# Appendix for Contextualising adverse events of special interest to characterise the baseline incidence rates in 24 million patients with COVID-19 across 26 databases: A multinational retrospective cohort study databases

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## Appendix 1 – Database Details

| Name and Country of Origin | Description |
|---|---|
| Health Data Warehouse of Assistance Publique - Hopitaux de Marseille (APHM)<br><br>From France | The Assistance Publique – Hôpitaux de Marseille (AP-HM) is a public university hospital system with 4 hospitals, 3,400 beds, and more than 12,000 health care professionals. The AP-HM is one the largest health centres in France (after Paris and Lyon). For adults and children, the AP-HM provide hospital care services going from primary care to cutting-edge treatments of complex and rare pathologies. Approximately 300,000 hospitalisations are recorded every year at the AP-HM, involving approximately 210,000 patients. Our information system includes multiple data sources with electronic medical record (Axigate), treatment prescription and deliverance (Pharma), oncology treatment (Chimio), Biology, PMSI (Programme de Médicalisation des Systèmes d'Information). The PMSI is the French medico-administrative database for all hospitalisations based on diagnosis related-groups (DRG) that we can group into significant diagnostic categories. All the stays are coded using the International Classification of Disease (ICD-10th version). Only ICD-10$^{th}$ version codes were used in this study. All these data are collected and stored for more than 10 years with more than 1 billion pieces of data. |
| Clinical Practice Research Datalink - AURUM (CPRD_AURUM)<br><br>From the United Kingdom | The Clinical Practice Research Datalink (CPRD) is a governmental, not-for-profit research service, jointly funded by the National Health Service (NHS) National Institute for Health Research (NIHR) and the Medicines and Healthcare products Regulatory Agency (MHRA), a part of the Department of Health, United Kingdom (UK). CPRD Aurum consists of data collected from UK primary care offices using EMIS software. This includes conditions, observations, measurements, and procedures that the general practitioner is made aware of in addition to any prescriptions as prescribed by the general practitioner. |
| University of Colorado Anschutz Medical Campus - Health Data Compass (CU_AMC)<br><br>From the United States | The Health Data Compass research data warehouse is an all-cloud data and analytics ecosystem that houses administrative, clinical, genomic, and public health registries data from the UCHealth system. UCHealth consists of 11 hospitals across Colorado including the University of Colorado Hospital, the only academic medical centre in the State of Colorado. The primary data source is the electronic medical record, where the same instance and configuration is used across all clinical care settings. Public health data includes linked records from the Colorado state death registry and the state immunization registry. Drug fulfilment data and census and social determinants data are incorporated from commercial vendors. Genomic data are incorporated from the Center for Personalized Medicine Biobank. |
| Columbia University Irving Medical Center (CUIMC)<br><br>From the United States | The Columbia University Irving Medical Center (CUIMC) database comprises electronic health records on 6,666,613 patients, with data collection starting in 1985. CUIMC is a northeast United States of America (US) quaternary care centre with primary care practices in northern Manhattan and surrounding areas, and the database includes inpatient and outpatient care. The database currently holds information about the person (demographics), visits (inpatient and outpatient), conditions (billing diagnoses and problem lists), drugs (outpatient prescriptions and inpatient orders and administrations), devices, measurements (laboratory tests and vital signs), and other observations (symptoms). The data sources include current and previous electronic health record systems (homegrown Clinical Information System, homegrown WebCIS, Allscripts Sunrise Clinical Manager, Allscripts TouchWorks, Epic Systems), administrative systems (IBM PCS-ADS, Eagle Registration, IDX Systems, Epic Systems), and ancillary systems (homegrown LIS, Sunquest, Cerner Laboratory). The data were extracted from each system and transformed to the Observational Health Data Science and Informatics (OHDSI) Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM): common data model source name Epic Legacy CUMC MERGE common data model ETL reference v1.3.0.cdm5.3 common data model release date 2020-05-22 vocabulary version v5.0 30-APR-20 with OMOP common data model version 5.3.1 and local version name ohdsi_cumc_2020q4r1. |

| Name and Country of Origin | Description |
|---|---|
| Fundación para la Investigación e Innovación Biosanitaria en Atención Primaria (FIIBAP) COVID19 (FIIBAP)*<br><br>From Spain | Database from the COVID-19 cohort from FIIBAP project. Contains data from COVID-19-related conditions from COVID-19 patients of the Madrid region and H12O full conditions for COVID-19 patients in hospital. |
| Health Informatics Centre (HIC)<br><br>From the United Kingdom | Health datasets from the Tayside and Fife regions of Scotland, provided by the Health Informatics Centre (HIC) at the University of Dundee. |
| IBM® MarketScan® Commercial Claims and Encounters Database (IBM_CCAE)<br><br>From the United States | The IBM® MarketScan® Commercial Database (CCAE) includes health insurance claims across the continuum of care (i.e., inpatient, outpatient, outpatient pharmacy, carve-out behavioural healthcare) as well as enrolment data from large employers and health plans across the United States who provide private healthcare coverage for more than 155 million employees, their spouses, and dependents. This administrative claims database includes a variety of fee-for-service, preferred provider organisations, and capitated health plans. |
| IBM® MarketScan® Multi-State Medicaid Database (IBM_MDCD)<br><br>From the United States | The IBM® MarketScan® Multi-State Medicaid Database (MDCD) reflects the healthcare service use of individuals covered by Medicaid programs in numerous geographically dispersed states. The database contains the pooled healthcare experience of Medicaid enrolees, covered under fee-for-service and managed care plans. It includes records of inpatient services, inpatient admissions, outpatient services, and prescription drug claims, as well as information on long-term care. Data on eligibility and service and provider type are also included. In addition to standard demographic variables such as age and gender, the database includes variables such as federal aid category (income based, disability, Temporary Assistance for Needy Families) and race. |
| IBM® MarketScan® Medicare Supplemental and Coordination of Benefits Database (IBM_MDCR)<br><br>From the United States | The IBM® MarketScan® Medicare Supplemental Database (MDCR) represents the health services of approximately 10 million retirees in the United States with Medicare supplemental coverage through employer-sponsored plans. This database contains primarily fee-for-service plans and includes health insurance claims across the continuum of care (e.g., inpatient, outpatient and outpatient pharmacy). |
| Parc de Salut Mar Barcelona Information System (IMASIS)<br><br>From Spain | The IMASIS database is the Electronic Health Record (EHR) system of the Parc Salut Mar Barcelona (PSMar), which is a complete healthcare services organisation including two general hospitals, one mental health care centre and one social-healthcare centre, which are offering specific and different healthcare services in the Barcelona city area (Spain). IMASIS includes information since 1990 and from different settings such as admissions, outpatients, emergency room, and major ambulatory surgery. Currently, the database contains hospital-based information on approximately 1 million patients. |

| Name and Country of Origin | Description |
|---|---|
| Integrated Primary Care Information (IPCI)<br><br>From the Netherlands | The Integrated Primary Care Information (IPCI) database started in 1992 and is collected from EHR records of patients registered with their general practitioners (GPs) throughout the Netherlands. The database contains records from in total 2.6 million patients (approximately 1.4 million are still active) out of a Dutch population of 17 million.<br>The observation period for a patient is determined by the date of registration at the GP and the date of leave/death. The observation period start date is refined by many quality indicators, e.g., exclusion of peaks of conditions when registering at the GP. All data before the observation period is kept as history data.<br><br>Drugs are captured as prescription records with product, quantity, dosing directions, strength, and indication. The duration of the drug exposure is determined for all drugs by: 1. The amount and dose extracted from the signature or if instruction is "see product instructions" we use the defined daily dose (DDD) and quantity; 2. Duration available in the record; 3. If option 1 and 2 is not possible we use the DDD derived duration, or default to 30 days otherwise. Drugs not prescribed in the GP setting might be underreported.<br><br>Indications are available as diagnoses by the GPs and, indirectly, from secondary care providers but the latter might not be complete.<br><br>Important citations:<br>de Ridder, M., de Wilde, M., de Ben, C., Leyba, A. R., Mosseveld, B., Verhamme, K., van der Lei, J., & Rijnbeek, P. R. (2022). Data Resource Profile: The Integrated Primary Care Information (IPCI) database, The Netherlands. *International journal of epidemiology*, dyac026. Advance online publication. https://doi.org/10.1093/ije/dyac026 |
| IQVIA® Disease Analyzer (DA) France (IQVIA_FRANCE_DA)<br><br>From France | The IQVIA® Disease Analyzer (DA) France database consists of data collected from French general practitioner (GP) offices for all ages. Data includes age, gender, medical history, diagnosis, prescriptions as prescribed, and device prescriptions as captured by the GP. No specialist data is collected on patients.<br><br>Important citations:<br>Becher, H., Kostev, K., & Schröder-Bernhardi, D. (2009). Validity and representativeness of the "Disease Analyzer" patient database for use in pharmacoepidemiological and pharmacoeconomic studies. *International journal of clinical pharmacology and therapeutics*, *47*(10), 617–626. https://doi.org/10.5414/cpp47617 |
| IQVIA® Disease Analyzer (DA) Germany (IQVIA_GERMANY_DA)<br><br>From Germany | The IQVIA® Disease Analyzer (DA) Germany database consists of data collected from physician practices and medical centres for all ages. Mostly primary care physician data however some data from specialty practices (where practices are electronically connected to each other) and some lab data is included. Key attributes include demographics, prescriptions as prescribed at brand level, diagnosis, lab measurements, and actions (e.g., referrals, sick notes).<br><br>Important citations:<br>Becher, H., Kostev, K., & Schröder-Bernhardi, D. (2009). Validity and representativeness of the "Disease Analyzer" patient database for use in pharmacoepidemiological and pharmacoeconomic studies. *International journal of clinical pharmacology and therapeutics*, *47*(10), 617–626. https://doi.org/10.5414/cpp47617 |
| IQVIA LRxDx Open Claims (IQVIA_OPENCLAIMS)<br><br>From the United States | Pre-adjudicated claims at the anonymised patient level collected from office-based physicians and specialists via office management software and clearinghouse switch sources for the purpose of reimbursement. A subset of medical claims data has adjudicated claims. |

| Name and Country of Origin | Description |
|---|---|
| The IQVIA Adjudicated Health Plan Claims Data (IQVIA_PHARMETRICS)<br><br>From the United States | The IQVIA Adjudicated Health Plan Claims Data (formerly PharMetrics Plus) – a United States of America (US) database comprised of fully adjudicated health plan claims data and enrolment information for commercial individuals. The information is comprised of over 70 contributing health plans and self-insured employer groups throughout the US for over more than 140 million unique enrolees since 2006. This anonymous, patient-centric database includes all medical and pharmacy claims data (costs and descriptive services). Claims represent payments to providers for services rendered to covered health plan individuals. The data also includes patient-level enrolment which is a record of demographic variables including eligibility status (year of birth, gender, US Census region, eligibility by month). The enrolee population in the database is generally representative of the less than 65 years of age, commercially insured population with a subset of Commercial Medicare and Medicaid in the US with respect to both age and gender. The average length of enrolment is 39 months, and 47 million patients have 3 or more years of continuous enrolment (medical and pharmacy coverage). Each contributing plan's data undergoes rigorous data quality review by IQVIA prior to its addition to the IQVIA Adjudicated Health Plan Claims - US database. |
| Istanbul Faculty of Medicine, Istanbul University (IU)<br><br>From Turkey | Istanbul University (IU) Istanbul Faculty of Medicine uses a bespoke EHR system (IU - Hospital Information Management System [HIS]). All IU hospitals' medical records are stored in a central data repository. When a patient visits the hospital, all her/his healthcare information is recorded in an Electronic Health Record (EHR). The 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) coding is the standard for the description of illness in these records. All doctor visits, diagnostics, treatments, prescriptions, and other relevant information are entered into the record. |
| JMDC<br><br>From Japan | JMDC database consists of data from 60 Society-Managed Health Insurances covering workers aged 18 to 65 and their dependents (children younger than 18 years old and elderly people older than 65 years old). Those aged 66 or older are less representative as compared with whole population in the nation. When estimated among the people who are younger than 66 years old, the proportion of children younger than 18 years old in JMDC is approximately the same as the proportion in the whole nation. JMDC data includes data on membership status of the insured people and claims data provided by insurers under contract. Claims data are derived from monthly claims issued by clinics, hospitals and community pharmacies. The number of claims issued and added to JMDC database is about 800,000 per month. The size of JMDC population is 1.9 million, 1.5% of about 120 million people in the whole nation.<br><br>Important citations:<br>Kimura, S., Sato, T., Ikeda, S., Noda, M., & Nakayama, T. (2010). Development of a database of health insurance claims: standardisation of disease classifications and anonymous record linkage. *Journal of epidemiology*, *20*(5), 413–419. https://doi.org/10.2188/jea.je20090066 |
| Medaman Hospital Data (MHD)<br><br>From Belgium | The data source consists of three parts. The main part is the so-called Minimal Hospital Data Set: a registration of all hospital stays from January 1, 2016, with information about the patient, the stay, the diseases (the 10th revision of the International Statistical Classification of Diseases and Related Health Problems [ICD-10-CM]) and procedures (ICD-10-PCS). The second part is a dataset about the medication administered during the hospital stay. The third part is data from the clinical laboratory. |

| Name and Country of Origin | Description |
|---|---|
| Optum® de-identified Electronic Health Record Dataset (OPTUM_EHR)<br><br>From the United States | Optum's longitudinal electronic health record (EHR) repository is derived from dozens of healthcare provider organisations in the United States (US), that include more than 700 hospitals and 7,000 clinics: treating more than 106 million patients receiving care in the US. The data is certified as de-identified by an independent statistical expert following the Health Insurance Portability and Accountability Act (HIPAA) statistical de-identification rules and managed according to Optum® customer data use agreements. Clinical, claims, and other medical administrative data is obtained from both Inpatient and Ambulatory EHRs, practice management systems and numerous other internal systems. Information is processed, normalised, and standardised across the continuum of care from both acute inpatient stays and outpatient visits. Optum® data elements include demographics, medications prescribed and administered, immunizations, allergies, lab results (including microbiology), vital signs and other observable measurements, clinical and inpatient stay administrative data, and coded diagnoses and procedures. In addition, Optum® uses natural language processing (NLP) computing technology to transform critical facts from physician notes into usable datasets. The NLP data provides detailed information regarding signs and symptoms, family history, disease related scores (i.e., RAPID3 for RA, or CHADS2 for stroke risk), genetic testing, medication changes, and physician rationale behind prescribing decisions that might never be recorded in the EHR. |
| Optum De-Identified Clinformatics® Data Mart Database - Socio-Economic Status (OPTUM_SES)<br><br>From the United States | Optum's Clinformatics® Data Mart is derived from a database of administrative health claims for members of large commercial and Medicare Advantage health plans. The database includes approximately 17-19 million annual covered lives, for a total of over 65 million unique lives over a 12-year period (1/2007 through 12/2019). Clinformatics® Data Mart is statistically de-identified under the Expert Determination method consistent with the Health Insurance Portability and Accountability Act (HIPAA) and managed according to Optum customer data use agreements. Administrative claims submitted for payment by providers and pharmacies are verified, adjudicated and de-identified prior to inclusion. This data, including patient-level enrolment information, is derived from claims submitted for all medical and pharmacy health care services with information related to healthcare costs and resource utilization. The population is geographically diverse, spanning all 50 states. Optum Clinformatics® Data Mart Socio-Economic Status provides socio-economic status for members with both medical and pharmacy coverage and location information for patients at the United States of America Census Division level. |
| The Information System for Research on Primary Care (SIDIAP)<br><br>From Spain | The Information System for Research in Primary Care (SIDIAP; www.sidiap.org) is a primary care records database that covers approximately 75% of the population of Catalonia, North-East Spain. Healthcare is universal and taxpayer funded in the region, and primary care physicians are gatekeepers for all care and responsible for repeat prescriptions.<br><br>Important citations:<br>Recalde, M., Rodríguez, C., Burn, E., Far, M., García, D., Carrere-Molina, J., Benítez, M., Moleras, A., Pistillo, A., Bolíbar, B., Aragón, M., & Duarte-Salles, T. (2022). Data Resource Profile: The Information System for Research in Primary Care (SIDIAP). *International journal of epidemiology*, dyac068. Advance online publication. https://doi.org/10.1093/ije/dyac068 |

| Name and Country of Origin | Description |
|---|---|
| Stanford STARR OMOP (STARR)<br><br>From the United States | STAnford medicine Research data Repository (STARR), a clinical data warehouse containing live Epic data from Stanford Health Care, the Stanford Children's Hospital, the University Healthcare Alliance and Packard Children's Health Alliance clinics and other auxiliary data from Hospital applications such as radiology picture archiving and communication system (PACS). STARR platform is developed and operated by Stanford Medicine Research IT team and is made possible by Stanford School of Medicine Research Office.<br><br>Important citations:<br>Datta, S., et al., *A new paradigm for accelerating clinical data science at Stanford Medicine.* arXiv preprint arXiv:2003.10534, 2020.<br>https://arxiv.org/abs/2003.10534 |
| University of Tartu (U_OF_TARTU)†<br><br>From Estonia | National health insurance claims for all Estonian COVID-19 cases before February 2021 and four controls (randomly selected from population) per every case. The database was updated in November 2021, where many of the original controls also contracted COVID-19 between February 2021 and November 2021. |
| University Clinical Center of Serbia (UCCS)<br><br>From Serbia | University Clinical Center of Serbia is the largest health care facility in Serbia and Europe (by number of beds). It covers all fields of medicine in a tertiary setting, using Heliant as HIS/EHR (Health information system / Electronic health record), which follows many hospital business processes, from patient care, financial information, and to drug and material maintenance. |
| University of California Health Data Warehouse (UCHDW)*<br><br>From the United States | The University of California Health System, with 20 health professional schools (6 medical schools), 6 academic health centres, and 12 hospitals, is the tenth largest health system in the United States by revenue and has built a secure central data warehouse (UC Health Data Warehouse, or UCHDW) for operational improvement, promotion of quality patient care, and to enable the next generation of clinical research. The repository currently securely holds data on over 8 million patients seen since 2012, treated by over a million health care providers across nearly 310 million encounters, with over 875 million procedures, nearly 1.1 billion medication orders and prescriptions, and with over 3 billion vital signs measurements and test results (including 19 thousand sequenced cancer genomes). Over 600,000 of these patients are primary care patients. The majority of these patients live in California, the most diverse state in the United States. De-identification of the data has already been completed to enable clinical research projects, under guidance from UC campus institutional reviews boards, privacy and compliance officers, and information security officers. This data is stored in the Observational Medical Outcomes Partnership (OMOP) vendor-neutral open data model, enabling a wide range of software tools and computational methods to be used consistently with other state and national efforts. This data is currently centralised and available in a Microsoft Azure Databricks secure cloud environment, enabling research and development in artificial intelligence and machine learning with a familiar notebook interface supporting R, Python, and SQL.<br><br>Since the start of the COVID-19 pandemic, the University of California has tested over a million of its patients (as of this writing) finding the virus in over 120 thousand of them. We have created a standardised HIPAA Limited Data Set (University of California COVID Research Data Set, or UC CORDS) with the appropriate information to let thousands of internal researchers, clinicians, and policy makers understand the impact and progression of COVID-19. Care practice data (medications, procedures, ventilators, laboratory data) and previous medical data is available on the over 11 thousand patients admitted to date. |

| Name and Country of Origin | Description |
|---|---|
| UK Biobank (UK_BIOBANK)<br><br>From the United Kingdom | The United Kingdom (UK) Biobank (UKB) is a population-level, longitudinal research study of 500,000 participants in age range 40-69 from England, Scotland, and Wales recruited between 2006 - 2010. The study contains detailed baseline phenotypic (physical and biomarker measurements, diet and alcohol, cognitive function, mental health, education and employment), imaging (abdomen, brain and heart MRI, DXA), and genotypic (imputed genome, whole genome, exome sequencing) information. All participants have longitudinal follow-up data through electronic health records containing events from primary (231k patients), secondary care (395k patients), and national death and cancer registration information data. Since 2012, UKB has approved over 13,000 registrations from researchers working in over 1,375 institutes in 68 countries and approved over 1,200 applications to enable these researchers to access the data. Recently, the UKB has made data from national COVID-19 testing on participants (at the moment containing test results from 1,474 participants). During the current COVID-19 pandemic, the UKB is releasing data from national COVID-19 testing, primary care EHR, hospital inpatient episodes, national mortality registers and intensive care data (for participants with confirmed COVID-19) on a monthly basis.<br><br>Important citations:<br>Sudlow, C., Gallacher, J., Allen, N., Beral, V., Burton, P., Danesh, J., Downey, P., Elliott, P., Green, J., Landray, M., Liu, B., Matthews, P., Ong, G., Pell, J., Silman, A., Young, A., Sprosen, T., Peakman, T., & Collins, R. (2015). UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. *PLoS medicine*, *12*(3), e1001779. https://doi.org/10.1371/journal.pmed.1001779 |

* COVID-19 only subset, † COVID-19 + Controls

## Appendix 2 – Evaluation of the Quality and Validity of 16 Adverse Events of Special Interest (AESI) across 26 Databases

All 16 AESIs were characterised for every data partner that participated in this study using the OHDSI CohortDiagnostics [1] tool. For each cohort within each database, CohortDiagnostics characterization includes descriptive statistics about the concepts used to define the cohorts, counts of individuals that make up the cohort, incidence rates, descriptive statistics about conditions, drug and device exposures, procedures, and other clinical observations that occur prior to index date. Upon review with the tool and each data partner, cohorts would be excluded for a particular database if an inappropriate pattern was observed. Specifically, 31 of 416 outcome-database combinations were excluded; 20 due to the database lacking inpatient records where the phenotype definition required it, 7 where the definition was not applicable for the database (e.g., a database could not be used for myocarditis and pericarditis because its local coding was not sufficiently specific, instead only capturing the broader concept of 'infection of heart'), and 4 where the database was completely unable to identify any qualifying patients. An example, IPCI lacks complete access to inpatient data, therefore an AESI that requires an inpatient stay such as haemorrhagic stroke is not appropriate for that dataset and therefore should be excluded. The Appendix 2 Table 1 highlights which outcomes were excluded for which databases. Results from each database were also restricted to age ranges applicable to each specific database; IBM_CCAE was limited to patients less than 65, and IBM_MDCR was restricted to patients >=65 years at index date. Once the exclusion rules were known, the incidence rates could be reviewed.

References:

Rao G, Schuemie MJ, Ryan PB, et al. CohortDiagnostics: Diagnostics for OHDSI Cohorts. 2022

**Appendix 2 Table 1 - Adverse Events of Special Interest (AESI) Evaluation for Quality and Validity by Database**

| DB | Pulmonary Embolism | † Haemorrhagic Stroke | † Non-Haemorrhagic Stroke | DVT | Appendicitis | DIC | Transverse Myelitis | Anaphylaxis | Bell' s Palsy | † Encephalomyelitis | Narcolepsy | † Guillain-Barré syndrome | † AMI | Myocarditis Pericarditis | ITP | TWT |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| APHM | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| CPRD_AURUM | ✓ | ✱ | ✱ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✱ | ✓ | ✱ | ✱ | ✓ | ✓ | ✓ |
| CU_AMC | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| CUIMC | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| FIIBAP | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| HIC | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✗ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| IBM_CCAE | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| IBM_MDCD | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| IBM_MDCR | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| IMASIS | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| IPCI | ✓ | ✱ | ✱ | ✗ | ✓ | ✗ | ✗ | ✓ | ✓ | ✱ | ✗ | ✱ | ✱ | ✗ | ✓ | ✓ |
| IQVIA_FRANCE_DA | ✓ | ✱ | ✱ | ✓ | ✓ | ❗ | ❗ | ✓ | ✓ | ✱ | ✓ | ✱ | ✱ | ✓ | ✓ | ✓ |
| IQVIA_GERMANY_DA | ✓ | ✱ | ✱ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✱ | ✓ | ✱ | ✱ | ✓ | ✓ | ✓ |
| IQVIA_OPENCLAIMS | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| IQVIA_PHARMETRICS | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| IU | ✓ | ✓ | ✓ | ✗ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| JMDC | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| MHD | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ❗ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| OPTUM_EHR | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| OPTUM_SES | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| SIDIAP | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ❗ | ✓ | ✓ | ✓ | ✓ | ✓ |
| STARR | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| U_OF_TARTU | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| UCCS | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| UCHDW | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| UK_BIOBANK | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |

† = definition is inpatient based, ✓= no censorship applied, ✱ = database had outpatient data only, ✗ = database requires different definition, ❗ = data absent from this database

APHM = Health Data Warehouse of Assistance Publique - Hopitaux de Marseille, AMI = Acute Myocardial Infarction, CPRD_AURUM = Clinical Practice Research Datalink AURUM, CU_AMC = University of Colorado Anschutz Medical Campus - Health Data Compass, CUIMC = Columbia University Irving Medical Center, DIC = Disseminated Intravascular Coagulation, DVT = Deep Vein Thrombosis, F = Female, FIIBAP = Fundación para la Investigación e Innovación Biosanitaria en Atención Primaria COVID19, ITP = Immune Thrombocytopenia, HIC = Health Informatics Centre, IBM_CCAE = IBM® MarketScan® Commercial Claims and Encounters Database, IBM_MDCD = IBM® MarketScan® Multi-State Medicaid Database, IBM_MDCR = IBM® MarketScan® Medicare Supplemental and Coordination of Benefits Database, IMASIS = Parc de Salut Mar Barcelona Information System, IPCI = Integrated Primary Care Information, IQVIA_FRANCE_DA = IQVIA Disease Analyzer France, IQVIA_GERMAN_DA = IQVIA Disease Analyzer Germany, IQVIA_OPENCLAIMS = IQVIA LRxDX Open Claims,

IQVIA_PHARMETRICS = IQVIA Pharmetrics, IU = Istanbul Faculty of Medicine, Istanbul University, M = Male, MHD = Medaman Hospital Data, OPTUM_EHR = Optum® de-identified Electronic Health Record Dataset, OPTUM_SES = Optum De-Identified Clinformatics® Data Mart Database - Socio-Economic Status, SIDIAP = The Information System for Research on Primary Care, STARR = STAnford medicine Research data Repository-OMOP, TWT = Thrombosis with Thrombocytopenia U_OF_TARTU = University of Tartu (U_OF_TARTU), UCCS = University Clinical Center of Serbia, UCHDW = University of California Health Data Warehouse, UK_BIOBANK = UK Biobank

## Appendix 3 – Negative Control Outcomes

Twenty negative control outcomes were selected as diseases with no *a priori* evidence of a causal relationship with COVID-19, based on literature review and clinician adjudication. The following outcomes were used as negative controls:

1. Alcoholic liver damage
2. Animal bite wound
3. Ankle ulcer
4. Benign neoplasm of ovary
5. Biliary calculus
6. Burn of digit of hand
7. Burn of lower leg
8. Cannabis abuse
9. Cervical spine ankylosis
10. Contusion of toe
11. Endometriosis of uterus
12. Hyperplasia of prostate
13. Intestinal parasitism
14. Leukaemia
15. Open wound of buttock
16. Poisoning by bee sting
17. Primary malignant neoplasm of pancreas
18. Prosthetic joint loosening
19. Sprain of spinal ligament
20. Tailor's bunion

## Appendix 4 – 'Patients with COVID-19' As well as 'Pre-Pandemic Background Population' Standardised Incidence Rates for each Adverse Events of Special Interest Across all Database, Age Groups, and Sexes

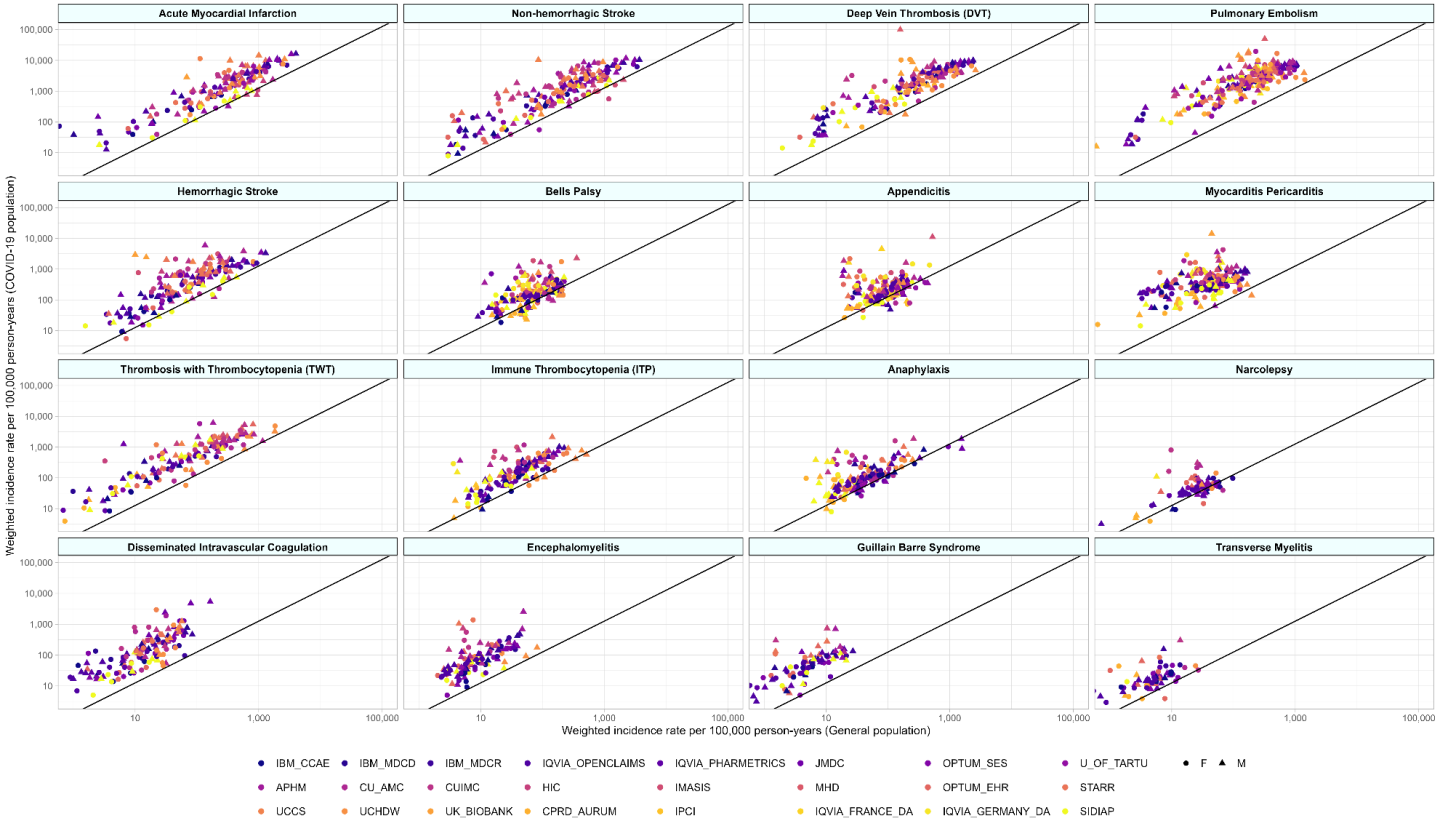
Appendix 4, Figure 1 compares the database-, age –group-, and sex-stratified incidence rates for 'Subjects with COVID-19' to the 'Pre-Pandemic Background Population'. If the two populations were similar the incidence rates would fall close to the 45-degree line, if the incidence rates are above the line this means they are higher for 'Patients with COVID-19', and if the incidence rates are below the line this means they are higher for the 'Pre-Pandemic Background Population'. For most outcomes, across all database/age group/sex combinations, the incidence rates are higher for the 'Patients with COVID-19' compared to the 'Pre-Pandemic Background Population'. Narcolepsy, appendicitis, Bell's palsy, and anaphylaxis demonstrated a smaller and less consistent positive trend.

The attached file are the details behind Figure 1 and Appendix 4, Figure 1. It contains the following columns:

- **databaseName** = lists the database each row was calculated from
- **sex** = lists if the row was calculated for females (F) or males (M)
- **ageGroup** = lists the age group the row was calculated for
- **outcomeName** = lists the Adverse Events of Special Interest the rows calculated for
- **incidenceRateP100py** = the incidence rate, per 100 person years, calculated for 'Patients with COVID-19'
- **incidenceRateP100pyGeneral** = the incidence rate, per 100 person years, calculated for 'Pre-Pandemic Background Population'

incidenceAnalysisCensoredCovidVsGen

**Appendix 4 – Figure 1 - Comparing the 'Patients with COVID-19' Stratified Incidence Rates (by Database*, 8 Age Groups, and Sex) for 16 Adverse Events of Special Interest to Those for 'Pre-Pandemic Background Population'**




* FIIBAP and IU did not contribute to the 'Pre-Pandemic Background Population' and thus and IR could not be calculated.

APHM = Health Data Warehouse of Assistance Publique - Hopitaux de Marseille, CPRD_AURUM = Clinical Practice Research Datalink AURUM, CU_AMC = University of Colorado Anschutz Medical Campus- Health Data Compass, CUIMC = Columbia University Irving Medical Center, F = Female, FIIBAP = Fundación para la Investigación e Innovación Biosanitaria en Atención Primaria COVID19, HIC = Health Informatics Centre, IBM_CCAE = IBM® MarketScan® Commercial Claims and Encounters Database, IBM_MDCD = IBM® MarketScan® Multi-State Medicaid Database, IBM_MDCR = IBM® MarketScan® Medicare Supplemental and Coordination of Benefits Database, IMASIS = Parc de Salut Mar Barcelona Information System, IPCI = Integrated Primary Care Information, IQVIA_FRANCE_DA = IQVIA Disease Analyzer France, IQVIA_GERMAN_DA = IQVIA Disease Analyzer Germany, IQVIA_OPENCLAIMS = IQVIA LRxDX Open Claims, IQVIA_PHARMETRICS = IQVIA Pharmetrics, IU = Istanbul Faculty of Medicine, Istanbul University, M = Male, MHD = Medaman Hospital Data, OPTUM_EHR = Optum® de-identified Electronic Health Record Dataset, OPTUM_SES = Optum De-

Identified Clinformatics® Data Mart Database - Socio-Economic Status, SIDIAP = The Information System for Research on Primary Care, STARR = STAnford medicine Research data Repository-OMOP, U_OF_TARTU = University of Tartu (U_OF_TARTU), UCCS = University Clinical Center of Serbia, UCHDW = University of California Health Data Warehouse, UK_BIOBANK = UK Biobank

## Appendix 5 - Pooled Estimated Age and Sex Stratified Incidence Rates Per 100000 person years (with 95% prediction intervals), calculated from meta-analyses for 'Pre-Pandemic General Population'

| Outcome by Sex | 0-5 Years | 6-17 Years | 18-34 Years | 35-54 Years | 55-64 Years | 65-74 Years | 75-84 Years | >=85 Years |
|---|---|---|---|---|---|---|---|---|
| Acute myocardial infarction (AMI) | | | | | | | | |
| Female | 6 (0 to 250) | 3 (0 to 40) | 11 (3 to 41) | 53 (14 to 211) | 151 (41 to 550) | 237 (94 to 600) | 532 (241 to 1172) | 996 (241 to 4111) |
| Male | 6 (0 to 219) | 3 (0 to 19) | 18 (6 to 52) | 152 (54 to 432) | 400 (166 to 965) | 539 (242 to 1202) | 789 (354 to 1758) | 1306 (292 to 5847) |
| Non-haemorrhagic stroke | | | | | | | | |
| Female | 12 (2 to 87) | 6 (2 to 21) | 19 (6 to 61) | 67 (16 to 278) | 152 (36 to 643) | 274 (95 to 792) | 647 (285 to 1472) | 1412 (322 to 6185) |
| Male | 12 (3 to 48) | 8 (2 to 28) | 17 (5 to 59) | 93 (29 to 301) | 252 (83 to 769) | 417 (173 to 1008) | 774 (334 to 1791) | 1246 (243 to 6382) |
| Deep vein thrombosis (DVT) | | | | | | | | |
| Female | 10 (2 to 58) | 8 (3 to 25) | 52 (19 to 141) | 91 (33 to 251) | 146 (55 to 393) | 224 (90 to 560) | 387 (169 to 888) | 378 (82 to 1753) |
| Male | 11 (2 to 57) | 10 (3 to 30) | 48 (17 to 134) | 107 (40 to 289) | 251 (105 to 602) | 302 (124 to 735) | 437 (188 to 1019) | 408 (81 to 2046) |
| Pulmonary embolism (PE) | | | | | | | | |
| Female | 5 (0 to 111) | 3 (1 to 11) | 43 (16 to 114) | 90 (32 to 253) | 155 (59 to 407) | 238 (120 to 475) | 430 (227 to 815) | 492 (161 to 1496) |
| Male | 5 (0 to 118) | 3 (1 to 13) | 29 (10 to 85) | 98 (37 to 256) | 199 (90 to 439) | 280 (143 to 549) | 409 (205 to 819) | 419 (124 to 1424) |
| Haemorrhagic stroke | | | | | | | | |
| Female | 17 (2 to 118) | 7 (2 to 23) | 15 (4 to 55) | 32 (10 to 103) | 64 (22 to 184) | 88 (33 to 232) | 196 (84 to 457) | 363 (84 to 1564) |
| Male | 14 (3 to 65) | 10 (3 to 37) | 21 (6 to 66) | 44 (15 to 124) | 94 (35 to 253) | 128 (55 to 298) | 272 (121 to 612) | 403 (85 to 1901) |
| Bell's palsy | | | | | | | | |
| Female | 19 (7 to 53) | 23 (11 to 47) | 44 (20 to 96) | 62 (25 to 158) | 79 (32 to 198) | 82 (30 to 224) | 100 (33 to 301) | 97 (29 to 321) |
| Male | 18 (6 to 54) | 20 (10 to 42) | 42 (19 to 92) | 64 (26 to 157) | 84 (34 to 209) | 93 (35 to 244) | 100 (33 to 302) | 106 (31 to 365) |
| Appendicitis | | | | | | | | |
| Female | 33 (13 to 82) | 161 (71 to 363) | 140 (69 to 286) | 89 (44 to 178) | 76 (38 to 153) | 55 (26 to 116) | 46 (20 to 105) | 40 (10 to 171) |
| Male | 37 (18 to 77) | 211 (119 to 371) | 152 (80 to 287) | 92 (48 to 177) | 70 (35 to 140) | 59 (28 to 121) | 49 (23 to 105) | 47 (12 to 189) |
| Myocarditis pericarditis | | | | | | | | |
| Female | 9 (1 to 68) | 9 (2 to 38) | 20 (6 to 66) | 29 (10 to 85) | 39 (14 to 108) | 41 (15 to 112) | 49 (18 to 133) | 43 (6 to 295) |
| Male | 9 (1 to 66) | 11 (4 to 36) | 40 (14 to 112) | 44 (15 to 132) | 53 (18 to 155) | 57 (21 to 154) | 64 (20 to 205) | 51 (8 to 338) |
| Thrombosis with Thrombocytopenia (TWT) | | | | | | | | |
| Female | 7 (0 to 779) | 3 (0 to 170) | 7 (1 to 91) | 12 (1 to 146) | 26 (2 to 281) | 37 (3 to 410) | 80 (8 to 810) | 174 (43 to 701) |
| Male | 6 (0 to 328) | 3 (0 to 140) | 7 (0 to 148) | 23 (1 to 422) | 54 (4 to 737) | 81 (6 to 1069) | 146 (14 to 1568) | 320 (88 to 1155) |
| Immune thrombocytopenia (ITP) | | | | | | | | |
| Female | 18 (6 to 52) | 12 (5 to 30) | 23 (7 to 73) | 23 (8 to 71) | 30 (11 to 87) | 36 (13 to 101) | 50 (18 to 141) | 45 (11 to 185) |
| Male | 20 (8 to 52) | 11 (4 to 31) | 11 (3 to 37) | 17 (5 to 56) | 29 (10 to 89) | 45 (15 to 137) | 76 (26 to 218) | 85 (22 to 334) |
| Anaphylaxis | | | | | | | | |
| Female | 85 (7 to 1002) | 66 (3 to 1556) | 47 (11 to 195) | 41 (11 to 146) | 38 (9 to 154) | 30 (9 to 95) | 25 (8 to 78) | 15 (2 to 99) |
| Male | 124 (9 to 1628) | 72 (2 to 3305) | 31 (7 to 134) | 26 (6 to 106) | 28 (5 to 168) | 25 (6 to 107) | 17 (6 to 44) | 12 (4 to 35) |
| Narcolepsy | | | | | | | | |
| Female | 5 (0 to 386) | 8 (3 to 27) | 28 (8 to 95) | 23 (7 to 80) | 19 (6 to 60) | 15 (5 to 44) | 16 (5 to 49) | 15 (3 to 81) |
| Male | 5 (0 to 179) | 8 (2 to 26) | 20 (6 to 61) | 19 (6 to 61) | 18 (6 to 56) | 15 (5 to 45) | 18 (6 to 55) | 21 (5 to 94) |
| Disseminated intravascular coagulation (DIC) | | | | | | | | |
| Female | 9 (0 to 397) | 4 (0 to 82) | 8 (0 to 141) | 9 (1 to 102) | 13 (2 to 94) | 14 (3 to 77) | 19 (5 to 72) | 25 (4 to 156) |
| Male | 9 (0 to 369) | 5 (0 to 109) | 5 (0 to 51) | 11 (1 to 106) | 19 (2 to 161) | 21 (3 to 165) | 28 (7 to 117) | 34 (8 to 145) |
| Encephalomyelitis | | | | | | | | |
| Female | 10 (2 to 68) | 9 (2 to 54) | 7 (1 to 37) | 8 (1 to 45) | 13 (3 to 64) | 14 (4 to 48) | 16 (4 to 59) | 25 (4 to 179) |
| Male | 9 (2 to 57) | 10 (2 to 57) | 8 (2 to 39) | 8 (2 to 37) | 15 (3 to 66) | 15 (4 to 53) | 22 (5 to 95) | 29 (6 to 151) |
| Guillain-Barré syndrome (BGS) | | | | | | | | |
| Female | 7 (0 to 507) | 3 (0 to 43) | 4 (1 to 16) | 4 (1 to 15) | 6 (2 to 24) | 7 (2 to 28) | 9 (3 to 32) | 16 (2 to 137) |
| Male | 8 (0 to 275) | 3 (0 to 20) | 3 (1 to 11) | 5 (2 to 16) | 9 (3 to 26) | 10 (4 to 28) | 16 (5 to 53) | 19 (5 to 65) |
| Transverse myelitis | | | | | | | | |
| Female | 4 (0 to 290) | 2 (0 to 20) | 5 (1 to 16) | 7 (2 to 24) | 7 (3 to 20) | 7 (3 to 20) | 5 (2 to 15) | 7 (0 to 198) |
| Male | 4 (0 to 283) | 2 (0 to 18) | 3 (1 to 8) | 4 (1 to 15) | 6 (2 to 20) | 5 (2 to 13) | 6 (1 to 22) | 7 (1 to 35) |
| Council of International Organizations of Medical Sciences frequency classification | | | | | | | | |
| Very rare (<1/10000) | Rare (>=10000 to <1/1000) | Uncommon (>= 1/1000 to <1/100) | Common (>= 1/100 to <1/10) | Very Common (>=1 /10) | | | | |

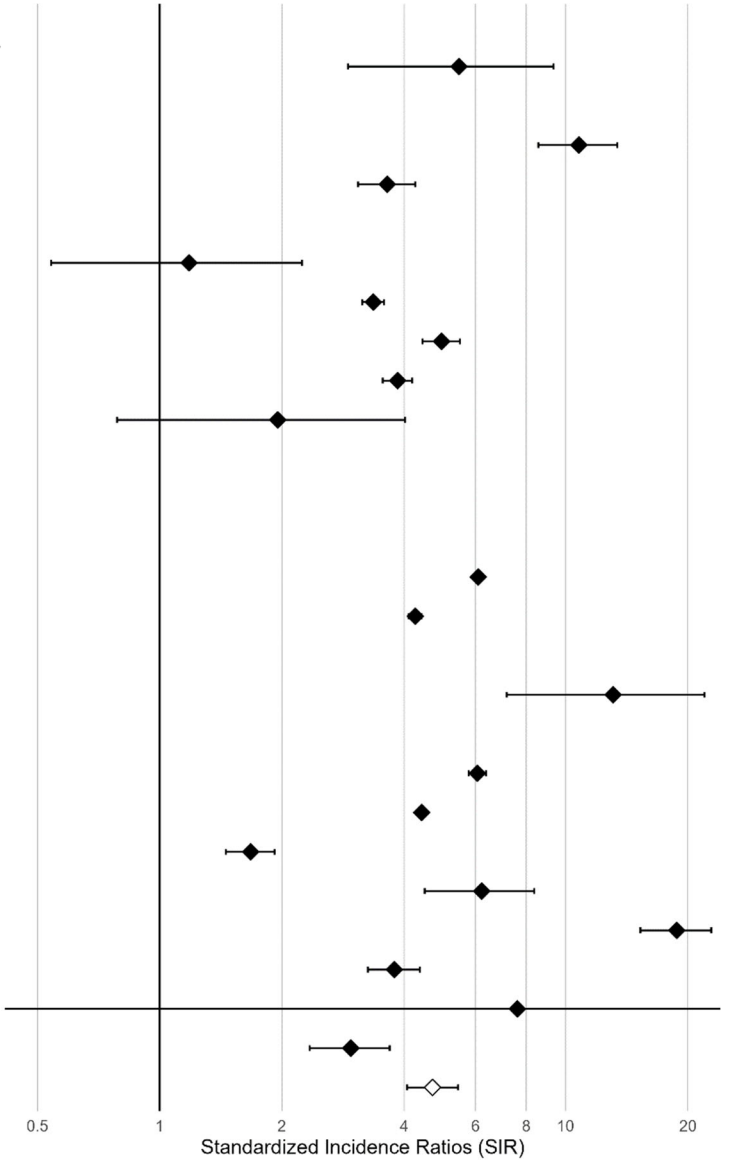
## Appendix 6 – Standardised Incidence Ratios Forest Plots across 26 databases for 16 Adverse Events of Special Interest comparing 'Patients with COVID-19' and 'Pre-Pandemic Background Population'

For each database, for each adverse event of special interest (AESI) results are either:

- Reported
- Labelled as "Results Censored" which is based on the exclusions applied from Appendix 2.
- Labelled as "Insufficient data" meaning there were too few cases to provide a valid standardised incidence ratio (SIR)

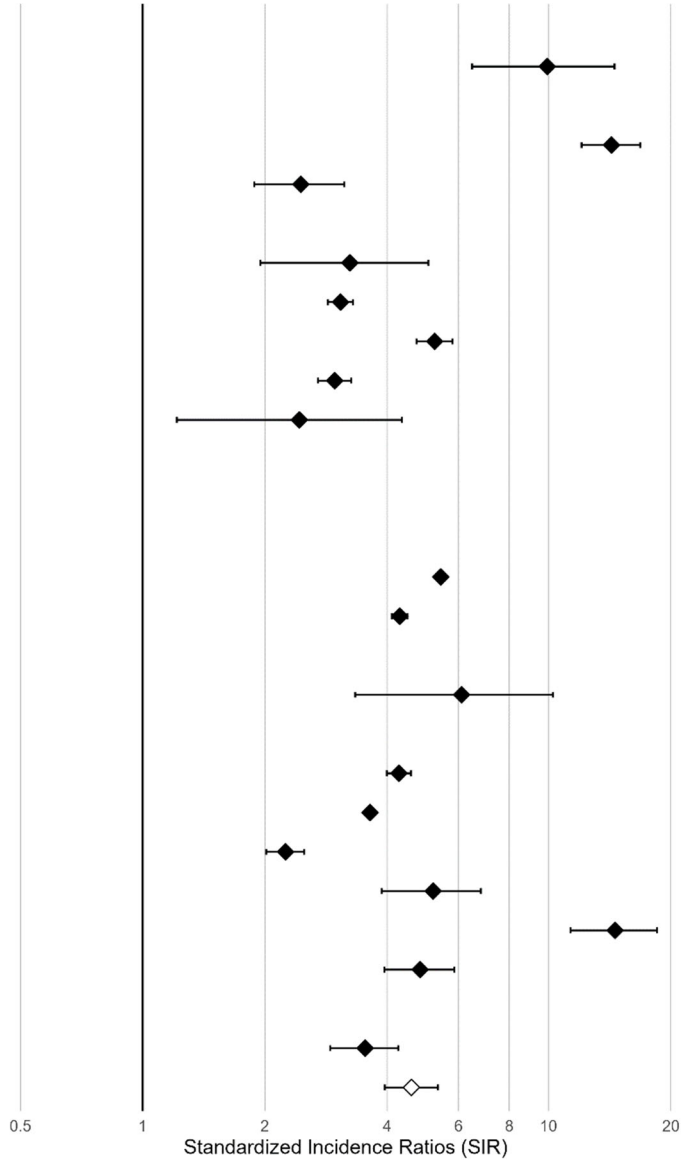
## Acute Myocardial Infarction

| Source | SIR (95% CI) |
|---|---|
| APHM | 5.46 (2.91 - 9.34) |
| CPRD_AURUM | Results Censored |
| CUIMC | 10.78 (8.56 - 13.40) |
| CU_AMC | 3.63 (3.08 - 4.26) |
| FIIBAP | Insufficient Data |
| HIC | 1.18 (0.54 - 2.24) |
| IBM_CCAE | 3.36 (3.16 - 3.57) |
| IBM_MDCD | 4.95 (4.44 - 5.49) |
| IBM_MDCR | 3.86 (3.54 - 4.19) |
| IMASIS | 1.95 (0.79 - 4.02) |
| IPCI | Results Censored |
| IQVIA_FRANCE_DA | Results Censored |
| IQVIA_GERMANY_DA | Results Censored |
| IQVIA_OPENCLAIMS | 6.09 (6.04 - 6.15) |
| IQVIA_PHARMETRICS | 4.26 (4.11 - 4.42) |
| IU | Insufficient Data |
| JMDC | 13.09 (7.16 - 21.97) |
| MHD | Insufficient Data |
| OPTUM_EHR | 6.06 (5.77 - 6.36) |
| OPTUM_SES | 4.42 (4.31 - 4.54) |
| SIDIAP | 1.68 (1.46 - 1.92) |
| STARR | 6.21 (4.49 - 8.37) |
| UCCS | 18.78 (15.28 - 22.84) |
| UCHDW | 3.79 (3.26 - 4.38) |
| UK_BIOBANK | 7.60 (0.19 - 42.37) |
| U_OF_TARTU | 2.96 (2.34 - 3.69) |
| Summary | 4.70 (4.07 - 5.43) |



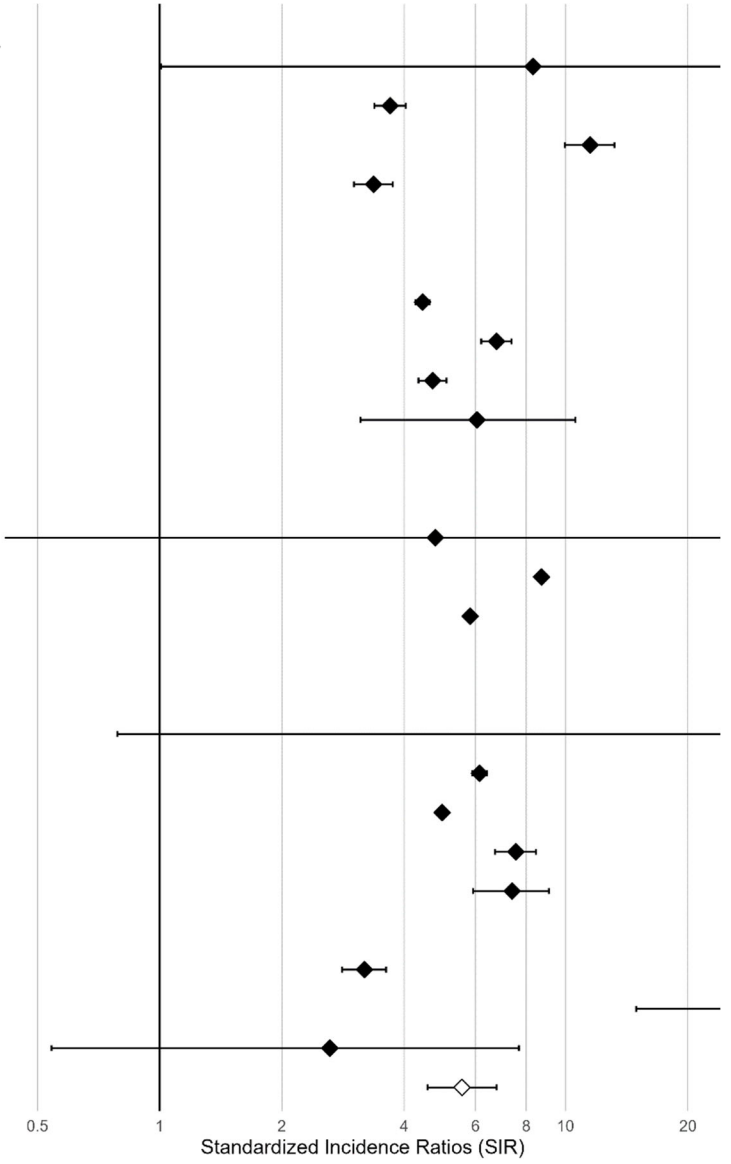
## Non-haemorrhagic Stroke

| Source | SIR (95% CI) |
|---|---|
| APHM | 9.92 (6.48 - 14.54) |
| CPRD_AURUM | Results Censored |
| CUIMC | 14.28 (12.05 - 16.80) |
| CU_AMC | 2.45 (1.88 - 3.14) |
| FIIBAP | Insufficient Data |
| HIC | 3.24 (1.95 - 5.06) |
| IBM_CCAE | 3.07 (2.86 - 3.30) |
| IBM_MDCD | 5.24 (4.73 - 5.79) |
| IBM_MDCR | 2.97 (2.70 - 3.26) |
| IMASIS | 2.43 (1.21 - 4.35) |
| IPCI | Results Censored |
| IQVIA_FRANCE_DA | Results Censored |
| IQVIA_GERMANY_DA | Results Censored |
| IQVIA_OPENCLAIMS | 5.42 (5.37 - 5.48) |
| IQVIA_PHARMETRICS | 4.30 (4.11 - 4.49) |
| IU | Insufficient Data |
| JMDC | 6.11 (3.34 - 10.24) |
| MHD | Insufficient Data |
| OPTUM_EHR | 4.28 (3.99 - 4.58) |
| OPTUM_SES | 3.63 (3.53 - 3.73) |
| SIDIAP | 2.25 (2.01 - 2.50) |
| STARR | 5.19 (3.88 - 6.81) |
| UCCS | 14.58 (11.32 - 18.48) |
| UCHDW | 4.83 (3.94 - 5.85) |
| UK_BIOBANK | Insufficient Data |
| U_OF_TARTU | 3.53 (2.90 - 4.26) |
| Summary | 4.59 (3.95 - 5.34) |



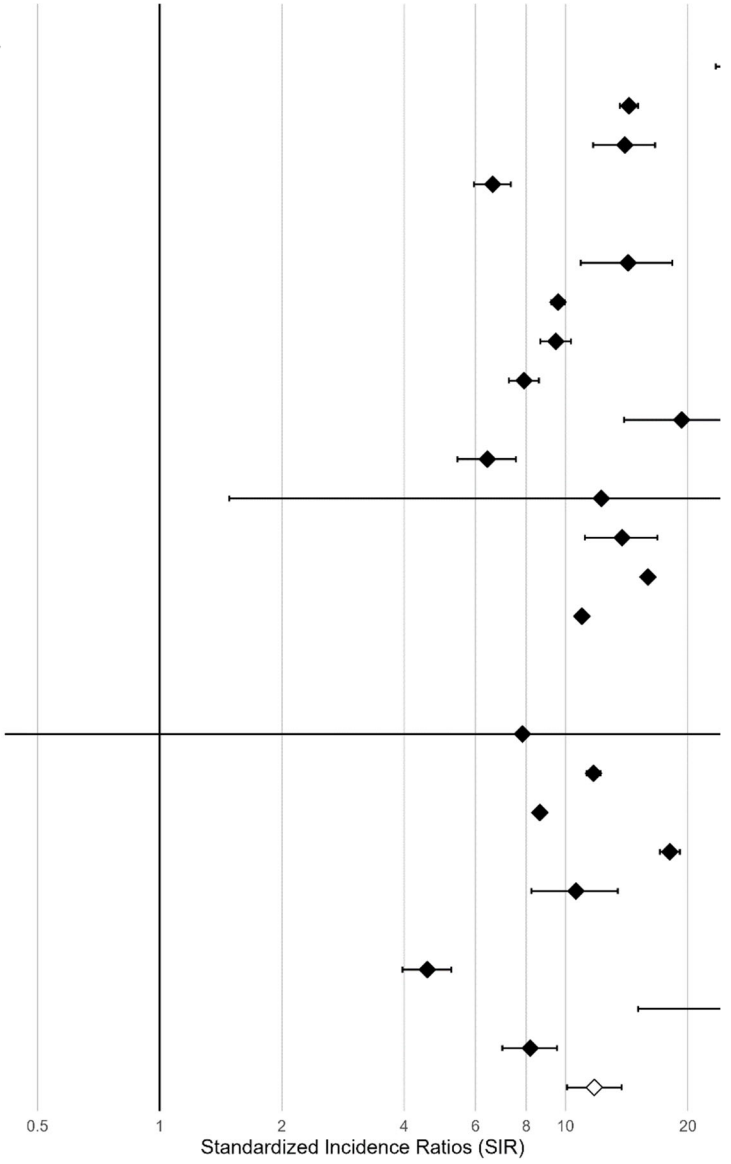
## Deep Vein Thrombosis (DVT)

| Source | SIR (95% CI) |
|---|---|
| APHM | 8.31 (1.01 - 30.03) |
| CPRD_AURUM | 3.70 (3.38 - 4.04) |
| CUIMC | 11.49 (9.96 - 13.18) |
| CU_AMC | 3.37 (3.01 - 3.75) |
| FIIBAP | Insufficient Data |
| HIC | Insufficient Data |
| IBM_CCAE | 4.44 (4.27 - 4.63) |
| IBM_MDCD | 6.76 (6.20 - 7.35) |
| IBM_MDCR | 4.70 (4.34 - 5.09) |
| IMASIS | 6.05 (3.13 - 10.57) |
| IPCI | Results Censored |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | 4.77 (0.12 - 26.60) |
| IQVIA_OPENCLAIMS | 8.72 (8.66 - 8.78) |
| IQVIA_PHARMETRICS | 5.82 (5.65 - 5.99) |
| IU | Results Censored |
| JMDC | Insufficient Data |
| MHD | 31.06 (0.79 - 173.07) |
| OPTUM_EHR | 6.14 (5.89 - 6.39) |
| OPTUM_SES | 4.96 (4.84 - 5.09) |
| SIDIAP | 7.54 (6.71 - 8.45) |
| STARR | 7.38 (5.92 - 9.09) |
| UCCS | Insufficient Data |
| UCHDW | 3.20 (2.82 - 3.61) |
| UK_BIOBANK | 28.87 (14.92 - 50.43) |
| U_OF_TARTU | 2.63 (0.54 - 7.67) |
| Summary | 5.56 (4.57 - 6.76) |



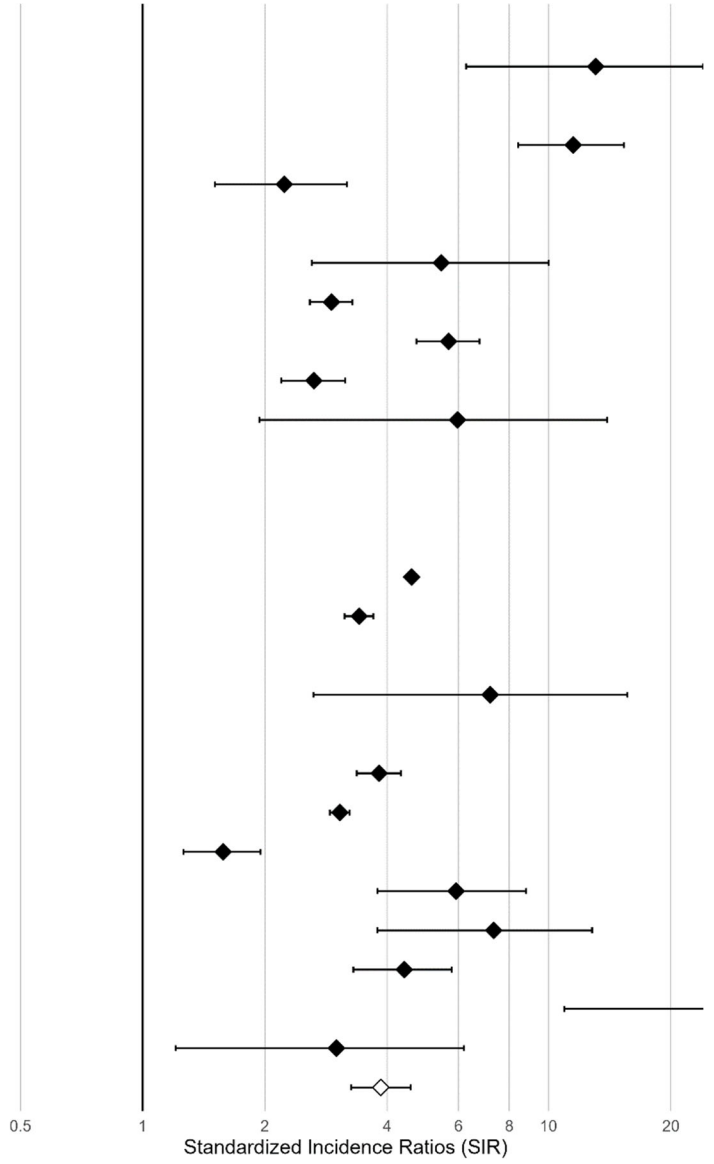
## Pulmonary Embolism (PE)

| Source | SIR (95% CI) |
|---|---|
| APHM | 32.64 (23.42 - 44.28) |
| CPRD_AURUM | 14.32 (13.61 - 15.07) |
| CUIMC | 13.99 (11.69 - 16.61) |
| CU_AMC | 6.61 (5.95 - 7.33) |
| FIIBAP | Insufficient Data |
| HIC | 14.25 (10.90 - 18.31) |
| IBM_CCAE | 9.58 (9.23 - 9.95) |
| IBM_MDCD | 9.46 (8.66 - 10.31) |
| IBM_MDCR | 7.90 (7.25 - 8.60) |
| IMASIS | 19.32 (13.92 - 26.11) |
| IPCI | 6.41 (5.42 - 7.54) |
| IQVIA_FRANCE_DA | 12.24 (1.48 - 44.23) |
| IQVIA_GERMANY_DA | 13.77 (11.16 - 16.82) |
| IQVIA_OPENCLAIMS | 15.95 (15.84 - 16.06) |
| IQVIA_PHARMETRICS | 10.97 (10.67 - 11.28) |
| IU | Insufficient Data |
| JMDC | 49.28 (32.47 - 71.70) |
| MHD | 7.83 (0.20 - 43.62) |
| OPTUM_EHR | 11.71 (11.26 - 12.18) |
| OPTUM_SES | 8.64 (8.42 - 8.86) |
| SIDIAP | 18.06 (17.06 - 19.11) |
| STARR | 10.60 (8.23 - 13.44) |
| UCCS | 34.58 (30.00 - 39.65) |
| UCHDW | 4.56 (3.97 - 5.23) |
| UK_BIOBANK | 26.94 (15.08 - 44.44) |
| U_OF_TARTU | 8.18 (6.98 - 9.53) |
| Summary | 11.77 (10.08 - 13.73) |



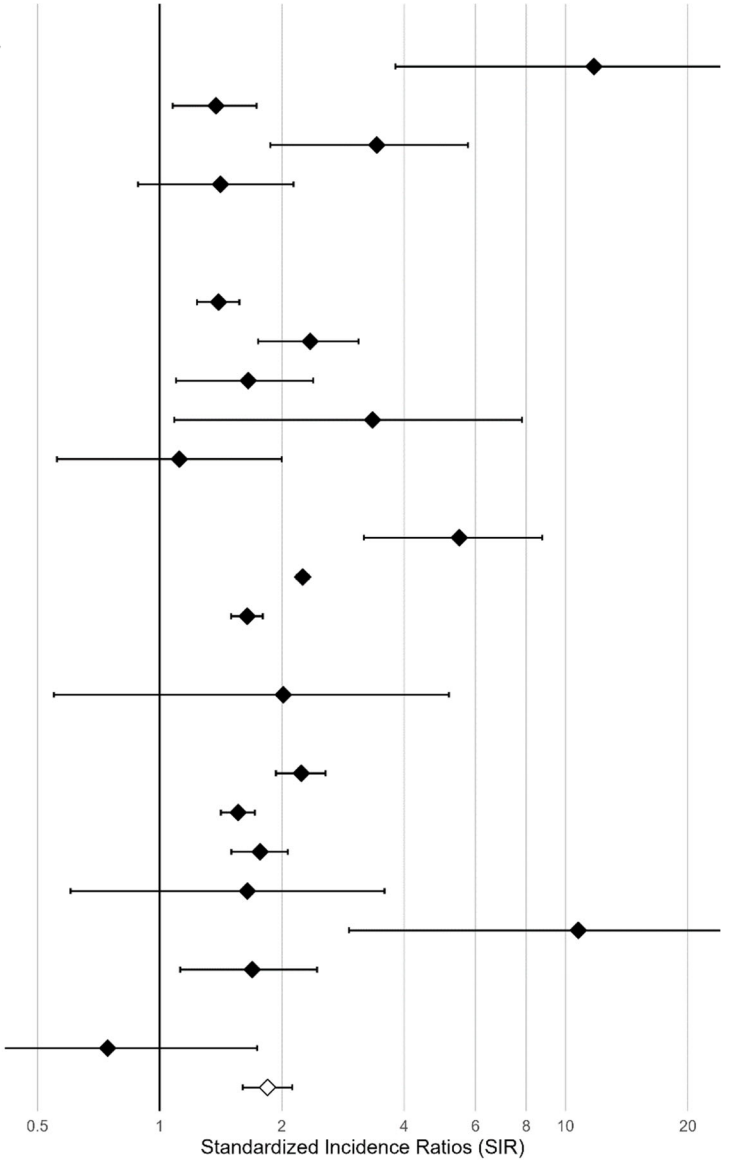
## Haemorrhagic Stroke

| Source | SIR (95% CI) |
|---|---|
| APHM | 13.06 (6.26 - 24.02) |
| CPRD_AURUM | Results Censored |
| CUIMC | 11.50 (8.42 - 15.33) |
| CU_AMC | 2.23 (1.51 - 3.19) |
| FIIBAP | Insufficient Data |
| HIC | 5.44 (2.61 - 10.00) |
| IBM_CCAE | 2.92 (2.58 - 3.29) |
| IBM_MDCD | 5.67 (4.72 - 6.75) |
| IBM_MDCR | 2.64 (2.19 - 3.15) |
| IMASIS | 5.97 (1.94 - 13.92) |
| IPCI | Results Censored |
| IQVIA_FRANCE_DA | Results Censored |
| IQVIA_GERMANY_DA | Results Censored |
| IQVIA_OPENCLAIMS | 4.60 (4.51 - 4.69) |
| IQVIA_PHARMETRICS | 3.41 (3.14 - 3.70) |
| IU | Insufficient Data |
| JMDC | 7.18 (2.63 - 15.62) |
| MHD | Insufficient Data |
| OPTUM_EHR | 3.82 (3.37 - 4.32) |
| OPTUM_SES | 3.06 (2.89 - 3.24) |
| SIDIAP | 1.58 (1.26 - 1.95) |
| STARR | 5.92 (3.79 - 8.80) |
| UCCS | 7.32 (3.78 - 12.79) |
| UCHDW | 4.41 (3.30 - 5.77) |
| UK_BIOBANK | 90.21 (10.92 - 325.87) |
| U_OF_TARTU | 3.00 (1.21 - 6.18) |
| Summary | 3.86 (3.26 - 4.57) |



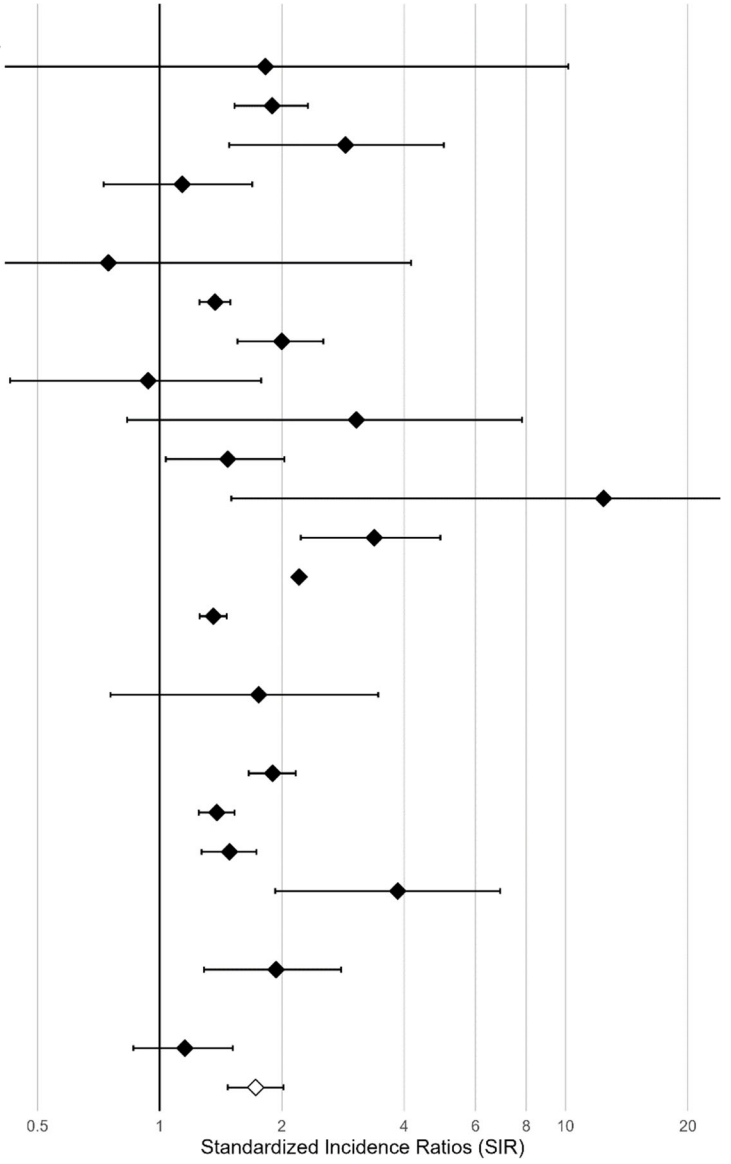
## Bell's Palsy

| Source | SIR (95% CI) |
|---|---|
| APHM | 11.74 (3.81 - 27.39) |
| CPRD_AURUM | 1.38 (1.08 - 1.73) |
| CUIMC | 3.43 (1.87 - 5.75) |
| CU_AMC | 1.41 (0.88 - 2.14) |
| FIIBAP | Insufficient Data |
| HIC | Insufficient Data |
| IBM_CCAE | 1.40 (1.24 - 1.57) |
| IBM_MDCD | 2.35 (1.75 - 3.09) |
| IBM_MDCR | 1.65 (1.10 - 2.39) |
| IMASIS | 3.34 (1.09 - 7.81) |
| IPCI | 1.12 (0.56 - 2.00) |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | 5.47 (3.19 - 8.76) |
| IQVIA_OPENCLAIMS | 2.25 (2.18 - 2.32) |
| IQVIA_PHARMETRICS | 1.64 (1.50 - 1.80) |
| IU | Insufficient Data |
| JMDC | 2.02 (0.55 - 5.16) |
| MHD | Insufficient Data |
| OPTUM_EHR | 2.23 (1.93 - 2.56) |
| OPTUM_SES | 1.56 (1.42 - 1.72) |
| SIDIAP | 1.77 (1.50 - 2.07) |
| STARR | 1.64 (0.60 - 3.58) |
| UCCS | 10.75 (2.93 - 27.51) |
| UCHDW | 1.69 (1.12 - 2.44) |
| UK_BIOBANK | Insufficient Data |
| U_OF_TARTU | 0.74 (0.24 - 1.74) |
| Summary | 1.84 (1.60 - 2.12) |



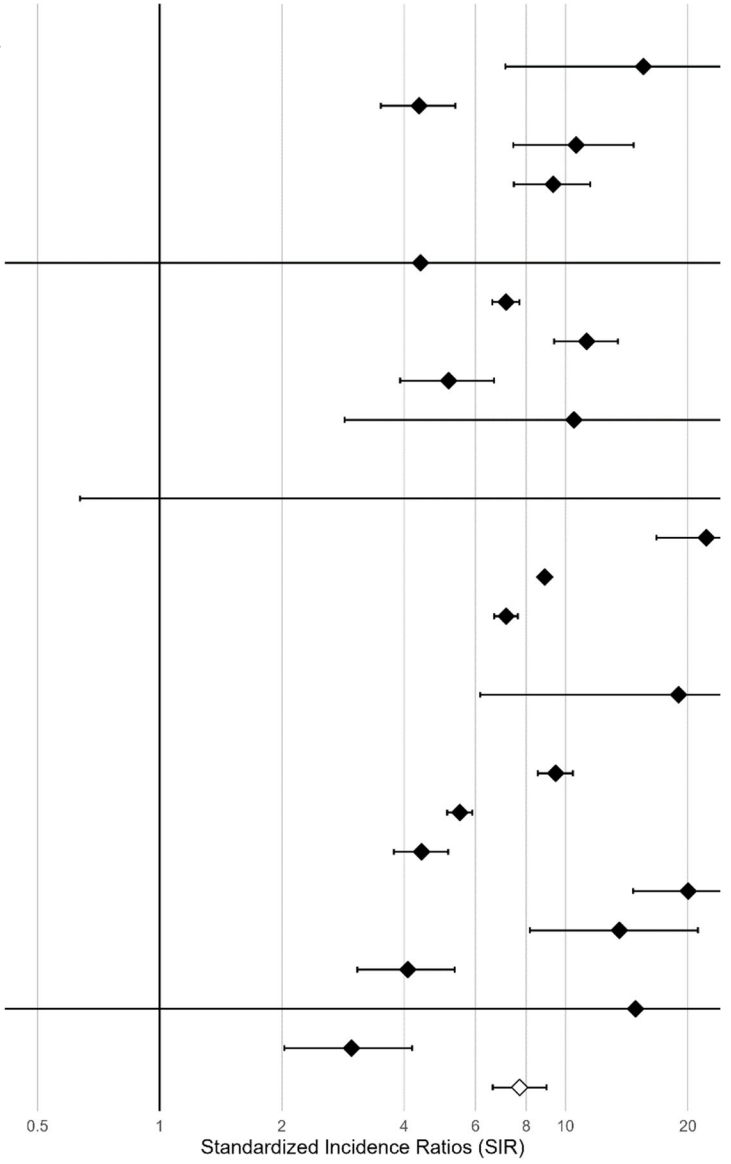
## Appendicitis

| Source | SIR (95% CI) |
|---|---|
| APHM | 1.82 (0.05 - 10.15) |
| CPRD_AURUM | 1.89 (1.53 - 2.32) |
| CUIMC | 2.87 (1.48 - 5.01) |
| CU_AMC | 1.14 (0.73 - 1.69) |
| FIIBAP | Insufficient Data |
| HIC | 0.75 (0.02 - 4.17) |
| IBM_CCAE | 1.37 (1.25 - 1.49) |
| IBM_MDCD | 2.00 (1.56 - 2.53) |
| IBM_MDCR | 0.94 (0.43 - 1.78) |
| IMASIS | 3.05 (0.83 - 7.81) |
| IPCI | 1.47 (1.04 - 2.03) |
| IQVIA_FRANCE_DA | 12.40 (1.50 - 44.80) |
| IQVIA_GERMANY_DA | 3.38 (2.23 - 4.91) |
| IQVIA_OPENCLAIMS | 2.20 (2.15 - 2.26) |
| IQVIA_PHARMETRICS | 1.36 (1.26 - 1.46) |
| IU | Insufficient Data |
| JMDC | 1.75 (0.76 - 3.45) |
| MHD | Insufficient Data |
| OPTUM_EHR | 1.90 (1.66 - 2.16) |
| OPTUM_SES | 1.38 (1.25 - 1.53) |
| SIDIAP | 1.49 (1.27 - 1.73) |
| STARR | 3.86 (1.93 - 6.90) |
| UCCS | Insufficient Data |
| UCHDW | 1.94 (1.29 - 2.80) |
| UK_BIOBANK | Insufficient Data |
| U_OF_TARTU | 1.15 (0.86 - 1.51) |
| Summary | 1.72 (1.47 - 2.02) |



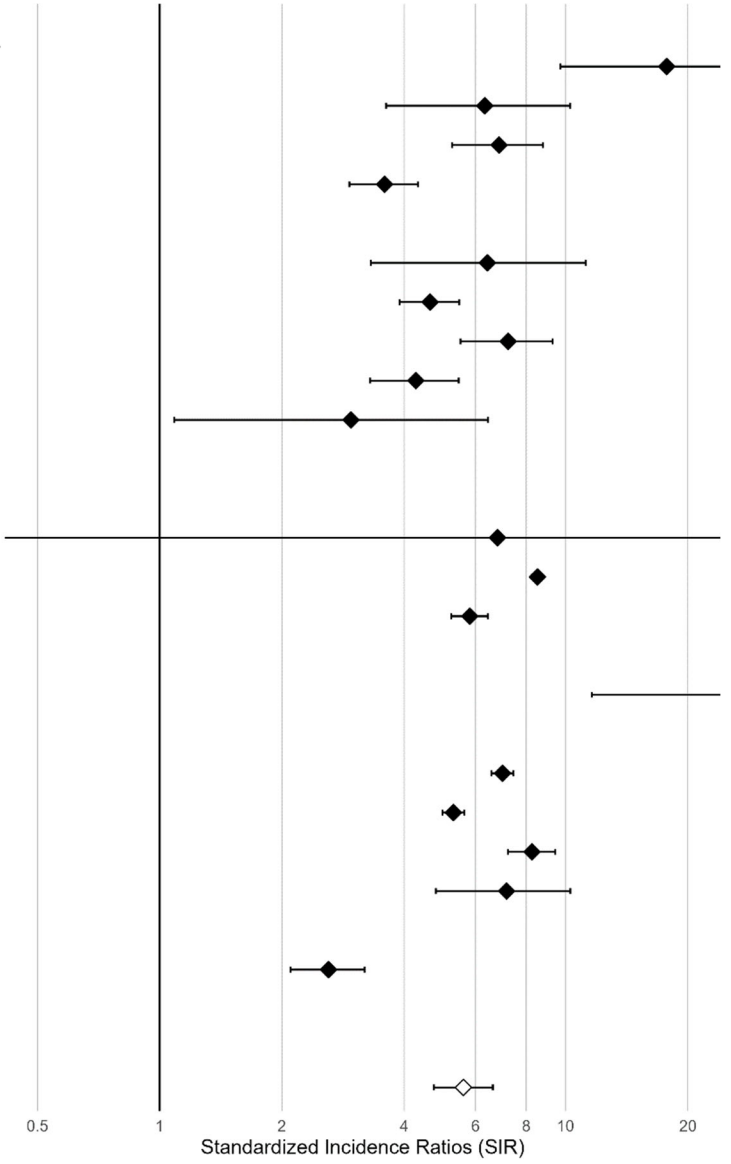
## Myocarditis and Pericarditis

| Source | SIR (95% CI) |
|---|---|
| APHM | 15.55 (7.11 - 29.51) |
| CPRD_AURUM | 4.36 (3.51 - 5.35) |
| CUIMC | 10.62 (7.44 - 14.70) |
| CU_AMC | 9.32 (7.45 - 11.51) |
| FIIBAP | Insufficient Data |
| HIC | 4.39 (0.11 - 24.47) |
| IBM_CCAE | 7.13 (6.60 - 7.70) |
| IBM_MDCD | 11.27 (9.36 - 13.44) |
| IBM_MDCR | 5.15 (3.91 - 6.66) |
| IMASIS | 10.48 (2.86 - 26.84) |
| IPCI | Results Censored |
| IQVIA_FRANCE_DA | 25.15 (0.64 - 140.13) |
| IQVIA_GERMANY_DA | 22.21 (16.73 - 28.91) |
| IQVIA_OPENCLAIMS | 8.88 (8.68 - 9.09) |
| IQVIA_PHARMETRICS | 7.14 (6.67 - 7.63) |
| IU | Insufficient Data |
| JMDC | 18.98 (6.16 - 44.30) |
| MHD | Insufficient Data |
| OPTUM_EHR | 9.45 (8.55 - 10.43) |
| OPTUM_SES | 5.49 (5.11 - 5.89) |
| SIDIAP | 4.42 (3.78 - 5.14) |
| STARR | 20.05 (14.68 - 26.74) |
| UCCS | 13.56 (8.17 - 21.18) |
| UCHDW | 4.08 (3.07 - 5.33) |
| UK_BIOBANK | 14.87 (0.38 - 82.84) |
| U_OF_TARTU | 2.97 (2.03 - 4.19) |
| Summary | 7.70 (6.61 - 8.98) |



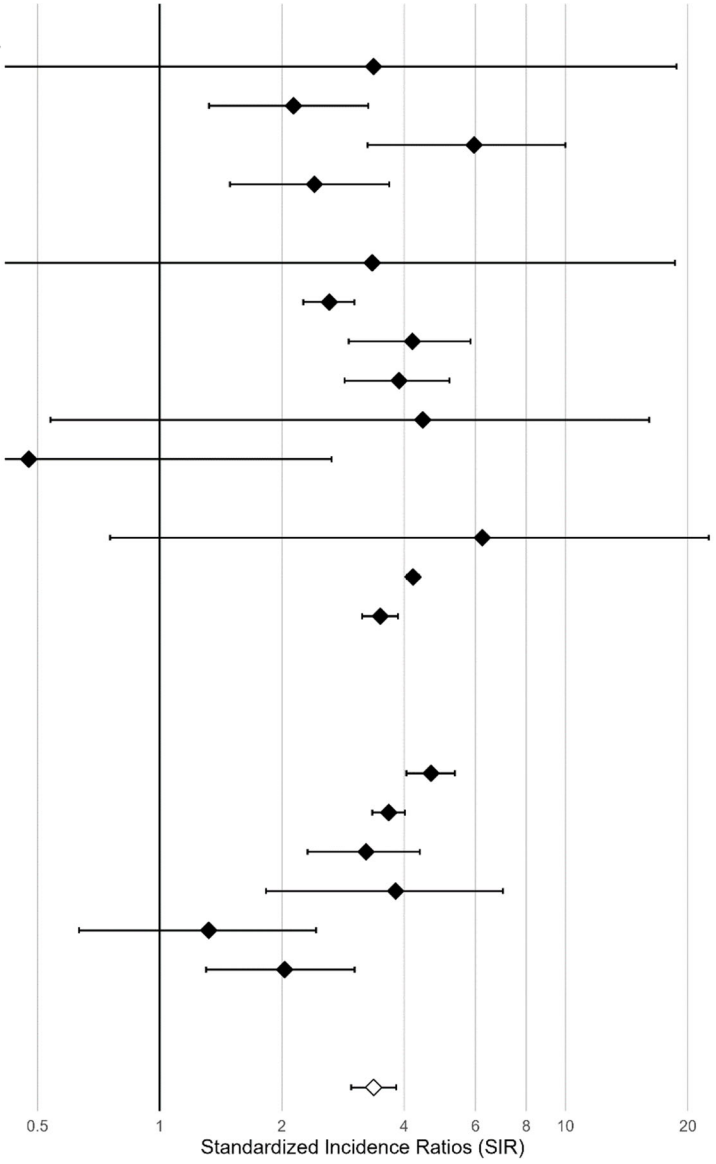
### Thrombosis with Thrombocytopenia (TWT)

| Source | SIR (95% CI) |
|---|---|
| APHM | 17.75 (9.70 - 29.77) |
| CPRD_AURUM | 6.32 (3.61 - 10.26) |
| CUIMC | 6.85 (5.26 - 8.79) |
| CU_AMC | 3.58 (2.93 - 4.33) |
| FIIBAP | Insufficient Data |
| HIC | 6.41 (3.31 - 11.20) |
| IBM_CCAE | 4.64 (3.90 - 5.47) |
| IBM_MDCD | 7.22 (5.51 - 9.29) |
| IBM_MDCR | 4.28 (3.30 - 5.45) |
| IMASIS | 2.96 (1.09 - 6.44) |
| IPCI | Insufficient Data |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | 6.79 (0.17 - 37.86) |
| IQVIA_OPENCLAIMS | 8.52 (8.25 - 8.81) |
| IQVIA_PHARMETRICS | 5.80 (5.23 - 6.43) |
| IU | Insufficient Data |
| JMDC | 42.58 (11.60 - 109.03) |
| MHD | Insufficient Data |
| OPTUM_EHR | 6.99 (6.57 - 7.44) |
| OPTUM_SES | 5.29 (4.97 - 5.63) |
| SIDIAP | 8.26 (7.20 - 9.43) |
| STARR | 7.15 (4.79 - 10.28) |
| UCCS | 232.94 (181.24 - 294.80) |
| UCHDW | 2.61 (2.10 - 3.20) |
| UK_BIOBANK | Insufficient Data |
| U_OF_TARTU | Insufficient Data |
| Summary | 5.60 (4.74 - 6.62) |



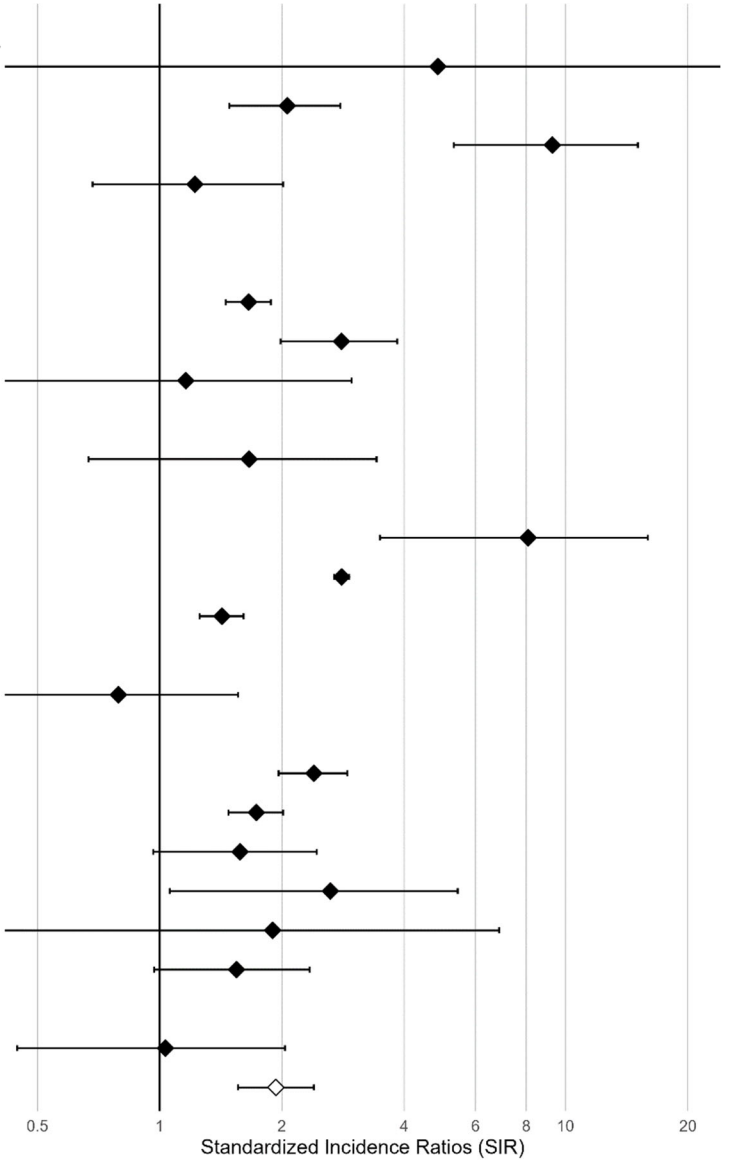
## Immune Thrombocytopenia (ITP)

| Source | SIR (95% CI) |
|---|---|
| APHM | 3.36 (0.09 - 18.74) |
| CPRD_AURUM | 2.14 (1.32 - 3.27) |
| CUIMC | 5.95 (3.25 - 9.98) |
| CU_AMC | 2.41 (1.49 - 3.68) |
| FIIBAP | Insufficient Data |
| HIC | 3.34 (0.08 - 18.60) |
| IBM_CCAE | 2.62 (2.26 - 3.02) |
| IBM_MDCD | 4.19 (2.92 - 5.83) |
| IBM_MDCR | 3.89 (2.86 - 5.17) |
| IMASIS | 4.45 (0.54 - 16.06) |
| IPCI | 0.48 (0.01 - 2.65) |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | 6.23 (0.75 - 22.52) |
| IQVIA_OPENCLAIMS | 4.21 (4.06 - 4.36) |
| IQVIA_PHARMETRICS | 3.50 (3.15 - 3.87) |
| IU | Insufficient Data |
| JMDC | Insufficient Data |
| MHD | Insufficient Data |
| OPTUM_EHR | 4.66 (4.05 - 5.34) |
| OPTUM_SES | 3.67 (3.34 - 4.02) |
| SIDIAP | 3.22 (2.31 - 4.37) |
| STARR | 3.81 (1.83 - 7.01) |
| UCCS | 1.32 (0.63 - 2.43) |
| UCHDW | 2.03 (1.30 - 3.02) |
| UK_BIOBANK | Insufficient Data |
| U_OF_TARTU | Insufficient Data |
| Summary | 3.37 (2.96 - 3.82) |



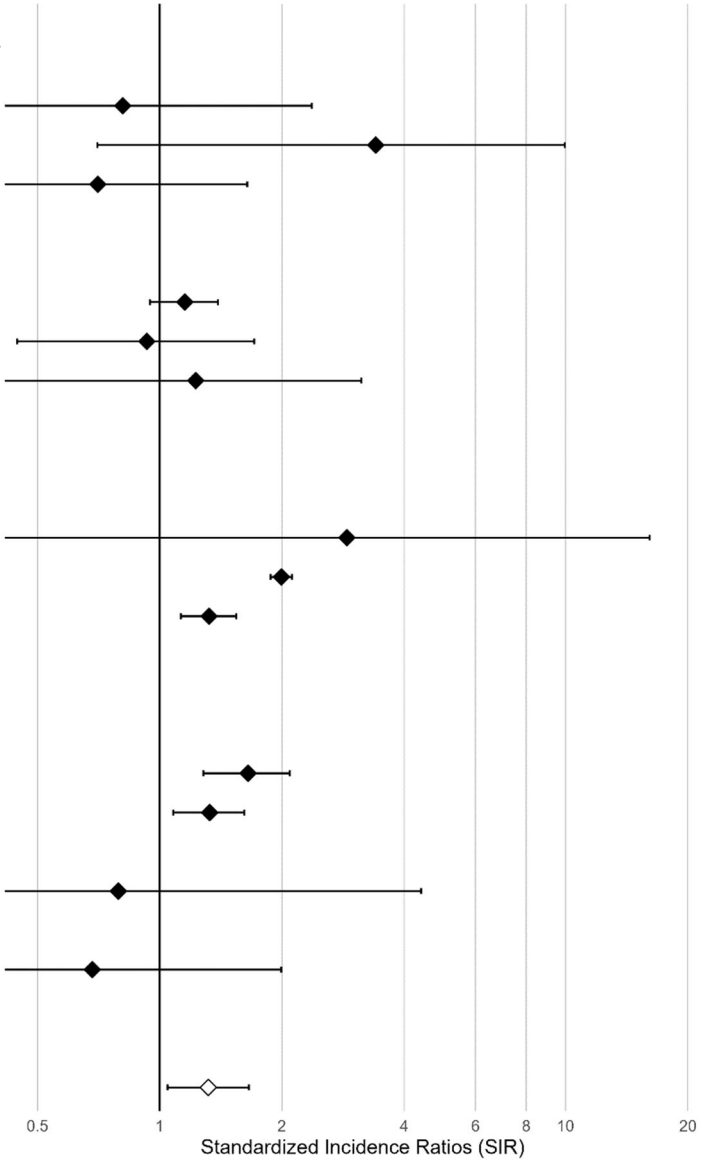
## Anaphylaxis

| Source | SIR (95% CI) |
|---|---|
| APHM | 4.85 (0.12 - 27.00) |
| CPRD_AURUM | 2.06 (1.49 - 2.79) |
| CUIMC | 9.27 (5.30 - 15.06) |
| CU_AMC | 1.22 (0.68 - 2.01) |
| FIIBAP | Insufficient Data |
| HIC | Results Censored |
| IBM_CCAE | 1.66 (1.45 - 1.88) |
| IBM_MDCD | 2.80 (1.98 - 3.85) |
| IBM_MDCR | 1.16 (0.32 - 2.97) |
| IMASIS | Insufficient Data |
| IPCI | 1.66 (0.67 - 3.42) |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | 8.08 (3.49 - 15.93) |
| IQVIA_OPENCLAIMS | 2.81 (2.69 - 2.93) |
| IQVIA_PHARMETRICS | 1.42 (1.25 - 1.61) |
| IU | Insufficient Data |
| JMDC | 0.79 (0.34 - 1.56) |
| MHD | Insufficient Data |
| OPTUM_EHR | 2.40 (1.96 - 2.90) |
| OPTUM_SES | 1.73 (1.48 - 2.01) |
| SIDIAP | 1.58 (0.96 - 2.44) |
| STARR | 2.63 (1.06 - 5.42) |
| UCCS | 1.90 (0.23 - 6.85) |
| UCHDW | 1.55 (0.97 - 2.34) |
| UK_BIOBANK | Insufficient Data |
| U_OF_TARTU | 1.03 (0.45 - 2.03) |
| Summary | 1.93 (1.56 - 2.40) |



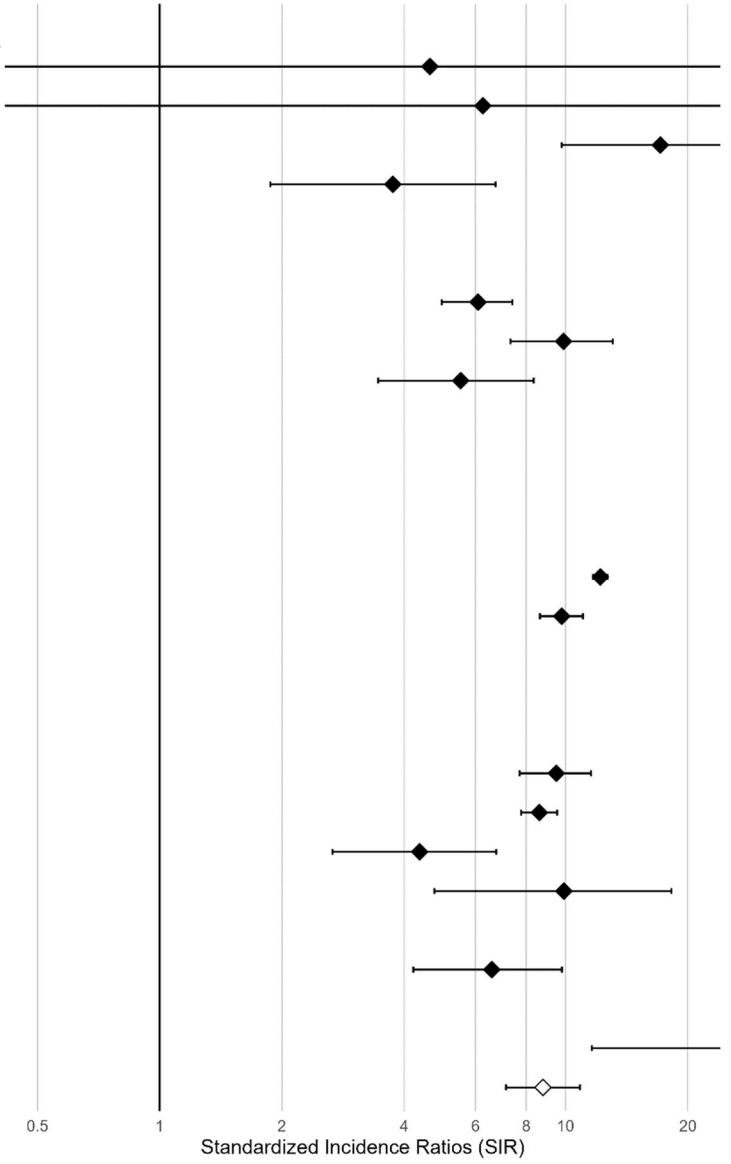
## Narcolepsy

| Source | SIR (95% CI) |
|---|---|
| APHM | Insufficient Data |
| CPRD_AURUM | 0.81 (0.17 - 2.37) |
| CUIMC | 3.41 (0.70 - 9.95) |
| CU_AMC | 0.70 (0.23 - 1.64) |
| FIIBAP | Insufficient Data |
| HIC | Insufficient Data |
| IBM_CCAE | 1.15 (0.95 - 1.39) |
| IBM_MDCD | 0.93 (0.45 - 1.71) |
| IBM_MDCR | 1.23 (0.33 - 3.14) |
| IMASIS | Insufficient Data |
| IPCI | Results Censored |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | 2.89 (0.07 - 16.11) |
| IQVIA_OPENCLAIMS | 1.99 (1.88 - 2.12) |
| IQVIA_PHARMETRICS | 1.32 (1.13 - 1.54) |
| IU | Insufficient Data |
| JMDC | Insufficient Data |
| MHD | Insufficient Data |
| OPTUM_EHR | 1.65 (1.28 - 2.09) |
| OPTUM_SES | 1.33 (1.08 - 1.62) |
| SIDIAP | Results Censored |
| STARR | 0.79 (0.02 - 4.41) |
| UCCS | Insufficient Data |
| UCHDW | 0.68 (0.14 - 1.99) |
| UK_BIOBANK | Insufficient Data |
| U_OF_TARTU | Insufficient Data |
| Summary | 1.32 (1.05 - 1.66) |



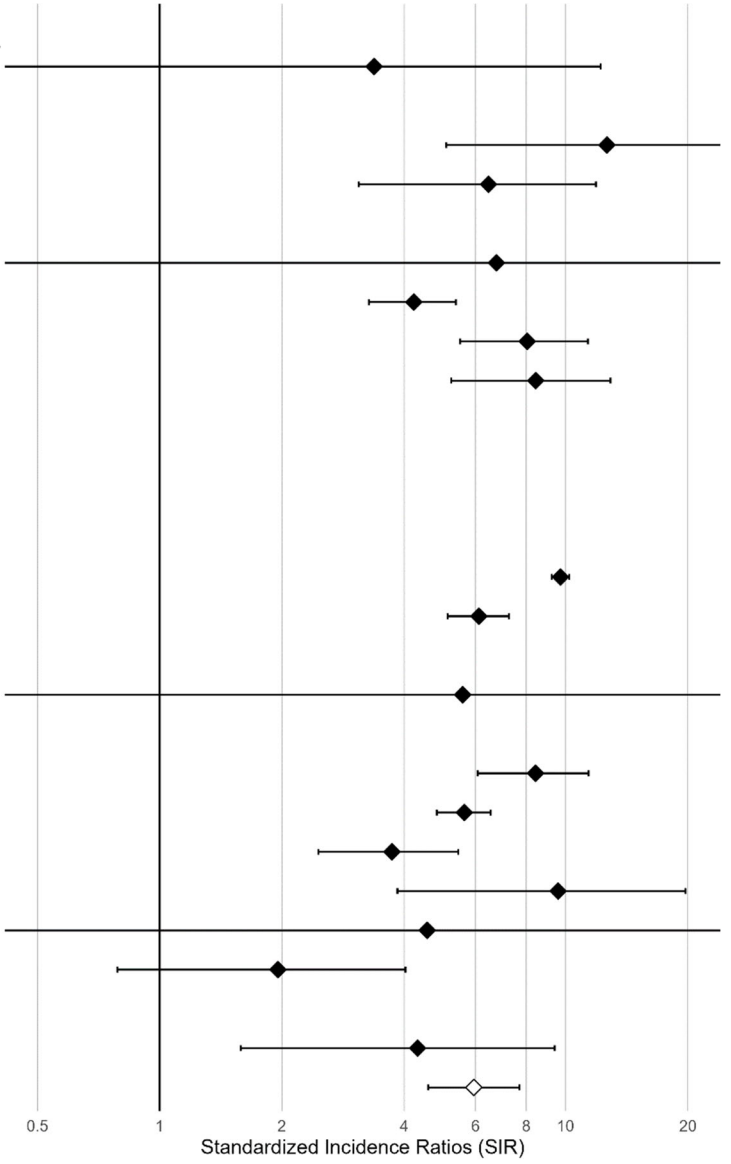
## Disseminated Intravascular Coagulation (DIC)

| Source | SIR (95% CI) |
|---|---|
| APHM | 4.63 (0.12 - 25.81) |
| CPRD_AURUM | 6.25 (0.16 - 34.83) |
| CUIMC | 17.11 (9.78 - 27.79) |
| CU_AMC | 3.75 (1.87 - 6.72) |
| FIIBAP | Insufficient Data |
| HIC | Insufficient Data |
| IBM_CCAE | 6.08 (4.96 - 7.39) |
| IBM_MDCD | 9.88 (7.31 - 13.06) |
| IBM_MDCR | 5.51 (3.45 - 8.35) |
| IMASIS | Insufficient Data |
| IPCI | Results Censored |
| IQVIA_FRANCE_DA | Results Censored |
| IQVIA_GERMANY_DA | Insufficient Data |
| IQVIA_OPENCLAIMS | 12.18 (11.69 - 12.68) |
| IQVIA_PHARMETRICS | 9.78 (8.64 - 11.02) |
| IU | Insufficient Data |
| JMDC | 33.56 (24.99 - 44.12) |
| MHD | Insufficient Data |
| OPTUM_EHR | 9.48 (7.71 - 11.55) |
| OPTUM_SES | 8.62 (7.77 - 9.54) |
| SIDIAP | 4.37 (2.67 - 6.75) |
| STARR | 9.90 (4.75 - 18.21) |
| UCCS | 63.87 (46.03 - 86.33) |
| UCHDW | 6.58 (4.21 - 9.79) |
| UK_BIOBANK | Insufficient Data |
| U_OF_TARTU | 42.57 (11.60 - 108.99) |
| Summary | 8.79 (7.13 - 10.85) |



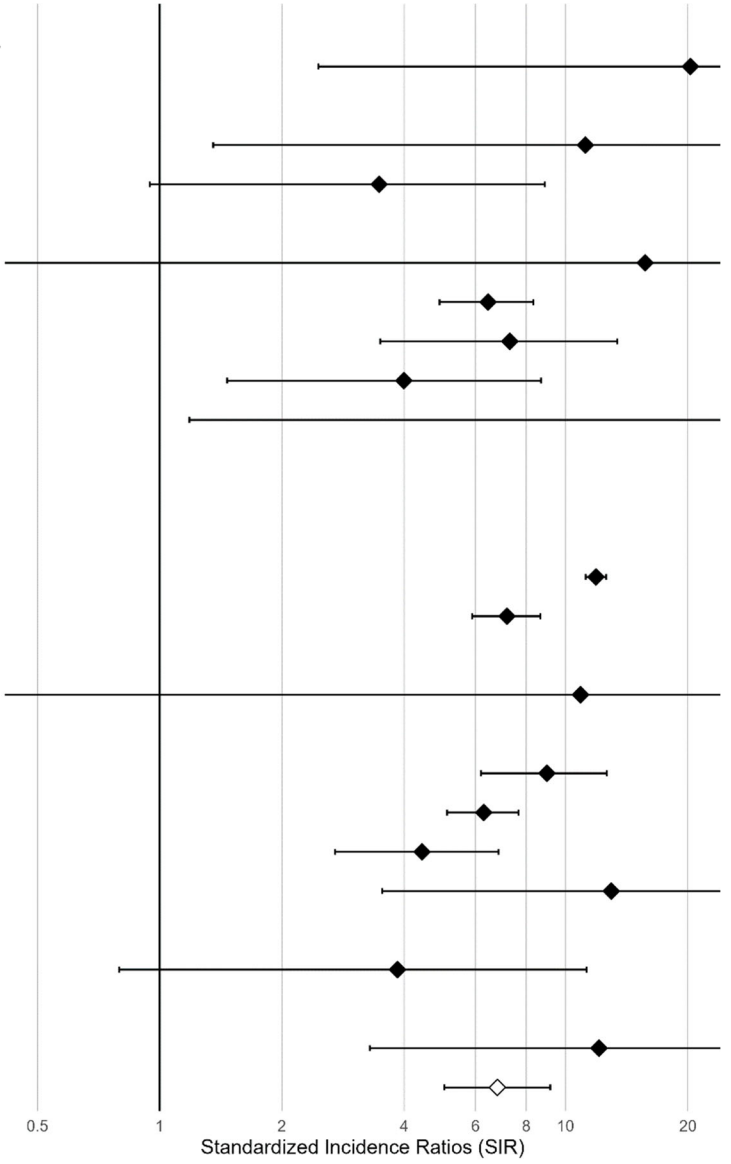
## Encephalomyelitis

| Source | SIR (95% CI) |
|---|---|
| APHM | 3.37 (0.41 - 12.19) |
| CPRD_AURUM | Results Censored |
| CUIMC | 12.64 (5.08 - 26.05) |
| CU_AMC | 6.46 (3.10 - 11.87) |
| FIIBAP | Insufficient Data |
| HIC | 6.76 (0.17 - 37.64) |
| IBM_CCAE | 4.23 (3.28 - 5.37) |
| IBM_MDCD | 8.04 (5.50 - 11.35) |
| IBM_MDCR | 8.44 (5.22 - 12.90) |
| IMASIS | Insufficient Data |
| IPCI | Results Censored |
| IQVIA_FRANCE_DA | Results Censored |
| IQVIA_GERMANY_DA | Results Censored |
| IQVIA_OPENCLAIMS | 9.71 (9.24 - 10.20) |
| IQVIA_PHARMETRICS | 6.12 (5.12 - 7.25) |
| IU | Insufficient Data |
| JMDC | 5.58 (0.14 - 31.08) |
| MHD | Insufficient Data |
| OPTUM_EHR | 8.43 (6.08 - 11.40) |
| OPTUM_SES | 5.63 (4.82 - 6.54) |
| SIDIAP | 3.73 (2.46 - 5.43) |
| STARR | 9.58 (3.85 - 19.75) |
| UCCS | 4.56 (0.12 - 25.40) |
| UCHDW | 1.96 (0.79 - 4.03) |
| UK_BIOBANK | Insufficient Data |
| U_OF_TARTU | 4.32 (1.58 - 9.40) |
| Summary | 5.94 (4.59 - 7.70) |



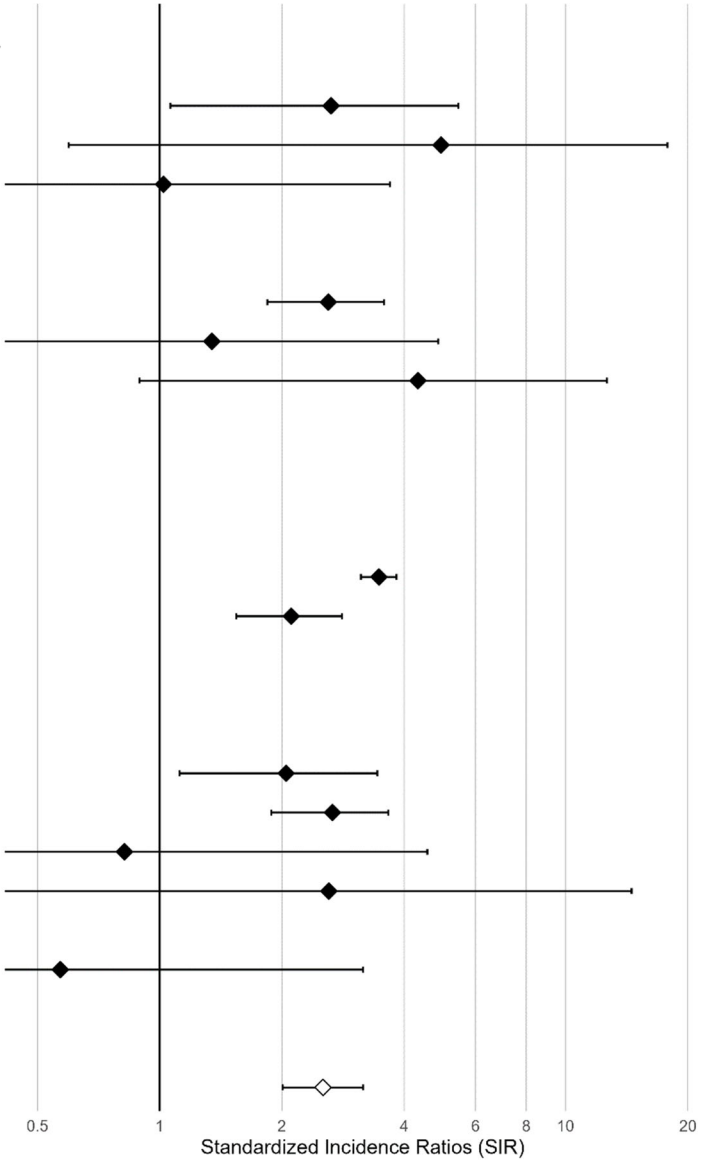
## Guillain-Barré Syndrome

| Source | SIR (95% CI) |
|---|---|
| APHM | 20.30 (2.46 - 73.32) |
| CPRD_AURUM | Results Censored |
| CUIMC | 11.19 (1.35 - 40.41) |
| CU_AMC | 3.47 (0.95 - 8.89) |
| FIIBAP | Insufficient Data |
| HIC | 15.70 (0.40 - 87.47) |
| IBM_CCAE | 6.44 (4.89 - 8.33) |
| IBM_MDCD | 7.28 (3.49 - 13.40) |
| IBM_MDCR | 3.99 (1.47 - 8.70) |
| IMASIS | 46.76 (1.18 - 260.53) |
| IPCI | Results Censored |
| IQVIA_FRANCE_DA | Results Censored |
| IQVIA_GERMANY_DA | Results Censored |
| IQVIA_OPENCLAIMS | 11.88 (11.20 - 12.59) |
| IQVIA_PHARMETRICS | 7.17 (5.88 - 8.66) |
| IU | Insufficient Data |
| JMDC | 10.88 (0.28 - 60.62) |
| MHD | Insufficient Data |
| OPTUM_EHR | 8.99 (6.19 - 12.63) |
| OPTUM_SES | 6.28 (5.11 - 7.65) |
| SIDIAP | 4.43 (2.70 - 6.84) |
| STARR | 12.96 (3.53 - 33.17) |
| UCCS | Insufficient Data |
| UCHDW | 3.85 (0.79 - 11.26) |
| UK_BIOBANK | Insufficient Data |
| U_OF_TARTU | 12.09 (3.29 - 30.95) |
| Summary | 6.79 (5.03 - 9.17) |



## Transverse Myelitis

| Source | SIR (95% CI) |
|---|---|
| APHM | Insufficient Data |
| CPRD_AURUM | 2.64 (1.06 - 5.45) |
| CUIMC | 4.93 (0.60 - 17.82) |
| CU_AMC | 1.02 (0.12 - 3.69) |
| FIIBAP | Insufficient Data |
| HIC | Insufficient Data |
| IBM_CCAE | 2.60 (1.84 - 3.57) |
| IBM_MDCD | 1.34 (0.16 - 4.86) |
| IBM_MDCR | 4.33 (0.89 - 12.64) |
| IMASIS | Insufficient Data |
| IPCI | Results Censored |
| IQVIA_FRANCE_DA | Results Censored |
| IQVIA_GERMANY_DA | Insufficient Data |
| IQVIA_OPENCLAIMS | 3.47 (3.13 - 3.83) |
| IQVIA_PHARMETRICS | 2.11 (1.54 - 2.81) |
| IU | Insufficient Data |
| JMDC | Insufficient Data |
| MHD | Results Censored |
| OPTUM_EHR | 2.05 (1.12 - 3.44) |
| OPTUM_SES | 2.66 (1.89 - 3.66) |
| SIDIAP | 0.82 (0.02 - 4.56) |
| STARR | 2.61 (0.07 - 14.54) |
| UCCS | Insufficient Data |
| UCHDW | 0.57 (0.01 - 3.17) |
| UK_BIOBANK | Insufficient Data |
| U_OF_TARTU | Insufficient Data |
| Summary | 2.53 (2.01 - 3.17) |

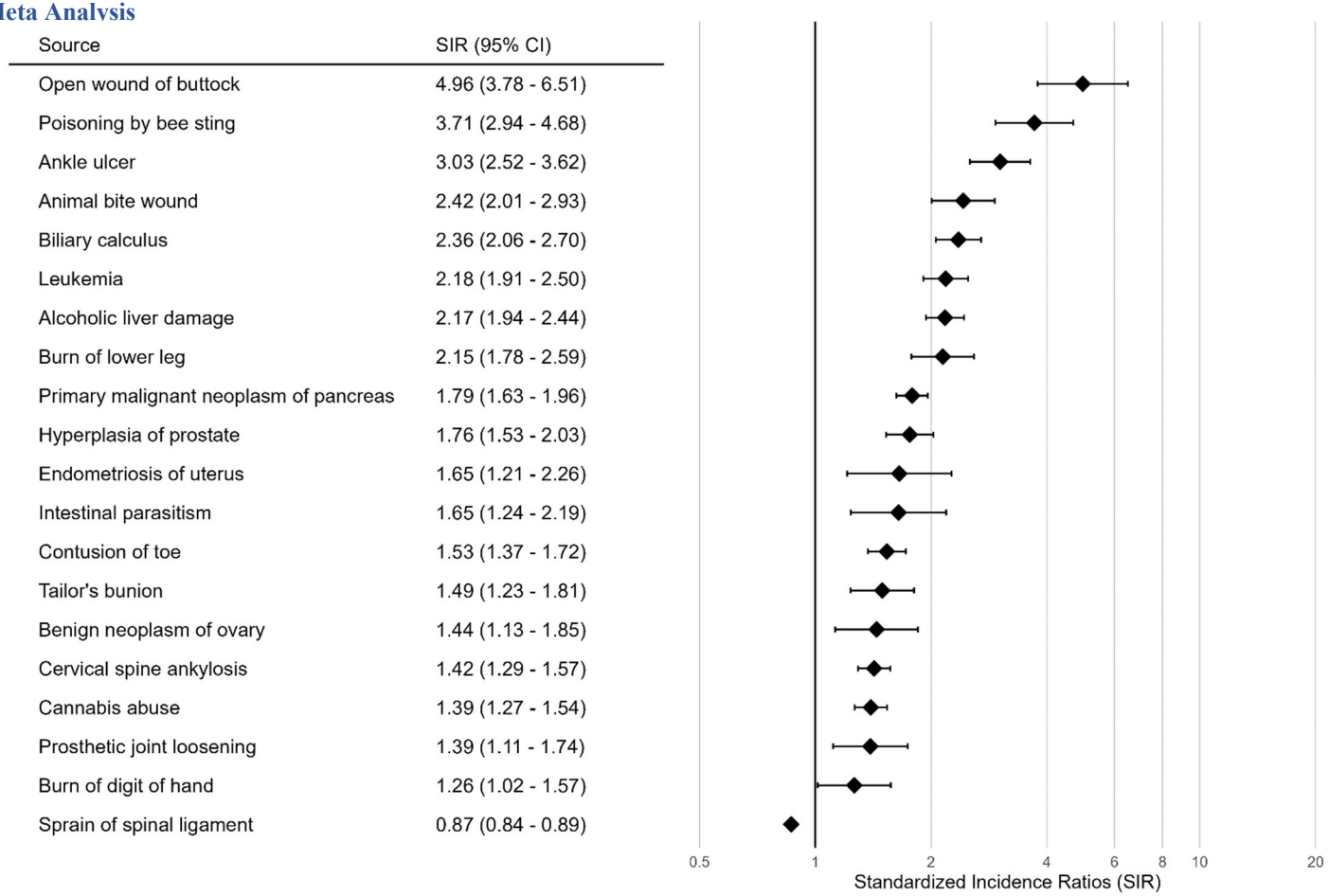


## Appendix 7 - Standardised Incidence Ratios Forest Plots across 9 databases (a subset of the 26 databases) for 20 Negative Controls comparing 'Patients with COVID-19' and 'Pre-Pandemic Background Population'

For each database, for each negative controls results are either:

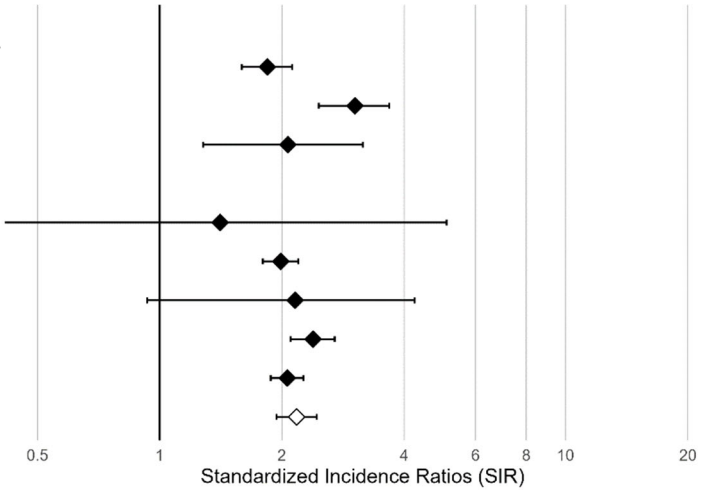
- Reported
- Labelled as "Results Censored" which is based on the exclusions applied from Appendix 2.
- Labelled as "Insufficient data" meaning there were too few cases to provide a valid standardised incidence ratio (SIR)

### Meta Analysis



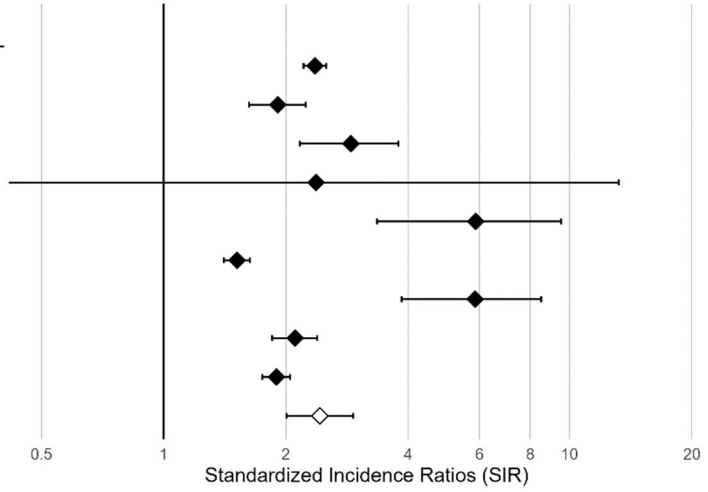
## Alcoholic liver damage

| Source | SIR (95% CI) |
|---|---|
| IBM_CCAE | 1.84 (1.59 - 2.12) |
| IBM_MDCD | 3.03 (2.47 - 3.68) |
| IBM_MDCR | 2.07 (1.28 - 3.16) |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | 1.41 (0.17 - 5.09) |
| IQVIA_PHARMETRICS | 1.99 (1.80 - 2.19) |
| JMDC | 2.16 (0.93 - 4.25) |
| OPTUM_EHR | 2.39 (2.10 - 2.70) |
| OPTUM_SES | 2.06 (1.88 - 2.26) |
| Summary | 2.17 (1.94 - 2.44) |



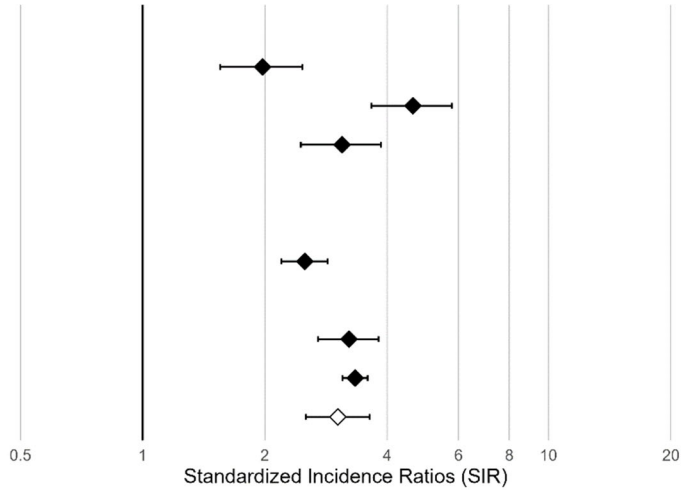

## Animal bite wound

| Source | SIR (95% CI) |
|---|---|
| IBM_CCAE | 2.36 (2.21 - 2.51) |
| IBM_MDCD | 1.91 (1.62 - 2.24) |
| IBM_MDCR | 2.89 (2.17 - 3.78) |
| IQVIA_FRANCE_DA | 2.37 (0.06 - 13.22) |
| IQVIA_GERMANY_DA | 5.87 (3.35 - 9.53) |
| IQVIA_PHARMETRICS | 1.52 (1.41 - 1.63) |
| JMDC | 5.85 (3.86 - 8.51) |
| OPTUM_EHR | 2.11 (1.85 - 2.39) |
| OPTUM_SES | 1.90 (1.75 - 2.05) |
| Summary | 2.42 (2.01 - 2.93) |



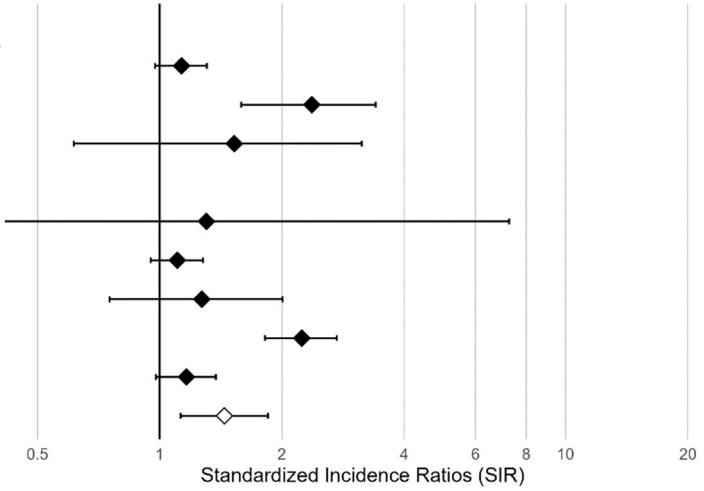
## Ankle ulcer

| Source | SIR (95% CI) |
|---|---|
| IBM_CCAE | 1.97 (1.55 - 2.47) |
| IBM_MDCD | 4.63 (3.66 - 5.78) |
| IBM_MDCR | 3.10 (2.45 - 3.86) |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | Insufficient Data |
| IQVIA_PHARMETRICS | 2.51 (2.20 - 2.85) |
| JMDC | Insufficient Data |
| OPTUM_EHR | 3.22 (2.70 - 3.81) |
| OPTUM_SES | 3.34 (3.11 - 3.58) |
| Summary | 3.03 (2.52 - 3.62) |



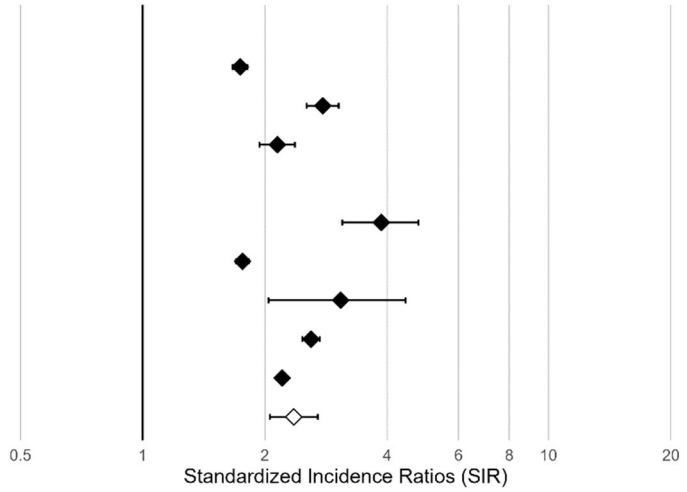

## Benign neoplasm of ovary

| Source | SIR (95% CI) |
|---|---|
| IBM_CCAE | 1.13 (0.97 - 1.31) |
| IBM_MDCD | 2.37 (1.59 - 3.40) |
| IBM_MDCR | 1.53 (0.61 - 3.15) |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | 1.30 (0.03 - 7.26) |
| IQVIA_PHARMETRICS | 1.11 (0.95 - 1.28) |
| JMDC | 1.27 (0.75 - 2.01) |
| OPTUM_EHR | 2.24 (1.82 - 2.73) |
| OPTUM_SES | 1.16 (0.98 - 1.38) |
| Summary | 1.44 (1.13 - 1.85) |



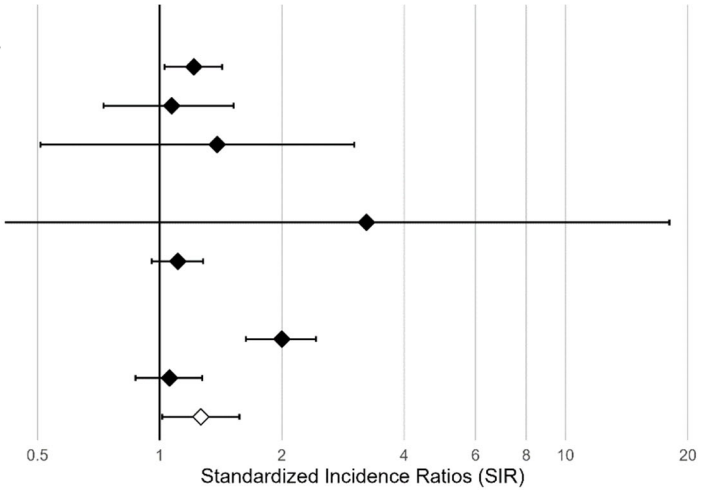
## Biliary calculus

| Source | SIR (95% CI) |
|---|---|
| IBM_CCAE | 1.74 (1.67 - 1.81) |
| IBM_MDCD | 2.78 (2.53 - 3.04) |
| IBM_MDCR | 2.15 (1.94 - 2.37) |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | 3.87 (3.10 - 4.78) |
| IQVIA_PHARMETRICS | 1.76 (1.70 - 1.83) |
| JMDC | 3.07 (2.04 - 4.44) |
| OPTUM_EHR | 2.60 (2.47 - 2.73) |
| OPTUM_SES | 2.21 (2.14 - 2.27) |
| Summary | 2.36 (2.06 - 2.70) |



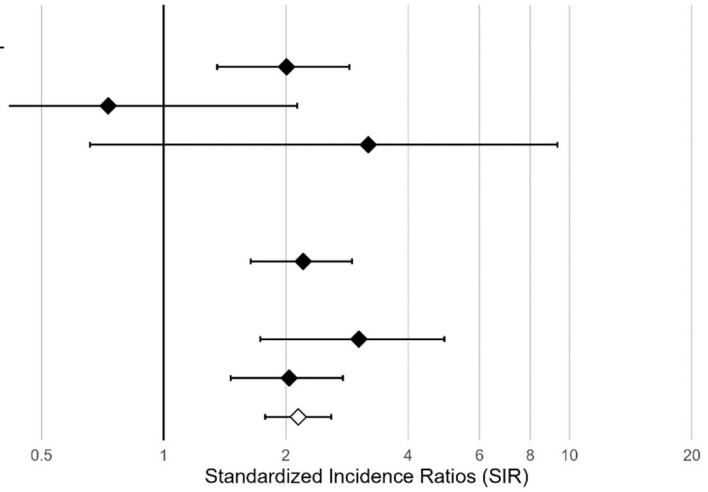

## Burn of digit of hand

| Source | SIR (95% CI) |
|---|---|
| IBM_CCAE | 1.21 (1.03 - 1.42) |
| IBM_MDCD | 1.07 (0.73 - 1.52) |
| IBM_MDCR | 1.39 (0.51 - 3.02) |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | 3.23 (0.08 - 18.01) |
| IQVIA_PHARMETRICS | 1.11 (0.96 - 1.28) |
| JMDC | Insufficient Data |
| OPTUM_EHR | 2.00 (1.63 - 2.43) |
| OPTUM_SES | 1.06 (0.87 - 1.27) |
| Summary | 1.26 (1.02 - 1.57) |



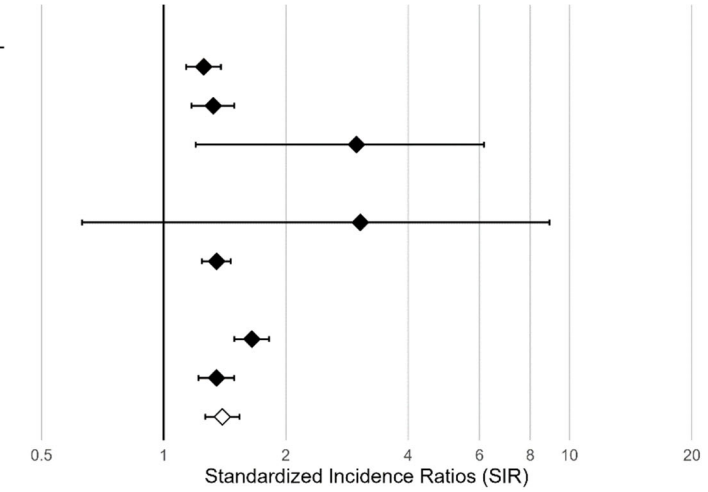
## Burn of lower leg

| Source | SIR (95% CI) |
|---|---|
| IBM_CCAE | 2.01 (1.35 - 2.87) |
| IBM_MDCD | 0.73 (0.15 - 2.13) |
| IBM_MDCR | 3.19 (0.66 - 9.33) |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | Insufficient Data |
| IQVIA_PHARMETRICS | 2.21 (1.64 - 2.91) |
| JMDC | Insufficient Data |
| OPTUM_EHR | 3.03 (1.73 - 4.91) |
| OPTUM_SES | 2.04 (1.46 - 2.76) |
| Summary | 2.15 (1.78 - 2.59) |



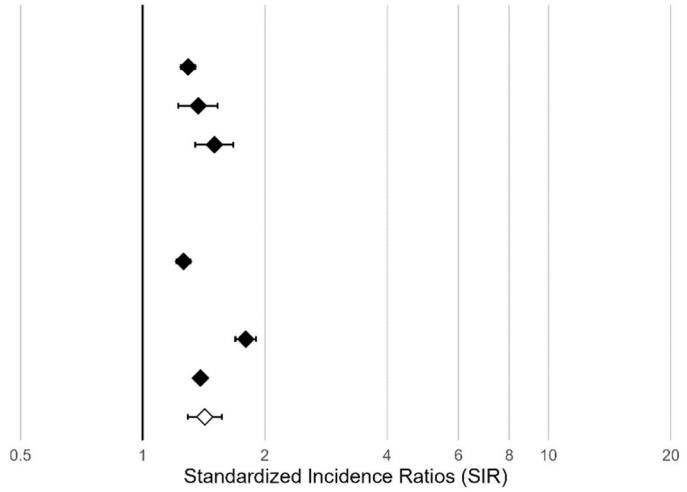

## Cannabis abuse

| Source | SIR (95% CI) |
|---|---|
| IBM_CCAE | 1.25 (1.14 - 1.38) |
| IBM_MDCD | 1.32 (1.17 - 1.49) |
| IBM_MDCR | 2.98 (1.20 - 6.15) |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | 3.05 (0.63 - 8.91) |
| IQVIA_PHARMETRICS | 1.35 (1.24 - 1.46) |
| JMDC | Insufficient Data |
| OPTUM_EHR | 1.65 (1.49 - 1.82) |
| OPTUM_SES | 1.35 (1.22 - 1.49) |
| Summary | 1.39 (1.27 - 1.54) |



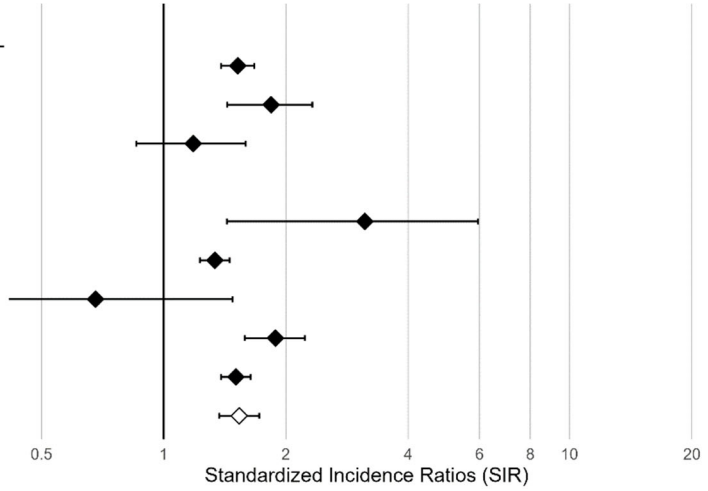
## Cervical spine ankylosis

| Source | SIR (95% CI) |
|---|---|
| IBM_CCAE | 1.29 (1.24 - 1.35) |
| IBM_MDCD | 1.37 (1.22 - 1.53) |
| IBM_MDCR | 1.50 (1.35 - 1.67) |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | Insufficient Data |
| IQVIA_PHARMETRICS | 1.26 (1.21 - 1.31) |
| JMDC | Insufficient Data |
| OPTUM_EHR | 1.79 (1.69 - 1.90) |
| OPTUM_SES | 1.39 (1.35 - 1.43) |
| Summary | 1.42 (1.29 - 1.57) |



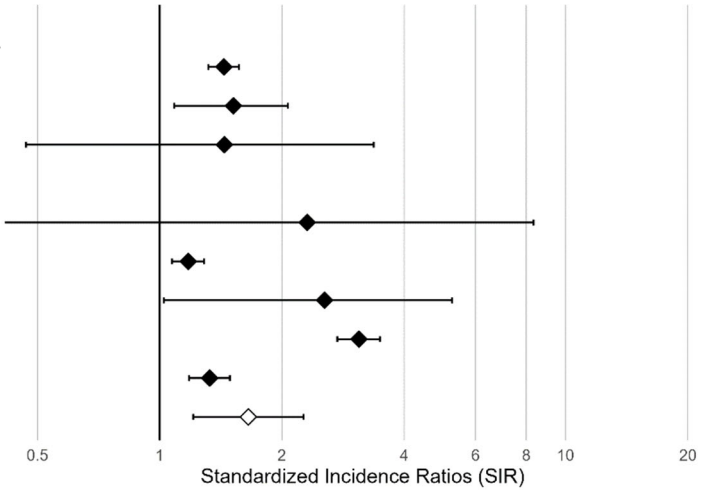

## Contusion of toe

| Source | SIR (95% CI) |
|---|---|
| IBM_CCAE | 1.52 (1.38 - 1.67) |
| IBM_MDCD | 1.84 (1.43 - 2.32) |
| IBM_MDCR | 1.18 (0.86 - 1.59) |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | 3.13 (1.43 - 5.94) |
| IQVIA_PHARMETRICS | 1.34 (1.23 - 1.45) |
| JMDC | 0.68 (0.25 - 1.48) |
| OPTUM_EHR | 1.89 (1.58 - 2.23) |
| OPTUM_SES | 1.51 (1.38 - 1.64) |
| Summary | 1.53 (1.37 - 1.72) |



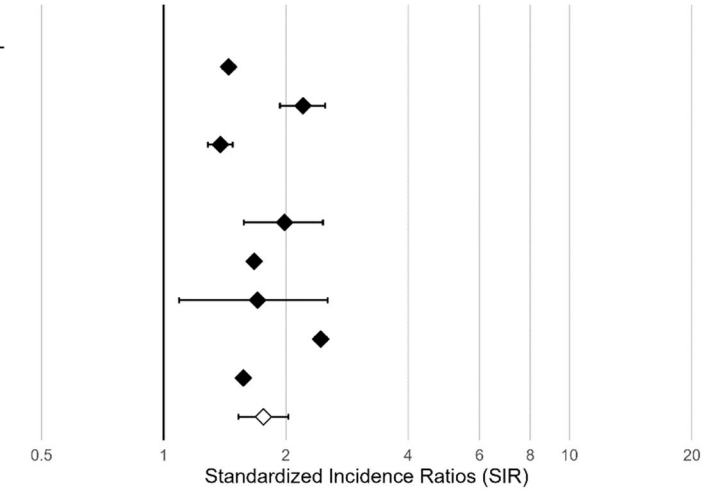
## Endometriosis of uterus

| Source | SIR (95% CI) |
|---|---|
| IBM_CCAE | 1.44 (1.32 - 1.57) |
| IBM_MDCD | 1.52 (1.09 - 2.07) |
| IBM_MDCR | 1.44 (0.47 - 3.37) |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | 2.31 (0.28 - 8.34) |
| IQVIA_PHARMETRICS | 1.18 (1.07 - 1.29) |
| JMDC | 2.55 (1.02 - 5.25) |
| OPTUM_EHR | 3.10 (2.74 - 3.49) |
| OPTUM_SES | 1.33 (1.18 - 1.49) |
| Summary | 1.65 (1.21 - 2.26) |



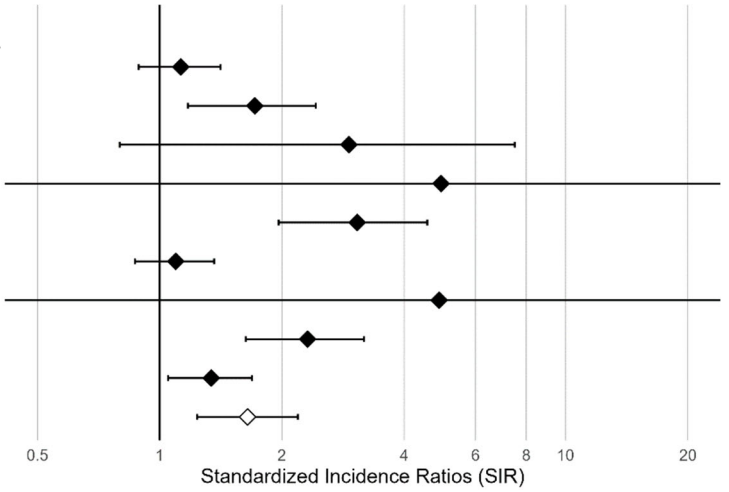

## Hyperplasia of prostate

| Source | SIR (95% CI) |
|---|---|
| IBM_CCAE | 1.45 (1.40 - 1.49) |
| IBM_MDCD | 2.20 (1.93 - 2.50) |
| IBM_MDCR | 1.38 (1.28 - 1.48) |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | 1.98 (1.58 - 2.47) |
| IQVIA_PHARMETRICS | 1.67 (1.63 - 1.71) |
| JMDC | 1.70 (1.09 - 2.53) |
| OPTUM_EHR | 2.44 (2.36 - 2.52) |
| OPTUM_SES | 1.57 (1.54 - 1.60) |
| Summary | 1.76 (1.53 - 2.03) |



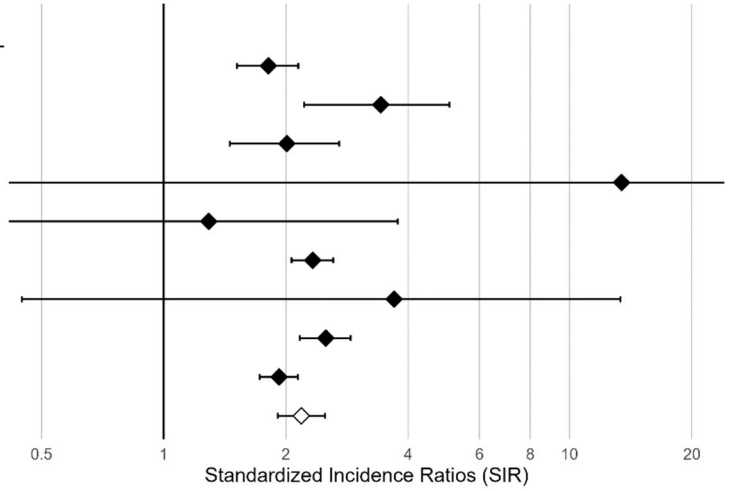
## Intestinal parasitism

| Source | SIR (95% CI) |
|---|---|
| IBM_CCAE | 1.13 (0.89 - 1.41) |
| IBM_MDCD | 1.72 (1.17 - 2.42) |
| IBM_MDCR | 2.93 (0.80 - 7.49) |
| IQVIA_FRANCE_DA | 4.93 (0.12 - 27.49) |
| IQVIA_GERMANY_DA | 3.07 (1.96 - 4.56) |
| IQVIA_PHARMETRICS | 1.10 (0.87 - 1.36) |
| JMDC | 4.88 (0.12 - 27.19) |
| OPTUM_EHR | 2.31 (1.63 - 3.19) |
| OPTUM_SES | 1.34 (1.05 - 1.69) |
| Summary | 1.65 (1.24 - 2.19) |



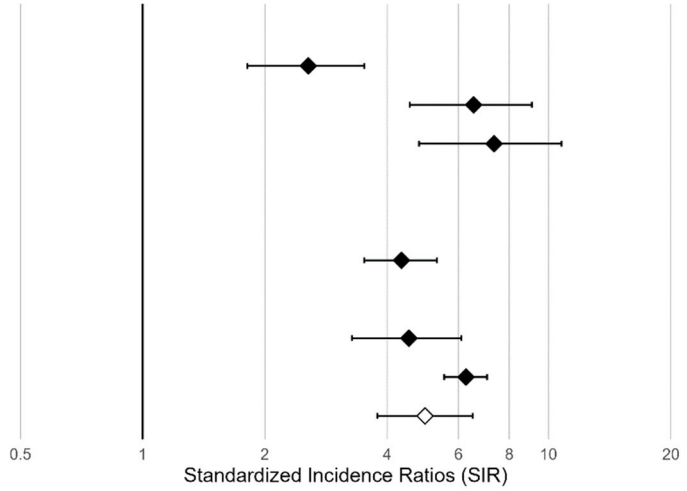

## Leukaemia

| Source | SIR (95% CI) |
|---|---|
| IBM_CCAE | 1.81 (1.52 - 2.15) |
| IBM_MDCD | 3.43 (2.22 - 5.06) |
| IBM_MDCR | 2.01 (1.46 - 2.71) |
| IQVIA_FRANCE_DA | 13.43 (0.34 - 74.80) |
| IQVIA_GERMANY_DA | 1.29 (0.27 - 3.77) |
| IQVIA_PHARMETRICS | 2.33 (2.06 - 2.62) |
| JMDC | 3.70 (0.45 - 13.35) |
| OPTUM_EHR | 2.51 (2.17 - 2.89) |
| OPTUM_SES | 1.92 (1.72 - 2.14) |
| Summary | 2.18 (1.91 - 2.50) |



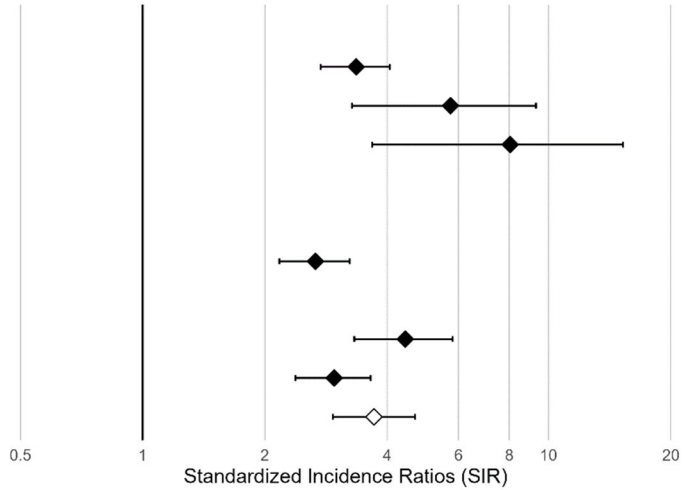
## Open wound of buttock

| Source | SIR (95% CI) |
|---|---|
| IBM_CCAE | 2.56 (1.81 - 3.51) |
| IBM_MDCD | 6.53 (4.55 - 9.09) |
| IBM_MDCR | 7.34 (4.79 - 10.75) |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | Insufficient Data |
| IQVIA_PHARMETRICS | 4.34 (3.51 - 5.31) |
| JMDC | Insufficient Data |
| OPTUM_EHR | 4.53 (3.28 - 6.10) |
| OPTUM_SES | 6.26 (5.53 - 7.05) |
| Summary | 4.96 (3.78 - 6.51) |



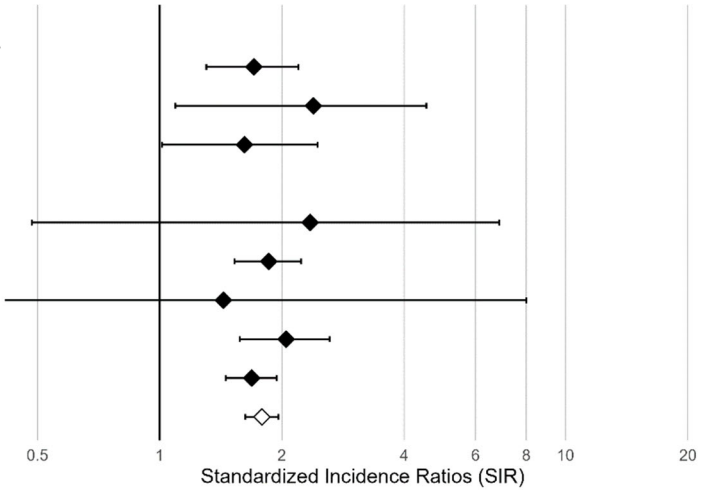

## Poisoning by bee sting

| Source | SIR (95% CI) |
|---|---|
| IBM_CCAE | 3.36 (2.75 - 4.06) |
| IBM_MDCD | 5.73 (3.28 - 9.31) |
| IBM_MDCR | 8.04 (3.68 - 15.26) |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | Insufficient Data |
| IQVIA_PHARMETRICS | 2.66 (2.17 - 3.24) |
| JMDC | Insufficient Data |
| OPTUM_EHR | 4.43 (3.32 - 5.80) |
| OPTUM_SES | 2.96 (2.38 - 3.65) |
| Summary | 3.71 (2.94 - 4.68) |



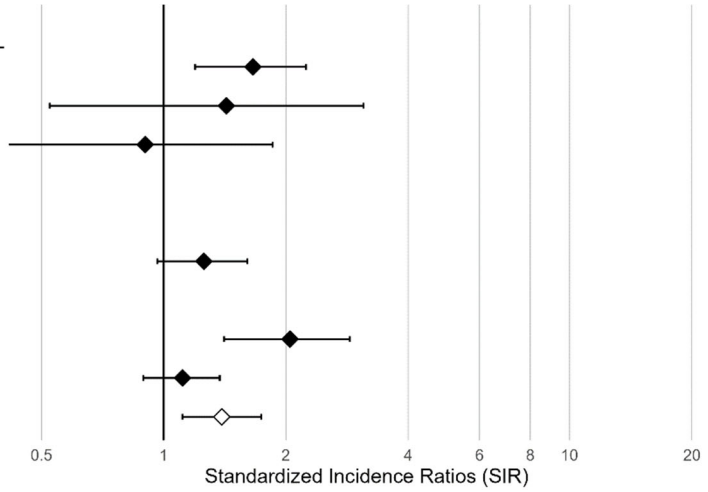
## Primary malignant neoplasm of pancreas

| Source | SIR (95% CI) |
|---|---|
| IBM_CCAE | 1.71 (1.30 - 2.20) |
| IBM_MDCD | 2.39 (1.09 - 4.54) |
| IBM_MDCR | 1.62 (1.01 - 2.45) |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | 2.35 (0.48 - 6.86) |
| IQVIA_PHARMETRICS | 1.86 (1.53 - 2.23) |
| JMDC | 1.44 (0.04 - 8.00) |
| OPTUM_EHR | 2.05 (1.57 - 2.62) |
| OPTUM_SES | 1.69 (1.45 - 1.94) |
| Summary | 1.79 (1.63 - 1.96) |



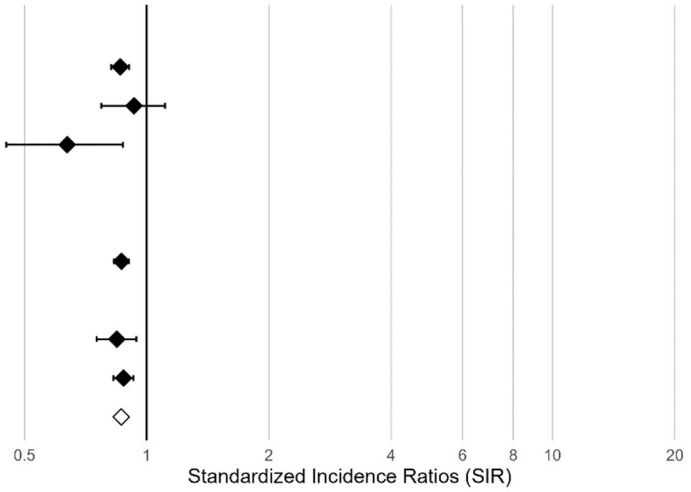

## Prosthetic joint loosening

| Source | SIR (95% CI) |
|---|---|
| IBM_CCAE | 1.66 (1.20 - 2.24) |
| IBM_MDCD | 1.43 (0.52 - 3.11) |
| IBM_MDCR | 0.90 (0.36 - 1.86) |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | Insufficient Data |
| IQVIA_PHARMETRICS | 1.26 (0.97 - 1.61) |
| JMDC | Insufficient Data |
| OPTUM_EHR | 2.05 (1.41 - 2.87) |
| OPTUM_SES | 1.11 (0.89 - 1.37) |
| Summary | 1.39 (1.11 - 1.74) |



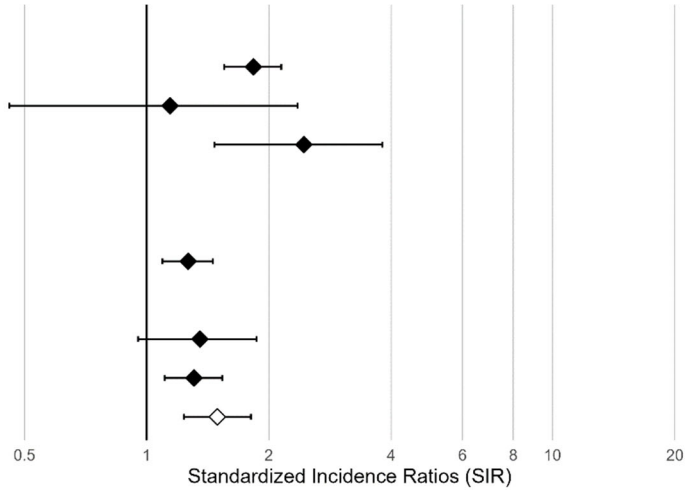
## Sprain of spinal ligament

| Source | SIR (95% CI) |
|---|---|
| IBM_CCAE | 0.86 (0.82 - 0.91) |
| IBM_MDCD | 0.93 (0.77 - 1.11) |
| IBM_MDCR | 0.64 (0.45 - 0.87) |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | Insufficient Data |
| IQVIA_PHARMETRICS | 0.87 (0.83 - 0.90) |
| JMDC | Insufficient Data |
| OPTUM_EHR | 0.84 (0.75 - 0.94) |
| OPTUM_SES | 0.88 (0.83 - 0.93) |
| Summary | 0.87 (0.84 - 0.89) |




## Tailor's bunion

| Source | SIR (95% CI) |
|---|---|
| IBM_CCAE | 1.83 (1.55 - 2.15) |
| IBM_MDCD | 1.14 (0.46 - 2.35) |
| IBM_MDCR | 2.44 (1.47 - 3.81) |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | Insufficient Data |
| IQVIA_PHARMETRICS | 1.27 (1.09 - 1.46) |
| JMDC | Insufficient Data |
| OPTUM_EHR | 1.35 (0.95 - 1.86) |
| OPTUM_SES | 1.31 (1.11 - 1.53) |
| Summary | 1.49 (1.23 - 1.81) |



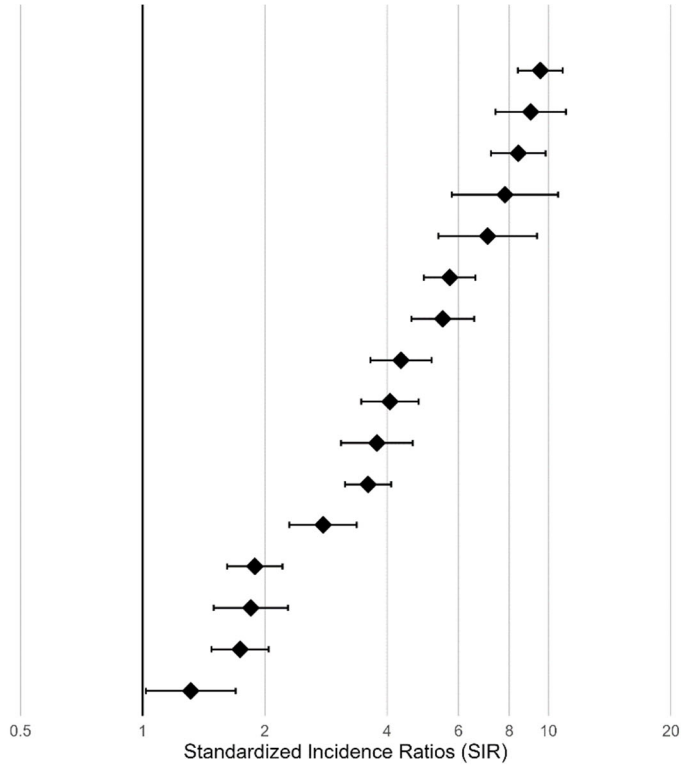
## Appendix 8 - Standardised Incidence Ratios Forest Plots across 26 databases for 16 Adverse Events of Special Interest comparing 'Patients with COVID-19' prior to 2021 and 'Pre-Pandemic Background Population'

For each database, for each adverse event of special interest (AESI) results are either:

- Reported
- Labelled as "Results Censored" which is based on the exclusions applied from Appendix 2.
- Labelled as "Insufficient data" meaning there were too few cases to provide a valid standardised incidence ratio (SIR)

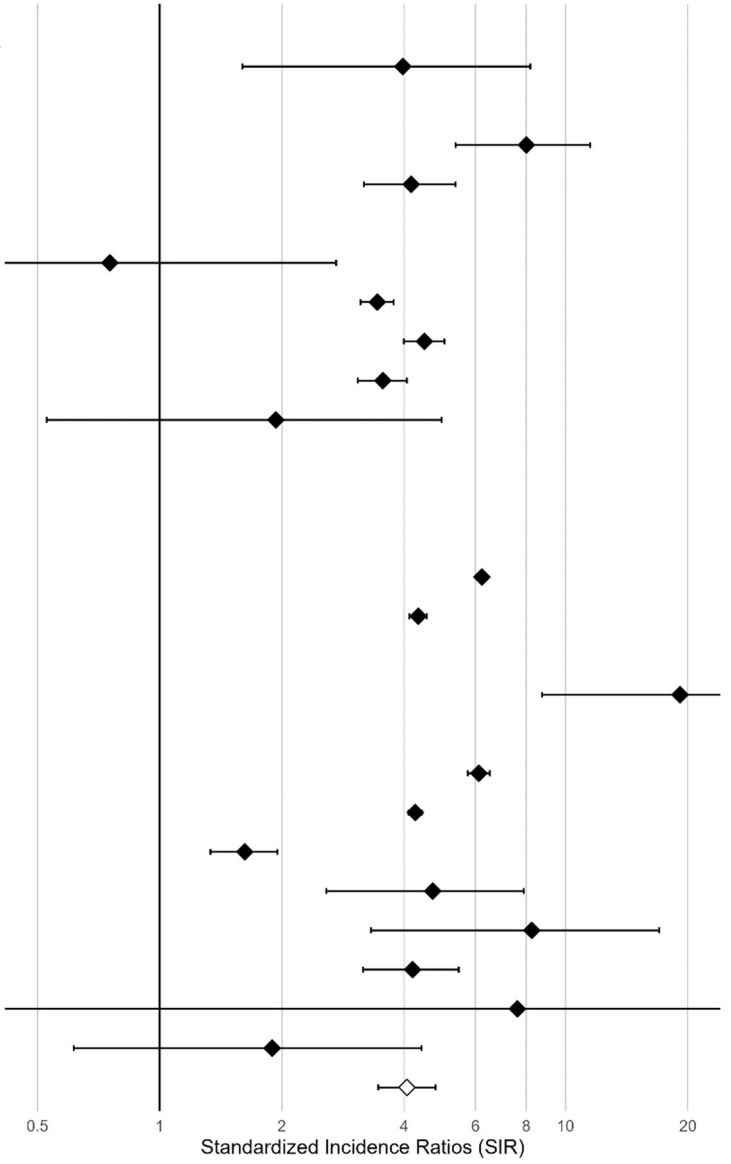
### Meta Analysis

| Source | SIR (95% CI) |
|---|---|
| Pulmonary Embolism | 9.54 (8.40 - 10.84) |
| Disseminated Intravascular Coagulation | 9.03 (7.40 - 11.03) |
| Myocarditis Pericarditis | 8.42 (7.21 - 9.83) |
| Guillain Barre Syndrome | 7.81 (5.78 - 10.55) |
| Encephalomyelitis | 7.08 (5.35 - 9.36) |
| Thrombosis with Thrombocytopenia (TWT) | 5.71 (4.93 - 6.61) |
| Deep Vein Thrombosis (DVT) | 5.49 (4.59 - 6.55) |
| Non-hemorrhagic Stroke | 4.33 (3.64 - 5.15) |
| Acute Myocardial Infarction | 4.07 (3.46 - 4.78) |
| Hemorrhagic Stroke | 3.78 (3.08 - 4.63) |
| Immune Thrombocytopenia (ITP) | 3.59 (3.15 - 4.09) |
| Transverse Myelitis | 2.78 (2.30 - 3.37) |
| Bells Palsy | 1.89 (1.61 - 2.21) |
| Anaphylaxis | 1.85 (1.50 - 2.28) |
| Appendicitis | 1.74 (1.48 - 2.04) |
| Narcolepsy | 1.31 (1.02 - 1.69) |



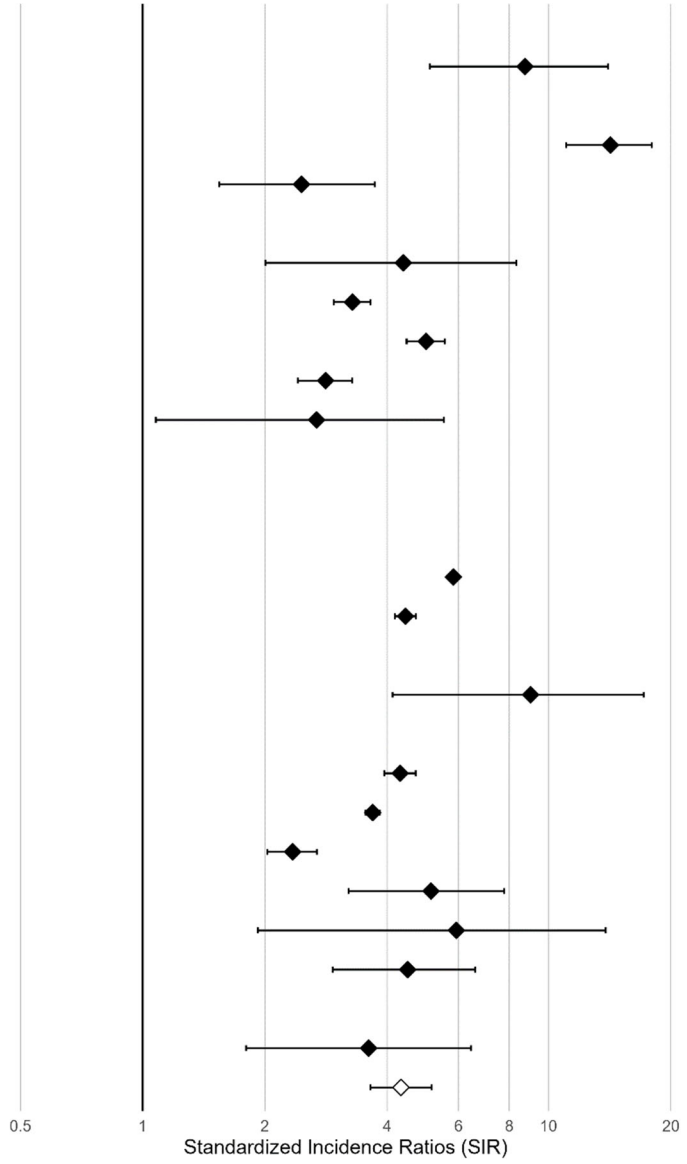
## Acute Myocardial Infarction

| Source | SIR (95% CI) |
|---|---|
| APHM | 3.97 (1.60 - 8.18) |
| CPRD_AURUM | Results Censored |
| CUIMC | 8.00 (5.36 - 11.50) |
| CU_AMC | 4.17 (3.19 - 5.35) |
| FIIBAP | Insufficient Data |
| HIC | 0.75 (0.09 - 2.72) |
| IBM_CCAE | 3.44 (3.13 - 3.77) |
| IBM_MDCD | 4.49 (3.99 - 5.03) |
| IBM_MDCR | 3.55 (3.08 - 4.07) |
| IMASIS | 1.93 (0.53 - 4.95) |
| IPCI | Results Censored |
| IQVIA_FRANCE_DA | Results Censored |
| IQVIA_GERMANY_DA | Results Censored |
| IQVIA_OPENCLAIMS | 6.22 (6.12 - 6.32) |
| IQVIA_PHARMETRICS | 4.33 (4.12 - 4.55) |
| IU | Insufficient Data |
| JMDC | 19.13 (8.75 - 36.31) |
| MHD | Insufficient Data |
| OPTUM_EHR | 6.11 (5.74 - 6.51) |
| OPTUM_SES | 4.26 (4.11 - 4.42) |
| SIDIAP | 1.62 (1.33 - 1.95) |
| STARR | 4.70 (2.57 - 7.89) |
| UCCS | 8.25 (3.32 - 17.00) |
| UCHDW | 4.20 (3.17 - 5.45) |
| UK_BIOBANK | 7.60 (0.19 - 42.37) |
| U_OF_TARTU | 1.89 (0.61 - 4.42) |
| Summary | 4.07 (3.46 - 4.78) |



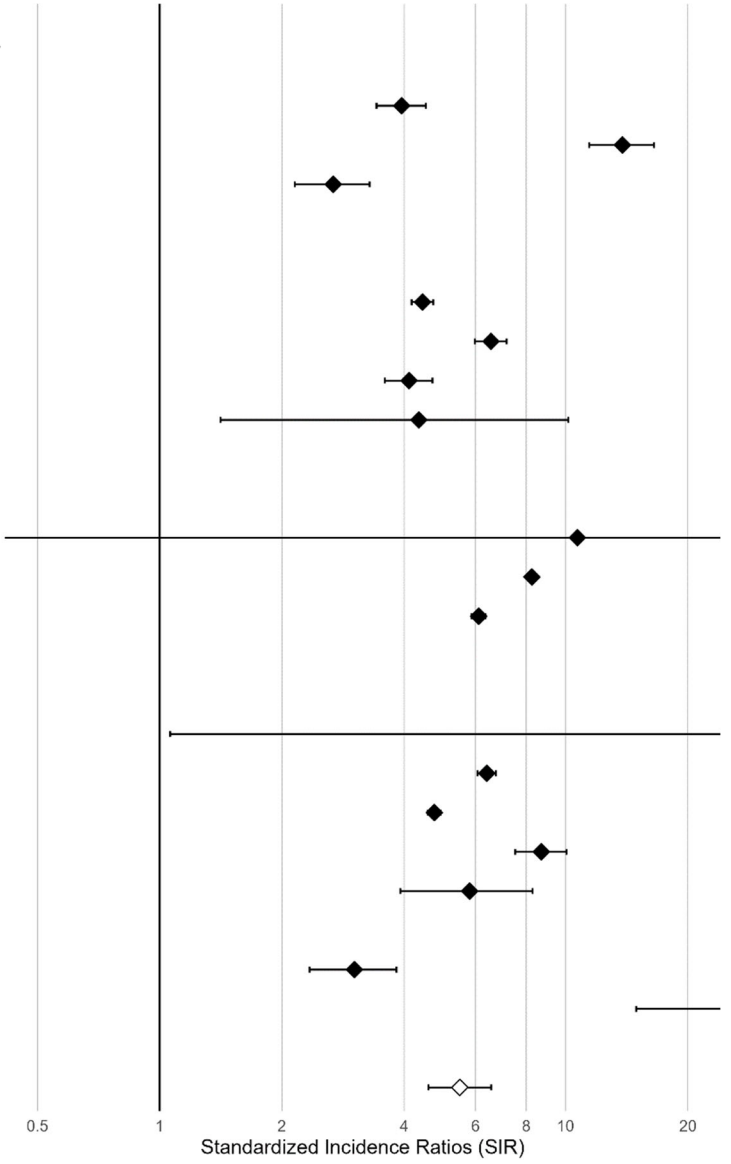
## Non-haemorrhagic Stroke

| Source | SIR (95% CI) |
|---|---|
| APHM | 8.75 (5.10 - 14.00) |
| CPRD_AURUM | Results Censored |
| CUIMC | 14.20 (11.05 - 17.97) |
| CU_AMC | 2.46 (1.54 - 3.73) |
| FIIBAP | Insufficient Data |
| HIC | 4.39 (2.01 - 8.33) |
| IBM_CCAE | 3.29 (2.96 - 3.64) |
| IBM_MDCD | 4.99 (4.47 - 5.55) |
| IBM_MDCR | 2.82 (2.41 - 3.28) |
| IMASIS | 2.68 (1.08 - 5.52) |
| IPCI | Results Censored |
| IQVIA_FRANCE_DA | Results Censored |
| IQVIA_GERMANY_DA | Results Censored |
| IQVIA_OPENCLAIMS | 5.83 (5.73 - 5.92) |
| IQVIA_PHARMETRICS | 4.44 (4.18 - 4.71) |
| IU | Insufficient Data |
| JMDC | 9.03 (4.13 - 17.14) |
| MHD | Insufficient Data |
| OPTUM_EHR | 4.31 (3.94 - 4.70) |
| OPTUM_SES | 3.69 (3.54 - 3.83) |
| SIDIAP | 2.34 (2.03 - 2.69) |
| STARR | 5.13 (3.22 - 7.77) |
| UCCS | 5.92 (1.92 - 13.82) |
| UCHDW | 4.50 (2.94 - 6.59) |
| UK_BIOBANK | Insufficient Data |
| U_OF_TARTU | 3.60 (1.80 - 6.44) |
| Summary | 4.33 (3.64 - 5.15) |



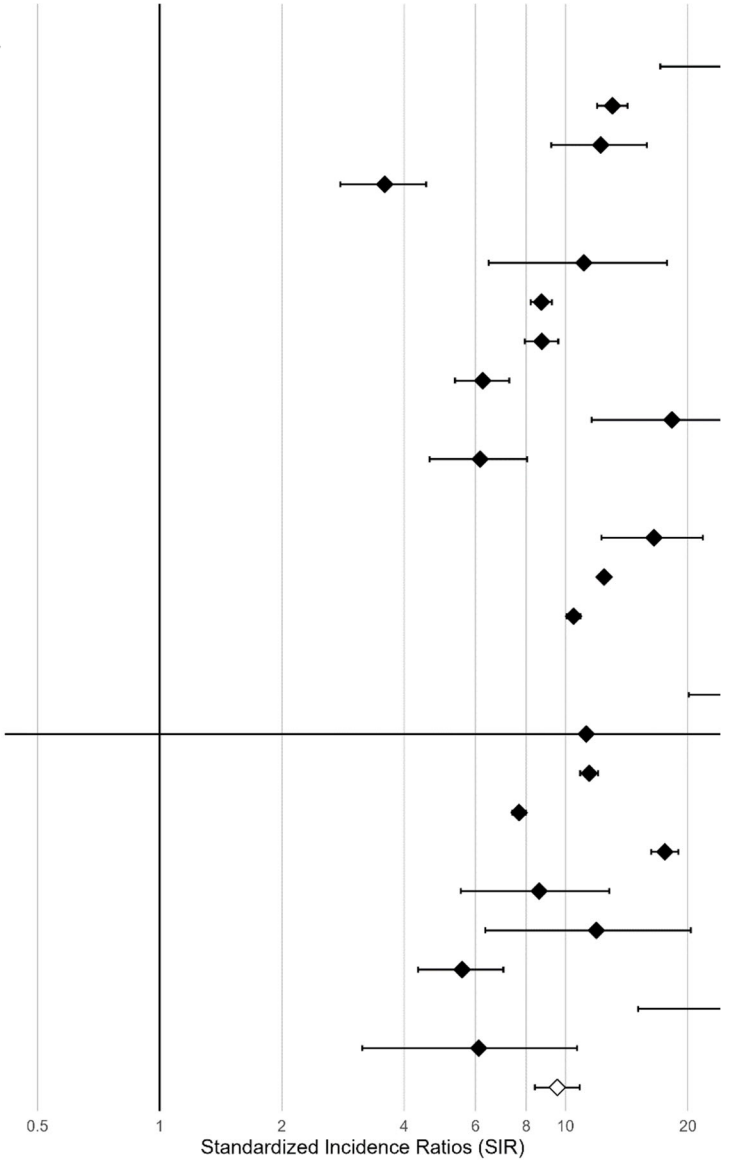
## Deep Vein Thrombosis (DVT)

| Source | SIR (95% CI) |
|---|---|
| APHM | Insufficient Data |
| CPRD_AURUM | 3.94 (3.42 - 4.52) |
| CUIMC | 13.80 (11.43 - 16.51) |
| CU_AMC | 2.68 (2.15 - 3.29) |
| FIIBAP | Insufficient Data |
| HIC | Insufficient Data |
| IBM_CCAE | 4.44 (4.17 - 4.72) |
| IBM_MDCD | 6.55 (5.98 - 7.16) |
| IBM_MDCR | 4.11 (3.59 - 4.70) |
| IMASIS | 4.35 (1.41 - 10.15) |
| IPCI | Results Censored |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | 10.69 (0.27 - 59.58) |
| IQVIA_OPENCLAIMS | 8.26 (8.15 - 8.37) |
| IQVIA_PHARMETRICS | 6.11 (5.87 - 6.35) |
| IU | Results Censored |
| JMDC | Insufficient Data |
| MHD | 41.94 (1.06 - 233.67) |
| OPTUM_EHR | 6.40 (6.07 - 6.74) |
| OPTUM_SES | 4.75 (4.58 - 4.92) |
| SIDIAP | 8.71 (7.52 - 10.04) |
| STARR | 5.80 (3.92 - 8.28) |
| UCCS | Insufficient Data |
| UCHDW | 3.02 (2.34 - 3.83) |
| UK_BIOBANK | 28.87 (14.92 - 50.43) |
| U_OF_TARTU | Insufficient Data |
| Summary | 5.49 (4.59 - 6.55) |



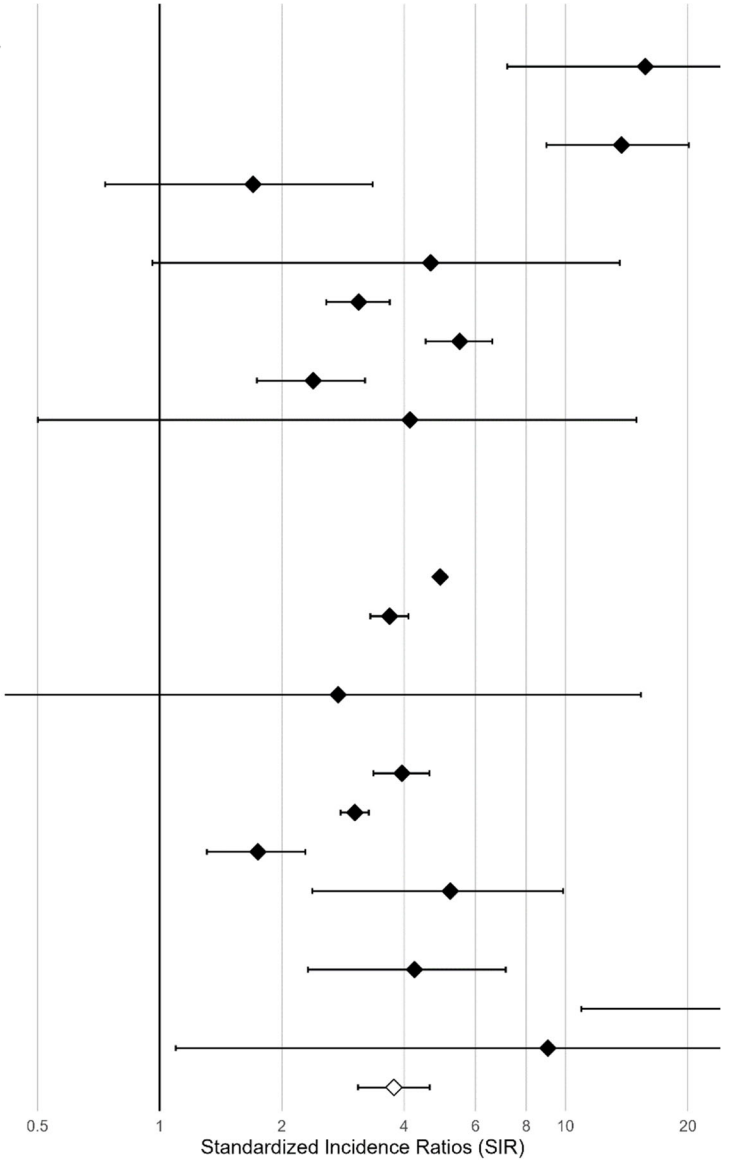
## Pulmonary Embolism (PE)

| Source | SIR (95% CI) |
|---|---|
| APHM | 26.45 (17.11 - 39.04) |
| CPRD_AURUM | 13.04 (11.95 - 14.20) |
| CUIMC | 12.20 (9.22 - 15.85) |
| CU_AMC | 3.58 (2.79 - 4.53) |
| FIIBAP | Insufficient Data |
| HIC | 11.09 (6.46 - 17.76) |
| IBM_CCAE | 8.72 (8.20 - 9.25) |
| IBM_MDCD | 8.74 (7.94 - 9.59) |
| IBM_MDCR | 6.25 (5.34 - 7.26) |
| IMASIS | 18.28 (11.59 - 27.42) |
| IPCI | 6.16 (4.63 - 8.03) |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | 16.51 (12.25 - 21.76) |
| IQVIA_OPENCLAIMS | 12.44 (12.27 - 12.61) |
| IQVIA_PHARMETRICS | 10.46 (10.06 - 10.87) |
| IU | Insufficient Data |
| JMDC | 41.92 (20.10 - 77.09) |
| MHD | 11.24 (0.28 - 62.63) |
| OPTUM_EHR | 11.43 (10.86 - 12.03) |
| OPTUM_SES | 7.68 (7.39 - 7.98) |
| SIDIAP | 17.56 (16.24 - 18.95) |
| STARR | 8.60 (5.51 - 12.80) |
| UCCS | 11.90 (6.34 - 20.36) |
| UCHDW | 5.56 (4.33 - 7.02) |
| UK_BIOBANK | 26.94 (15.08 - 44.44) |
| U_OF_TARTU | 6.11 (3.16 - 10.67) |
| Summary | 9.54 (8.40 - 10.84) |



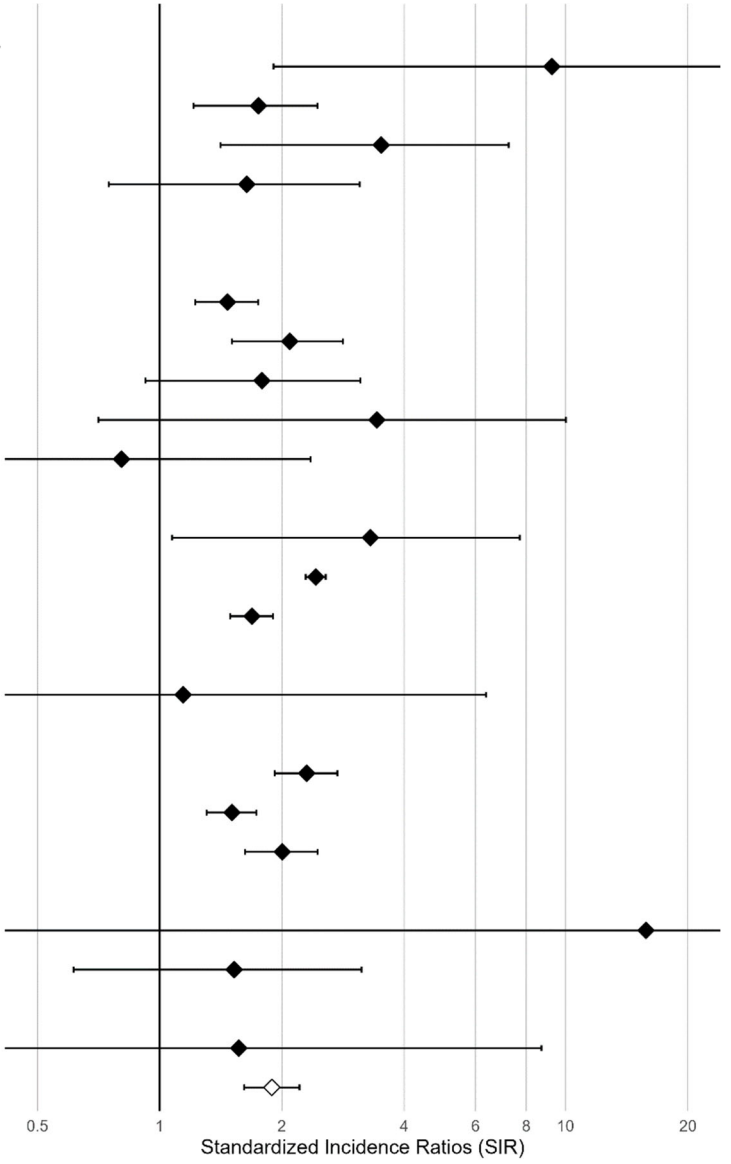
## Haemorrhagic Stroke

| Source | SIR (95% CI) |
|---|---|
| APHM | 15.71 (7.18 - 29.82) |
| CPRD_AURUM | Results Censored |
| CUIMC | 13.73 (8.97 - 20.11) |
| CU_AMC | 1.70 (0.73 - 3.35) |
| FIIBAP | Insufficient Data |
| HIC | 4.65 (0.96 - 13.59) |
| IBM_CCAE | 3.09 (2.57 - 3.69) |
| IBM_MDCD | 5.48 (4.52 - 6.59) |
| IBM_MDCR | 2.39 (1.74 - 3.21) |
| IMASIS | 4.14 (0.50 - 14.94) |
| IPCI | Results Censored |
| IQVIA_FRANCE_DA | Results Censored |
| IQVIA_GERMANY_DA | Results Censored |
| IQVIA_OPENCLAIMS | 4.91 (4.75 - 5.07) |
| IQVIA_PHARMETRICS | 3.68 (3.30 - 4.10) |
| IU | Insufficient Data |
| JMDC | 2.75 (0.07 - 15.33) |
| MHD | Insufficient Data |
| OPTUM_EHR | 3.95 (3.36 - 4.62) |
| OPTUM_SES | 3.03 (2.79 - 3.27) |
| SIDIAP | 1.75 (1.31 - 2.28) |
| STARR | 5.20 (2.38 - 9.86) |
| UCCS | Insufficient Data |
| UCHDW | 4.24 (2.32 - 7.12) |
| UK_BIOBANK | 90.21 (10.92 - 325.87) |
| U_OF_TARTU | 9.04 (1.10 - 32.66) |
| Summary | 3.78 (3.08 - 4.63) |



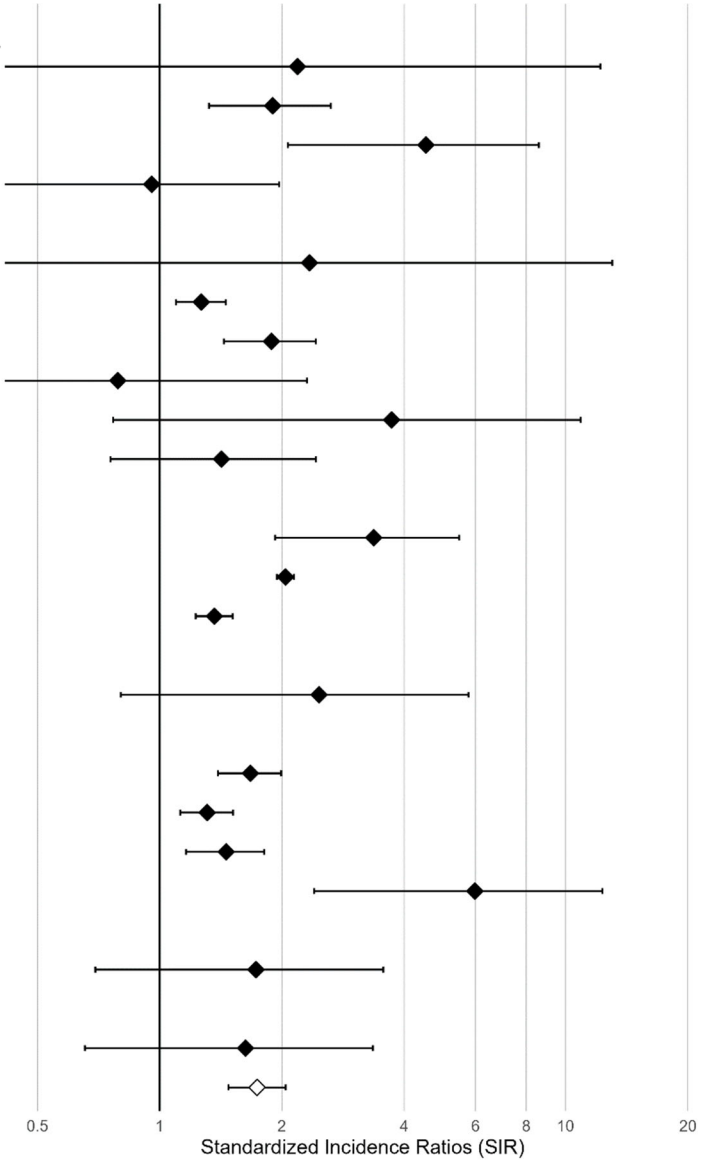
## Bell's Palsy

| Source | SIR (95% CI) |
|---|---|
| APHM | 9.25 (1.91 - 27.03) |
| CPRD_AURUM | 1.75 (1.21 - 2.45) |
| CUIMC | 3.51 (1.41 - 7.24) |
| CU_AMC | 1.64 (0.75 - 3.11) |
| FIIBAP | Insufficient Data |
| HIC | Insufficient Data |
| IBM_CCAE | 1.47 (1.22 - 1.75) |
| IBM_MDCD | 2.09 (1.51 - 2.83) |
| IBM_MDCR | 1.79 (0.92 - 3.12) |
| IMASIS | 3.43 (0.71 - 10.02) |
| IPCI | 0.81 (0.17 - 2.35) |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | 3.30 (1.07 - 7.71) |
| IQVIA_OPENCLAIMS | 2.42 (2.29 - 2.57) |
| IQVIA_PHARMETRICS | 1.69 (1.49 - 1.90) |
| IU | Insufficient Data |
| JMDC | 1.14 (0.03 - 6.37) |
| MHD | Insufficient Data |
| OPTUM_EHR | 2.30 (1.92 - 2.74) |
| OPTUM_SES | 1.51 (1.31 - 1.73) |
| SIDIAP | 2.00 (1.62 - 2.45) |
| STARR | Insufficient Data |
| UCCS | 15.78 (0.40 - 87.91) |
| UCHDW | 1.53 (0.61 - 3.14) |
| UK_BIOBANK | Insufficient Data |
| U_OF_TARTU | 1.57 (0.04 - 8.72) |
| Summary | 1.89 (1.61 - 2.21) |



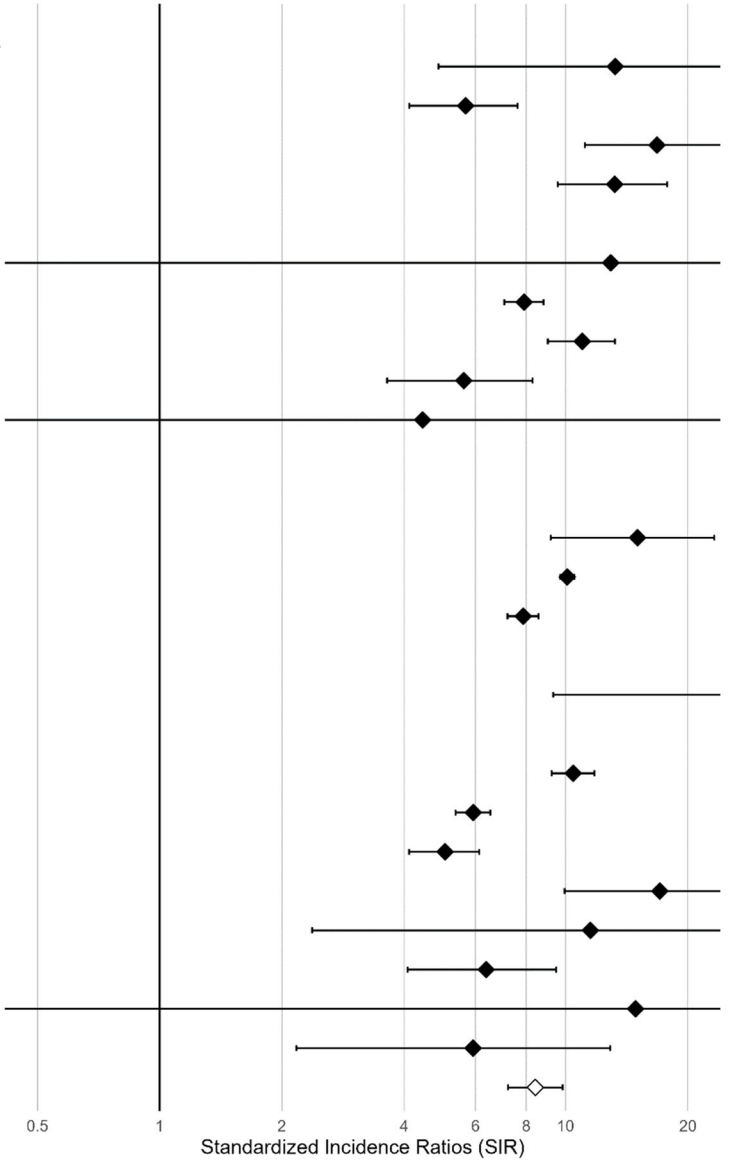
## Appendicitis

| Source | SIR (95% CI) |
|---|---|
| APHM | 2.19 (0.06 - 12.18) |
| CPRD_AURUM | 1.90 (1.32 - 2.64) |
| CUIMC | 4.53 (2.07 - 8.60) |
| CU_AMC | 0.96 (0.38 - 1.97) |
| FIIBAP | Insufficient Data |
| HIC | 2.34 (0.06 - 13.04) |
| IBM_CCAE | 1.27 (1.10 - 1.45) |
| IBM_MDCD | 1.89 (1.44 - 2.43) |
| IBM_MDCR | 0.79 (0.16 - 2.30) |
| IMASIS | 3.73 (0.77 - 10.89) |
| IPCI | 1.42 (0.76 - 2.43) |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | 3.37 (1.93 - 5.47) |
| IQVIA_OPENCLAIMS | 2.04 (1.94 - 2.14) |
| IQVIA_PHARMETRICS | 1.36 (1.23 - 1.51) |
| IU | Insufficient Data |
| JMDC | 2.47 (0.80 - 5.76) |
| MHD | Insufficient Data |
| OPTUM_EHR | 1.67 (1.39 - 1.99) |
| OPTUM_SES | 1.31 (1.12 - 1.52) |
| SIDIAP | 1.46 (1.16 - 1.81) |
| STARR | 5.98 (2.40 - 12.31) |
| UCCS | Insufficient Data |
| UCHDW | 1.73 (0.69 - 3.56) |
| UK_BIOBANK | Insufficient Data |
| U_OF_TARTU | 1.63 (0.65 - 3.35) |
| Summary | 1.74 (1.48 - 2.04) |



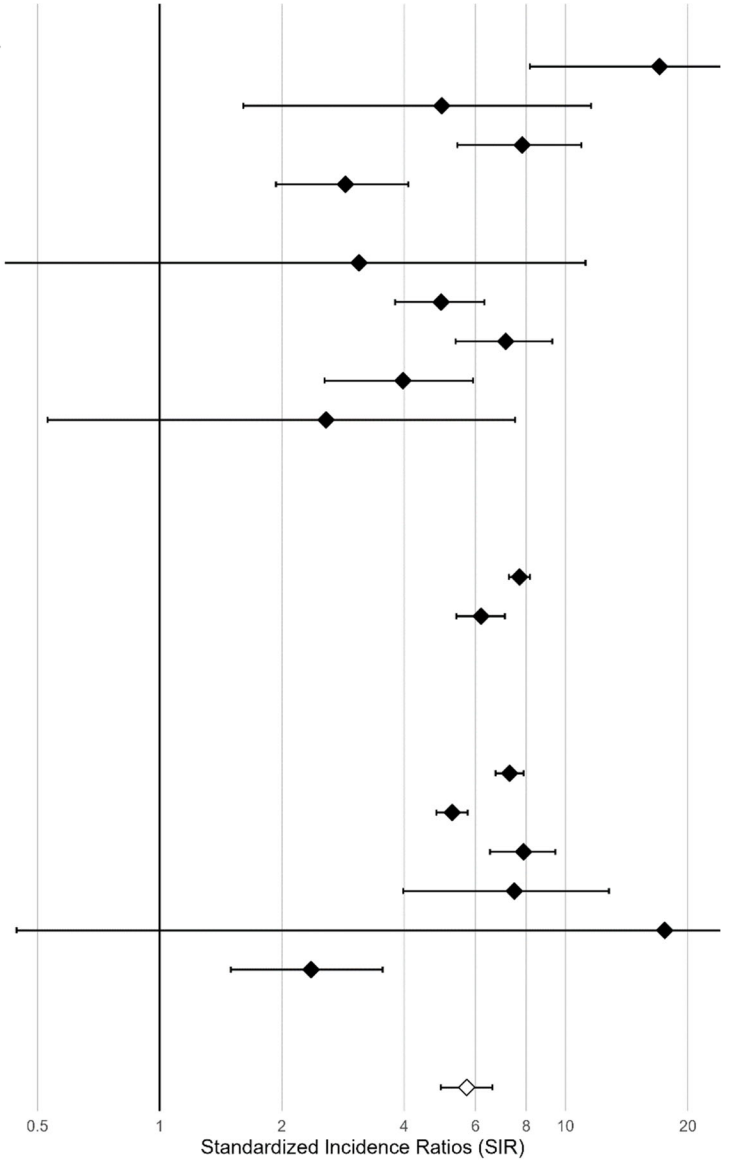
## Myocarditis and Pericarditis

| Source | SIR (95% CI) |
|---|---|
| APHM | 13.25 (4.86 - 28.84) |
| CPRD_AURUM | 5.67 (4.12 - 7.61) |
| CUIMC | 16.79 (11.16 - 24.27) |
| CU_AMC | 13.21 (9.56 - 17.80) |
| FIIBAP | Insufficient Data |
| HIC | 12.92 (0.33 - 71.99) |
| IBM_CCAE | 7.90 (7.06 - 8.82) |
| IBM_MDCD | 10.99 (9.04 - 13.23) |
| IBM_MDCR | 5.61 (3.63 - 8.29) |
| IMASIS | 4.44 (0.11 - 24.76) |
| IPCI | Results Censored |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | 15.04 (9.19 - 23.23) |
| IQVIA_OPENCLAIMS | 10.09 (9.70 - 10.50) |
| IQVIA_PHARMETRICS | 7.86 (7.19 - 8.57) |
| IU | Insufficient Data |
| JMDC | 34.20 (9.32 - 87.57) |
| MHD | Insufficient Data |
| OPTUM_EHR | 10.44 (9.24 - 11.76) |
| OPTUM_SES | 5.92 (5.36 - 6.52) |
| SIDIAP | 5.05 (4.11 - 6.13) |
| STARR | 17.06 (9.94 - 27.31) |
| UCCS | 11.51 (2.37 - 33.63) |
| UCHDW | 6.37 (4.08 - 9.48) |
| UK_BIOBANK | 14.87 (0.38 - 82.84) |
| U_OF_TARTU | 5.92 (2.17 - 12.87) |
| Summary | 8.42 (7.21 - 9.83) |



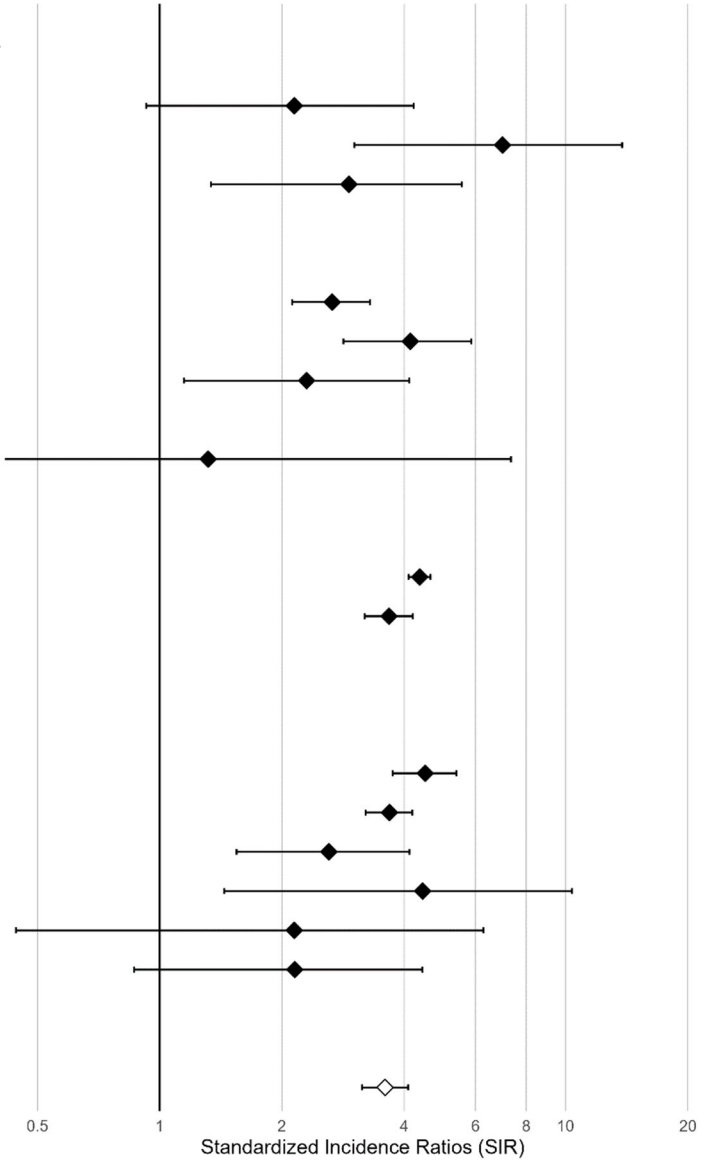
### Thrombosis with Thrombocytopenia (TWT)

| Source | SIR (95% CI) |
|---|---|
| APHM | 17.03 (8.16 - 31.31) |
| CPRD_AURUM | 4.95 (1.61 - 11.56) |
| CUIMC | 7.82 (5.41 - 10.92) |
| CU_AMC | 2.87 (1.93 - 4.09) |
| FIIBAP | Insufficient Data |
| HIC | 3.10 (0.38 - 11.19) |
| IBM_CCAE | 4.93 (3.80 - 6.30) |
| IBM_MDCD | 7.12 (5.36 - 9.27) |
| IBM_MDCR | 3.97 (2.55 - 5.91) |
| IMASIS | 2.57 (0.53 - 7.51) |
| IPCI | Insufficient Data |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | Insufficient Data |
| IQVIA_OPENCLAIMS | 7.70 (7.25 - 8.17) |
| IQVIA_PHARMETRICS | 6.19 (5.38 - 7.09) |
| IU | Insufficient Data |
| JMDC | 98.34 (26.79 - 251.79) |
| MHD | Insufficient Data |
| OPTUM_EHR | 7.28 (6.72 - 7.87) |
| OPTUM_SES | 5.25 (4.81 - 5.73) |
| SIDIAP | 7.88 (6.51 - 9.44) |
| STARR | 7.48 (3.98 - 12.78) |
| UCCS | 17.54 (0.44 - 97.72) |
| UCHDW | 2.36 (1.50 - 3.54) |
| UK_BIOBANK | Insufficient Data |
| U_OF_TARTU | Insufficient Data |
| Summary | 5.71 (4.93 - 6.61) |



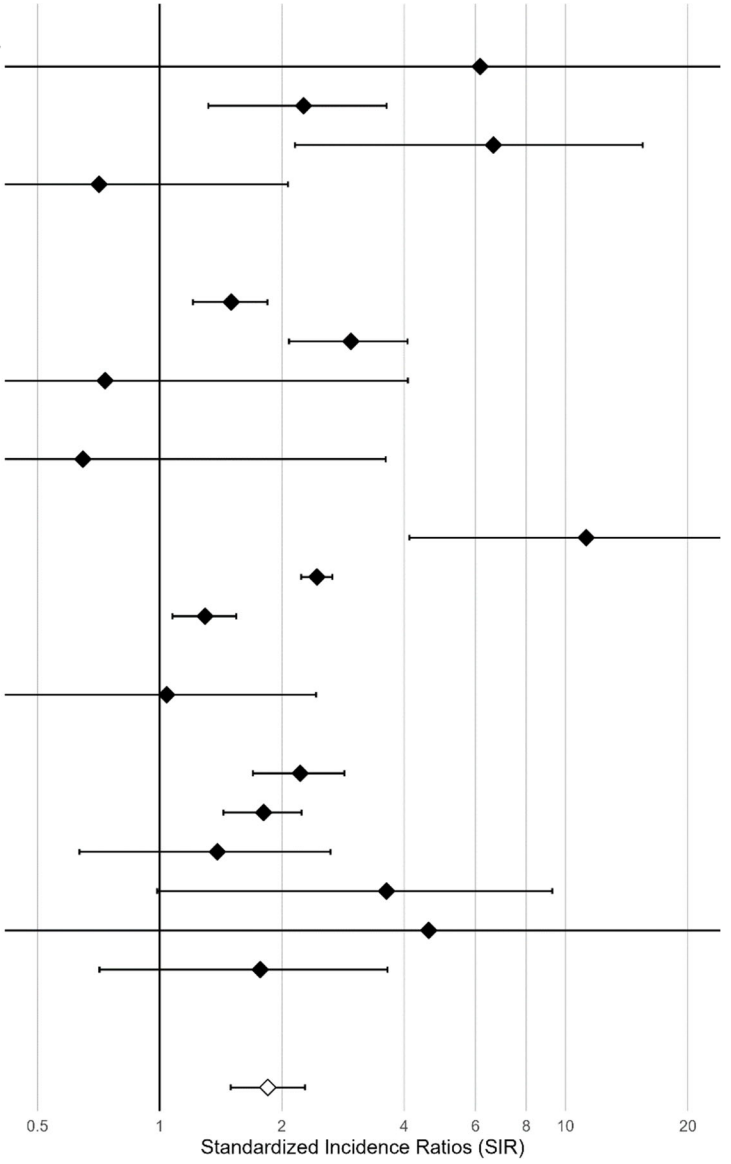
## Immune Thrombocytopenia (ITP)

| Source | SIR (95% CI) |
|---|---|
| APHM | Insufficient Data |
| CPRD_AURUM | 2.15 (0.93 - 4.23) |
| CUIMC | 6.99 (3.02 - 13.77) |
| CU_AMC | 2.92 (1.34 - 5.55) |
| FIIBAP | Insufficient Data |
| HIC | Insufficient Data |
| IBM_CCAE | 2.66 (2.12 - 3.30) |
| IBM_MDCD | 4.14 (2.83 - 5.85) |
| IBM_MDCR | 2.30 (1.15 - 4.12) |
| IMASIS | Insufficient Data |
| IPCI | 1.32 (0.03 - 7.34) |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | Insufficient Data |
| IQVIA_OPENCLAIMS | 4.37 (4.11 - 4.65) |
| IQVIA_PHARMETRICS | 3.67 (3.20 - 4.20) |
| IU | Insufficient Data |
| JMDC | Insufficient Data |
| MHD | Insufficient Data |
| OPTUM_EHR | 4.51 (3.75 - 5.38) |
| OPTUM_SES | 3.68 (3.22 - 4.19) |
| SIDIAP | 2.61 (1.55 - 4.13) |
| STARR | 4.44 (1.44 - 10.37) |
| UCCS | 2.15 (0.44 - 6.27) |
| UCHDW | 2.15 (0.87 - 4.43) |
| UK_BIOBANK | Insufficient Data |
| U_OF_TARTU | Insufficient Data |
| Summary | 3.59 (3.15 - 4.09) |



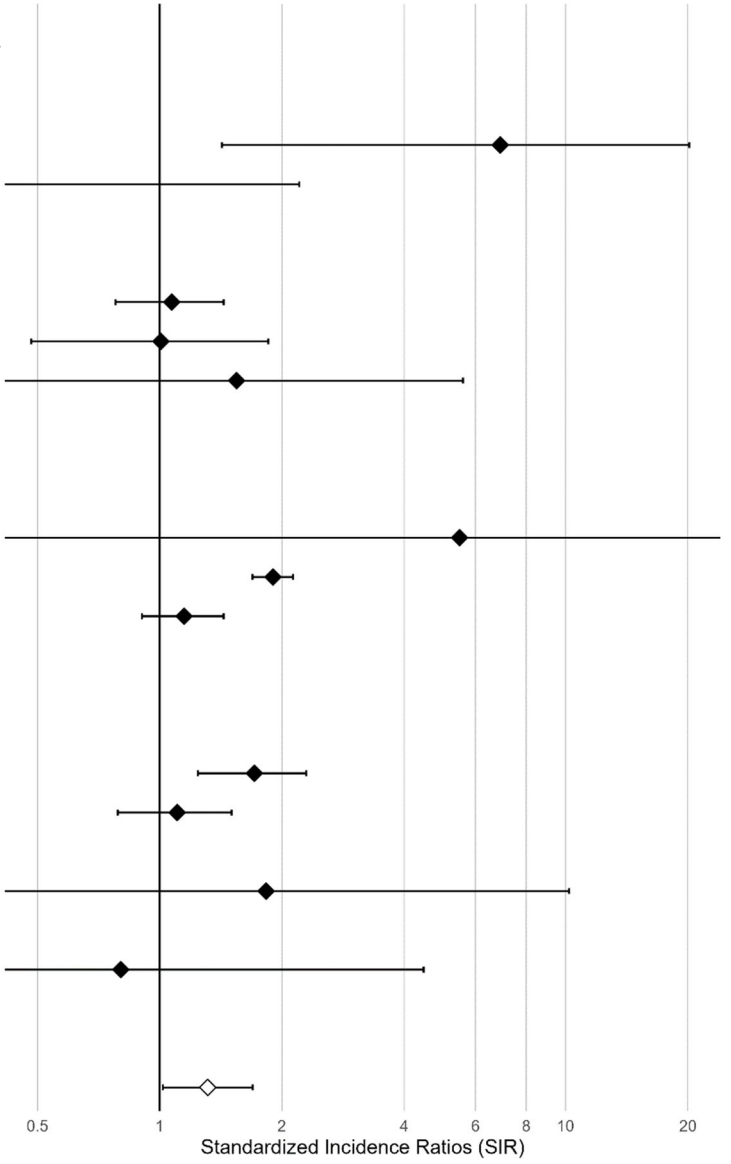
## Anaphylaxis

| Source | SIR (95% CI) |
|---|---|
| APHM | 6.16 (0.16 - 34.30) |
| CPRD_AURUM | 2.26 (1.32 - 3.62) |
| CUIMC | 6.64 (2.16 - 15.49) |
| CU_AMC | 0.71 (0.15 - 2.07) |
| FIIBAP | Insufficient Data |
| HIC | Results Censored |
| IBM_CCAE | 1.50 (1.21 - 1.84) |
| IBM_MDCD | 2.96 (2.08 - 4.08) |
| IBM_MDCR | 0.73 (0.02 - 4.09) |
| IMASIS | Insufficient Data |
| IPCI | 0.65 (0.02 - 3.60) |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | 11.24 (4.12 - 24.46) |
| IQVIA_OPENCLAIMS | 2.44 (2.23 - 2.66) |
| IQVIA_PHARMETRICS | 1.29 (1.07 - 1.54) |
| IU | Insufficient Data |
| JMDC | 1.04 (0.34 - 2.43) |
| MHD | Insufficient Data |
| OPTUM_EHR | 2.22 (1.70 - 2.85) |
| OPTUM_SES | 1.80 (1.44 - 2.24) |
| SIDIAP | 1.39 (0.63 - 2.63) |
| STARR | 3.62 (0.99 - 9.27) |
| UCCS | 4.60 (0.12 - 25.62) |
| UCHDW | 1.77 (0.71 - 3.64) |
| UK_BIOBANK | Insufficient Data |
| U_OF_TARTU | Insufficient Data |
| Summary | 1.85 (1.50 - 2.28) |



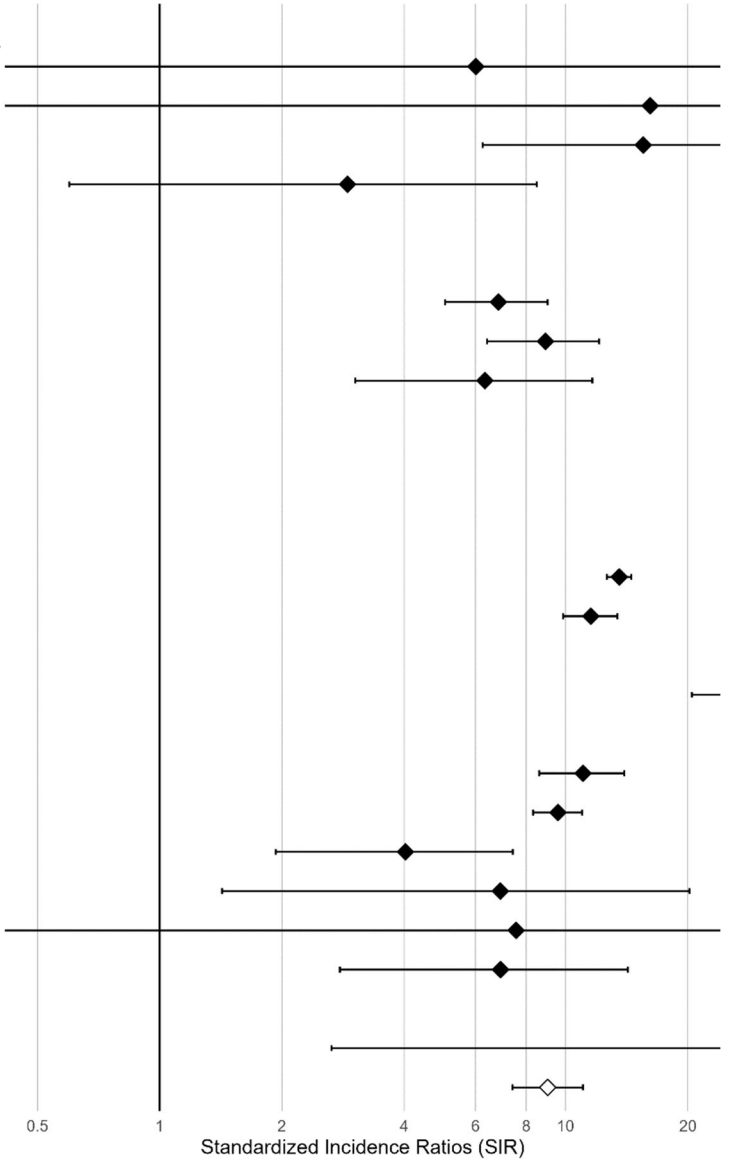
## Narcolepsy

| Source | SIR (95% CI) |
|---|---|
| APHM | Insufficient Data |
| CPRD_AURUM | Insufficient Data |
| CUIMC | 6.90 (1.42 - 20.17) |
| CU_AMC | 0.40 (0.01 - 2.21) |
| FIIBAP | Insufficient Data |
| HIC | Insufficient Data |
| IBM_CCAE | 1.07 (0.78 - 1.44) |
| IBM_MDCD | 1.01 (0.48 - 1.85) |
| IBM_MDCR | 1.55 (0.19 - 5.59) |
| IMASIS | Insufficient Data |
| IPCI | Results Censored |
| IQVIA_FRANCE_DA | Insufficient Data |
| IQVIA_GERMANY_DA | 5.48 (0.14 - 30.53) |
| IQVIA_OPENCLAIMS | 1.90 (1.69 - 2.13) |
| IQVIA_PHARMETRICS | 1.15 (0.90 - 1.44) |
| IU | Insufficient Data |
| JMDC | Insufficient Data |
| MHD | Insufficient Data |
| OPTUM_EHR | 1.71 (1.24 - 2.30) |
| OPTUM_SES | 1.10 (0.79 - 1.50) |
| SIDIAP | Results Censored |
| STARR | 1.83 (0.05 - 10.19) |
| UCCS | Insufficient Data |
| UCHDW | 0.80 (0.02 - 4.47) |
| UK_BIOBANK | Insufficient Data |
| U_OF_TARTU | Insufficient Data |
| Summary | 1.31 (1.02 - 1.69) |



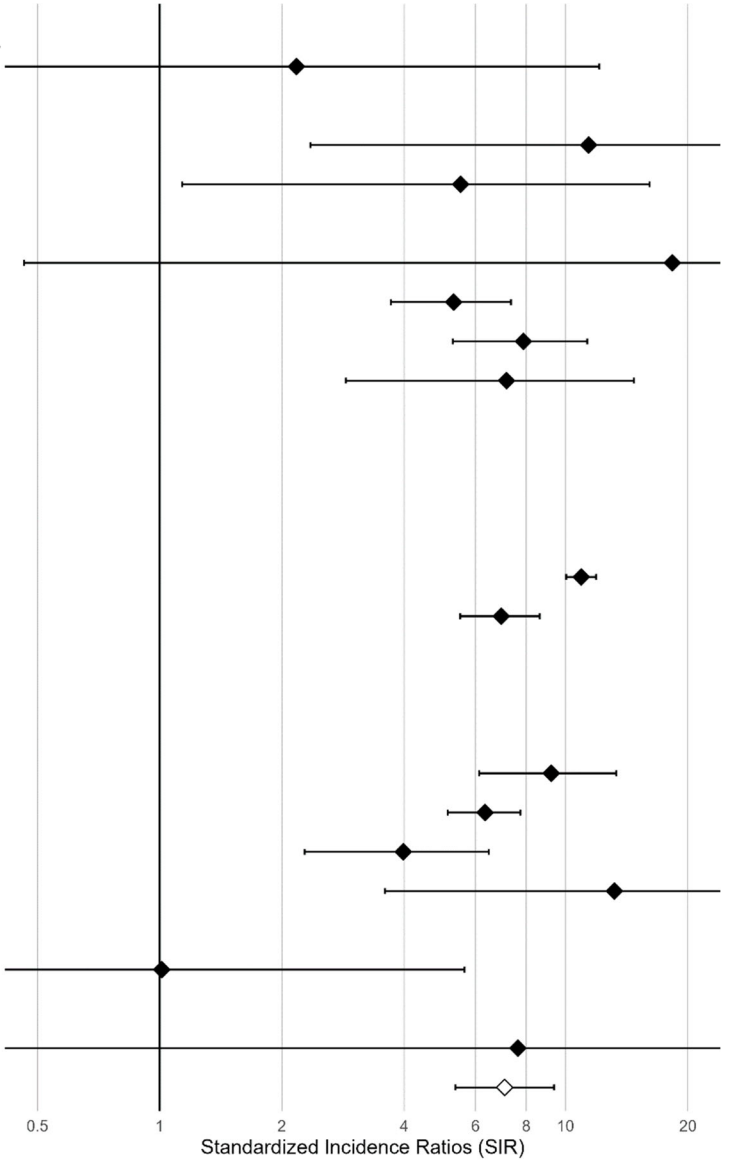
## Disseminated Intravascular Coagulation (DIC)

| Source | SIR (95% CI) |
|---|---|
| APHM | 6.01 (0.15 - 33.48) |
| CPRD_AURUM | 16.16 (0.41 - 90.02) |
| CUIMC | 15.53 (6.24 - 31.99) |
| CU_AMC | 2.90 (0.60 - 8.48) |
| FIIBAP | Insufficient Data |
| HIC | Insufficient Data |
| IBM_CCAE | 6.83 (5.05 - 9.03) |
| IBM_MDCD | 8.92 (6.40 - 12.10) |
| IBM_MDCR | 6.33 (3.03 - 11.64) |
| IMASIS | Insufficient Data |
| IPCI | Results Censored |
| IQVIA_FRANCE_DA | Results Censored |
| IQVIA_GERMANY_DA | Insufficient Data |
| IQVIA_OPENCLAIMS | 13.56 (12.64 - 14.52) |
| IQVIA_PHARMETRICS | 11.54 (9.87 - 13.42) |
| IU | Insufficient Data |
| JMDC | 32.67 (20.47 - 49.46) |
| MHD | Insufficient Data |
| OPTUM_EHR | 11.04 (8.61 - 13.95) |
| OPTUM_SES | 9.57 (8.31 - 10.97) |
| SIDIAP | 4.03 (1.93 - 7.41) |
| STARR | 6.91 (1.42 - 20.18) |
| UCCS | 7.55 (0.19 - 42.07) |
| UCHDW | 6.91 (2.78 - 14.24) |
| UK_BIOBANK | Insufficient Data |
| U_OF_TARTU | 104.59 (2.65 - 582.72) |
| Summary | 9.03 (7.40 - 11.03) |



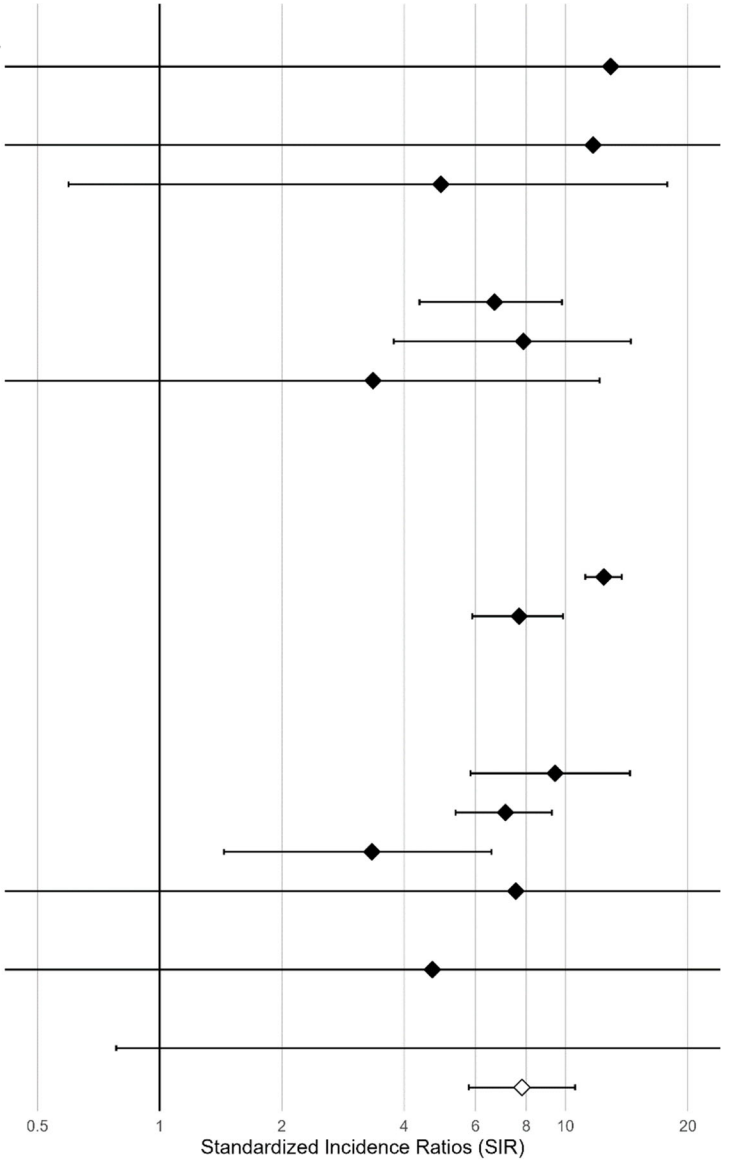
## Encephalomyelitis

| Source | SIR (95% CI) |
|---|---|
| APHM | 2.17 (0.05 - 12.10) |
| CPRD_AURUM | Results Censored |
| CUIMC | 11.40 (2.35 - 33.30) |
| CU_AMC | 5.51 (1.14 - 16.10) |
| FIIBAP | Insufficient Data |
| HIC | 18.31 (0.46 - 102.03) |
| IBM_CCAE | 5.30 (3.71 - 7.34) |
| IBM_MDCD | 7.87 (5.27 - 11.30) |
| IBM_MDCR | 7.15 (2.88 - 14.74) |
| IMASIS | Insufficient Data |
| IPCI | Results Censored |
| IQVIA_FRANCE_DA | Results Censored |
| IQVIA_GERMANY_DA | Results Censored |
| IQVIA_OPENCLAIMS | 10.93 (10.03 - 11.88) |
| IQVIA_PHARMETRICS | 6.94 (5.50 - 8.64) |
| IU | Insufficient Data |
| JMDC | Insufficient Data |
| MHD | Insufficient Data |
| OPTUM_EHR | 9.21 (6.12 - 13.32) |
| OPTUM_SES | 6.33 (5.12 - 7.74) |
| SIDIAP | 3.98 (2.28 - 6.47) |
| STARR | 13.18 (3.59 - 33.75) |
| UCCS | Insufficient Data |
| UCHDW | 1.01 (0.03 - 5.64) |
| UK_BIOBANK | Insufficient Data |
| U_OF_TARTU | 7.63 (0.19 - 42.51) |
| Summary | 7.08 (5.35 - 9.36) |



## Guillain-Barré Syndrome

| Source | SIR (95% CI) |
|---|---|
| APHM | 12.91 (0.33 - 71.94) |
| CPRD_AURUM | Results Censored |
| CUIMC | 11.69 (0.30 - 65.11) |
| CU_AMC | 4.93 (0.60 - 17.81) |
| FIIBAP | Insufficient Data |
| HIC | Insufficient Data |
| IBM_CCAE | 6.68 (4.36 - 9.79) |
| IBM_MDCD | 7.87 (3.77 - 14.47) |
| IBM_MDCR | 3.35 (0.41 - 12.12) |
| IMASIS | Insufficient Data |
| IPCI | Results Censored |
| IQVIA_FRANCE_DA | Results Censored |
| IQVIA_GERMANY_DA | Results Censored |
| IQVIA_OPENCLAIMS | 12.42 (11.18 - 13.76) |
| IQVIA_PHARMETRICS | 7.68 (5.89 - 9.85) |
| IU | Insufficient Data |
| JMDC | Insufficient Data |
| MHD | Insufficient Data |
| OPTUM_EHR | 9.42 (5.83 - 14.40) |
| OPTUM_SES | 7.11 (5.35 - 9.25) |
| SIDIAP | 3.33 (1.44 - 6.57) |
| STARR | 7.54 (0.19 - 41.99) |
| UCCS | Insufficient Data |
| UCHDW | 4.69 (0.12 - 26.16) |
| UK_BIOBANK | Insufficient Data |
| U_OF_TARTU | 30.86 (0.78 - 171.94) |
| Summary | 7.81 (5.78 - 10.55) |



## Transverse Myelitis

| Source | SIR (95% CI) |
|---|---|
| APHM | Insufficient Data |
| CPRD_AURUM | 3.10 (0.64 - 9.06) |
| CUIMC | 9.83 (1.19 - 35.49) |
| CU_AMC | 1.45 (0.04 - 8.05) |
| FIIBAP | Insufficient Data |
| HIC | Insufficient Data |
| IBM_CCAE | 2.21 (1.21 - 3.72) |
| IBM_MDCD | 0.73 (0.02 - 4.05) |
| IBM_MDCR | Insufficient Data |
| IMASIS | Insufficient Data |
| IPCI | Results Censored |
| IQVIA_FRANCE_DA | Results Censored |
| IQVIA_GERMANY_DA | Insufficient Data |
| IQVIA_OPENCLAIMS | 3.29 (2.70 - 3.97) |
| IQVIA_PHARMETRICS | 2.23 (1.45 - 3.26) |
| IU | Insufficient Data |
| JMDC | Insufficient Data |
| MHD | Results Censored |
| OPTUM_EHR | 2.14 (0.98 - 4.06) |
| OPTUM_SES | 2.90 (1.77 - 4.47) |
| SIDIAP | 1.56 (0.04 - 8.70) |
| STARR | 5.97 (0.15 - 33.25) |
| UCCS | Insufficient Data |
| UCHDW | 2.11 (0.05 - 11.74) |
| UK_BIOBANK | Insufficient Data |
| U_OF_TARTU | Insufficient Data |
| Summary | 2.78 (2.30 - 3.37) |