| Urinary tract infectious disease | 15.2 | 17.1 | -0.05 | 15.6 | 16.1 | -0.01 |
| Viral hepatitis C | 0.4 | 0.5 | -0.02 | 0.4 | 0.5 | -0.01 |
| Visual system disorder | 61.5 | 61.0 | 0.01 | 61.3 | 60.8 | 0.01 |
| Medical history: Cardiovascular disease |  |  |  |  |  |  |
| Atrial fibrillation | 9.6 | 11.3 | -0.06 | 10.3 | 10.6 | -0.01 |
| Cerebrovascular disease | 12.0 | 11.3 | 0.02 | 11.8 | 11.3 | 0.02 |
| Coronary arteriosclerosis | 19.8 | 20.3 | -0.01 | 20.7 | 20.5 | 0.01 |
| Heart disease | 44.9 | 46.4 | -0.03 | 45.7 | 46.0 | -0.01 |
| Heart failure | 11.9 | 10.5 | 0.04 | 11.4 | 11.2 | 0.01 |
| Ischemic heart disease | 10.5 | 10.0 | 0.02 | 10.7 | 10.2 | 0.02 |
| Peripheral vascular disease | 6.3 | 6.4 | 0.00 | 6.5 | 6.0 | 0.02 |
| Pulmonary embolism | 1.4 | 1.4 | 0.01 | 1.5 | 1.3 | 0.02 |
| Venous thrombosis | 3.2 | 3.8 | -0.04 | 3.5 | 3.7 | -0.02 |
| Medical history: Neoplasms |  |  |  |  |  |  |
| Hematologic neoplasm | 2.0 | 2.3 | -0.02 | 2.1 | 2.2 | -0.01 |
| Malignant lymphoma | 1.5 | 1.4 | 0.01 | 1.6 | 1.4 | 0.02 |
| Malignant neoplasm of anorectum | 0.3 | 0.4 | -0.02 | 0.3 | 0.4 | -0.02 |
| Malignant neoplastic disease | 18.8 | 19.7 | -0.02 | 19.4 | 19.1 | 0.01 |
| Malignant tumor of breast | 4.1 | 3.9 | 0.01 | 4.3 | 3.9 | 0.02 |
| Malignant tumor of colon | 0.6 | 0.8 | -0.02 | 0.7 | 0.8 | -0.01 |
| Malignant tumor of lung | 0.8 | 0.9 | -0.01 | 0.8 | 1.0 | -0.03 |
| Malignant tumor of urinary bladder | 0.9 | 0.9 | 0.00 | 0.9 | 0.9 | 0.00 |
| Primary malignant neoplasm of prostate | 1.9 | 2.4 | -0.03 | 2.2 | 2.1 | 0.01 |
| Medication use |  |  |  |  |  |  |
| Agents acting on the renin-angiotensin system | 48.0 | 47.7 | 0.00 | 47.7 | 48.3 | -0.01 |
| Antibacterials for systemic use | 53.1 | 51.8 | 0.03 | 52.4 | 52.7 | -0.01 |
| Antidepressants | 36.6 | 35.7 | 0.02 | 36.2 | 37.1 | -0.02 |
| Antiepileptics | 23.7 | 23.4 | 0.01 | 23.9 | 23.7 | 0.01 |
| Antiinflammatory and antirheumatic products | 37.0 | 41.3 | -0.09 | 40.3 | 39.5 | 0.02 |
| Antineoplastic agents | 37.1 | 36.1 | 0.02 | 36.5 | 37.2 | -0.02 |
| Antipsoriatics | 1.3 | 1.2 | 0.01 | 1.3 | 1.3 | 0.00 |
| Antithrombotic agents | 23.3 | 26.2 | -0.07 | 24.7 | 24.6 | 0.00 |
| Beta blocking agents | 40.3 | 41.7 | -0.03 | 41.4 | 41.0 | 0.01 |
| Calcium channel blockers | 30.5 | 29.5 | 0.02 | 30.2 | 29.9 | 0.01 |
| Diuretics | 48.1 | 47.5 | 0.01 | 47.6 | 48.4 | -0.02 |
| Drugs for acid related disorders | 52.0 | 49.7 | 0.05 | 51.2 | 51.6 | -0.01 |
| Drugs for obstructive airway diseases | 49.3 | 36.0 | 0.27 | 41.8 | 43.0 | -0.02 |
| Drugs used in diabetes | 15.5 | 15.1 | 0.01 | 15.5 | 15.1 | 0.01 |
| Immunosuppressants | 49.6 | 47.6 | 0.04 | 48.5 | 49.3 | -0.02 |
| Lipid modifying agents | 47.4 | 47.6 | 0.00 | 48.0 | 47.9 | 0.00 |
| Opioids | 41.9 | 44.9 | -0.06 | 42.9 | 43.2 | 0.00 |
| Psycholeptics | 38.7 | 37.1 | 0.03 | 37.9 | 38.2 | -0.01 |
| Psychostimulants, agents used for adhd and nootropics | 2.3 | 2.6 | -0.02 | 2.4 | 2.7 | -0.02 |

### **S6.2.9. OpenClaims**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Before stratification |  |  | After stratification |  |  |
|  | AZM | AMX |  | AZM | AMX |  |
| Characteristic | % | % | Std. diff | % | % | Std. diff |
| Age group |  |  |  |  |  |  |
| 15-19 | 0.3 | 0.3 | 0.00 | 0.3 | 0.3 | 0.00 |
| 20-24 | 1.0 | 1.0 | 0.00 | 1.0 | 1.0 | 0.00 |
| 25-29 | 1.8 | 1.7 | 0.00 | 1.8 | 1.8 | 0.00 |
| 30-34 | 3.0 | 2.9 | 0.01 | 3.0 | 2.9 | 0.00 |
| 40-44 | 6.1 | 5.7 | 0.02 | 6.0 | 5.9 | 0.00 |
| 50-54 | 11.7 | 11.1 | 0.02 | 11.5 | 11.5 | 0.00 |
| 55-59 | 14.0 | 13.9 | 0.00 | 14.0 | 14.0 | 0.00 |
| 60-64 | 13.8 | 14.1 | -0.01 | 13.9 | 14.1 | 0.00 |
| 65-69 | 12.4 | 13.0 | -0.02 | 12.7 | 12.7 | 0.00 |
| 80-84 | 4.0 | 4.6 | -0.03 | 4.3 | 4.2 | 0.00 |
| 85-89 | 0.2 | 0.2 | 0.00 | 0.2 | 0.2 | 0.01 |
| Gender: female | 84.7 | 82.1 | 0.07 | 83.5 | 83.5 | 0.00 |
| Medical history: General |  |  |  |  |  |  |
| Acute respiratory disease | 36.6 | 27.3 | 0.20 | 33.1 | 31.5 | 0.03 |
| Attention deficit hyperactivity disorder | 0.9 | 0.8 | 0.00 | 0.9 | 0.8 | 0.00 |
| Chronic liver disease | 2.1 | 2.2 | -0.01 | 2.2 | 2.2 | 0.00 |
| Chronic obstructive lung disease | 10.6 | 8.0 | 0.09 | 9.4 | 9.3 | 0.00 |
| Crohn's disease | 0.5 | 0.5 | 0.00 | 0.5 | 0.5 | 0.00 |
| Dementia | 0.9 | 1.0 | -0.01 | 0.9 | 0.9 | 0.00 |
| Depressive disorder | 11.3 | 11.6 | -0.01 | 11.7 | 11.5 | 0.01 |
| Diabetes mellitus | 16.5 | 16.9 | -0.01 | 16.8 | 16.7 | 0.00 |
| Gastroesophageal reflux disease | 5.5 | 6.4 | -0.04 | 6.0 | 5.9 | 0.00 |
| Gastrointestinal hemorrhage | 2.5 | 2.7 | -0.01 | 2.6 | 2.6 | 0.00 |
| Hyperlipidemia | 26.6 | 27.3 | -0.02 | 27.1 | 26.8 | 0.01 |
| Hypertensive disorder | 37.0 | 38.1 | -0.02 | 37.9 | 37.4 | 0.01 |
| Lesion of liver | 0.8 | 0.9 | -0.01 | 0.9 | 0.9 | 0.00 |
| Obesity | 7.6 | 7.8 | -0.01 | 7.8 | 7.7 | 0.00 |
| Osteoarthritis | 35.5 | 38.0 | -0.05 | 37.0 | 36.6 | 0.01 |
| Pneumonia | 7.1 | 4.8 | 0.10 | 6.1 | 5.8 | 0.01 |
| Psoriasis | 1.9 | 1.9 | 0.00 | 2.0 | 1.9 | 0.00 |
| Renal impairment | 7.2 | 7.7 | -0.02 | 7.5 | 7.5 | 0.00 |
| Rheumatoid arthritis | 68.4 | 67.8 | 0.01 | 68.1 | 68.0 | 0.00 |
| Schizophrenia | 0.2 | 0.2 | 0.01 | 0.2 | 0.2 | 0.01 |
| Ulcerative colitis | 0.5 | 0.5 | 0.00 | 0.5 | 0.5 | 0.00 |
| Urinary tract infectious disease | 10.0 | 11.0 | -0.03 | 10.6 | 10.5 | 0.00 |
| Viral hepatitis C | 1.0 | 1.1 | -0.01 | 1.0 | 1.0 | 0.00 |
| Visual system disorder | 26.7 | 27.3 | -0.01 | 27.1 | 27.0 | 0.00 |
| Medical history: Cardiovascular disease |  |  |  |  |  |  |
| Atrial fibrillation | 3.5 | 4.4 | -0.05 | 4.0 | 4.0 | 0.00 |
| Cerebrovascular disease | 3.5 | 3.5 | 0.00 | 3.6 | 3.5 | 0.00 |
| Coronary arteriosclerosis | 7.3 | 7.7 | -0.02 | 7.7 | 7.6 | 0.00 |
| Heart disease | 19.8 | 20.8 | -0.02 | 20.4 | 20.3 | 0.00 |
| Ischemic heart disease | 3.9 | 3.9 | 0.00 | 4.0 | 3.9 | 0.00 |
| Peripheral vascular disease | 10.4 | 11.2 | -0.03 | 11.0 | 10.8 | 0.00 |
| Pulmonary embolism | 0.9 | 1.0 | -0.01 | 1.0 | 1.0 | 0.00 |
| Venous thrombosis | 1.6 | 1.8 | -0.01 | 1.7 | 1.7 | 0.00 |
| Medical history: Neoplasms |  |  |  |  |  |  |
| Hematologic neoplasm | 1.0 | 1.1 | -0.01 | 1.1 | 1.1 | 0.00 |
| Malignant lymphoma | 0.7 | 0.7 | 0.00 | 0.7 | 0.7 | 0.00 |
| Malignant neoplasm of anorectum | 0.1 | 0.1 | 0.00 | 0.1 | 0.1 | 0.00 |
| Malignant neoplastic disease | 8.0 | 8.4 | -0.01 | 8.3 | 8.2 | 0.00 |
| Malignant tumor of breast | 2.1 | 2.1 | 0.00 | 2.2 | 2.1 | 0.00 |
| Malignant tumor of colon | 0.3 | 0.3 | -0.01 | 0.3 | 0.3 | 0.00 |
| Malignant tumor of lung | 0.4 | 0.3 | 0.01 | 0.4 | 0.4 | 0.00 |
| Malignant tumor of urinary bladder | 0.2 | 0.3 | -0.01 | 0.2 | 0.3 | 0.00 |
| Primary malignant neoplasm of prostate | 0.6 | 0.7 | -0.01 | 0.6 | 0.6 | 0.00 |
| Medication use |  |  |  |  |  |  |
| Agents acting on the renin-angiotensin system | 37.3 | 38.2 | -0.02 | 38.0 | 37.9 | 0.00 |
| Antibacterials for systemic use | 49.3 | 49.7 | -0.01 | 49.9 | 49.9 | 0.00 |
| Antidepressants | 45.6 | 45.4 | 0.00 | 46.0 | 45.8 | 0.00 |
| Antiepileptics | 32.9 | 33.3 | -0.01 | 33.5 | 33.3 | 0.00 |
| Antiinflammatory and antirheumatic products | 45.3 | 47.7 | -0.05 | 46.8 | 46.6 | 0.00 |
| Antineoplastic agents | 38.6 | 35.9 | 0.06 | 37.0 | 37.3 | 0.00 |
| Antithrombotic agents | 15.7 | 18.3 | -0.07 | 17.2 | 17.0 | 0.00 |
| Beta blocking agents | 28.8 | 30.2 | -0.03 | 29.7 | 29.6 | 0.00 |
| Calcium channel blockers | 21.7 | 22.0 | -0.01 | 22.0 | 21.9 | 0.00 |
| Diuretics | 35.6 | 35.8 | 0.00 | 35.9 | 35.9 | 0.00 |
| Drugs for acid related disorders | 47.6 | 47.4 | 0.00 | 47.7 | 47.8 | 0.00 |
| Drugs for obstructive airway diseases | 50.2 | 40.6 | 0.19 | 45.8 | 45.5 | 0.01 |
| Immunosuppressants | 52.8 | 50.2 | 0.05 | 51.4 | 51.5 | 0.00 |
| Lipid modifying agents | 34.8 | 35.9 | -0.02 | 35.6 | 35.5 | 0.00 |
| Opioids | 41.8 | 44.3 | -0.05 | 43.5 | 43.2 | 0.01 |
| Psycholeptics | 39.2 | 38.4 | 0.02 | 39.3 | 39.2 | 0.00 |
| Psychostimulants, agents used for adhd and nootropics | 6.7 | 6.5 | 0.01 | 6.8 | 6.7 | 0.00 |

### **S6.2.10. Optum**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Before stratification |  |  | After stratification |  |  |
|  | AZM | AMX |  | AZM | AMX |  |
| Characteristic | % | % | Std. diff | % | % | Std. diff |
| Age group |  |  |  |  |  |  |
| 15-19 | 0.3 | 0.2 | 0.00 | 0.2 | 0.3 | 0.00 |
| 20-24 | 0.8 | 0.8 | 0.00 | 0.9 | 1.0 | -0.01 |
| 25-29 | 1.5 | 1.4 | 0.01 | 1.5 | 1.4 | 0.01 |
| 30-34 | 3.1 | 2.7 | 0.02 | 3.0 | 2.8 | 0.01 |
| 35-39 | 4.4 | 4.2 | 0.01 | 4.3 | 4.4 | -0.01 |
| 40-44 | 6.8 | 6.0 | 0.03 | 6.6 | 6.4 | 0.01 |
| 45-49 | 8.6 | 8.6 | 0.00 | 8.6 | 8.9 | -0.01 |
| 55-59 | 14.0 | 13.5 | 0.01 | 13.9 | 13.6 | 0.01 |
| 60-64 | 13.3 | 13.2 | 0.00 | 13.3 | 13.0 | 0.01 |
| 65-69 | 12.1 | 12.8 | -0.02 | 12.4 | 12.6 | -0.01 |
| 70-74 | 10.2 | 10.8 | -0.02 | 10.2 | 10.3 | 0.00 |
| 75-79 | 7.2 | 7.8 | -0.02 | 7.2 | 7.4 | -0.01 |
| 80-84 | 4.4 | 4.8 | -0.02 | 4.4 | 4.5 | -0.01 |
| 85-89 | 1.7 | 1.9 | -0.02 | 1.8 | 1.8 | 0.00 |
| Gender: female | 84.9 | 82.9 | 0.06 | 84.0 | 83.9 | 0.00 |
| Medical history: General |  |  |  |  |  |  |
| Acute respiratory disease | 64.9 | 48.7 | 0.33 | 57.7 | 57.7 | 0.00 |
| Chronic obstructive lung disease | 14.8 | 11.0 | 0.11 | 13.0 | 13.1 | 0.00 |
| Crohn's disease | 0.7 | 0.7 | 0.01 | 0.8 | 0.6 | 0.02 |
| Dementia | 1.5 | 1.9 | -0.03 | 1.7 | 1.9 | -0.02 |
| Depressive disorder | 20.7 | 21.4 | -0.02 | 21.3 | 21.2 | 0.00 |
| Diabetes mellitus | 20.4 | 20.7 | -0.01 | 20.4 | 20.7 | -0.01 |
| Gastroesophageal reflux disease | 25.6 | 26.1 | -0.01 | 26.1 | 25.8 | 0.01 |
| Gastrointestinal hemorrhage | 4.2 | 4.5 | -0.02 | 4.4 | 4.5 | 0.00 |
| Human immunodeficiency virus infection | 0.2 | 0.2 | 0.00 | 0.2 | 0.2 | 0.00 |
| Hyperlipidemia | 46.3 | 46.7 | -0.01 | 46.4 | 46.3 | 0.00 |
| Hypertensive disorder | 53.9 | 55.5 | -0.03 | 54.6 | 54.8 | 0.00 |
| Lesion of liver | 1.1 | 1.3 | -0.02 | 1.1 | 1.3 | -0.02 |
| Osteoarthritis | 52.5 | 56.2 | -0.07 | 54.5 | 54.5 | 0.00 |
| Pneumonia | 10.7 | 7.2 | 0.12 | 9.0 | 9.0 | 0.00 |
| Psoriasis | 3.3 | 3.0 | 0.01 | 3.2 | 3.1 | 0.01 |
| Renal impairment | 11.1 | 12.4 | -0.04 | 11.5 | 11.7 | -0.01 |
| Rheumatoid arthritis | 84.5 | 83.3 | 0.03 | 84.0 | 84.0 | 0.00 |
| Schizophrenia | 0.2 | 0.2 | -0.01 | 0.2 | 0.2 | 0.00 |
| Ulcerative colitis | 0.7 | 0.8 | -0.01 | 0.8 | 0.8 | 0.00 |
| Urinary tract infectious disease | 17.6 | 19.3 | -0.04 | 18.6 | 18.5 | 0.00 |
| Viral hepatitis C | 1.1 | 1.4 | -0.03 | 1.2 | 1.3 | -0.01 |
| Medical history: Cardiovascular disease |  |  |  |  |  |  |
| Atrial fibrillation | 4.7 | 6.0 | -0.06 | 5.2 | 5.5 | -0.01 |
| Cerebrovascular disease | 6.5 | 7.0 | -0.02 | 6.6 | 6.8 | -0.01 |
| Coronary arteriosclerosis | 11.4 | 12.1 | -0.02 | 11.6 | 11.8 | 0.00 |
| Heart disease | 29.8 | 31.2 | -0.03 | 30.4 | 30.6 | 0.00 |
| Heart failure | 7.5 | 7.4 | 0.00 | 7.6 | 7.4 | 0.01 |
| Ischemic heart disease | 7.0 | 7.3 | -0.01 | 7.1 | 7.3 | 0.00 |
| Peripheral vascular disease | 4.9 | 5.2 | -0.02 | 5.1 | 5.0 | 0.01 |
| Pulmonary embolism | 1.3 | 1.4 | -0.01 | 1.3 | 1.4 | 0.00 |
| Venous thrombosis | 2.5 | 2.9 | -0.02 | 2.6 | 2.8 | -0.01 |
| Medical history: Neoplasms |  |  |  |  |  |  |
| Hematologic neoplasm | 1.6 | 1.5 | 0.01 | 1.7 | 1.5 | 0.01 |
| Malignant lymphoma | 0.9 | 0.9 | 0.00 | 0.9 | 0.9 | 0.01 |
| Malignant neoplasm of anorectum | 0.1 | 0.2 | -0.02 | 0.1 | 0.2 | -0.01 |
| Malignant neoplastic disease | 11.3 | 11.9 | -0.02 | 11.4 | 11.6 | -0.01 |
| Malignant tumor of breast | 2.7 | 2.7 | 0.00 | 2.6 | 2.7 | 0.00 |
| Malignant tumor of colon | 0.4 | 0.4 | -0.01 | 0.3 | 0.4 | -0.01 |
| Malignant tumor of lung | 0.6 | 0.4 | 0.02 | 0.5 | 0.5 | -0.01 |
| Malignant tumor of urinary bladder | 0.3 | 0.4 | -0.03 | 0.3 | 0.4 | -0.01 |
| Primary malignant neoplasm of prostate | 0.8 | 0.9 | -0.02 | 0.8 | 0.8 | 0.00 |
| Medication use |  |  |  |  |  |  |
| Antidepressants | 42.5 | 42.6 | 0.00 | 43.0 | 42.8 | 0.00 |
| Antiepileptics | 27.7 | 28.2 | -0.01 | 28.4 | 27.9 | 0.01 |
| Antiinflammatory and antirheumatic products | 44.2 | 45.7 | -0.03 | 45.5 | 45.2 | 0.01 |
| Antineoplastic agents | 35.2 | 33.1 | 0.04 | 33.4 | 34.2 | -0.02 |
| Antipsoriatics | 1.1 | 1.0 | 0.01 | 1.1 | 1.1 | 0.01 |
| Antithrombotic agents | 13.1 | 15.4 | -0.07 | 14.0 | 14.2 | 0.00 |
| Beta blocking agents | 25.8 | 27.1 | -0.03 | 26.5 | 26.4 | 0.00 |
| Drugs for acid related disorders | 41.8 | 41.9 | 0.00 | 41.9 | 41.8 | 0.00 |
| Drugs for obstructive airway diseases | 45.4 | 36.4 | 0.18 | 41.2 | 41.1 | 0.00 |
| Immunosuppressants | 49.8 | 47.4 | 0.05 | 48.3 | 48.4 | 0.00 |
| Lipid modifying agents | 32.4 | 33.2 | -0.02 | 32.6 | 32.6 | 0.00 |
| Opioids | 41.0 | 43.3 | -0.05 | 42.7 | 42.0 | 0.01 |
| Psycholeptics | 35.8 | 36.3 | -0.01 | 36.5 | 36.6 | 0.00 |
| Psychostimulants, agents used for adhd and nootropics | 5.2 | 4.8 | 0.02 | 5.3 | 5.0 | 0.02 |

### **S6.2.11. PanTher**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Before stratification |  |  | After stratification |  |  |
|  | AZM | AMX |  | AZM | AMX |  |
| Characteristic | % | % | Std. diff | % | % | Std. diff |
| Age group |  |  |  |  |  |  |
| 15-19 | 0.2 | 0.3 | -0.02 | 0.2 | 0.3 | -0.02 |
| 20-24 | 0.9 | 0.9 | 0.00 | 1.1 | 0.8 | 0.03 |
| 25-29 | 1.6 | 1.7 | 0.00 | 1.9 | 1.6 | 0.02 |
| 30-34 | 2.7 | 3.1 | -0.03 | 2.9 | 2.9 | 0.00 |
| 35-39 | 3.7 | 4.5 | -0.04 | 4.1 | 4.1 | 0.00 |
| 40-44 | 5.3 | 5.9 | -0.03 | 5.7 | 6.0 | -0.01 |
| 45-49 | 7.1 | 7.4 | -0.01 | 7.3 | 7.4 | 0.00 |
| 50-54 | 10.5 | 10.5 | 0.00 | 10.5 | 10.3 | 0.01 |
| 55-59 | 13.1 | 13.8 | -0.02 | 13.2 | 13.9 | -0.02 |
| 60-64 | 13.7 | 13.6 | 0.00 | 13.9 | 13.8 | 0.00 |
| 65-69 | 12.6 | 12.2 | 0.01 | 12.4 | 12.5 | 0.00 |
| 70-74 | 10.9 | 10.5 | 0.01 | 10.5 | 10.6 | 0.00 |
| 75-79 | 8.6 | 7.6 | 0.04 | 8.2 | 7.9 | 0.01 |
| 80-84 | 6.4 | 6.0 | 0.02 | 5.9 | 5.8 | 0.00 |
| 85-89 | 2.6 | 2.1 | 0.04 | 2.3 | 2.0 | 0.02 |
| Gender: female | 82.3 | 82.1 | 0.00 | 82.9 | 82.7 | 0.01 |
| Race |  |  |  |  |  |  |
| race = Asian | 1.1 | 1.0 | 0.01 | 1.0 | 1.0 | 0.01 |
| race = Black or African American | 10.5 | 9.4 | 0.04 | 10.0 | 9.4 | 0.02 |
| race = White | 83.4 | 84.3 | -0.02 | 84.1 | 84.4 | -0.01 |
| Ethnicity |  |  |  |  |  |  |
| ethnicity = Hispanic or Latino | 4.6 | 4.4 | 0.01 | 4.5 | 4.5 | 0.00 |
| Medical history: General |  |  |  |  |  |  |
| Acute respiratory disease | 57.2 | 43.2 | 0.28 | 52.6 | 51.8 | 0.02 |
| Attention deficit hyperactivity disorder | 1.0 | 1.5 | -0.04 | 1.1 | 1.4 | -0.03 |
| Chronic liver disease | 3.3 | 3.4 | -0.01 | 3.4 | 3.4 | 0.00 |
| Chronic obstructive lung disease | 19.5 | 11.0 | 0.24 | 15.2 | 15.1 | 0.00 |
| Crohn's disease | 0.6 | 0.6 | 0.00 | 0.7 | 0.5 | 0.02 |
| Dementia | 2.2 | 1.9 | 0.02 | 1.9 | 1.9 | 0.00 |
| Depressive disorder | 23.7 | 23.4 | 0.01 | 23.9 | 23.4 | 0.01 |
| Diabetes mellitus | 19.3 | 18.3 | 0.03 | 18.8 | 18.4 | 0.01 |
| Gastroesophageal reflux disease | 29.6 | 28.1 | 0.03 | 29.2 | 28.8 | 0.01 |
| Human immunodeficiency virus infection | 0.2 | 0.1 | 0.01 | 0.2 | 0.2 | 0.00 |
| Hyperlipidemia | 40.8 | 38.8 | 0.04 | 39.7 | 39.4 | 0.01 |
| Hypertensive disorder | 51.4 | 49.7 | 0.03 | 50.4 | 50.4 | 0.00 |
| Lesion of liver | 1.5 | 1.5 | 0.00 | 1.6 | 1.4 | 0.01 |
| Obesity | 17.5 | 18.1 | -0.02 | 17.6 | 17.8 | -0.01 |
| Osteoarthritis | 41.1 | 42.2 | -0.02 | 41.4 | 41.0 | 0.01 |
| Pneumonia | 20.6 | 7.6 | 0.38 | 14.7 | 12.4 | 0.07 |
| Psoriasis | 2.1 | 2.1 | 0.00 | 2.2 | 2.1 | 0.01 |
| Renal impairment | 14.7 | 12.8 | 0.06 | 13.2 | 12.6 | 0.02 |
| Rheumatoid arthritis | 84.8 | 83.4 | 0.04 | 84.0 | 84.3 | -0.01 |
| Schizophrenia | 0.3 | 0.3 | -0.01 | 0.2 | 0.3 | -0.01 |
| Ulcerative colitis | 0.5 | 0.7 | -0.03 | 0.6 | 0.6 | 0.00 |
| Urinary tract infectious disease | 13.1 | 14.1 | -0.03 | 13.7 | 13.2 | 0.02 |
| Viral hepatitis C | 1.3 | 1.1 | 0.02 | 1.3 | 1.1 | 0.01 |
| Visual system disorder | 21.4 | 22.6 | -0.03 | 21.5 | 21.6 | 0.00 |
| Medical history: Cardiovascular disease |  |  |  |  |  |  |
| Atrial fibrillation | 7.5 | 6.9 | 0.02 | 6.9 | 7.1 | -0.01 |
| Cerebrovascular disease | 5.1 | 4.5 | 0.03 | 4.8 | 4.5 | 0.01 |
| Coronary arteriosclerosis | 13.4 | 12.1 | 0.04 | 12.5 | 12.5 | 0.00 |
| Heart disease | 33.3 | 29.6 | 0.08 | 31.1 | 30.3 | 0.02 |
| Heart failure | 11.3 | 8.0 | 0.12 | 9.4 | 8.6 | 0.03 |
| Ischemic heart disease | 8.0 | 6.7 | 0.05 | 7.2 | 7.0 | 0.01 |
| Pulmonary embolism | 1.7 | 1.8 | -0.01 | 1.7 | 1.7 | 0.00 |
| Venous thrombosis | 3.3 | 3.4 | -0.01 | 3.3 | 3.1 | 0.01 |
| Medical history: Neoplasms |  |  |  |  |  |  |
| Hematologic neoplasm | 1.7 | 1.7 | 0.00 | 1.8 | 1.6 | 0.01 |
| Malignant lymphoma | 0.8 | 1.0 | -0.02 | 0.8 | 0.9 | -0.02 |
| Malignant neoplasm of anorectum | 0.4 | 0.5 | -0.02 | 0.3 | 0.4 | 0.00 |
| Malignant neoplastic disease | 11.8 | 13.3 | -0.05 | 12.2 | 12.5 | -0.01 |
| Malignant tumor of breast | 2.5 | 3.1 | -0.03 | 2.7 | 2.8 | -0.01 |
| Malignant tumor of colon | 0.5 | 0.6 | -0.01 | 0.5 | 0.5 | 0.01 |
| Malignant tumor of lung | 1.0 | 0.7 | 0.04 | 0.9 | 0.9 | -0.01 |
| Malignant tumor of urinary bladder | 0.3 | 0.4 | -0.02 | 0.3 | 0.3 | -0.01 |
| Primary malignant neoplasm of prostate | 0.8 | 0.8 | 0.00 | 0.9 | 0.7 | 0.02 |
| Medication use |  |  |  |  |  |  |
| Agents acting on the renin-angiotensin system | 37.6 | 36.5 | 0.02 | 36.9 | 36.5 | 0.01 |
| Antibacterials for systemic use | 53.0 | 51.6 | 0.03 | 52.1 | 50.8 | 0.03 |
| Antidepressants | 47.6 | 48.1 | -0.01 | 48.1 | 48.3 | 0.00 |
| Antiepileptics | 33.3 | 34.7 | -0.03 | 33.8 | 34.1 | 0.00 |
| Antiinflammatory and antirheumatic products | 47.1 | 50.6 | -0.07 | 48.8 | 49.7 | -0.02 |
| Antineoplastic agents | 39.5 | 36.8 | 0.06 | 38.1 | 38.6 | -0.01 |
| Antithrombotic agents | 47.7 | 44.7 | 0.06 | 45.4 | 44.1 | 0.03 |
| Beta blocking agents | 35.2 | 35.8 | -0.01 | 35.0 | 34.9 | 0.00 |
| Calcium channel blockers | 24.0 | 22.2 | 0.04 | 22.9 | 22.8 | 0.00 |
| Diuretics | 40.3 | 38.3 | 0.04 | 39.3 | 38.9 | 0.01 |
| Drugs for acid related disorders | 61.8 | 61.0 | 0.02 | 61.0 | 61.0 | 0.00 |
| Drugs for obstructive airway diseases | 64.7 | 52.3 | 0.25 | 58.6 | 59.1 | -0.01 |
| Drugs used in diabetes | 19.7 | 19.2 | 0.02 | 19.1 | 19.1 | 0.00 |
| Immunosuppressants | 56.0 | 53.6 | 0.05 | 55.1 | 55.5 | -0.01 |
| Lipid modifying agents | 37.0 | 36.1 | 0.02 | 36.2 | 35.9 | 0.01 |
| Opioids | 52.5 | 53.9 | -0.03 | 52.3 | 52.2 | 0.00 |
| Psycholeptics | 49.8 | 49.6 | 0.00 | 49.2 | 49.5 | -0.01 |
| Psychostimulants, agents used for adhd and nootropics | 5.6 | 6.6 | -0.04 | 6.0 | 6.3 | -0.01 |

### **S6.2.12. SIDIAP**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Before stratification |  |  | After stratification |  |  |
|  | AZM | AMX |  | AZM | AMX |  |
| Characteristic | % | % | Std. diff | % | % | Std. diff |
| Age group |  |  |  |  |  |  |
| 20-24 | <3.8 | <0.7 | 0.09 | <2.8 | <0.7 | 0.07 |
| 30-34 | <3.8 | 4.1 | -0.10 | <2.8 | 4.0 | -0.12 |
| 35-39 | 3.8 | 5.5 | -0.08 | 6.1 | 5.4 | 0.03 |
| 40-44 | 6.2 | 6.3 | 0.00 | 3.3 | 6.1 | -0.13 |
| 45-49 | 4.6 | 6.0 | -0.06 | 5.7 | 5.8 | -0.01 |
| 50-54 | 13.1 | 8.3 | 0.16 | 17.6 | 8.3 | 0.28 |
| 55-59 | 15.4 | 10.3 | 0.15 | 17.5 | 10.5 | 0.20 |
| 60-64 | 10.8 | 12.7 | -0.06 | 12.9 | 12.9 | 0.00 |
| 65-69 | 7.7 | 12.2 | -0.15 | 5.0 | 12.5 | -0.27 |
| 70-74 | 12.3 | 11.1 | 0.04 | 10.0 | 11.0 | -0.03 |
| 75-79 | 7.7 | 8.9 | -0.04 | 4.5 | 8.6 | -0.17 |
| 80-84 | 7.7 | 8.2 | -0.02 | 9.0 | 8.3 | 0.03 |
| 85-89 | 6.2 | 3.1 | 0.15 | 4.0 | 3.3 | 0.03 |
| 90-94 | <3.8 | <0.7 | 0.09 | <2.8 | <0.7 | 0.12 |
| Gender: female | 80.0 | 77.6 | 0.06 | 79.9 | 77.9 | 0.05 |
| Medical history: General |  |  |  |  |  |  |
| Acute respiratory disease | 26.9 | 20.1 | 0.16 | 29.4 | 20.6 | 0.20 |
| Chronic liver disease | <3.8 | 1.2 | -0.04 | <2.8 | 1.2 | -0.09 |
| Chronic obstructive lung disease | 4.6 | 2.6 | 0.11 | 3.7 | 2.7 | 0.05 |
| Dementia | <3.8 | 0.9 | -0.01 | <2.8 | 0.9 | -0.06 |
| Depressive disorder | <3.8 | 4.7 | -0.08 | <2.8 | 4.9 | -0.11 |
| Diabetes mellitus | <3.8 | 3.6 | -0.13 | <2.8 | 3.5 | -0.10 |
| Gastroesophageal reflux disease | <3.8 | 1.3 | 0.02 | <2.8 | 1.3 | -0.04 |
| Gastrointestinal hemorrhage | 5.4 | 2.0 | 0.18 | 5.5 | 2.1 | 0.18 |
| Hyperlipidemia | 4.6 | 6.4 | -0.08 | 3.8 | 6.3 | -0.12 |
| Hypertensive disorder | 6.2 | 7.1 | -0.04 | 6.3 | 7.0 | -0.03 |
| Obesity | 7.7 | 8.0 | -0.01 | 9.8 | 7.9 | 0.07 |
| Osteoarthritis | 4.6 | 3.8 | 0.04 | 5.2 | 3.7 | 0.07 |
| Pneumonia | <3.8 | 3.4 | -0.06 | <2.8 | 3.4 | -0.14 |
| Renal impairment | <3.8 | 2.9 | -0.04 | <2.8 | 2.8 | -0.03 |
| Rheumatoid arthritis | 20.8 | 29.3 | -0.20 | 22.9 | 28.8 | -0.13 |
| Urinary tract infectious disease | 8.5 | 10.8 | -0.08 | 5.5 | 10.8 | -0.19 |
| Viral hepatitis C | <3.8 | <0.7 | 0.02 | <2.8 | <0.7 | -0.04 |
| Visual system disorder | 17.7 | 20.8 | -0.08 | 14.6 | 20.9 | -0.16 |
| Medical history: Cardiovascular disease |  |  |  |  |  |  |
| Cerebrovascular disease | 4.6 | 4.1 | 0.03 | 5.5 | 4.3 | 0.06 |
| Heart disease | 6.9 | 10.1 | -0.11 | 6.9 | 10.0 | -0.11 |
| Heart failure | <3.8 | 1.5 | -0.07 | <2.8 | 1.5 | -0.10 |
| Ischemic heart disease | <3.8 | 3.4 | -0.02 | <2.8 | 3.4 | -0.09 |
| Peripheral vascular disease | 8.5 | 6.4 | 0.08 | 5.8 | 6.4 | -0.02 |
| Venous thrombosis | <3.8 | <0.7 | 0.04 | <2.8 | <0.7 | -0.01 |
| Medical history: Neoplasms |  |  |  |  |  |  |
| Malignant neoplastic disease | <3.8 | 4.7 | -0.13 | <2.8 | 4.8 | -0.18 |
| Medication use |  |  |  |  |  |  |
| Agents acting on the renin-angiotensin system | 26.9 | 31.2 | -0.09 | 21.0 | 31.1 | -0.23 |
| Antibacterials for systemic use | 27.7 | 27.1 | 0.01 | 23.2 | 27.6 | -0.10 |
| Antidepressants | 30.8 | 28.9 | 0.04 | 33.8 | 29.2 | 0.10 |
| Antiepileptics | 16.2 | 14.0 | 0.06 | 14.3 | 14.2 | 0.00 |
| Antiinflammatory and antirheumatic products | 62.3 | 64.4 | -0.04 | 55.1 | 64.6 | -0.20 |
| Antineoplastic agents | 27.7 | 17.6 | 0.24 | 18.1 | 19.1 | -0.03 |
| Antipsoriatics | <3.8 | 1.2 | -0.04 | <2.8 | 1.1 | 0.08 |
| Antithrombotic agents | 20.8 | 25.2 | -0.11 | 22.5 | 25.0 | -0.06 |
| Beta blocking agents | 15.4 | 15.0 | 0.01 | 15.3 | 14.9 | 0.01 |
| Calcium channel blockers | 9.2 | 9.8 | -0.02 | 10.1 | 9.5 | 0.02 |
| Diuretics | 30.0 | 29.3 | 0.02 | 30.3 | 29.3 | 0.02 |
| Drugs for acid related disorders | 89.2 | 83.2 | 0.18 | 82.0 | 83.9 | -0.05 |
| Drugs for obstructive airway diseases | 48.5 | 38.9 | 0.19 | 34.3 | 41.2 | -0.14 |
| Drugs used in diabetes | 11.5 | 14.7 | -0.09 | 11.8 | 14.5 | -0.08 |
| Immunosuppressants | 37.7 | 29.4 | 0.18 | 26.9 | 30.8 | -0.08 |
| Lipid modifying agents | 26.9 | 27.4 | -0.01 | 27.1 | 27.4 | -0.01 |
| Opioids | 16.2 | 22.2 | -0.15 | 13.2 | 22.5 | -0.24 |
| Psycholeptics | 43.8 | 41.3 | 0.05 | 41.1 | 41.6 | -0.01 |
| Psychostimulants, agents used for adhd and nootropics | 5.4 | 2.5 | 0.15 | 3.6 | 2.5 | 0.06 |

### **S6.2.13. VA**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Before stratification |  |  | After stratification |  |  |
|  | AZM | AMX |  | AZM | AMX |  |
| Characteristic | % | % | Std. diff | % | % | Std. diff |
| Age group |  |  |  |  |  |  |
| 20-24 | <0.1 | 0.1 | 0.00 | <0.1 | 0.1 | 0.00 |
| 25-29 | 0.4 | 0.2 | 0.03 | 0.4 | 0.3 | 0.03 |
| 30-34 | 1.0 | 1.0 | 0.00 | 1.2 | 1.1 | 0.02 |
| 35-39 | 1.3 | 1.5 | -0.02 | 1.3 | 1.4 | -0.01 |
| 40-44 | 2.5 | 2.8 | -0.02 | 3.1 | 2.7 | 0.02 |
| 45-49 | 4.9 | 5.5 | -0.03 | 5.9 | 5.4 | 0.02 |
| 50-54 | 8.8 | 9.1 | -0.01 | 9.6 | 9.0 | 0.02 |
| 55-59 | 13.4 | 14.6 | -0.03 | 12.9 | 14.3 | -0.04 |
| 60-64 | 17.6 | 17.2 | 0.01 | 17.1 | 18.0 | -0.02 |
| 65-69 | 18.2 | 17.5 | 0.02 | 17.2 | 17.0 | 0.00 |
| 70-74 | 13.7 | 13.9 | -0.01 | 14.5 | 14.2 | 0.01 |
| 75-79 | 8.9 | 8.6 | 0.01 | 8.2 | 8.6 | -0.01 |
| 80-84 | 5.7 | 5.4 | 0.02 | 5.4 | 5.2 | 0.00 |
| 85-89 | 2.9 | 2.0 | 0.05 | 2.5 | 2.0 | 0.03 |
| 90-94 | 0.6 | 0.5 | 0.02 | 0.5 | 0.6 | -0.01 |
| 95-99 | <0.1 | <0.1 | 0.01 | <0.1 | <0.1 | 0.00 |
| Gender: female | 18.6 | 16.7 | 0.05 | 18.7 | 17.5 | 0.03 |
| Race |  |  |  |  |  |  |
| race = Asian | 0.4 | 0.3 | 0.01 | 0.3 | 0.3 | 0.01 |
| race = Black or African American | 16.5 | 17.8 | -0.04 | 17.0 | 17.7 | -0.02 |
| race = White | 74.0 | 71.1 | 0.06 | 73.2 | 71.8 | 0.03 |
| race = Unknown | 7.7 | 8.9 | -0.04 | 8.0 | 8.4 | -0.02 |
| race = Native Hawaiian or Other Pacific Islander | 0.6 | 0.8 | -0.02 | 0.7 | 0.8 | -0.01 |
| race = American Indian or Alaska Native | 0.8 | 1.1 | -0.02 | 0.8 | 1.0 | -0.02 |
| Ethnicity |  |  |  |  |  |  |
| ethnicity = Hispanic or Latino | 4.7 | 5.2 | -0.02 | 3.9 | 4.8 | -0.04 |
| ethnicity = Not Hispanic or Latino | 91.1 | 89.3 | 0.06 | 91.6 | 89.9 | 0.06 |
| Medical history: General |  |  |  |  |  |  |
| Acute respiratory disease | 48.2 | 29.9 | 0.38 | 40.3 | 40.4 | 0.00 |
| Attention deficit hyperactivity disorder | 0.4 | 0.6 | -0.04 | 0.4 | 0.6 | -0.03 |
| Chronic liver disease | 3.7 | 4.6 | -0.04 | 3.7 | 4.2 | -0.03 |
| Chronic obstructive lung disease | 33.7 | 22.5 | 0.25 | 26.1 | 27.6 | -0.03 |
| Crohn's disease | 0.4 | 0.4 | 0.00 | 0.4 | 0.3 | 0.02 |
| Depressive disorder | 28.4 | 27.9 | 0.01 | 29.5 | 28.5 | 0.02 |
| Diabetes mellitus | 27.4 | 29.5 | -0.05 | 28.0 | 28.2 | 0.00 |
| Gastroesophageal reflux disease | 7.2 | 8.0 | -0.03 | 7.4 | 7.7 | -0.01 |
| Gastrointestinal hemorrhage | 3.2 | 3.7 | -0.03 | 3.8 | 3.2 | 0.03 |
| Human immunodeficiency virus infection | 0.3 | 0.4 | -0.02 | 0.3 | 0.4 | -0.02 |
| Hyperlipidemia | 48.8 | 46.6 | 0.04 | 47.0 | 47.0 | 0.00 |
| Hypertensive disorder | 64.7 | 63.3 | 0.03 | 63.8 | 63.3 | 0.01 |
| Lesion of liver | 1.5 | 1.9 | -0.03 | 1.7 | 1.9 | -0.02 |
| Obesity | 18.4 | 18.4 | 0.00 | 17.8 | 18.5 | -0.02 |
| Osteoarthritis | 42.8 | 43.8 | -0.02 | 42.6 | 42.9 | 0.00 |
| Pneumonia | 18.2 | 7.9 | 0.31 | 12.9 | 11.4 | 0.04 |
| Psoriasis | 2.4 | 2.5 | 0.00 | 2.5 | 2.2 | 0.02 |
| Renal impairment | 11.9 | 11.8 | 0.00 | 11.4 | 11.2 | 0.01 |
| Rheumatoid arthritis | 87.3 | 86.0 | 0.04 | 86.0 | 86.7 | -0.02 |
| Schizophrenia | 0.7 | 1.1 | -0.04 | 1.1 | 1.1 | 0.00 |
| Ulcerative colitis | 0.4 | 0.5 | -0.02 | 0.5 | 0.4 | 0.01 |
| Urinary tract infectious disease | 5.9 | 8.3 | -0.09 | 7.4 | 7.2 | 0.01 |
| Visual system disorder | 65.7 | 65.2 | 0.01 | 65.2 | 64.9 | 0.01 |
| Medical history: Cardiovascular disease |  |  |  |  |  |  |
| Atrial fibrillation | 7.4 | 8.3 | -0.03 | 7.9 | 8.1 | -0.01 |
| Cerebrovascular disease | 6.1 | 5.6 | 0.02 | 6.1 | 5.4 | 0.03 |
| Coronary arteriosclerosis | 19.5 | 18.3 | 0.03 | 18.6 | 18.0 | 0.02 |
| Heart disease | 39.8 | 38.2 | 0.03 | 38.7 | 37.7 | 0.02 |
| Heart failure | 11.8 | 9.9 | 0.06 | 11.3 | 10.2 | 0.04 |
| Ischemic heart disease | 15.7 | 15.2 | 0.01 | 15.2 | 15.1 | 0.00 |
| Peripheral vascular disease | 17.6 | 18.4 | -0.02 | 18.1 | 18.0 | 0.00 |
| Pulmonary embolism | 1.5 | 1.6 | -0.01 | 1.7 | 1.5 | 0.02 |
| Venous thrombosis | 2.3 | 2.5 | -0.01 | 2.4 | 2.2 | 0.01 |
| Medical history: Neoplasms |  |  |  |  |  |  |
| Hematologic neoplasm | 1.8 | 2.2 | -0.03 | 1.9 | 2.2 | -0.02 |
| Malignant lymphoma | 1.2 | 1.3 | -0.01 | 1.2 | 1.2 | 0.00 |
| Malignant neoplasm of anorectum | 0.2 | 0.2 | 0.00 | 0.1 | 0.1 | 0.00 |
| Malignant neoplastic disease | 16.3 | 16.4 | 0.00 | 17.1 | 16.0 | 0.03 |
| Malignant tumor of breast | 0.8 | 0.4 | 0.06 | 0.8 | 0.4 | 0.05 |
| Malignant tumor of colon | 0.6 | 0.8 | -0.03 | 0.5 | 0.7 | -0.03 |
| Malignant tumor of lung | 1.1 | 1.0 | 0.00 | 1.0 | 1.2 | -0.02 |
| Malignant tumor of urinary bladder | 1.2 | 1.1 | 0.00 | 1.3 | 1.1 | 0.02 |
| Primary malignant neoplasm of prostate | 4.6 | 5.0 | -0.02 | 5.0 | 4.9 | 0.01 |
| Medication use |  |  |  |  |  |  |
| Agents acting on the renin-angiotensin system | 45.4 | 45.3 | 0.00 | 44.8 | 44.9 | 0.00 |
| Antiepileptics | 29.8 | 31.3 | -0.03 | 32.1 | 30.4 | 0.04 |
| Antiinflammatory and antirheumatic products | 49.5 | 51.7 | -0.04 | 51.6 | 51.5 | 0.00 |
| Antineoplastic agents | 45.5 | 39.0 | 0.13 | 41.5 | 42.1 | -0.01 |
| Antipsoriatics | 1.8 | 1.6 | 0.02 | 2.2 | 1.4 | 0.06 |
| Antithrombotic agents | 45.3 | 45.3 | 0.00 | 45.7 | 43.9 | 0.04 |
| Beta blocking agents | 40.4 | 41.4 | -0.02 | 41.0 | 40.2 | 0.02 |
| Calcium channel blockers | 27.4 | 27.6 | -0.01 | 28.2 | 27.0 | 0.03 |
| Diuretics | 42.4 | 41.4 | 0.02 | 42.3 | 41.3 | 0.02 |
| Drugs for acid related disorders | 71.1 | 70.4 | 0.01 | 71.1 | 70.3 | 0.02 |
| Drugs for obstructive airway diseases | 57.5 | 41.7 | 0.32 | 48.3 | 49.0 | -0.01 |
| Drugs used in diabetes | 23.1 | 25.1 | -0.05 | 24.4 | 23.9 | 0.01 |
| Immunosuppressants | 58.8 | 52.8 | 0.12 | 54.7 | 55.5 | -0.02 |
| Lipid modifying agents | 51.9 | 49.9 | 0.04 | 50.4 | 49.7 | 0.01 |
| Opioids | 43.7 | 46.6 | -0.06 | 45.3 | 44.1 | 0.02 |
| Psycholeptics | 35.3 | 36.3 | -0.02 | 36.2 | 35.7 | 0.01 |
| Psychostimulants, agents used for adhd and nootropics | 2.7 | 2.9 | -0.02 | 2.9 | 2.9 | 0.00 |

# **S7. Patient counts, events, incident rates**

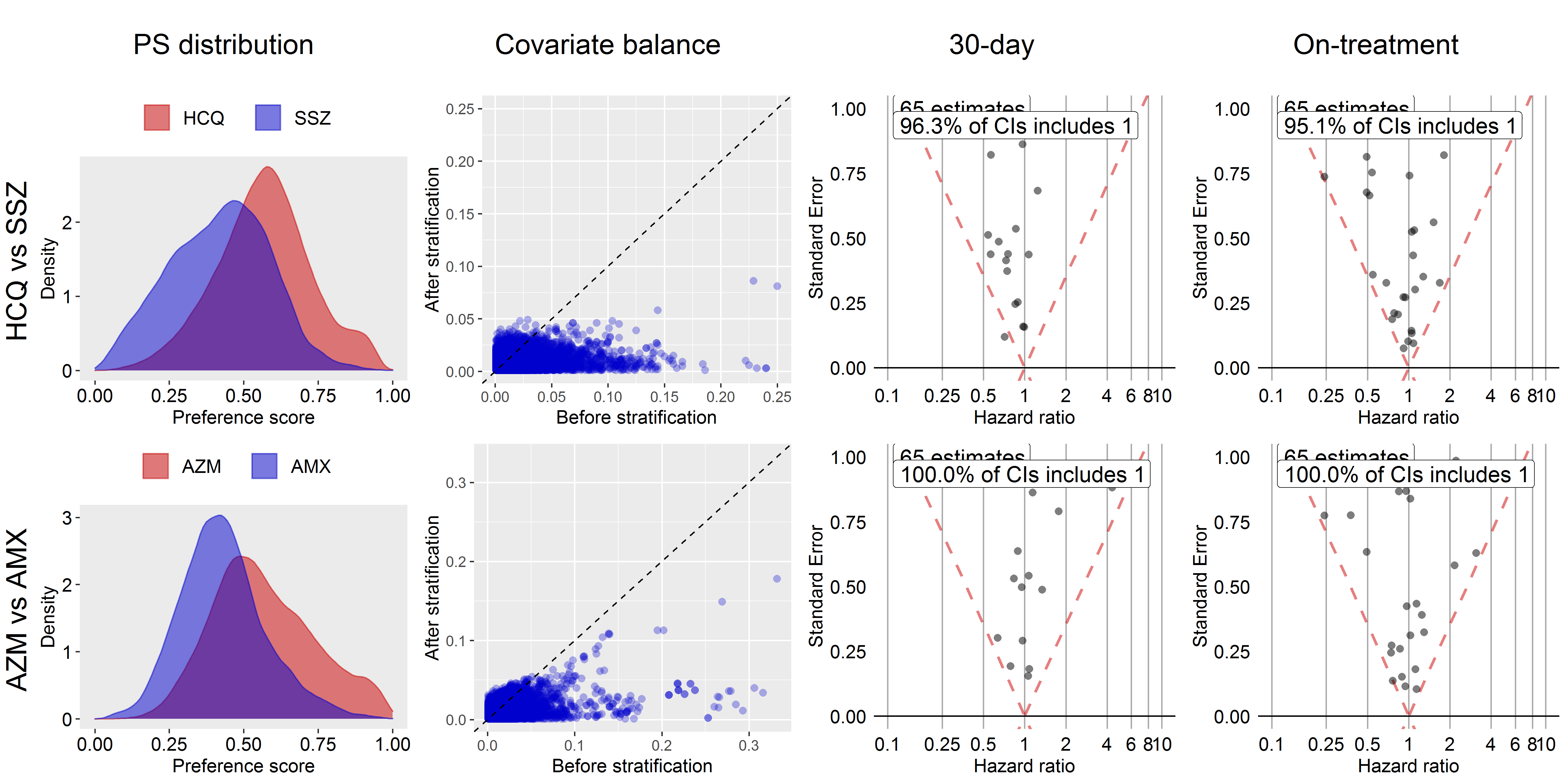
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | 30-day follow-up | | | | | | On-treatment follow-up | | | | | |
| Comparison | Outcome | Database | Patients | | Events | | IR | | Patients | | Events | | IR | |
|  |  |  | T | C | T | C | T | C | T | C | T | C | T | C |
| HCQ vs SSZ | All-cause mortality | CPRD | 9,127 | 11,398 | 6 | 5 | 8.03 | 5.35 | 9,127 | 11,398 | 253 | 386 | 14.02 | 14.56 |
| IMRD | 8,851 | 8,460 | <5 | 6 | <6.91 | 8.66 | 8,851 | 8,460 | 214 | 241 | 12.32 | 12.72 |
| Optum | 51,280 | 17,389 | 20 | 10 | 4.81 | 7.09 | 51,280 | 17,389 | 527 | 66 | 9.88 | 5.29 |
| VA | 32,028 | 14,349 | 45 | 17 | 17.13 | 14.45 | 32,028 | 14,349 | 1,356 | 327 | 24.51 | 18.65 |
| Meta-analysis | 101,286 | 51,596 | <76 | 38 | <9.20 | 9.02 |  |  |  |  |  |  |
| Myocardial infarction | CCAE | 66,630 | 22,374 | 29 | 11 | 5.36 | 6.05 | 66,630 | 22,374 | 240 | 48 | 3.64 | 3.28 |
| MDCD | 8,079 | 2,196 | 13 | 5 | 19.75 | 27.98 | 8,079 | 2,196 | 83 | 14 | 14.32 | 11.39 |
| MDCR | 15,827 | 5,190 | 26 | 10 | 20.17 | 23.68 | 15,827 | 5,190 | 287 | 70 | 15.93 | 17.55 |
| OpenClaims | 620,751 | 183,482 | 369 | 89 | 7.24 | 5.91 | 620,751 | 183,482 | 5,396 | 956 | 6.25 | 5.57 |
| Optum | 51,244 | 17,380 | 51 | 20 | 12.27 | 14.19 | 51,244 | 17,380 | 517 | 121 | 9.79 | 9.81 |
| PanTher | 78,424 | 21,885 | 59 | 12 | 9.29 | 6.77 |  |  |  |  |  |  |
| VA | 32,009 | 14,342 | 30 | 9 | 11.43 | 7.65 | 32,009 | 14,342 | 395 | 137 | 7.22 | 7.89 |
| Meta-analysis | 872,964 | 266,849 | 577 | 156 | 8.08 | 7.14 | 794,540 | 244,964 | 6,918 | 1,346 | 6.52 | 6.08 |
| Cardiovascular events | CCAE | 66,533 | 22,357 | 97 | 36 | 17.96 | 19.83 | 66,533 | 22,357 | 839 | 197 | 12.86 | 13.6 |
| MDCD | 8,041 | 2,186 | 35 | 11 | 53.5 | 61.95 | 8,041 | 2,186 | 388 | 78 | 70.54 | 66.08 |
| MDCR | 15,759 | 5,167 | 117 | 39 | 91.39 | 93.05 | 15,759 | 5,167 | 1,295 | 310 | 76.12 | 82.67 |
| OpenClaims | 619,493 | 183,209 | 1,636 | 470 | 32.2 | 31.28 | 619,493 | 183,209 | 22,657 | 4,394 | 26.94 | 26.16 |
| Optum | 51,095 | 17,340 | 215 | 76 | 51.96 | 54.11 | 51,095 | 17,340 | 2,232 | 490 | 43.8 | 40.92 |
| PanTher | 77,825 | 21,752 | 294 | 70 | 46.7 | 39.79 |  |  |  |  |  |  |
| VA | 31,913 | 14,300 | 120 | 46 | 45.92 | 39.28 | 31,913 | 14,300 | 1,577 | 546 | 29.84 | 32.57 |
| Meta-analysis | 870,659 | 266,311 | 2,514 | 748 | 35.31 | 34.35 | 792,834 | 244,559 | 28,988 | 6,015 | 28.07 | 27.83 |
| Cardiac arrhythmia | AmbEMR | 56,743 | 15,208 | 147 | 43 | 31.61 | 34.5 | 56,743 | 15,208 | 467 | 163 | 25.54 | 29.19 |
| CCAE | 66,430 | 22,337 | 153 | 58 | 28.38 | 32 | 66,430 | 22,337 | 1,301 | 348 | 20.3 | 24.42 |
| CPRD | 9,120 | 11,390 | 7 | 14 | 9.38 | 15 | 9,120 | 11,390 | 113 | 180 | 6.37 | 6.95 |
| DAGermany | 3,883 | 5,040 | <5 | 5 | <15.70 | 12.09 | 3,883 | 5,040 | 22 | 38 | 8.68 | 10.82 |
| IMRD | 8,847 | 8,452 | 8 | 12 | 11.06 | 17.35 | 8,847 | 8,452 | 101 | 123 | 5.9 | 6.64 |
| MDCD | 8,051 | 2,191 | 37 | 10 | 56.48 | 56.15 | 8,051 | 2,191 | 232 | 40 | 41.47 | 33.06 |
| MDCR | 15,763 | 5,165 | 73 | 24 | 56.93 | 57.2 | 15,763 | 5,165 | 726 | 183 | 42.35 | 48.33 |
| OpenClaims | 619,285 | 183,147 | 1,505 | 490 | 29.63 | 32.62 | 619,285 | 183,147 | 19,445 | 4,134 | 23.37 | 24.86 |
| Optum | 51,069 | 17,320 | 159 | 61 | 38.43 | 43.46 | 51,069 | 17,320 | 1,557 | 461 | 30.64 | 39.13 |
| PanTher | 77,008 | 21,581 | 472 | 115 | 75.89 | 65.97 |  |  |  |  |  |  |
| VA | 31,766 | 14,275 | 107 | 45 | 41.12 | 38.48 | 31,766 | 14,275 | 1,391 | 508 | 26.84 | 30.95 |
| Meta-analysis | 947,965 | 306,106 | <2,673 | 877 | <34.48 | 35.03 |  |  |  |  |  |  |
| Bradycardia | AmbEMR | 57,594 | 15,350 | 17 | <5 | 3.6 | <3.97 | 57,594 | 15,350 | 60 | 15 | 3.2 | 2.63 |
| CCAE | 66,640 | 22,373 | 5 | <5 | 0.92 | <2.75 | 66,640 | 22,373 | 69 | 13 | 1.04 | 0.89 |
| CPRD |  |  |  |  |  |  | 9,127 | 11,398 | <5 | <5 | <0.28 | <0.19 |
| IMRD |  |  |  |  |  |  | 8,852 | 8,460 | <5 | <5 | <0.29 | <0.26 |
| MDCD | 8,085 | 2,197 | 6 | <5 | 9.1 | <27.96 | 8,085 | 2,197 | 30 | <5 | 5.14 | <4.02 |
| MDCR |  |  |  |  |  |  | 15,830 | 5,190 | 106 | 25 | 5.84 | 6.21 |
| OpenClaims | 620,919 | 183,510 | 155 | 56 | 3.04 | 3.72 | 620,919 | 183,510 | 2,791 | 507 | 3.22 | 2.95 |
| Optum | 51,259 | 17,386 | 23 | <5 | 5.53 | <3.54 | 51,259 | 17,386 | 256 | 55 | 4.83 | 4.43 |
| PanTher | 78,425 | 21,911 | 62 | 16 | 9.76 | 9.02 |  |  |  |  |  |  |
| VA | 32,018 | 14,345 | 9 | <5 | 3.43 | <4.25 | 32,018 | 14,345 | 231 | 62 | 4.21 | 3.56 |
| Meta-analysis | 914,940 | 277,072 | 277 | <97 | 3.7 | <4.28 | 870,324 | 280,209 | <3,553 | <692 | <3.18 | <2.53 |
| Transient ischemic attack | CCAE | 66,617 | 22,372 | 23 | 6 | 4.25 | 3.3 | 66,617 | 22,372 | 187 | 35 | 2.84 | 2.39 |
| MDCD | 8,078 | 2,198 | 7 | <5 | 10.63 | <27.96 | 8,078 | 2,198 | 58 | 10 | 9.97 | 8.08 |
| MDCR | 15,821 | 5,187 | 17 | 7 | 13.19 | 16.59 | 15,821 | 5,187 | 202 | 47 | 11.18 | 11.74 |
| OpenClaims | 620,812 | 183,511 | 261 | 56 | 5.12 | 3.72 | 620,812 | 183,511 | 3,381 | 615 | 3.91 | 3.58 |
| Optum | 51,235 | 17,377 | 38 | 9 | 9.14 | 6.38 | 51,235 | 17,377 | 375 | 75 | 7.09 | 6.06 |
| PanTher | 78,520 | 21,921 | 26 | 7 | 4.09 | 3.94 |  |  |  |  |  |  |
| VA | 32,010 | 14,346 | 10 | 5 | 3.81 | 4.25 | 32,010 | 14,346 | 153 | 49 | 2.78 | 2.81 |
| Meta-analysis | 873,093 | 266,912 | 382 | <95 | 5.34 | <4.35 | 794,573 | 244,991 | 4,356 | 831 | 4.1 | 3.75 |
| Stroke | CCAE | 66,619 | 22,374 | 26 | 8 | 4.8 | 4.4 | 66,619 | 22,374 | 221 | 41 | 3.35 | 2.81 |
| MDCD | 8,073 | 2,196 | 13 | <5 | 19.76 | <27.98 | 8,073 | 2,196 | 103 | 15 | 17.82 | 12.13 |
| MDCR | 15,825 | 5,186 | 29 | 9 | 22.5 | 21.34 | 15,825 | 5,186 | 300 | 66 | 16.64 | 16.53 |
| OpenClaims | 620,748 | 183,482 | 383 | 98 | 7.52 | 6.51 | 620,748 | 183,482 | 5,413 | 1,122 | 6.27 | 6.54 |
| Optum | 51,239 | 17,376 | 41 | 12 | 9.86 | 8.51 | 51,239 | 17,376 | 562 | 106 | 10.66 | 8.56 |
| PanTher | 78,442 | 21,897 | 52 | 10 | 8.18 | 5.64 |  |  |  |  |  |  |
| VA | 32,008 | 14,341 | 19 | 8 | 7.24 | 6.8 | 32,008 | 14,341 | 241 | 70 | 4.38 | 4.01 |
| Meta-analysis | 872,954 | 266,852 | 563 | <150 | 7.88 | <6.87 |  |  |  |  |  |  |
| Venous thromboembolism | AmbEMR | 57,262 | 15,281 | 52 | 17 | 11.07 | 13.56 | 57,262 | 15,281 | 201 | 68 | 10.81 | 12.05 |
| CCAE | 66,528 | 22,358 | 70 | 23 | 12.96 | 12.67 | 66,528 | 22,358 | 650 | 152 | 9.96 | 10.48 |
| CPRD | 9,118 | 11,390 | <5 | 11 | <6.70 | 11.79 | 9,118 | 11,390 | 130 | 177 | 7.35 | 6.79 |
| DAGermany | 3,881 | 5,033 | <5 | 6 | <15.70 | 14.53 | 3,881 | 5,033 | 34 | 47 | 13.56 | 13.43 |
| IMRD | 8,841 | 8,455 | 5 | 10 | 6.92 | 14.45 | 8,841 | 8,455 | 116 | 123 | 6.79 | 6.59 |
| MDCD | 8,059 | 2,196 | 24 | <5 | 36.57 | <27.98 | 8,059 | 2,196 | 157 | 19 | 27.6 | 15.47 |
| MDCR | 15,780 | 5,176 | 41 | 8 | 31.9 | 18.99 | 15,780 | 5,176 | 442 | 89 | 24.86 | 22.63 |
| OpenClaims | 620,093 | 183,330 | 788 | 237 | 15.48 | 15.75 | 620,093 | 183,330 | 10,006 | 2,001 | 11.74 | 11.77 |
| Optum | 51,153 | 17,355 | 104 | 31 | 25.08 | 22.03 | 51,153 | 17,355 | 949 | 207 | 18.23 | 16.87 |
| PanTher | 78,092 | 21,804 | 241 | 52 | 38.15 | 29.47 |  |  |  |  |  |  |
| VA | 31,962 | 14,328 | 42 | 22 | 16.03 | 18.73 | 31,962 | 14,328 | 583 | 208 | 10.76 | 12.09 |
| Meta-analysis | 950,769 | 306,706 | <1,377 | <422 | <17.70 | <16.81 | 872,677 | 284,902 | 13,268 | 3,091 | 12.03 | 11.32 |
| Gastrointestil bleeding | CCAE | 66,621 | 22,357 | 40 | 12 | 7.39 | 6.61 | 66,621 | 22,357 | 332 | 54 | 5.05 | 3.69 |
| MDCD | 8,071 | 2,191 | 16 | <5 | 24.33 | <28.05 | 8,071 | 2,191 | 109 | 13 | 18.9 | 10.51 |
| MDCR | 15,813 | 5,177 | 31 | 7 | 24.06 | 16.62 | 15,813 | 5,177 | 350 | 62 | 19.49 | 15.49 |
| OpenClaims | 620,631 | 183,371 | 438 | 126 | 8.6 | 8.37 | 620,631 | 183,371 | 6,086 | 1,108 | 7.06 | 6.46 |
| Optum | 51,218 | 17,345 | 68 | 13 | 16.37 | 9.24 | 51,218 | 17,345 | 658 | 118 | 12.51 | 9.53 |
| PanTher | 78,411 | 21,890 | 78 | 18 | 12.28 | 10.15 |  |  |  |  |  |  |
| VA | 31,993 | 14,334 | 26 | 16 | 9.91 | 13.62 | 31,993 | 14,334 | 390 | 143 | 7.12 | 8.23 |
| Meta-analysis | 872,758 | 266,665 | 697 | <197 | 9.76 | <9.03 |  |  |  |  |  |  |
| Acute rel failure | CCAE | 66,584 | 22,362 | 72 | 27 | 13.32 | 14.87 | 66,584 | 22,362 | 526 | 96 | 8.01 | 6.59 |
| MDCD | 8,051 | 2,189 | 41 | 13 | 62.61 | 73.1 | 8,051 | 2,189 | 256 | 44 | 45.23 | 36.48 |
| MDCR | 15,797 | 5,181 | 60 | 17 | 46.67 | 40.37 | 15,797 | 5,181 | 608 | 133 | 34.22 | 33.69 |
| OpenClaims | 620,101 | 183,354 | 1,061 | 308 | 20.85 | 20.47 | 620,101 | 183,354 | 13,812 | 2,404 | 16.18 | 14.1 |
| Optum | 51,166 | 17,353 | 163 | 54 | 39.32 | 38.39 | 51,166 | 17,353 | 1,377 | 298 | 26.47 | 24.32 |
| PanTher | 78,010 | 21,797 | 186 | 42 | 29.45 | 23.81 |  |  |  |  |  |  |
| VA | 31,947 | 14,317 | 102 | 35 | 38.98 | 29.84 | 31,947 | 14,317 | 1,214 | 307 | 22.63 | 17.85 |
| Meta-analysis | 871,656 | 266,553 | 1,685 | 496 | 23.63 | 22.75 | 793,646 | 244,756 | 17,793 | 3,282 | 16.97 | 14.94 |
| End stage rel disease | AmbEMR |  |  |  |  |  |  | 57,647 | 15,355 | 12 | <5 | 0.64 | <0.88 |
| CCAE | 66,641 | 22,378 | <5 | <5 | <0.92 | <2.75 | 66,641 | 22,378 | 48 | 8 | 0.73 | 0.55 |
| MDCD |  |  |  |  |  |  | 8,087 | 2,198 | 15 | <5 | 2.56 | <4.01 |
| MDCR | 15,838 | 5,191 | <5 | <5 | <3.87 | <11.83 | 15,838 | 5,191 | 56 | 7 | 3.07 | 1.73 |
| OpenClaims | 621,009 | 183,543 | 70 | 8 | 1.37 | 0.53 | 621,009 | 183,543 | 1,298 | 174 | 1.49 | 1.01 |
| Optum | 51,271 | 17,389 | 7 | <5 | 1.68 | <3.54 | 51,271 | 17,389 | 118 | 19 | 2.22 | 1.52 |
| PanTher | 78,526 | 21,924 | 27 | <5 | 4.24 | <2.82 |  |  |  |  |  |  |
| VA | 32,020 | 14,348 | 5 | <5 | 1.9 | <4.25 | 32,020 | 14,348 | 86 | 27 | 1.56 | 1.54 |
| Meta-analysis | 865,305 | 264,773 | <119 | <33 | <1.68 | <1.52 | 852,513 | 260,402 | 1,633 | <245 | 1.5 | <1.07 |
| Hepatic failure | CCAE | 66,638 | 22,378 | 6 | <5 | 1.11 | <2.75 | 66,638 | 22,378 | 50 | 11 | 0.76 | 0.75 |
| DAGermany |  |  |  |  |  |  | 3,887 | 5,047 | <5 | <5 | <1.95 | <1.40 |
| MDCD | 8,085 | 2,198 | <5 | <5 | <7.58 | <27.95 | 8,085 | 2,198 | 25 | 6 | 4.26 | 4.82 |
| MDCR |  |  |  |  |  |  | 15,841 | 5,189 | 32 | 5 | 1.75 | 1.23 |
| OpenClaims | 621,042 | 183,551 | 42 | 23 | 0.82 | 1.53 | 621,042 | 183,551 | 729 | 151 | 0.84 | 0.87 |
| Optum | 51,267 | 17,387 | 13 | <5 | 3.13 | <3.54 | 51,267 | 17,387 | 102 | 26 | 1.92 | 2.09 |
| PanTher | 78,529 | 21,916 | 32 | 9 | 5.03 | 5.07 |  |  |  |  |  |  |
| VA | 32,025 | 14,348 | 5 | <5 | 1.9 | <4.25 | 32,025 | 14,348 | 61 | 14 | 1.1 | 0.8 |
| Meta-analysis | 857,586 | 261,778 | <103 | <52 | <1.47 | <2.43 | 798,785 | 250,098 | <1,004 | <218 | <0.94 | <0.96 |
| Acute pancreatitis | CCAE | 66,637 | 22,374 | 22 | 7 | 4.06 | 3.85 | 66,637 | 22,374 | 143 | 34 | 2.17 | 2.32 |
| MDCD | 8,077 | 2,196 | 10 | <5 | 15.19 | <27.97 | 8,077 | 2,196 | 55 | 8 | 9.47 | 6.45 |
| MDCR | 15,833 | 5,188 | 6 | <5 | 4.65 | <11.84 | 15,833 | 5,188 | 62 | 15 | 3.4 | 3.7 |
| OpenClaims | 620,956 | 183,525 | 155 | 50 | 3.04 | 3.32 | 620,956 | 183,525 | 1,881 | 390 | 2.17 | 2.26 |
| Optum | 51,259 | 17,384 | 21 | 9 | 5.05 | 6.38 | 51,259 | 17,384 | 171 | 50 | 3.22 | 4.02 |
| PanTher | 78,522 | 21,921 | 21 | 5 | 3.3 | 2.82 |  |  |  |  |  |  |
| VA | 32,023 | 14,347 | 12 | <5 | 4.57 | <4.25 | 32,023 | 14,347 | 106 | 46 | 1.92 | 2.63 |
| Meta-analysis | 873,307 | 266,935 | 247 | <86 | 3.45 | <3.94 | 794,785 | 245,014 | 2,418 | 543 | 2.27 | 2.44 |
| AZM vs AMX | All-cause mortality | Optum | 23,597 | 24,521 | 17 | 17 | 8.88 | 8.55 | 23,597 | 24,521 | 268 | 276 | 15.56 | 18.85 |
| VA | 6,234 | 8,005 | 91 | 52 | 179.23 | 79.42 | 6,234 | 8,005 | 550 | 518 | 51.16 | 45.97 |
| Meta-analysis | 29,831 | 32,526 | 108 | 69 | 44.58 | 26.12 | 29,831 | 32,526 | 818 | 794 | 29.24 | 30.64 |
| Myocardial infarction | CCAE | 32,610 | 32,507 | 13 | 11 | 4.92 | 4.17 | 32,610 | 32,507 | 117 | 94 | 4.33 | 4.33 |
| MDCD | 3,803 | 3,808 | <5 | 6 | <16.21 | 19.4 | 3,803 | 3,808 | 29 | 27 | 11.46 | 13.46 |
| MDCR | 8,119 | 9,254 | 16 | 9 | 24.33 | 11.96 | 8,119 | 9,254 | 166 | 140 | 20.41 | 17.34 |
| OpenClaims | 216,028 | 232,938 | 182 | 173 | 10.26 | 9.05 | 216,028 | 232,938 | 2,065 | 1,732 | 8.11 | 7.94 |
| Optum | 23,565 | 24,484 | 30 | 29 | 15.7 | 14.62 | 23,565 | 24,484 | 179 | 147 | 10.6 | 10.19 |
| PanTher | 18,477 | 16,424 | 26 | 20 | 17.35 | 15.01 |  |  |  |  |  |  |
| VA | 6,203 | 7,978 | 33 | 19 | 65.53 | 29.15 | 6,203 | 7,978 | 154 | 127 | 14.79 | 11.59 |
| Meta-analysis | 308,805 | 327,393 | <305 | 267 | <12.08 | 9.97 | 290,328 | 310,969 | 2,710 | 2,267 | 8.48 | 8.24 |
| Cardiovascular events | CCAE | 32,540 | 32,453 | 68 | 57 | 25.8 | 21.67 | 32,540 | 32,453 | 467 | 351 | 17.73 | 16.54 |
| MDCD | 3,759 | 3,781 | 31 | 30 | 102.07 | 97.98 | 3,759 | 3,781 | 157 | 122 | 69.38 | 67.74 |
| MDCR | 8,030 | 9,188 | 93 | 59 | 143.76 | 79.2 | 8,030 | 9,188 | 657 | 573 | 92.6 | 78.6 |
| OpenClaims | 215,278 | 232,274 | 901 | 784 | 51.08 | 41.18 | 215,278 | 232,274 | 7,835 | 6,884 | 32.54 | 33.34 |
| Optum | 23,434 | 24,361 | 147 | 137 | 77.54 | 69.59 | 23,434 | 24,361 | 723 | 669 | 45.56 | 49.38 |
| PanTher | 17,963 | 16,221 | 123 | 80 | 84.71 | 60.92 |  |  |  |  |  |  |
| VA | 6,047 | 7,866 | 183 | 87 | 378.81 | 136.03 | 6,047 | 7,866 | 544 | 445 | 58.44 | 44.08 |
| Meta-analysis |  |  |  |  |  |  | 289,088 | 309,923 | 10,383 | 9,044 | 34.42 | 34.73 |
| Cardiac arrhythmia | AmbEMR | 13,076 | 11,977 | 27 | 25 | 25.18 | 25.46 | 13,076 | 11,977 | 116 | 90 | 20.7 | 18.79 |
| CCAE | 32,510 | 32,423 | 113 | 67 | 42.94 | 25.5 | 32,510 | 32,423 | 711 | 486 | 28.53 | 23.76 |
| MDCD | 3,781 | 3,787 | 14 | 18 | 45.72 | 58.59 | 3,781 | 3,787 | 88 | 77 | 37.42 | 41.8 |
| MDCR | 8,084 | 9,210 | 45 | 48 | 68.86 | 64.24 | 8,084 | 9,210 | 354 | 361 | 47.87 | 49.98 |
| OpenClaims | 215,473 | 232,391 | 568 | 589 | 32.15 | 30.91 | 215,473 | 232,391 | 5,724 | 4,989 | 23.82 | 24.22 |
| Optum | 23,475 | 24,403 | 90 | 76 | 47.34 | 38.49 | 23,475 | 24,403 | 556 | 482 | 35.52 | 36.2 |
| PanTher | 18,022 | 16,138 | 153 | 111 | 105.13 | 85.09 |  |  |  |  |  |  |
| VA | 6,168 | 7,935 | 58 | 47 | 116.1 | 72.64 | 6,168 | 7,935 | 297 | 289 | 31.93 | 29.25 |
| Bradycardia | AmbEMR |  |  |  |  |  |  | 13,193 | 12,080 | 14 | 14 | 2.36 | 2.81 |
| CCAE | 32,619 | 32,516 | <5 | <5 | <1.89 | <1.90 | 32,619 | 32,516 | 43 | 50 | 1.58 | 2.29 |
| MDCD | 3,807 | 3,810 | <5 | <5 | <16.19 | <16.15 | 3,807 | 3,810 | 19 | 11 | 7.41 | 5.42 |
| MDCR | 8,124 | 9,268 | 5 | <5 | 7.59 | <6.63 | 8,124 | 9,268 | 70 | 86 | 8.51 | 10.63 |
| OpenClaims | 216,124 | 233,035 | 72 | 78 | 4.06 | 4.08 | 216,124 | 233,035 | 1,115 | 1,069 | 4.35 | 4.88 |
| Optum | 23,580 | 24,509 | 10 | 17 | 5.23 | 8.56 | 23,580 | 24,509 | 108 | 96 | 6.34 | 6.61 |
| PanTher | 18,546 | 16,432 | 15 | 23 | 9.97 | 17.26 |  |  |  |  |  |  |
| VA | 6,227 | 8,000 | <5 | <5 | <9.86 | <7.64 | 6,227 | 8,000 | 64 | 60 | 6.1 | 5.42 |
| Meta-analysis | 309,027 | 327,570 | <117 | <138 | <4.63 | <5.15 | 303,674 | 323,218 | 1,433 | 1,386 | 4.37 | 4.93 |
| Transient ischemic attack | CCAE | 32,609 | 32,505 | 5 | 11 | 1.89 | 4.17 | 32,609 | 32,505 | 111 | 77 | 4.11 | 3.55 |
| MDCD | 3,802 | 3,808 | 7 | <5 | 22.72 | <16.16 | 3,802 | 3,808 | 27 | 15 | 10.62 | 7.51 |
| MDCR | 8,121 | 9,259 | 9 | 10 | 13.67 | 13.28 | 8,121 | 9,259 | 118 | 102 | 14.53 | 12.6 |
| OpenClaims | 216,102 | 232,985 | 96 | 102 | 5.41 | 5.33 | 216,102 | 232,985 | 1,306 | 1,102 | 5.11 | 5.04 |
| Optum | 23,577 | 24,501 | 20 | 24 | 10.46 | 12.09 | 23,577 | 24,501 | 122 | 120 | 7.18 | 8.32 |
| PanTher | 18,563 | 16,456 | 9 | 5 | 5.98 | 3.74 |  |  |  |  |  |  |
| VA | 6,231 | 8,000 | 12 | 5 | 23.67 | 7.64 | 6,231 | 8,000 | 54 | 41 | 5.11 | 3.69 |
| Meta-analysis | 309,005 | 327,514 | 158 | <162 | 6.25 | <6.05 | 290,442 | 311,058 | 1,738 | 1,457 | 5.42 | 5.28 |
| Stroke | CCAE | 32,609 | 32,508 | 12 | 11 | 4.54 | 4.17 | 32,609 | 32,508 | 131 | 94 | 4.85 | 4.33 |
| MDCD | 3,803 | 3,808 | 7 | 7 | 22.71 | 22.63 | 3,803 | 3,808 | 36 | 29 | 14.16 | 14.55 |
| MDCR | 8,118 | 9,257 | 17 | 13 | 25.85 | 17.27 | 8,118 | 9,257 | 156 | 173 | 19.33 | 21.57 |
| OpenClaims | 216,089 | 232,948 | 155 | 159 | 8.74 | 8.32 | 216,089 | 232,948 | 2,063 | 1,858 | 8.12 | 8.55 |
| Optum | 23,572 | 24,490 | 33 | 34 | 17.26 | 17.14 | 23,572 | 24,490 | 174 | 157 | 10.28 | 10.87 |
| PanTher | 18,538 | 16,433 | 25 | 9 | 16.63 | 6.75 |  |  |  |  |  |  |
| VA | 6,215 | 7,995 | 10 | 15 | 19.77 | 22.96 | 6,215 | 7,995 | 76 | 83 | 7.23 | 7.5 |
| Meta-analysis | 308,944 | 327,439 | 259 | 248 | 10.25 | 9.26 | 290,406 | 311,006 | 2,636 | 2,394 | 8.26 | 8.72 |
| Venous thromboembolism | AmbEMR | 13,133 | 12,024 | 11 | 19 | 10.21 | 19.27 | 13,133 | 12,024 | 51 | 57 | 8.71 | 11.72 |
| CCAE | 32,559 | 32,467 | 40 | 40 | 15.16 | 15.2 | 32,559 | 32,467 | 339 | 227 | 12.8 | 10.59 |
| MDCD | 3,793 | 3,797 | 8 | 18 | 26.03 | 58.49 | 3,793 | 3,797 | 81 | 61 | 33.31 | 31.49 |
| MDCR | 8,104 | 9,239 | 23 | 24 | 35.04 | 31.96 | 8,104 | 9,239 | 228 | 204 | 28.93 | 26.03 |
| OpenClaims | 215,805 | 232,676 | 320 | 357 | 18.07 | 18.7 | 215,805 | 232,676 | 3,662 | 3,137 | 14.74 | 14.73 |
| Optum | 23,540 | 24,459 | 54 | 63 | 28.3 | 31.82 | 23,540 | 24,459 | 330 | 303 | 20.08 | 21.49 |
| PanTher | 18,394 | 16,335 | 112 | 57 | 75.28 | 43.08 |  |  |  |  |  |  |
| VA | 6,203 | 7,977 | 32 | 23 | 63.53 | 35.31 | 6,203 | 7,977 | 175 | 165 | 17.32 | 15.45 |
| Meta-analysis | 321,531 | 338,974 | 600 | 601 | 22.82 | 21.68 | 303,137 | 322,639 | 4,866 | 4,154 | 15.32 | 15.17 |
| Gastrointestil bleeding | CCAE | 32,609 | 32,486 | 20 | 31 | 7.56 | 11.77 | 32,609 | 32,486 | 137 | 128 | 5.08 | 5.9 |
| MDCD | 3,805 | 3,797 | 8 | 11 | 25.93 | 35.67 | 3,805 | 3,797 | 58 | 35 | 23.17 | 17.82 |
| MDCR | 8,118 | 9,231 | 16 | 28 | 24.33 | 37.34 | 8,118 | 9,231 | 172 | 170 | 21.23 | 21.34 |
| OpenClaims | 216,032 | 232,795 | 213 | 220 | 12.01 | 11.52 | 216,032 | 232,795 | 2,245 | 2,009 | 8.85 | 9.26 |
| Optum | 23,568 | 24,453 | 39 | 37 | 20.41 | 18.68 | 23,568 | 24,453 | 227 | 189 | 13.45 | 13.14 |
| PanTher | 18,530 | 16,391 | 37 | 22 | 24.62 | 16.54 |  |  |  |  |  |  |
| VA | 6,211 | 7,952 | 31 | 31 | 61.43 | 47.76 | 6,211 | 7,952 | 122 | 125 | 11.67 | 11.44 |
| Meta-analysis | 308,873 | 327,105 | 364 | 380 | 14.41 | 14.2 | 290,343 | 310,714 | 2,961 | 2,656 | 9.3 | 9.69 |
| Acute rel failure | CCAE | 32,576 | 32,451 | 50 | 36 | 18.94 | 13.68 | 32,576 | 32,451 | 286 | 220 | 10.67 | 10.23 |
| MDCD | 3,774 | 3,789 | 21 | 27 | 68.81 | 87.98 | 3,774 | 3,789 | 110 | 77 | 46.36 | 40.34 |
| MDCR | 8,091 | 9,224 | 47 | 31 | 71.85 | 41.38 | 8,091 | 9,224 | 348 | 311 | 44.2 | 40.07 |
| OpenClaims | 215,716 | 232,429 | 500 | 603 | 28.26 | 31.64 | 215,716 | 232,429 | 4,977 | 4,565 | 20.04 | 21.49 |
| Optum | 23,534 | 24,413 | 104 | 87 | 54.57 | 44.05 | 23,534 | 24,413 | 476 | 444 | 28.9 | 31.72 |
| PanTher | 18,134 | 16,262 | 86 | 70 | 58.59 | 53.16 |  |  |  |  |  |  |
| VA | 6,133 | 7,907 | 146 | 117 | 296.69 | 182.62 | 6,133 | 7,907 | 416 | 410 | 42.7 | 39.97 |
| Meta-analysis |  |  |  |  |  |  | 289,824 | 310,213 | 6,613 | 6,027 | 21.22 | 22.5 |
| End stage rel disease | AmbEMR |  |  |  |  |  |  | 13,197 | 12,079 | 7 | 5 | 1.18 | 1 |
| CCAE | 32,620 | 32,518 | <5 | <5 | <1.89 | <1.90 | 32,620 | 32,518 | 30 | 20 | 1.1 | 0.91 |
| MDCD | 3,806 | 3,809 | <5 | <5 | <16.20 | <16.15 | 3,806 | 3,809 | 18 | 10 | 6.96 | 4.96 |
| MDCR | 8,130 | 9,270 | 7 | <5 | 10.62 | <6.63 | 8,130 | 9,270 | 23 | 28 | 2.75 | 3.4 |
| OpenClaims | 216,166 | 233,078 | 36 | 41 | 2.03 | 2.14 | 216,166 | 233,078 | 558 | 507 | 2.16 | 2.3 |
| Optum | 23,594 | 24,521 | <5 | 6 | <2.61 | 3.02 | 23,594 | 24,521 | 31 | 36 | 1.8 | 2.46 |
| PanTher | 18,557 | 16,465 | 9 | 5 | 5.98 | 3.74 |  |  |  |  |  |  |
| VA | 6,232 | 8,003 | 8 | <5 | 15.77 | <7.64 | 6,232 | 8,003 | 37 | 38 | 3.48 | 3.39 |
| Meta-analysis | 309,105 | 327,664 | <75 | <72 | <2.97 | <2.69 | 303,745 | 323,278 | 704 | 644 | 2.13 | 2.27 |
| Hepatic failure | CCAE | 32,621 | 32,519 | <5 | 5 | <1.89 | 1.9 | 32,621 | 32,519 | 30 | 28 | 1.1 | 1.28 |
| MDCD | 3,807 | 3,809 | <5 | <5 | <16.19 | <16.15 | 3,807 | 3,809 | 6 | 6 | 2.3 | 2.94 |
| MDCR | 8,130 | 9,269 | <5 | <5 | <7.58 | <6.63 | 8,130 | 9,269 | 18 | 15 | 2.15 | 1.81 |
| OpenClaims | 216,181 | 233,088 | 22 | 27 | 1.24 | 1.41 | 216,181 | 233,088 | 306 | 311 | 1.18 | 1.41 |
| Optum | 23,592 | 24,516 | <5 | <5 | <2.61 | <2.52 | 23,592 | 24,516 | 38 | 27 | 2.2 | 1.84 |
| PanTher | 18,548 | 16,466 | 15 | 11 | 9.97 | 8.23 |  |  |  |  |  |  |
| VA | 6,233 | 8,005 | 6 | <5 | 11.82 | <7.64 | 6,233 | 8,005 | 26 | 19 | 2.42 | 1.69 |
| Meta-analysis | 309,112 | 327,672 | <63 | <63 | <2.49 | <2.35 | 290,564 | 311,206 | 424 | 406 | 1.31 | 1.45 |
| Acute pancreatitis | CCAE | 32,611 | 32,513 | 6 | 8 | 2.27 | 3.03 | 32,611 | 32,513 | 70 | 55 | 2.58 | 2.52 |
| MDCD | 3,800 | 3,808 | <5 | 5 | <16.22 | 16.16 | 3,800 | 3,808 | 23 | 21 | 9.06 | 10.48 |
| MDCR | 8,129 | 9,268 | <5 | <5 | <7.59 | <6.63 | 8,129 | 9,268 | 32 | 32 | 3.84 | 3.89 |
| OpenClaims | 216,145 | 232,998 | 64 | 80 | 3.61 | 4.18 | 216,145 | 232,998 | 713 | 595 | 2.77 | 2.7 |
| Optum | 23,590 | 24,511 | 11 | 10 | 5.75 | 5.03 | 23,590 | 24,511 | 62 | 49 | 3.62 | 3.36 |
| PanTher | 18,572 | 16,463 | 7 | 9 | 4.65 | 6.74 |  |  |  |  |  |  |
| VA | 6,232 | 7,995 | 7 | 6 | 13.8 | 9.18 | 6,232 | 7,995 | 39 | 41 | 3.68 | 3.68 |
| Meta-analysis | 309,079 | 327,556 | <105 | <123 | <4.15 | <4.59 | 290,507 | 311,093 | 939 | 793 | 2.91 | 2.85 |

# **S8. Calibrated hazard ratio forest plots**

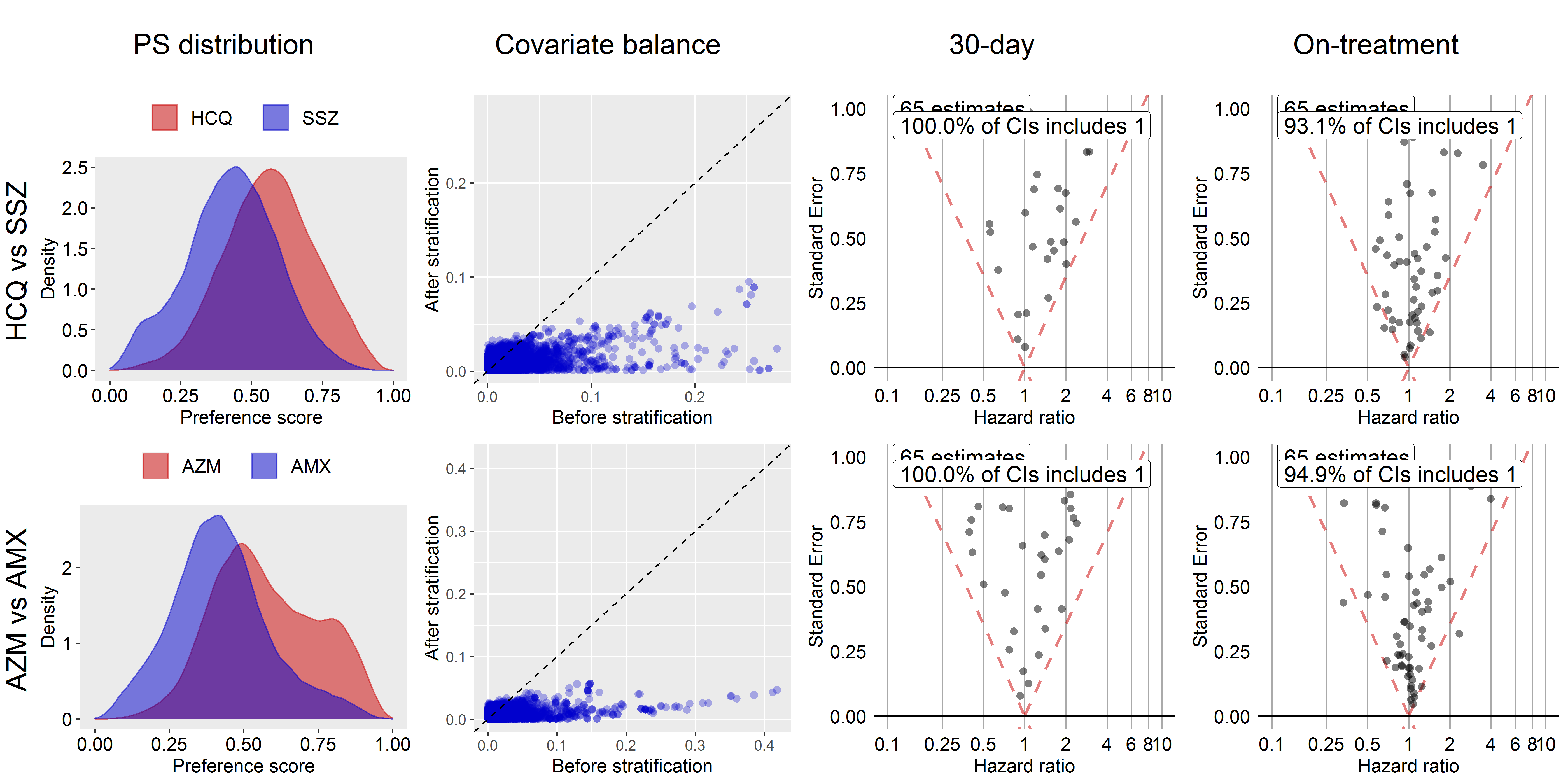
Blah

# **S9. Evidence evaluation diagnostics**

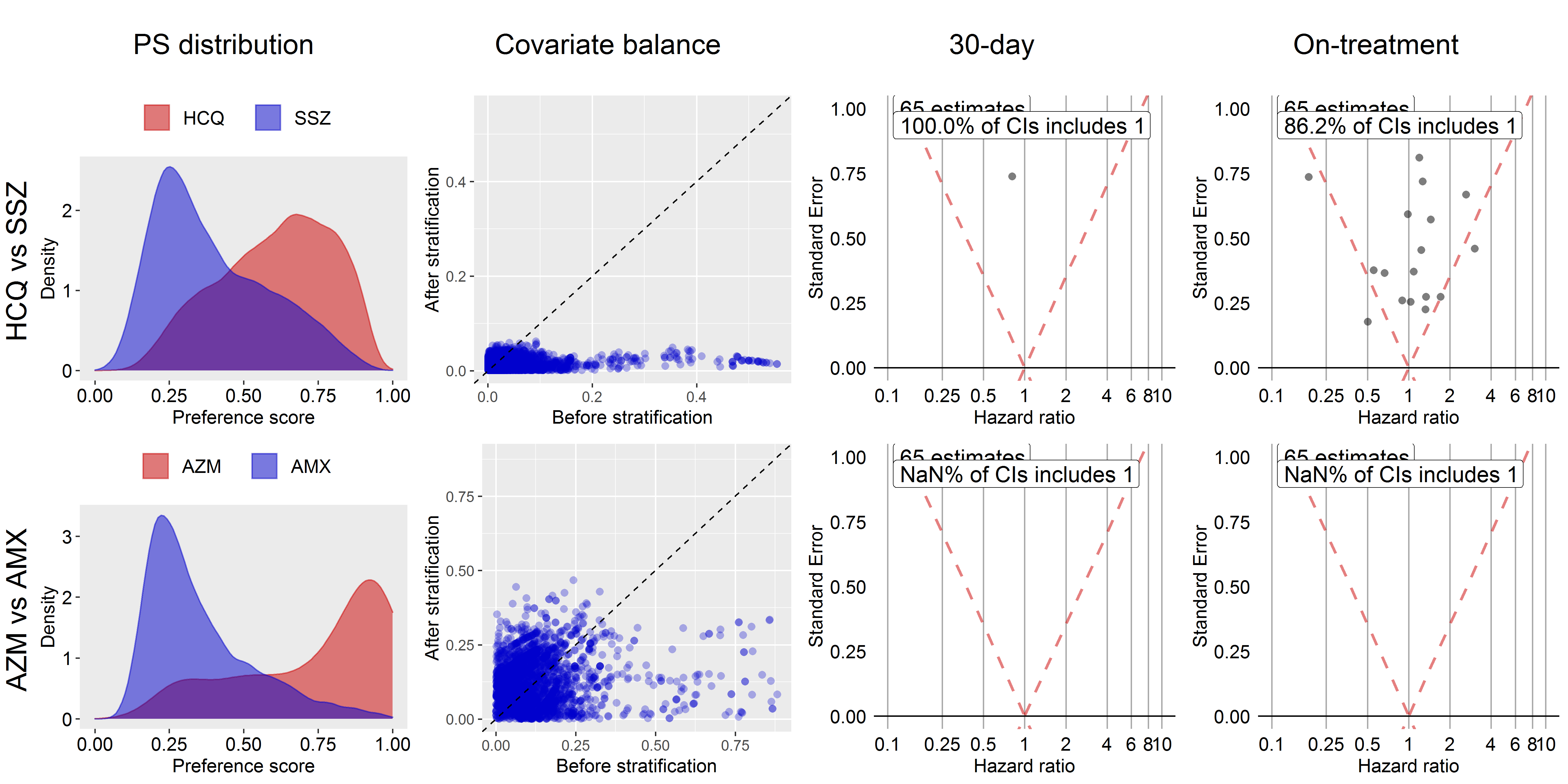
## **S9.1. AmbEMR**



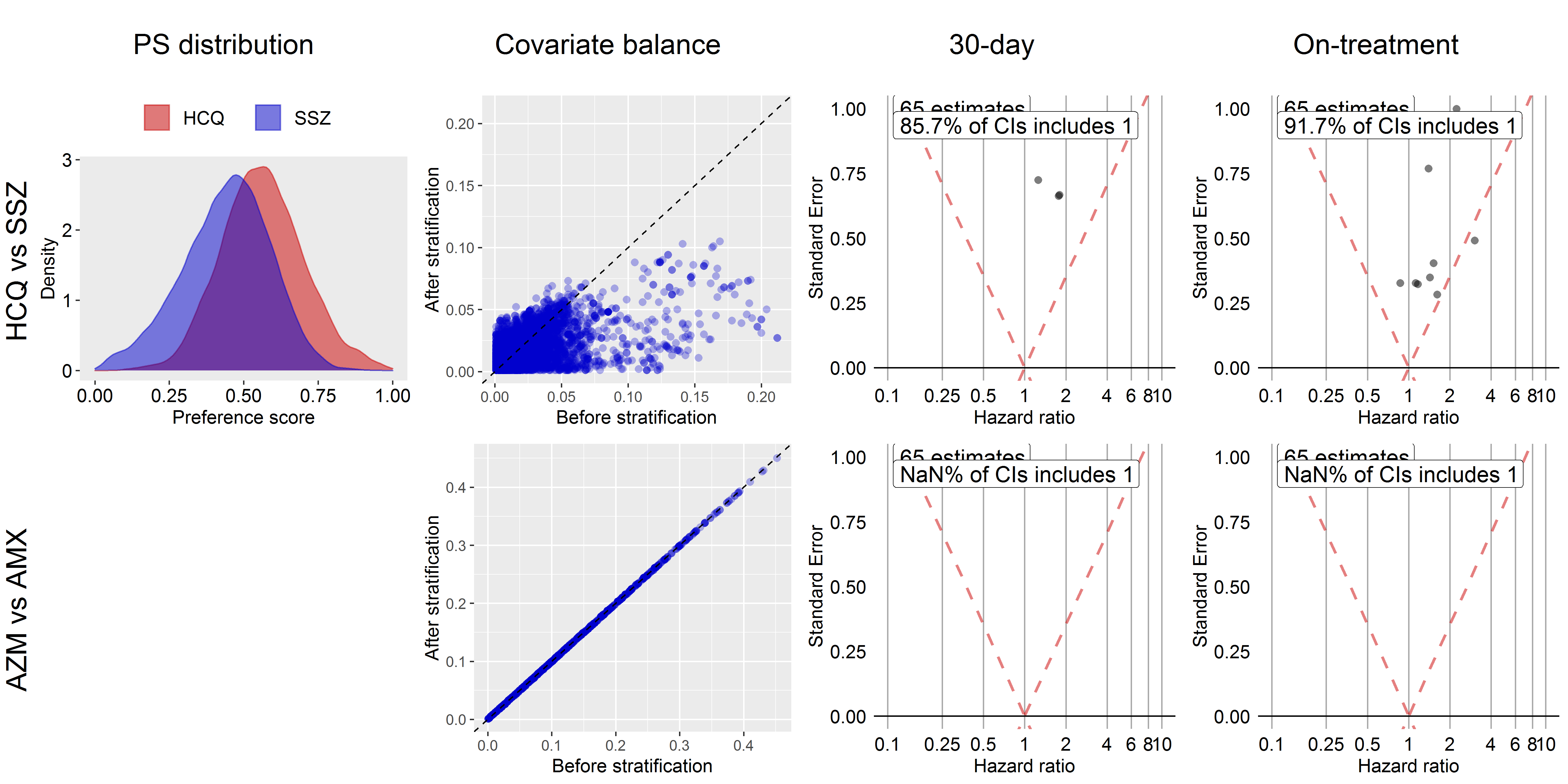
## **S9.2. CCAE**



## **S9.3. CPRD**



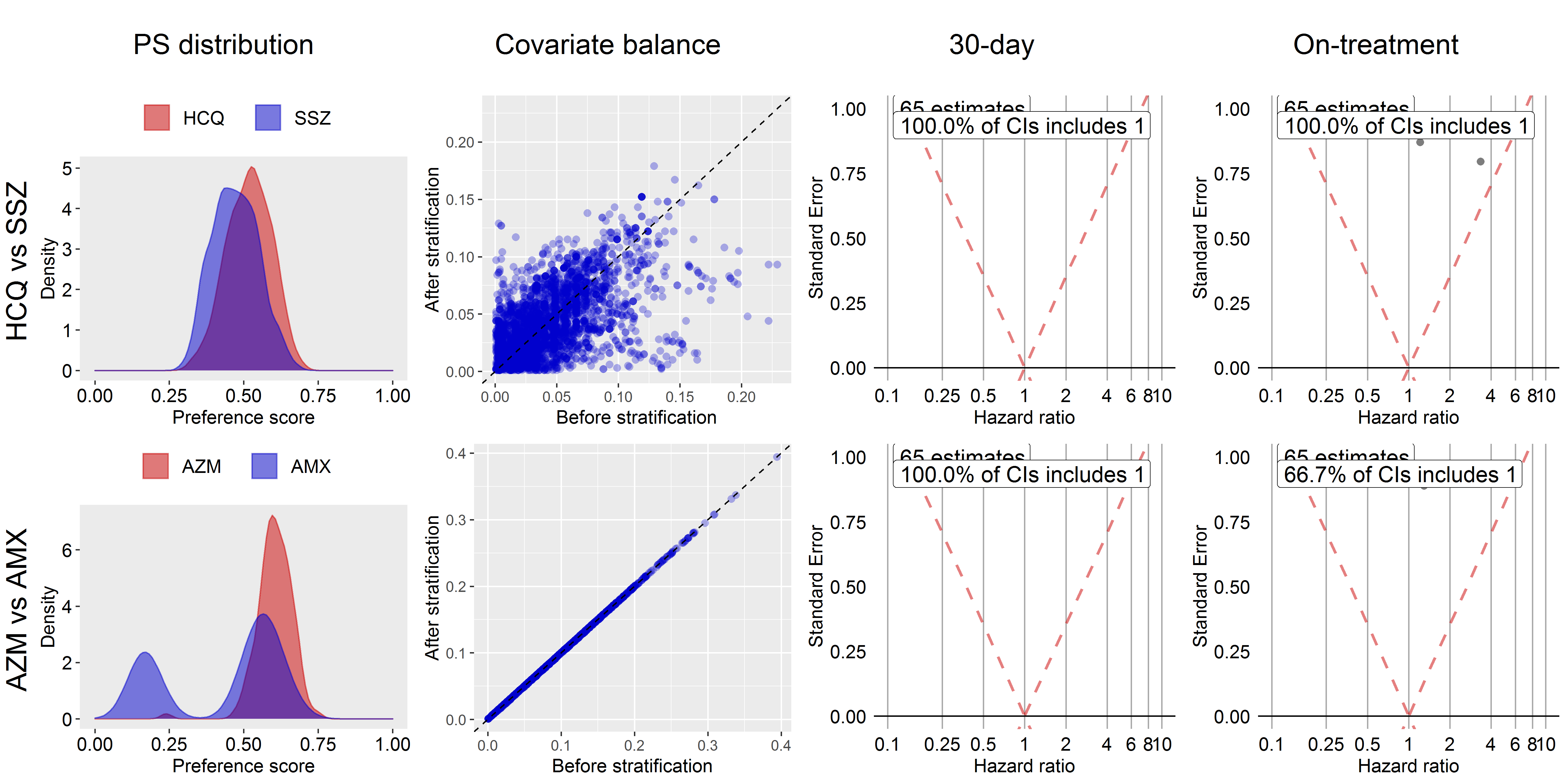
## **S9.4. DAGermany**



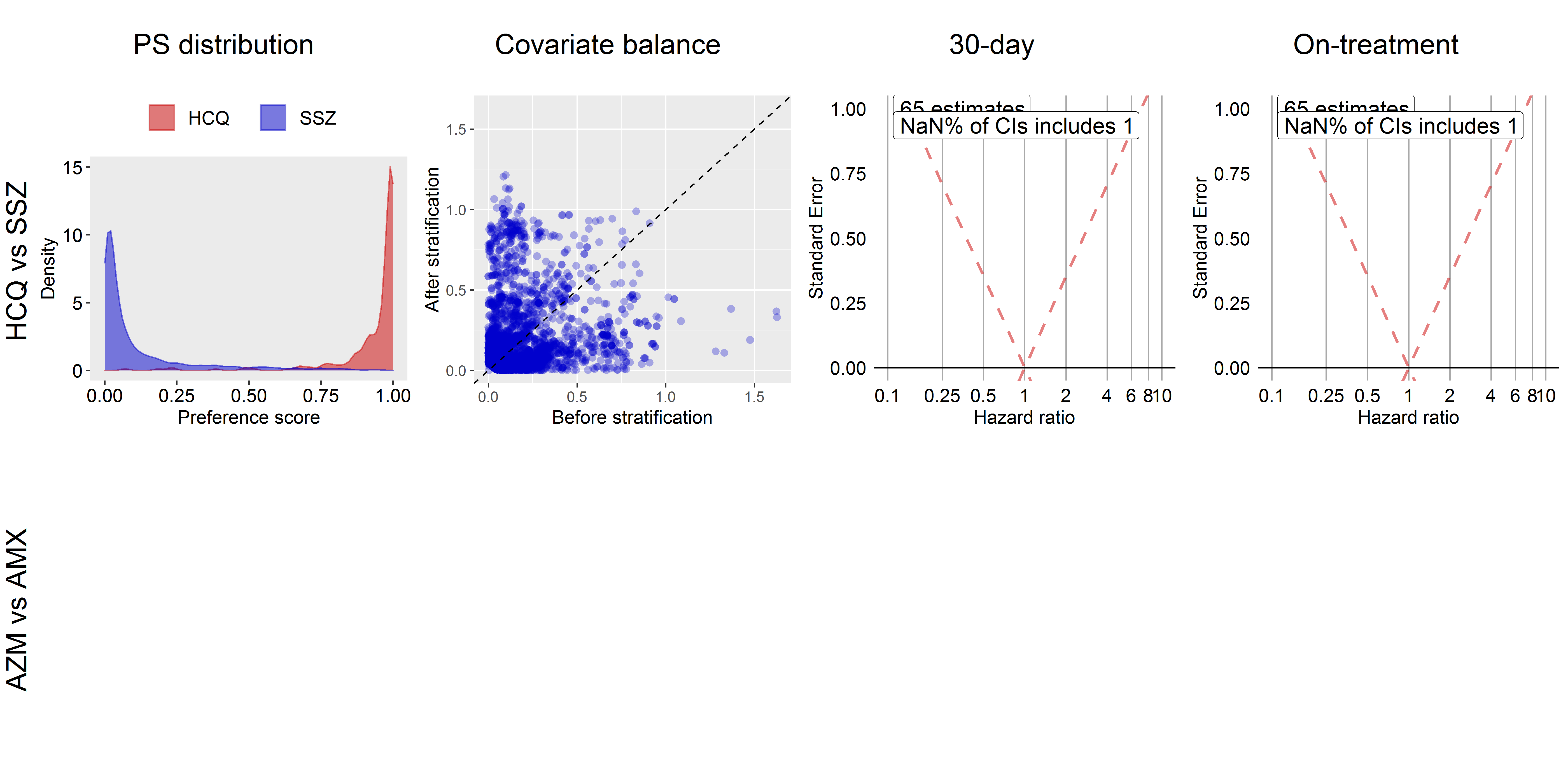
## **S9.5. IMRD**



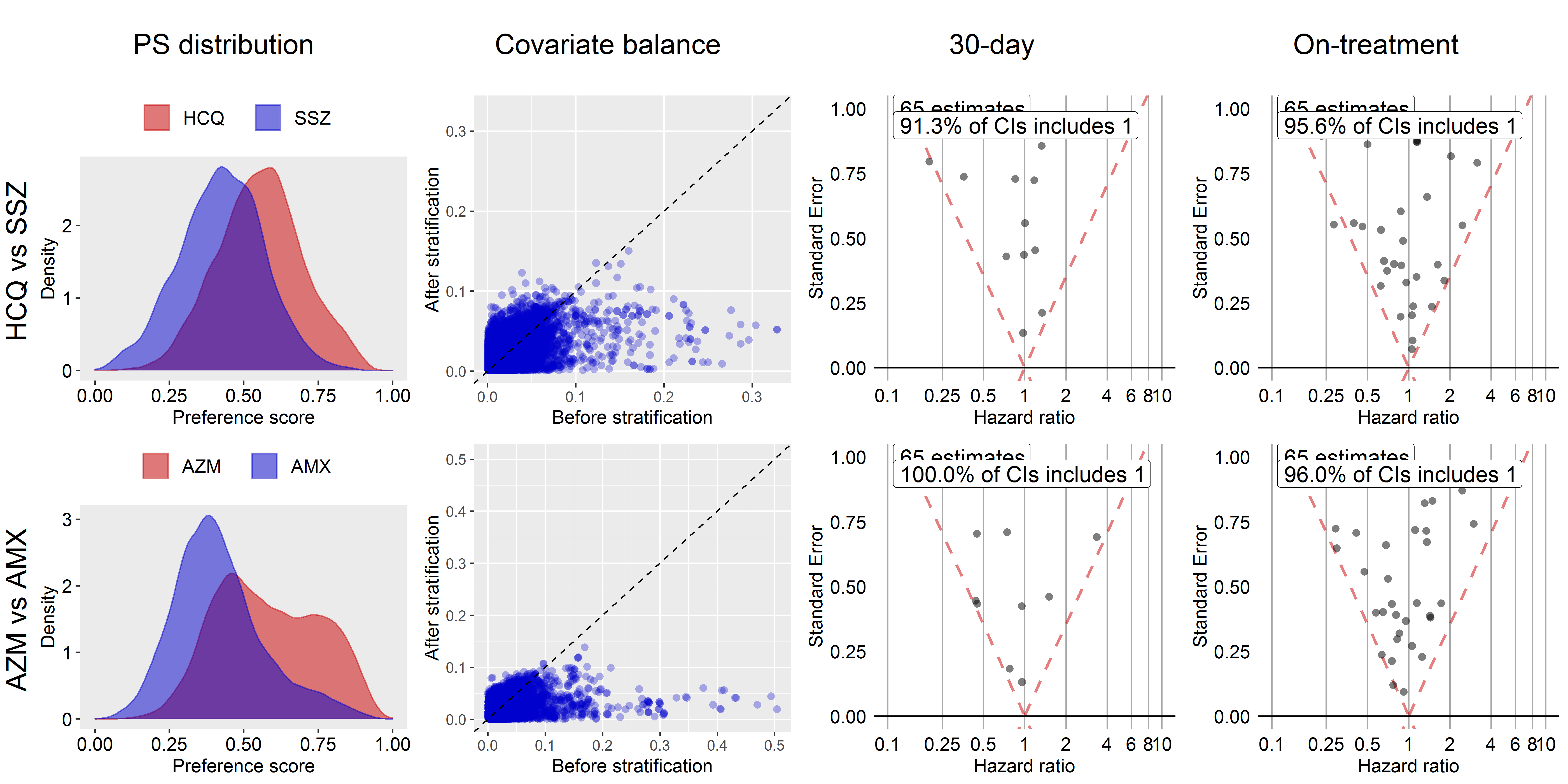
## **S9.6. IPCI**



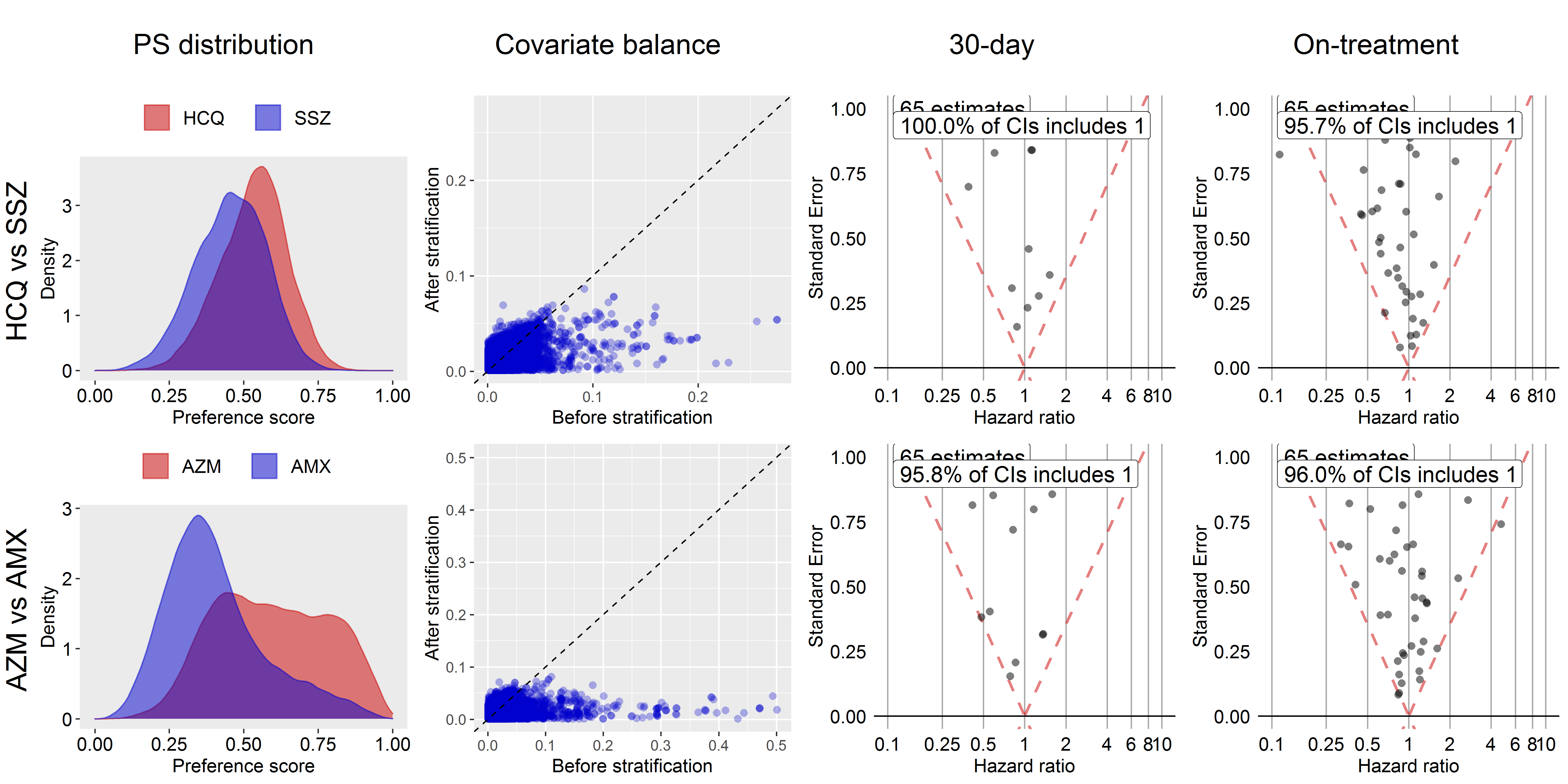
## **S9.7. JMDC**



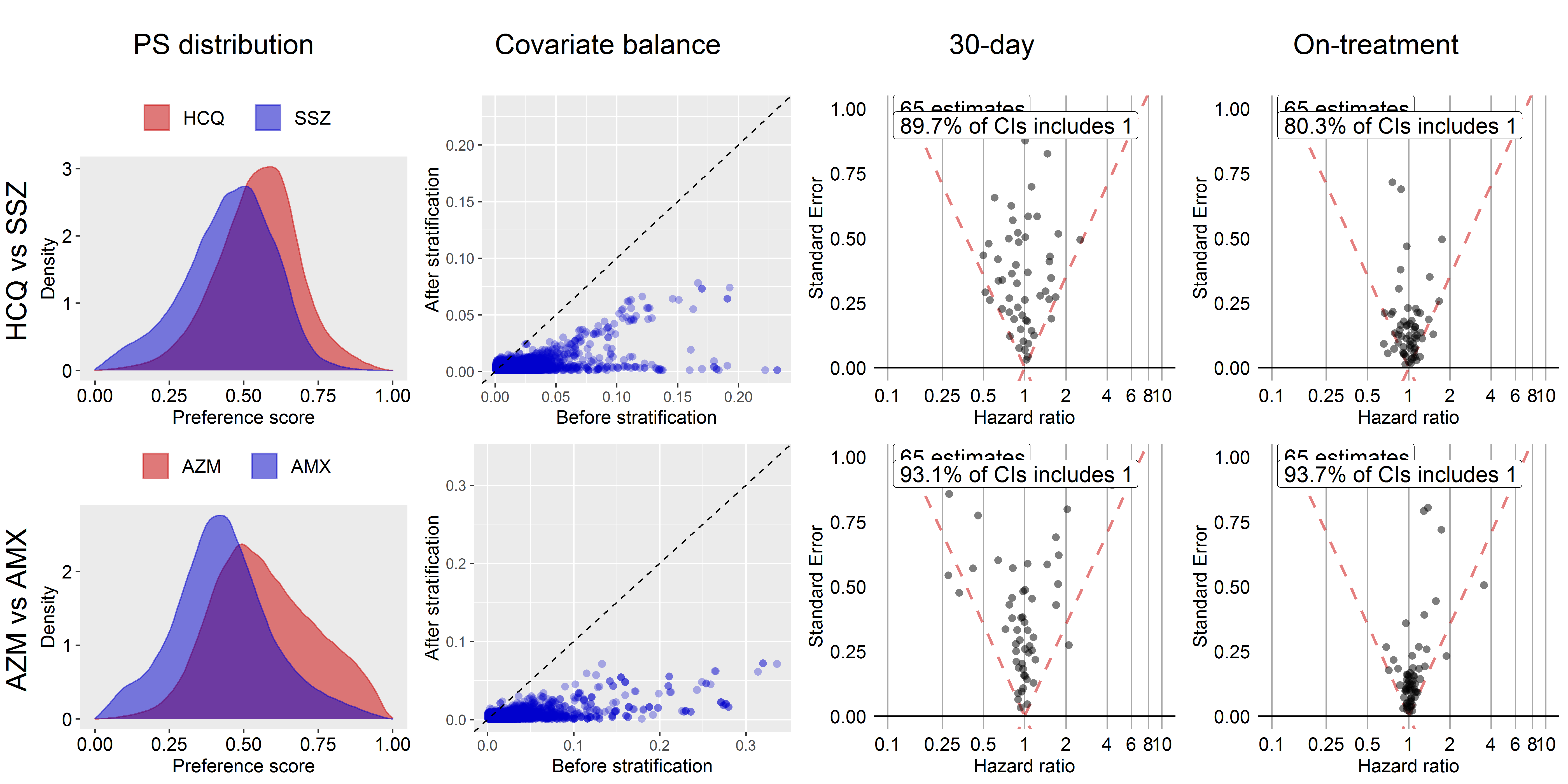
## **S9.8. MDCD**



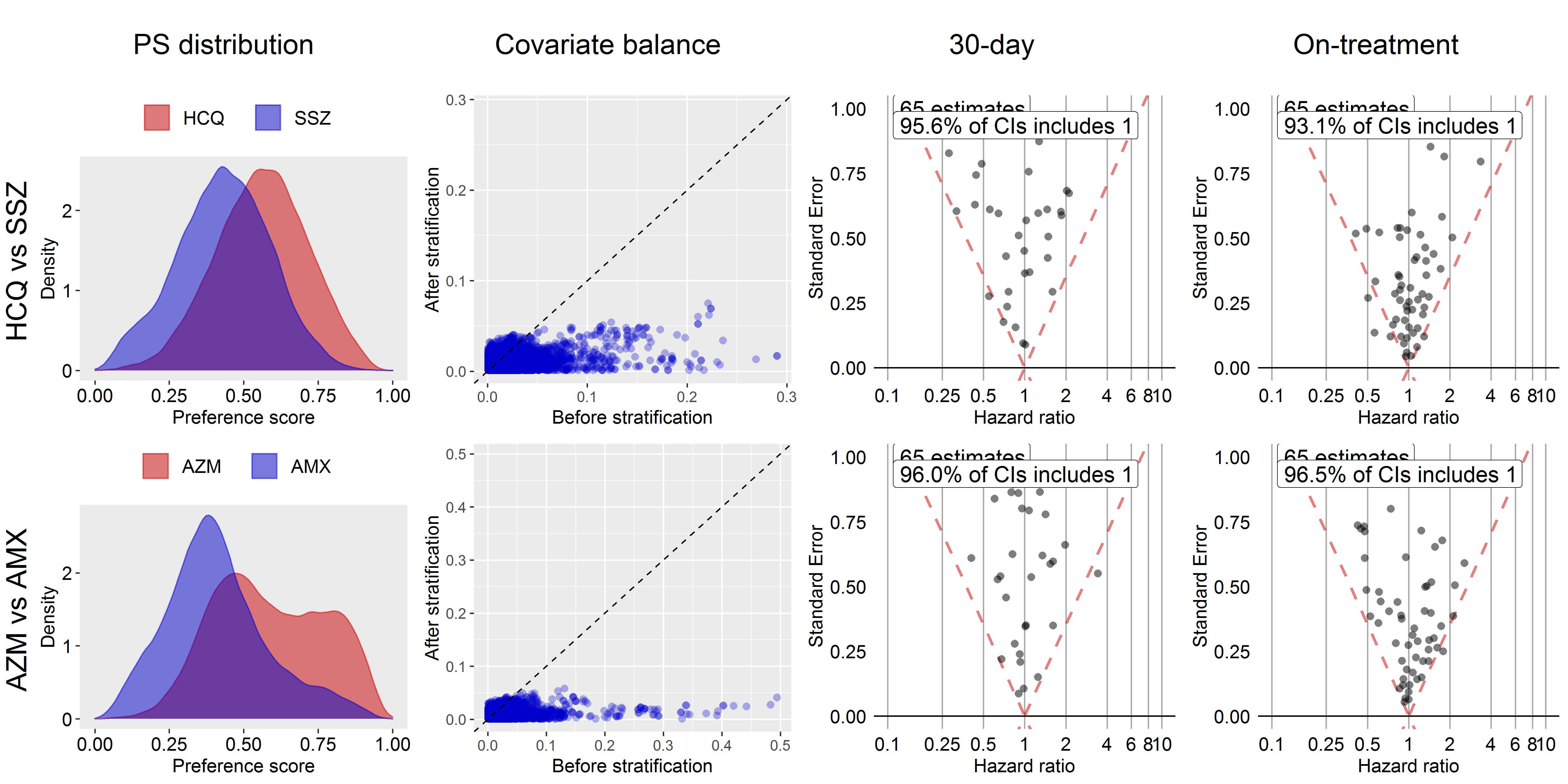
## **S9.9. MDCR**



## **S9.10. OpenClaims**



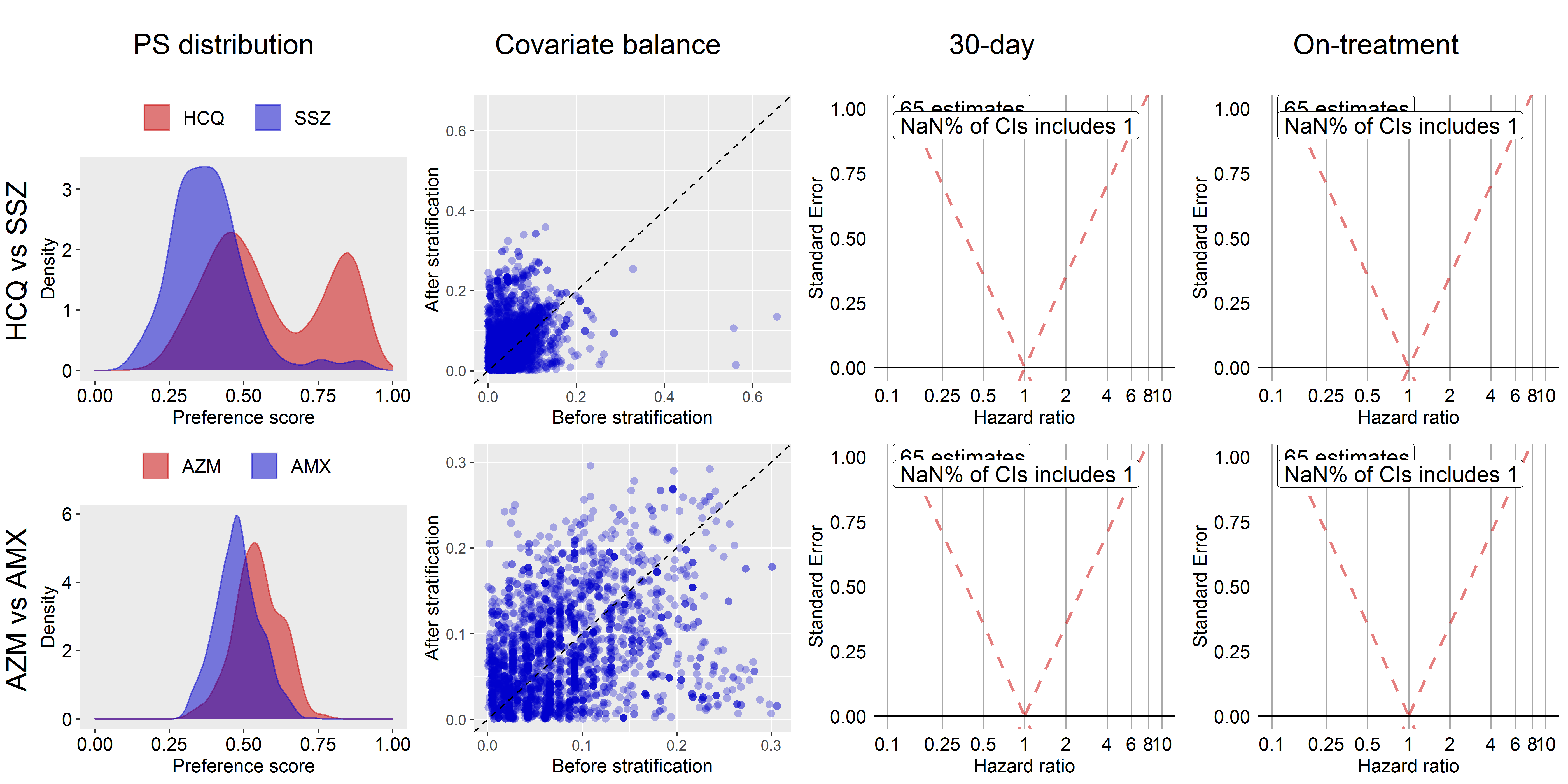
## **S9.11. Optum**



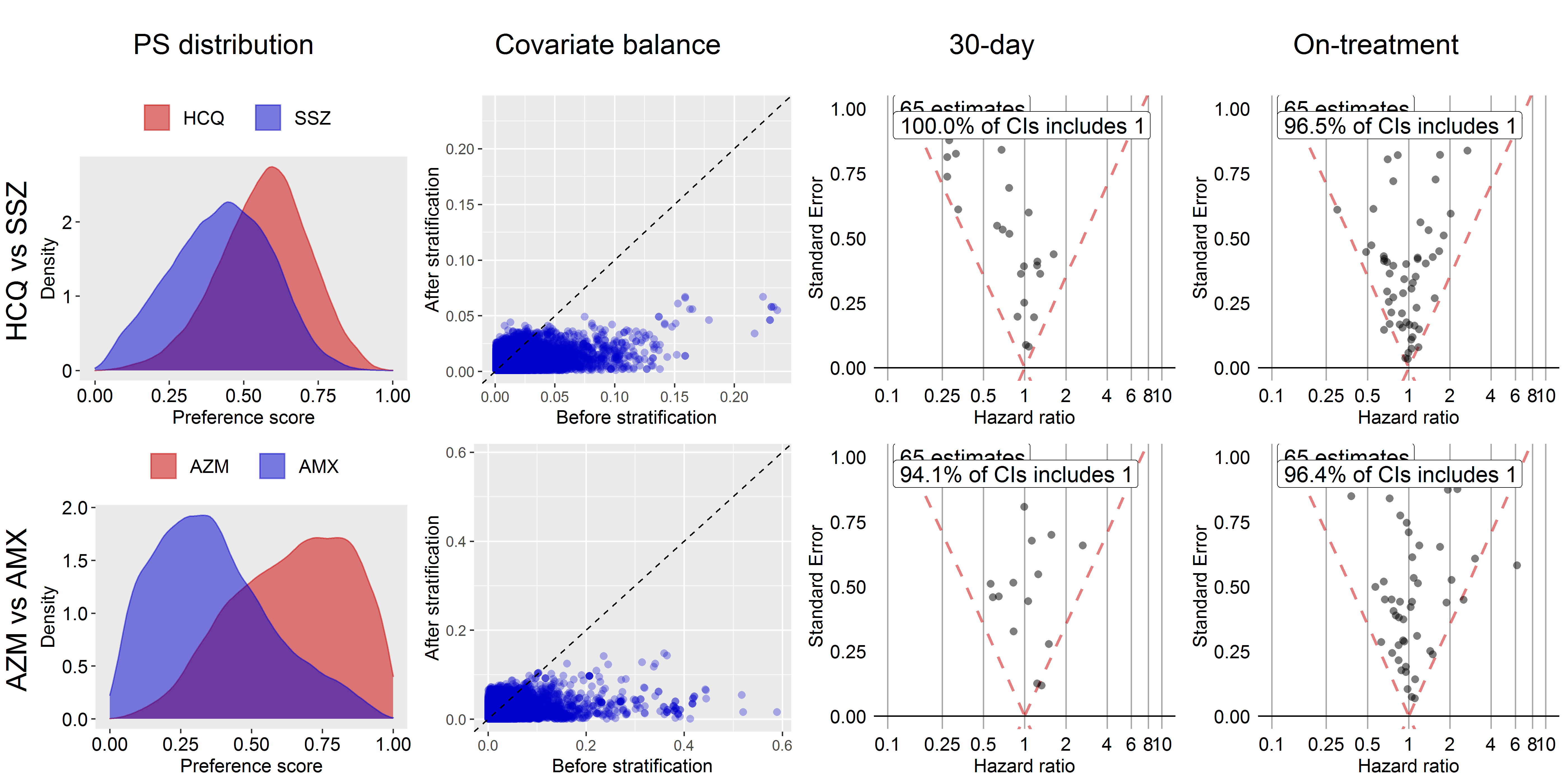
## **S9.12. PanTher**



## **S9.13. SIDIAP**



## **S9.14. VA**



# **S10. Self-Controlled Case Series (SCCS) results: Hydroxychloroquine**

## **S10.1 CPRD**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Outcome** | **Analysis** | **Cases** | **IRR** | **95% CI LB** | **95% CI UB** | **Calibrated P** | **Calibrated IRR** | | **Calibrated 95% CI LB** | **Calibrated 95% CI UB** |
| Myocardial infarction | Adjusting for event-dependent observation | 0 | NA | NA | NA | NA | NA | NA | | NA |
| Myocardial infarction | Primary analysis | 0 | NA | NA | NA | NA | NA | NA | | NA |
| Acute pancreatitis events | Adjusting for event-dependent observation | 0 | NA | NA | NA | NA | NA | NA | | NA |
| Acute pancreatitis event | Primary analysis | 0 | NA | NA | NA | NA | NA | NA | | NA |
| Acute renal failure | Adjusting for event-dependent observation | 0 | NA | NA | NA | NA | NA | NA | | NA |
| Acute renal failure | Primary analysis | 0 | NA | NA | NA | NA | NA | NA | | NA |
| Gastrointestinal bleeding | Adjusting for event-dependent observation | 0 | NA | NA | NA | NA | NA | NA | | NA |
| Gastrointestinal bleeding | Primary analysis | 0 | NA | NA | NA | NA | NA | NA | | NA |
| Cardiac arrhythmia | Adjusting for event-dependent observation | 12,614 | 0.86 | 0.77 | 0.97 | 0.81 | 0.95 | 0.61 | | 1.47 |
| Cardiac arrhythmia | Primary analysis | 12,614 | 0.87 | 0.77 | 0.98 | 0.83 | 0.95 | 0.61 | | 1.48 |
| Bradycardia | Adjusting for event-dependent observation | 7,094 | 0.6 | 0.18 | 1.68 | 0.49 | 0.65 | 0.2 | | 2.16 |
| Bradycardia | Primary analysis | 7,094 | 0.62 | 0.19 | 1.69 | 0.51 | 0.68 | 0.21 | | 2.18 |
| Chest pain or angina | Adjusting for event-dependent observation | 13,376 | 0.89 | 0.8 | 1 | 0.9 | 0.98 | 0.63 | | 1.52 |
| Chest pain or angina | Primary analysis | 13,376 | 0.89 | 0.8 | 1 | 0.9 | 0.98 | 0.63 | | 1.52 |
| End stage renal disease | Adjusting for event-dependent observation | 1,496 | 0.84 | 0.14 | 4.51 | 0.92 | 0.91 | 0.15 | | 5.49 |
| End stage renal disease | Primary analysis | 1,496 | 0.83 | 0.14 | 4.41 | 0.91 | 0.91 | 0.15 | | 5.31 |
| Heart failure | Adjusting for event-dependent observation | 10,215 | 1.1 | 0.76 | 1.56 | 0.53 | 1.2 | 0.69 | | 2.09 |
| Heart failure | Primary analysis | 10,215 | 1.1 | 0.77 | 1.58 | 0.52 | 1.21 | 0.69 | | 2.11 |
| Hepatic failure | Adjusting for event-dependent observation | 2,710 | 1 | NA | NA | NA | NA | NA | | NA |
| Hepatic failure | Primary analysis | 2,710 | 0.09 | 0 | 0.77 | 0.08 | 0.09 | 0.01 | | 1.35 |
| Stroke | Adjusting for event-dependent observation | 0 | NA | NA | NA | NA | NA | NA | | NA |
| Stroke | Primary analysis | 0 | NA | NA | NA | NA | NA | NA | | NA |
| Cardiovascular events | Adjusting for event-dependent observation | 0 | NA | NA | NA | NA | NA | NA | | NA |
| Cardiovascular events | Primary analysis | 0 | NA | NA | NA | NA | NA | NA | | NA |
| Transient ischemic attack | Adjusting for event-dependent observation | 0 | NA | NA | NA | NA | NA | NA | | NA |
| Transient ischemic attack | Primary analysis | 0 | NA | NA | NA | NA | NA | NA | | NA |
| Venous thromboembolism | Adjusting for event-dependent observation | 12,454 | 0.64 | 0.56 | 0.72 | 0.12 | 0.7 | 0.45 | | 1.09 |
| Venous thromboembolism | Primary analysis | 12,454 | 0.63 | 0.55 | 0.71 | 0.11 | 0.69 | 0.44 | | 1.07 |
| **IRR**= Incidence Rate Ratio **95%CI LB**= 95% Confidence Interval Lower Boundary **95%CI UB**= 95% Confidence Interval Upper Boundary | | | | | | | | | | |

## **S10.2 JMDC**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Outcome** | **Analysis** | **Cases** | **IRR** | **95% CI LB** | **95% CI UB** | **Calibrated P** | **Calibrated IRR** | **Calibrated 95% CI LB** | **Calibrated 95% CI UB** |
| Myocardial infarction | Adjusting for event-dependent observation | 5,788 | 0 | NA | 0 | NA | NA | NA | NA |
| Myocardial infarction | Primary analysis | 5,789 | 0 | NA | 1.19 | NA | NA | NA | NA |
| Acute pancreatitis events | Adjusting for event-dependent observation | 5,307 | 1.42 | 0.06 | 25.06 | 0.62 | 2.18 | 0.11 | 43.82 |
| Acute pancreatitis event | Primary analysis | 5,307 | 1.38 | 0.06 | 13.42 | 0.6 | 2.11 | 0.14 | 31.5 |
| Acute renal failure | Adjusting for event-dependent observation | 3,598 | 0.86 | 0.18 | 3.12 | 0.73 | 1.33 | 0.31 | 5.71 |
| Acute renal failure | Primary analysis | 3,598 | 0.91 | 0.19 | 3.37 | 0.69 | 1.39 | 0.32 | 6.12 |
| Gastrointestinal bleeding | Adjusting for event-dependent observation | 10,009 | 0.16 | 0.01 | 0.82 | 0.25 | 0.25 | 0.03 | 2.44 |
| Gastrointestinal bleeding | Primary analysis | 10,009 | 0.16 | 0.01 | 0.79 | 0.24 | 0.24 | 0.03 | 2.38 |
| Cardiac arrhythmia | Adjusting for event-dependent observation | 10,034 | 0.4 | 0.11 | 1.2 | 0.5 | 0.62 | 0.18 | 2.15 |
| Cardiac arrhythmia | Primary analysis | 10,034 | 0.38 | 0.1 | 1.11 | 0.43 | 0.58 | 0.17 | 1.98 |
| Bradycardia | Adjusting for event-dependent observation | 5,813 | 2.4 | 0.11 | 20.87 | 0.35 | 3.67 | 0.26 | 50.91 |
| Bradycardia | Primary analysis | 5,813 | 2.41 | 0.11 | 21.25 | 0.35 | 3.69 | 0.26 | 51.54 |
| Chest pain or angina | Adjusting for event-dependent observation | 10,082 | 0.6 | 0.32 | 1.09 | 0.74 | 0.92 | 0.45 | 1.85 |
| Chest pain or angina | Primary analysis | 10,082 | 0.6 | 0.31 | 1.08 | 0.74 | 0.91 | 0.45 | 1.84 |
| End stage renal disease | Adjusting for event-dependent observation | 2,439 | NA | NA | NA | NA | NA | NA | NA |
| End stage renal disease | Primary analysis | 2,445 | NA | NA | NA | NA | NA | NA | NA |
| Heart failure | Adjusting for event-dependent observation | 10,071 | 0.67 | 0.34 | 1.23 | 0.77 | 1.02 | 0.5 | 2.1 |
| Heart failure | Primary analysis | 10,071 | 0.66 | 0.34 | 1.22 | 0.76 | 1.02 | 0.49 | 2.08 |
| Hepatic failure | Adjusting for event-dependent observation | 3,014 | 1 | 0.04 | 15.31 | 0.79 | 1.54 | 0.08 | 30.15 |
| Hepatic failure | Primary analysis | 3,014 | 0.97 | 0.04 | 18.75 | 0.81 | 1.48 | 0.07 | 33.23 |
| Stroke | Adjusting for event-dependent observation | 10,001 | 0.74 | 0.23 | 2.1 | 0.8 | 1.13 | 0.36 | 3.55 |
| Stroke | Primary analysis | 10,001 | 0.74 | 0.23 | 2.12 | 0.8 | 1.14 | 0.36 | 3.59 |
| Cardiovascular events | Adjusting for event-dependent observation | 10,035 | 0.33 | 0.13 | 0.72 | 0.21 | 0.51 | 0.21 | 1.25 |
| Cardiovascular events | Primary analysis | 10,035 | 0.33 | 0.13 | 0.72 | 0.2 | 0.5 | 0.2 | 1.25 |
| Transient ischemic attack | Adjusting for event-dependent observation | 2,208 | 0 | NA | 0 | NA | NA | NA | NA |
| Transient ischemic attack | Primary analysis | 2,208 | 0 | NA | 38.67 | NA | NA | NA | NA |
| Venous thromboembolism | Adjusting for event-dependent observation | 10,029 | 0.98 | 0.41 | 2.14 | 0.45 | 1.51 | 0.62 | 3.67 |
| Venous thromboembolism | Primary analysis | 10,029 | 0.98 | 0.41 | 2.14 | 0.45 | 1.51 | 0.62 | 3.67 |
| **IRR**= Incidence Rate Ratio **95%CI LB**= 95% Confidence Interval Lower Boundary **95%CI UB**= 95% Confidence Interval Upper Boundary | | | | | | | | | |
|  |  |  |  |  |  |  |  |  |  |

## **S10.3 CCAE**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Outcome** | **Analysis** | **Cases** | **IRR** | **95% CI LB** | **95% CI UB** | **Calibrated P** | **Calibrated IRR** | **Calibrated 95% CI LB** | **Calibrated 95% CI UB** |
| Myocardial infarction | Adjusting for event-dependent observation | 14,483 | 0.91 | 0.83 | 0.99 | 0.53 | 0.91 | 0.69 | 1.21 |
| Myocardial infarction | Primary analysis | 14,483 | 0.91 | 0.84 | 1 | 0.57 | 0.92 | 0.7 | 1.22 |
| Acute pancreatitis events | Adjusting for event-dependent observation | 13,221 | NA | NA | NA | NA | NA | NA | NA |
| Acute pancreatitis event | Primary analysis | 13,221 | 0.89 | 0.81 | 0.99 | 0.48 | 0.9 | 0.68 | 1.2 |
| Acute renal failure | Adjusting for event-dependent observation | 17,178 | 0.88 | 0.82 | 0.94 | 0.38 | 0.88 | 0.67 | 1.16 |
| Acute renal failure | Primary analysis | 17,178 | 0.9 | 0.84 | 0.96 | 0.47 | 0.9 | 0.69 | 1.19 |
| Gastrointestinal bleeding | Adjusting for event-dependent observation | 15,638 | NA | NA | NA | NA | NA | NA | NA |
| Gastrointestinal bleeding | Primary analysis | 15,638 | 1 | 0.92 | 1.07 | 0.94 | 1.01 | 0.76 | 1.32 |
| Cardiac arrhythmia | Adjusting for event-dependent observation | 14,328 | 0.94 | 0.86 | 1.03 | 0.71 | 0.95 | 0.72 | 1.25 |
| Cardiac arrhythmia | Primary analysis | 14,328 | 0.94 | 0.86 | 1.03 | 0.74 | 0.95 | 0.72 | 1.26 |
| Bradycardia | Adjusting for event-dependent observation | 12,248 | NA | NA | NA | NA | NA | NA | NA |
| Bradycardia | Primary analysis | 12,248 | 0.71 | 0.63 | 0.81 | 0.03 | 0.72 | 0.54 | 0.96 |
| Chest pain or angina | Adjusting for event-dependent observation | 13,399 | 0.9 | 0.81 | 1 | 0.53 | 0.91 | 0.69 | 1.21 |
| Chest pain or angina | Primary analysis | 13,399 | 0.9 | 0.81 | 1 | 0.52 | 0.91 | 0.69 | 1.21 |
| End stage renal disease | Adjusting for event-dependent observation | 11,303 | 1.01 | 0.65 | 1.16 | 0.93 | 1.02 | 0.69 | 1.51 |
| End stage renal disease | Primary analysis | 11,303 | 1.02 | 0.88 | 1.18 | 0.85 | 1.03 | 0.76 | 1.39 |
| Heart failure | Adjusting for event-dependent observation | 15,626 | 0.98 | 0.9 | 1.05 | 0.91 | 0.99 | 0.75 | 1.29 |
| Heart failure | Primary analysis | 15,626 | 0.98 | 0.91 | 1.06 | 0.93 | 0.99 | 0.75 | 1.3 |
| Hepatic failure | Adjusting for event-dependent observation | 11,254 | 0.67 | 0.57 | 0.78 | 0.01 | 0.68 | 0.5 | 0.92 |
| Hepatic failure | Primary analysis | 11,254 | 0.64 | 0.54 | 0.75 | 0.01 | 0.64 | 0.47 | 0.88 |
| Stroke | Adjusting for event-dependent observation | 15,535 | NA | NA | NA | NA | NA | NA | NA |
| Stroke | Primary analysis | 15,535 | 0.79 | 0.73 | 0.86 | 0.12 | 0.8 | 0.61 | 1.06 |
| Cardiovascular events | Adjusting for event-dependent observation | 15,200 | NA | NA | NA | NA | NA | NA | NA |
| Cardiovascular events | Primary analysis | 15,200 | 0.86 | 0.79 | 0.93 | 0.3 | 0.86 | 0.66 | 1.14 |
| Transient ischemic attack | Adjusting for event-dependent observation | 14,563 | 0.9 | 0.85 | 0.98 | 0.51 | 0.91 | 0.69 | 1.2 |
| Transient ischemic attack | Primary analysis | 14,563 | 0.91 | 0.83 | 0.99 | 0.55 | 0.92 | 0.7 | 1.21 |
| Venous thromboembolism | Adjusting for event-dependent observation | 16,595 | 0.78 | 0.5 | 0.84 | 0.22 | 0.79 | 0.54 | 1.15 |
| Venous thromboembolism | Primary analysis | 16,595 | 0.8 | 0.75 | 0.86 | 0.14 | 0.81 | 0.62 | 1.07 |
| **IRR**= Incidence Rate Ratio **95%CI LB**= 95% Confidence Interval Lower Boundary **95%CI UB**= 95% Confidence Interval Upper Boundary | | | | | | | | | |

## **S10.4 MDCD**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Outcome** | **Analysis** | **Cases** | **IRR** | **95% CI LB** | **95% CI UB** | **Calibrated P** | **Calibrated IRR** | **Calibrated 95% CI LB** | **Calibrated 95% CI UB** |
| Myocardial infarction | Adjusting for event-dependent observation | 11,276 | NA | NA | NA | NA | NA | NA | NA |
| Myocardial infarction | Primary analysis | 11,276 | 0.97 | 0.83 | 1.13 | 0.39 | 0.89 | 0.7 | 1.15 |
| Acute pancreatitis events | Adjusting for event-dependent observation | 10,851 | 1.22 | 1.02 | 1.46 | 0.39 | 1.13 | 0.86 | 1.47 |
| Acute pancreatitis event | Primary analysis | 10,851 | 1.22 | 1.02 | 1.45 | 0.4 | 1.12 | 0.86 | 1.46 |
| Acute renal failure | Adjusting for event-dependent observation | 12,714 | NA | NA | NA | NA | NA | NA | NA |
| Acute renal failure | Primary analysis | 12,714 | 1.09 | 0.98 | 1.21 | 0.92 | 1 | 0.8 | 1.25 |
| Gastrointestinal bleeding | Adjusting for event-dependent observation | 12,000 | 1.03 | 0.91 | 1.16 | 0.66 | 0.95 | 0.75 | 1.2 |
| Gastrointestinal bleeding | Primary analysis | 12,000 | 1.03 | 0.91 | 1.17 | 0.69 | 0.95 | 0.76 | 1.2 |
| Cardiac arrhythmia | Adjusting for event-dependent observation | 12,340 | 1.01 | 0.89 | 1.13 | 0.53 | 0.93 | 0.74 | 1.17 |
| Cardiac arrhythmia | Primary analysis | 12,340 | 1.01 | 0.89 | 1.13 | 0.54 | 0.93 | 0.74 | 1.17 |
| Bradycardia | Adjusting for event-dependent observation | 10,541 | NA | NA | NA | NA | NA | NA | NA |
| Bradycardia | Primary analysis | 10,541 | 0.8 | 0.64 | 1 | 0.05 | 0.74 | 0.55 | 0.99 |
| Chest pain or angina | Adjusting for event-dependent observation | 11,642 | 1.17 | 0.98 | 1.34 | 0.59 | 1.07 | 0.84 | 1.38 |
| Chest pain or angina | Primary analysis | 11,642 | 1.16 | 1.01 | 1.34 | 0.58 | 1.07 | 0.84 | 1.36 |
| End stage renal disease | Adjusting for event-dependent observation | 10,562 | NA | NA | NA | NA | NA | NA | NA |
| End stage renal disease | Primary analysis | 10,562 | 1.34 | 1.1 | 1.64 | 0.15 | 1.24 | 0.93 | 1.64 |
| Heart failure | Adjusting for event-dependent observation | 12,030 | 1.03 | 0.91 | 1.17 | 0.68 | 0.95 | 0.75 | 1.2 |
| Heart failure | Primary analysis | 12,030 | 1.03 | 0.91 | 1.17 | 0.68 | 0.95 | 0.75 | 1.2 |
| Hepatic failure | Adjusting for event-dependent observation | 10,278 | 0.91 | 0.7 | 1.17 | 0.29 | 0.83 | 0.6 | 1.16 |
| Hepatic failure | Primary analysis | 10,278 | 0.83 | 0.64 | 1.09 | 0.13 | 0.77 | 0.55 | 1.07 |
| Stroke | Adjusting for event-dependent observation | 11,662 | 0.98 | 0.86 | 1.12 | 0.4 | 0.9 | 0.71 | 1.14 |
| Stroke | Primary analysis | 11,662 | 0.92 | 0.81 | 1.06 | 0.2 | 0.85 | 0.67 | 1.08 |
| Cardiovascular events | Adjusting for event-dependent observation | 12,067 | 0.99 | 0.88 | 1.12 | 0.46 | 0.91 | 0.73 | 1.15 |
| Cardiovascular events | Primary analysis | 12,067 | 0.93 | 0.82 | 1.05 | 0.21 | 0.86 | 0.68 | 1.08 |
| Transient ischemic attack | Adjusting for event-dependent observation | 10,938 | 1.02 | 0.86 | 1.22 | 0.66 | 0.94 | 0.72 | 1.23 |
| Transient ischemic attack | Primary analysis | 10,938 | 1 | 0.84 | 1.19 | 0.57 | 0.92 | 0.71 | 1.2 |
| Venous thromboembolism | Adjusting for event-dependent observation | 12,646 | 0.96 | 0.86 | 1.07 | 0.29 | 0.88 | 0.71 | 1.1 |
| Venous thromboembolism | Primary analysis | 12,646 | 0.95 | 0.85 | 1.05 | 0.25 | 0.87 | 0.7 | 1.09 |
| **IRR**= Incidence Rate Ratio **95%CI LB**= 95% Confidence Interval Lower Boundary **95%CI UB**= 95% Confidence Interval Upper Boundary | | | | | | | | | |

## **S10.5 MDCR**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Outcome** | **Analysis** | **Cases** | **IRR** | **CI95LB** | **CI95UB** | **Calibrated P** | **Calibrated IRR** | **Calibrated CI95LB** | **Calibrated CI95UB** |
| Myocardial infarction | Adjusting for event-dependent observation | 14,554 | 1.04 | 0.96 | 1.13 | 0.47 | 1.09 | 0.86 | 1.39 |
| Myocardial infarction | Primary analysis | 14,554 | 0.94 | 0.86 | 1.03 | 0.91 | 0.99 | 0.78 | 1.26 |
| Acute pancreatitis events | Adjusting for event-dependent observation | 10,998 | 0.98 | 0.82 | 1.16 | 0.86 | 1.03 | 0.77 | 1.36 |
| Acute pancreatitis event | Primary analysis | 10,998 | 0.94 | 0.79 | 1.12 | 0.93 | 0.99 | 0.74 | 1.32 |
| Acute renal failure | Adjusting for event-dependent observation | 15,657 | 1.03 | 0.95 | 1.11 | 0.53 | 1.08 | 0.85 | 1.37 |
| Acute renal failure | Primary analysis | 15,657 | 0.92 | 0.85 | 1 | 0.8 | 0.97 | 0.76 | 1.23 |
| Gastrointestinal bleeding | Adjusting for event-dependent observation | 15,255 | 0.97 | 0.9 | 1.05 | 0.85 | 1.02 | 0.81 | 1.3 |
| Gastrointestinal bleeding | Primary analysis | 15,255 | 0.92 | 0.84 | 0.99 | 0.75 | 0.96 | 0.76 | 1.22 |
| Cardiac arrhythmia | Adjusting for event-dependent observation | 13,552 | 0.81 | 0.73 | 0.9 | 0.22 | 0.85 | 0.67 | 1.09 |
| Cardiac arrhythmia | Primary analysis | 13,552 | 0.82 | 0.74 | 0.9 | 0.24 | 0.86 | 0.67 | 1.1 |
| Bradycardia | Adjusting for event-dependent observation | 12,752 | 0.83 | 0.74 | 0.93 | 0.29 | 0.87 | 0.68 | 1.12 |
| Bradycardia | Primary analysis | 12,752 | 0.83 | 0.74 | 0.93 | 0.28 | 0.87 | 0.68 | 1.12 |
| Chest pain or angina | Adjusting for event-dependent observation | 14,060 | 0.91 | 0.82 | 0.99 | 0.69 | 0.95 | 0.75 | 1.21 |
| Chest pain or angina | Primary analysis | 14,060 | 0.9 | 0.82 | 0.99 | 0.65 | 0.94 | 0.74 | 1.2 |
| End stage renal disease | Adjusting for event-dependent observation | 10,839 | 0.84 | 0.69 | 1.01 | 0.41 | 0.88 | 0.66 | 1.18 |
| End stage renal disease | Primary analysis | 10,839 | 0.84 | 0.7 | 1.02 | 0.42 | 0.88 | 0.66 | 1.19 |
| Heart failure | Adjusting for event-dependent observation | 14,531 | 1.06 | 0.98 | 1.16 | 0.37 | 1.12 | 0.88 | 1.42 |
| Heart failure | Primary analysis | 14,531 | 1.04 | 0.96 | 1.13 | 0.48 | 1.09 | 0.86 | 1.39 |
| Hepatic failure | Adjusting for event-dependent observation | 10,325 | 0.78 | 0.6 | 1.03 | 0.28 | 0.82 | 0.58 | 1.17 |
| Hepatic failure | Primary analysis | 10,325 | 0.77 | 0.59 | 1.01 | 0.25 | 0.81 | 0.57 | 1.15 |
| Stroke | Adjusting for event-dependent observation | 14,536 | 0.96 | 0.88 | 1.05 | 0.91 | 1.01 | 0.8 | 1.29 |
| Stroke | Primary analysis | 14,536 | 0.89 | 0.81 | 0.97 | 0.57 | 0.93 | 0.73 | 1.18 |
| Cardiovascular events | Adjusting for event-dependent observation | 14,573 | 1.05 | 0.97 | 1.14 | 0.43 | 1.1 | 0.87 | 1.4 |
| Cardiovascular events | Primary analysis | 14,573 | 0.97 | 0.89 | 1.05 | 0.89 | 1.02 | 0.8 | 1.29 |
| Transient ischemic attack | Adjusting for event-dependent observation | 13,727 | 0.95 | 0.87 | 1.05 | 0.93 | 1 | 0.79 | 1.28 |
| Transient ischemic attack | Primary analysis | 13,727 | 0.93 | 0.84 | 1.02 | 0.82 | 0.97 | 0.76 | 1.24 |
| Venous thromboembolism | Adjusting for event-dependent observation | 16,067 | 0.72 | 0.67 | 0.78 | 0.02 | 0.76 | 0.6 | 0.96 |
| Venous thromboembolism | Primary analysis | 16,067 | 0.68 | 0.63 | 0.73 | 0.01 | 0.71 | 0.56 | 0.91 |
| **IRR**= Incidence Rate Ratio **95%CI LB**= 95% Confidence Interval Lower Boundary **95%CI UB**= 95% Confidence Interval Upper Boundary | | | | | | | | | |

## **S10.6 Optum**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Outcome** | **Analysis** | **Cases** | **IRR** | **CI95LB** | | **CI95UB** | | **Calibrated P** | | **Calibrated IRR** | | **Calibrated CI95LB** | | **Calibrated CI95UB** | |
| Myocardial infarction | Adjusting for event-dependent observation | 14,351 | 1.11 | 1.02 | 1.21 | | 0.51 | | 1.11 | | 0.81 | | 1.54 | |
| Myocardial infarction | Primary analysis | 14,351 | 1.01 | 0.92 | 1.1 | | 0.92 | | 1.02 | | 0.74 | | 1.4 | |
| Acute pancreatitis events | Adjusting for event-dependent observation | 12,730 | 1.04 | 0.93 | 1.16 | | 0.78 | | 1.05 | | 0.75 | | 1.46 | |
| Acute pancreatitis event | Primary analysis | 12,730 | 1.04 | 0.93 | 1.16 | | 0.78 | | 1.05 | | 0.75 | | 1.46 | |
| Acute renal failure | Adjusting for event-dependent observation | 14,919 | 0.96 | 0.48 | 1.04 | | 0.88 | | 0.96 | | 0.58 | | 1.59 | |
| Acute renal failure | Primary analysis | 14,919 | 0.99 | 0.91 | 1.07 | | 0.94 | | 0.99 | | 0.72 | | 1.37 | |
| Gastrointestinal bleeding | Adjusting for event-dependent observation | 14,884 | 1.12 | 1.03 | 1.22 | | 0.46 | | 1.13 | | 0.82 | | 1.55 | |
| Gastrointestinal bleeding | Primary analysis | 14,884 | 1.05 | 0.97 | 1.14 | | 0.74 | | 1.06 | | 0.77 | | 1.46 | |
| Cardiac arrhythmia | Adjusting for event-dependent observation | 13,388 | 1.02 | 0.92 | 1.13 | | 0.88 | | 1.03 | | 0.74 | | 1.42 | |
| Cardiac arrhythmia | Primary analysis | 13,388 | 1.03 | 0.93 | 1.13 | | 0.85 | | 1.03 | | 0.74 | | 1.43 | |
| Bradycardia | Adjusting for event-dependent observation | 13,682 | 0.9 | 0.77 | 1 | | 0.58 | | 0.91 | | 0.65 | | 1.27 | |
| Bradycardia | Primary analysis | 13,682 | 0.92 | 0.83 | 1.01 | | 0.63 | | 0.92 | | 0.67 | | 1.28 | |
| Chest pain or angina | Adjusting for event-dependent observation | 13,093 | 1.06 | 0.96 | 1.18 | | 0.7 | | 1.07 | | 0.77 | | 1.48 | |
| Chest pain or angina | Primary analysis | 13,093 | 1.06 | 0.95 | 1.17 | | 0.72 | | 1.06 | | 0.76 | | 1.47 | |
| End stage renal disease | Adjusting for event-dependent observation | 11,891 | NA | NA | NA | | NA | | NA | | NA | | NA | |
| End stage renal disease | Primary analysis | 11,891 | 1.26 | 1.11 | 1.42 | | 0.17 | | 1.26 | | 0.9 | | 1.76 | |
| Heart failure | Adjusting for event-dependent observation | 13,817 | 1.14 | 1.04 | 1.25 | | 0.41 | | 1.15 | | 0.83 | | 1.58 | |
| Heart failure | Primary analysis | 13,817 | 1.12 | 1.02 | 1.23 | | 0.47 | | 1.13 | | 0.82 | | 1.56 | |
| Hepatic failure | Adjusting for event-dependent observation | 11,571 | NA | NA | NA | | NA | | NA | | NA | | NA | |
| Hepatic failure | Primary analysis | 11,571 | 0.72 | 0.62 | 0.83 | | 0.07 | | 0.73 | | 0.52 | | 1.02 | |
| Stroke | Adjusting for event-dependent observation | 14,342 | 0.97 | 0.89 | 1.05 | | 0.86 | | 0.97 | | 0.7 | | 1.34 | |
| Stroke | Primary analysis | 14,342 | 0.89 | 0.82 | 0.97 | | 0.51 | | 0.9 | | 0.65 | | 1.24 | |
| Cardiovascular events | Adjusting for event-dependent observation | 14,189 | 0.9 | 0.18 | 0.98 | | 0.82 | | 0.9 | | 0.37 | | 2.21 | |
| Cardiovascular events | Primary analysis | 14,189 | 0.94 | 0.86 | 1.03 | | 0.75 | | 0.95 | | 0.69 | | 1.31 | |
| Transient ischemic attack | Adjusting for event-dependent observation | 14,895 | 0.94 | 0.86 | 1.02 | | 0.73 | | 0.94 | | 0.68 | | 1.3 | |
| Transient ischemic attack | Primary analysis | 14,895 | 0.93 | 0.85 | 1.01 | | 0.68 | | 0.93 | | 0.68 | | 1.29 | |
| Venous thromboembolism | Adjusting for event-dependent observation | 15,377 | 0.85 | 0.79 | 0.92 | | 0.36 | | 0.86 | | 0.62 | | 1.18 | |
| Venous thromboembolism | Primary analysis | 15,377 | 0.84 | 0.77 | 0.91 | | 0.3 | | 0.84 | | 0.61 | | 1.16 | |
| **IRR**= Incidence Rate Ratio **95%CI LB**= 95% Confidence Interval Lower Boundary **95%CI UB**= 95% Confidence Interval Upper Boundary | | | | | | | | | | | | | | |

# **S11. Literature review search**

## **S11.1 Pubmed search strategy**

((((((((("Antirheumatic Agents"[Mesh]) OR (((disease modifying antirheumatic drug\*[Title/Abstract] OR disease modifying anti-rheumatic drug\*[Title/Abstract] OR disease modifying antirheumatic agent\*[Title/Abstract] OR disease modifying anti-rheumatic agent\*[Title/Abstract]) OR (DMARD\*[Title/Abstract])))) OR (((((((((("hydroxychloroquine"[MeSH Terms]) OR Hydroxychloroquine[Title/Abstract]) OR chloroquinol[Title/Abstract]) OR ercoquin[Title/Abstract]) OR hydrochloroquine[Title/Abstract]) OR hydrocloroquine[Title/Abstract]) OR oxychloroquine[Title/Abstract]) OR plaquenil[Title/Abstract]) OR quensyl[Title/Abstract]) OR "sn 8137"[Title/Abstract])) OR (((((((("tocilizumab"[MeSH Terms]) OR tocilizumab[Title/Abstract]) OR actemra\*[Title/Abstract]) OR atlizumab[Title/Abstract]) OR lusinex[Title/Abstract]) OR "r 1569"[Title/Abstract]) OR r1569[Title/Abstract]) OR roactemra[Title/Abstract])) OR "baricitinib"[Supplementary Concept]) OR ((((((((baricitinib[Title/Abstract]) OR "incb 028050"[Title/Abstract]) OR "incb 28050"[Title/Abstract]) OR "incb028050"[Title/Abstract]) OR "incb28050"[Title/Abstract]) OR "ly 3009104"[Title/Abstract]) OR "ly3009104"[Title/Abstract]) OR olumiant[Title/Abstract])) OR (((((((((((((((((((((((("methotrexate"[MeSH Terms]) OR methotrexate[Title/Abstract]) OR "a methopterine"[Title/Abstract]) OR abitrexate[Title/Abstract]) OR amethopterin\*[Title/Abstract]) OR ametopterine[Title/Abstract]) OR antifolan[Title/Abstract]) OR biotrexate[Title/Abstract]) OR canceren[Title/Abstract]) OR "cl 14377"[Title/Abstract]) OR cl14377[Title/Abstract]) OR emtexate[Title/Abstract]) OR emthexat\*[Title/Abstract]) OR enthexate[Title/Abstract]) OR emtrexate[Title/Abstract]) OR farmitrexat\*[Title/Abstract]) OR farmotrex[Title/Abstract]) OR folex\*[Title/Abstract]) OR ifamet[Title/Abstract]) OR imeth[Title/Abstract]) OR "intradose MTX"[Title/Abstract]) OR jylamvo[Title/Abstract]) OR lantarel[Title/Abstract]) OR ledertrexate[Title/Abstract])) OR (((((((((((((((((((((((((((((maxtrex[Title/Abstract]) OR metex[Title/Abstract]) OR methoblastin[Title/Abstract]) OR methohexate[Title/Abstract]) OR methotrate[Title/Abstract]) OR methotrexat\*[Title/Abstract]) OR methoxtrexate[Title/Abstract]) OR methrotrexate[Title/Abstract]) OR methylaminopterin\*[Title/Abstract]) OR meticil[Title/Abstract]) OR metoject[Title/Abstract]) OR metothrexate[Title/Abstract]) OR metotrex\*[Title/Abstract]) OR metrex[Title/Abstract]) OR mexate\*[Title/Abstract]) OR "mpi 5004"[Title/Abstract]) OR mpi5004[Title/Abstract]) OR MTX[Title/Abstract]) OR neotrexate[Title/Abstract]) OR nordimet[Title/Abstract]) OR novatrex[Title/Abstract]) OR "nsc 740"[Title/Abstract]) OR nsc740 AND "[Title/Abstract]) OR otrexup[Title/Abstract]) OR rasuvo[Title/Abstract]) OR reumatrex[Title/Abstract]) OR rheumatrex[Title/Abstract]) OR texate\*[Title/Abstract]) OR texorate[Title/Abstract]) OR trexall[Title/Abstract]) OR xaken[Title/Abstract]) OR xatmep[Title/Abstract]) OR zexate[Title/Abstract])) OR (((((((((((((((((((((((((((((((sulfasalazine[MeSH Terms]) OR salazosulfapyridine[Title/Abstract]) OR " AND azlufidine en-tabs AND "[Title/Abstract]) OR azopyrin\*[Title/Abstract]) OR azosulfidine[Title/Abstract]) OR azulfid\*[Title/Abstract]) OR azulfin[Title/Abstract]) OR benzosulfa[Title/Abstract]) OR " AND colo pleon AND "[Title/Abstract]) OR " AND colo-pleon AND "[Title/Abstract]) OR colopleon[Title/Abstract]) OR disalazin[Title/Abstract]) OR gastropyrin[Title/Abstract]) OR " AND pleon ra AND "[Title/Abstract]) OR " AND pyralin en AND "[Title/Abstract]) OR rorasul[Title/Abstract]) OR rosulfant[Title/Abstract]) OR " AND s.a.s.-500 AND "[Title/Abstract]) OR salaz\*[Title/Abstract]) OR " AND salicyl azo sulfapyridine AND "[Title/Abstract]) OR salicylazosulfapyridin\*[Title/Abstract]) OR salisulf[Title/Abstract]) OR salopyr[Title/Abstract]) OR saridine[Title/Abstract]) OR " AND sas 500 Title/Abstract) OR sulcolon[Title/Abstract]) OR sulfasalazine[Title/Abstract]) OR sulfasalizine[Title/Abstract]) OR sulfosalazine[Title/Abstract]) OR sulphasalazine[Title/Abstract]) OR zopyrin[Title/Abstract]))) AND ((((((((((((((((((((((((((((("coronavirus infections"[MeSH Terms]) OR coronavirus\*[Title/Abstract]) OR coronovirus\*[Title/Abstract]) OR "2019-nCoV"[Title/Abstract]) OR "COVID-19"[Title/Abstract]) OR "CORVID-19"[Title/Abstract]) OR "WN-CoV"[Title/Abstract]) OR "HCoV-19"[Title/Abstract]) OR CoV[Title/Abstract]) OR ncov[Title/Abstract]) OR "SARS-CoV-2"[Title/Abstract]) OR SARSCov19[Title/Abstract]) OR ncov\*wuhan[Title/Abstract]) OR "severe acute respiratory syndrome"[MeSH Terms]) OR "severe acute respiratory syndrome"[Title/Abstract]) OR "sudden acute respiratory syndrome"[Title/Abstract]) OR SARS[Title/Abstract]) OR MERS[Title/Abstract]) OR "Middle East Respiratory Syndrome"[Title/Abstract]) OR sars coronavirus[MeSH Terms]) OR viral infection[Title/Abstract]) OR viral disease[Title/Abstract]) OR virus infection[Title/Abstract]) OR virus disease[Title/Abstract]) OR viral pneumonia[MeSH Terms]) OR viral pneumonia[Title/Abstract]) OR influenza[MeSH Terms]) OR influenza[Title/Abstract]) OR flu[Title])

Limit to: Chinese, English, Italian, Spanish

## **S11.2 Embase (1974 to present) search strategy**

|  |
| --- |
| 1 disease modifying antirheumatic drug/ (16237) |
| 2 disease modifying antirheumatic drug\*.ti,ab. (6045) |
| 3 disease modifying anti-rheumatic drug\*.ti,ab. (3750) |
| 4 disease modifying antirheumatic agent\*.ti,ab. (38) |
| 5 disease modifying anti-rheumatic agent\*.ti,ab. (37) |
| 6 DMARD\*.ti,ab. (14249) |
| 7 hydroxychloroquine/ (23310) |
| 8 Hydroxychloroquine.ti,ab. (7610) |
| 9 chloroquinol.ti,ab. (2) |
| 10 ercoquin.ti,ab. (0) |
| 11 hydrochloroquine.ti,ab. (56) |
| 12 hydrocloroquine.ti,ab. (0) |
| 13 oxychloroquine.ti,ab. (6) |
| 14 plaquenil.ti,ab. (305) |
| 15 quensyl.ti,ab. (4) |
| 16 "sn 8137".ti,ab. (1) |
| 17 tocilizumab/ (10914) |
| 18 tocilizumab.ti,ab. (6966) |
| 19 actemra\*.ti,ab. (71) |
| 20 atlizumab.ti,ab. (21) |
| 21 lusinex.ti,ab. (0) |
| 22 "r 1569".ti,ab. (0) |
| 23 r1569.ti,ab. (0) |
| 24 roactemra.ti,ab. (43) |
| 25 baricitinib/ (944) |
| 26 Baricitinib.ti,ab. (600) |
| 27 "incb 028050".ti,ab. (2) |
| 28 "incb 28050".ti,ab. (1) |
| 29 "incb028050".ti,ab. (18) |
| 30 "incb28050".ti,ab. (0) |
| 31 "ly 3009104".ti,ab. (2) |
| 32 "ly3009104".ti,ab. (19) |
| 33 olumiant.ti,ab. (8) |
| 34 methotrexate/ (173846) |
| 35 methotrexate.ti,ab. (65636) |
| 36 "a methopterine".ti,ab. (0) |
| 37 abitrexate.ti,ab. (0) |
| 38 amethopterin\*.ti,ab. (232) |
| 39 ametopterine.ti,ab. (1) |
| 40 antifolan.ti,ab. (0) |
| 41 biotrexate.ti,ab. (3) |
| 42 canceren.ti,ab. (1) |
| 43 "cl 14377".ti,ab. (0) |
| 44 cl14377.ti,ab. (0) |
| 45 emtexate.ti,ab. (0) |
| 46 emthexat\*.ti,ab. (2) |
| 47 emtrexate.ti,ab. (1) |
| 48 enthexate.ti,ab. (0) |
| 49 farmitrexat\*.ti,ab. (0) |
| 50 farmotrex.ti,ab. (0) |
| 51 folex\*.ti,ab. (3) |
| 52 ifamet.ti,ab. (0) |
| 53 imeth.ti,ab. (2) |
| 54 "intradose MTX".ti,ab. (0) |
| 55 jylamvo.ti,ab. (0) |
| 56 lantarel.ti,ab. (3) |
| 57 ledertrexate.ti,ab. (4) |
| 58 maxtrex.ti,ab. (0) |
| 59 metex.ti,ab. (12) |
| 60 methoblastin.ti,ab. (0) |
| 61 methohexate.ti,ab. (0) |
| 62 methotrate.ti,ab. (4) |
| 63 methotrexat\*.ti,ab. (65844) |
| 64 methoxtrexate.ti,ab. (3) |
| 65 methrotrexate.ti,ab. (62) |
| 66 methylaminopterin\*.ti,ab. (6) |
| 67 meticil.ti,ab. (0) |
| 68 metoject.ti,ab. (13) |
| 69 metothrexate.ti,ab. (108) |
| 70 metotrex\*.ti,ab. (257) |
| 71 metrex.ti,ab. (18) |
| 72 mexate\*.ti,ab. (1) |
| 73 "mpi 5004".ti,ab. (0) |
| 74 mpi5004.ti,ab. (0) |
| 75 MTX.ti,ab. (23376) |
| 76 neotrexate.ti,ab. (0) |
| 77 nordimet.ti,ab. (1) |
| 78 novatrex.ti,ab. (0) |
| 79 "nsc 740".ti,ab. (34) |
| 80 "nsc740".ti,ab. (0) |
| 81 otrexup.ti,ab. (2) |
| 82 rasuvo.ti,ab. (1) |
| 83 reumatrex.ti,ab. (0) |
| 84 rheumatrex.ti,ab. (6) |
| 85 texate\*.ti,ab. (2) |
| 86 texorate.ti,ab. (0) |
| 87 trexall.ti,ab. (3) |
| 88 xaken.ti,ab. (0) |
| 89 xatmep.ti,ab. (0) |
| 90 zexate.ti,ab. (0) |
| 91 salazosulfapyridine/ (24991) |
| 92 salazosulfapyridine.ti,ab. (403) |
| 93 "azlufidine en-tabs".ti,ab. (0) |
| 94 azopyrin\*.ti,ab. (0) |
| 95 azosulfidine.ti,ab. (1) |
| 96 azulfid\*.ti,ab. (81) |
| 97 azulfin.ti,ab. (0) |
| 98 benzosulfa.ti,ab. (0) |
| 99 "colo pleon".ti,ab. (2) |
| 100 "colo-pleon".ti,ab. (2) |
| 101 colopleon.ti,ab. (0) |
| 102 disalazin.ti,ab. (0) |
| 103 gastropyrin.ti,ab. (0) |
| 104 "pleon ra".ti,ab. (0) |
| 105 "pyralin en".ti,ab. (0) |
| 106 rorasul.ti,ab. (0) |
| 107 rosulfant.ti,ab. (0) |
| 108 "s.a.s.-500".ti,ab. (2) |
| 109 salaz\*.ti,ab. (1188) |
| 110 "salicyl azo sulfapyridine".ti,ab. (2) |
| 111 salicylazosulfapyridin\*.ti,ab. (181) |
| 112 salisulf.ti,ab. (0) |
| 113 salopyr.ti,ab. (0) |
| 114 saridine.ti,ab. (0) |
| 115 "sas 500".ti,ab. (2) |
| 116 sulcolon.ti,ab. (0) |
| 117 sulfasalazine.ti,ab. (5325) |
| 118 sulfasalizine.ti,ab. (4) |
| 119 sulfosalazine.ti,ab. (5) |
| 120 sulphasalazine.ti,ab. (1742) |
| 121 zopyrin.ti,ab. (0) |
| 122 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99 or 100 or 101 or 102 or 103 or 104 or 105 or 106 or 107 or 108 or 109 or 110 or 111 or 112 or 113 or 114 or 115 or 116 or 117 or 118 or 119 or 120 or 121 (226851) |
| 123 Coronavirus infection/ (1778) |
| 124 coronavirus\*.ti,ab. (11962) |
| 125 coronovirus\*.ti,ab. (19) |
| 126 "2019-nCoV".ti,ab. (233) |
| 127 "COVID-19".ti,ab. (255) |
| 128 "CORVID-19".ti,ab. (0) |
| 129 "WN-CoV".ti,ab. (0) |
| 130 "HCoV-19".ti,ab. (0) |
| 131 CoV.ti,ab. (6191) |
| 132 ncov.ti,ab. (246) |
| 133 "SARS-CoV-2".ti,ab. (102) |
| 134 SARSCov19.ti,ab. (0) |
| 135 ncov\*wuhan.ti,ab. (0) |
| 136 ((outbreak\* or "respiratory illness" or "respiratory disease" or respiratory symptom\* or seafood market or food market or wildlife) and (Wuhan or China or Chinese)).ti,ab. (5699) |
| 137 severe acute respiratory syndrome/ (8192) |
| 138 "severe acute respiratory syndrome".ti,ab. (4884) |
| 139 "sudden acute respiratory syndrome".ti,ab. (9) |
| 140 SARS.ti,ab. (9457) |
| 141 MERS.ti,ab. (4478) |
| 142 "Middle East Respiratory Syndrome".ti,ab. (1889) |
| 143 SARS coronavirus/ (4579) |
| 144 virus infection/ (158726) |
| 145 ((virus\* or viral) adj (infection\* or disease\*)).ti,ab. (154324) |
| 146 virus pneumonia/ (6683) |
| 147 ((viral or virus) adj3 pneumonia).ti,ab. (2989) |
| 148 exp influenza/ (83690) |
| 149 influenza.ti,ab. (103586) |
| 150 flu.ti,ab. (19565) |
| 151 123 or 124 or 125 or 126 or 127 or 128 or 129 or 131 or 132 or 133 or 134 or 135 or 136 or 137 or 138 or 139 or 140 or 141 or 142 or 143 or 144 or 145 or 146 or 147 or 148 or 149 or 150 (408377) |
| 152 122 and 151 (4890) |
| 153 limit 152 to (chinese or english or italian or spanish) (4681) |

## **S11.3 Clinicaltrials search strategy**

for: "disease modifying antirheumatic drug" OR "disease modifying anti-rheumatic drug" OR DMARD OR Hydroxychloroquine OR tocilizumab OR baricitinib OR methotrexate OR Sulfasalazine | Corona Virus Infection OR coronavirus OR coronovirus OR Covid-19 OR "2019-nCoV" OR "SARS-CoV-2" OR "SARSCov19" OR SARS OR "severe acute respiratory syndrome" OR MERS OR "Middle East Respiratory Syndrome" OR viral pneumonia OR influenza

## **S11.2 ICTRP search strategy**

CORONAVIRUS INFECTIONS, CORONAVIRUS SARS-ASSOCIATED, CORONAVIRUS SARS-ASSOCIATED (DIAGNOSIS), MERS, RESPIRATORY SYNDROME, ACUTE, SEVERE, RESPIRATORY SYNDROME, SEVERE ACUTE, SARS, SARS ASSOC CORONAVIRUS, SARS-ASSOCIATED CORONAVIRUS, severe acute respiratory syndrome - middle east respiratory syndrome - CORONAVIRUS INFECT, CORONAVIRUS INFECTION, CORONAVIRUS INFECTION (DIAGNOSIS), CORONAVIRUS INFECTION (DISORDER), CORONAVIRUS INFECTION, UNSPECIFIED, CORONAVIRUS INFECTIONS, CORONAVIRUS INFECTIONS [DISEASE/FINDING], INFECT CORONAVIRUS, INFECTION, CORONAVIRUS, INFECTION; VIRAL, CORONAVIRUS, INFECTIONS, CORONAVIRUS, corona virus infection - PNEUMONIA VIRAL, PNEUMONIA VIRAL NOS, PNEUMONIA, VIRAL, PNEUMONIA, VIRAL [DISEASE/FINDING], PNEUMONIA; VIRAL, PNEUMONIA; VIRUS, PNEUMONIA;VIRAL, PNEUMONIAS, VIRAL, VIRAL PNEUMONITIS, VIRAL; PNEUMONIA, VIRUS; PNEUMONIA, viral pneumonia - coronovirus - CORONA VIRUS INFECTION, CORONAVIRIDAE, FAMILY CORONAVIRIDAE, FAMILY CORONAVIRIDAE (ORGANISM), coronavirus - sars-cov-2 - sarscov19 - AIDS, FLU, FLU SYNDROME, FLU VACCINE, FLU VACCINES, FLU, HUMAN, GRIPPE, HUMAN FLU, SYNDROME FLU, VACCINES, FLU, influenza - 2019-ncov - covid-19 - CORONAVIRUS INFECTIONS, FLJ20450, MERS, MITOCHONDRIAL SERRS, MTSERRS, RESPIRATORY SYNDROME, ACUTE, SEVERE, RESPIRATORY SYNDROME, SEVERE ACUTE, SERINE TRNA LIGASE 1, CYTOPLASMIC, SERINE TRNA LIGASE 2, MITOCHONDRIAL, SERRS, SERRSMT, SERS, SERYL-TRNA SYNTHETASE, SERYL-TRNA SYNTHETASE 2, SERYL-TRNA SYNTHETASE 2, MITOCHONDRIAL, SERYL-TRNA SYNTHETASE, MITOCHONDRIAL, SEVERE ACUTE RESPIRATORY SYNDROME, SEVERE ACUTE RESPIRATORY SYNDROME (DISORDER), SEVERE ACUTE RESPIRATORY SYNDROME [DISEASE/FINDING], SEVERE ACUTE RESPIRATORY SYNDROME NOS, SEVERE ACUTE RESPIRATORY SYNDROME VIRUS, SEVERE ACUTE RESPIRATORY SYNDROME-RELATED CORONAVIRUS, SEVERE ACUTE RESPIRATORY SYNDROME-RELATED CORONAVIRUS (ORGANISM), SYS, sars - CORONA VIRUS INFECTION, CORONAVIRUS INFECT, CORONAVIRUS INFECTION, CORONAVIRUS INFECTION (DIAGNOSIS), CORONAVIRUS INFECTION (DISORDER), CORONAVIRUS INFECTION, UNSPECIFIED, CORONAVIRUS INFECTIONS, CORONAVIRUS INFECTIONS [DISEASE/FINDING], CORONAVIRUS SARS-ASSOCIATED, CORONAVIRUS SARS-ASSOCIATED (DIAGNOSIS), INFECT CORONAVIRUS, INFECTION, CORONAVIRUS, INFECTION; VIRAL, CORONAVIRUS, INFECTIONS, CORONAVIRUS, RESPIRATORY SYNDROME, ACUTE, SEVERE, RESPIRATORY SYNDROME, SEVERE ACUTE, SARS, SARS (SEVERE ACUTE RESPIRATORY SYNDROME), SARS ASSOC CORONAVIRUS, SARS-ASSOCIATED CORONAVIRUS, SEA, SEA (ENVIRONMENT), SEAS, SEVERE ACUTE RESPIRATORY SYNDROME, SEVERE ACUTE RESPIRATORY SYNDROME (DISORDER), SEVERE ACUTE RESPIRATORY SYNDROME (SARS), SEVERE ACUTE RESPIRATORY SYNDROME (SARS) (DIAGNOSIS), SEVERE ACUTE RESPIRATORY SYNDROME [DISEASE/FINDING], SEVERE ACUTE RESPIRATORY SYNDROME NOS, mers - disease modifying anti-rheumatic drug - disease modifying antirheumatic drug - CHLOROQUINE, HCQ, HYDROXYCHLOROCHIN, OXYCHLOROCHIN, OXYCHLOROQUINE, hydroxychloroquine - SALAZOSULFAPYRIDINE, SALAZOSULPHAPYRIDINE, SALICYLAZOSULFAPYRIDINE, SALICYLAZOSULPHAPYRIDINE, SULFANILAMIDE, SULPHASALAZINE, sulfasalazine - AMETHOPTERIN, MTX, methotrexate - ATLIZUMAB, MONOCLONAL ANTIBODY, MRA, MRA, tocilizumab - baricitinib - [MS100] ANTIRHEUMATICS, AGENTS, ANTI-RHEUMATIC, AGENTS, ANTIRHEUMATIC, ANTI RHEUMATIC AGENTS, ANTI RHEUMATIC DRUGS, ANTI-RHEUMATIC AGENT, ANTI-RHEUMATIC AGENT (PRODUCT), ANTI-RHEUMATIC AGENT, NOS, ANTI-RHEUMATIC AGENTS, ANTI-RHEUMATIC DRUGS, ANTIRHEUMATIC AGENT, ANTIRHEUMATIC AGENT [TC], ANTIRHEUMATIC AGENTS, ANTIRHEUMATIC DISEASE MODIFYING SECOND LINE DRUGS, ANTIRHEUMATIC DISEASE-MODIFYING SECOND-LINE DRUGS, ANTIRHEUMATIC DRUGS, ANTIRHEUMATIC DRUGS DIS MODIFYING, ANTIRHEUMATIC DRUGS, DISEASE MODIFYING, ANTIRHEUMATIC DRUGS, DISEASE-MODIFYING, ANTIRHEUMATICS, DIS MODIFYING ANTIRHEUMATIC DRUGS, DISEASE MODIFYING ANTIRHEUMATIC DRUGS, DISEASE MODIFYING, ANTIRHEUMATIC SECOND LINE DRUGS, DISEASE-MODIFYING ANTIRHEUMATIC DRUG, DISEASE-MODIFYING ANTIRHEUMATIC DRUGS, DISEASE-MODIFYING, ANTIRHEUMATIC SECOND-LINE DRUGS, DRUGS, ANTI-RHEUMATIC, DRUGS, ANTIRHEUMATIC, DRUGS, DISEASE-MODIFYING ANTIRHEUMATIC, dmard